Supporting Information for

Copper-catalysed selective C5−H bromination and difluoromethylation of 8-aminoquinoline amides employing ethyl bromodifluoroacetate as the bifunctional reagent

Changdong Shao,* Tianyi Xu, Chen Chen, Qionglin Yang, Chao Tang, Ping Chen, Mingzhu Lu, Zhengsong Hu, Huayou Hu and Tingting Zhang*

Jiangsu Provincial Key Laboratory for Chemistry of Low-Dimensional Materials, School of Chemistry and Chemical Engineering, Huaiyin Normal University, Huai'an, 223300, Jiangsu, China. E-mail: shaochangdong@hytc.edu.cn

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1. General information

^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded on Bruker ARX400 instrument. High resolution mass spectra were obtained on a Bruker micrOTOF II ESI mass spectrometer. NMR spectra were recorded in $CDCl_3$. ^{1}H NMR spectra were referenced to residual $CHCl_3$ at 7.26 ppm, and ^{13}C NMR spectra were referenced to the central peak of $CDCl_3$ at 77.16 ppm. Chemical shifts (δ) are reported in ppm, and coupling constants (J) are in Hertz (Hz). Multiplicities are reported using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet.

8-Aminoquinoline amides were synthesized according to the previously reported protocol. [1-2] All other chemicals were purchased from commercial sources and used directly without further purification.

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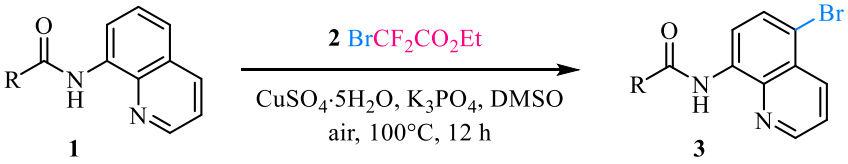
2. General procedure for the C5-bromination of 8-aminoquinoline amides



1 **3**

A 35 mL sealed tube equipped with a stir bar was charged with 8-amidequinolines (0.2 mmol, 1.0 equiv.), $BrCF_2CO_2Et$ (104 μL, 0.8 mmol, 4.0 equiv.), $CuSO_4·5H_2O$ (10.0 mg, 0.04 mmol, 20 mol%), K_3PO_4 (42.5 mg, 0.2 mmol, 1.0 equiv.) and DMSO (1.0 mL). The tube was sealed with a Teflon cap under air, then the mixture was stirred at 100ºC for 12 h. After completion, the reaction mixture was diluted with ethyl acetate (20 mL) and washed with saturated sodium bicarbonate, saturated sodium sulfide and brine successively. The organic layer was dried over anhydrous sodium sulfate and concentrated *in vacuo*. The residue was purified on preparative thin layer chromatography (PTLC) to afford the desired product **3**.

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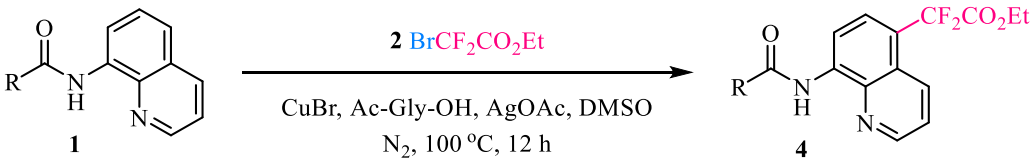
3. General Procedure for the C5-difluoromethylation of 8-aminoquinoline amides

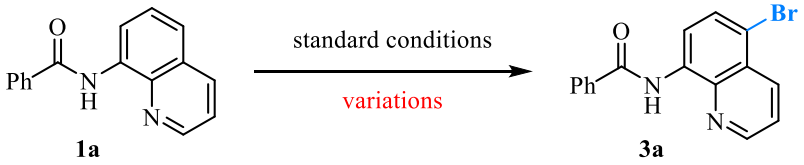


1 **4**

A 35 mL Schlenk tube equipped with a stir bar was charged with 8-amidequinolines (0.2 mmol, 1.0 equiv.), CuBr (5.8 mg, 0.04 mmol, 20 mol%), Ac-Gly-OH (9.4 mg, 0.08 mmol, 40 mol%) and AgOAc (67 mg, 0.4 mmol, 2.0 equiv.) under air. The tube was sealed with a rubber stopper and then evacuated and backfilled with N_2 (5 times). $BrCF_2CO_2Et$ (104 μL, 0.8 mmol, 4.0 equiv.) and DMSO (1.0 mL) were injected *via* syringe. After the reaction was stirred at 100ºC for 12 h, it was allowed to cool down to room temperature. The reaction mixture was diluted with ethyl acetate (20 mL) and then washed with saturated sodium bicarbonate, saturated sodium sulfide and brine successively.

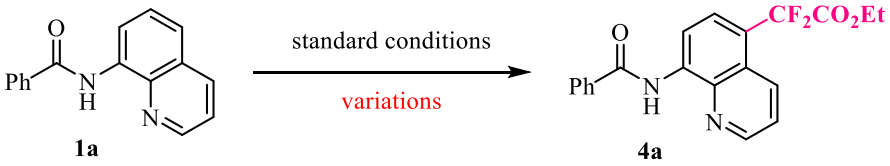
The organic layer was dried over anhydrous sodium sulfate and concentrated *in vacuo*. The residue was purified on preparative thin layer chromatography (PTLC) to afford the desired product **4**.

4. Preliminary mechanistic studies



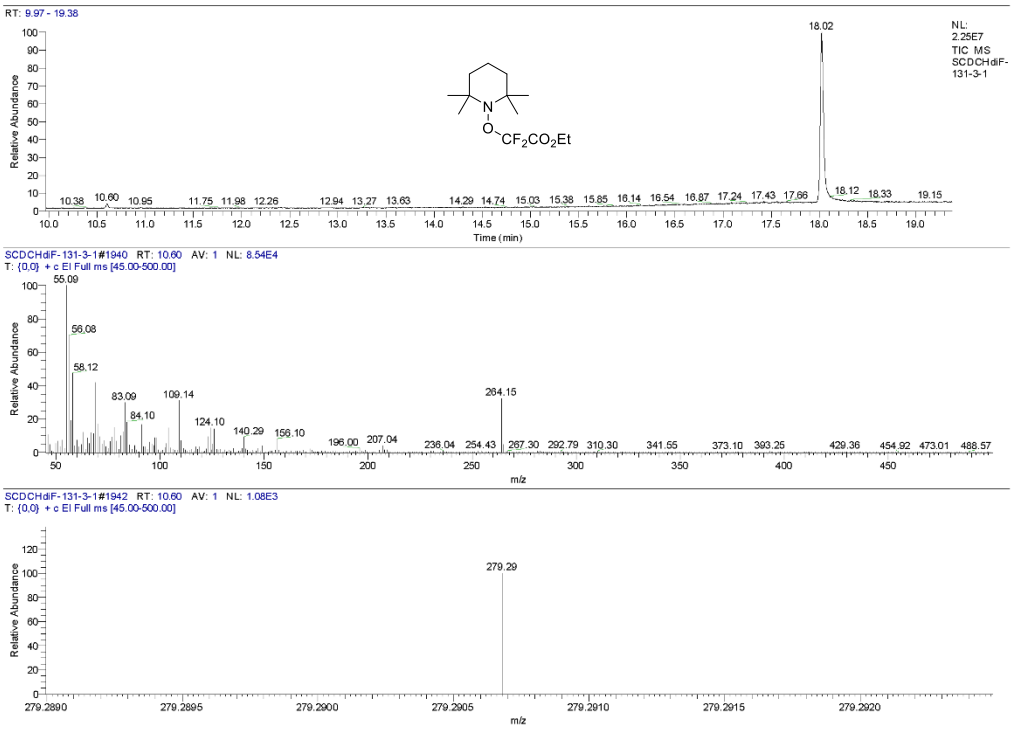
1a **3a**

+ TEMPO (2.0 equivalent)	23% yield
+ BHT (2.0 equivalent)	75% yield
under N_2	90% yield



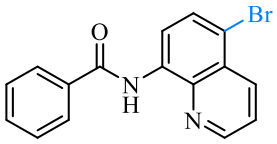
1a **4a**

+ TEMPO (2.0 equivalent)	0% yield
+ BHT (2.0 equivalent)	0% yield
under Air	0% yield



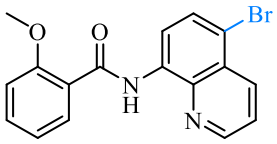
5. Characterization of isolated products

N-(5-bromoquinolin-8-yl)benzamide (**3a**)



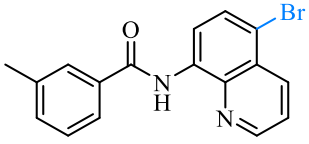
Purified with PTLC (PE/EA = 5/1, R_f = 0.76) to afford the title compound as a white solid (60.5 mg, 93%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.65 (s, 1H), 8.84 – 8.77 (m, 2H), 8.48 (dd, *J* = 8.5, 1.3 Hz, 1H), 8.05 (d, *J* = 6.8 Hz, 2H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.58 – 7.49 (m, 4H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 165.39, 148.82, 139.48, 136.03, 134.94, 134.58, 132.08, 131.02, 128.92, 127.36, 127.30, 122.78, 117.08, 114.48. Characterization data were consistent with a previous report. [3]

N-(5-bromoquinolin-8-yl)-2-methoxybenzamide (**3b**)



Purified with PTLC (PE/DCM = 1/1, R_f = 0.36) to afford the title compound as a white solid (61.4 mg, 86%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 12.26 (s, 1H), 8.87 (d, *J* = 8.4 Hz, 1H), 8.77 (d, *J* = 3.1 Hz, 1H), 8.42 (d, *J* = 7.6 Hz, 1H), 8.30 (d, *J* = 6.5 Hz, 1H), 7.77 (d, *J* = 8.4 Hz, 1H), 7.49 – 7.43 (m, 2H), 7.10 (t, *J* = 7.5 Hz, 1H), 6.99 (d, *J* = 8.3 Hz, 1H), 4.11 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 163.62, 157.81, 148.68, 139.94, 135.83, 135.71, 133.36, 132.42, 131.08, 127.27, 122.50, 122.11, 121.36, 117.75, 114.12, 111.67, 56.14. **HRMS (ESI-TOF)** m/z: calculated for $C_{17}H_{13}BrN_2NaO_2^+$: 379.0053 $(M + Na)^+$, found: 379.0065.

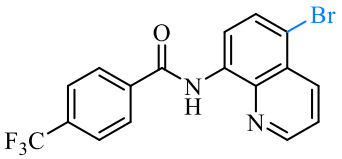
N-(5-bromoquinolin-8-yl)-3-methylbenzamide (**3c**)



Purified with PTLC (PE/EA = 5/1, R_f = 0.71) to afford the title compound as a white solid (62.8 mg, 92%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.63 (s, 1H), 8.83 (d, *J* = 4.0 Hz, 1H), 8.80 (d, *J* = 8.4 Hz, 1H), 8.50 (d, *J* = 8.4 Hz, 1H), 7.87 – 7.79 (m, 3H), 7.54 (dd, *J* = 8.5, 4.2 Hz, 1H), 7.44 – 7.36 (m,

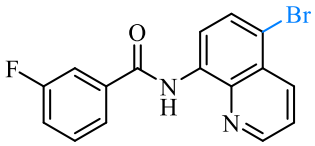
2H), 2.47 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 165.66, 148.83, 139.54, 138.83, 136.04, 134.98, 134.69, 132.86, 131.06, 128.78, 128.15, 127.33, 124.30, 122.77, 117.12, 114.42, 21.58. Characterization data were consistent with a previous report. [3]

N-(5-bromoquinolin-8-yl)-4-(trifluoromethyl)benzamide (**3d**)



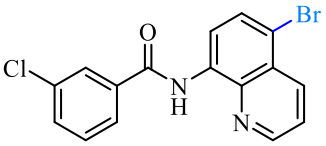
Purified with PTLC (PE/EA = 5/1, R_f = 0.77) to afford the title compound as a white solid (68.8 mg, 87%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.70 (s, 1H), 8.84 (dd, *J* = 4.1, 1.1 Hz, 1H), 8.77 (d, *J* = 8.3 Hz, 1H), 8.52 (dd, *J* = 8.5, 1.1 Hz, 1H), 8.15 (d, *J* = 8.1 Hz, 2H), 7.84 – 7.77 (m, 3H), 7.58 (dd, *J* = 8.5, 4.2 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 164.03, 149.03, 139.47, 138.22 (q, *J* = 0.8 Hz), 136.23, 134.18, 133.79 (q, *J* = 32.7 Hz), 131.04, 127.86, 127.41, 126.03 (q, *J* = 3.8 Hz), 122.97, 123.83 (q, *J* = 273.7 Hz), 117.34, 115.11. Characterization data were consistent with a previous report. [3]

N-(5-bromoquinolin-8-yl)-3-fluorobenzamide (**3e**)



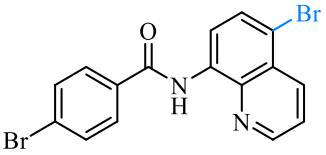
Purified with PTLC (PE/EA = 5/1, R_f = 0.67) to afford the title compound as a white solid (63.5 mg, 92%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.65 (s, 1H), 8.85 (dd, *J* = 4.1, 1.3 Hz, 1H), 8.77 (d, *J* = 8.4 Hz, 1H), 8.52 (dd, *J* = 8.5, 1.3 Hz, 1H), 7.82 (d, *J* = 8.3 Hz, 2H), 7.75 (dt, *J* = 9.3, 1.9 Hz, 1H), 7.57 (dd, *J* = 8.5, 4.2 Hz, 1H), 7.52 (td, *J* = 8.0, 5.7 Hz, 1H), 7.32 – 7.24 (m, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 164.06 (d, *J* = 2.6 Hz), 163.11 (d, *J* = 248.0 Hz), 148.99, 139.50, 137.27 (d, *J* = 6.8 Hz), 136.18, 134.32, 131.06, 130.63 (d, *J* = 7.9 Hz), 127.40, 122.92, 122.83 (d, *J* = 3.1 Hz), 119.15 (d, *J* = 21.4 Hz), 117.26, 114.91 (d, *J* = 4.9 Hz), 114.71. Characterization data were consistent with a previous report. [3]

N-(5-bromoquinolin-8-yl)-3-chlorobenzamide (**3f**)



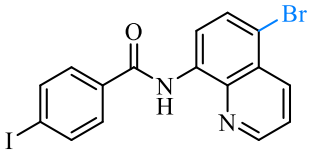
Purified with PTLC (PE/EA = 5/1, R_f = 0.66) to afford the title compound as a white solid (71.6 mg, 99%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.61 (s, 1H), 8.84 (dd, *J* = 4.1, 1.3 Hz, 1H), 8.75 (d, *J* = 8.4 Hz, 1H), 8.51 (dd, *J* = 8.5, 1.3 Hz, 1H), 8.02 (s, 1H), 7.90 (d, *J* = 7.7 Hz, 1H), 7.80 (d, *J* = 8.4 Hz, 1H), 7.59 – 7.52 (m, 2H), 7.46 (t, *J* = 7.8 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 163.96, 148.98, 139.45, 136.73, 136.15, 135.23, 134.27, 132.13, 131.02, 130.22, 127.81, 127.36, 125.33, 122.91, 117.27, 114.91. Characterization data were consistent with a previous report. [3]

4-bromo-N-(5-bromoquinolin-8-yl)benzamide (**3g**)



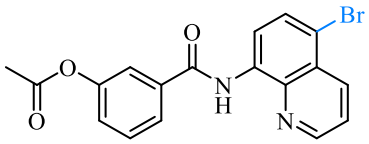
Purified with PTLC (PE/DCM = 1/1, R_f = 0.66) to afford the title compound as a white solid (79.6 mg, 98%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.64 (s, 1H), 8.91 – 8.82 (m, 1H), 8.80 – 8.75 (m, 1H), 8.59 – 8.47 (m, 1H), 7.91 (dd, *J* = 8.6, 2.0 Hz, 2H), 7.82 (dd, *J* = 8.4, 2.9 Hz, 1H), 7.67 (dd, *J* = 8.6, 2.0 Hz, 2H), 7.59 – 7.55 (m, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 164.37, 148.92, 139.45, 136.15, 134.34, 133.78, 132.20, 131.05, 128.95, 127.36, 126.94, 122.88, 117.19, 114.79. Characterization data were consistent with a previous report. [3]

N-(5-bromoquinolin-8-yl)-4-iodobenzamide (**3h**)



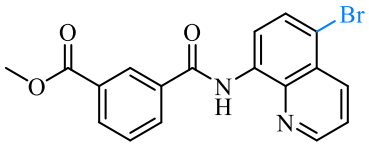
Purified with PTLC (PE/DCM = 1/1, R_f = 0.63) to afford the title compound as a white solid (87.0 mg, 96%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.63 (s, 1H), 8.84 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.76 (d, *J* = 8.4 Hz, 1H), 8.52 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.88 (d, *J* = 8.4 Hz, 2H), 7.81 (d, *J* = 8.4 Hz, 1H), 7.76 (d, *J* = 8.5 Hz, 2H), 7.57 (dd, *J* = 8.5, 4.2 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 164.63, 148.95, 139.48, 138.21, 136.19, 134.39, 134.35, 131.08, 128.93, 127.39, 122.91, 117.23, 114.81, 99.28. **HRMS (ESI-TOF)** m/z: calculated for $C_{16}H_{10}BrIN_2NaO^+$: 474.8913 $(M + Na)^+$, found: 474.8923.

3-((5-bromoquinolin-8-yl)carbamoyl)phenyl acetate (**3i**)



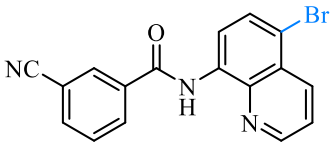
Purified with PTLC (DCM, R_f = 0.72) to afford the title compound as a white solid (64.7 mg, 84%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.62 (s, 1H), 8.83 (dd, *J* = 4.3, 1.6 Hz, 1H), 8.77 (d, *J* = 8.4 Hz, 1H), 8.50 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.90 (d, *J* = 7.8 Hz, 1H), 7.85 – 7.75 (m, 2H), 7.59 – 7.52 (m, 2H), 7.38 – 7.29 (m, 1H), 2.35 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 169.27, 164.34, 151.23, 148.93, 139.48, 136.60, 136.10, 134.39, 131.02, 129.95, 127.34, 125.48, 124.45, 122.86, 121.02, 117.23, 114.75, 21.22. **HRMS (ESI-TOF)** m/z: calculated for $C_{18}H_{13}BrN_2NaO_3^+$: 407.0002 $(M + Na)^+$, found: 407.0008.

methyl 3-((5-bromoquinolin-8-yl)carbamoyl)benzoate (**3j**)



Purified with PTLC (DCM, R_f = 0.75) to afford the title compound as a white solid (72.4 mg, 94%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.65 (s, 1H), 8.82 (d, *J* = 3.2 Hz, 1H), 8.75 (d, *J* = 8.4 Hz, 1H), 8.66 (s, 1H), 8.47 (d, *J* = 8.3 Hz, 1H), 8.21 (d, *J* = 7.7 Hz, 2H), 7.78 (d, *J* = 8.4 Hz, 1H), 7.59 (t, *J* = 7.7 Hz, 1H), 7.53 (dd, *J* = 8.5, 4.2 Hz, 1H), 3.97 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 166.32, 164.35, 148.95, 139.41, 136.04, 135.32, 134.31, 132.90, 131.68, 131.01, 130.96, 129.12, 128.36, 127.28, 122.84, 117.24, 114.80, 52.50. **HRMS (ESI-TOF)** m/z: calculated for $C_{18}H_{13}BrN_2NaO_3^+$: 407.0002 $(M + Na)^+$, found: 407.0010.

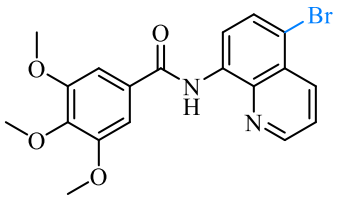
N-(5-bromoquinolin-8-yl)-3-cyanobenzamide (**3k**)



Purified with PTLC (DCM, R_f = 0.80) to afford the title compound as a white solid (68.3 mg, 97%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.72 (s, 1H), 8.90 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.78 (d, *J* = 8.4 Hz, 1H), 8.57 (dd, *J* = 8.5, 1.6 Hz, 1H), 8.34 (t, *J* = 1.8 Hz, 1H), 8.30 (dt, *J* = 7.9, 1.5 Hz, 1H), 7.95 –

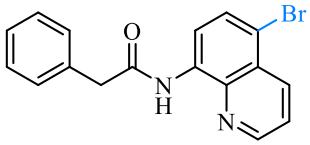
7.78 (m, 2H), 7.70 (t, J = 7.8 Hz, 1H), 7.63 (dd, J = 8.5, 4.3 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 163.10, 149.19, 139.45, 136.34, 136.23, 135.24, 133.98, 131.62, 131.11, 131.06, 130.01, 127.47, 123.11, 118.14, 117.44, 115.37, 113.51. **HRMS (ESI-TOF)** m/z: calculated for $C_{17}H_{10}BrN_3NaO^+$: 373.9899 $(M + Na)^+$, found: 373.9889.

N-(5-bromoquinolin-8-yl)-3,4,5-trimethoxybenzamide (**3l**)



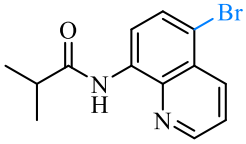
Purified with PTLC (DCM, R_f = 0.43) to afford the title compound as a white solid (80.1 mg, 96%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.55 (s, 1H), 8.81 (dd, J = 4.1, 1.4 Hz, 1H), 8.74 (d, J = 8.4 Hz, 1H), 8.50 (d, J = 8.5 Hz, 1H), 7.80 (d, J = 8.4 Hz, 1H), 7.54 (dd, J = 8.5, 4.2 Hz, 1H), 7.26 (s, 2H), 3.98 (s, 6H), 3.93 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 165.12, 153.48, 148.87, 141.75, 139.46, 136.07, 134.54, 131.02, 130.35, 127.31, 122.78, 117.00, 114.45, 105.03, 61.03, 56.55. **HRMS (ESI-TOF)** m/z: calculated for $C_{19}H_{17}BrN_2NaO_4^+$: 439.0264 $(M + Na)^+$, found: 439.0288.

N-(5-bromoquinolin-8-yl)-2-phenylacetamide (**3m**)



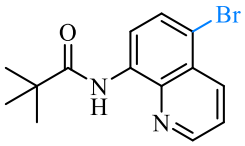
Purified with PTLC (PE/EA = 5/1, R_f = 0.59) to afford the title compound as a white solid (53.2 mg, 78%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.86 (s, 1H), 8.67 (dd, J = 4.1, 1.4 Hz, 1H), 8.64 (d, J = 8.4 Hz, 1H), 8.44 (dd, J = 8.5, 1.4 Hz, 1H), 7.74 (d, J = 8.4 Hz, 1H), 7.47 (dd, J = 8.5, 4.2 Hz, 1H), 7.45 – 7.38 (m, 4H), 7.38 – 7.31 (m, 1H), 3.88 (s, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 169.59, 148.71, 139.22, 135.90, 134.59, 134.42, 130.92, 129.65, 129.13, 127.53, 127.19, 122.65, 116.92, 114.38, 45.47. Characterization data were consistent with a previous report. [3]

N-(5-bromoquinolin-8-yl)isobutyramide (**3n**)



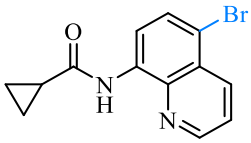
Purified with PTLC (PE/EA = 5/1, R_f = 0.75) to afford the title compound as a white solid (51.6 mg, 88%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.85 (s, 1H), 8.79 (dd, *J* = 4.1, 1.4 Hz, 1H), 8.66 (d, *J* = 8.4 Hz, 1H), 8.48 (dd, *J* = 8.5, 1.4 Hz, 1H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.52 (dd, *J* = 8.5, 4.2 Hz, 1H), 2.82 – 2.68 (m, 1H), 1.35 (s, 3H), 1.33 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 175.79, 148.69, 139.30, 136.02, 134.70, 131.04, 127.26, 122.68, 117.01, 114.04, 37.25, 19.76. Characterization data were consistent with a previous report. [4]

N-(5-bromoquinolin-8-yl)pivalamide (**3o**)



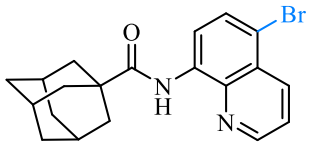
Purified with PTLC (PE/EA = 5/1, R_f = 0.84) to afford the title compound as a white solid (51.0 mg, 83%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.22 (s, 1H), 8.81 (dd, *J* = 4.1, 1.2 Hz, 1H), 8.68 (d, *J* = 8.4 Hz, 1H), 8.49 (dd, *J* = 8.5, 1.2 Hz, 1H), 7.77 (d, *J* = 8.4 Hz, 1H), 7.53 (dd, *J* = 8.5, 4.2 Hz, 1H), 1.42 (s, 9H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 177.36, 148.79, 139.63, 136.02, 134.81, 131.06, 127.29, 122.67, 116.87, 113.99, 40.51, 27.81. Characterization data were consistent with a previous report. [3]

N-(5-bromoquinolin-8-yl)cyclopropanecarboxamide (**3p**)



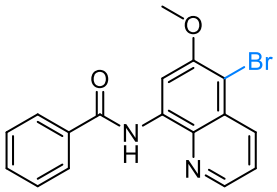
Purified with PTLC (PE/EA = 5/1, R_f = 0.64) to afford the title compound as a white solid (52.9 mg, 91%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.95 (s, 1H), 8.78 (dd, *J* = 4.1, 1.4 Hz, 1H), 8.60 (d, *J* = 8.4 Hz, 1H), 8.47 (dd, *J* = 8.5, 1.4 Hz, 1H), 7.73 (d, *J* = 8.4 Hz, 1H), 7.51 (dd, *J* = 8.5, 4.2 Hz, 1H), 1.82 – 1.74 (m, 1H), 1.19 – 1.12 (m, 2H), 0.95 – 0.88 (m, 2H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 172.33, 148.61, 139.00, 135.98, 134.73, 131.02, 127.23, 122.67, 116.95, 113.88, 16.40, 8.37. **HRMS (ESI-TOF)** m/z: calculated for $C_{13}H_{11}BrN_2NaO^+$: 312.9947 $(M + Na)^+$, found: 312.9940.

N-(5-bromoquinolin-8-yl)adamantane-1-carboxamide (**3q**)



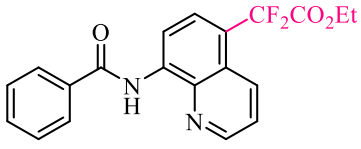
Purified with PTLC (PE/EA = 5/1, R_f = 0.84) to afford the title compound as a white solid (62.4 mg, 81%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.17 (s, 1H), 8.82 (d, *J* = 3.2 Hz, 1H), 8.70 (d, *J* = 8.4 Hz, 1H), 8.48 (d, *J* = 8.5 Hz, 1H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.53 (dd, *J* = 8.5, 4.2 Hz, 1H), 2.14 (s, 3H), 2.09 (s, 6H), 1.80 (s, 6H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 176.83, 148.75, 139.69, 135.99, 134.77, 131.06, 127.27, 122.63, 117.00, 113.92, 42.43, 39.45, 36.65, 28.36. Characterization data were consistent with a previous report. [5]

N-(5-bromo-6-methoxyquinolin-8-yl)benzamide (**3r**)



Purified with PTLC (DCM, R_f = 0.61) to afford the title compound as a white solid (65.6 mg, 92%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.74 (s, 1H), 8.93 (s, 1H), 8.66 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.47 (dd, *J* = 8.6, 1.5 Hz, 1H), 8.09 – 8.02 (m, 2H), 7.64 – 7.51 (m, 3H), 7.48 (dd, *J* = 8.6, 4.2 Hz, 1H), 4.10 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 165.58, 154.66, 146.36, 135.47, 135.04, 134.83, 134.75, 132.24, 129.01, 128.17, 127.35, 123.21, 104.55, 99.84, 57.12. Characterization data were consistent with a previous report. [3]

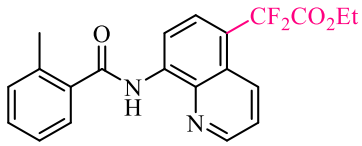
ethyl 2-(8-benzamidoquinolin-5-yl)-2,2-difluoroacetate (**4a**)



Purified with PTLC (PE/EA = 10/1, R_f = 0.42) to afford the title compound as a white solid (46 mg, 62%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.93 (s, 1H), 8.97 (d, *J* = 8.2 Hz, 1H), 8.89 (dd, *J* = 4.0, 1.1 Hz, 1H), 8.69 (dd, *J* = 8.6, 0.9 Hz, 1H), 8.15 – 8.02 (m, 2H), 7.93 (d, *J* = 8.3 Hz, 1H), 7.67 – 7.51 (m, 4H), 4.29 (q, *J* = 7.1 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -99.13. **^{13}C NMR (101 MHz, $CDCl_3$)** δ 165.61, 164.20 (t, *J* = 35.1 Hz), 148.44, 138.60, 137.45, 134.68, 133.79 (t, *J* = 3.5 Hz), 132.15, 128.86, 127.32, 126.88 (t, *J* = 9.1 Hz), 124.75, 122.50, 122.11 (t, *J* =

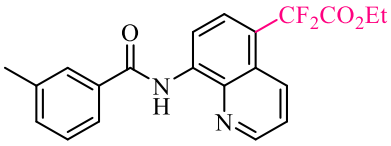
24.6 Hz), 114.75, 114.03 (t, J = 252.7 Hz), 63.40, 13.83. Characterization data were consistent with a previous report. [6]

ethyl 2,2-difluoro-2-(8-(2-methylbenzamido)quinolin-5-yl)acetate (**4b**)



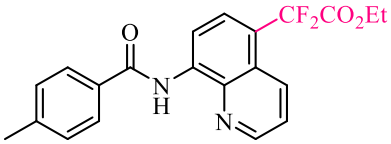
Purified with PTLC (PE/EA = 10/1, R_f = 0.54) to afford the title compound as a white solid (48 mg, 63%). **^{1}H NMR (400 MHz, CDCl$_3$)** δ 10.41 (s, 1H), 8.98 (d, J = 8.2 Hz, 1H), 8.82 (d, J = 4.1 Hz, 1H), 8.68 (d, J = 8.7 Hz, 1H), 7.94 (d, J = 8.3 Hz, 1H), 7.68 (d, J = 7.6 Hz, 1H), 7.55 (dd, J = 8.7, 4.2 Hz, 1H), 7.42 (t, J = 7.0 Hz, 1H), 7.33 (t, J = 7.7 Hz, 2H), 4.29 (q, J = 7.1 Hz, 2H), 2.60 (s, 3H), 1.26 (t, J = 7.1 Hz, 3H). **^{19}F NMR (376 MHz, CDCl$_3$)** δ -99.17. **^{13}C NMR (101 MHz, CDCl$_3$)** δ 168.28, 164.18 (t, J = 35.2 Hz), 148.40, 138.43, 137.56, 136.84, 136.09, 133.70 (t, J = 3.6 Hz), 131.47, 130.59, 127.22, 126.82 (t, J = 9.0 Hz), 126.05, 124.73 (t, J = 1.8 Hz), 122.46, 122.18 (t, J = 24.7 Hz), 114.68, 114.00 (t, J = 252.7 Hz), 63.39, 20.20, 13.82. Characterization data were consistent with a previous report. [6]

ethyl 2,2-difluoro-2-(8-(3-methylbenzamido)quinolin-5-yl)acetate (**4c**)



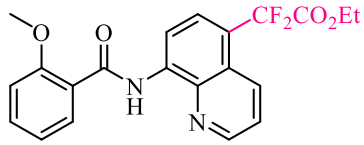
Purified with PTLC (PE/EA = 10/1, R_f = 0.45) to afford the title compound as a white solid (53 mg, 69%). **^{1}H NMR (400 MHz, CDCl$_3$)** δ 10.89 (s, 1H), 8.97 (d, J = 8.2 Hz, 1H), 8.90 (dd, J = 4.0, 1.1 Hz, 1H), 8.69 (d, J = 7.7 Hz, 1H), 7.93 (d, J = 8.3 Hz, 1H), 7.90 – 7.81 (m, 2H), 7.57 (dd, J = 8.7, 4.2 Hz, 1H), 7.49 – 7.36 (m, 2H), 4.29 (q, J = 7.1 Hz, 2H), 2.49 (s, 3H), 1.26 (t, J = 7.1 Hz, 3H). **^{19}F NMR (376 MHz, CDCl$_3$)** δ -99.12. **^{13}C NMR (101 MHz, CDCl$_3$)** δ 165.85, 164.22 (t, J = 35.3 Hz), 148.43, 138.78, 138.62, 137.52, 134.69, 133.77 (t, J = 3.6 Hz), 132.92, 128.71, 128.10, 126.89 (t, J = 9.0 Hz), 124.75 (t, J = 1.9 Hz), 124.24, 122.47, 122.03 (t, J = 24.5 Hz), 114.75, 114.04 (t, J = 252.6 Hz), 63.39, 21.46, 13.83. Characterization data were consistent with a previous report. [6]

ethyl 2,2-difluoro-2-(8-(4-methylbenzamido)quinolin-5-yl)acetate (**4d**)



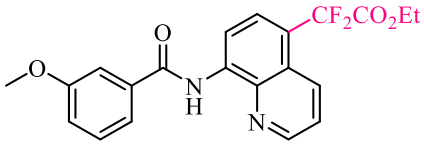
Purified with PTLC (PE/EA = 10/1, R_f = 0.43) to afford the title compound as a white solid (45 mg, 58%). **^{1}H NMR (400 MHz, CDCl$_3$)** δ 10.90 (s, 1H), 8.97 (d, *J* = 8.2 Hz, 1H), 8.90 (d, *J* = 3.0 Hz, 1H), 8.69 (d, *J* = 8.6 Hz, 1H), 7.98 (d, *J* = 8.1 Hz, 2H), 7.93 (d, *J* = 8.3 Hz, 1H), 7.57 (dd, *J* = 8.7, 4.2 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 2H), 4.29 (q, *J* = 7.1 Hz, 2H), 2.46 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR (376 MHz, CDCl$_3$)** δ -99.12. **^{13}C NMR (101 MHz, CDCl$_3$)** δ 165.62, 164.24 (t, *J* = 35.3 Hz), 148.40, 142.76, 138.62, 137.58, 133.78 (t, *J* = 3.6 Hz), 131.89, 129.54, 127.36, 126.92 (t, *J* = 9.0 Hz), 124.76 (t, *J* = 1.9 Hz), 122.47, 121.93 (t, *J* = 24.6 Hz), 114.68, 114.05 (t, *J* = 252.6 Hz), 63.39, 21.56, 13.84. Characterization data were consistent with a previous report. [6]

ethyl 2,2-difluoro-2-(8-(2-methoxybenzamido)quinolin-5-yl)acetate (**4e**)



Purified with PTLC (PE/EA = 5/1, R_f = 0.36) to afford the title compound as a white solid (57 mg, 71%). **^{1}H NMR (400 MHz, CDCl$_3$)** δ 12.49 (s, 1H), 9.05 (d, *J* = 8.3 Hz, 1H), 8.88 (dd, *J* = 3.9, 1.1 Hz, 1H), 8.65 (d, *J* = 8.6 Hz, 1H), 8.32 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.90 (d, *J* = 8.3 Hz, 1H), 7.60 – 7.42 (m, 2H), 7.13 (t, *J* = 7.5 Hz, 1H), 7.06 (d, *J* = 8.3 Hz, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 4.17 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR (376 MHz, CDCl$_3$)** δ -98.95. **^{13}C NMR (101 MHz, CDCl$_3$)** δ 164.26 (t, *J* = 35.2 Hz), 163.89, 157.73, 148.30, 139.03, 138.67, 133.45 (t, *J* = 3.4 Hz), 132.38, 126.98 (t, *J* = 8.9 Hz), 124.78 (t, *J* = 1.9 Hz), 122.19, 121.89, 121.65, 121.41, 121.30, 115.40, 114.15 (t, *J* = 252.5 Hz), 111.59, 63.32, 56.06, 13.80. Characterization data were consistent with a previous report. [6]

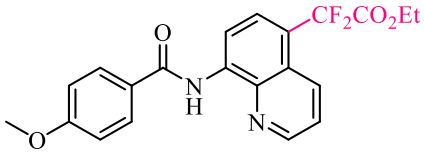
ethyl 2,2-difluoro-2-(8-(3-methoxybenzamido)quinolin-5-yl)acetate (**4f**)



Purified with PTLC (PE/EA = 5/1, R_f = 0.31) to afford the title compound as a white solid (54 mg, 67%). **^{1}H NMR (400 MHz, CDCl$_3$)** δ 10.91 (s, 1H), 8.96 (d, *J* = 8.2 Hz, 1H), 8.89 (dd, *J* = 4.1, 1.2

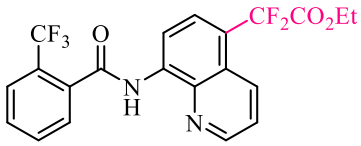
Hz, 1H), 8.69 (dd, *J* = 8.7, 1.0 Hz, 1H), 7.93 (d, *J* = 8.3 Hz, 1H), 7.67 – 7.61 (m, 2H), 7.57 (dd, *J* = 8.7, 4.2 Hz, 1H), 7.47 (t, *J* = 8.2 Hz, 1H), 7.17 – 7.09 (m, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 3.91 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR (377 MHz, $CDCl_3$)** δ -99.12. **^{13}C NMR (101 MHz, $CDCl_3$)** δ 165.44, 164.19 (t, *J* = 35.2 Hz), 160.03, 148.46, 138.59, 137.41, 136.15, 133.76 (t, *J* = 3.4 Hz), 129.84, 126.85 (t, *J* = 9.0 Hz), 124.74 (t, *J* = 1.7 Hz), 122.50, 122.13 (t, *J* = 24.5 Hz), 119.07, 118.26, 114.73, 114.02 (t, *J* = 252.5 Hz), 112.76, 63.39, 55.49, 13.82. Characterization data were consistent with a previous report. [6]

ethyl 2,2-difluoro-2-(8-(4-methoxybenzamido)quinolin-5-yl)acetate (**4g**)



Purified with PTLC (PE/EA = 5/1, R_f = 0.42) to afford the title compound as a white solid (54 mg, 67%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.86 (s, 1H), 8.96 (d, *J* = 8.3 Hz, 1H), 8.90 (dd, *J* = 4.1, 1.2 Hz, 1H), 8.69 (d, *J* = 7.8 Hz, 1H), 8.06 (d, *J* = 8.8 Hz, 2H), 7.92 (d, *J* = 8.3 Hz, 1H), 7.57 (dd, *J* = 8.7, 4.2 Hz, 1H), 7.05 (d, *J* = 8.8 Hz, 2H), 4.29 (q, *J* = 7.1 Hz, 2H), 3.91 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 5H). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -99.09. **^{13}C NMR (101 MHz, $CDCl_3$)** δ 165.17, 164.26 (t, *J* = 35.2 Hz), 162.78, 148.37, 138.63, 137.67, 133.80 (t, *J* = 3.6 Hz), 129.28, 126.99, 126.96 (t, *J* = 9.1 Hz), 124.78, 122.46, 121.79, 114.57, 114.12 (t, *J* = 251.1 Hz), 114.09, 63.39, 55.50, 13.84. Characterization data were consistent with a previous report. [6]

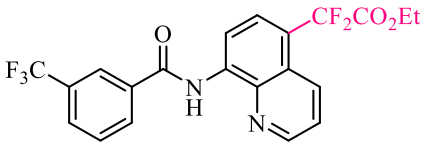
ethyl 2,2-difluoro-2-(8-(2-(trifluoromethyl)benzamido)quinolin-5-yl)acetate (**4h**)



Purified with PTLC (PE/EA = 10/1, R_f = 0.36) to afford the title compound as a white solid (50 mg, 57%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.35 (s, 1H), 8.96 (d, *J* = 8.2 Hz, 1H), 8.80 (d, *J* = 2.9 Hz, 1H), 8.69 (d, *J* = 7.8 Hz, 1H), 7.94 (d, *J* = 8.3 Hz, 1H), 7.82 (d, *J* = 7.7 Hz, 1H), 7.76 (d, *J* = 7.4 Hz, 1H), 7.71 (t, *J* = 7.3 Hz, 1H), 7.65 (t, *J* = 7.5 Hz, 1H), 7.55 (dd, *J* = 8.7, 4.2 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 1.27 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -58.82, -99.27. **^{13}C NMR (101 MHz, $CDCl_3$)** δ 166.13, 164.16 (t, *J* = 35.4 Hz), 148.51, 138.32, 137.12, 135.75 (q, *J* = 2.2 Hz), 133.78 (t, *J* =4.0 Hz), 132.23, 130.39, 128.48, 127.70 (q, *J* = 32.3 Hz), 126.79 (t, *J* = 9.1 Hz), 126.75 (q, *J* = 5.0 Hz), 124.74 (t, *J* = 2.1 Hz), 123.54 (q, *J* = 274.7 Hz), 122.83 (t, *J* = 24.2 Hz), 122.56,

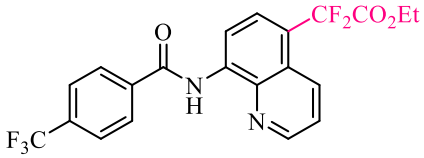
115.16, 113.93 (t, J = 254.5 Hz), 63.46, 13.84. Characterization data were consistent with a previous report. [7]

ethyl 2,2-difluoro-2-(8-(3-(trifluoromethyl)benzamido)quinolin-5-yl)acetate (**4i**)



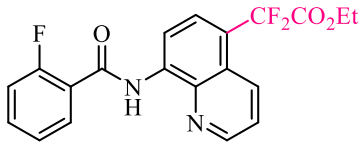
Purified with PTLC (PE/EA = 10/1, R_f = 0.39) to afford the title compound as a white solid (52 mg, 59%). **^{1}H NMR (400 MHz, CDCl$_3$)** δ 10.94 (s, 1H), 8.94 (d, J = 8.2 Hz, 1H), 8.91 (d, J = 3.7 Hz, 1H), 8.70 (d, J = 8.6 Hz, 1H), 8.34 (s, 1H), 8.24 (d, J = 7.8 Hz, 1H), 7.94 (d, J = 8.3 Hz, 1H), 7.86 (d, J = 7.8 Hz, 1H), 7.71 (t, J = 7.8 Hz, 1H), 7.59 (dd, J = 8.7, 4.2 Hz, 1H), 4.29 (q, J = 7.1 Hz, 2H), 1.26 (t, J = 7.1 Hz, 3H). **^{19}F NMR (376 MHz, CDCl$_3$)** δ -62.70, -99.19. **^{13}C NMR (101 MHz, CDCl$_3$)** δ 164.14 (t, J = 35.1 Hz), 164.07, 148.63, 138.53, 136.98, 135.53, 133.89 (t, J = 3.6 Hz), 131.54 (q, J = 33.0 Hz), 130.28, 129.50, 128.70 (q, J = 3.6 Hz), 126.80 (t, J = 9.0 Hz), 124.75 (t, J = 2.0 Hz), 124.61 (q, J = 3.8 Hz), 123.67 (q, J = 272.6 Hz), 122.65 (t, J = 24.6 Hz), 122.64, 115.00, 113.95 (t, J = 252.8 Hz), 63.46, 13.83. Characterization data were consistent with a previous report. [7]

ethyl 2,2-difluoro-2-(8-(4-(trifluoromethyl)benzamido)quinolin-5-yl)acetate (**4j**)



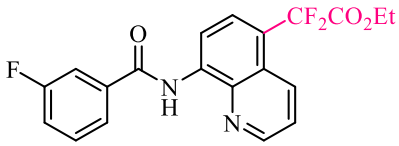
Purified with PTLC (PE/EA = 10/1, R_f = 0.58) to afford the title compound as a white solid (46 mg, 53%). **^{1}H NMR (400 MHz, CDCl$_3$)** δ 10.96 (s, 1H), 8.95 (d, J = 8.2 Hz, 1H), 8.90 (d, J = 4.1 Hz, 1H), 8.70 (d, J = 8.7 Hz, 1H), 8.19 (d, J = 8.1 Hz, 2H), 7.94 (d, J = 8.3 Hz, 1H), 7.83 (d, J = 8.2 Hz, 2H), 7.59 (dd, J = 8.7, 4.2 Hz, 1H), 4.29 (q, J = 7.1 Hz, 2H), 1.26 (t, J = 7.1 Hz, 3H). **^{19}F NMR (376 MHz, CDCl$_3$)** δ -62.95, -99.21. **^{13}C NMR (101 MHz, CDCl$_3$)** δ 164.21, 164.13 (t, J = 35.2 Hz), 148.60, 138.53, 137.93, 136.98, 133.92 (t, J = 4.0 Hz), 133.75 (q, J = 32.7 Hz), 127.80, 126.80 (t, J = 9.0 Hz), 125.94 (q, J = 3.7 Hz), 124.76, 123.62 (q, J = 272.6 Hz), 122.69 (t, J = 24.6 Hz), 122.64, 114.98, 113.94 (t, J = 252.8 Hz), 63.45, 13.83. Characterization data were consistent with a previous report. [6]

ethyl 2,2-difluoro-2-(8-(2-fluorobenzamido)quinolin-5-yl)acetate (**4k**)



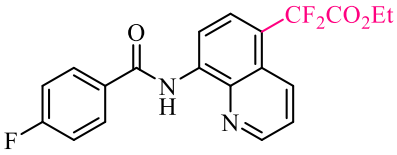
Purified with PTLC (PE/EA = 10/1, R_f = 0.50) to afford the title compound as a clear oil (46 mg, 60%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 11.33 (d, *J* = 12.6 Hz, 1H), 9.00 (d, *J* = 8.3 Hz, 1H), 8.90 (d, *J* = 3.0 Hz, 1H), 8.67 (d, *J* = 8.6 Hz, 1H), 8.21 (td, *J* = 7.8, 1.6 Hz, 1H), 7.92 (d, *J* = 8.3 Hz, 1H), 7.61 – 7.50 (m, 2H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.24 (dd, *J* = 11.8, 8.3 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 1.25 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -99.19, -111.92. **^{13}C NMR (101 MHz, $CDCl_3$)** δ 164.18 (t, *J* = 35.2 Hz), 161.85 (d, *J* = 3.2 Hz), 160.56 (d, *J* = 249.4 Hz), 148.60, 138.61, 137.70, 133.90 (d, *J* = 9.2 Hz), 133.57 (t, *J* = 3.6 Hz), 132.06 (d, *J* = 1.7 Hz), 126.77 (t, *J* = 9.0 Hz), 124.91 (d, *J* = 3.3 Hz), 124.69 (t, *J* = 1.9 Hz), 122.46, 122.41 (t, *J* = 24.5 Hz), 121.64 (d, *J* = 11.5 Hz), 116.36 (d, *J* = 24.5 Hz), 115.42, 114.00 (t, *J* = 252.6 Hz), 63.39, 13.81. Characterization data were consistent with a previous report. [7]

ethyl 2,2-difluoro-2-(8-(3-fluorobenzamido)quinolin-5-yl)acetate (**4l**)



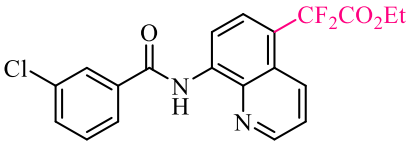
Purified with PTLC (PE/EA = 10/1, R_f = 0.42) to afford the title compound as a white solid (36 mg, 47%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.90 (s, 1H), 8.94 (d, *J* = 8.2 Hz, 1H), 8.90 (dd, *J* = 4.1, 1.2 Hz, 1H), 8.70 (dd, *J* = 8.7, 1.0 Hz, 1H), 7.93 (d, *J* = 8.3 Hz, 1H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.81 – 7.81 (m, 1H), 7.78 (dt, *J* = 9.3, 1.9 Hz, 1H), 7.62 – 7.50 (m, 2H), 7.30 (td, *J* = 8.3, 1.9 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 1.25 (q, *J* = 7.4 Hz, 3H). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -99.18, -111.26. **^{13}C NMR (101 MHz, $CDCl_3$)** δ 164.17, 164.15 (t, *J* = 35.2 Hz), 162.95 (d, *J* = 252.5 Hz), 148.55, 138.54, 137.11, 136.93 (d, *J* = 6.8 Hz), 133.84 (t, *J* = 3.6 Hz), 130.54 (d, *J* = 7.9 Hz), 126.81 (t, *J* = 9.0 Hz), 124.74, 122.75 (d, *J* = 3.0 Hz), 122.70, 122.46 (t, *J* = 24.5 Hz), 119.18 (d, *J* = 21.4 Hz), 114.88, 114.73 (d, *J* = 23.1 Hz), 113.97 (t, *J* = 252.8 Hz), 63.42, 13.82. Characterization data were consistent with a previous report. [6]

ethyl 2,2-difluoro-2-(8-(4-fluorobenzamido)quinolin-5-yl)acetate (**4m**)



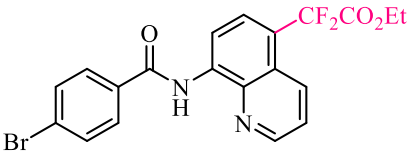
Purified with PTLC (PE/EA = 10/1, R_f = 0.45) to afford the title compound as a white solid (40 mg, 51%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.87 (s, 1H), 8.94 (d, *J* = 8.3 Hz, 1H), 8.89 (d, *J* = 3.0 Hz, 1H), 8.69 (d, *J* = 8.7 Hz, 1H), 8.09 (dd, *J* = 8.7, 5.3 Hz, 2H), 7.93 (d, *J* = 8.3 Hz, 1H), 7.58 (dd, *J* = 8.7, 4.2 Hz, 1H), 7.24 (t, *J* = 8.7 Hz, 2H), 4.29 (q, *J* = 7.1 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -99.14, -106.91. **^{13}C NMR (101 MHz, $CDCl_3$)** δ 165.17 (d, *J* = 254.5 Hz), 164.47, 164.17 (t, *J* = 36.1 Hz), 148.48, 138.57, 137.30, 133.87, 130.87, 129.76 (d, *J* = 9.2 Hz), 126.87 (t, *J* = 9.0 Hz), 124.76, 122.54, 122.25 (t, *J* = 25.0 Hz), 115.97 (d, *J* = 22.0 Hz), 114.76, 114.00 (t, *J* = 254.6 Hz), 63.42, 13.83. Characterization data were consistent with a previous report. [6]

ethyl 2-(8-(3-chlorobenzamido)quinolin-5-yl)-2,2-difluoroacetate (**4n**)



Purified with PTLC (PE/EA = 10/1, R_f = 0.50) to afford the title compound as a white solid (48 mg, 59%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.87 (s, 1H), 8.93 (d, *J* = 8.3 Hz, 1H), 8.91 (dd, *J* = 4.1, 1.1 Hz, 1H), 8.69 (d, *J* = 7.9 Hz, 1H), 8.05 (s, 1H), 7.96 – 7.90 (m, 2H), 7.63 – 7.55 (m, 2H), 7.50 (t, *J* = 7.8 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -99.18. **^{13}C NMR (101 MHz, $CDCl_3$)** δ 164.17, 164.15 (t, *J* = 35.2 Hz), 148.57, 138.53, 137.09, 136.44, 135.12, 133.85 (t, *J* = 3.7 Hz), 132.18, 130.15, 127.74, 126.81 (t, *J* = 9.1 Hz), 125.28, 124.74 (t, *J* = 1.9 Hz), 122.59, 122.49 (t, *J* = 24.6 Hz), 114.93, 113.96 (t, *J* = 252.7 Hz), 63.43, 13.83. Characterization data were consistent with a previous report. [6]

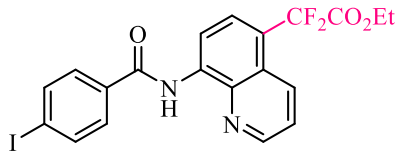
ethyl 2-(8-(4-bromobenzamido)quinolin-5-yl)-2,2-difluoroacetate (**4o**)



Purified with PTLC (PE/EA = 10/1, R_f = 0.55) to afford the title compound as a white solid (56 mg, 62%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.89 (s, 1H), 8.94 (d, *J* = 8.2 Hz, 1H), 8.90 (dd, *J* = 4.1, 1.2

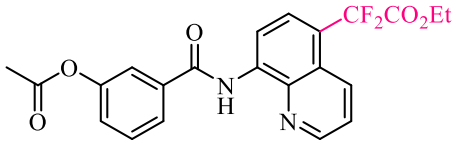
Hz, 1H), 8.70 (dd, *J* = 8.7, 1.0 Hz, 1H), 7.94 (dd, *J* = 8.3, 6.6 Hz, 3H), 7.70 (d, *J* = 8.5 Hz, 2H), 7.59 (dd, *J* = 8.7, 4.2 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -99.17. **^{13}C NMR (101 MHz, $CDCl_3$)** δ 164.62, 164.17 (t, *J* = 35.1 Hz), 148.52, 138.54, 137.17, 133.88 (t, *J* = 3.8 Hz), 133.52, 132.14, 128.92, 127.01, 126.85 (t, *J* = 9.1 Hz), 124.76 (t, *J* = 2.0 Hz), 122.59, 122.39 (t, *J* = 24.5 Hz), 114.85, 113.97 (t, *J* = 252.8 Hz), 63.44, 13.84. Characterization data were consistent with a previous report. [6]

ethyl 2,2-difluoro-2-(8-(4-iodobenzamido)quinolin-5-yl)acetate (**4p**)



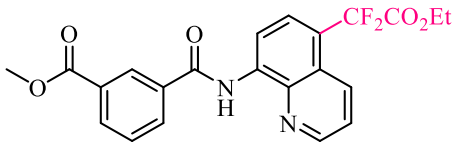
Purified with PTLC (PE/EA = 10/1, R_f = 0.55) to afford the title compound as a white solid (50 mg, 51%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.88 (s, 1H), 8.93 (d, *J* = 8.2 Hz, 1H), 8.89 (d, *J* = 3.0 Hz, 1H), 8.69 (d, *J* = 8.6 Hz, 1H), 7.98 – 7.87 (m, 3H), 7.79 (d, *J* = 8.4 Hz, 2H), 7.58 (dd, *J* = 8.7, 4.2 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 1.25 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -99.17. **^{13}C NMR (101 MHz, $CDCl_3$)** δ 164.82, 164.17 (t, *J* = 35.1 Hz), 148.52, 138.54, 138.13, 137.15, 134.10, 133.87 (t, *J* = 3.6 Hz), 128.86, 126.84 (t, *J* = 8.9 Hz), 124.75 (t, *J* = 1.8 Hz), 122.58, 122.38 (t, *J* = 24.5 Hz), 114.85, 113.97 (t, *J* = 252.9 Hz), 99.38, 63.43, 13.84. Characterization data were consistent with a previous report. [7]

ethyl 2-(8-(3-acetoxybenzamido)quinolin-5-yl)-2,2-difluoroacetate (**4q**)



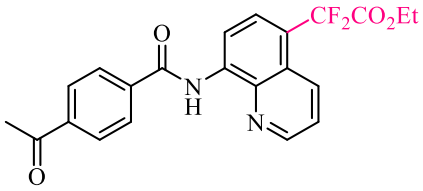
Purified with PTLC (PE/EA = 5/1, R_f = 0.31) to afford the title compound as a clear oil (41 mg, 48%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.88 (s, 1H), 8.94 (d, *J* = 8.2 Hz, 1H), 8.89 (dd, *J* = 4.0, 1.2 Hz, 1H), 8.69 (dd, *J* = 8.7, 0.9 Hz, 1H), 7.92 (d, *J* = 8.2 Hz, 2H), 7.80 (t, *J* = 1.7 Hz, 1H), 7.62 – 7.53 (m, 2H), 7.34 (dd, *J* = 8.1, 1.5 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 2.36 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -99.15. **^{13}C NMR (101 MHz, $CDCl_3$)** δ 169.18, 164.47, 164.14 (t, *J* = 35.3 Hz), 151.06, 148.50, 138.53, 137.19, 136.27, 133.77 (t, *J* = 3.6 Hz), 129.86, 126.79 (t, *J* = 9.1 Hz), 125.52, 124.70, 124.39, 122.52, 122.32, 120.95, 114.85, 113.97 (t, *J* = 252.6 Hz), 63.40, 21.08, 13.80. **HRMS (ESI-TOF)** m/z: calculated for $C_{22}H_{18}F_2N_2NaO_5^+$: 451.1076 (M + Na)$^+$, found 451.1088.

methyl 3-((5-(2-ethoxy-1,1-difluoro-2-oxoethyl)quinolin-8-yl)carbamoyl)benzoate (**4r**)



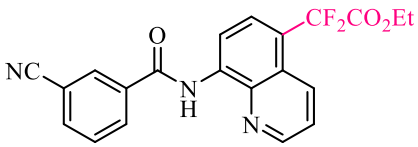
Purified with PTLC (PE/EA = 5/1, R_f = 0.33) to afford the title compound as a white solid (43 mg, 50%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.95 (s, 1H), 8.95 (d, *J* = 8.2 Hz, 1H), 8.91 (d, *J* = 3.2 Hz, 1H), 8.72 (s, 1H), 8.69 (d, *J* = 8.7 Hz, 1H), 8.26 (d, *J* = 7.8 Hz, 2H), 7.93 (d, *J* = 8.3 Hz, 1H), 7.65 (t, *J* = 7.8 Hz, 1H), 7.58 (dd, *J* = 8.7, 4.1 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 3.99 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -99.22. **^{13}C NMR (101 MHz, $CDCl_3$)** δ 166.21, 164.62, 164.14 (t, *J* = 35.2 Hz), 148.57, 138.52, 137.14, 135.06, 133.78 (t, *J* = 3.6 Hz), 132.97, 131.67, 130.89, 129.09, 128.32, 126.78 (t, *J* = 9.0 Hz), 124.69, 122.57, 122.39 (t, *J* = 24.5 Hz), 114.91, 113.94 (t, *J* = 252.8 Hz), 63.42, 52.45, 13.81. **HRMS (ESI-TOF)** m/z: calculated for $C_{22}H_{18}F_2N_2NaO_5^+$: 451.1076 $(M + Na)^+$, found 451.1084.

ethyl 2-(8-(4-acetylbenzamido)quinolin-5-yl)-2,2-difluoroacetate (**4s**)



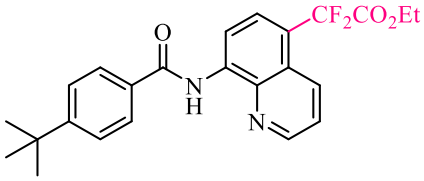
Purified with PTLC (PE/EA = 3/1, R_f = 0.57) to afford the title compound as a white solid (34 mg, 41%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.98 (s, 1H), 8.96 (d, *J* = 8.2 Hz, 1H), 8.91 (d, *J* = 3.1 Hz, 1H), 8.70 (d, *J* = 8.5 Hz, 1H), 8.15 (q, *J* = 8.5 Hz, 4H), 7.94 (d, *J* = 8.3 Hz, 1H), 7.60 (dd, *J* = 8.7, 4.2 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 2.69 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -99.19. **^{13}C NMR (101 MHz, $CDCl_3$)** δ 197.30, 164.56, 164.16 (t, *J* = 35.1 Hz), 148.59, 139.65, 138.58, 138.47, 137.09, 133.91 (t, *J* = 3.4 Hz), 128.80, 127.66, 126.84 (t, *J* = 9.0 Hz), 126.75, 124.78 (t, *J* = 2.0 Hz), 122.63, 114.97, 113.96 (t, *J* = 252.6 Hz), 63.45, 26.86, 13.84. Characterization data were consistent with a previous report. [8]

ethyl 2-(8-(3-cyanobenzamido)quinolin-5-yl)-2,2-difluoroacetate (**4t**)



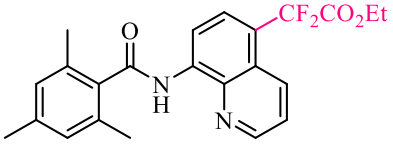
Purified with PTLC (PE/EA = 5/1, R_f = 0.25) to afford the title compound as a white solid (47 mg, 60%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.95 (s, 1H), 8.99 – 8.89 (m, 2H), 8.71 (d, *J* = 8.6 Hz, 1H), 8.36 (s, 1H), 8.32 (d, *J* = 7.9 Hz, 1H), 7.95 (d, *J* = 8.3 Hz, 1H), 7.90 (d, *J* = 7.7 Hz, 1H), 7.72 (t, *J* = 7.8 Hz, 1H), 7.62 (dd, *J* = 8.7, 4.2 Hz, 1H), 4.30 (q, *J* = 7.1 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -99.27. **^{13}C NMR (101 MHz, $CDCl_3$)** δ 164.09 (t, *J* = 35.0 Hz), 163.20, 148.70, 138.48, 136.74, 135.89, 135.23, 133.95 (t, *J* = 3.6 Hz), 131.51, 131.02, 129.90, 126.75 (t, *J* = 9.0 Hz), 124.76 (t, *J* = 1.9 Hz), 122.89 (t, *J* = 24.6 Hz), 122.72, 117.94, 115.06, 113.90 (t, *J* = 252.9 Hz), 113.37, 63.47, 13.82. **HRMS (ESI-TOF)** m/z: calculated for $C_{21}H_{15}F_2N_3NaO_3^+$: 418.0974 $(M + Na)^+$, found 418.0959.

ethyl 2-(8-(4-(tert-butyl)benzamido)quinolin-5-yl)-2,2-difluoroacetate (**4u**)



Purified with PTLC (PE/EA = 10/1, R_f = 0.54) to afford the title compound as a clear oil (61 mg, 72%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.91 (s, 1H), 8.97 (d, *J* = 8.2 Hz, 1H), 8.88 (d, *J* = 4.0 Hz, 1H), 8.68 (d, *J* = 8.6 Hz, 1H), 8.02 (d, *J* = 8.1 Hz, 2H), 7.92 (d, *J* = 8.3 Hz, 1H), 7.63 – 7.53 (m, 3H), 4.28 (q, *J* = 7.1 Hz, 2H), 1.38 (s, 9H), 1.25 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -99.14. **^{13}C NMR (101 MHz, $CDCl_3$)** δ 165.57, 164.20 (t, *J* = 35.2 Hz), 155.74, 148.37, 138.56, 137.54, 133.72 (t, *J* = 3.5 Hz), 131.81, 127.18, 126.86 (t, *J* = 9.0 Hz), 125.80, 124.70, 122.45, 121.86 (t, *J* = 24.6 Hz), 114.60, 114.01 (t, *J* = 252.7 Hz), 63.37, 35.01, 31.12, 13.81. Characterization data were consistent with a previous report. [6]

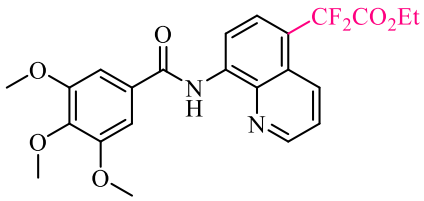
ethyl 2,2-difluoro-2-(8-(2,4,6-trimethylbenzamido)quinolin-5-yl)acetate (**4v**)



Purified with PTLC (PE/EA = 10/1, R_f = 0.60) to afford the title compound as a clear oil (57 mg, 69%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.10 (s, 1H), 9.03 (d, *J* = 8.2 Hz, 1H), 8.77 (d, *J* = 3.3 Hz,

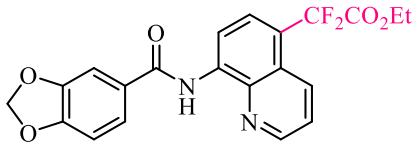
1H), 8.68 (d, *J* = 8.5 Hz, 1H), 7.94 (d, *J* = 8.3 Hz, 1H), 7.53 (dd, *J* = 8.7, 4.1 Hz, 1H), 6.94 (s, 2H), 4.29 (q, *J* = 7.1 Hz, 2H), 2.39 (s, 6H), 2.34 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -99.15. **^{13}C NMR (101 MHz, $CDCl_3$)** δ 169.35, 164.20 (t, *J* = 35.2 Hz), 148.39, 139.03, 138.36, 137.31, 134.98, 134.50, 133.69 (t, *J* = 3.6 Hz), 128.49, 126.83 (t, *J* = 9.0 Hz), 124.76 (t, *J* = 1.7 Hz), 122.44, 122.29 (t, *J* = 24.6 Hz), 114.86, 114.00 (t, *J* = 252.7 Hz), 63.41, 21.14, 19.39, 13.84. **HRMS (ESI-TOF)** m/z: calculated for $C_{23}H_{22}F_2N_2NaO_3^+$: 435.1491 $(M + Na)^+$, found 435.1499.

ethyl 2,2-difluoro-2-(8-(3,4,5-trimethoxybenzamido)quinolin-5-yl)acetate (**4w**)



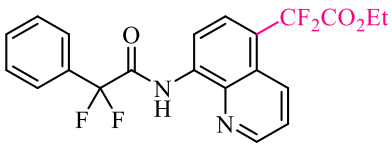
Purified with PTLC (PE/EA = 3/1, R_f = 0.55) to afford the title compound as a white solid (54 mg, 59%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.80 (s, 1H), 8.91 (d, *J* = 8.2 Hz, 1H), 8.87 (dd, *J* = 4.0, 1.2 Hz, 1H), 8.68 (d, *J* = 7.8 Hz, 1H), 7.92 (d, *J* = 8.3 Hz, 1H), 7.56 (dd, *J* = 8.7, 4.2 Hz, 1H), 7.28 (s, 2H), 4.28 (q, *J* = 7.1 Hz, 2H), 3.98 (s, 6H), 3.93 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -99.10. **^{13}C NMR (101 MHz, $CDCl_3$)** δ 165.29, 164.14 (t, *J* = 35.2 Hz), 153.35, 148.47, 141.62, 138.52, 137.36, 133.78 (t, *J* = 3.5 Hz), 130.08, 126.84 (t, *J* = 9.0 Hz), 124.72, 122.47, 122.06 (t, *J* = 24.6 Hz), 114.62, 113.98 (t, *J* = 252.7 Hz), 104.85, 63.37, 60.92, 56.39, 13.79. **HRMS (ESI-TOF)** m/z: calculated for $C_{23}H_{22}F_2N_2NaO_6^+$: 483.1338 $(M + Na)^+$, found 483.1365.

ethyl 2-(8-(benzo[d][1,3]dioxole-5-carboxamido)quinolin-5-yl)-2,2-difluoroacetate (**4x**)



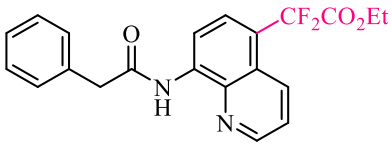
Purified with PTLC (PE/EA = 5/1, R_f = 0.60) to afford the title compound as a white solid (44 mg, 53%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.81 (s, 1H), 8.92 (d, *J* = 8.2 Hz, 1H), 8.89 (dd, *J* = 4.1, 1.1 Hz, 1H), 8.69 (dd, *J* = 8.7, 0.7 Hz, 1H), 7.92 (d, *J* = 8.3 Hz, 1H), 7.65 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.61 – 7.53 (m, 2H), 6.96 (d, *J* = 8.1 Hz, 1H), 6.09 (s, 2H), 4.29 (q, *J* = 7.1 Hz, 2H), 1.25 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR (377 MHz, $CDCl_3$)** δ -99.11. **^{13}C NMR (101 MHz, $CDCl_3$)** δ 164.80, 164.23 (t, *J* = 35.2 Hz), 150.99, 148.41, 148.27, 138.58, 137.53, 133.81 (t, *J* = 3.6 Hz), 128.92, 126.91 (t, *J* = 9.0 Hz), 124.76 (t, *J* = 1.8 Hz), 122.49, 122.32, 114.62, 114.05 (t, *J* = 252.6 Hz), 108.28, 107.87, 101.89, 63.39, 13.84. Characterization data were consistent with a previous report. [6]

ethyl 2-(8-(2,2-difluoro-2-phenylacetamido)quinolin-5-yl)-2,2-difluoroacetate (**4y**)



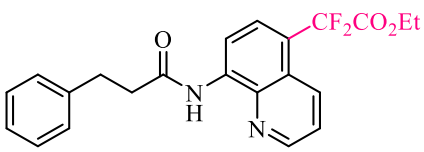
Purified with PTLC (PE/EA = 10/1, R_f = 0.58) to afford the title compound as a white solid (50 mg, 60%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 11.04 (s, 1H), 8.92 (d, *J* = 3.9 Hz, 1H), 8.78 (d, *J* = 8.2 Hz, 1H), 8.68 (d, *J* = 8.7 Hz, 1H), 7.89 (d, *J* = 8.2 Hz, 1H), 7.76 (d, *J* = 6.6 Hz, 2H), 7.59 (dd, *J* = 8.7, 4.1 Hz, 1H), 7.54 – 7.43 (m, 3H), 4.27 (q, *J* = 7.1 Hz, 2H), 1.24 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -99.46, -103.25. **^{13}C NMR (101 MHz, $CDCl_3$)** δ 164.01 (t, *J* = 35.0 Hz), 162.48 (t, *J* = 31.8 Hz), 148.96, 138.51, 135.75, 133.76 (t, *J* = 3.6 Hz), 132.78 (t, *J* = 25.6 Hz), 131.04, 128.71, 126.44 (t, *J* = 9.1 Hz), 125.60 (t, *J* = 6.1 Hz), 124.69, 123.70 (t, *J* = 24.6 Hz), 122.77, 115.44, 114.73 (t, *J* = 254.4 Hz), 113.77 (t, *J* = 252.9 Hz), 63.48, 13.80. **HRMS (ESI-TOF)** m/z: calculated for $C_{21}H_{16}F_4N_2NaO_3^+$: 443.0989 $(M + Na)^+$, found 443.1012.

ethyl 2,2-difluoro-2-(8-(2-phenylacetamido)quinolin-5-yl)acetate (**4z**)



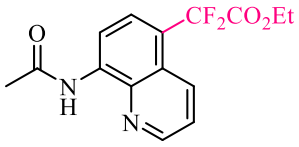
Purified with PTLC (PE/EA = 10/1, R_f = 0.33) to afford the title compound as a white solid (50 mg, 65%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.08 (s, 1H), 8.79 (d, *J* = 8.3 Hz, 1H), 8.71 (d, *J* = 3.0 Hz, 1H), 8.61 (d, *J* = 8.6 Hz, 1H), 7.84 (d, *J* = 8.3 Hz, 1H), 7.48 (dd, *J* = 8.7, 4.2 Hz, 1H), 7.46 – 7.30 (m, 5H), 4.26 (q, *J* = 7.1 Hz, 2H), 3.90 (s, 2H), 1.22 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -99.19. **^{13}C NMR (101 MHz, $CDCl_3$)** δ 169.75, 164.12 (t, *J* = 35.2 Hz), 148.25, 138.21, 137.17, 134.28, 133.52 (t, *J* = 3.6 Hz), 129.46, 128.98, 127.41, 126.67 (t, *J* = 9.0 Hz), 124.54 (t, *J* = 1.9 Hz), 122.30, 121.99 (t, *J* = 24.6 Hz), 114.46, 113.94 (t, *J* = 252.6 Hz), 63.32, 45.33, 13.76. Characterization data were consistent with a previous report. [8]

ethyl 2,2-difluoro-2-(8-(3-phenylpropanamido)quinolin-5-yl)acetate (**4aa**)



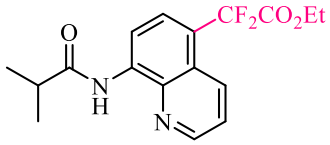
Purified with PTLC (PE/EA = 10/1, R_f = 0.32) to afford the title compound as a white solid (55 mg, 69%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.96 (s, 1H), 8.82 (d, *J* = 8.3 Hz, 1H), 8.79 (dd, *J* = 4.1, 1.1 Hz, 1H), 8.65 (d, *J* = 8.6 Hz, 1H), 7.87 (d, *J* = 8.3 Hz, 1H), 7.52 (dd, *J* = 8.7, 4.1 Hz, 1H), 7.30 (d, *J* = 4.4 Hz, 4H), 7.24 – 7.18 (m, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 3.15 (t, *J* = 7.8 Hz, 2H), 2.91 (t, *J* = 7.8 Hz, 2H), 1.25 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -99.10. **^{13}C NMR (101 MHz, $CDCl_3$)** δ 170.98, 164.16 (t, *J* = 35.2 Hz), 148.19, 140.48, 138.03, 137.20, 133.62 (t, *J* = 3.6 Hz), 128.53, 128.33, 126.77 (t, *J* = 9.0 Hz), 126.26, 124.59 (t, *J* = 1.9 Hz), 122.36, 121.81 (t, *J* = 24.6 Hz), 114.59, 113.97 (t, *J* = 252.6 Hz), 63.35, 39.65, 31.25, 13.79. Characterization data were consistent with a previous report. [7]

ethyl 2-(8-acetamidoquinolin-5-yl)-2,2-difluoroacetate (**4ab**)



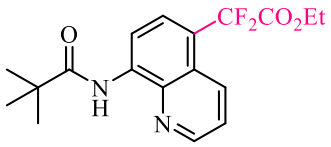
Purified with PTLC (PE/EA = 5/1, R_f = 0.37) to afford the title compound as a white solid (38 mg, 62%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.97 (s, 1H), 8.84 (d, *J* = 3.1 Hz, 1H), 8.79 (d, *J* = 8.3 Hz, 1H), 8.66 (d, *J* = 8.7 Hz, 1H), 7.86 (d, *J* = 8.3 Hz, 1H), 7.55 (dd, *J* = 8.7, 4.2 Hz, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 2.37 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -99.12. **^{13}C NMR (101 MHz, $CDCl_3$)** δ 169.01, 164.19 (t, *J* = 35.4 Hz), 148.25, 138.04, 137.33, 133.71 (t, *J* = 3.5 Hz), 126.82 (t, *J* = 9.0 Hz), 124.65, 122.40, 121.86 (t, *J* = 24.6 Hz), 114.56, 113.99 (t, *J* = 252.6 Hz), 63.38, 25.18, 13.82. Characterization data were consistent with a previous report. [7]

ethyl 2,2-difluoro-2-(8-isobutyramidoquinolin-5-yl)acetate (**4ac**)



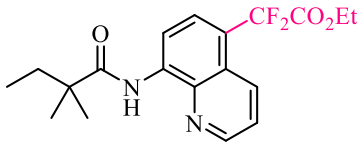
Purified with PTLC (PE/EA = 10/1, R_f = 0.30) to afford the title compound as a white solid (46 mg, 69%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.08 (s, 1H), 8.90 – 8.78 (m, 2H), 8.65 (dd, *J* = 8.7, 1.3 Hz, 1H), 7.86 (d, *J* = 8.3 Hz, 1H), 7.54 (dd, *J* = 8.7, 4.2 Hz, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 2.84 – 2.72 (m, 1H), 1.35 (d, *J* = 6.9 Hz, 6H), 1.24 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -99.17. **^{13}C NMR (101 MHz, $CDCl_3$)** δ 176.00, 164.22 (t, *J* = 35.3 Hz), 148.27, 138.28, 137.47, 133.69 (t, *J* = 3.7 Hz), 126.85 (t, *J* = 9.0 Hz), 124.66 (t, *J* = 2.0 Hz), 122.37, 121.70 (t, *J* = 24.5 Hz), 114.57, 114.01 (t, *J* = 252.6 Hz), 63.35, 37.16, 19.61, 13.81. Characterization data were consistent with a previous report. [8]

ethyl 2,2-difluoro-2-(8-pivalamidoquinolin-5-yl)acetate (**4ad**)



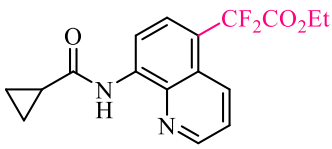
Purified with PTLC (PE/EA = 10/1, R_f = 0.48) to afford the title compound as a clear oil (47 mg, 67%). **^{1}H NMR (400 MHz, CDCl$_3$)** δ 10.44 (s, 1H), 8.86 (dd, *J* = 4.1, 1.3 Hz, 1H), 8.82 (d, *J* = 8.3 Hz, 1H), 8.65 (dd, *J* = 8.7, 1.2 Hz, 1H), 7.87 (d, *J* = 8.3 Hz, 1H), 7.54 (dd, *J* = 8.7, 4.2 Hz, 1H), 4.26 (q, *J* = 7.1 Hz, 2H), 1.42 (s, 9H), 1.23 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR (376 MHz, CDCl$_3$)** δ -99.19. **^{13}C NMR (101 MHz, CDCl$_3$)** δ 177.53, 164.22 (t, *J* = 35.3 Hz), 148.36, 138.59, 137.55, 133.65 (t, *J* = 3.6 Hz), 126.84 (t, *J* = 9.0 Hz), 124.64 (t, *J* = 1.9 Hz), 122.34, 121.62 (t, *J* = 24.5 Hz), 114.38, 114.02 (t, *J* = 252.5 Hz), 63.33, 40.45, 27.63, 13.80. Characterization data were consistent with a previous report. [7]

ethyl 2-(8-(2,2-dimethylbutanamido)quinolin-5-yl)-2,2-difluoroacetate (**4ae**)



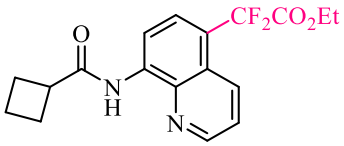
Purified with PTLC (PE/EA = 10/1, R_f = 0.43) to afford the title compound as a clear oil (45 mg, 62%). **^{1}H NMR (400 MHz, CDCl$_3$)** δ 10.41 (s, 1H), 8.89 – 8.80 (m, 2H), 8.65 (d, *J* = 8.0 Hz, 1H), 7.86 (d, *J* = 8.3 Hz, 1H), 7.54 (dd, *J* = 8.7, 4.2 Hz, 1H), 4.26 (q, *J* = 7.1 Hz, 2H), 1.76 (q, *J* = 7.1 Hz, 2H), 1.38 (s, 6H), 1.23 (t, *J* = 7.1 Hz, 3H), 0.94 (t, *J* = 7.5 Hz, 3H). **^{19}F NMR (376 MHz, CDCl$_3$)** δ -99.19. **^{13}C NMR (101 MHz, CDCl$_3$)** δ 176.94, 164.22 (t, *J* = 35.3 Hz), 148.36, 138.57, 137.51, 133.64 (t, *J* = 3.7 Hz), 126.85 (t, *J* = 9.0 Hz), 124.65 (t, *J* = 1.9 Hz), 122.32, 121.56 (t, *J* = 24.5 Hz), 114.34, 114.02 (t, *J* = 252.5 Hz), 63.33, 44.19, 34.05, 25.00, 13.80, 9.25. **HRMS (ESI-TOF)** m/z: calculated for $C_{19}H_{22}F_2N_2NaO_3^+$: 387.1491 $(M + Na)^+$, found 387.1496.

ethyl 2-(8-(cyclopropanecarboxamido)quinolin-5-yl)-2,2-difluoroacetate (**4af**)



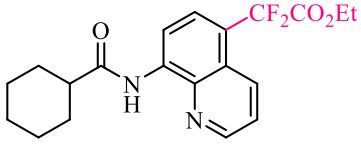
Purified with PTLC (PE/EA = 5/1, R_f = 0.46) to afford the title compound as a white solid (47 mg, 70%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.21 (s, 1H), 8.85 (dd, *J* = 4.1, 1.2 Hz, 1H), 8.77 (d, *J* = 8.3 Hz, 1H), 8.66 (dd, *J* = 8.7, 1.1 Hz, 1H), 7.85 (d, *J* = 8.3 Hz, 1H), 7.55 (dd, *J* = 8.7, 4.2 Hz, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 1.89 – 1.75 (m, 1H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.20 – 1.14 (m, 2H), 0.98 – 0.92 (m, 2H). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -99.13. **^{13}C NMR (101 MHz, $CDCl_3$)** δ 172.61, 164.24 (t, *J* = 35.2 Hz), 148.22, 138.05, 137.50, 133.71 (t, *J* = 3.6 Hz), 126.89 (t, *J* = 9.0 Hz), 124.70, 122.39, 121.57 (t, *J* = 24.5 Hz), 114.55, 114.04 (t, *J* = 252.5 Hz), 63.36, 16.36, 13.83, 8.49. Characterization data were consistent with a previous report. [7]

ethyl 2-(8-(cyclobutanecarboxamido)quinolin-5-yl)-2,2-difluoroacetate (**4ag**)



Purified with PTLC (PE/EA = 10/1, R_f = 0.32) to afford the title compound as a white solid (50 mg, 72%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.91 (s, 1H), 8.83 (dd, *J* = 4.7, 3.3 Hz, 2H), 8.64 (dd, *J* = 8.7, 1.1 Hz, 1H), 7.86 (d, *J* = 8.3 Hz, 1H), 7.53 (dd, *J* = 8.7, 4.2 Hz, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 3.49 – 3.32 (m, 1H), 2.56 – 2.41 (m, 2H), 2.40 – 2.26 (m, 2H), 2.14 – 1.92 (m, 2H), 1.23 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -99.14. **^{13}C NMR (101 MHz, $CDCl_3$)** δ 174.00, 164.21 (t, *J* = 35.3 Hz), 148.24, 138.21, 137.42, 133.66 (t, *J* = 3.6 Hz), 126.84 (t, *J* = 9.0 Hz), 124.66 (t, *J* = 1.9 Hz), 122.35, 121.65 (t, *J* = 24.6 Hz), 114.51, 114.02 (t, *J* = 252.6 Hz), 63.35, 41.35, 25.41, 18.12, 13.81. **HRMS (ESI-TOF)** m/z: calculated for $C_{18}H_{18}F_2N_2NaO_3^+$: 371.1178 $(M + Na)^+$, found 371.1188.

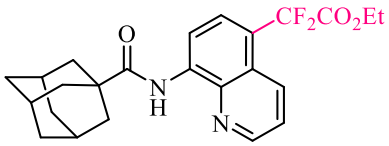
ethyl 2-(8-(cyclohexanecarboxamido)quinolin-5-yl)-2,2-difluoroacetate (**4ah**)



Purified with PTLC (PE/EA = 10/1, R_f = 0.39) to afford the title compound as a white solid (48 mg, 64%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.06 (s, 1H), 8.89 – 8.79 (m, 2H), 8.65 (d, *J* = 7.7 Hz, 1H), 7.86 (d, *J* = 8.3 Hz, 1H), 7.54 (dd, *J* = 8.7, 4.2 Hz, 1H), 4.26 (q, *J* = 7.1 Hz, 2H), 2.49 (tt, *J* = 11.7, 3.4 Hz, 1H), 2.08 (d, *J* = 12.0 Hz, 2H), 1.88 (dd, *J* = 9.9, 3.0 Hz, 2H), 1.74 (d, *J* = 11.3 Hz, 1H), 1.69 – 1.55 (m, 2H), 1.47 – 1.27 (m, 3H), 1.24 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR (376 MHz, $CDCl_3$)** δ -99.17. **^{13}C NMR (101 MHz, $CDCl_3$)** δ 175.14, 164.23 (t, *J* = 35.3 Hz), 148.25, 138.31, 137.50, 133.70 (t, *J* = 3.6 Hz), 126.87 (t, *J* = 9.0 Hz), 124.67, 122.36, 121.64 (t, *J* = 24.5 Hz), 114.59, 114.02

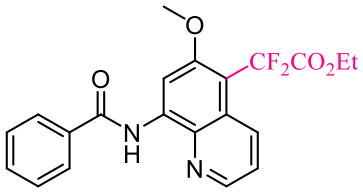
(t, J = 252.4 Hz), 63.35, 46.88, 29.66, 25.71, 25.68, 13.82. Characterization data were consistent with a previous report. [7]

ethyl 2-((8-adamantane-1-carboxamido)quinolin-5-yl)-2,2-difluoroacetate (**4ai**)



Purified with PTLC (PE/EA = 10/1, R_f = 0.60) to afford the title compound as a white solid (51 mg, 60%). **^{1}H NMR (400 MHz, CDCl$_3$)** δ 10.40 (s, 1H), 8.87 (dd, J = 4.1, 1.3 Hz, 1H), 8.84 (d, J = 8.3 Hz, 1H), 8.65 (dd, J = 8.7, 1.1 Hz, 1H), 7.86 (d, J = 8.3 Hz, 1H), 7.54 (dd, J = 8.7, 4.2 Hz, 1H), 4.26 (q, J = 7.1 Hz, 2H), 2.15 (s, 3H), 2.09 (s, 6H), 1.80 (s, 6H), 1.23 (t, J = 7.1 Hz, 3H). **^{19}F NMR (376 MHz, CDCl$_3$)** δ -99.18. **^{13}C NMR (101 MHz, CDCl$_3$)** δ 177.03, 164.24 (t, J = 35.3 Hz), 148.33, 138.67, 137.54, 133.64 (t, J = 3.6 Hz), 126.87 (t, J = 9.0 Hz), 124.66 (t, J = 2.0 Hz), 122.31, 121.55 (t, J = 24.5 Hz), 114.53, 114.04 (t, J = 252.6 Hz), 63.33, 42.36, 39.26, 36.45, 28.15, 13.81. **HRMS (ESI-TOF)** m/z: calculated for $C_{24}H_{26}F_2N_2NaO_3^+$: 451.1804 $(M + Na)^+$, found 451.1804.

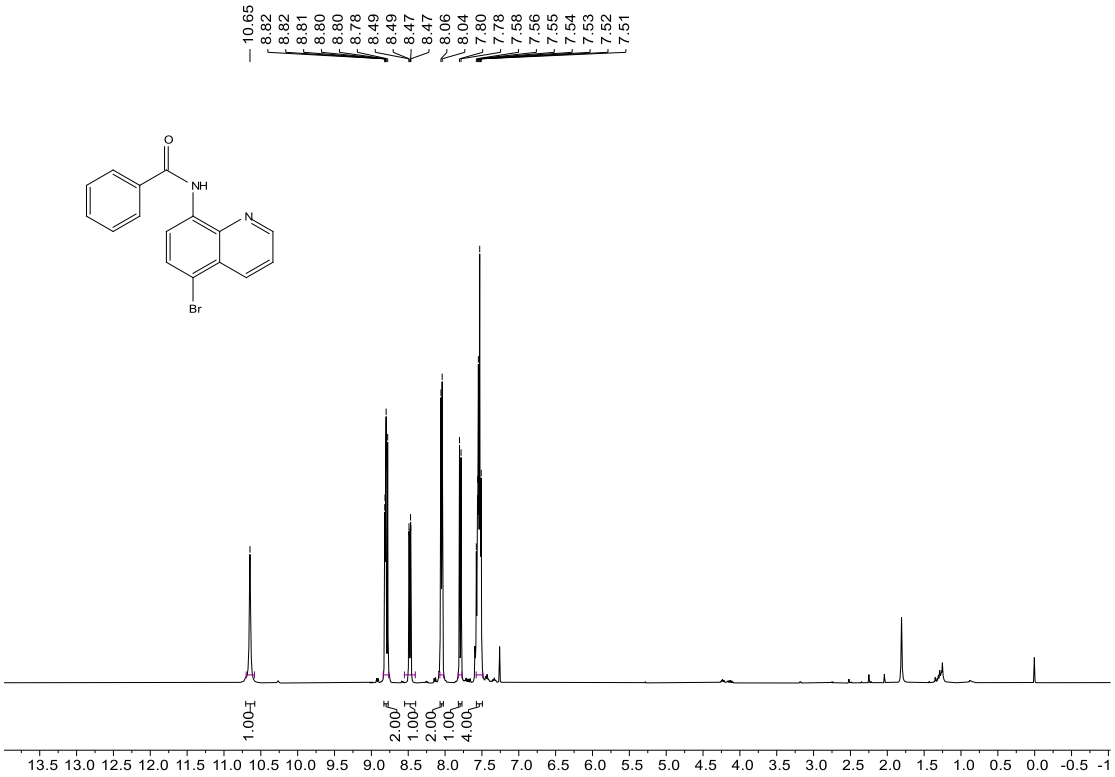
ethyl 2-(8-benzamido-6-methoxyquinolin-5-yl)-2,2-difluoroacetate (**4aj**)



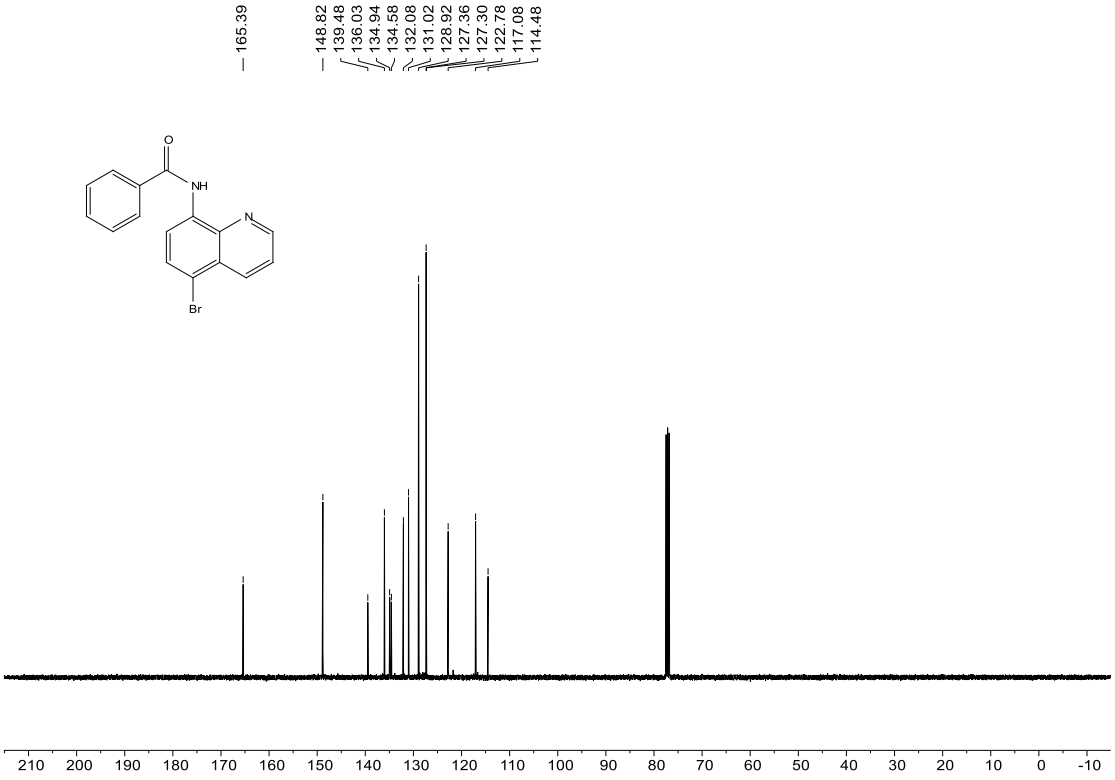
Purified with PTLC (PE/EA = 5/1, R_f = 0.28) to afford the title compound as a white solid (57 mg, 71%). **^{1}H NMR (400 MHz, CDCl$_3$)** δ 11.03 (s, 1H), 8.87 (s, 1H), 8.79 (d, J = 8.6 Hz, 1H), 8.74 (dd, J = 4.0, 1.1 Hz, 1H), 8.08 (d, J = 7.0 Hz, 2H), 7.66 – 7.48 (m, 4H), 4.41 (q, J = 7.1 Hz, 2H), 4.00 (s, 3H), 1.37 (t, J = 7.2 Hz, 3H). **^{19}F NMR (376 MHz, CDCl$_3$)** δ -91.84. **^{13}C NMR (101 MHz, CDCl$_3$)** δ 165.99, 164.34 (t, J = 32.8 Hz), 156.94 (t, J = 6.7 Hz), 146.38, 139.17, 134.88, 134.59, 133.55 (t, J = 8.2 Hz), 132.49, 129.10, 127.46, 126.99, 123.24, 114.68 (t, J = 247.3 Hz), 107.72 (t, J = 24.5 Hz), 103.71, 62.91, 57.22, 14.18. Characterization data were consistent with a previous report. [6]

6. Copies of NMR spectra

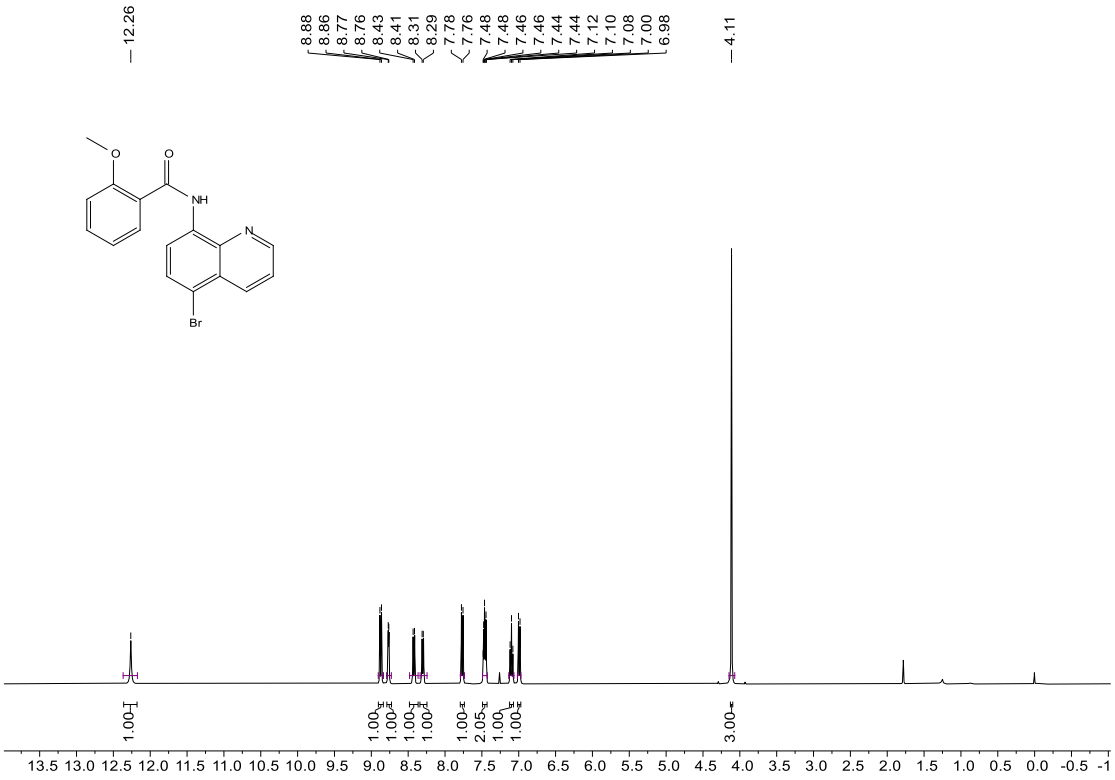
^{1}H NMR for N-(5-bromoquinolin-8-yl)benzamide (**3a**)



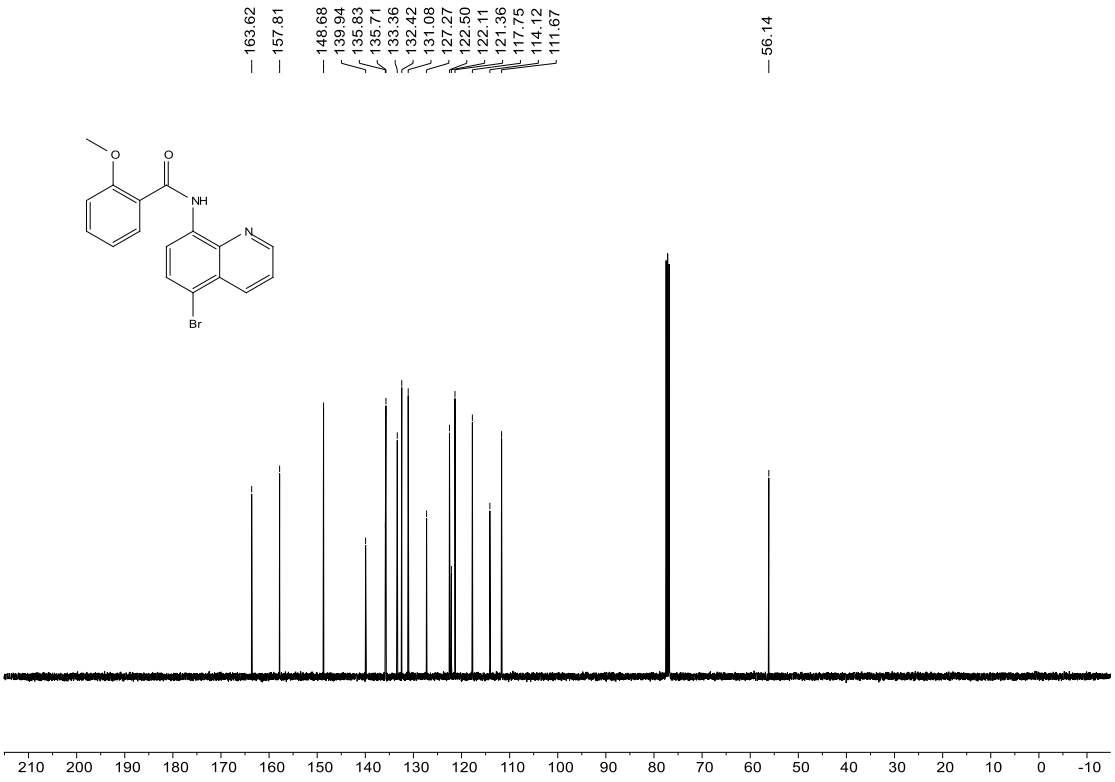
^{13}C NMR for N-(5-bromoquinolin-8-yl)benzamide (**3a**)



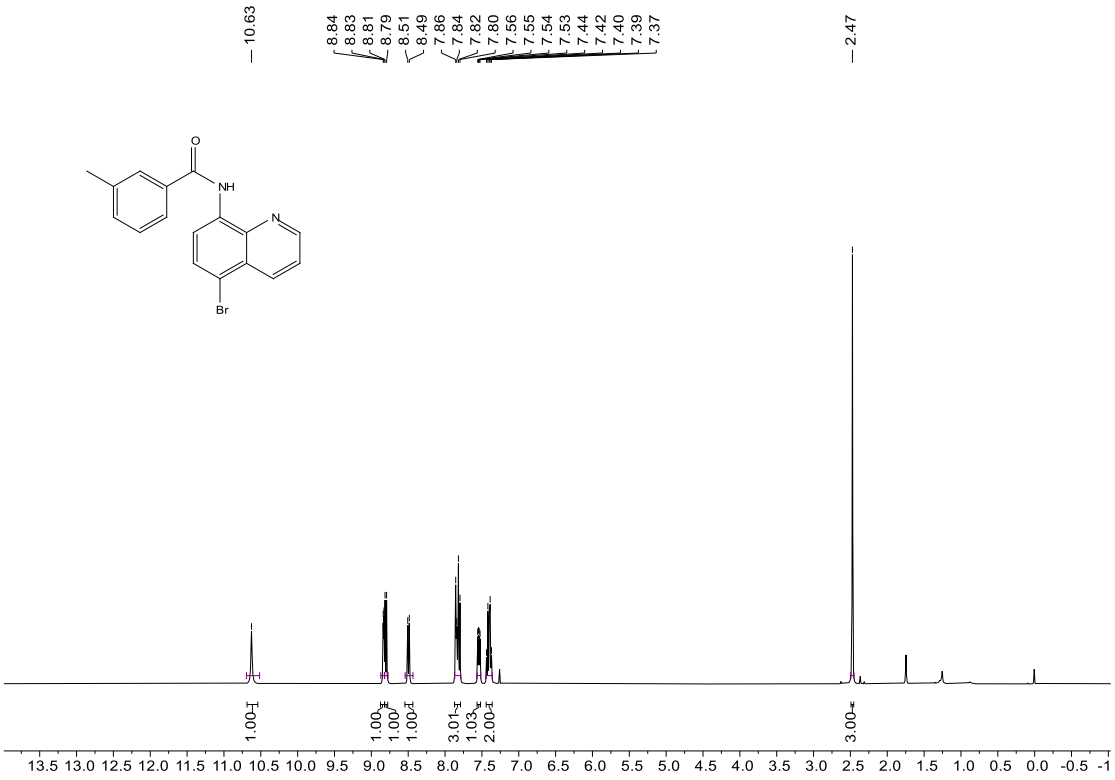
^{1}H NMR for N-(5-bromoquinolin-8-yl)-2-methoxybenzamide (**3b**)



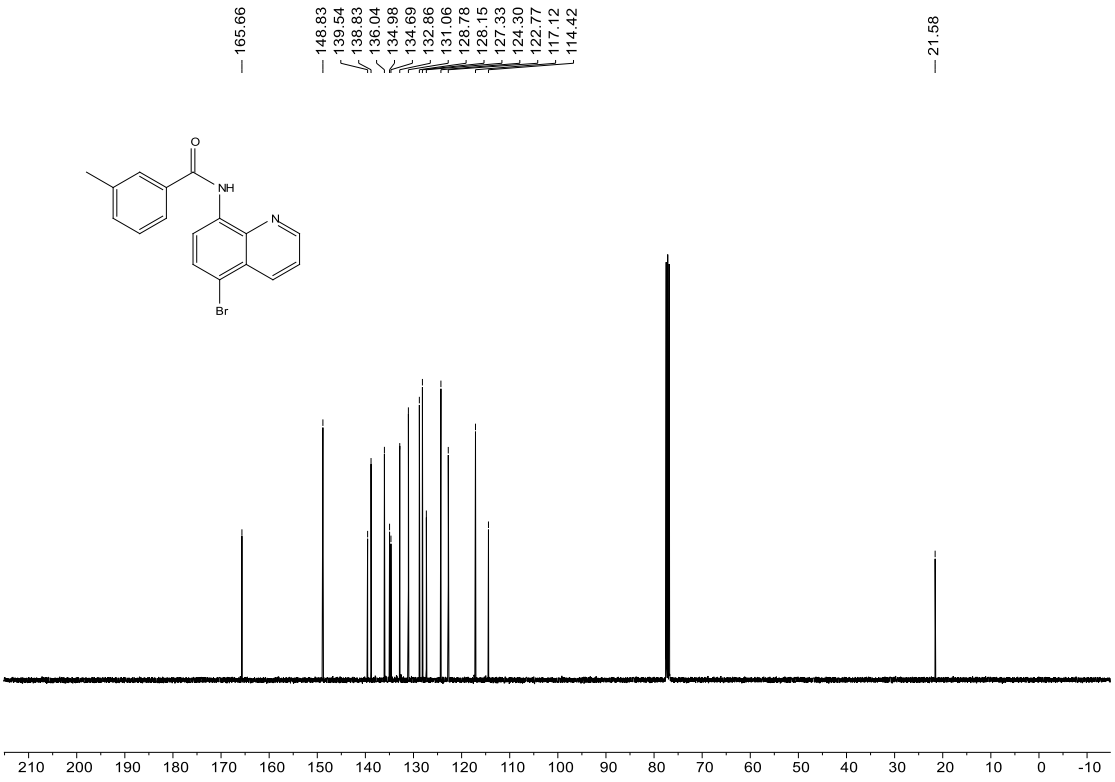
^{13}C NMR for N-(5-bromoquinolin-8-yl)-2-methoxybenzamide (**3b**)



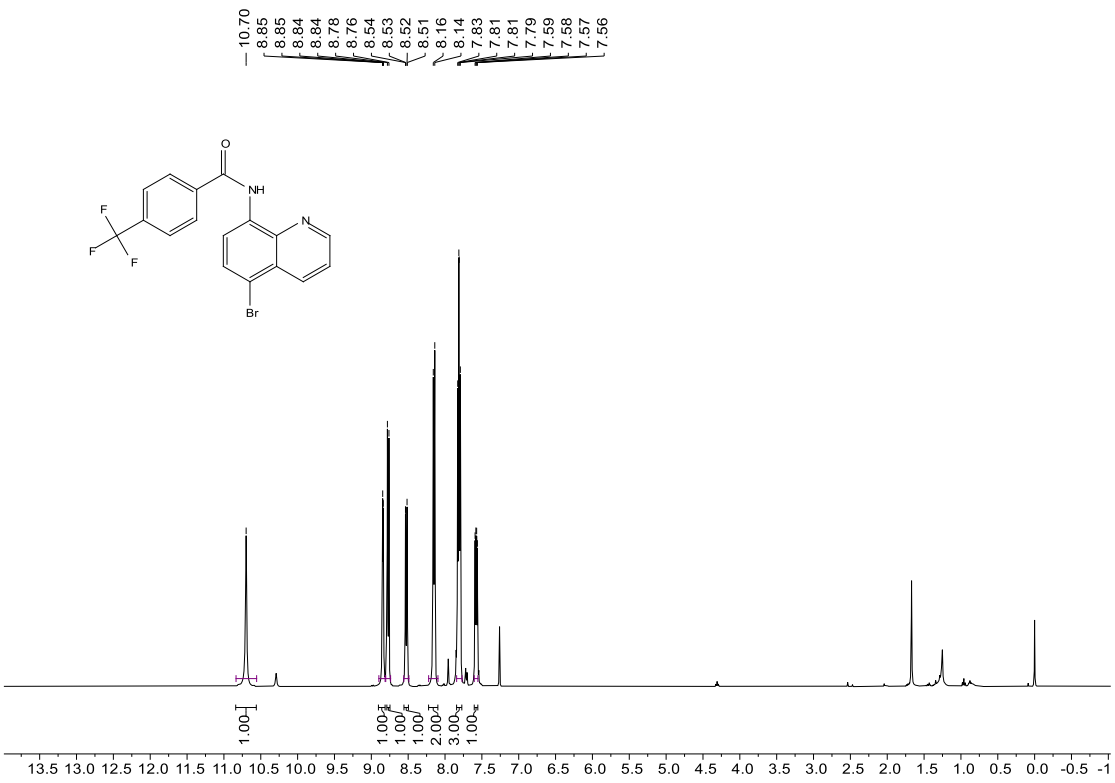
^{1}H NMR for N-(5-bromoquinolin-8-yl)-3-methylbenzamide (**3c**)



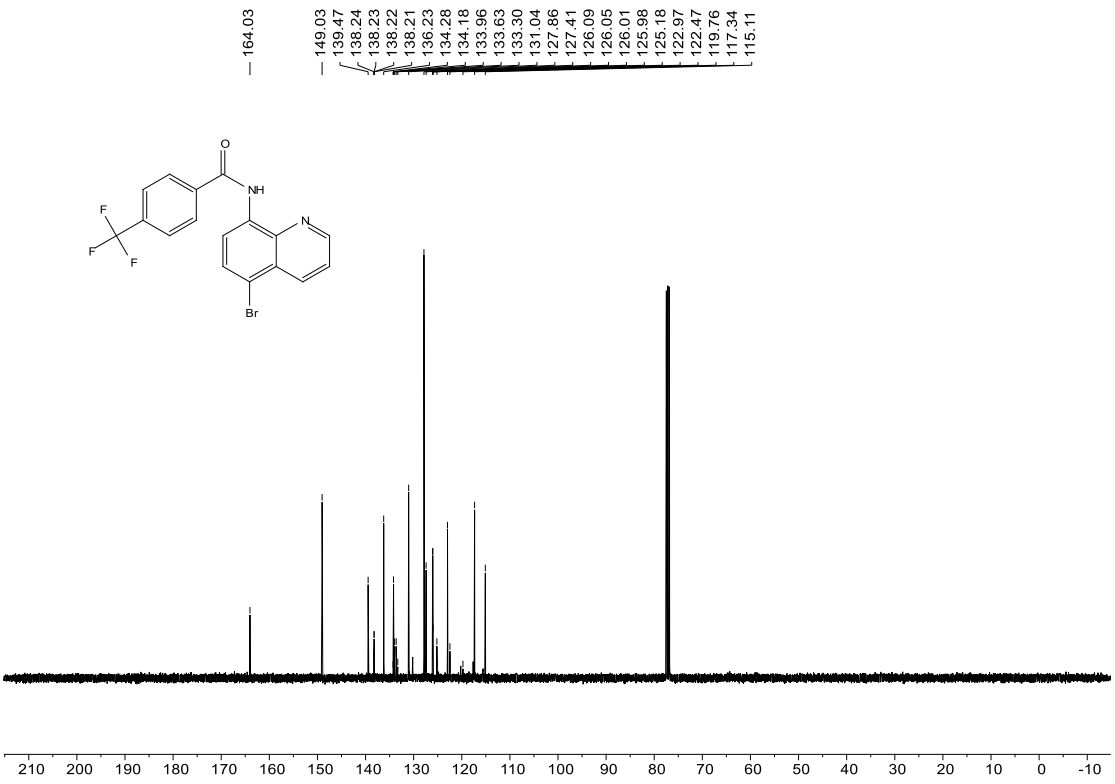
^{13}C NMR for N-(5-bromoquinolin-8-yl)-3-methylbenzamide (**3c**)



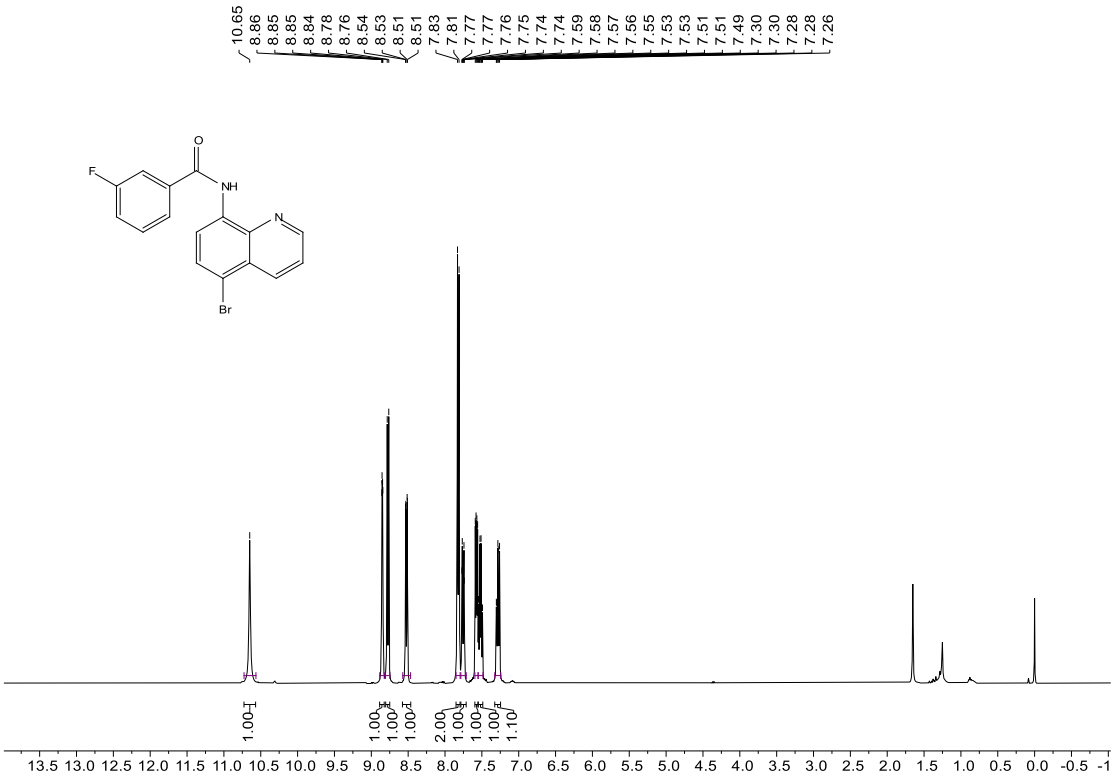
^{1}H NMR for N-(5-bromoquinolin-8-yl)-4-(trifluoromethyl)benzamide (**3d**)



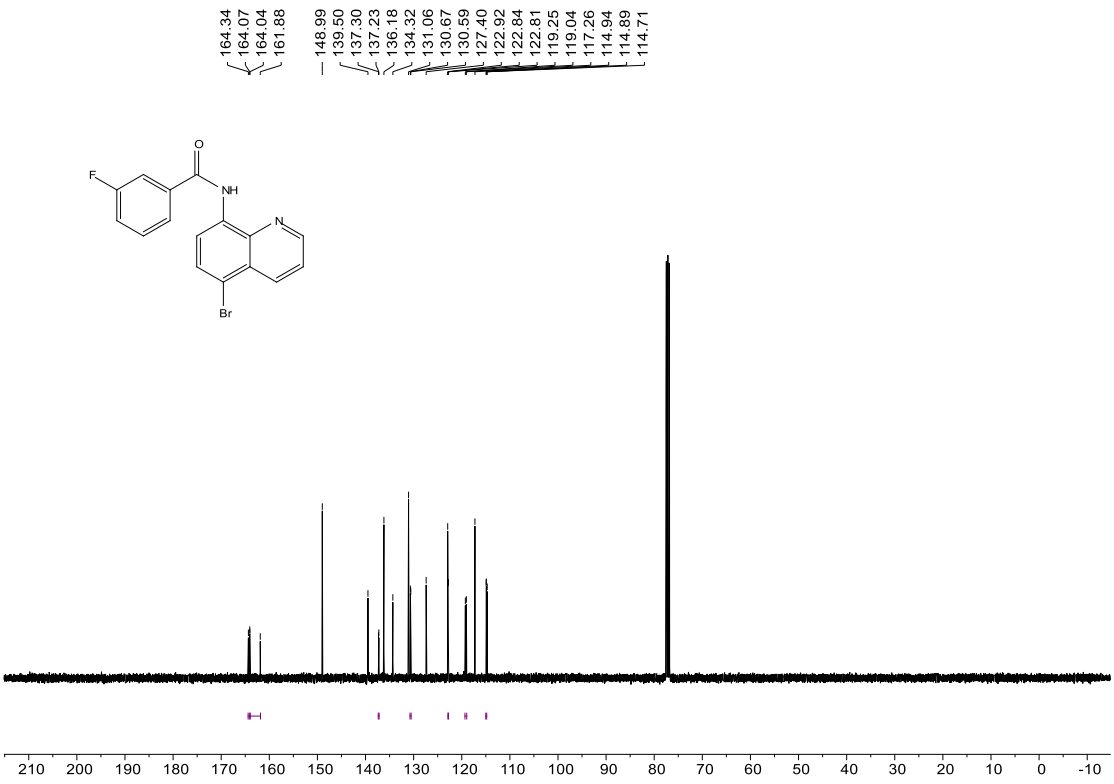
^{13}C NMR for N-(5-bromoquinolin-8-yl)-4-(trifluoromethyl)benzamide (**3d**)



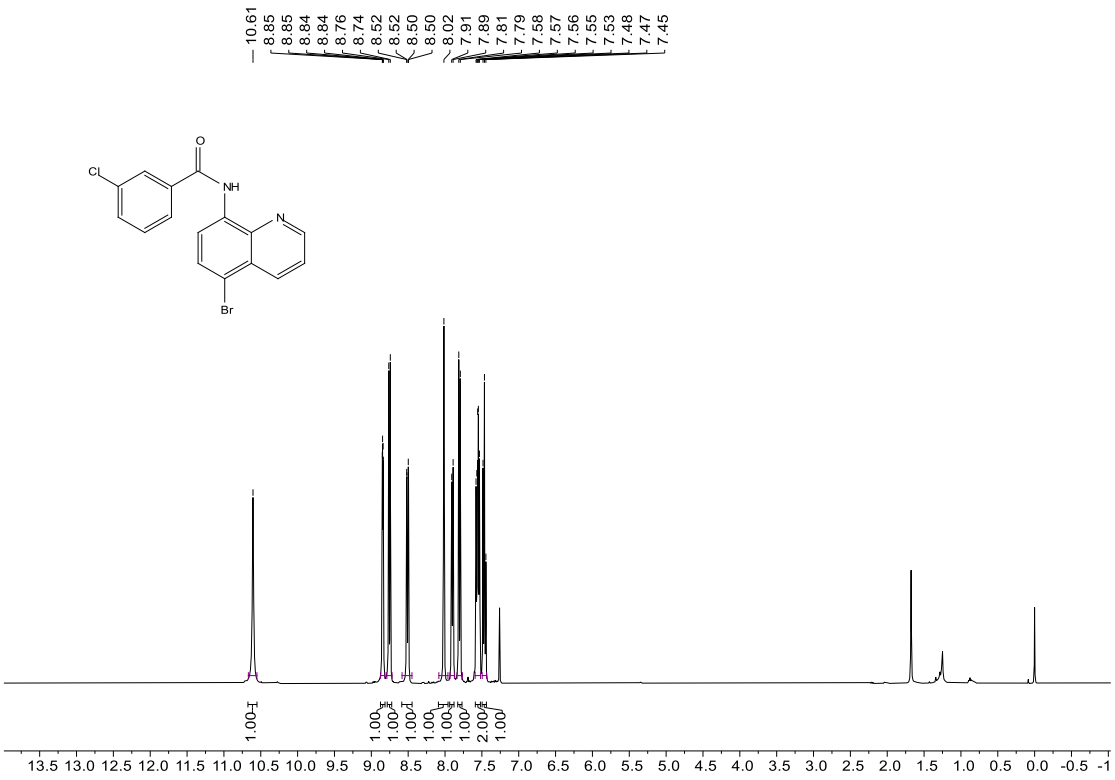
^{1}H NMR for N-(5-bromoquinolin-8-yl)-3-fluorobenzamide (**3e**)



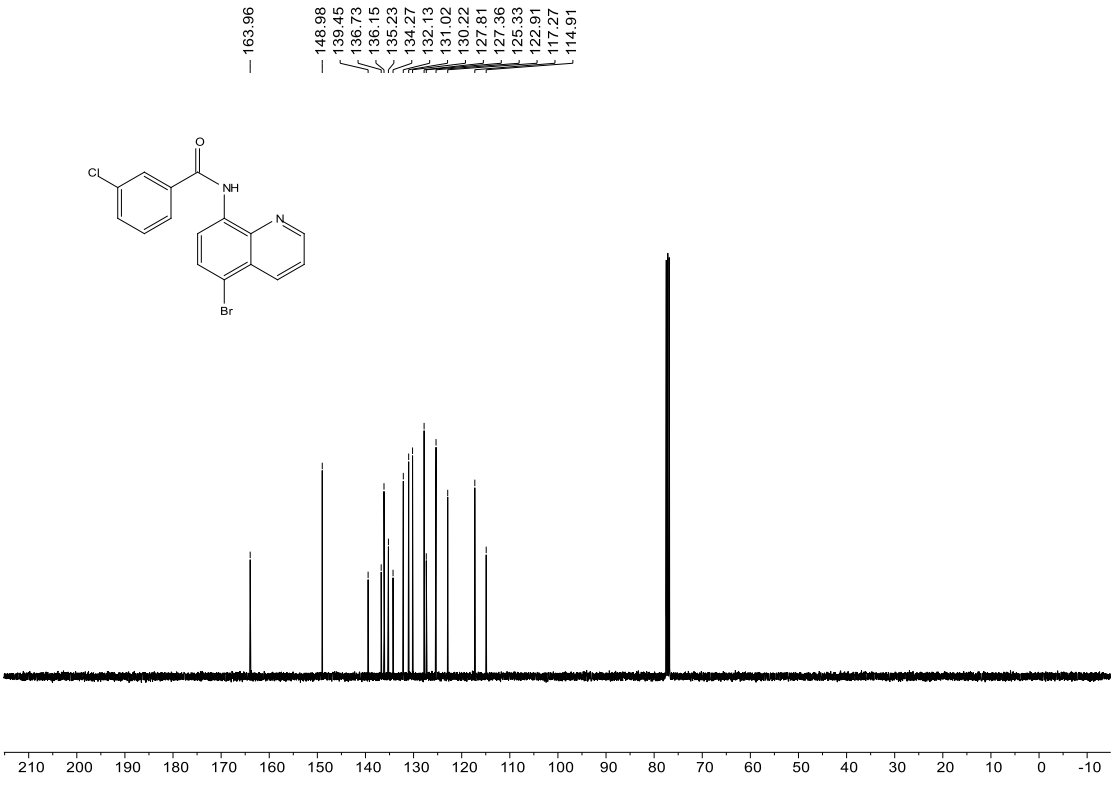
^{13}C NMR for N-(5-bromoquinolin-8-yl)-3-fluorobenzamide (**3e**)



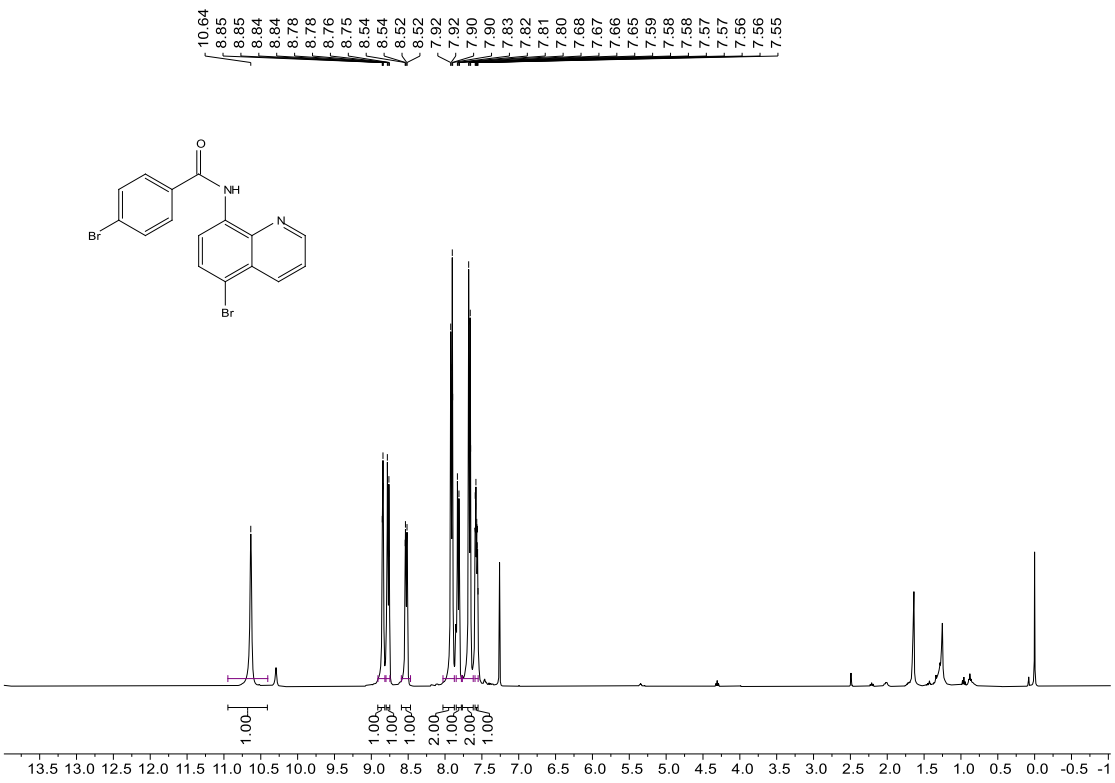
^{1}H NMR for N-(5-bromoquinolin-8-yl)-3-chlorobenzamide (**3f**)



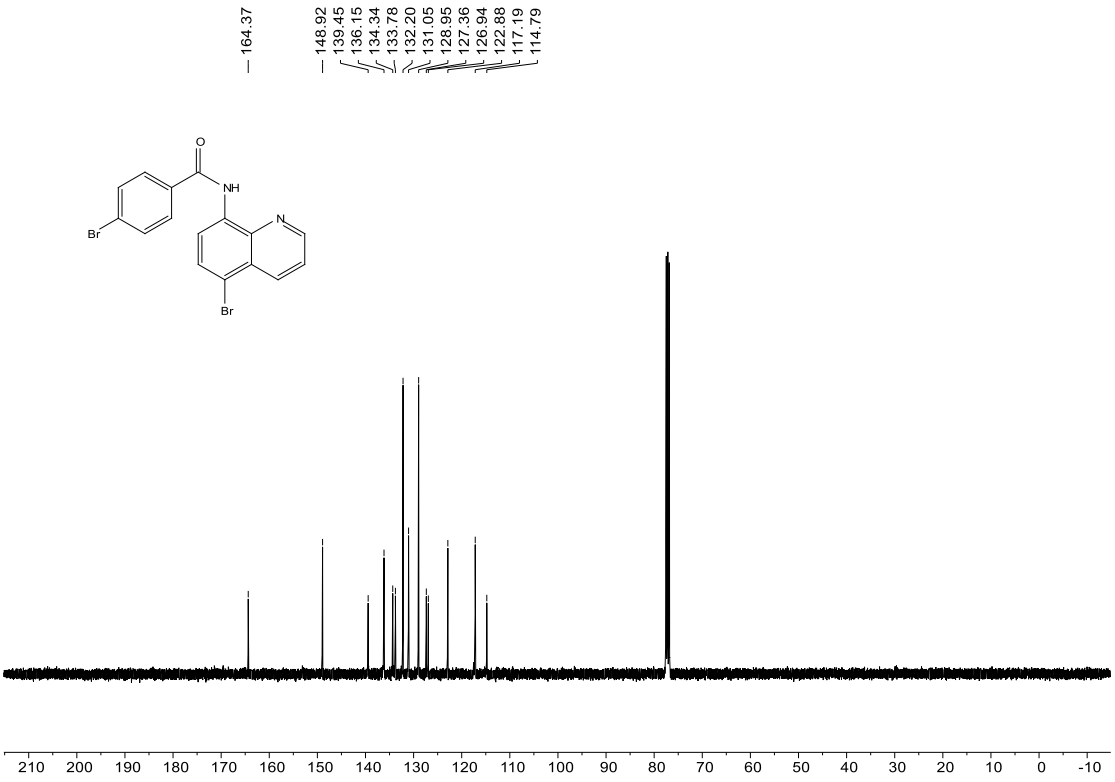
^{13}C NMR for N-(5-bromoquinolin-8-yl)-3-chlorobenzamide (**3f**)



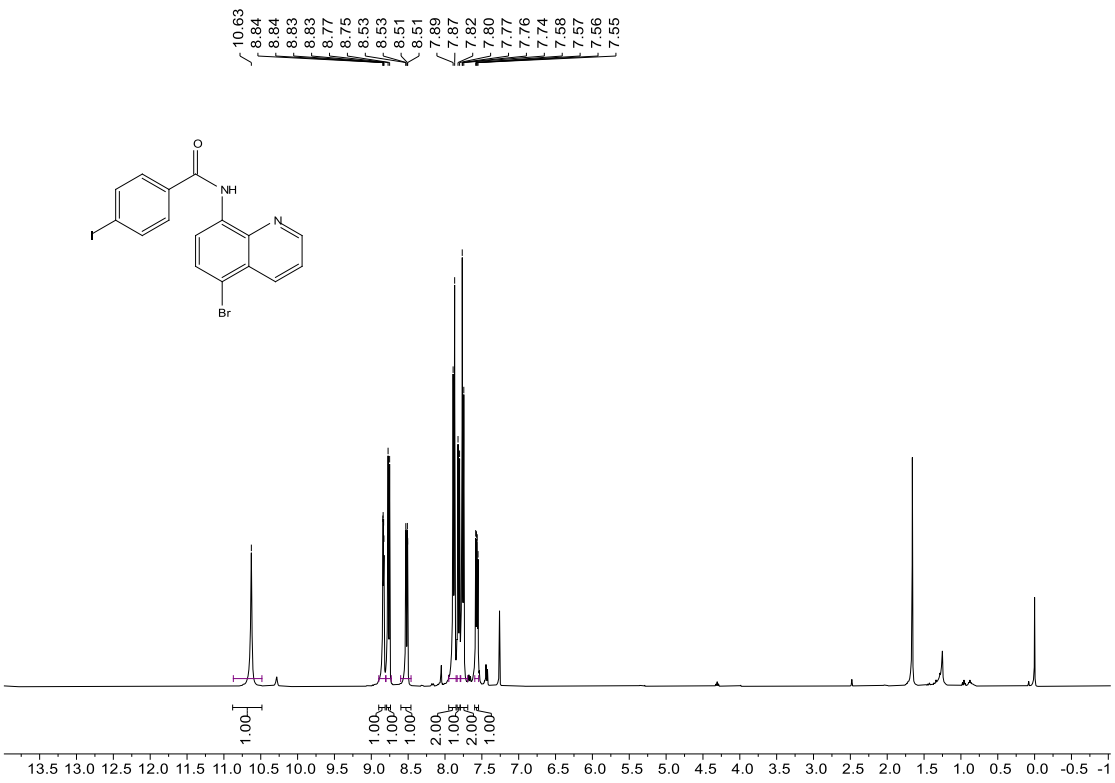
^{1}H NMR for 4-bromo-N-(5-bromoquinolin-8-yl)benzamide (**3g**)



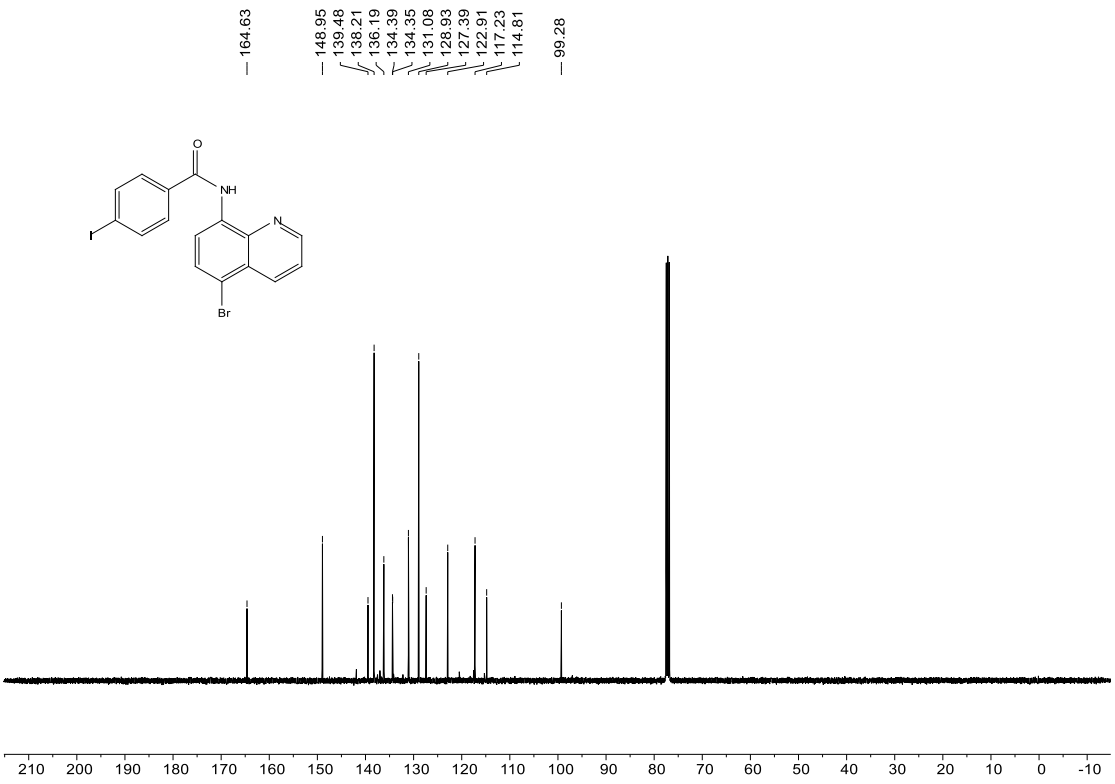
^{13}C NMR for 4-bromo-N-(5-bromoquinolin-8-yl)benzamide (**3g**)



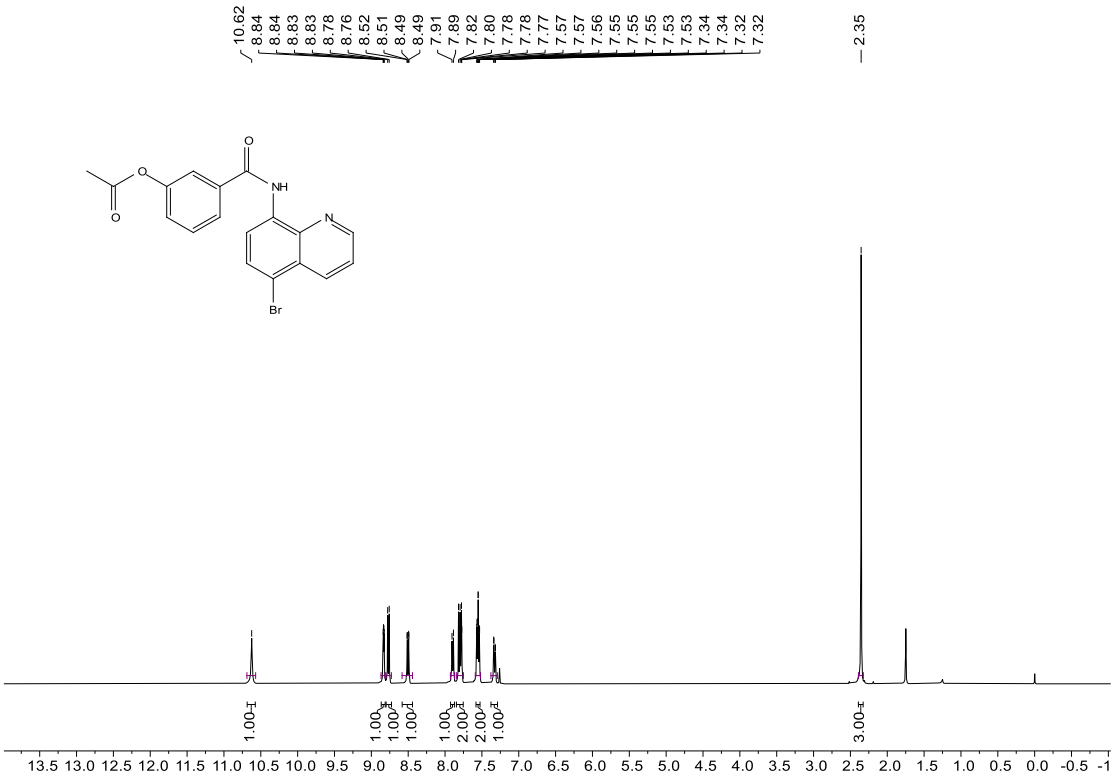
^{1}H NMR for N-(5-bromoquinolin-8-yl)-4-iodobenzamide (**3h**)



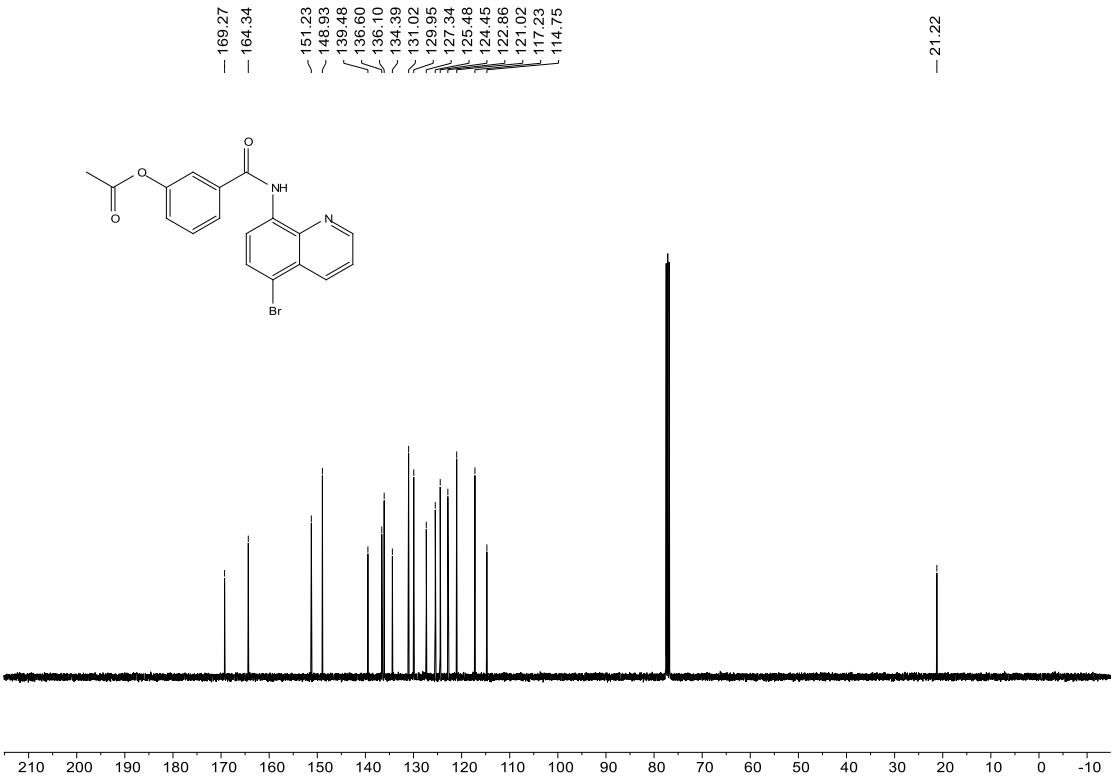
^{13}C NMR for N-(5-bromoquinolin-8-yl)-4-iodobenzamide (**3h**)



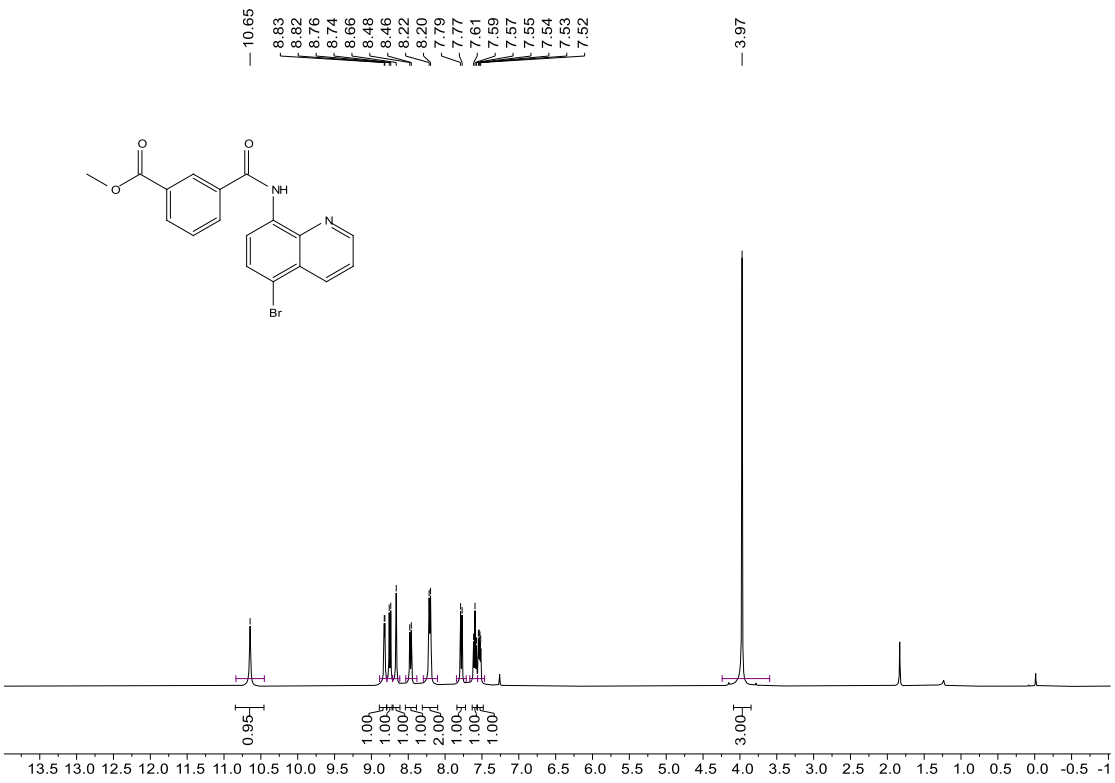
^{1}H NMR for 3-((5-bromoquinolin-8-yl)carbamoyl)phenyl acetate (**3i**)



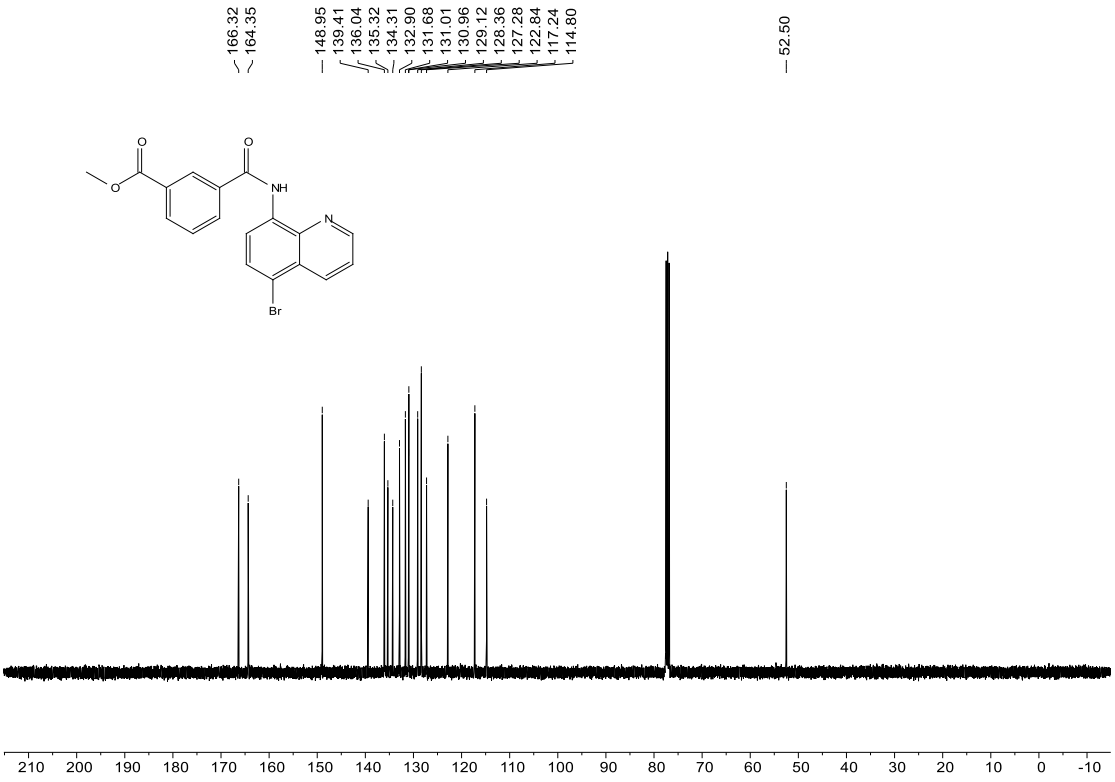
^{13}C NMR for 3-((5-bromoquinolin-8-yl)carbamoyl)phenyl acetate (**3i**)



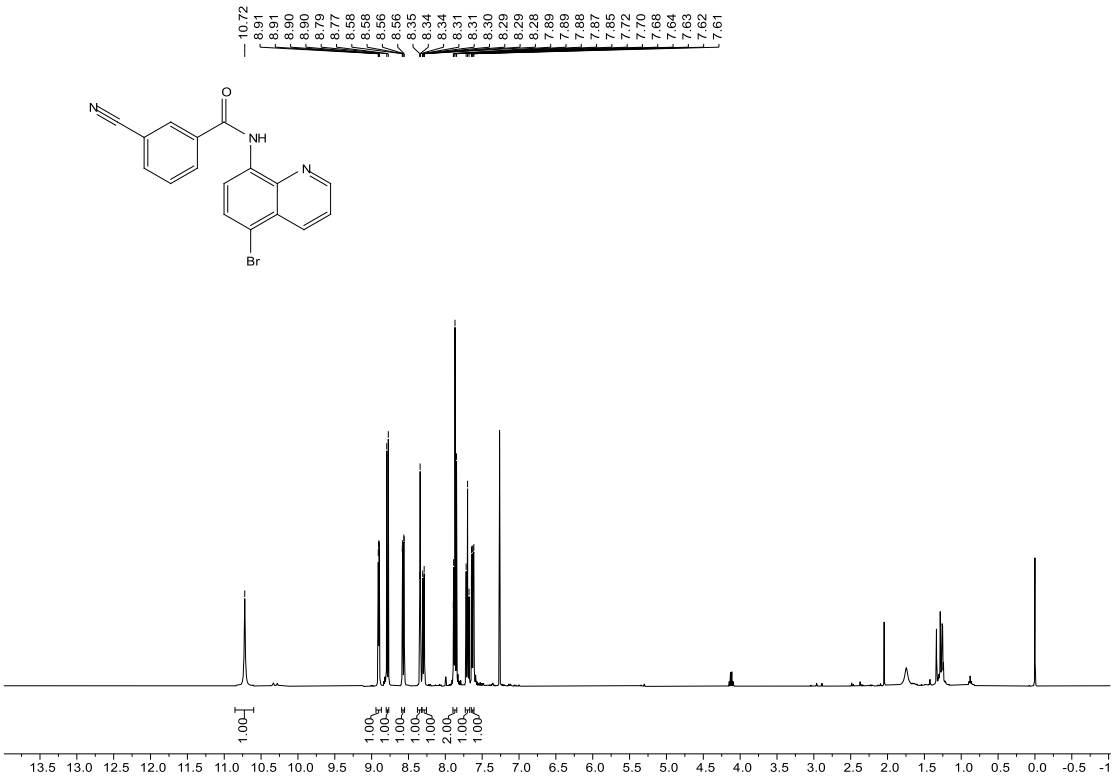
^{1}H NMR for methyl 3-((5-bromoquinolin-8-yl)carbamoyl)benzoate (**3j**)



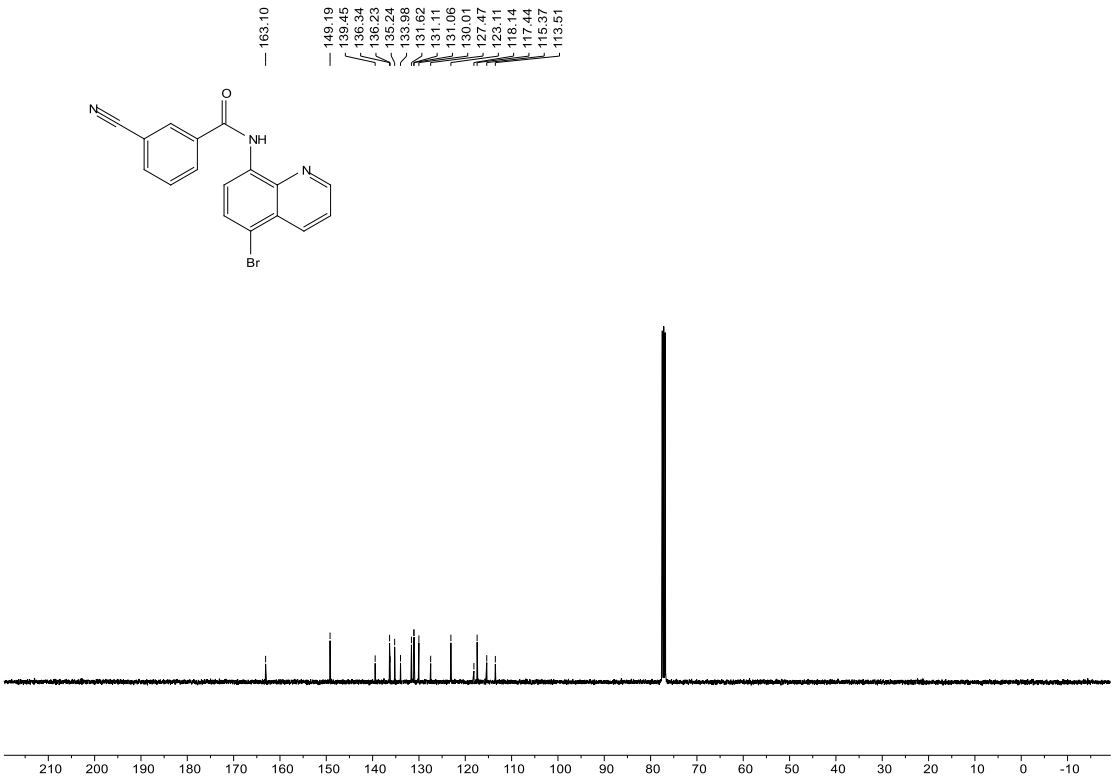
^{13}C NMR for methyl 3-((5-bromoquinolin-8-yl)carbamoyl)benzoate (**3j**)



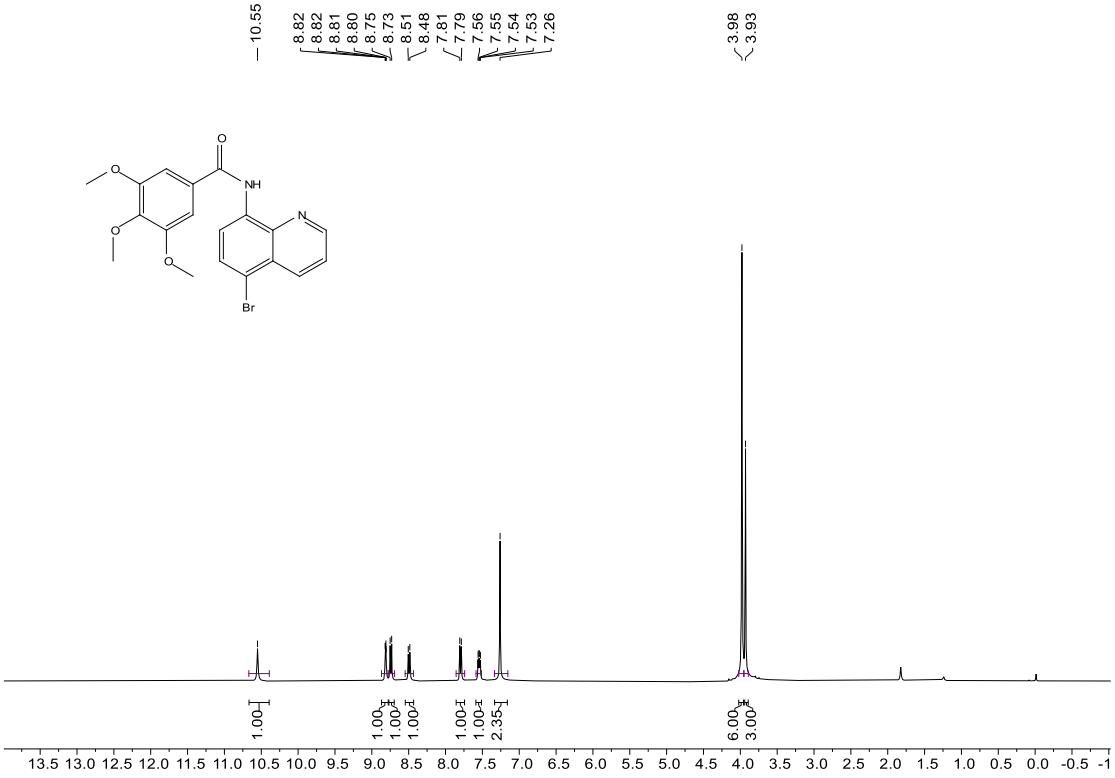
^{1}H NMR for N-(5-bromoquinolin-8-yl)-3-cyanobenzamide (**3k**)



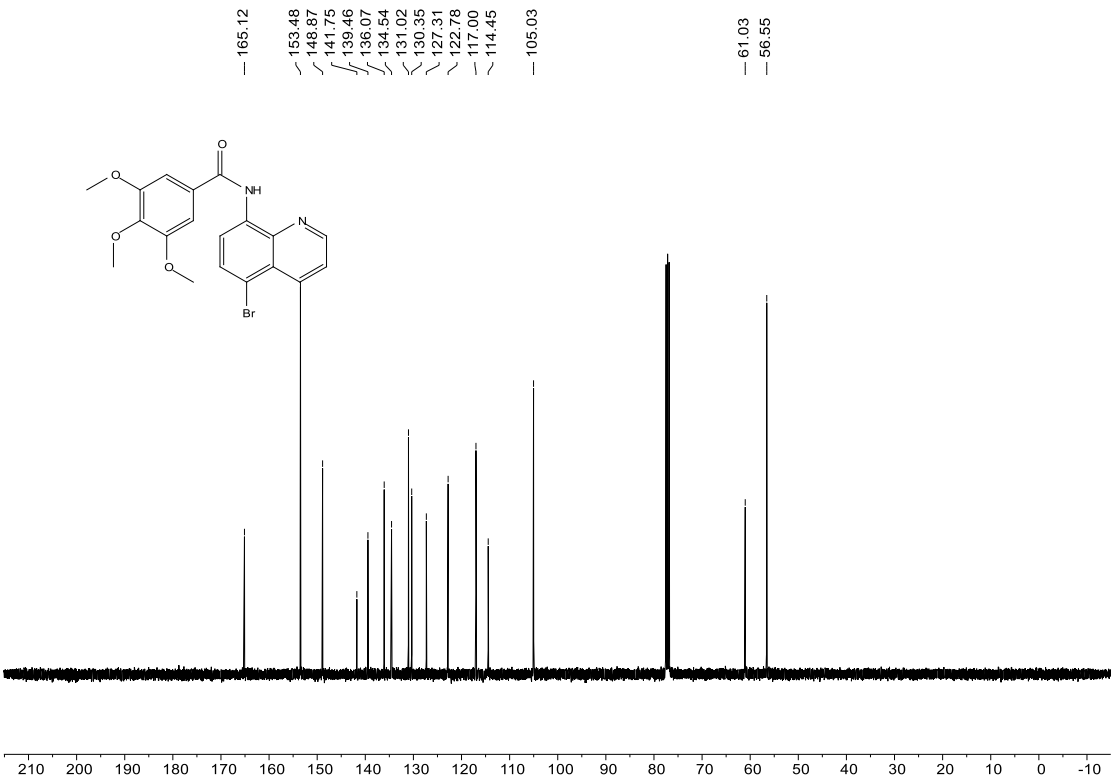
^{13}C NMR for N-(5-bromoquinolin-8-yl)-3-cyanobenzamide (**3k**)



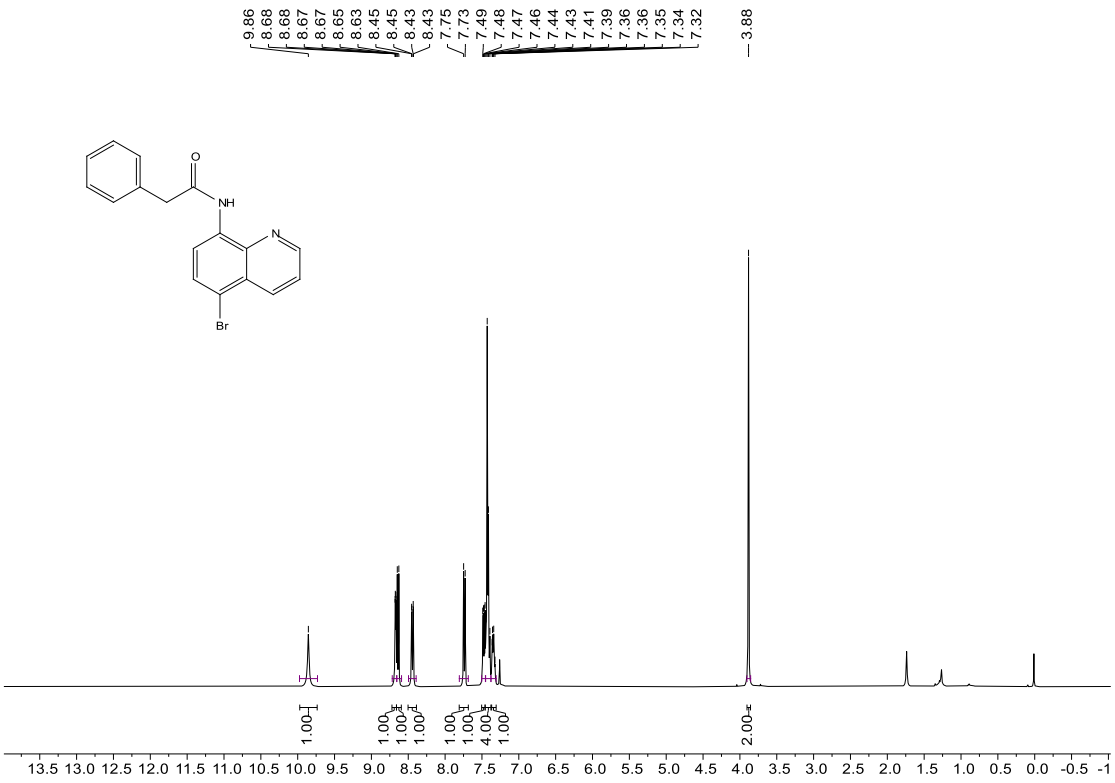
^{1}H NMR for N-(5-bromoquinolin-8-yl)-3,4,5-trimethoxybenzamide (**3l**)



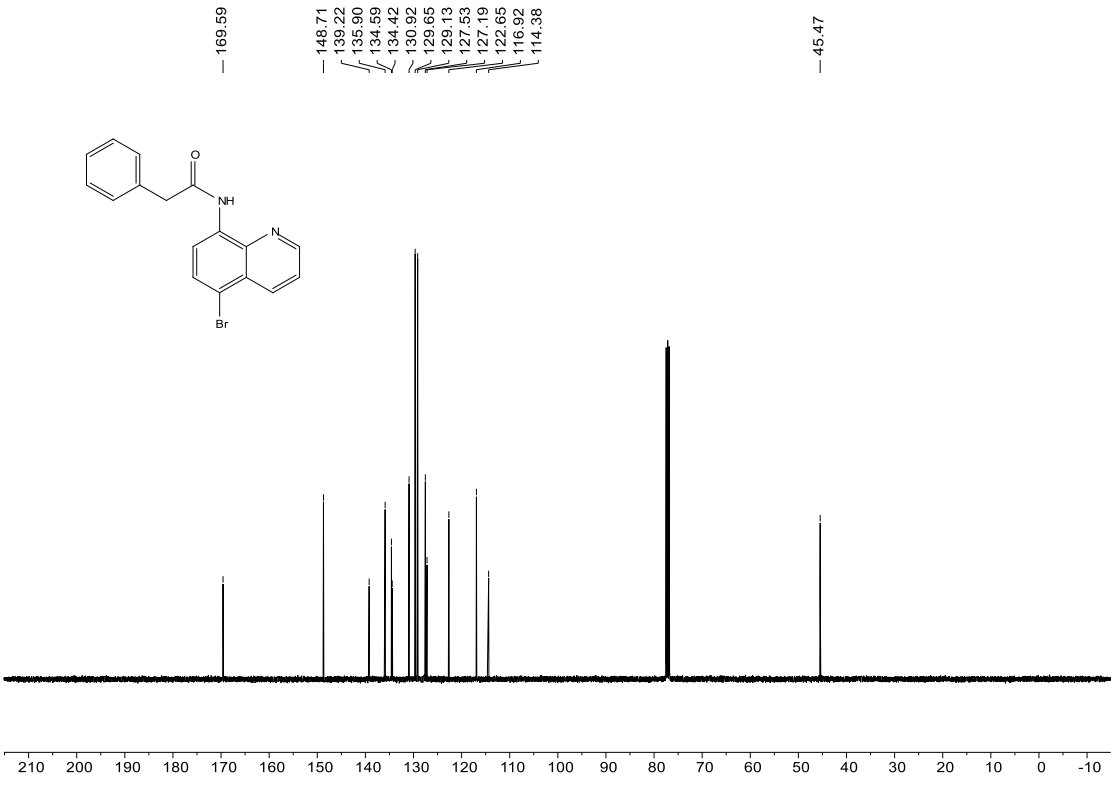
^{13}C NMR for N-(5-bromoquinolin-8-yl)-3,4,5-trimethoxybenzamide (**3l**)



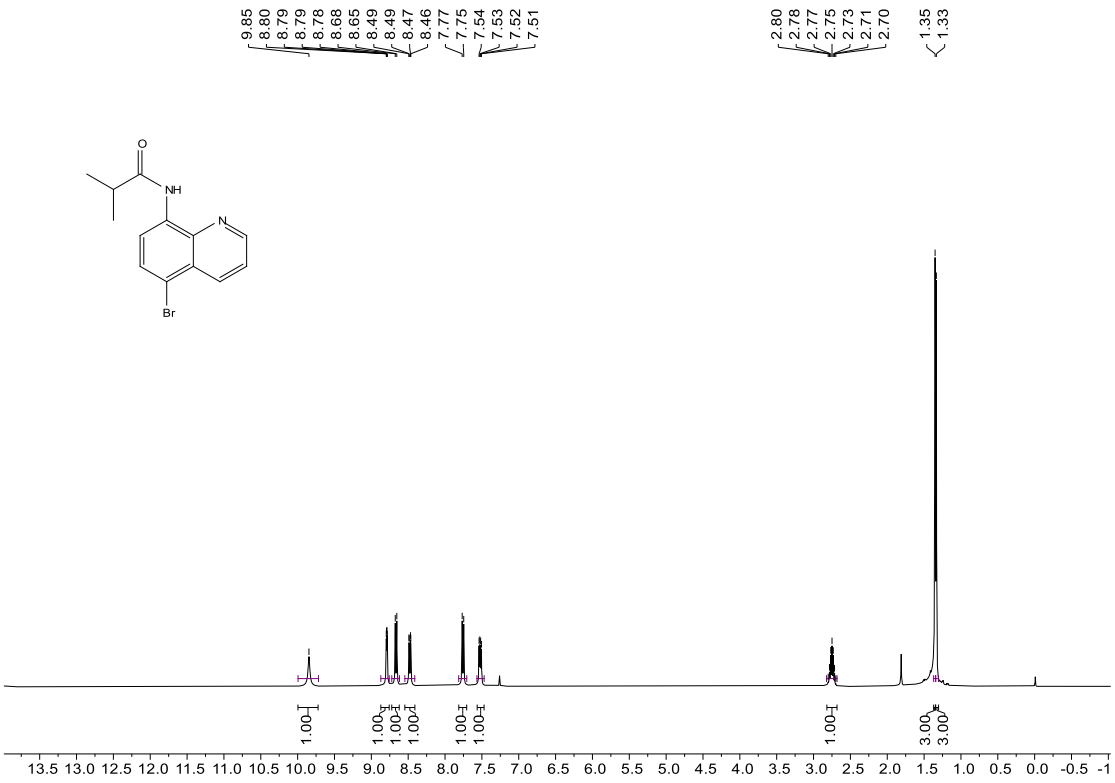
^{1}H NMR for N-(5-bromoquinolin-8-yl)-2-phenylacetamide (**3m**)



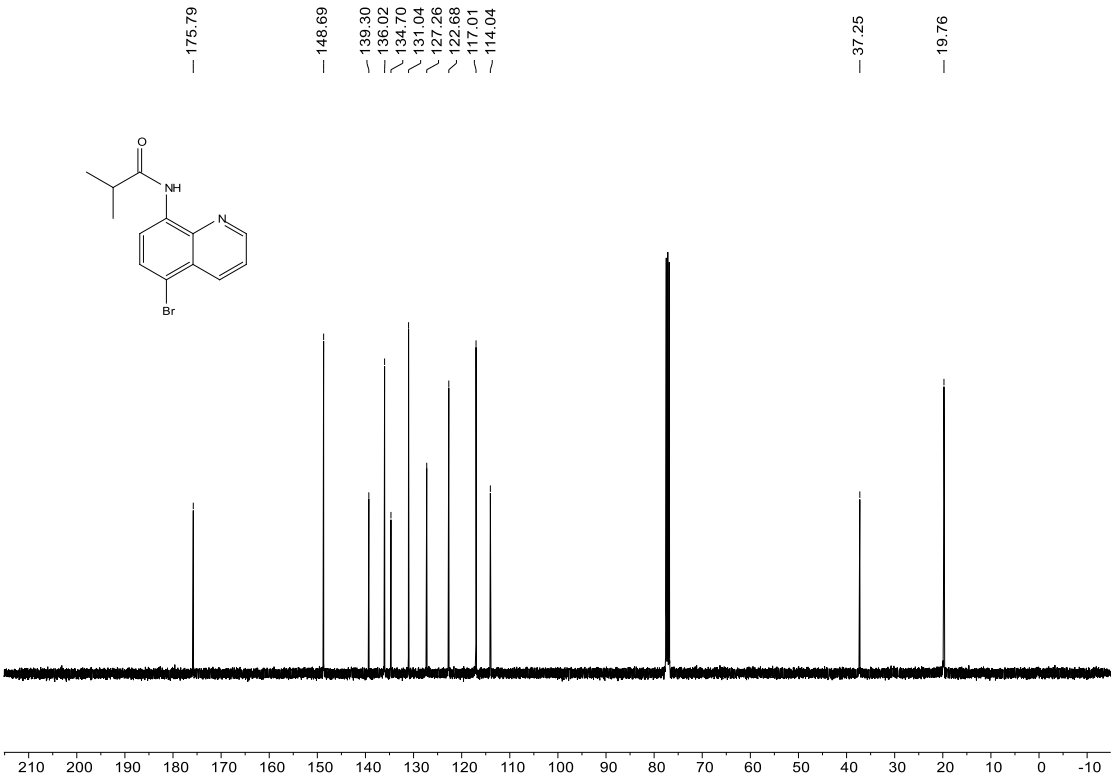
^{13}C NMR for N-(5-bromoquinolin-8-yl)-2-phenylacetamide (**3m**)



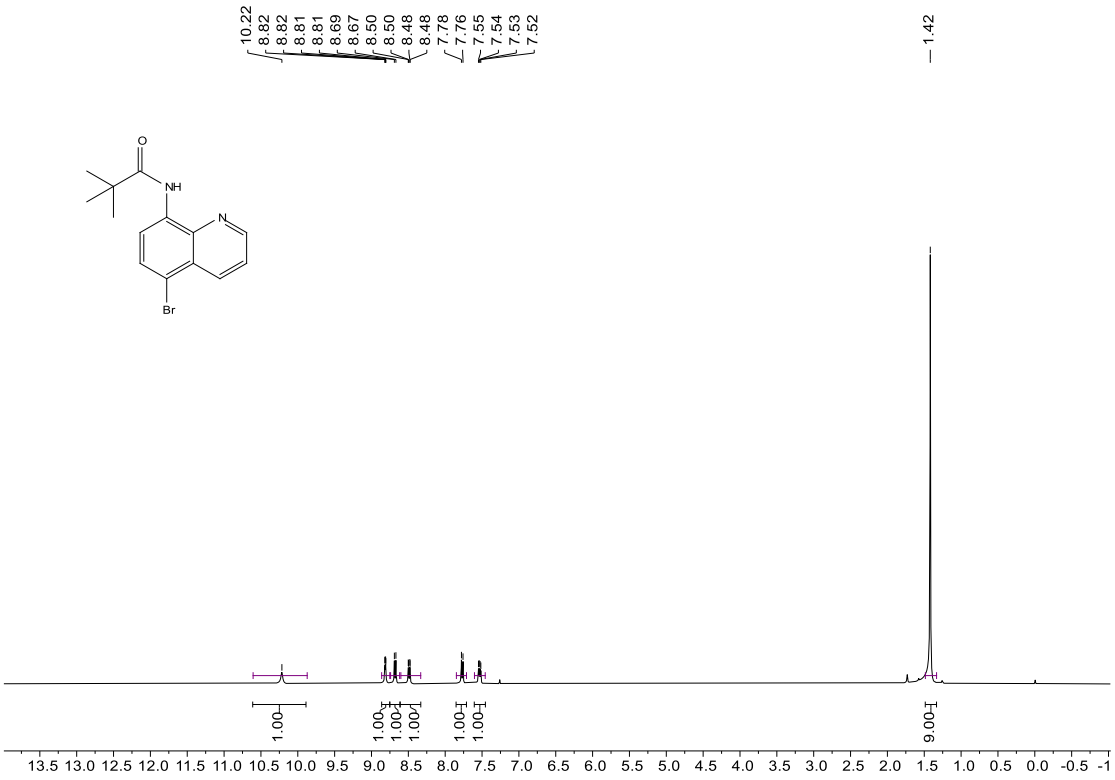
^{1}H NMR for N-(5-bromoquinolin-8-yl)isobutyramide (**3n**)



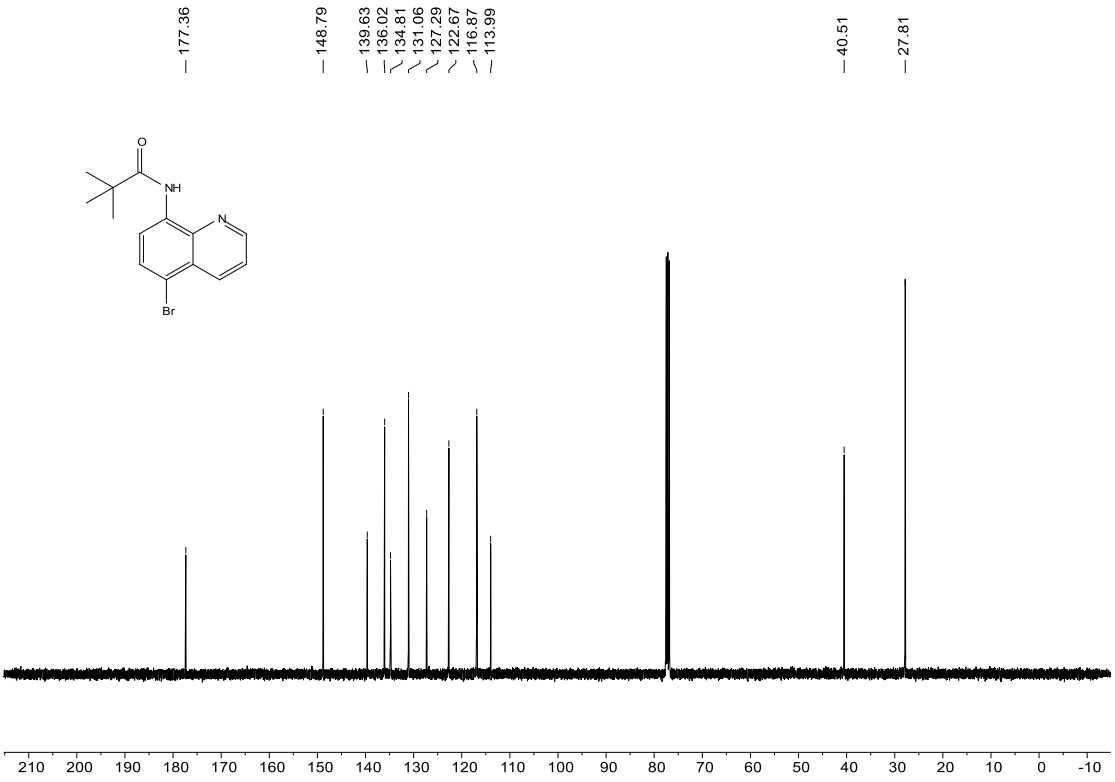
^{13}C NMR for N-(5-bromoquinolin-8-yl)isobutyramide (**3n**)



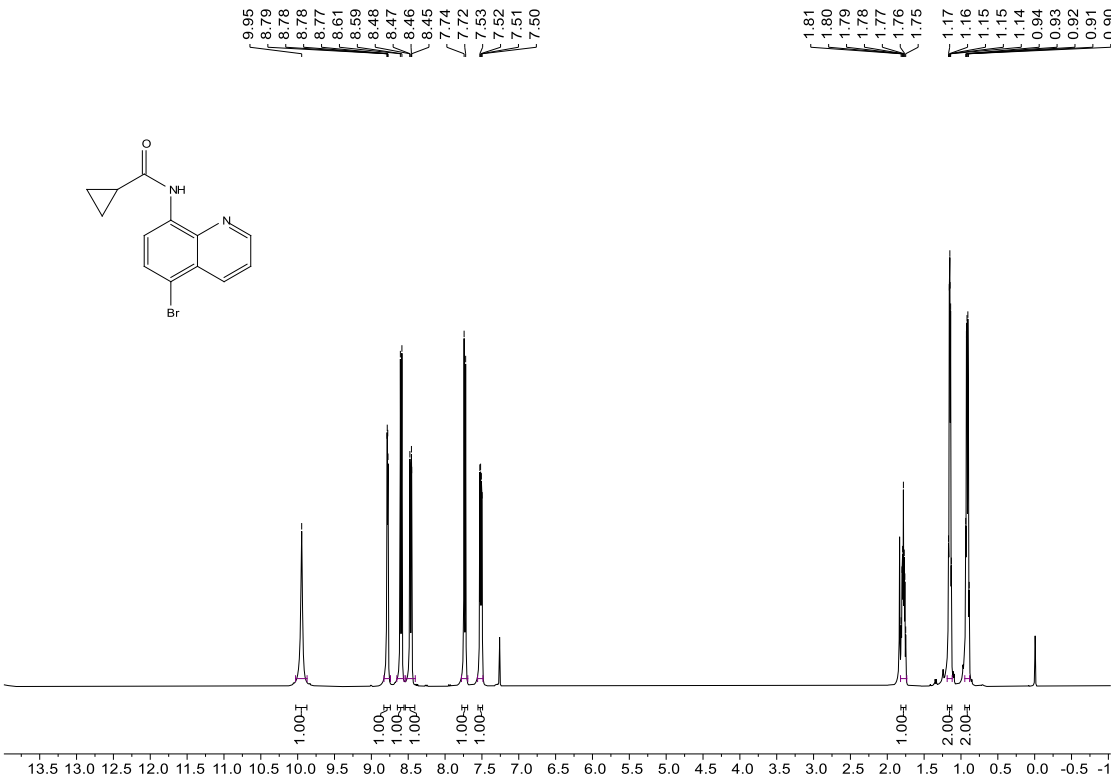
^{1}H NMR for N-(5-bromoquinolin-8-yl)pivalamide (**3o**)



^{13}C NMR for N-(5-bromoquinolin-8-yl)pivalamide (**3o**)

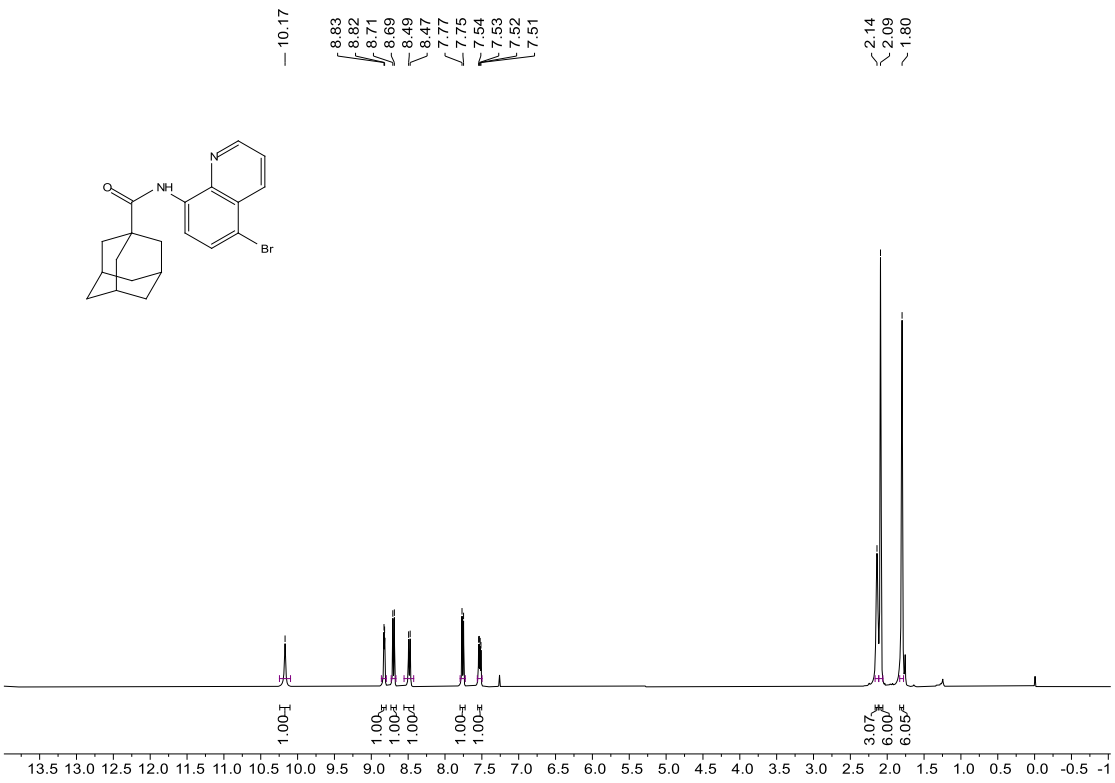


^{1}H NMR for N-(5-bromoquinolin-8-yl)cyclopropanecarboxamide (**3p**)

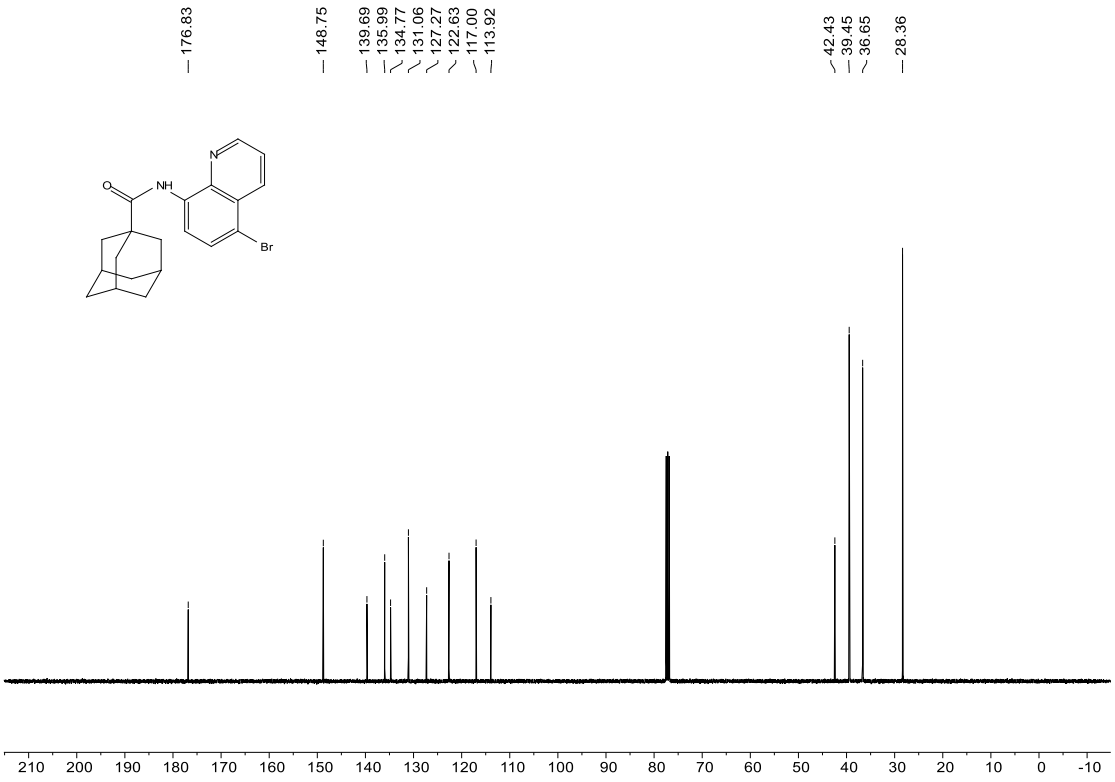


^{13}C NMR for N-(5-bromoquinolin-8-yl)cyclopropanecarboxamide (**3p**)

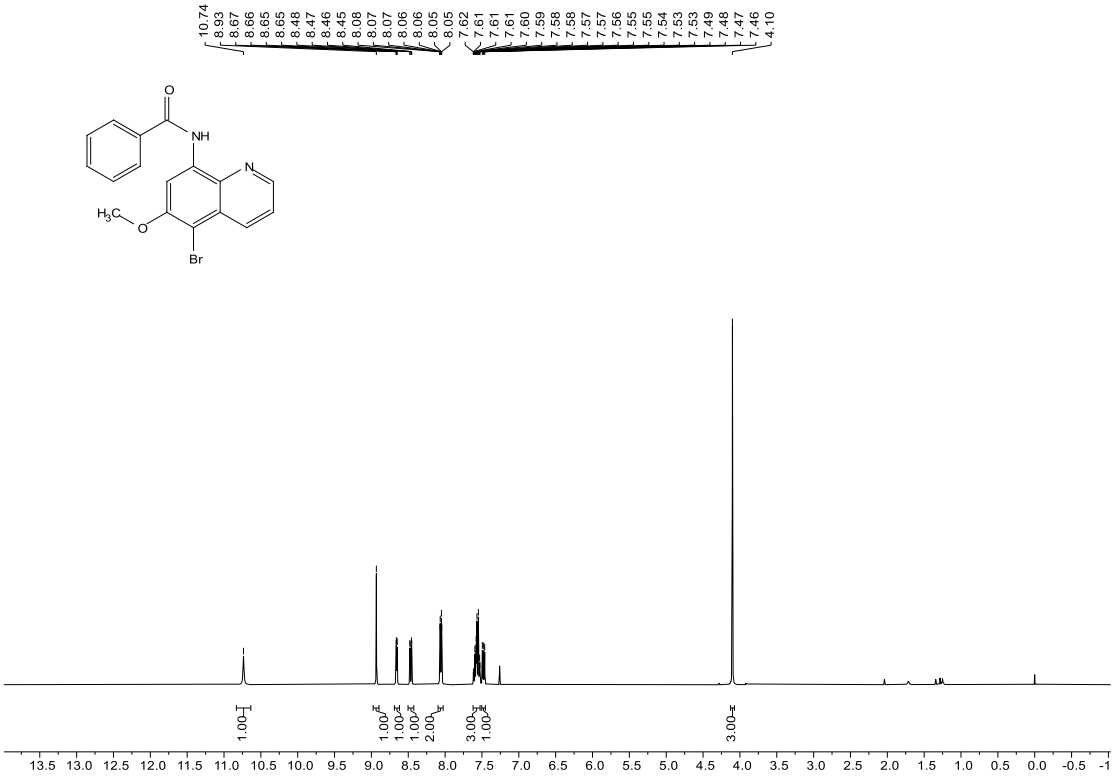
^{1}H NMR for N-(5-bromoquinolin-8-yl)adamantane-1-carboxamide (**3q**)



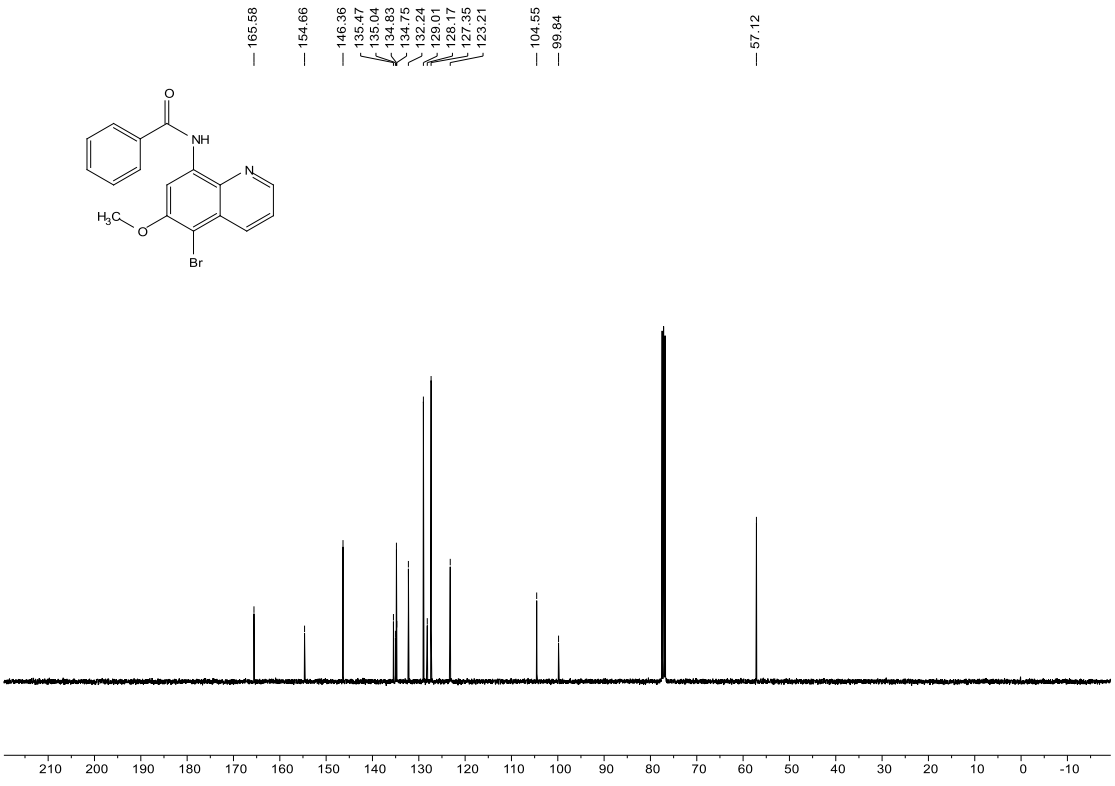
^{13}C NMR for N-(5-bromoquinolin-8-yl)adamantane-1-carboxamide (**3q**)



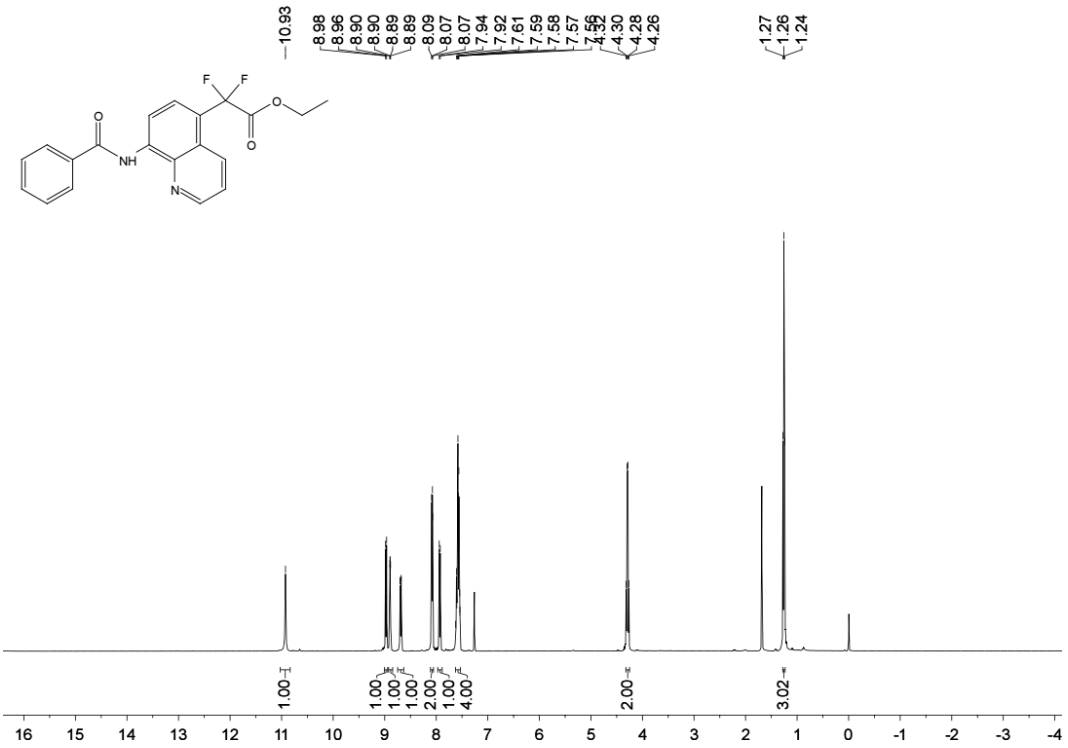
^{1}H NMR for N-(5-bromo-6-methoxyquinolin-8-yl)benzamide (**3r**)



^{13}C NMR for N-(5-bromo-6-methoxyquinolin-8-yl)benzamide (**3r**)

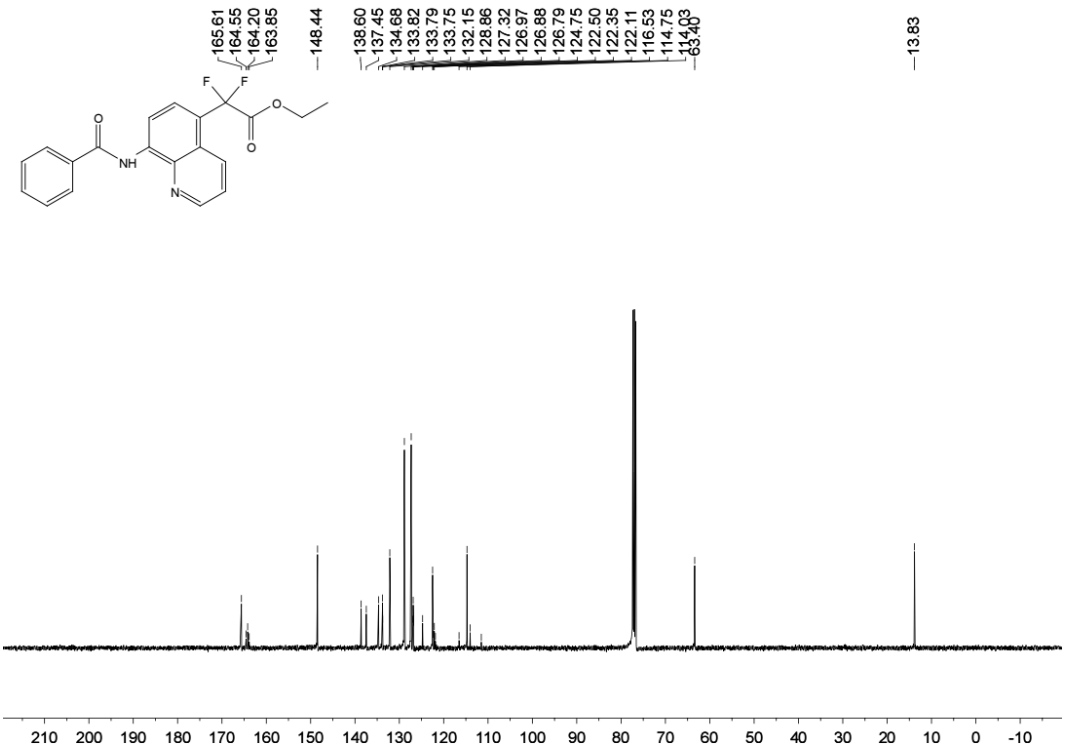


^{1}H NMR for ethyl 2-(8-benzamidoquinolin-5-yl)-2,2-difluoroacetate (**4a**)

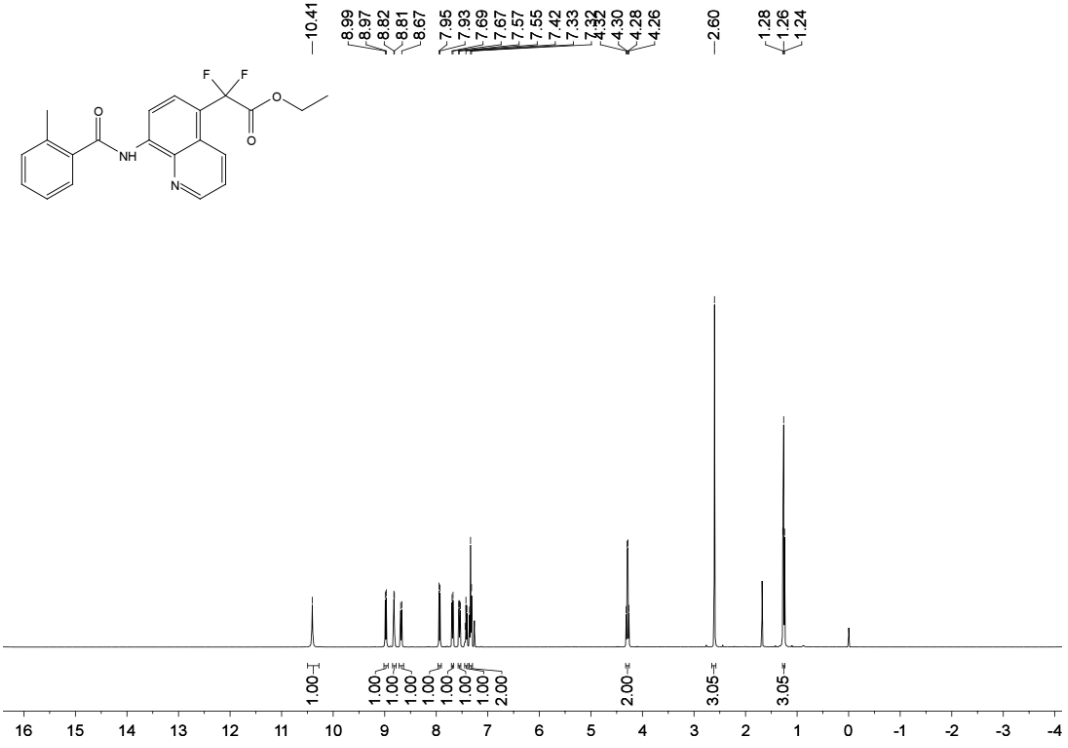


^{19}F NMR for ethyl 2-(8-benzamidoquinolin-5-yl)-2,2-difluoroacetate (**4a**)

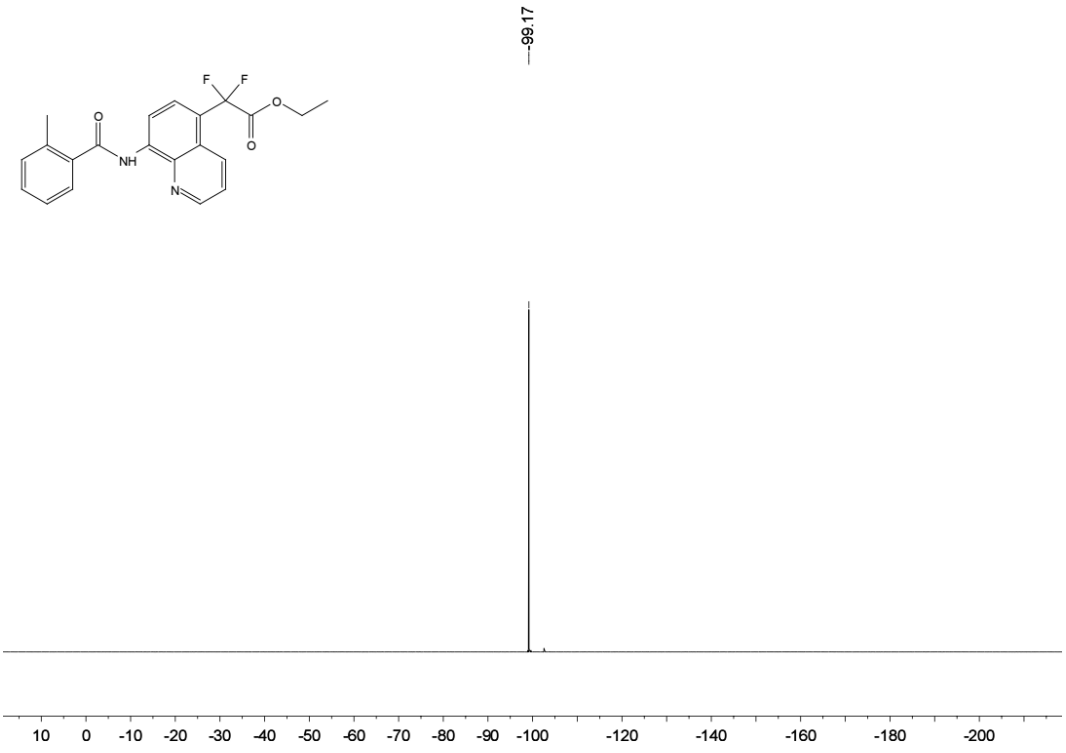
^{13}C NMR for ethyl 2-(8-benzamidoquinolin-5-yl)-2,2-difluoroacetate (**4a**)



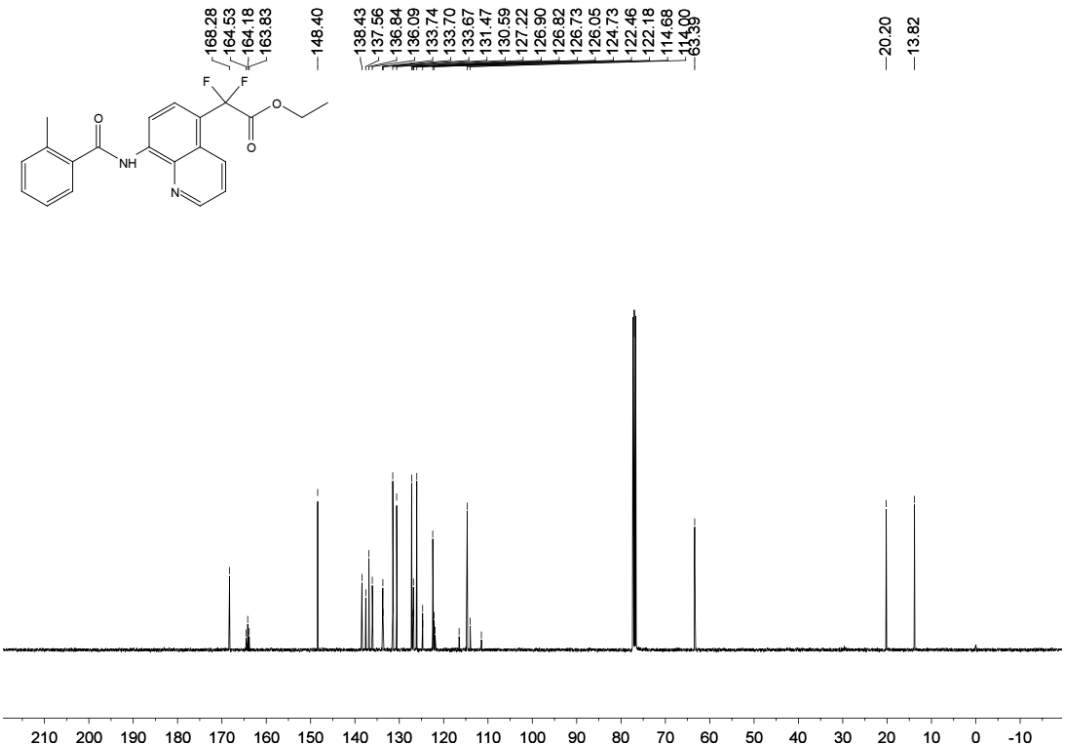
^{1}H NMR for ethyl 2,2-difluoro-2-(8-(2-methylbenzamido)quinolin-5-yl)acetate (**4b**)



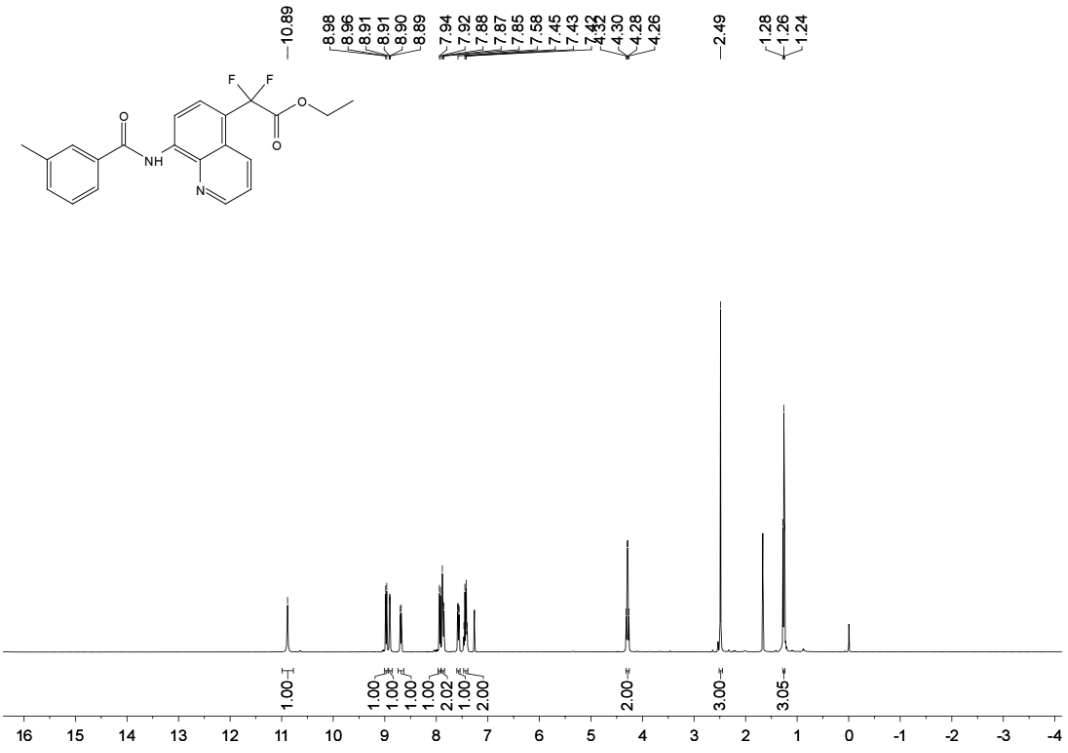
^{19}F NMR for ethyl 2,2-difluoro-2-(8-(2-methylbenzamido)quinolin-5-yl)acetate (**4b**)



^{13}C NMR for ethyl 2,2-difluoro-2-(8-(2-methylbenzamido)quinolin-5-yl)acetate (**4b**)

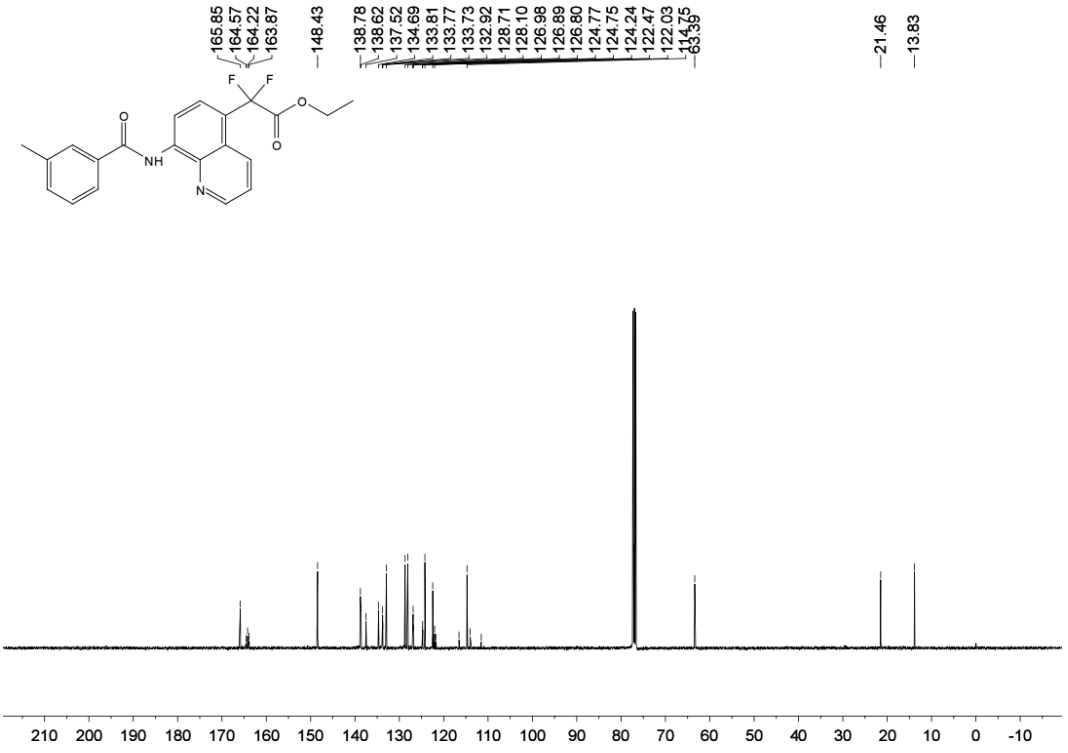


^{1}H NMR for ethyl 2,2-difluoro-2-(8-(3-methylbenzamido)quinolin-5-yl)acetate (**4c**)

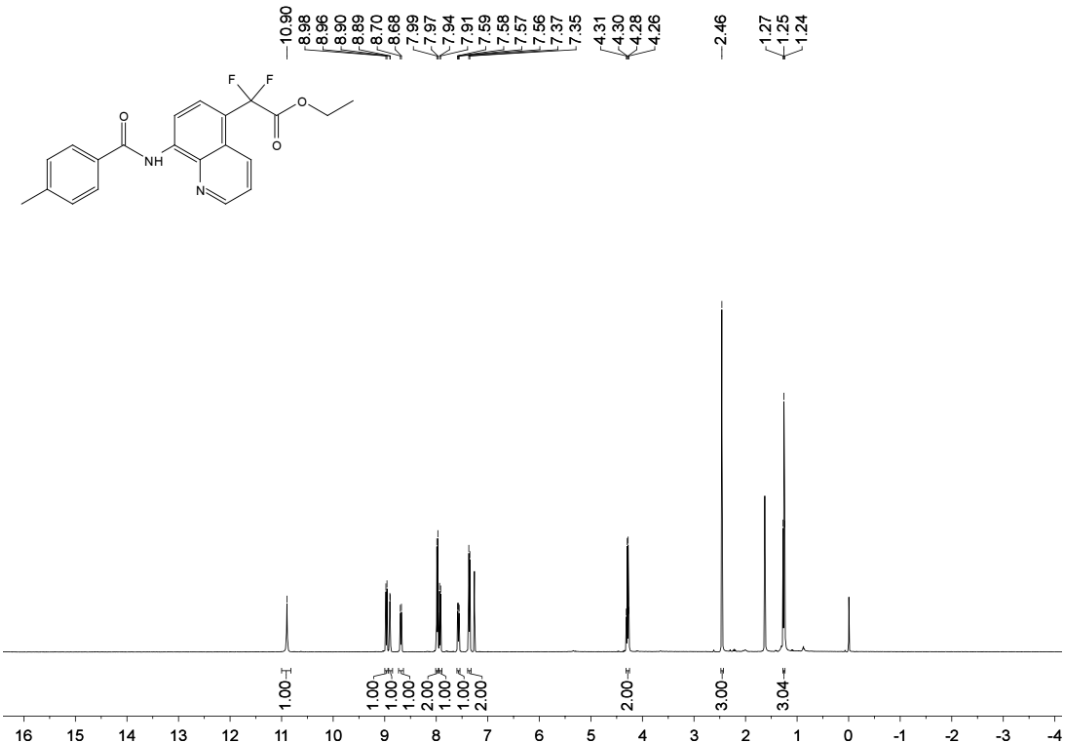


^{19}F NMR for ethyl 2,2-difluoro-2-(8-(3-methylbenzamido)quinolin-5-yl)acetate (**4c**)

^{13}C NMR for ethyl 2,2-difluoro-2-(8-(3-methylbenzamido)quinolin-5-yl)acetate (**4c**)

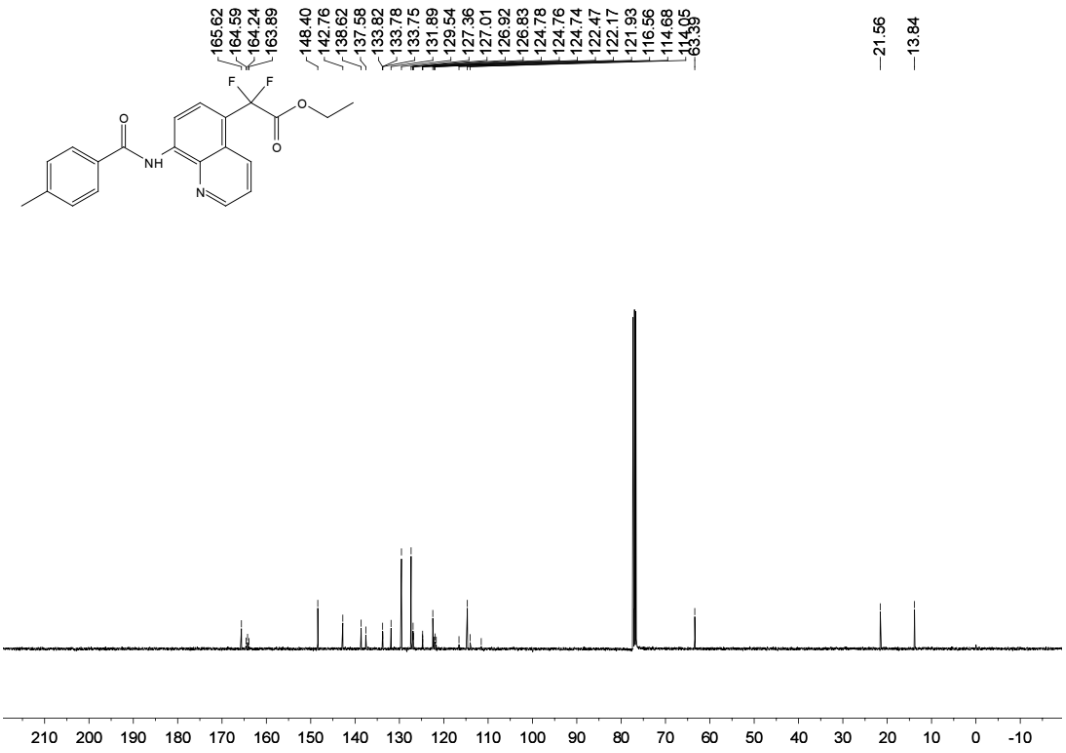


^{1}H NMR for ethyl 2,2-difluoro-2-(8-(4-methylbenzamido)quinolin-5-yl)acetate (**4d**)

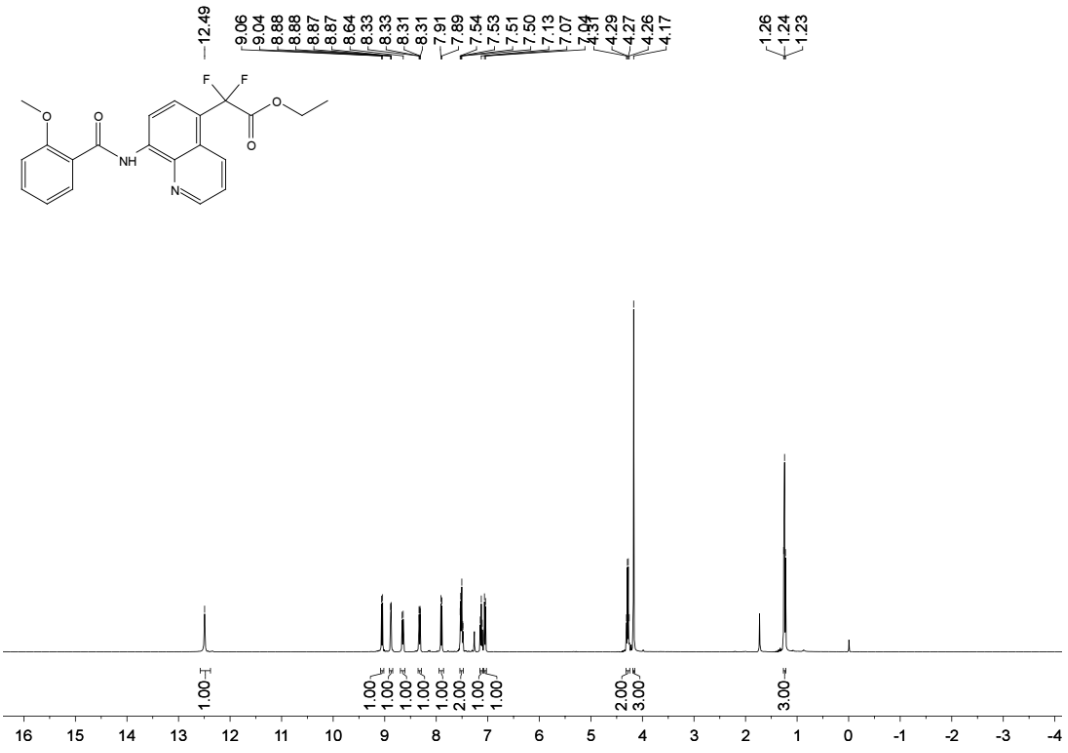


^{19}F NMR for ethyl 2,2-difluoro-2-(8-(4-methylbenzamido)quinolin-5-yl)acetate (**4d**)

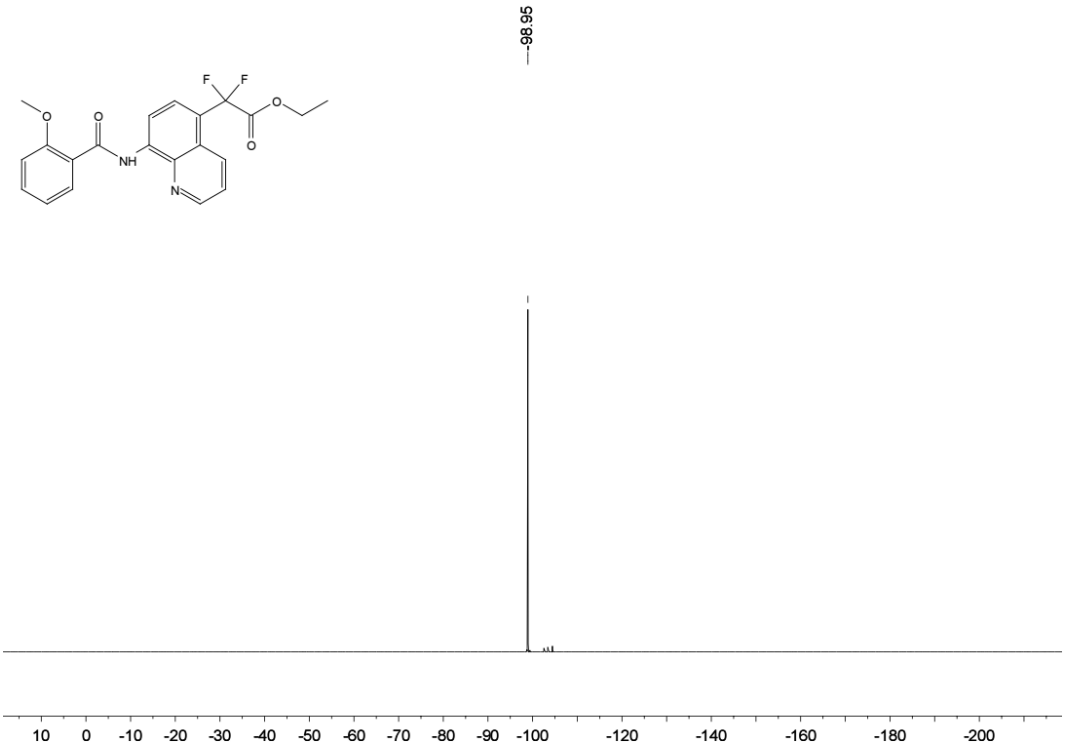
^{13}C NMR for ethyl 2,2-difluoro-2-(8-(4-methylbenzamido)quinolin-5-yl)acetate (**4d**)



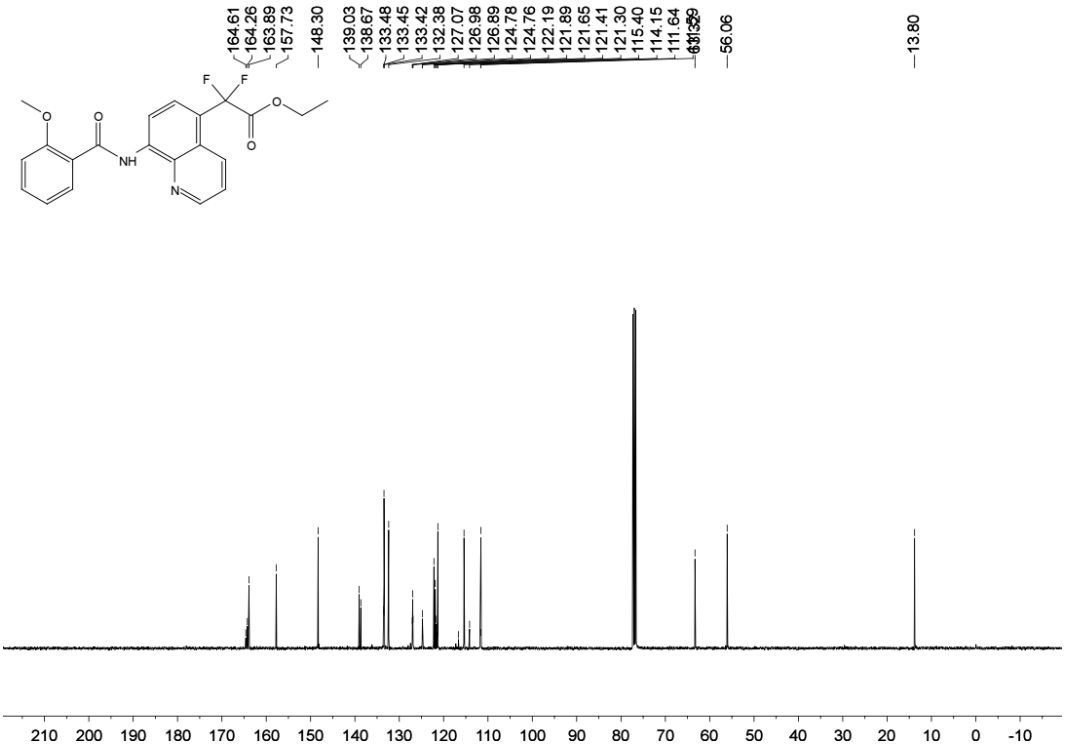
^{1}H NMR for ethyl 2,2-difluoro-2-(8-(2-methoxybenzamido)quinolin-5-yl)acetate (**4e**)



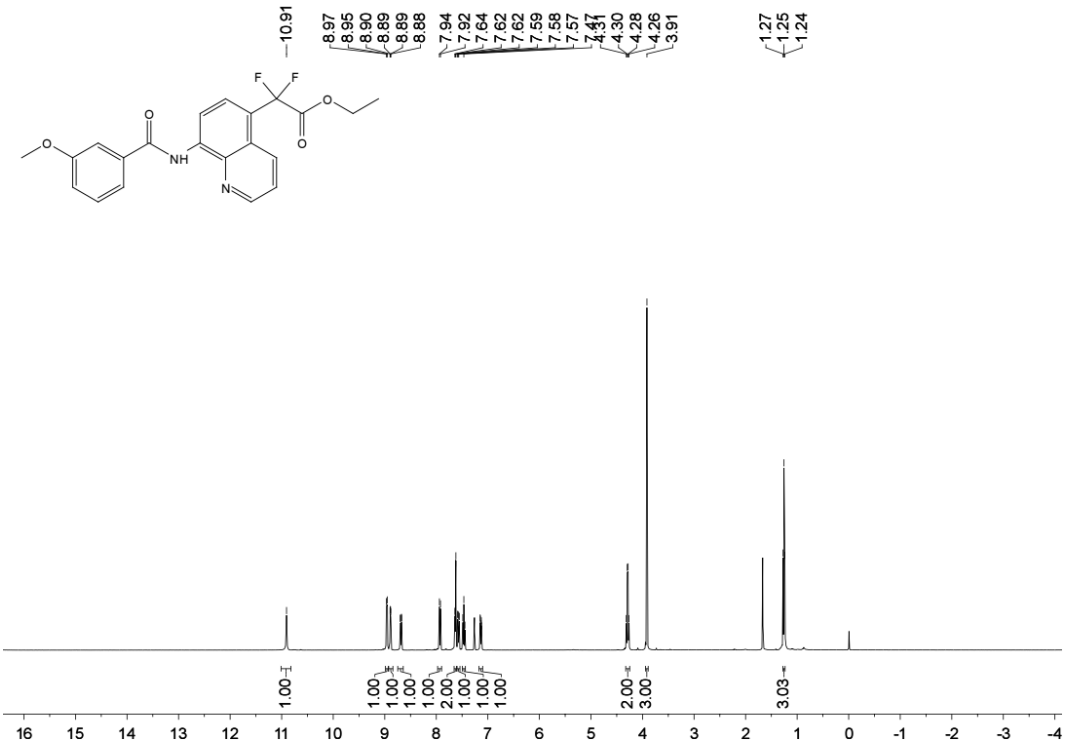
^{19}F NMR for ethyl 2,2-difluoro-2-(8-(2-methoxybenzamido)quinolin-5-yl)acetate (**4e**)



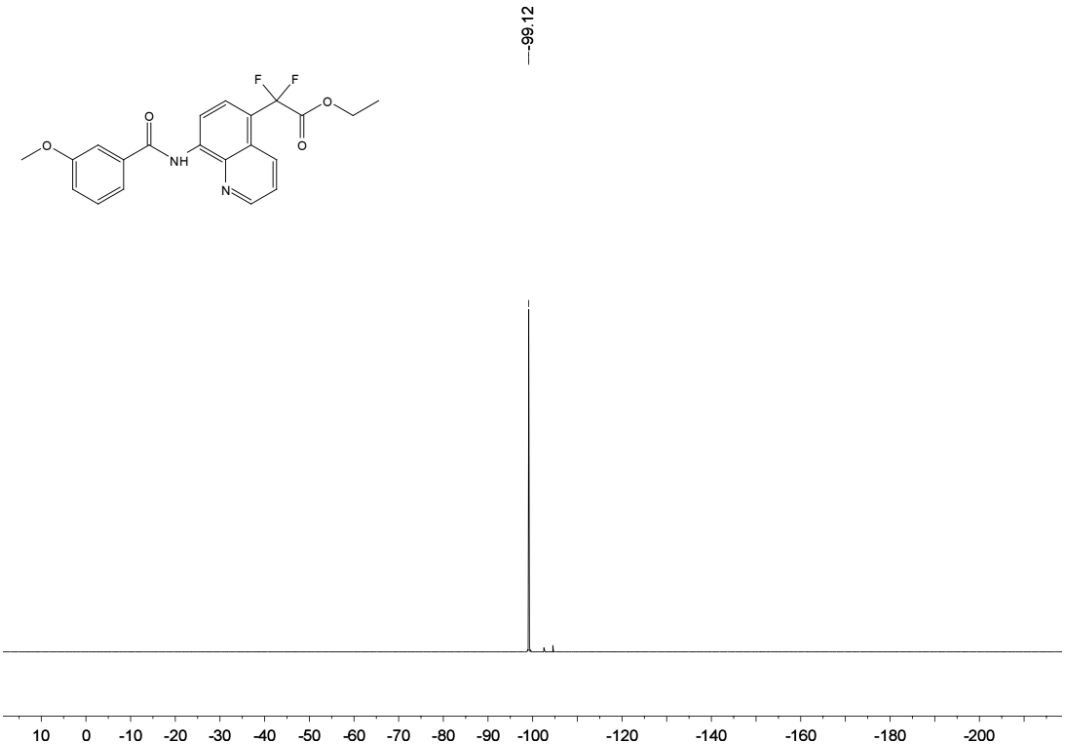
^{13}C NMR for ethyl 2,2-difluoro-2-(8-(2-methoxybenzamido)quinolin-5-yl)acetate (**4e**)



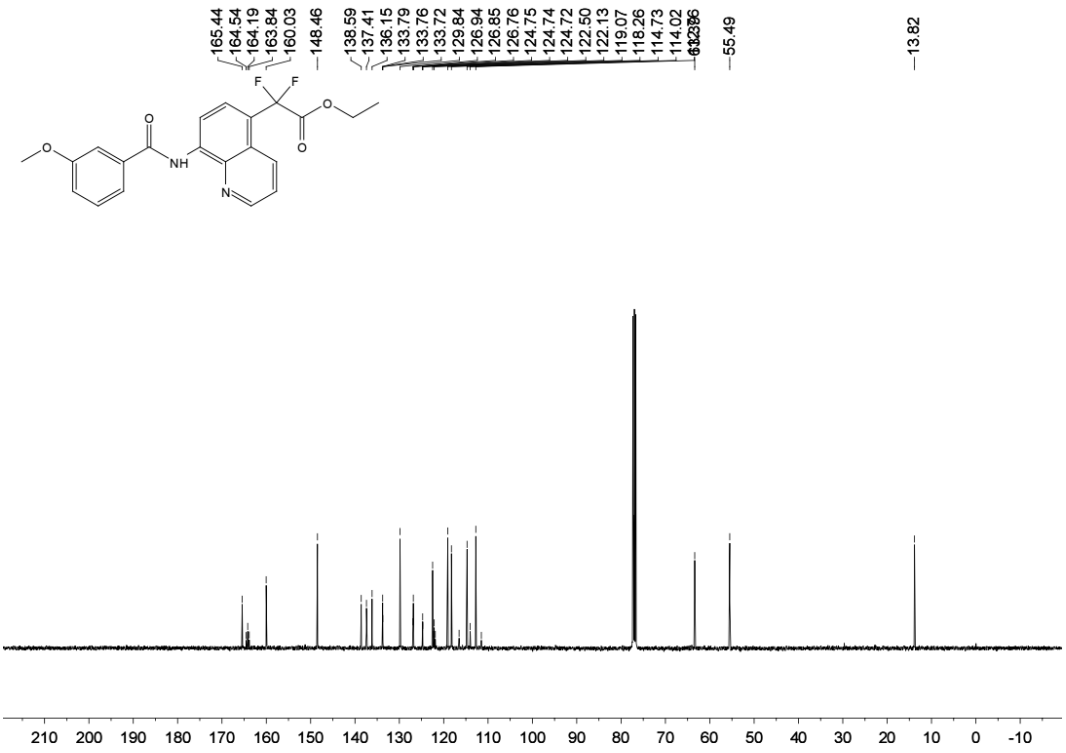
^{1}H NMR for ethyl 2,2-difluoro-2-(8-(3-methoxybenzamido)quinolin-5-yl)acetate (**4f**)



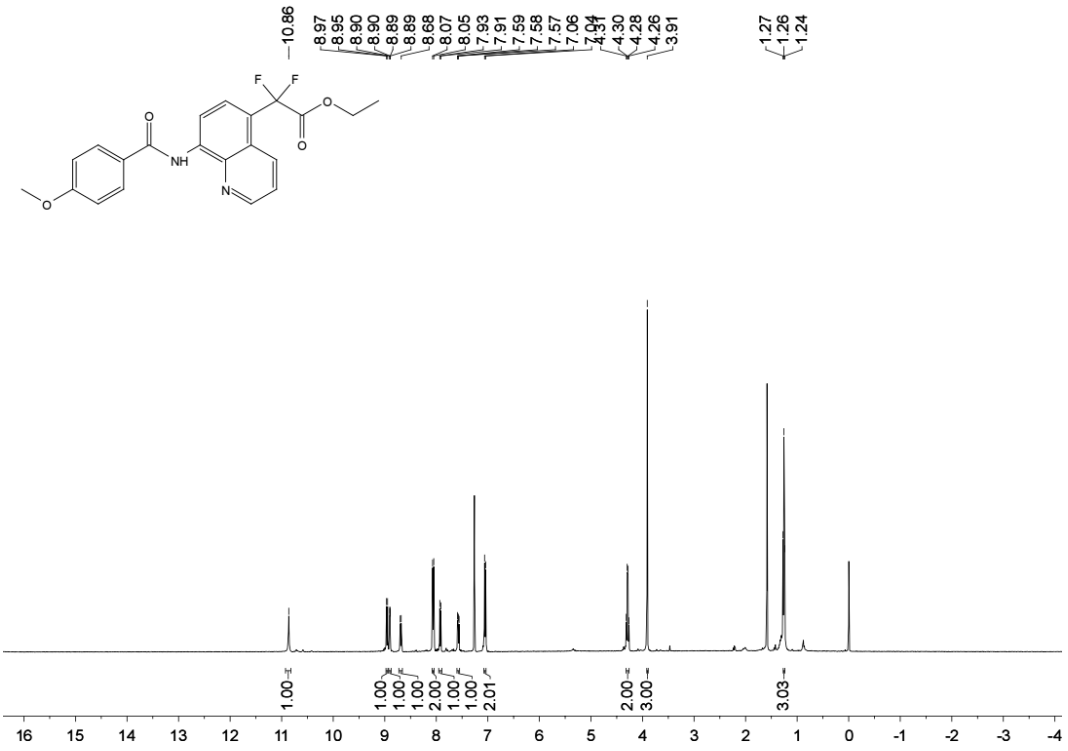
^{19}F NMR for ethyl 2,2-difluoro-2-(8-(3-methoxybenzamido)quinolin-5-yl)acetate (**4f**)



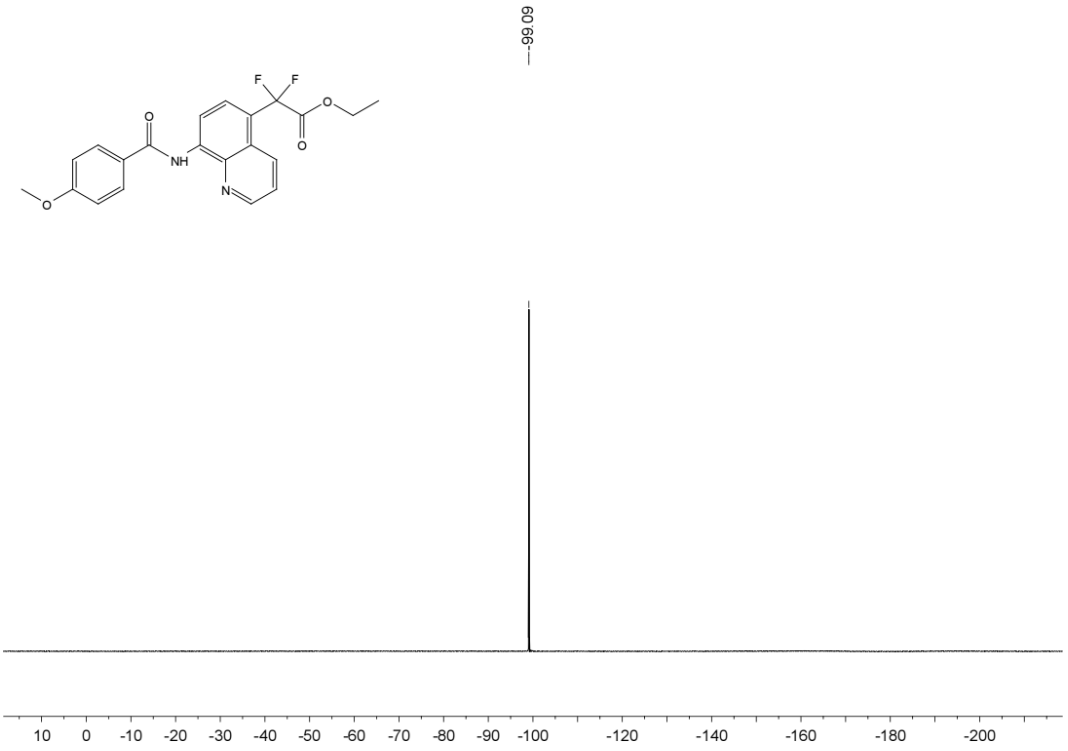
^{13}C NMR for ethyl 2,2-difluoro-2-(8-(3-methoxybenzamido)quinolin-5-yl)acetate (**4f**)



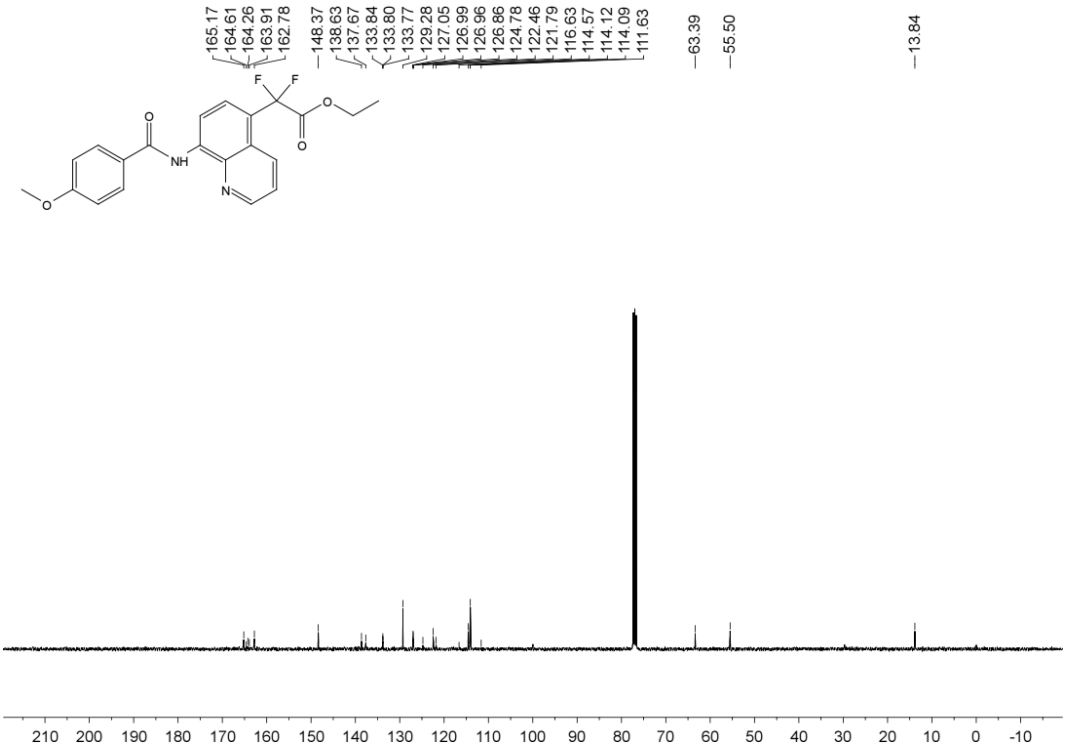
^{1}H NMR for ethyl 2,2-difluoro-2-(8-(4-methoxybenzamido)quinolin-5-yl)acetate (**4g**)



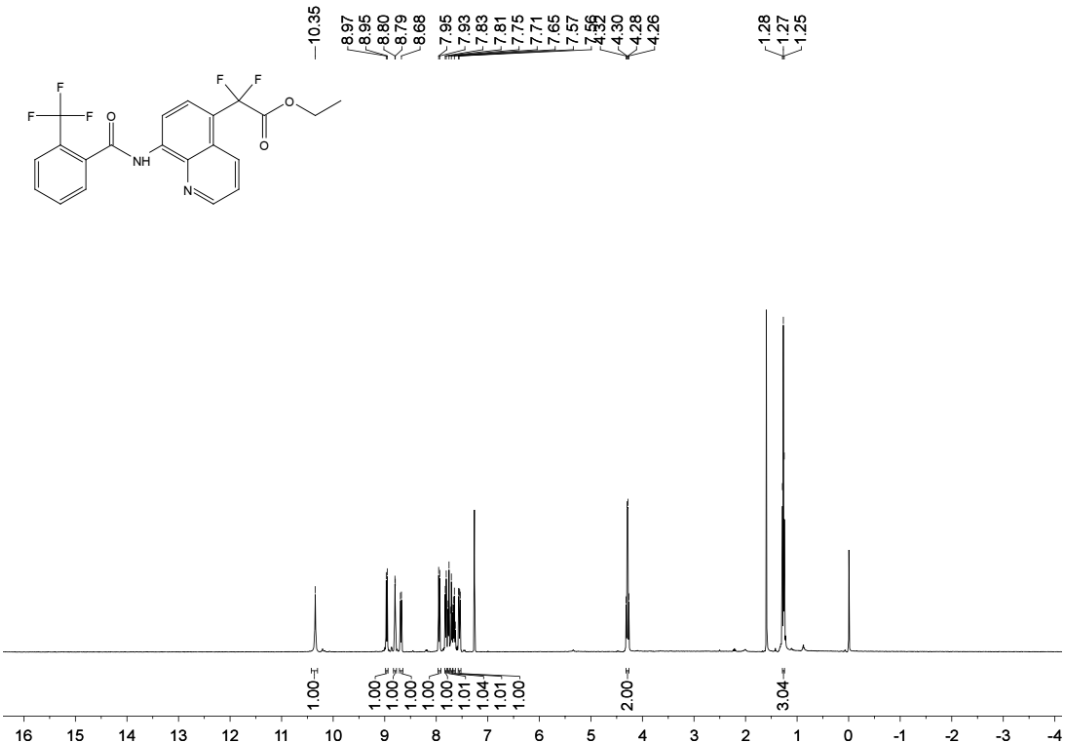
^{19}F NMR for ethyl 2,2-difluoro-2-(8-(4-methoxybenzamido)quinolin-5-yl)acetate (**4g**)



^{13}C NMR for ethyl 2,2-difluoro-2-(8-(4-methoxybenzamido)quinolin-5-yl)acetate (**4g**)

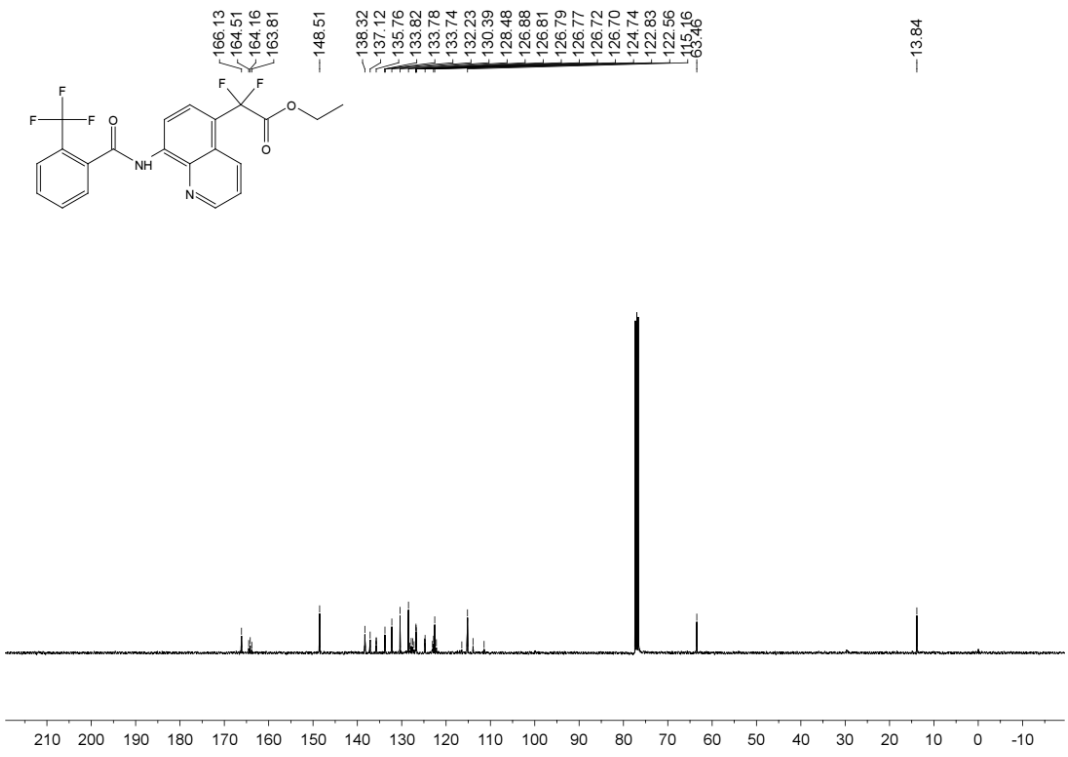


^{1}H NMR for ethyl 2,2-difluoro-2-(8-(2-(trifluoromethyl)benzamido)quinolin-5-yl)acetate (**4h**)

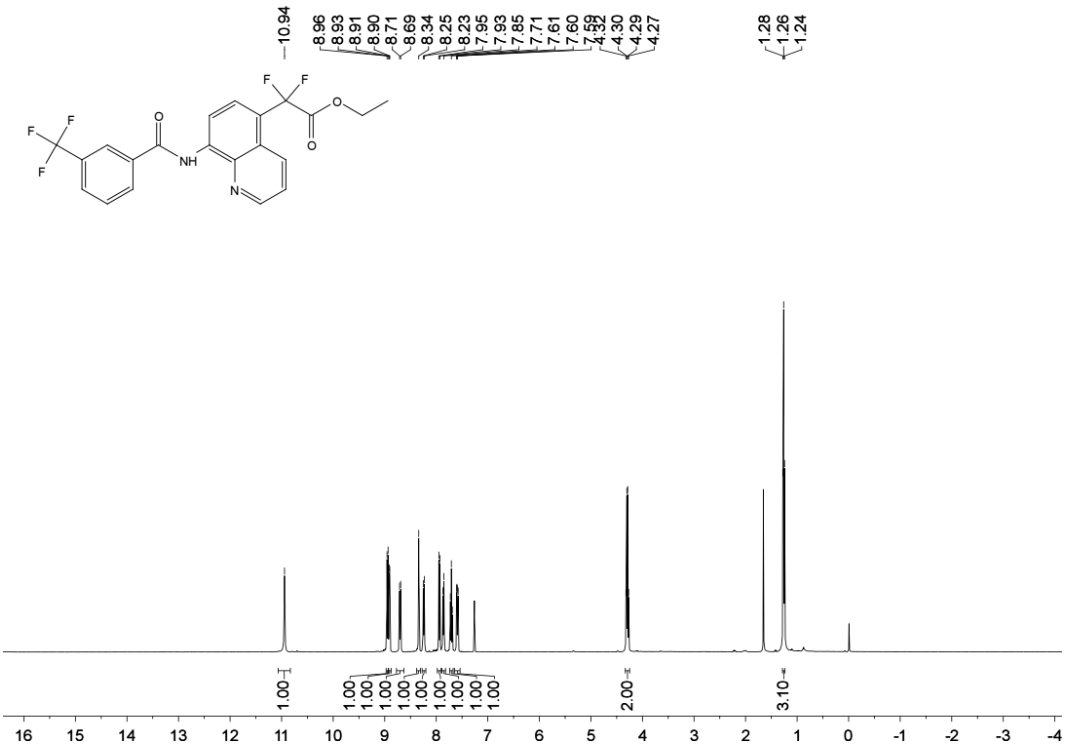


^{19}F NMR for ethyl 2,2-difluoro-2-(8-(2-(trifluoromethyl)benzamido)quinolin-5-yl)acetate (**4h**)

^{13}C NMR for ethyl 2,2-difluoro-2-(8-(2-(trifluoromethyl)benzamido)quinolin-5-yl)acetate (**4h**)

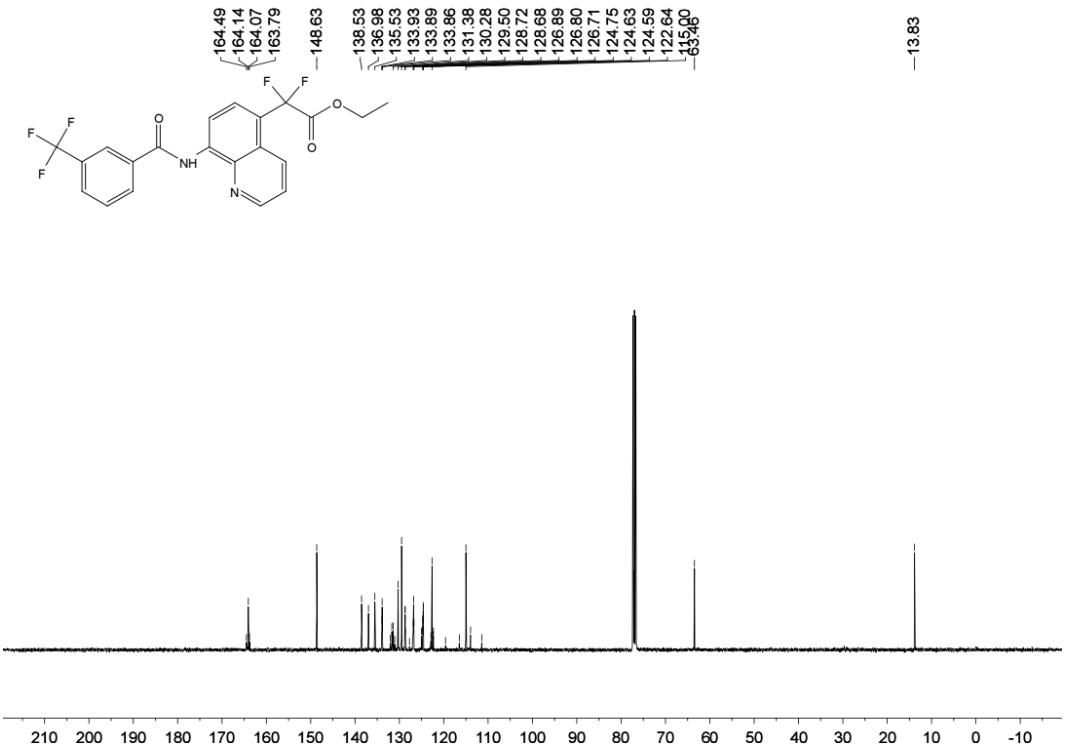


^{1}H NMR for ethyl 2,2-difluoro-2-(8-(3-(trifluoromethyl)benzamido)quinolin-5-yl)acetate (**4i**)

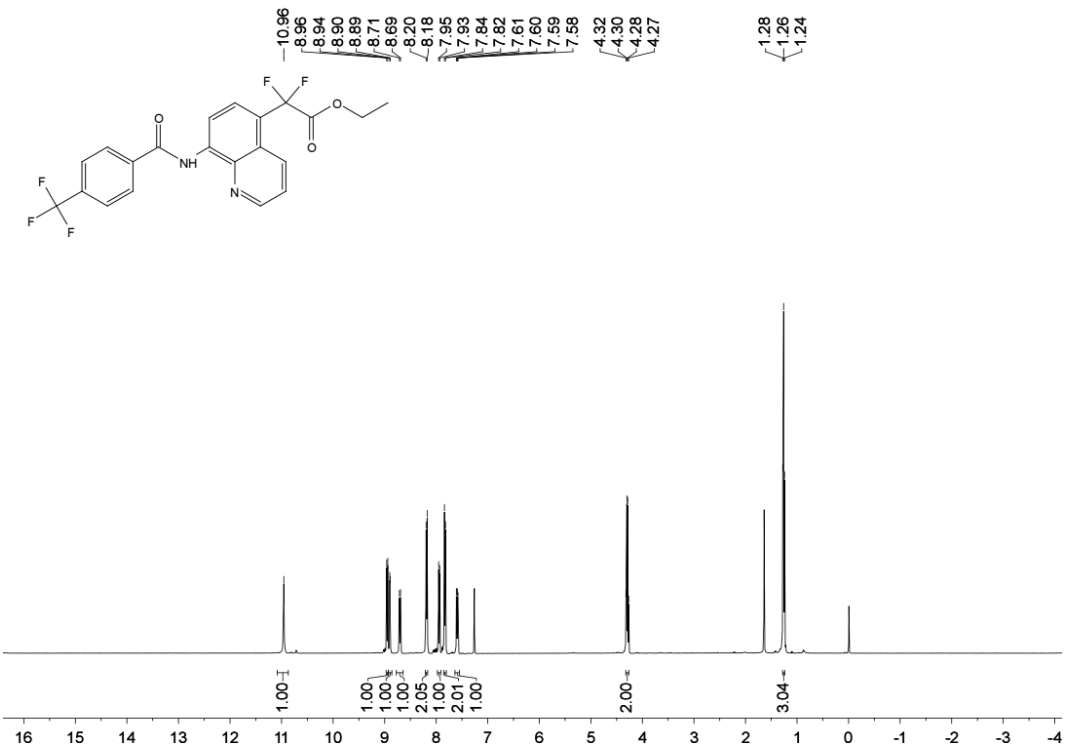


^{19}F NMR for ethyl 2,2-difluoro-2-(8-(3-(trifluoromethyl)benzamido)quinolin-5-yl)acetate (**4i**)

^{13}C NMR for ethyl 2,2-difluoro-2-(8-(3-(trifluoromethyl)benzamido)quinolin-5-yl)acetate (**4i**)

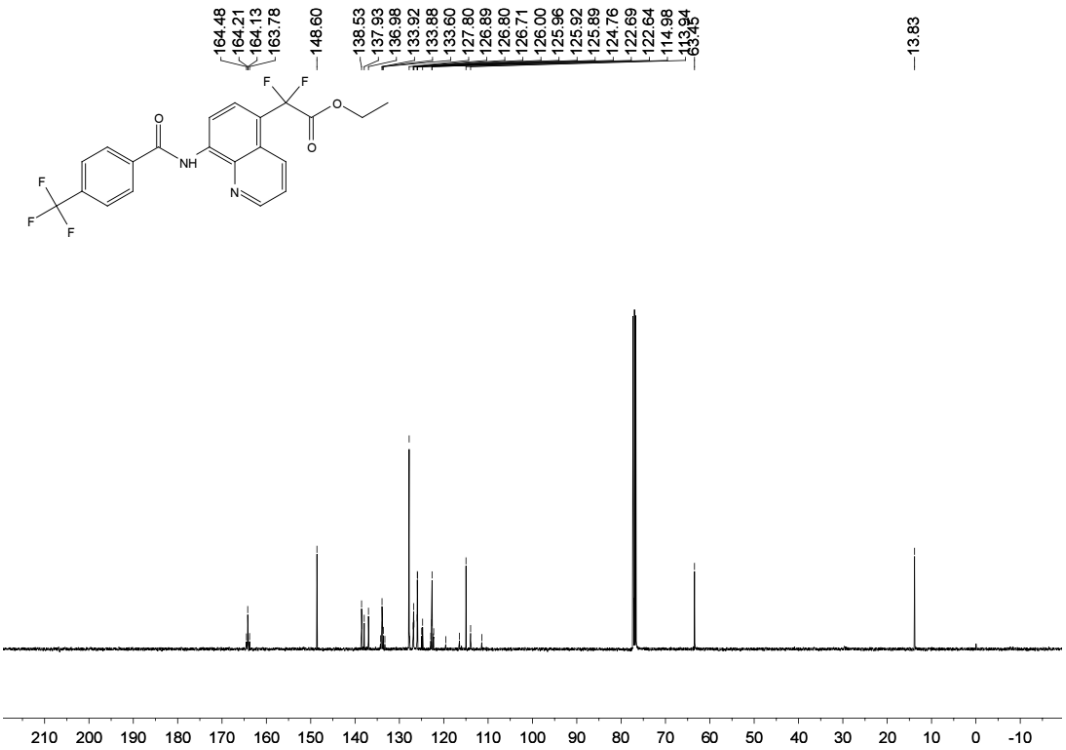


^{1}H NMR for ethyl 2,2-difluoro-2-(8-(4-(trifluoromethyl)benzamido)quinolin-5-yl)acetate (**4j**)

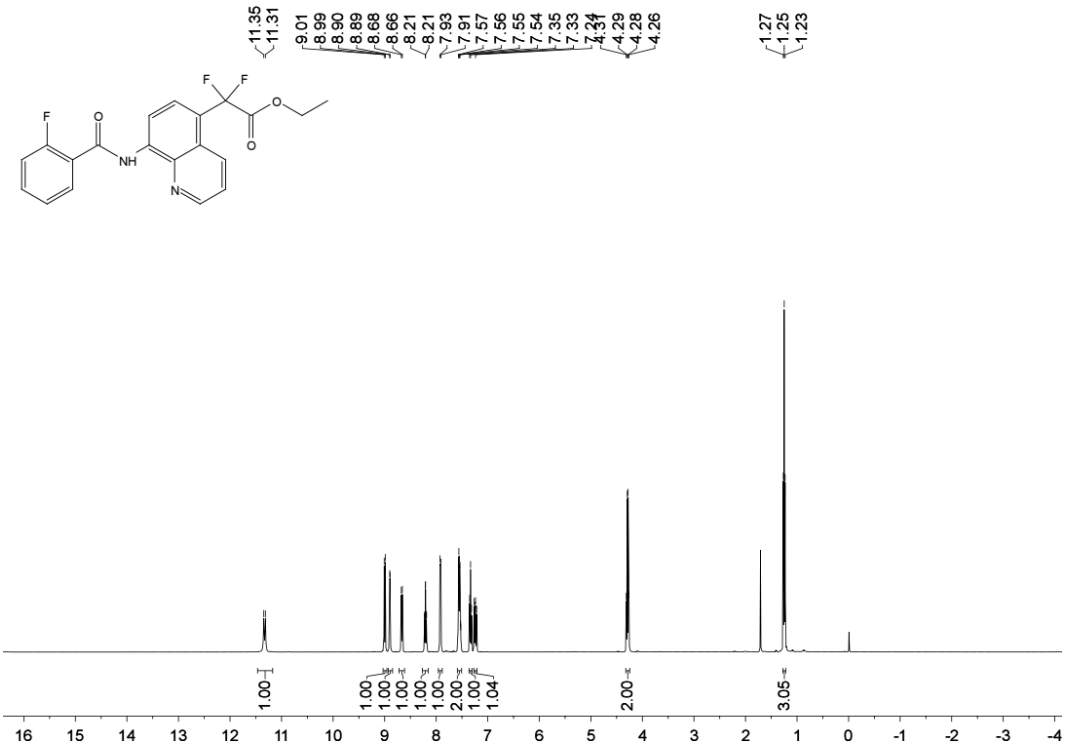


^{19}F NMR for ethyl 2,2-difluoro-2-(8-(4-(trifluoromethyl)benzamido)quinolin-5-yl)acetate (**4j**)

^{13}C NMR for ethyl 2,2-difluoro-2-(8-(4-(trifluoromethyl)benzamido)quinolin-5-yl)acetate (**4j**)

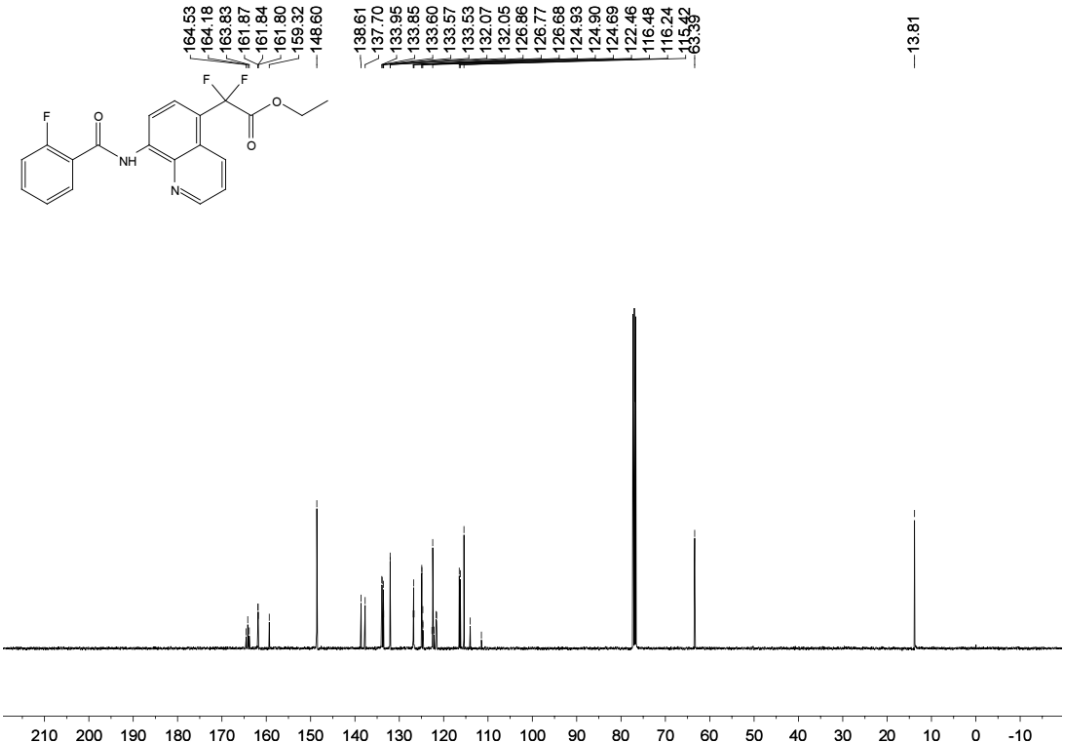


^{1}H NMR for ethyl 2,2-difluoro-2-(8-(2-fluorobenzamido)quinolin-5-yl)acetate (**4k**)

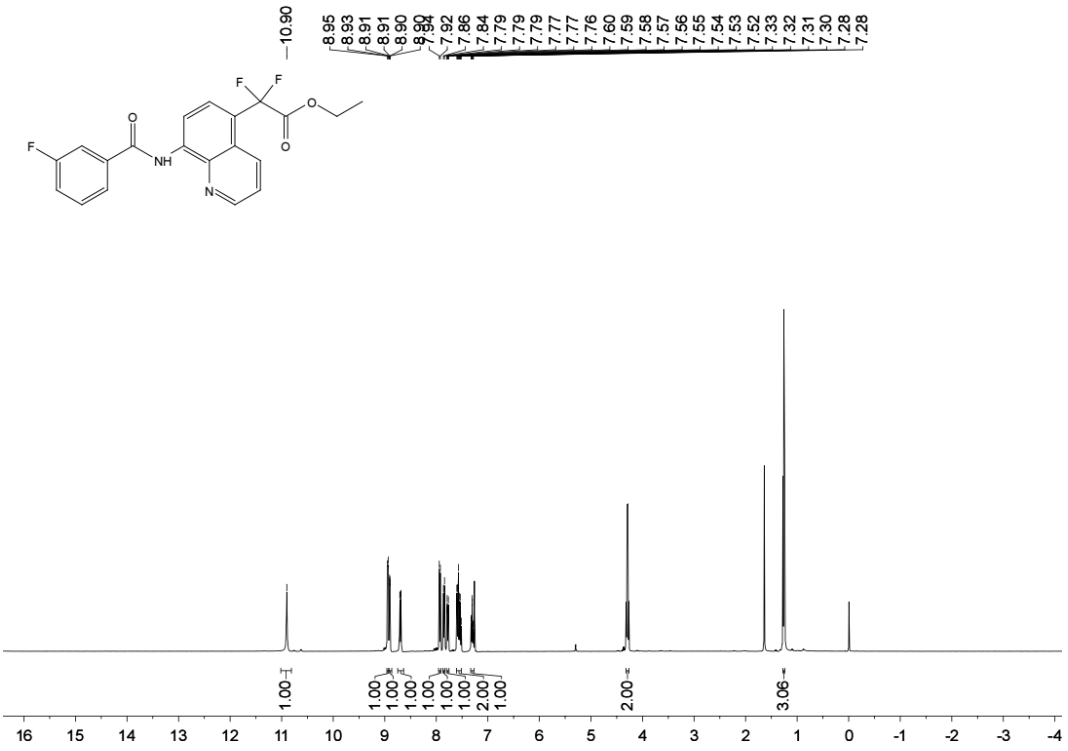


^{19}F NMR for ethyl 2,2-difluoro-2-(8-(2-fluorobenzamido)quinolin-5-yl)acetate (**4k**)

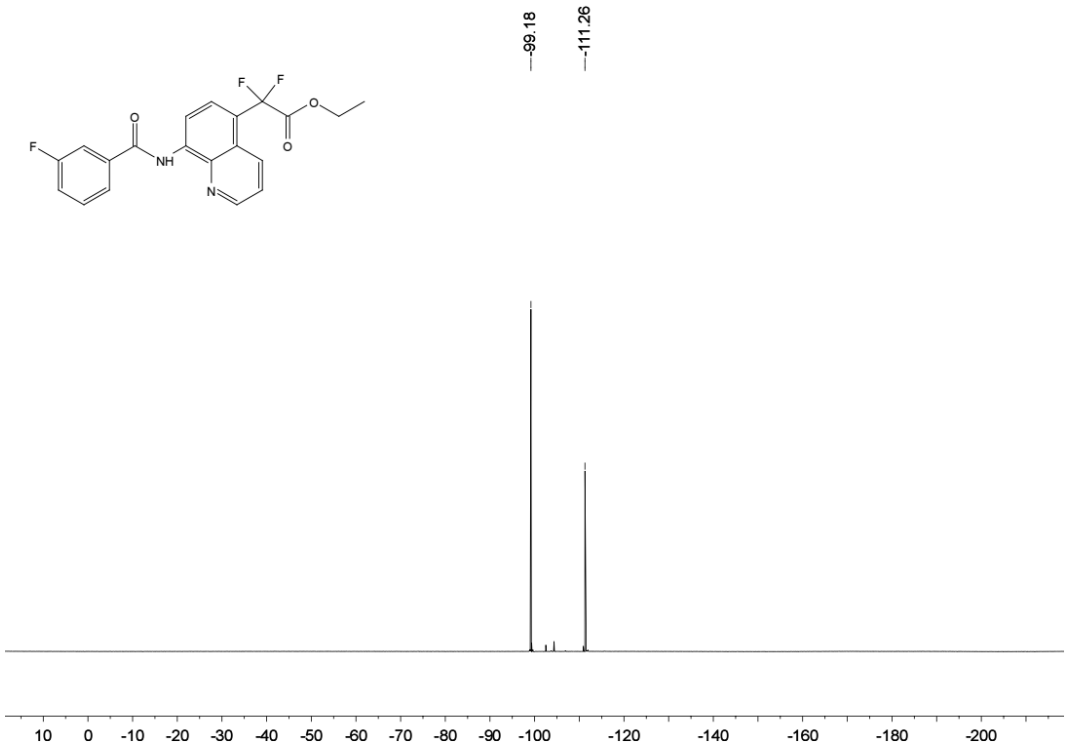
^{13}C NMR for ethyl 2,2-difluoro-2-(8-(2-fluorobenzamido)quinolin-5-yl)acetate (**4k**)



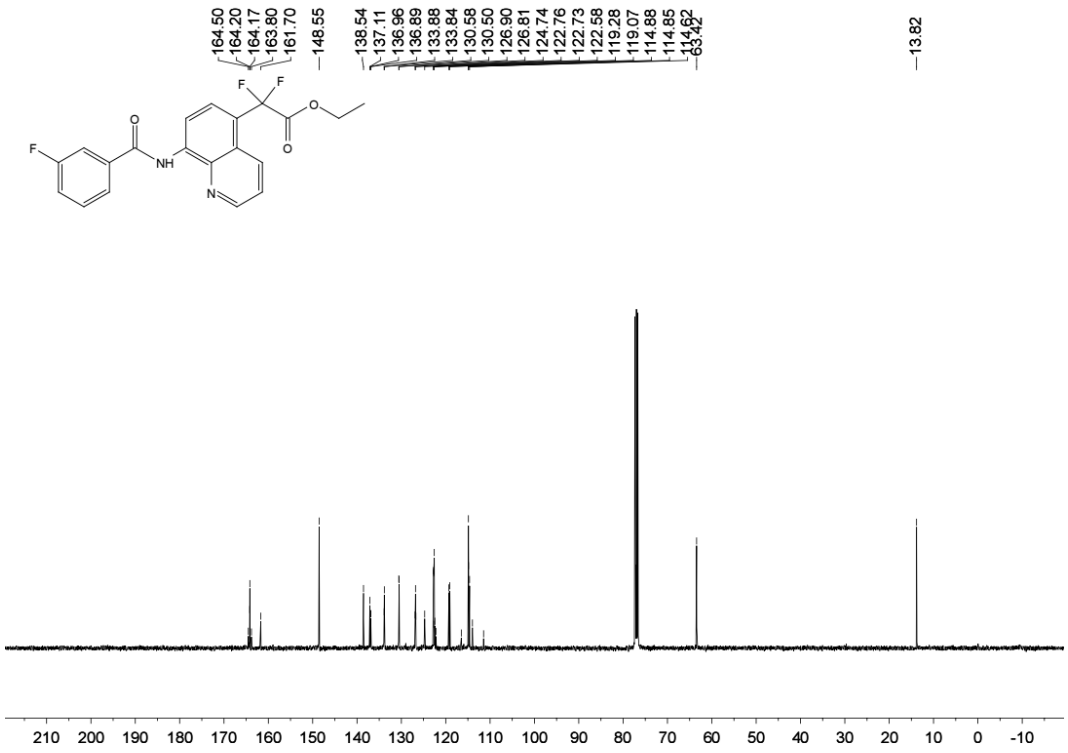
^{1}H NMR for ethyl 2,2-difluoro-2-(8-(3-fluorobenzamido)quinolin-5-yl)acetate (**4l**)



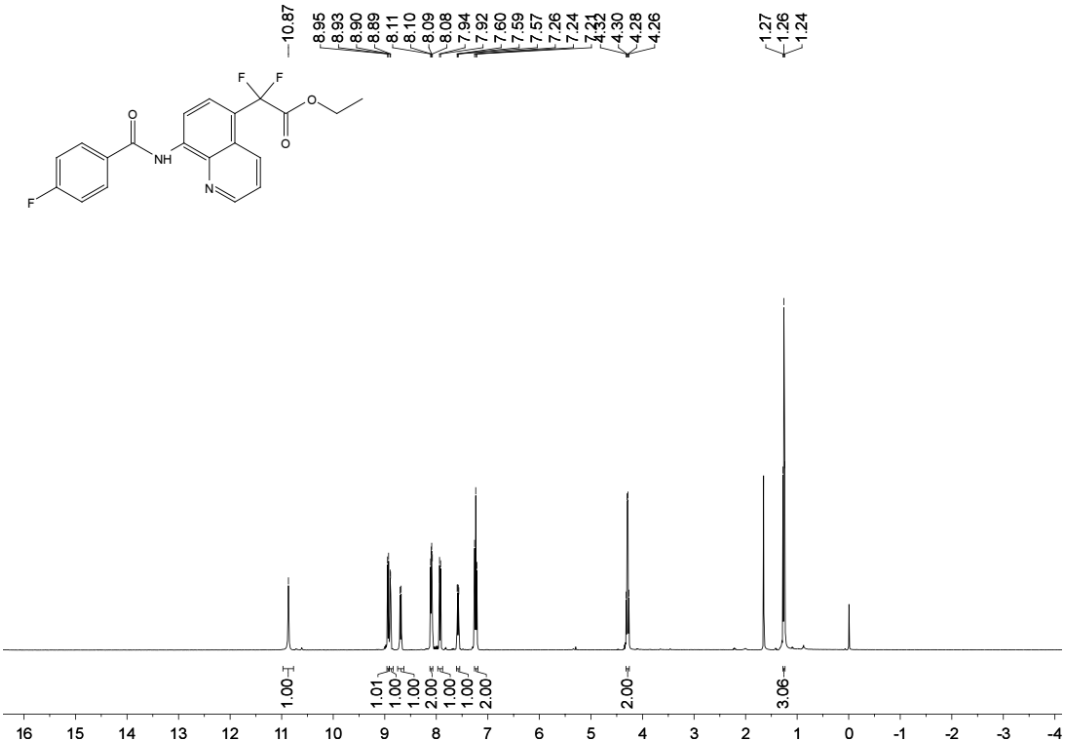
^{19}F NMR for ethyl 2,2-difluoro-2-(8-(3-fluorobenzamido)quinolin-5-yl)acetate (**4l**)



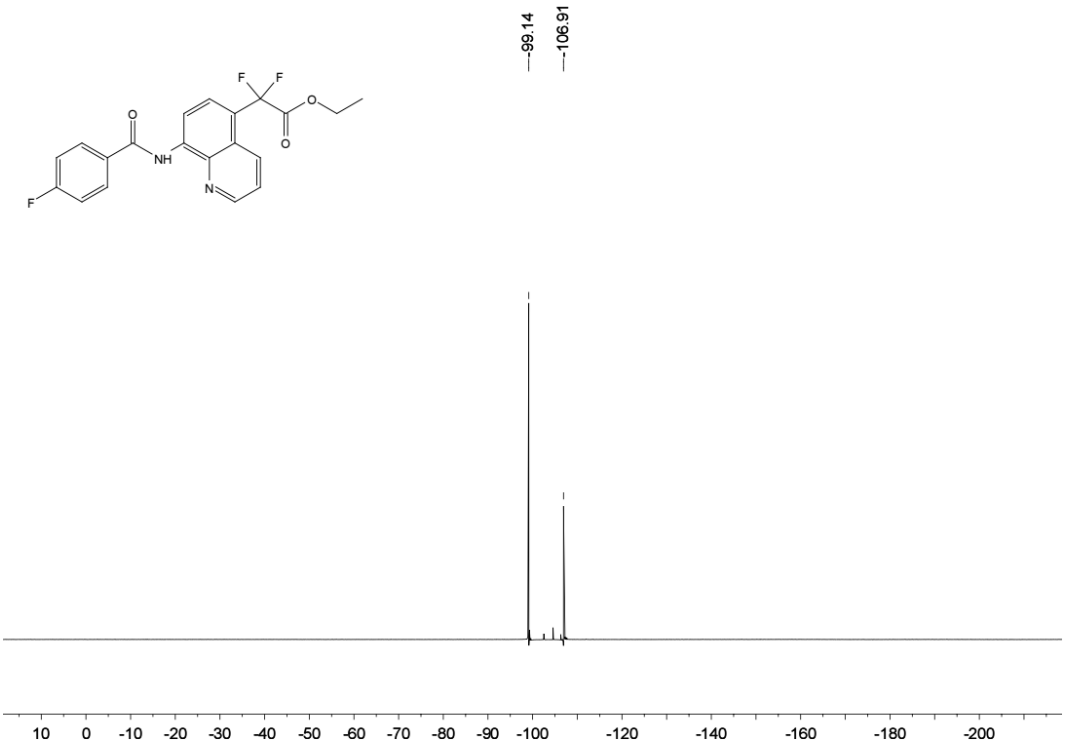
^{13}C NMR for ethyl 2,2-difluoro-2-(8-(3-fluorobenzamido)quinolin-5-yl)acetate (**4l**)



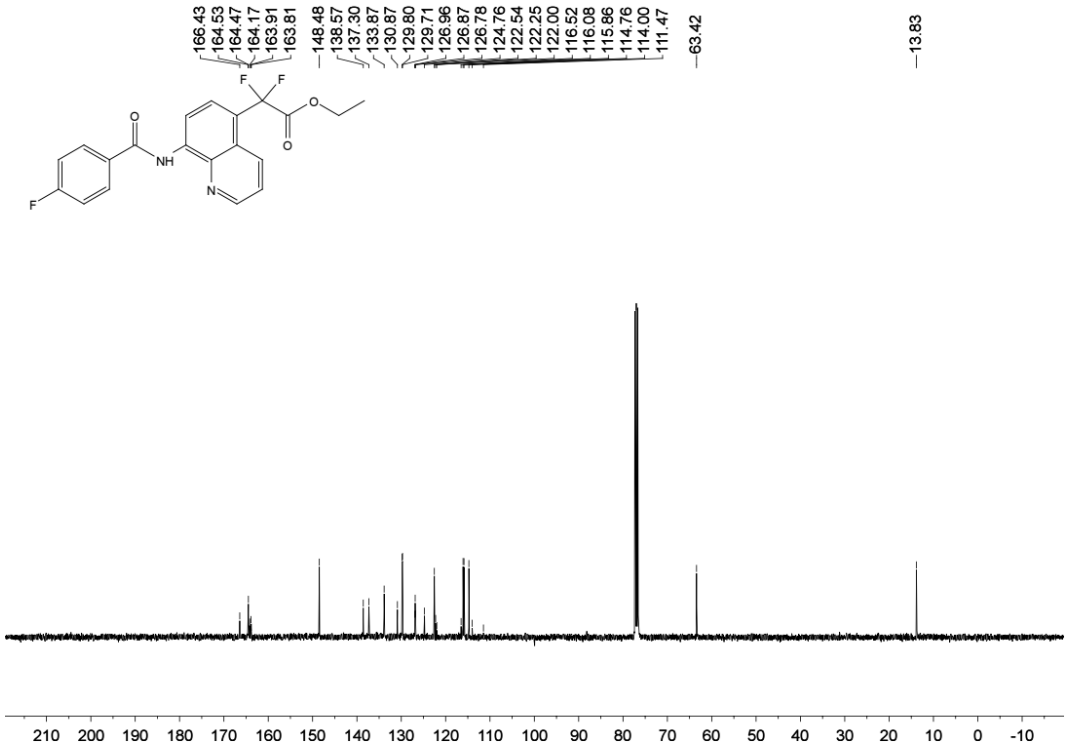
^{1}H NMR for ethyl 2,2-difluoro-2-(8-(4-fluorobenzamido)quinolin-5-yl)acetate (**4m**)



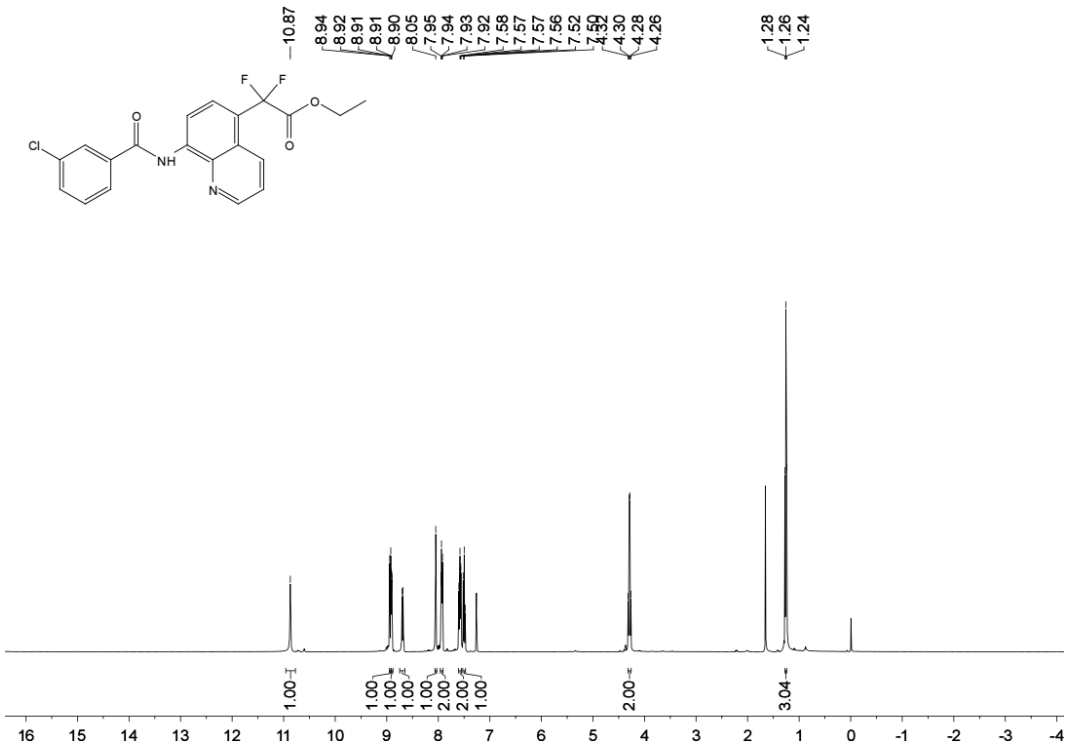
^{19}F NMR for ethyl 2,2-difluoro-2-(8-(4-fluorobenzamido)quinolin-5-yl)acetate (**4m**)



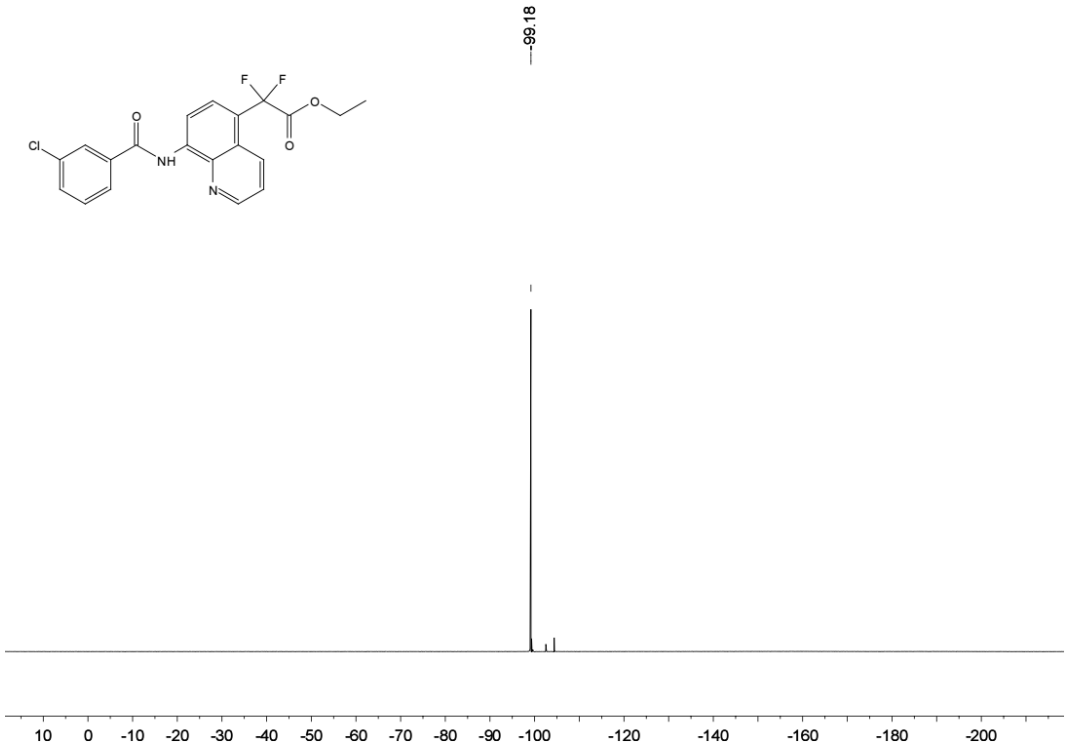
^{13}C NMR for ethyl 2,2-difluoro-2-(8-(4-fluorobenzamido)quinolin-5-yl)acetate (**4m**)



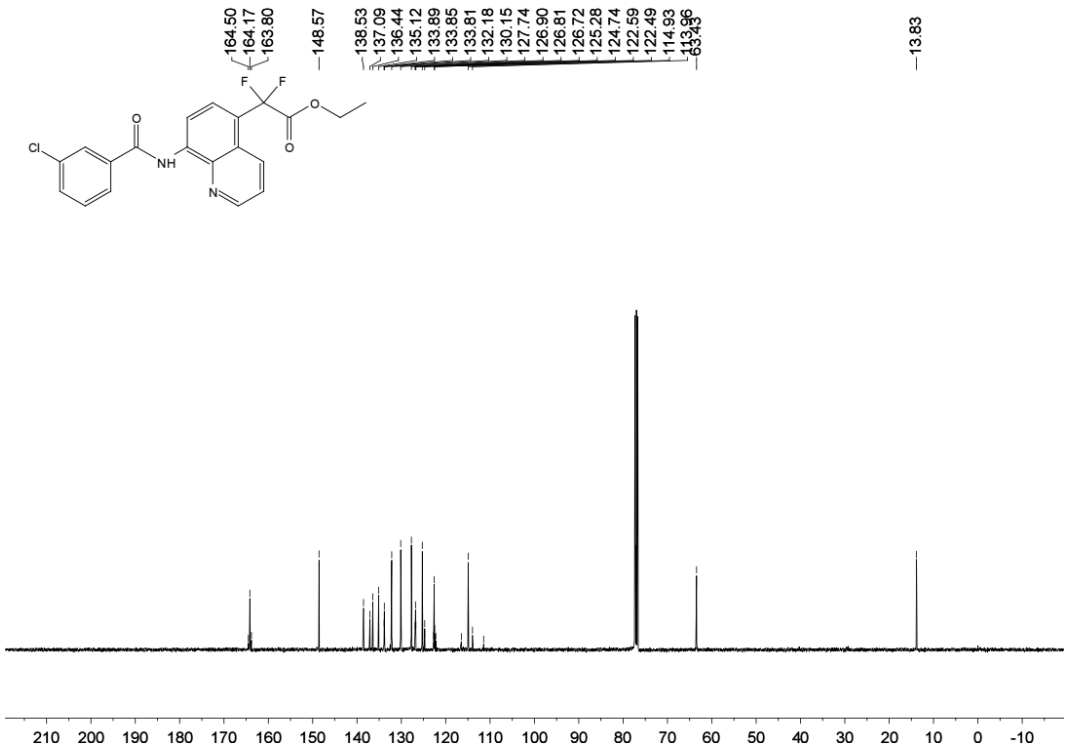
^{1}H NMR for ethyl 2-(8-(3-chlorobenzamido)quinolin-5-yl)-2,2-difluoroacetate (**4n**)



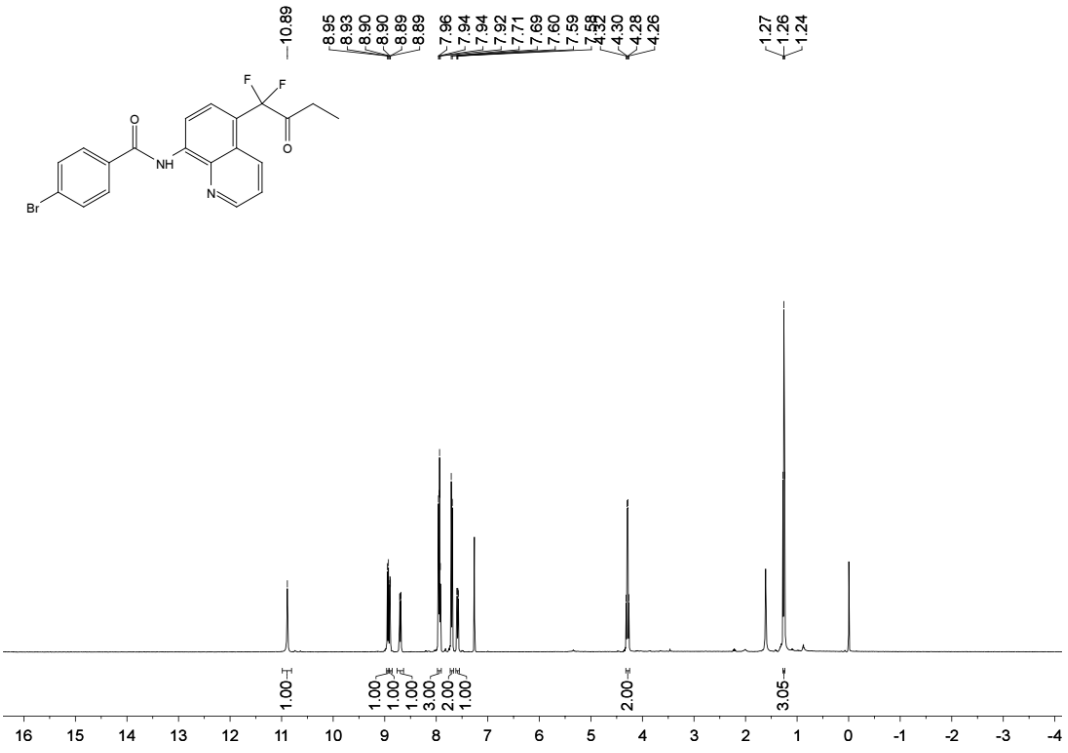
^{19}F NMR for ethyl 2-(8-(3-chlorobenzamido)quinolin-5-yl)-2,2-difluoroacetate (**4n**)



^{13}C NMR for ethyl 2-(8-(3-chlorobenzamido)quinolin-5-yl)-2,2-difluoroacetate (**4n**)

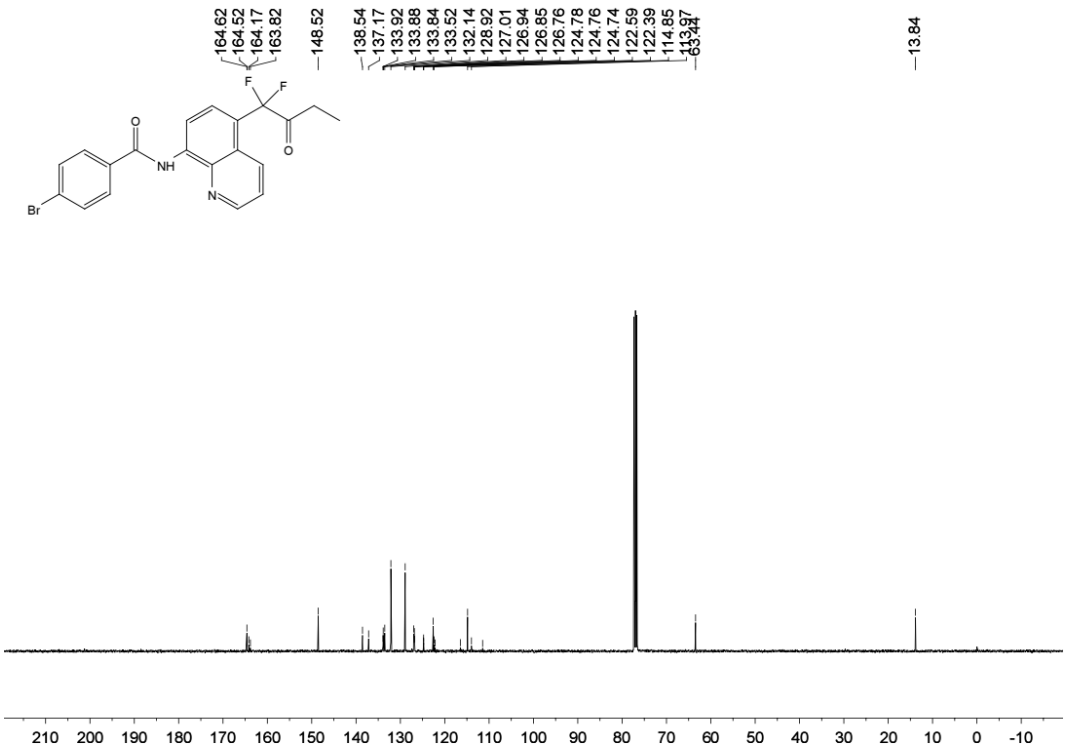


^{1}H NMR for ethyl 2-(8-(4-bromobenzamido)quinolin-5-yl)-2,2-difluoroacetate (**4o**)

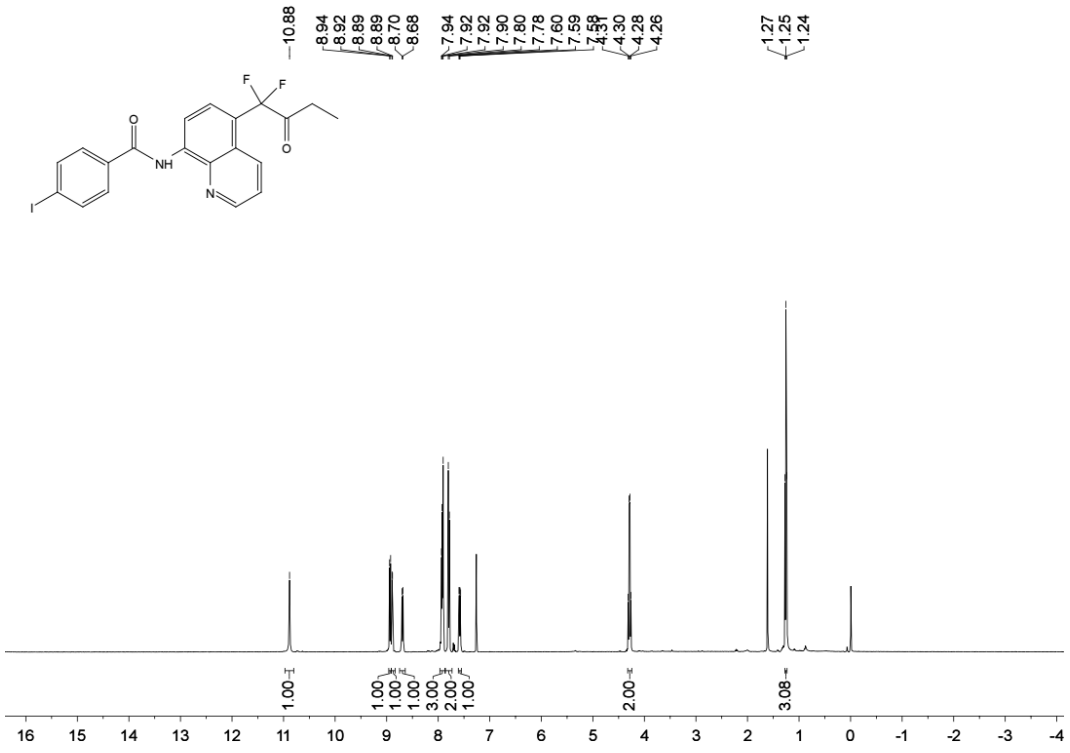


^{19}F NMR for ethyl 2-(8-(4-bromobenzamido)quinolin-5-yl)-2,2-difluoroacetate (**4o**)

^{13}C NMR for ethyl 2-(8-(4-bromobenzamido)quinolin-5-yl)-2,2-difluoroacetate (**4o**)

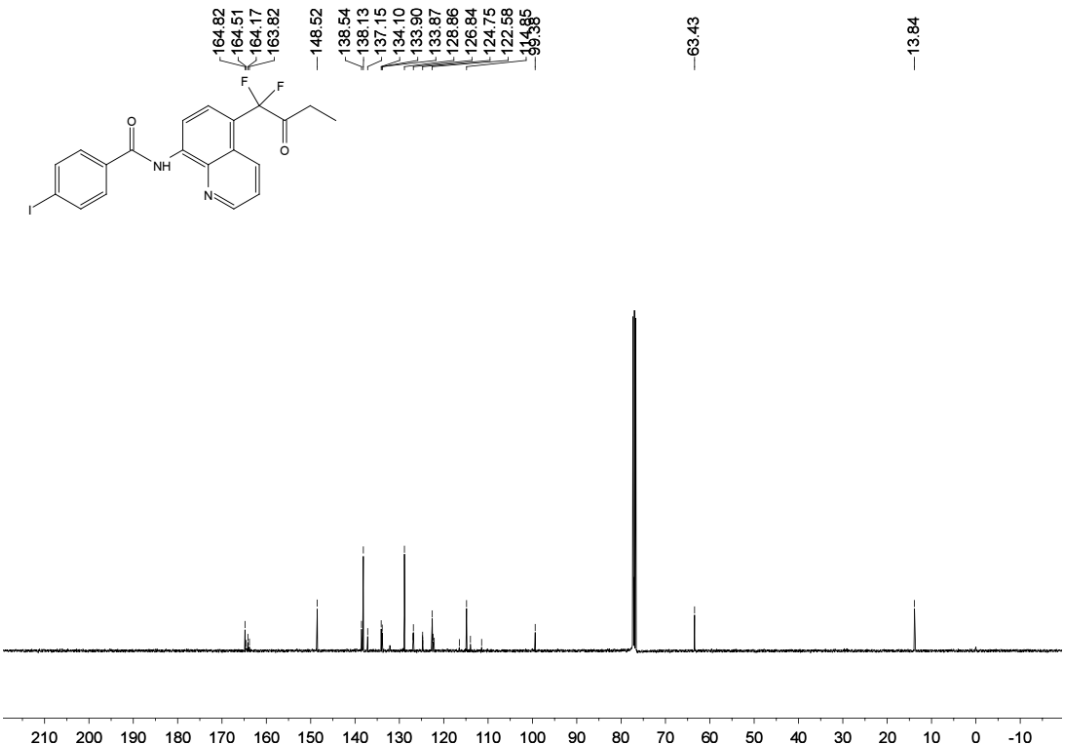


^{1}H NMR for ethyl 2,2-difluoro-2-(8-(4-iodobenzamido)quinolin-5-yl)acetate (**4p**)

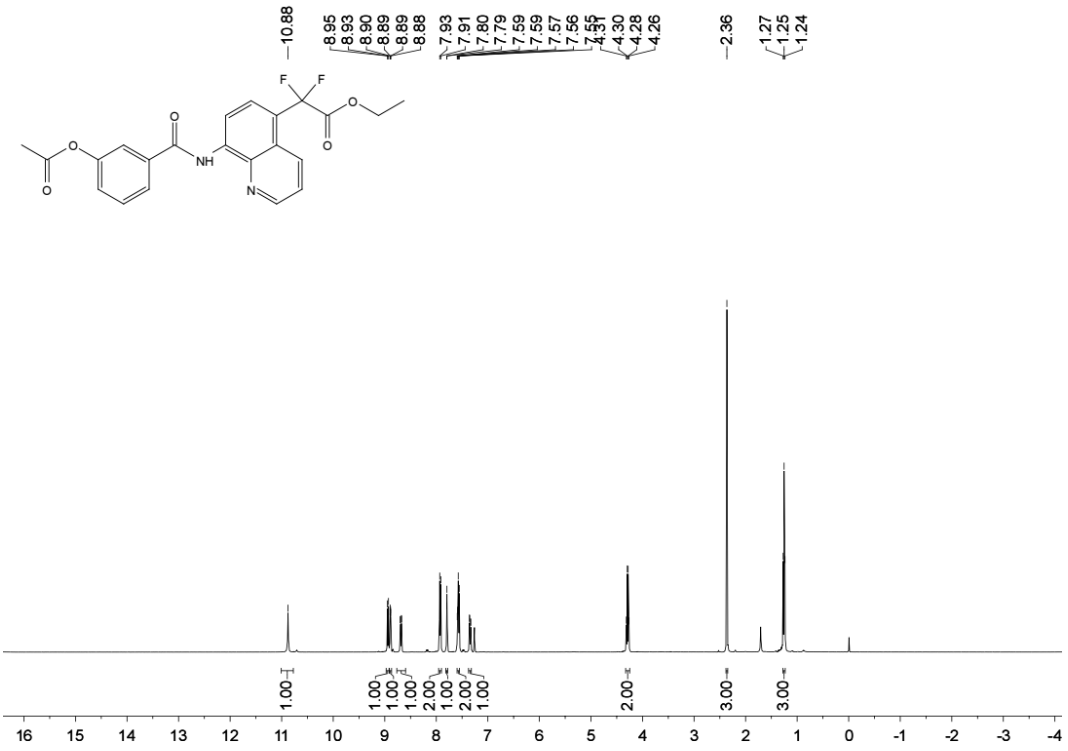


^{19}F NMR for ethyl 2,2-difluoro-2-(8-(4-iodobenzamido)quinolin-5-yl)acetate (**4p**)

^{13}C NMR for ethyl 2,2-difluoro-2-(8-(4-iodobenzamido)quinolin-5-yl)acetate (**4p**)

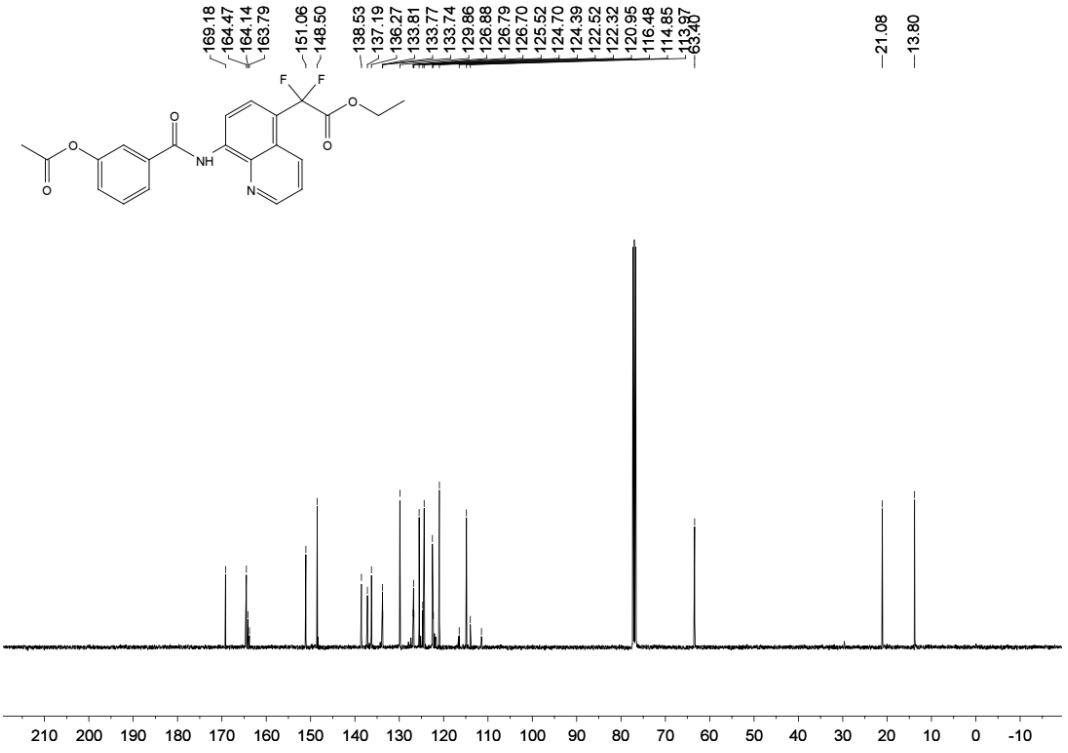


^{1}H NMR for ethyl 2-(8-(3-acetoxybenzamido)quinolin-5-yl)-2,2-difluoroacetate (**4q**)

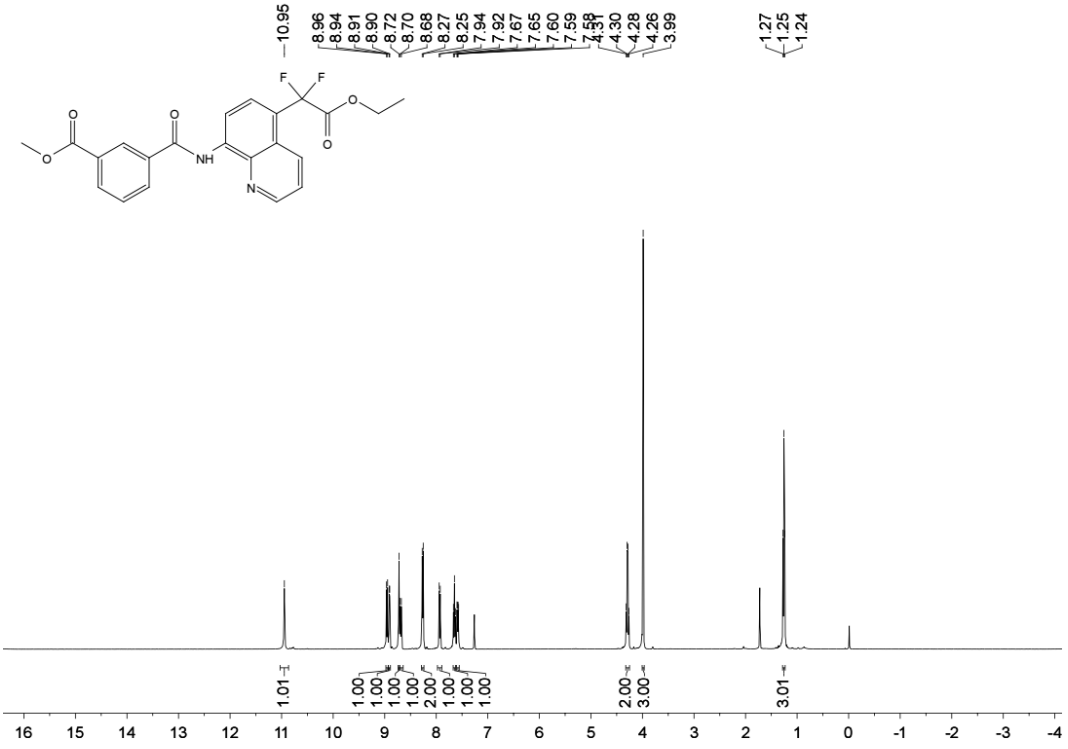


^{19}F NMR for ethyl 2-(8-(3-acetoxybenzamido)quinolin-5-yl)-2,2-difluoroacetate (**4q**)

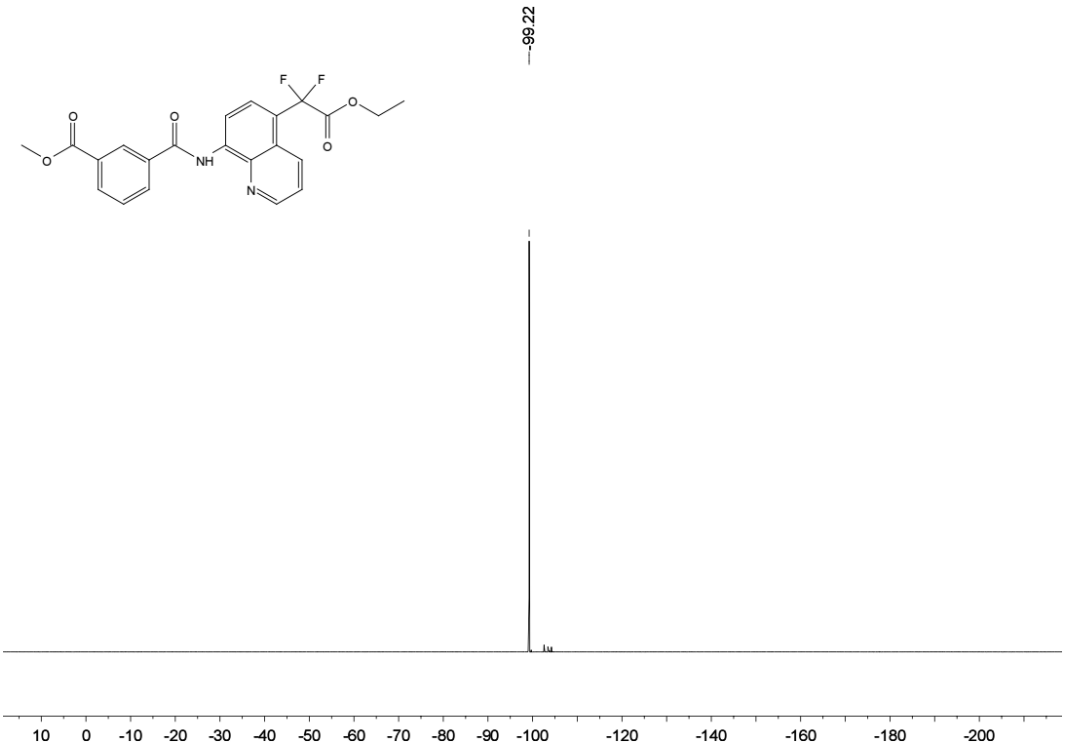
^{13}C NMR for ethyl 2-(8-(3-acetoxybenzamido)quinolin-5-yl)-2,2-difluoroacetate (**4q**)



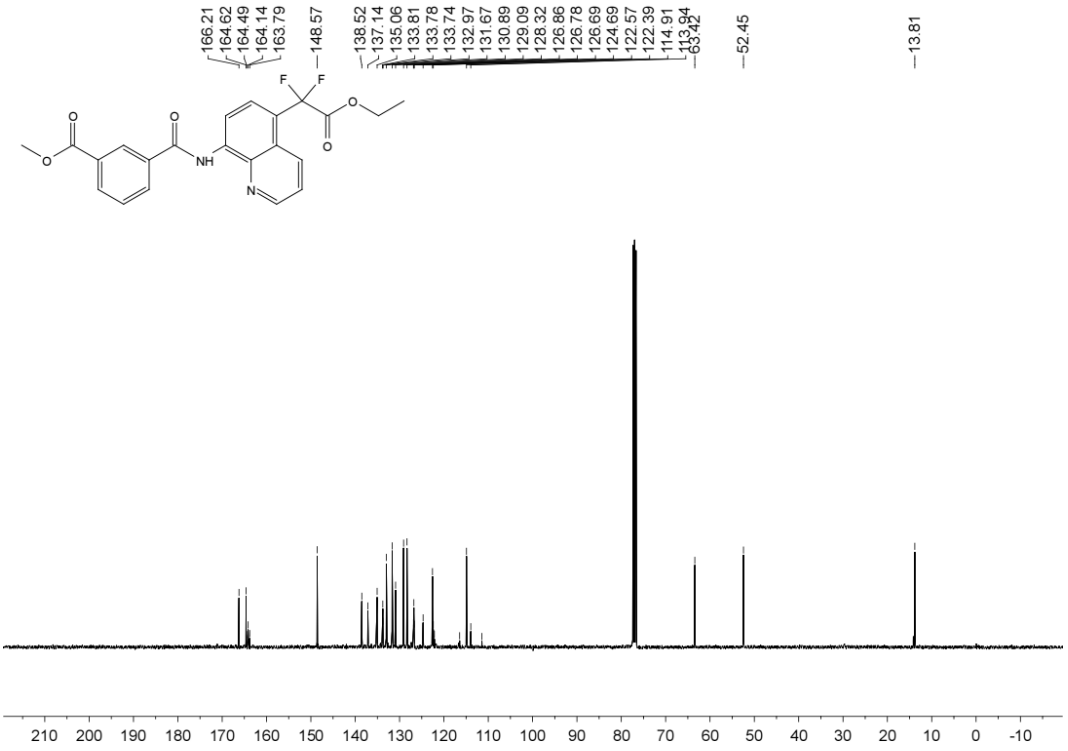
^{1}H NMR for methyl 3-((5-(2-ethoxy-1,1-difluoro-2-oxoethyl)quinolin-8-yl)carbamoyl)benzoate (**4r**)



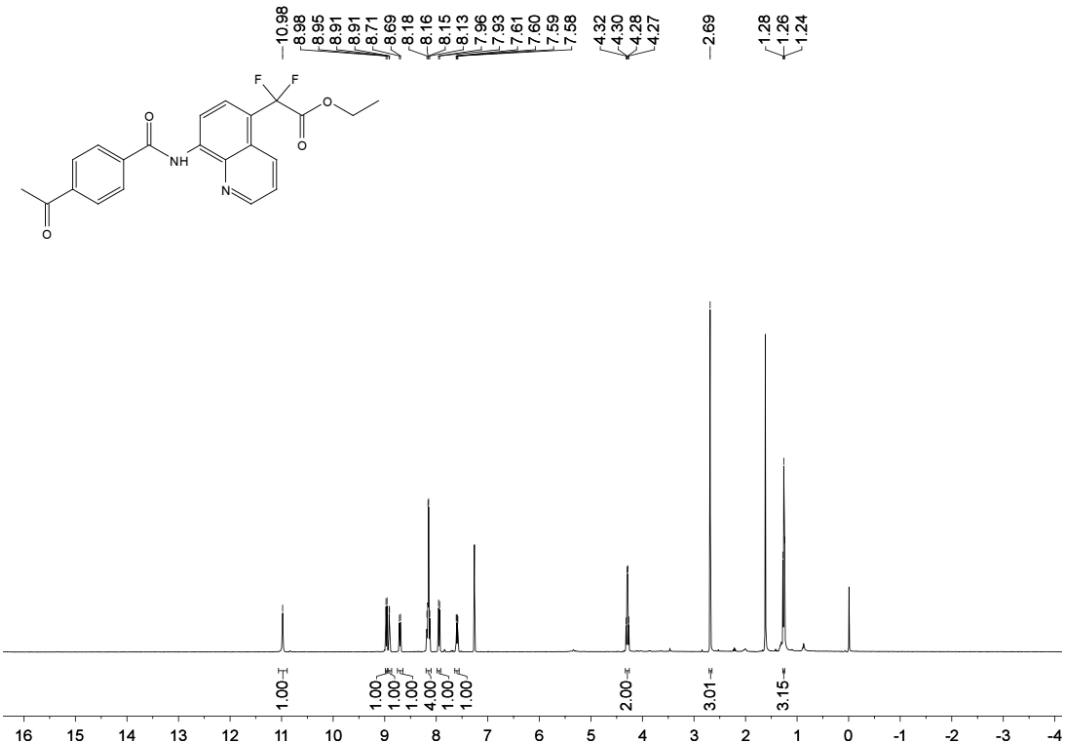
^{19}F NMR for methyl 3-((5-(2-ethoxy-1,1-difluoro-2-oxoethyl)quinolin-8-yl)carbamoyl)benzoate (**4r**)



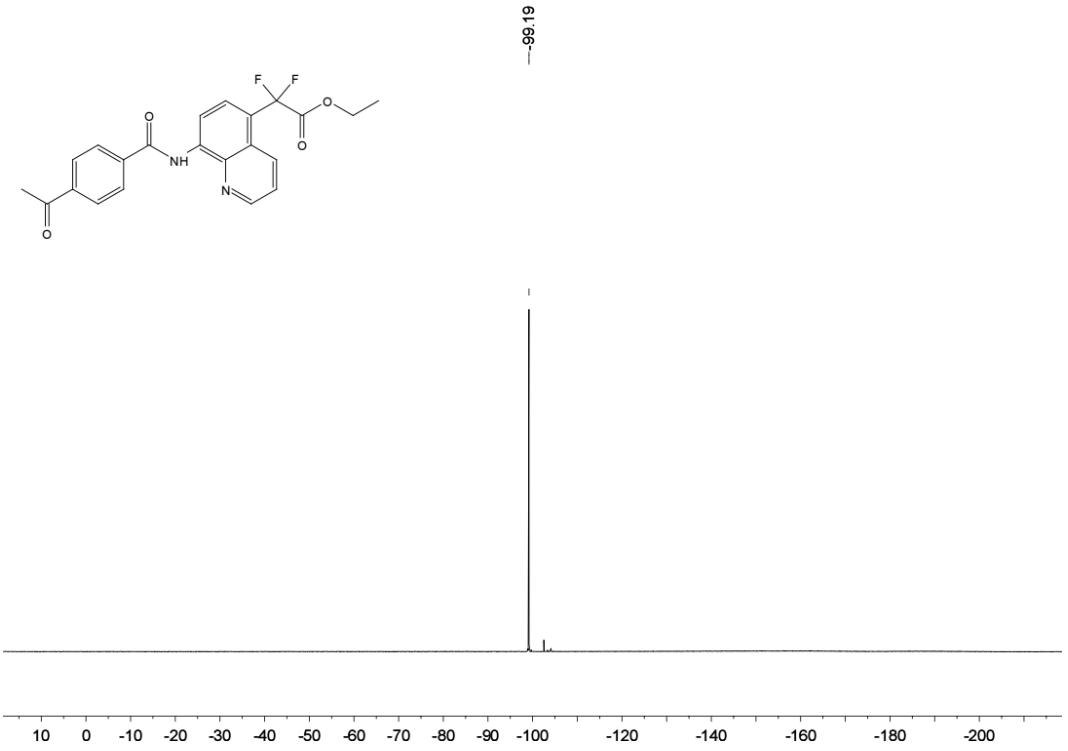
^{13}C NMR for methyl 3-((5-(2-ethoxy-1,1-difluoro-2-oxoethyl)quinolin-8-yl)carbamoyl)benzoate (**4r**)



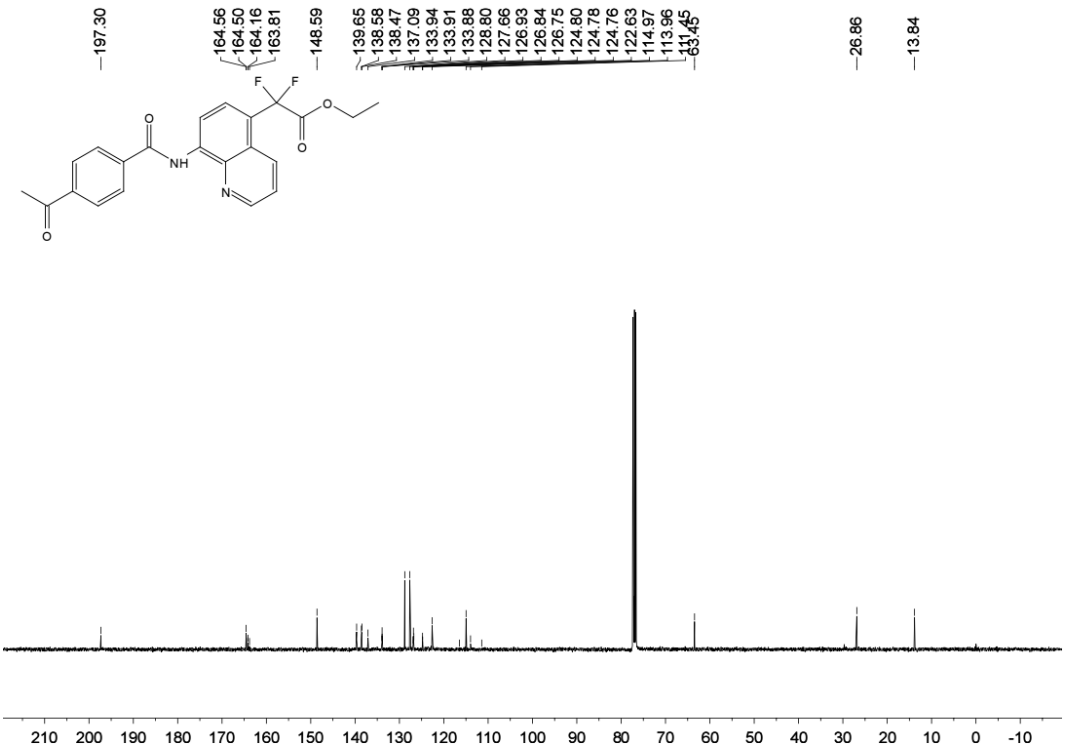
^{1}H NMR for ethyl 2-(8-(4-acetylbenzamido)quinolin-5-yl)-2,2-difluoroacetate (**4s**)



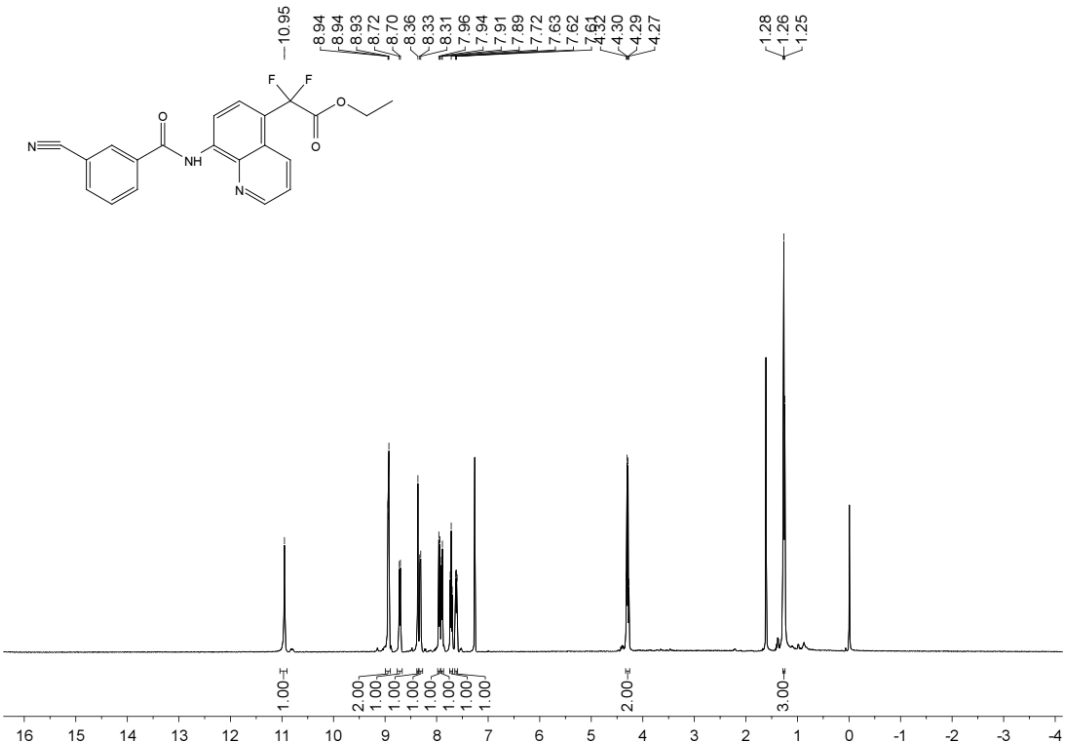
^{19}F NMR for ethyl 2-(8-(4-acetylbenzamido)quinolin-5-yl)-2,2-difluoroacetate (**4s**)



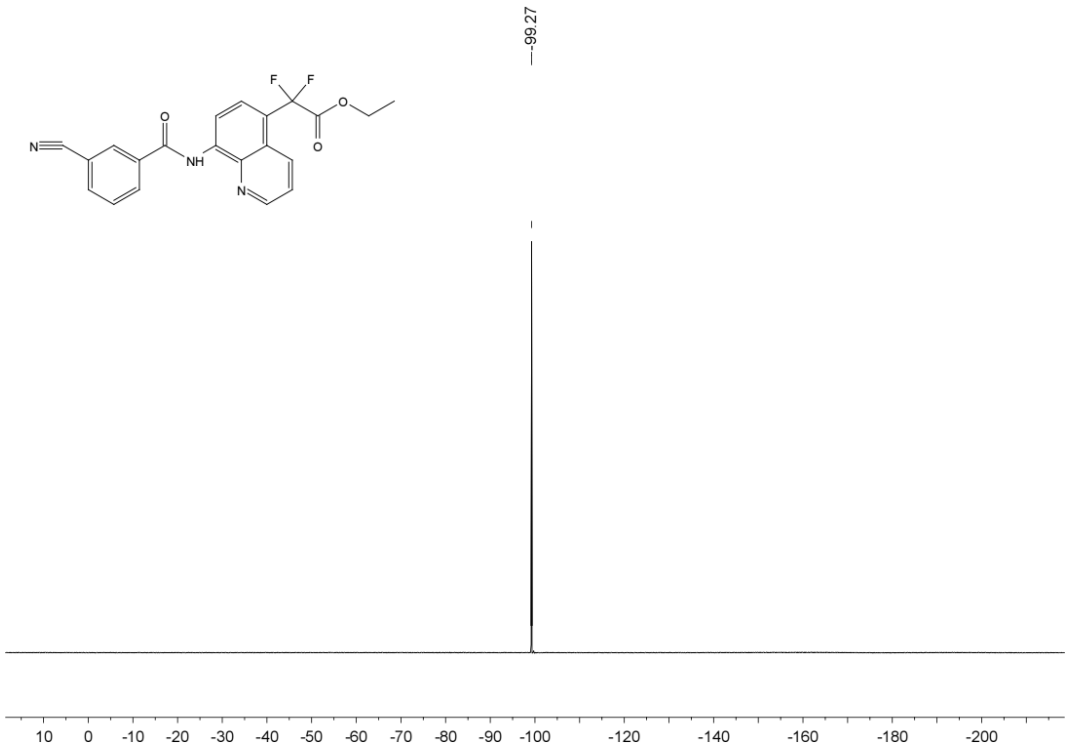
^{13}C NMR for ethyl 2-(8-(4-acetylbenzamido)quinolin-5-yl)-2,2-difluoroacetate (**4s**)



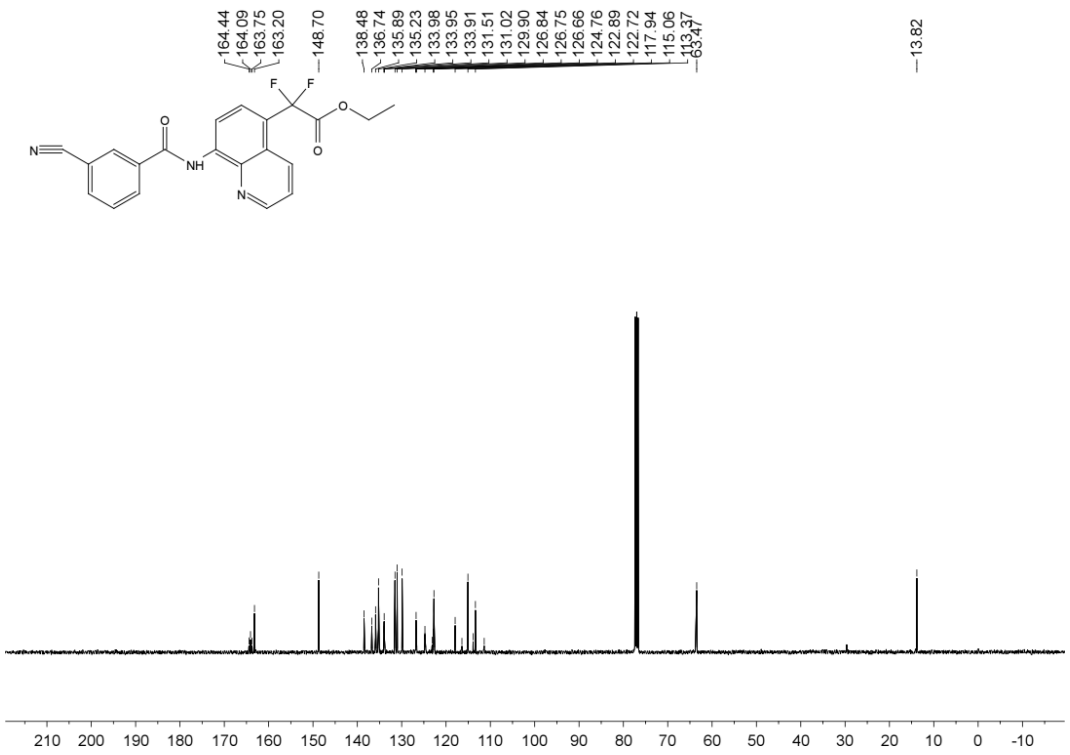
^{1}H NMR for ethyl 2-(8-(3-cyanobenzamido)quinolin-5-yl)-2,2-difluoroacetate (**4t**)



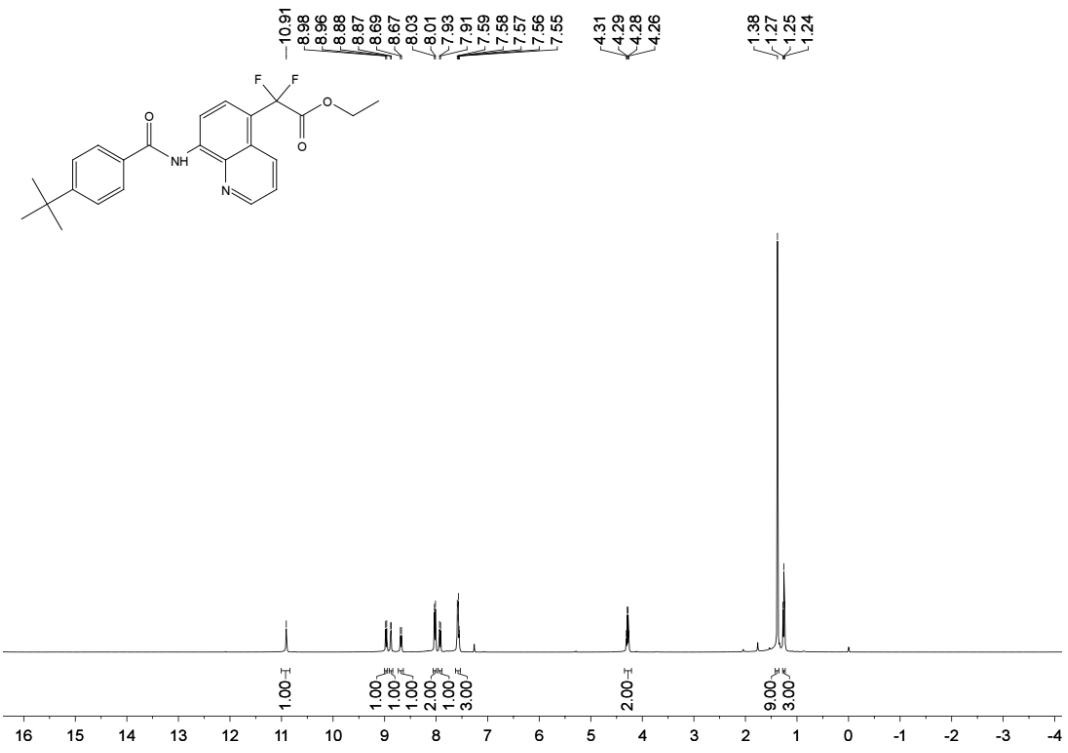
^{19}F NMR for ethyl 2-(8-(3-cyanobenzamido)quinolin-5-yl)-2,2-difluoroacetate (**4t**)



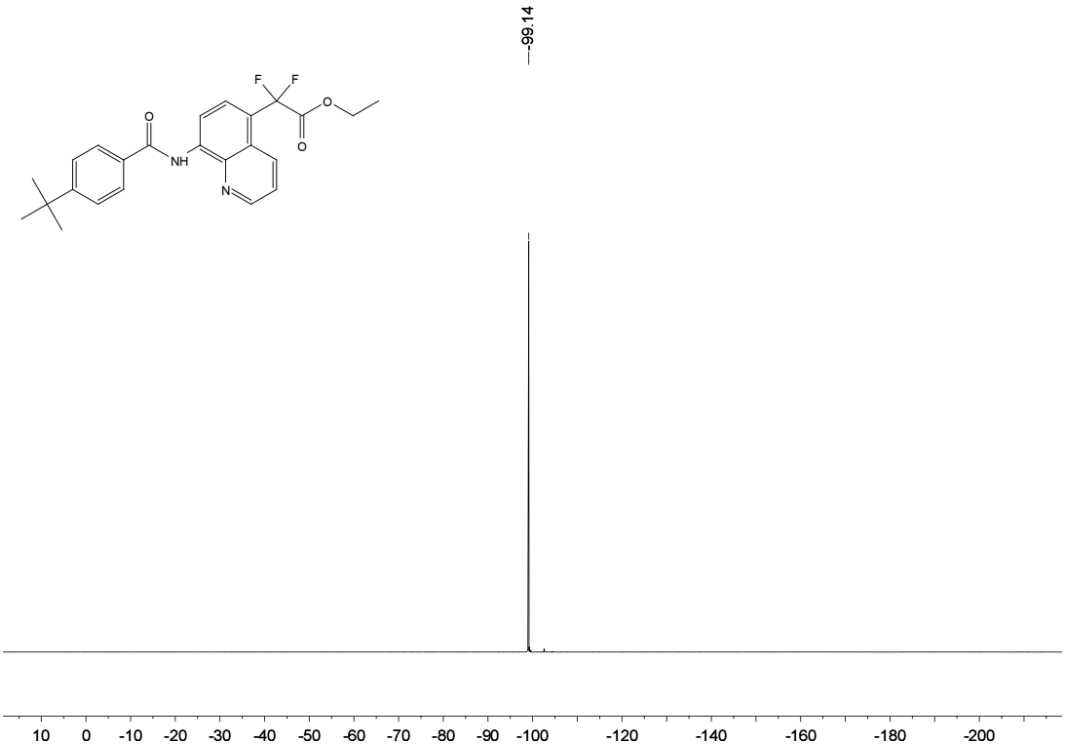
^{13}C NMR for ethyl 2-(8-(3-cyanobenzamido)quinolin-5-yl)-2,2-difluoroacetate (**4t**)



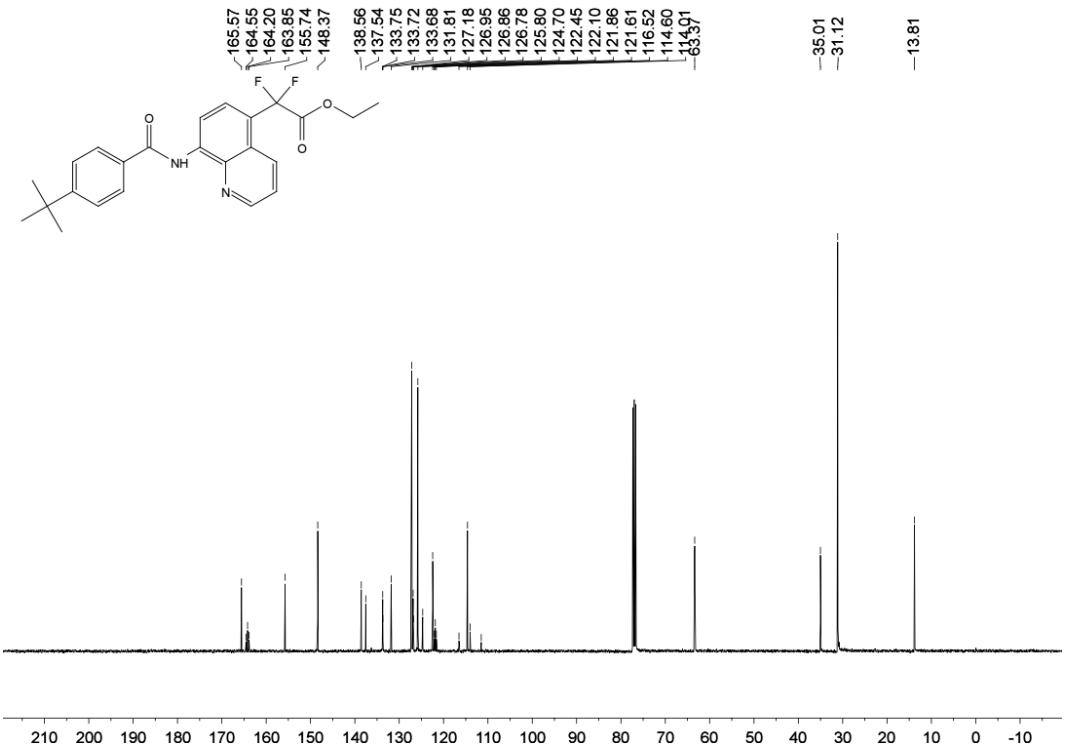
^{1}H NMR for ethyl 2-(8-(4-(tert-butyl)benzamido)quinolin-5-yl)-2,2-difluoroacetate (**4u**)



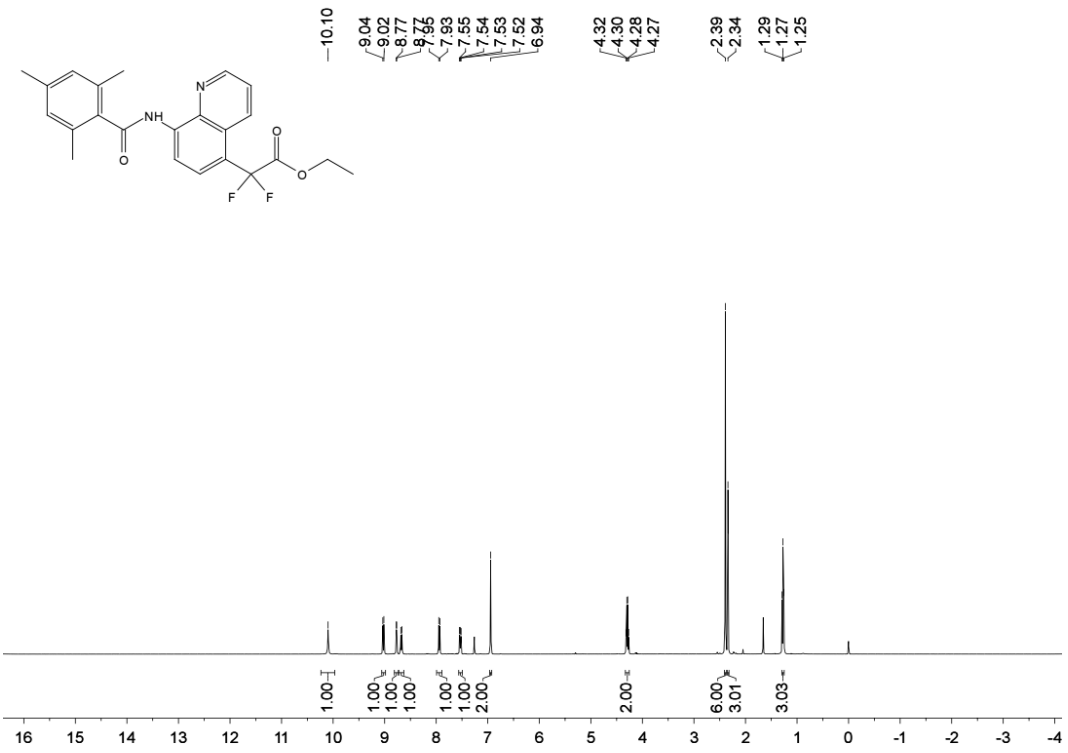
^{19}F NMR for ethyl 2-(8-(4-(tert-butyl)benzamido)quinolin-5-yl)-2,2-difluoroacetate (**4u**)



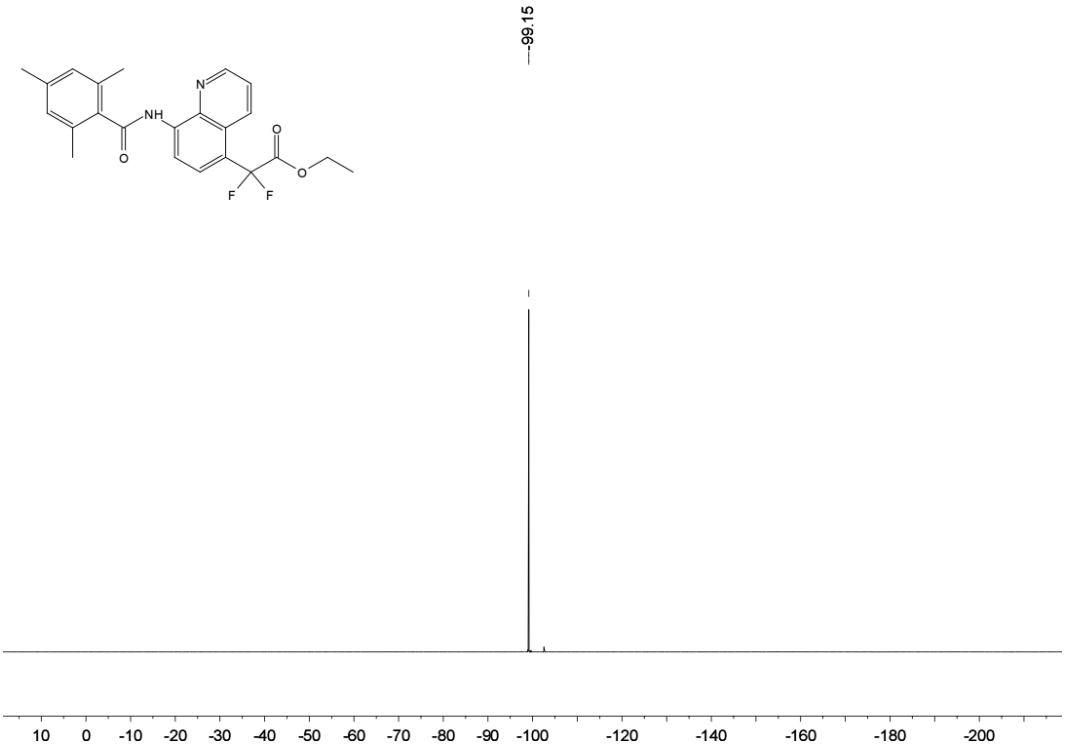
^{13}C NMR for ethyl 2-(8-(4-(tert-butyl)benzamido)quinolin-5-yl)-2,2-difluoroacetate (**4u**)



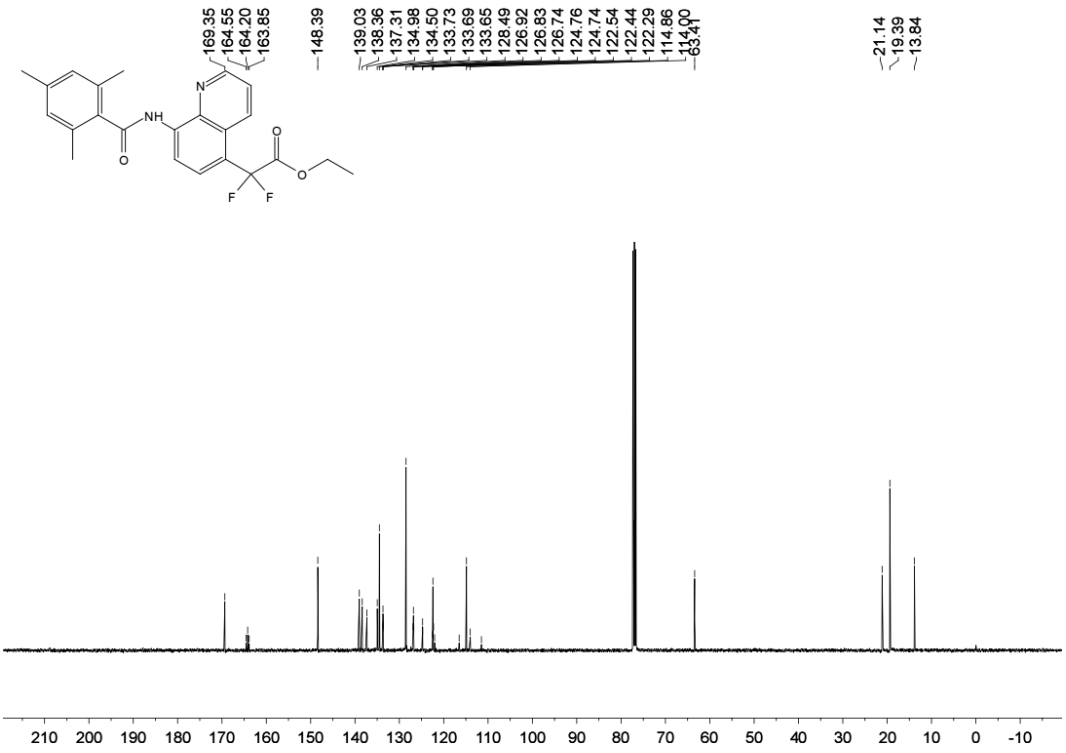
^{1}H NMR for ethyl 2,2-difluoro-2-(8-(2,4,6-trimethylbenzamido)quinolin-5-yl)acetate (**4v**)



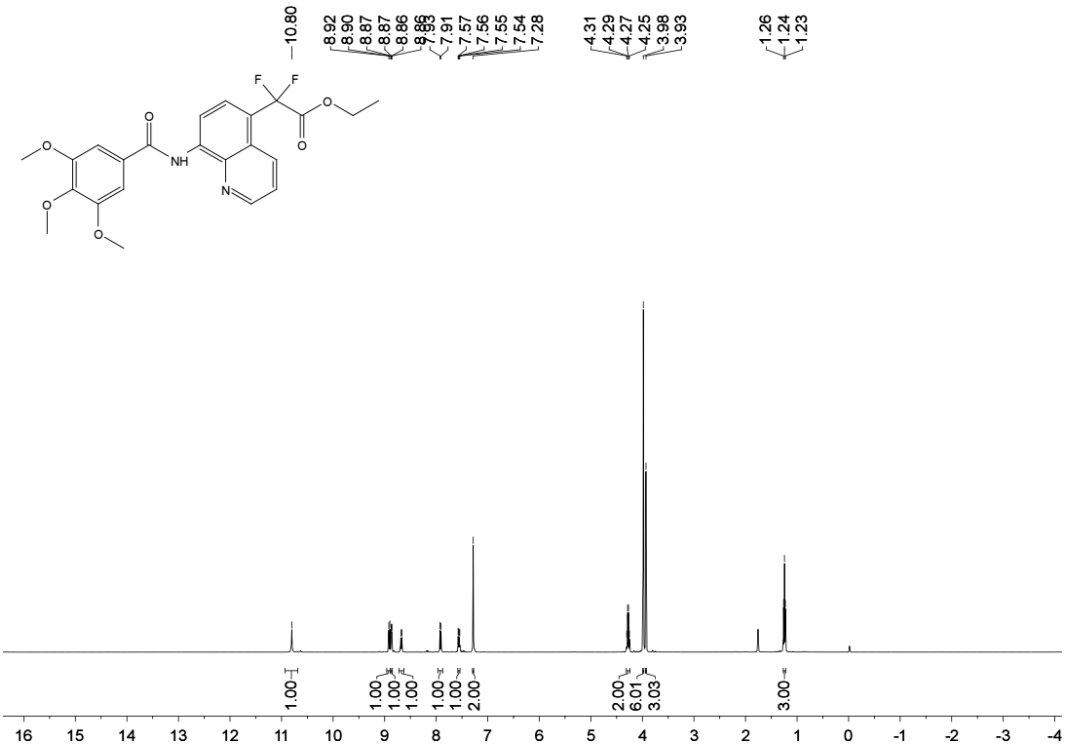
^{19}F NMR for ethyl 2,2-difluoro-2-(8-(2,4,6-trimethylbenzamido)quinolin-5-yl)acetate (**4v**)



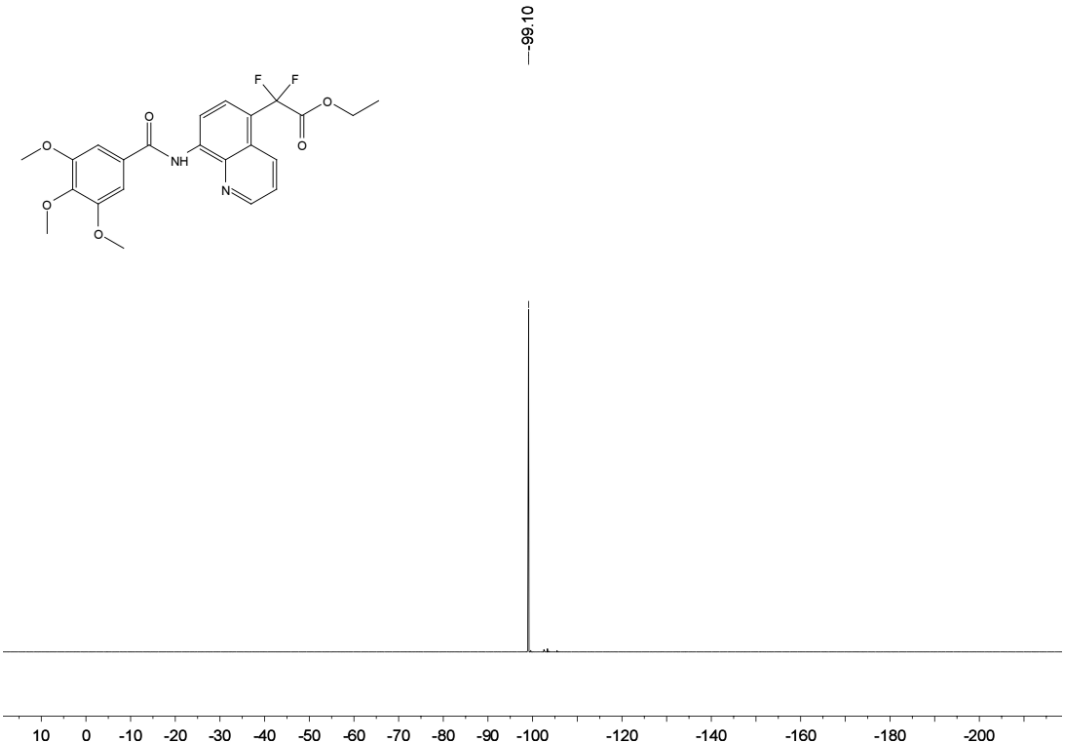
^{13}C NMR for ethyl 2,2-difluoro-2-(8-(2,4,6-trimethylbenzamido)quinolin-5-yl)acetate (**4v**)



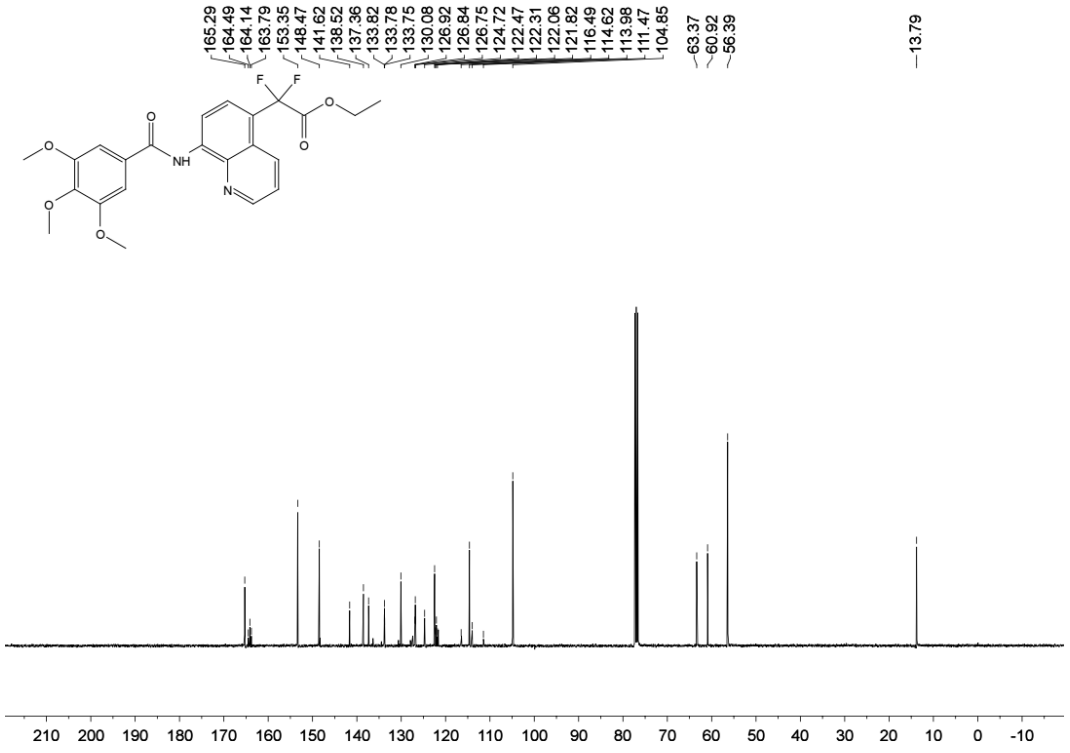
^{1}H NMR for ethyl 2,2-difluoro-2-(8-(3,4,5-trimethoxybenzamido)quinolin-5-yl)acetate (**4w**)



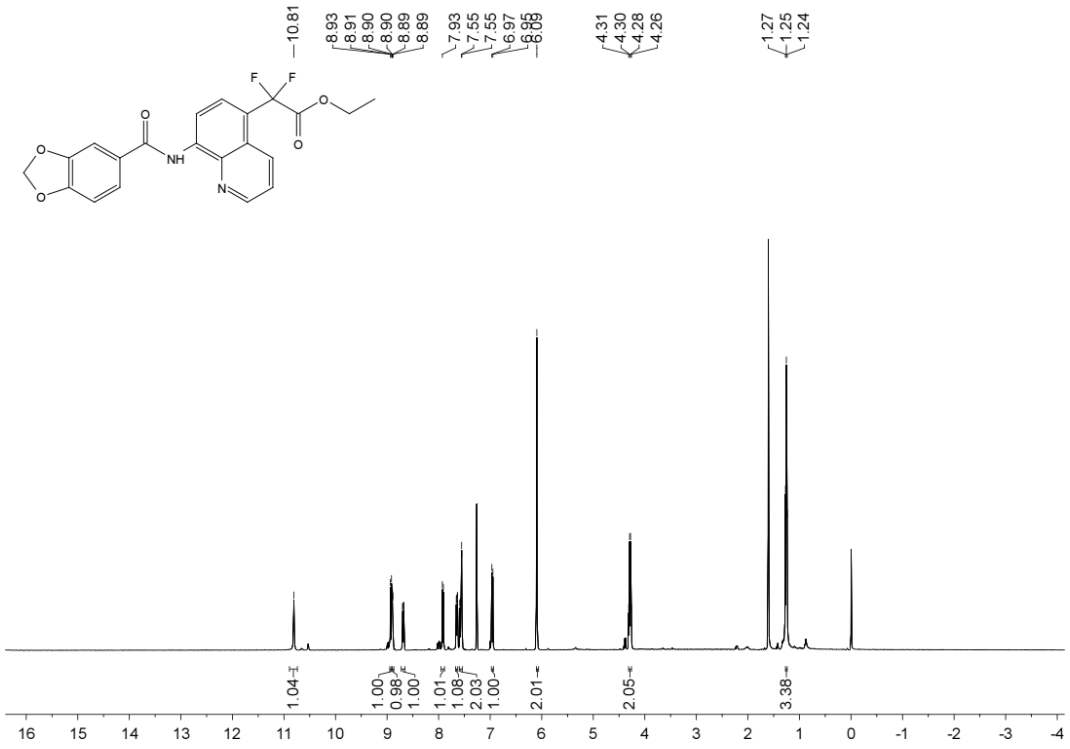
^{19}F NMR for ethyl 2,2-difluoro-2-(8-(3,4,5-trimethoxybenzamido)quinolin-5-yl)acetate (**4w**)



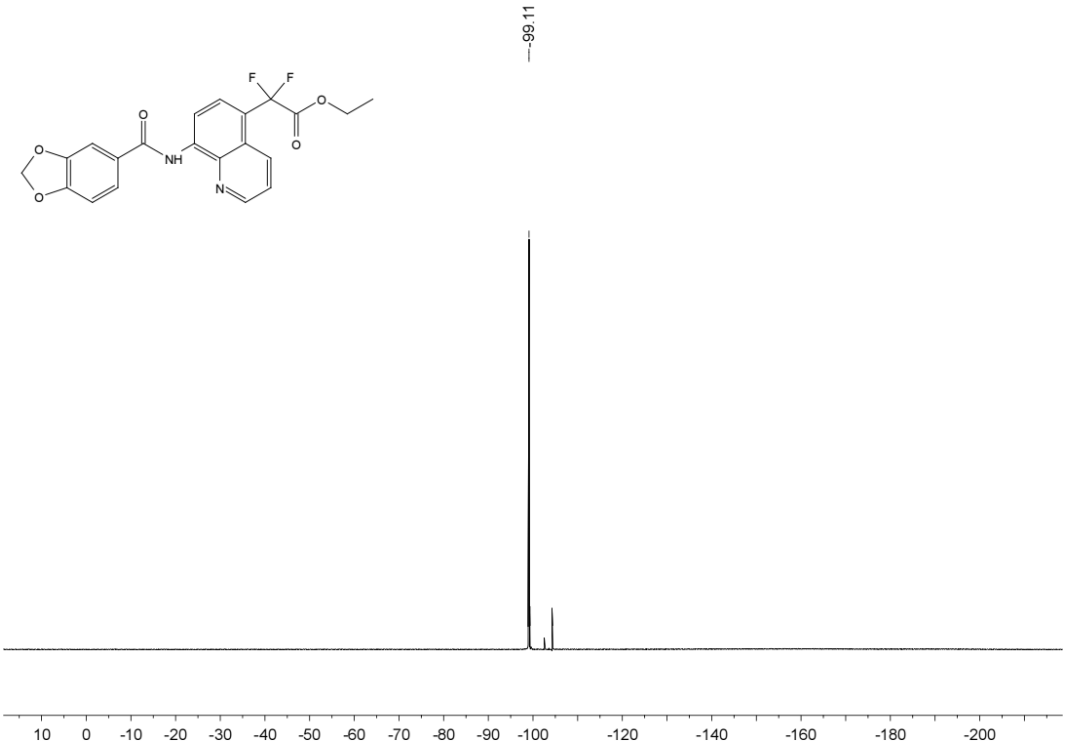
^{13}C NMR for ethyl 2,2-difluoro-2-(8-(3,4,5-trimethoxybenzamido)quinolin-5-yl)acetate (**4w**)



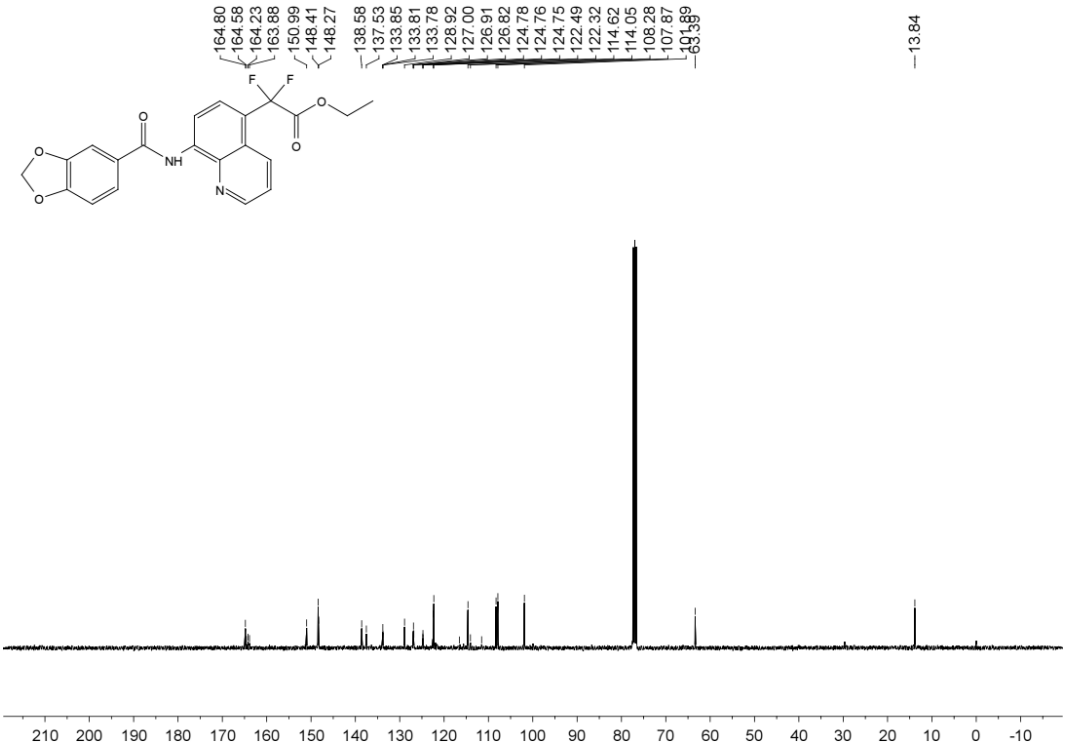
^{1}H NMR for ethyl 2-(8-(benzo[d][1,3]dioxole-5-carboxamido)quinolin-5-yl)-2,2-difluoroacetate (**4x**)



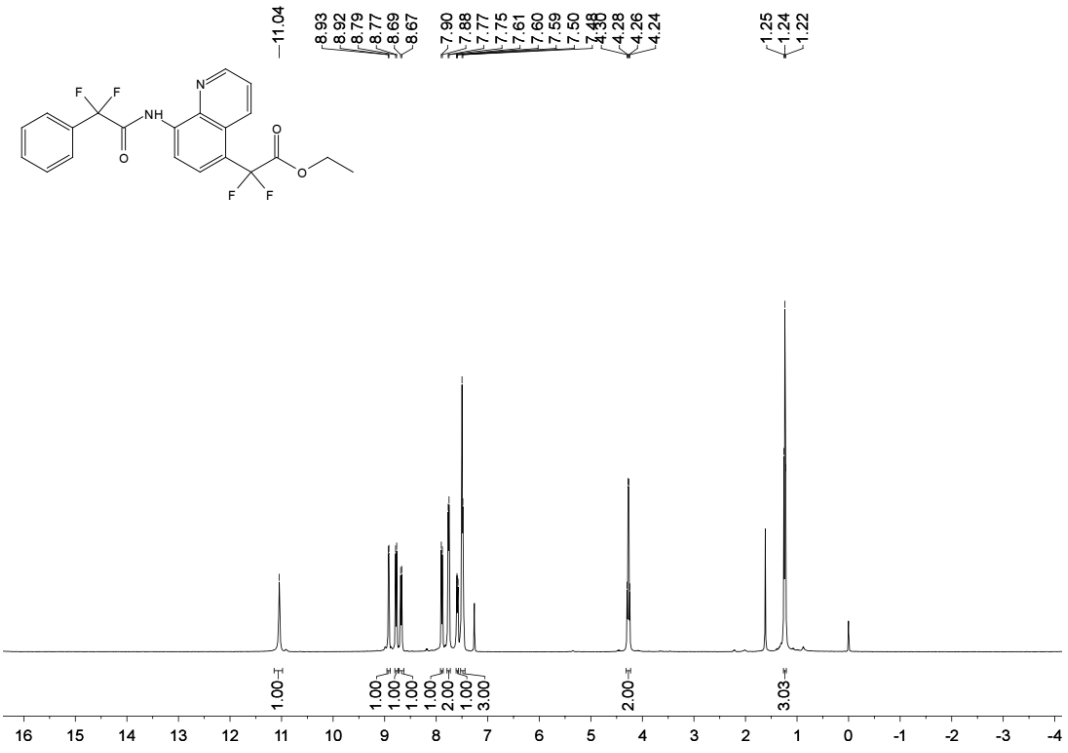
^{19}F NMR for ethyl 2-(8-(benzo[d][1,3]dioxole-5-carboxamido)quinolin-5-yl)-2,2-difluoroacetate (**4x**)



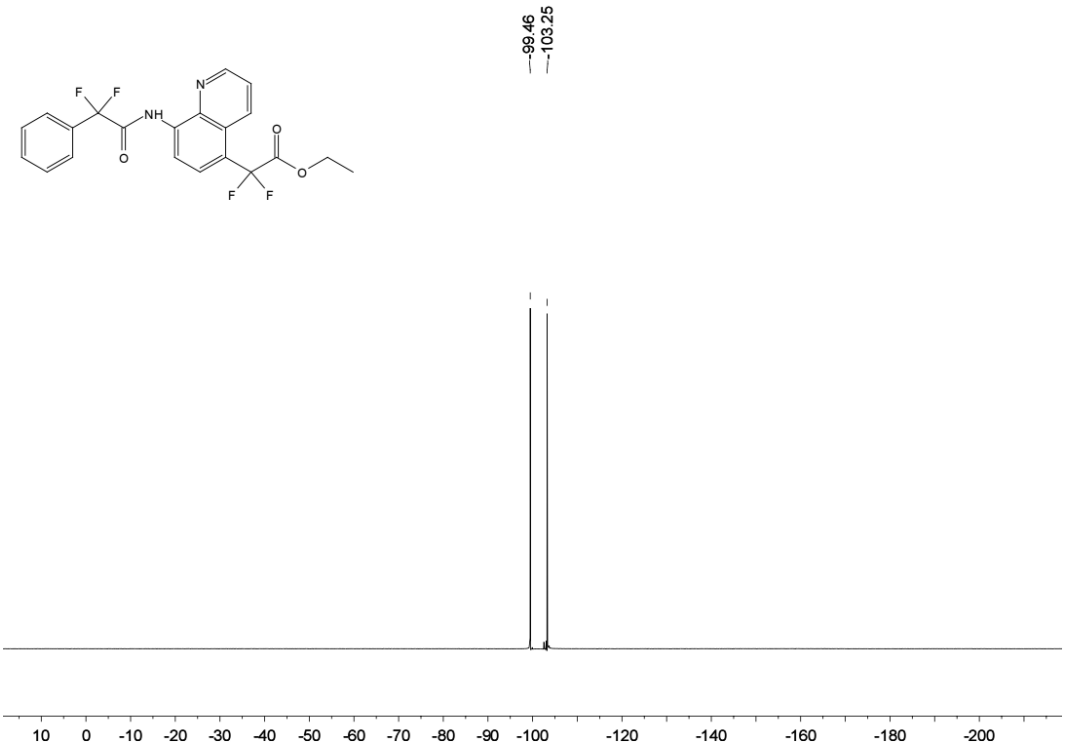
^{13}C NMR for ethyl 2-(8-(benzo[d][1,3]dioxole-5-carboxamido)quinolin-5-yl)-2,2-difluoroacetate (**4x**)



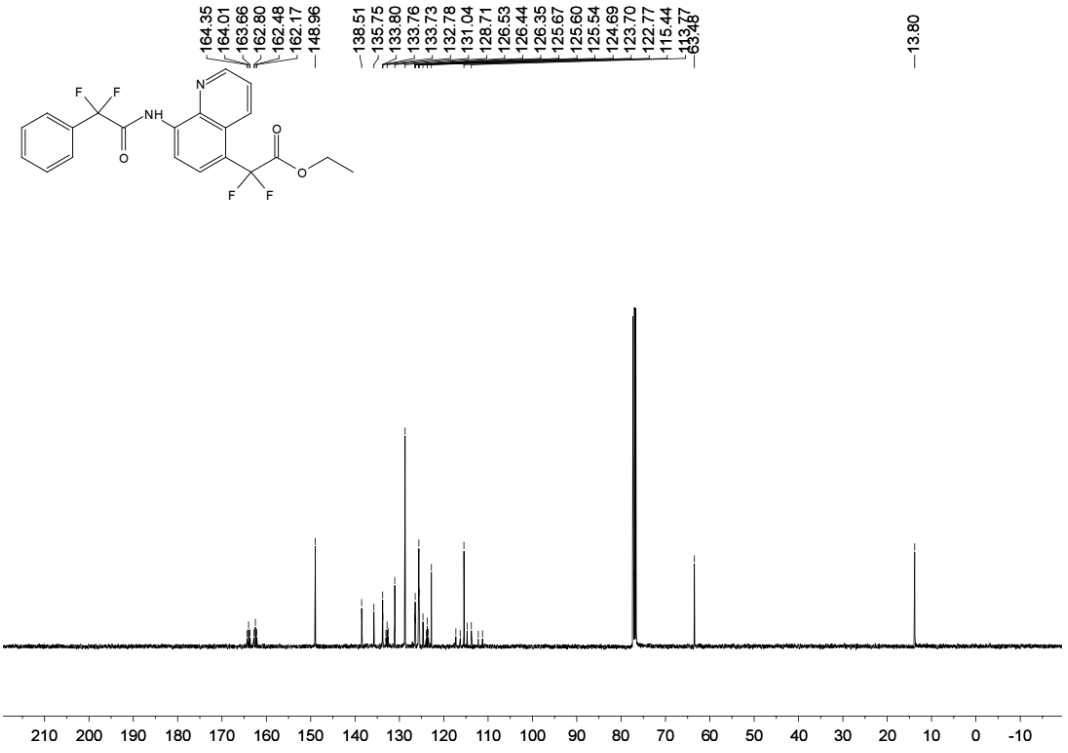
^{1}H NMR for ethyl 2-(8-(2,2-difluoro-2-phenylacetamido)quinolin-5-yl)-2,2-difluoroacetate (**4y**)



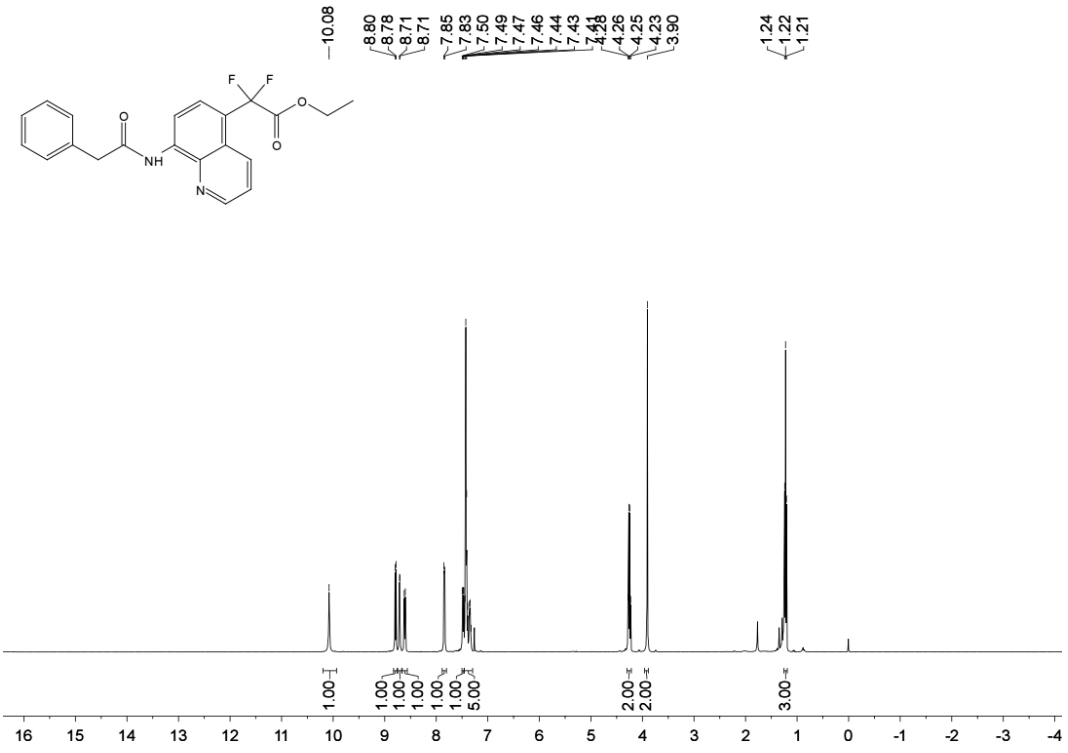
^{19}F NMR for ethyl 2-(8-(2,2-difluoro-2-phenylacetamido)quinolin-5-yl)-2,2-difluoroacetate (**4y**)



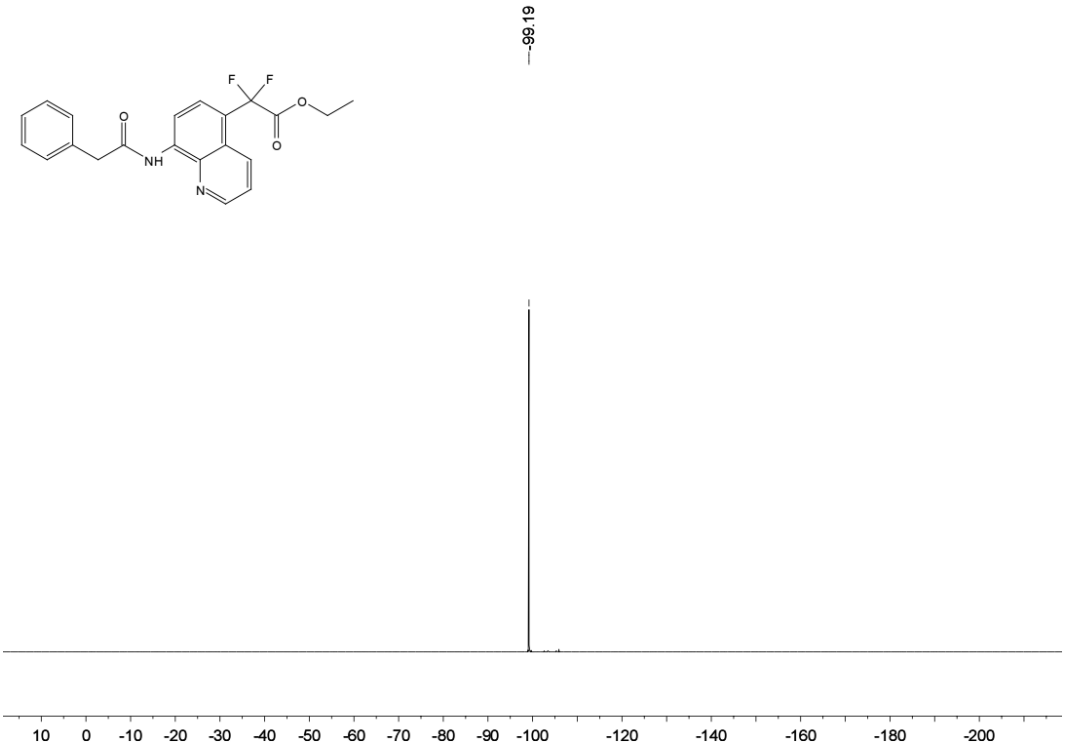
^{13}C NMR for ethyl 2-(8-(2,2-difluoro-2-phenylacetamido)quinolin-5-yl)-2,2-difluoroacetate (**4y**)



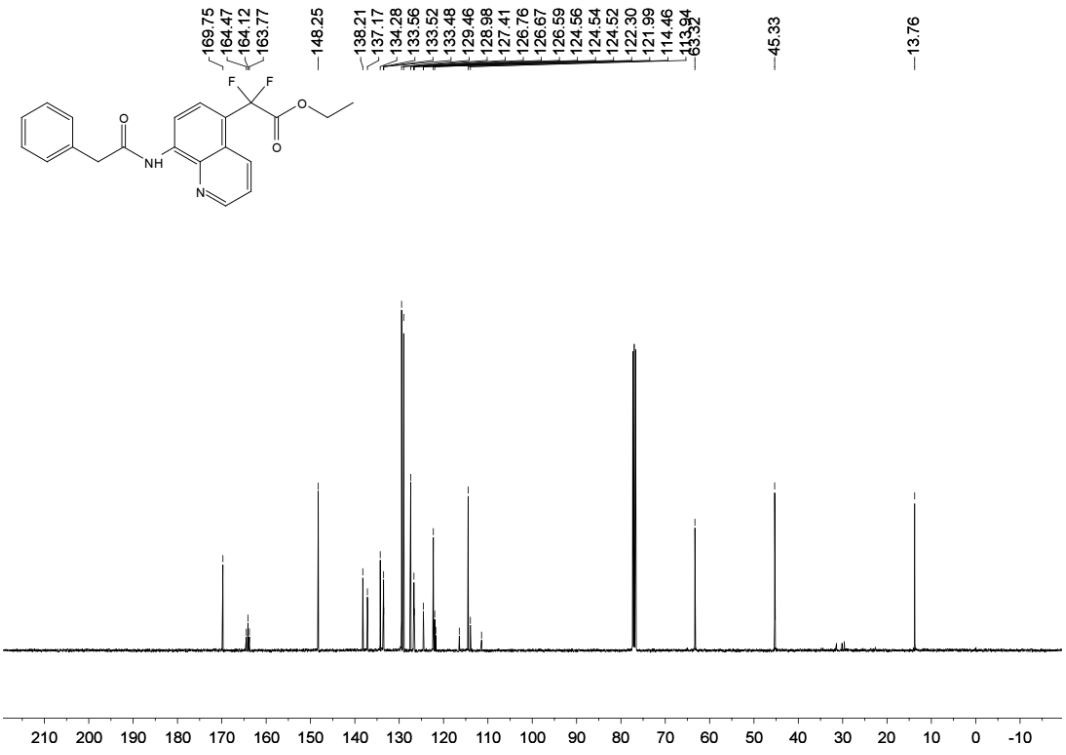
^{1}H NMR for ethyl 2,2-difluoro-2-(8-(2-phenylacetamido)quinolin-5-yl)acetate (**4z**)



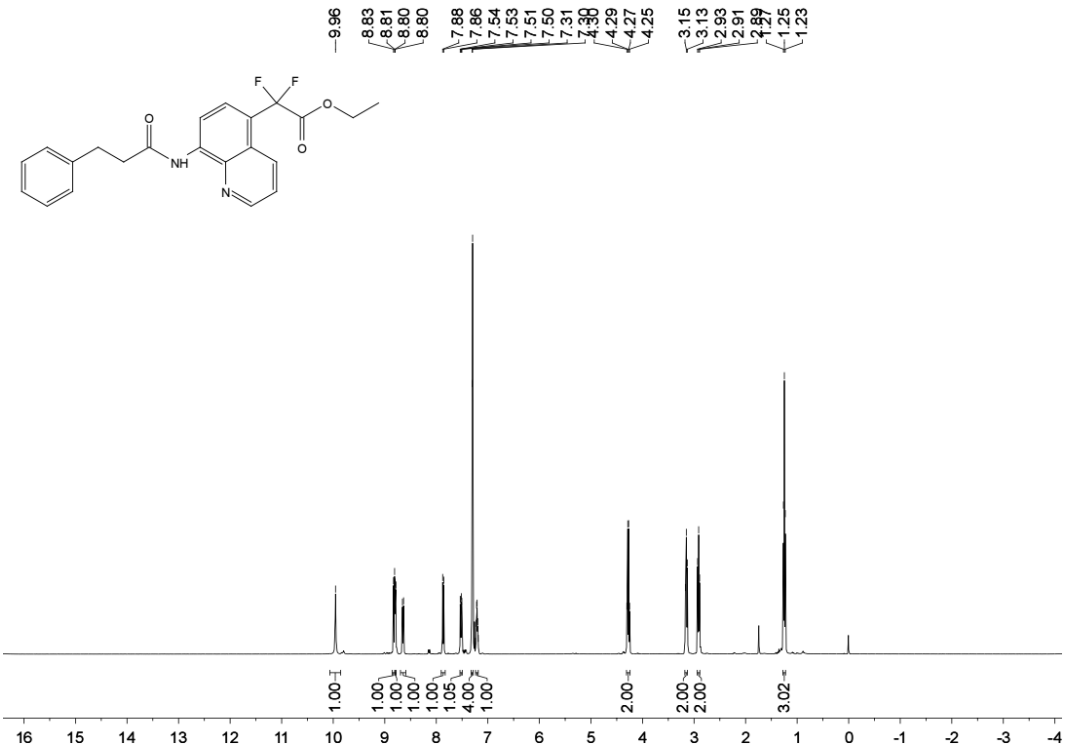
^{19}F NMR for ethyl 2,2-difluoro-2-(8-(2-phenylacetamido)quinolin-5-yl)acetate (**4z**)



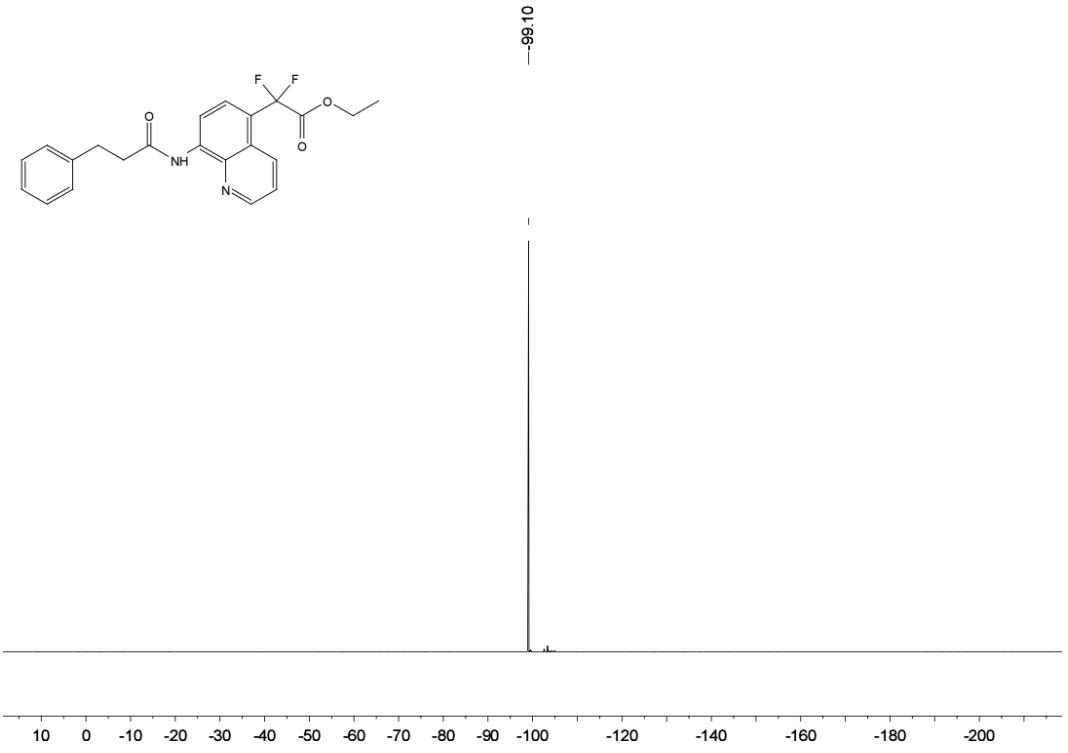
^{13}C NMR for ethyl 2,2-difluoro-2-(8-(2-phenylacetamido)quinolin-5-yl)acetate (**4z**)



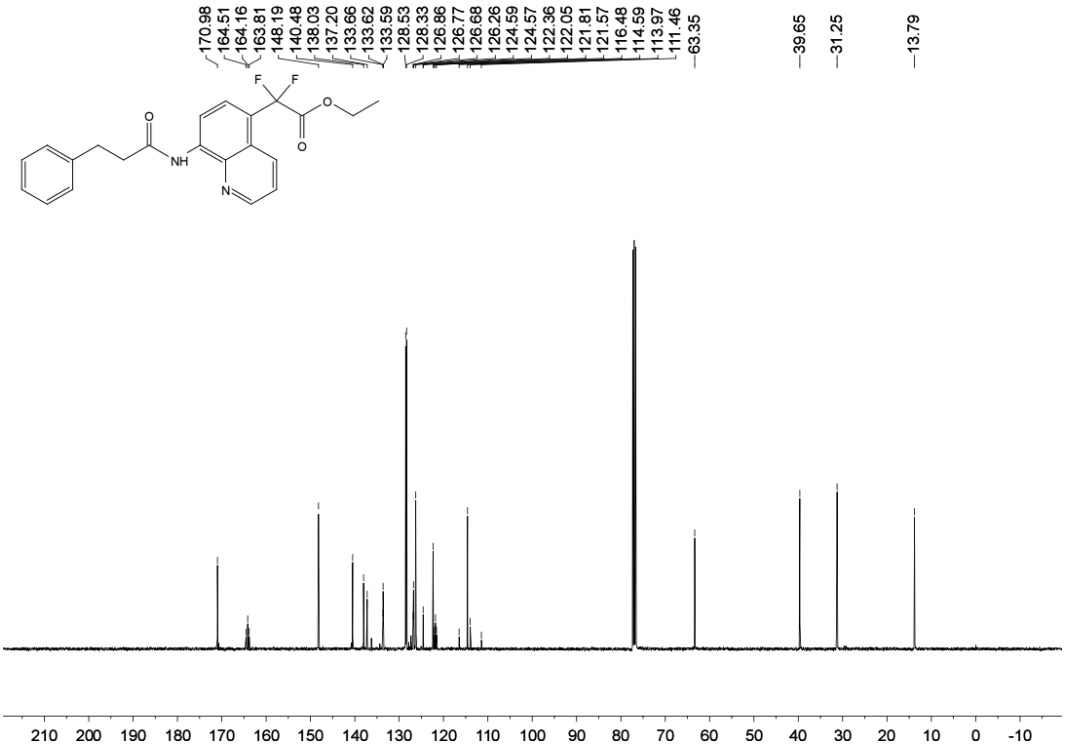
^{1}H NMR for ethyl 2,2-difluoro-2-(8-(3-phenylpropanamido)quinolin-5-yl)acetate (**4aa**)



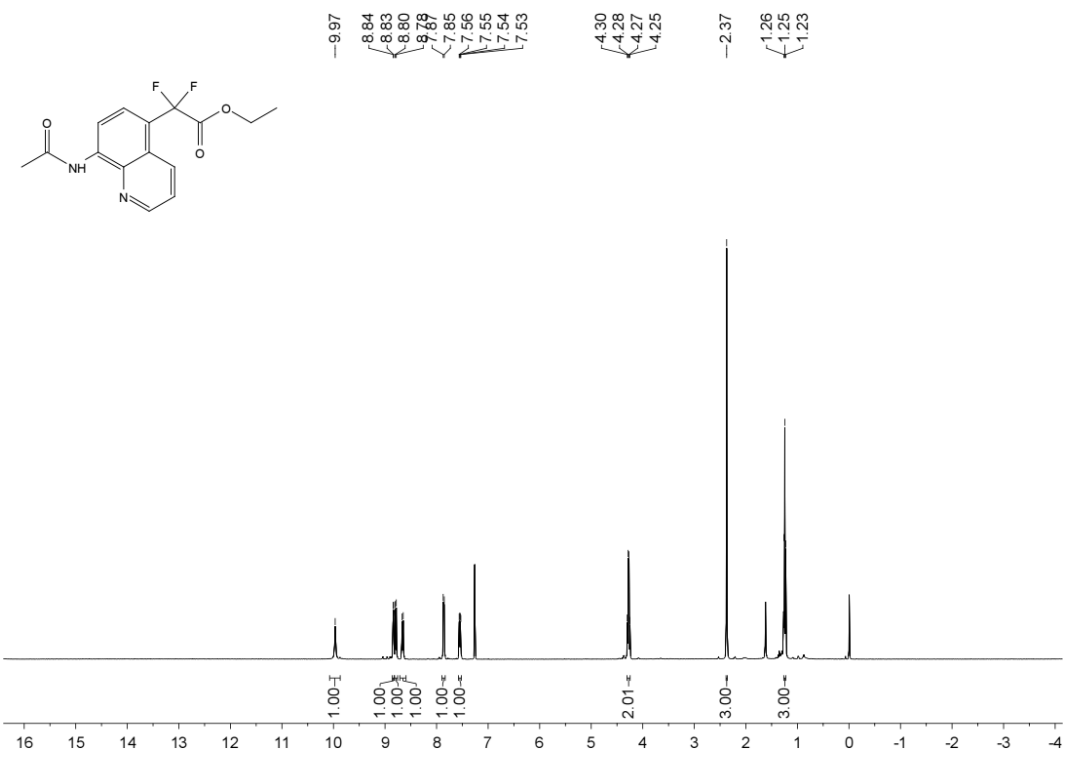
^{19}F NMR for ethyl 2,2-difluoro-2-(8-(3-phenylpropanamido)quinolin-5-yl)acetate (**4aa**)



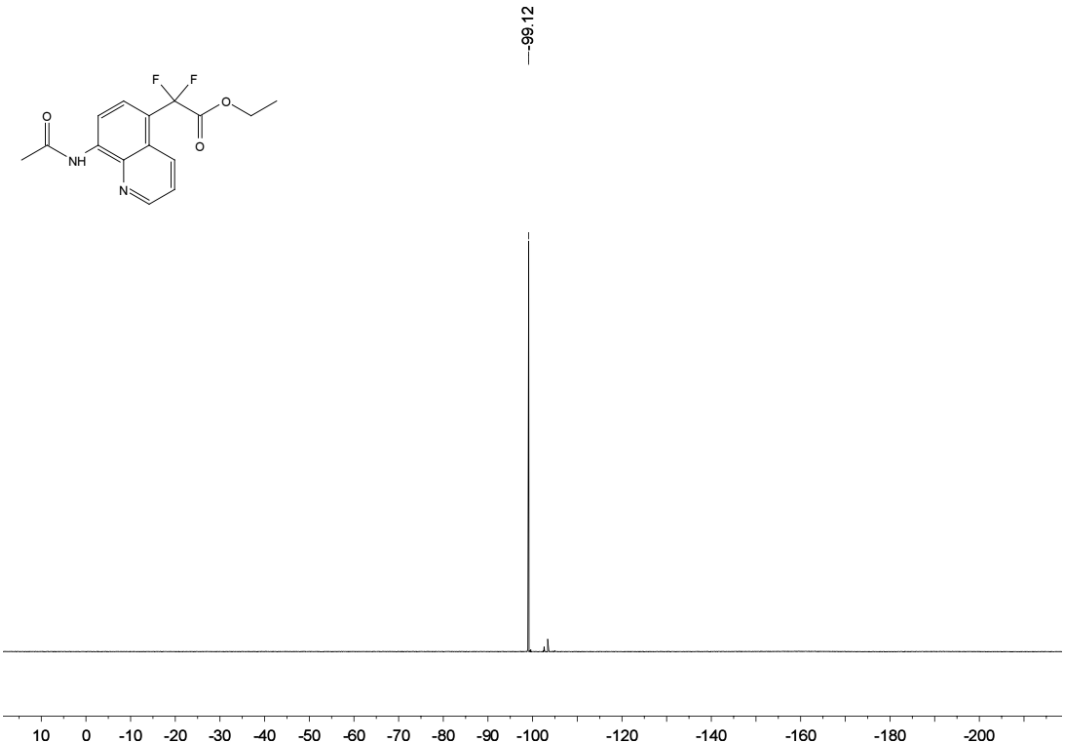
^{13}C NMR for ethyl 2,2-difluoro-2-(8-(3-phenylpropanamido)quinolin-5-yl)acetate (**4aa**)



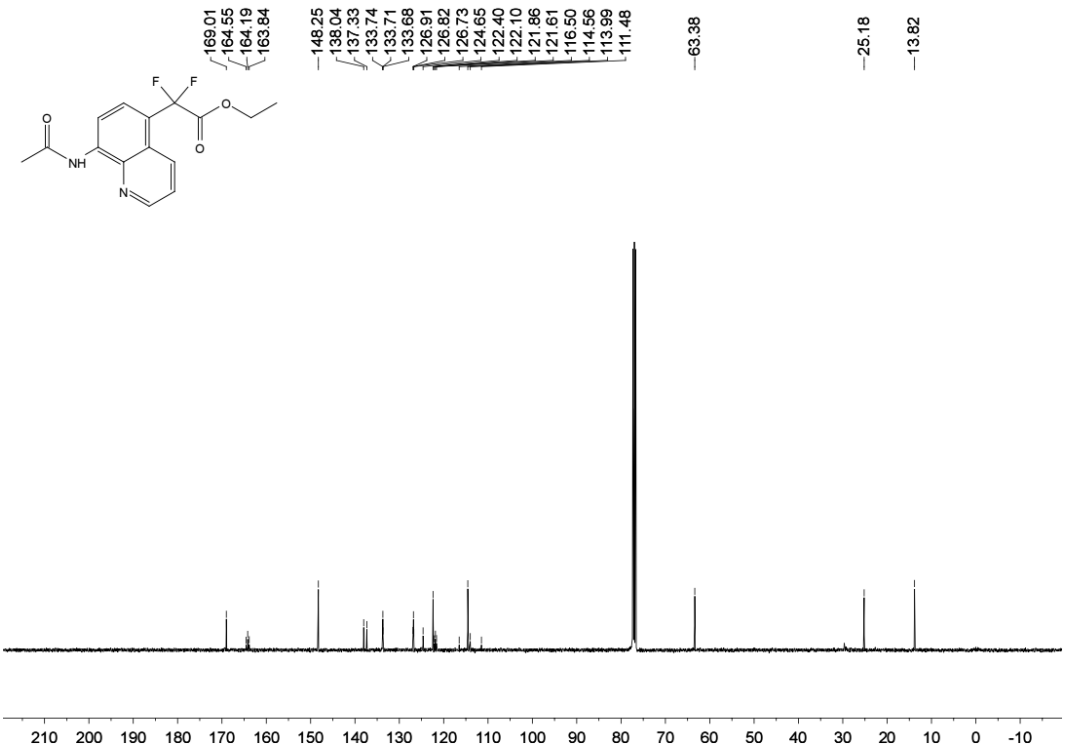
^{1}H NMR for ethyl 2-(8-acetamidoquinolin-5-yl)-2,2-difluoroacetate (**4ab**)



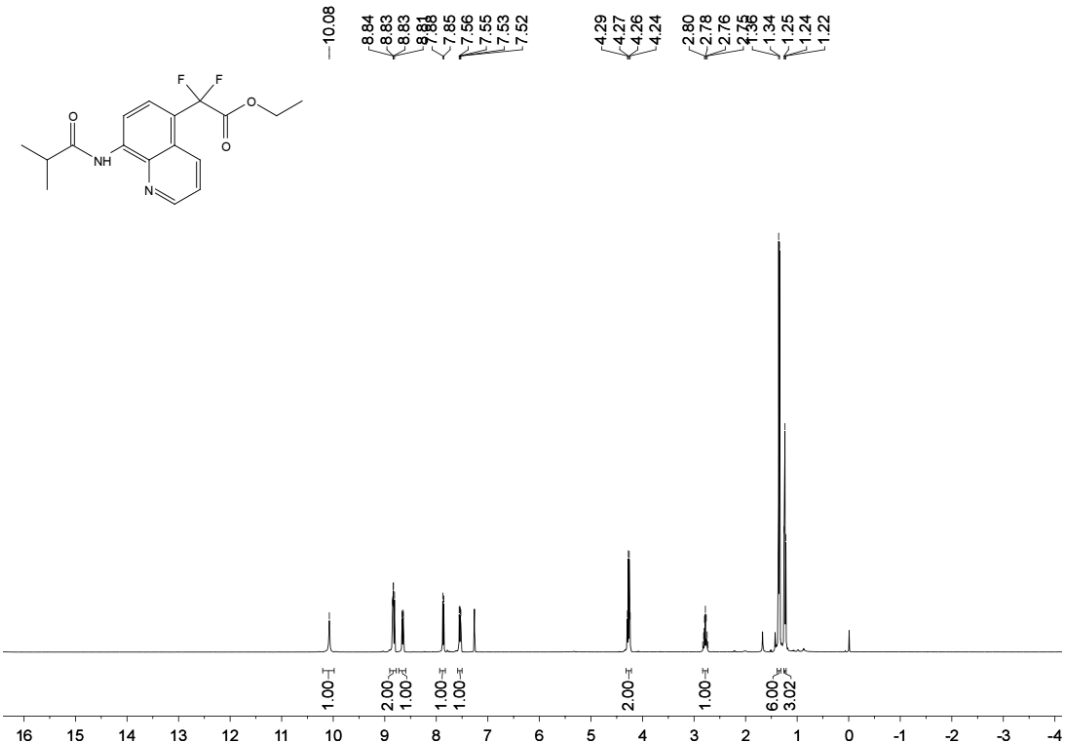
^{19}F NMR for ethyl 2-(8-acetamidoquinolin-5-yl)-2,2-difluoroacetate (**4ab**)



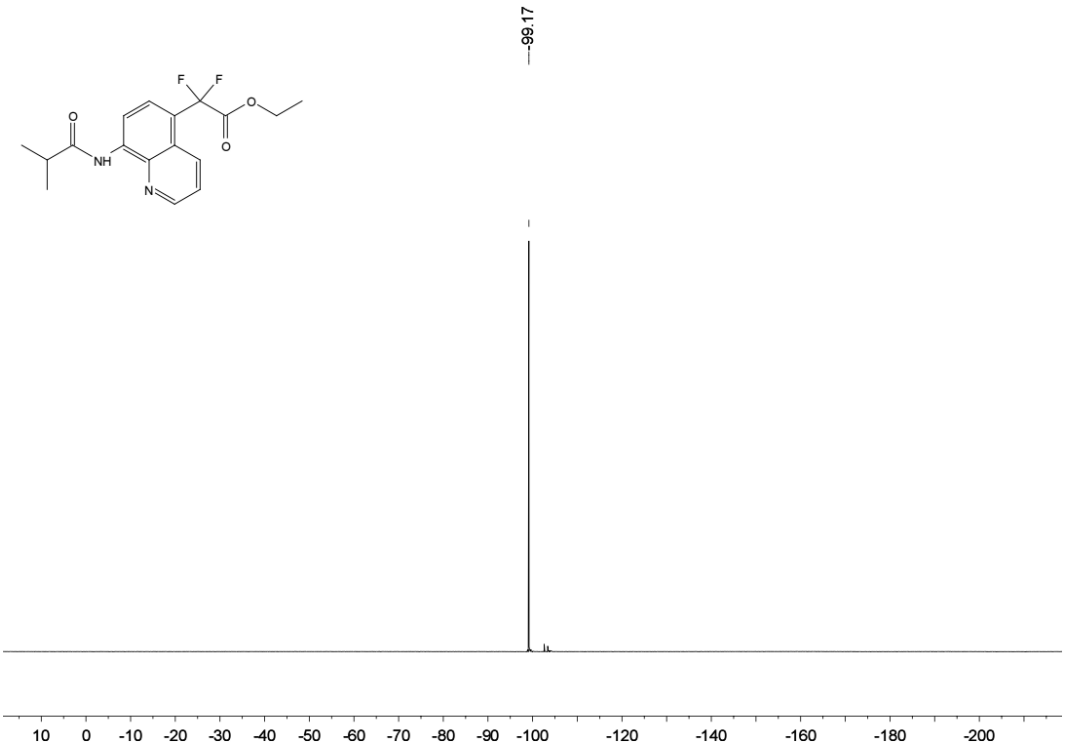
^{13}C NMR for ethyl 2-(8-acetamidoquinolin-5-yl)-2,2-difluoroacetate (**4ab**)



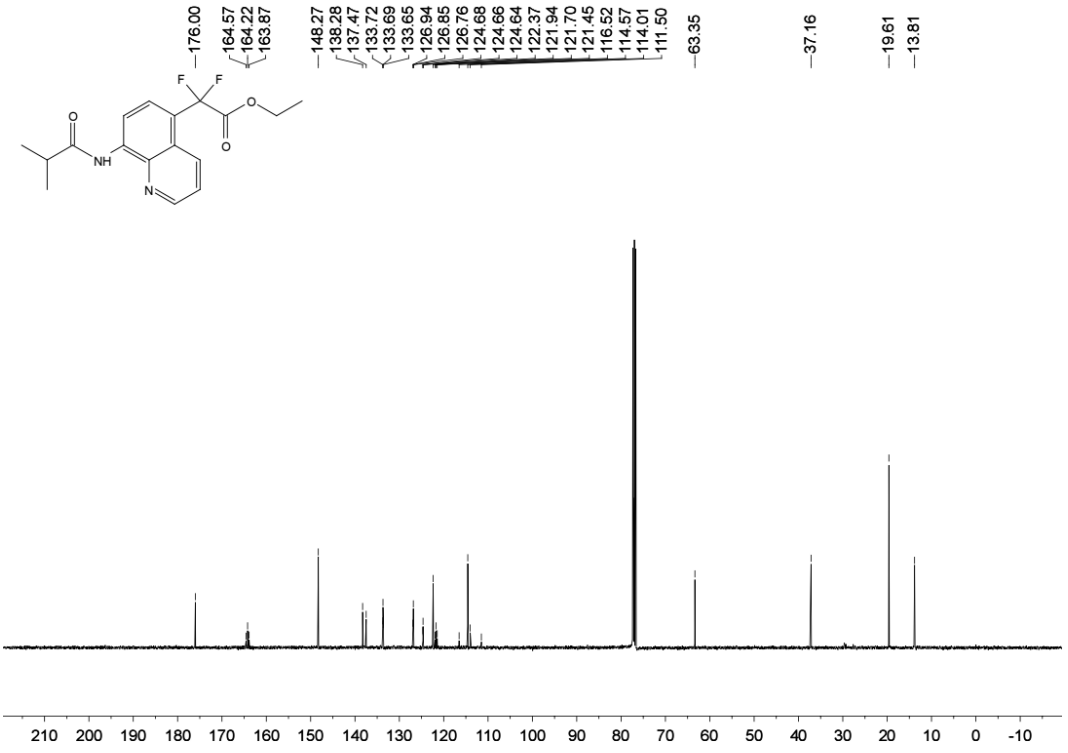
^{1}H NMR for ethyl 2,2-difluoro-2-(8-isobutyramidoquinolin-5-yl)acetate (**4ac**)



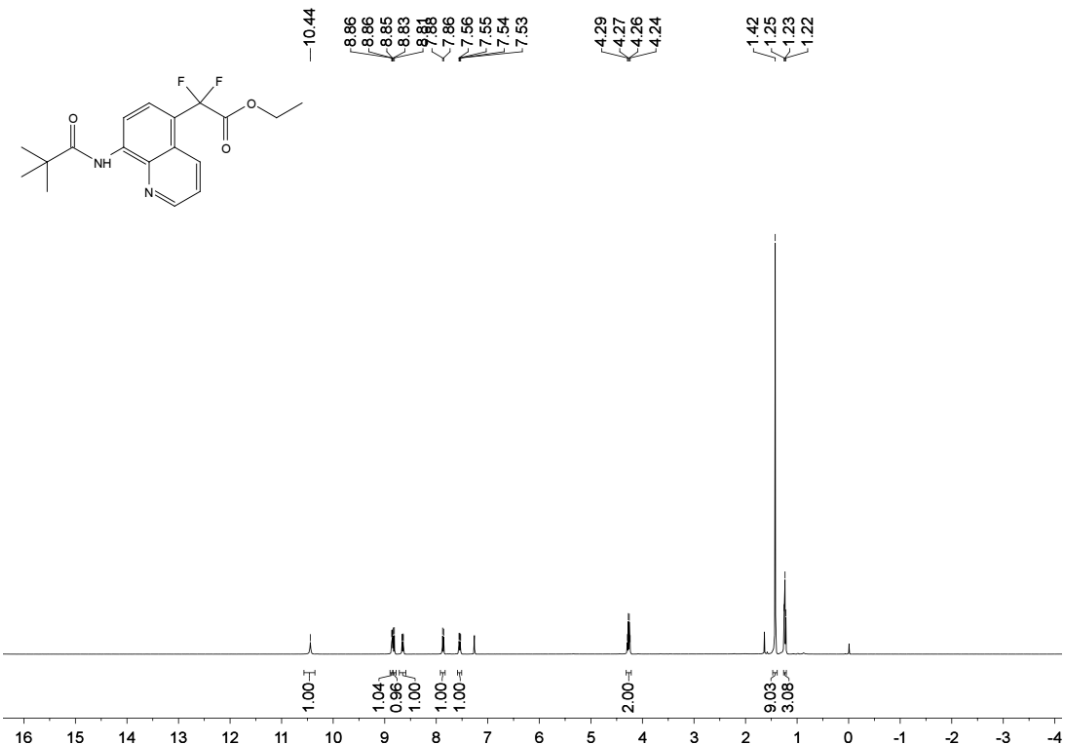
^{19}F NMR for ethyl 2,2-difluoro-2-(8-isobutyramidoquinolin-5-yl)acetate (**4ac**)



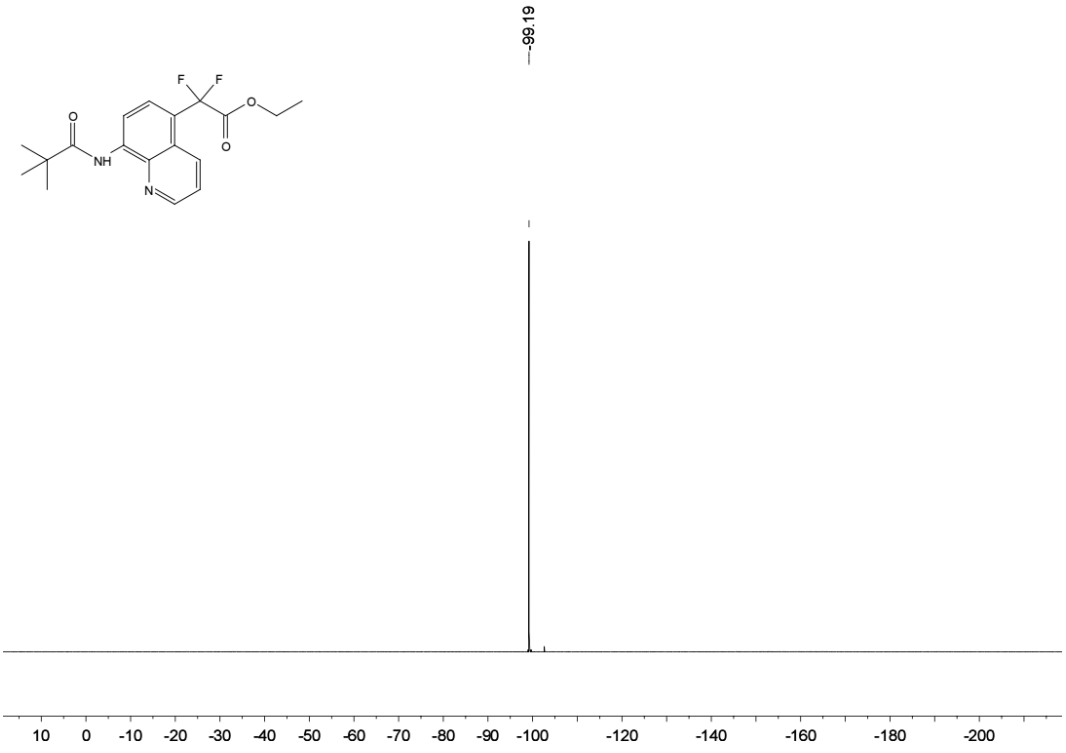
^{13}C NMR for ethyl 2,2-difluoro-2-(8-isobutyramidoquinolin-5-yl)acetate (**4ac**)



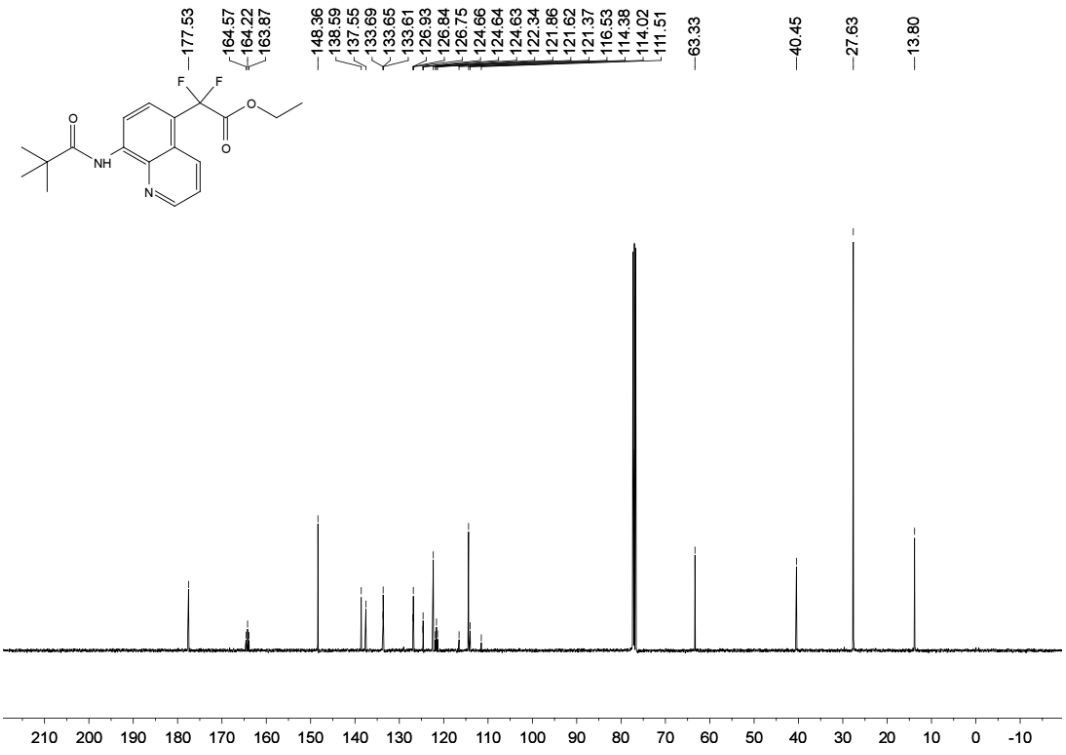
^{1}H NMR for ethyl 2,2-difluoro-2-(8-pivalamidoquinolin-5-yl)acetate (**4ad**)



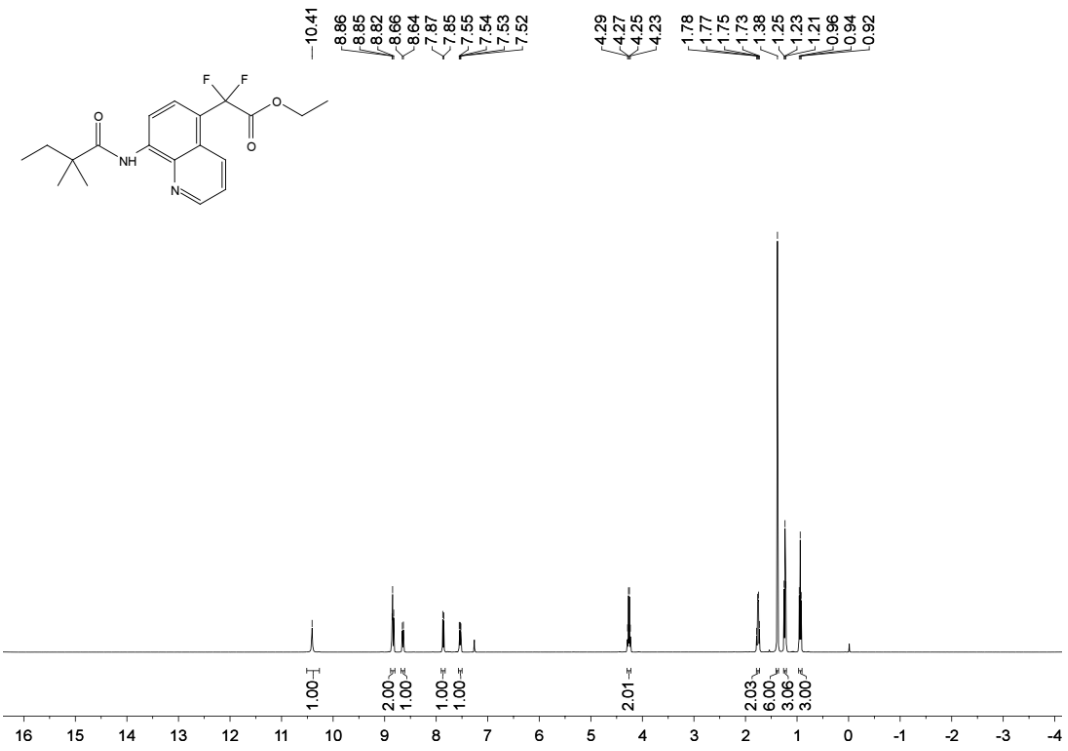
^{19}F NMR for ethyl 2,2-difluoro-2-(8-pivalamidoquinolin-5-yl)acetate (**4ad**)



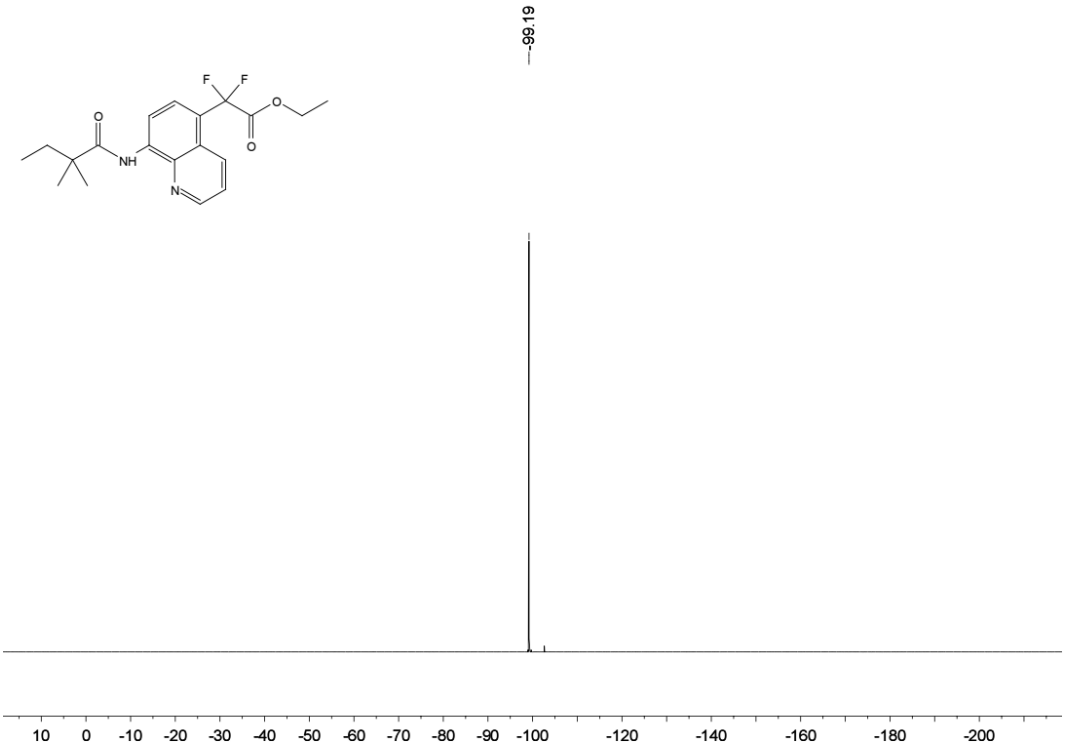
^{13}C NMR for ethyl 2,2-difluoro-2-(8-pivalamidoquinolin-5-yl)acetate (**4ad**)



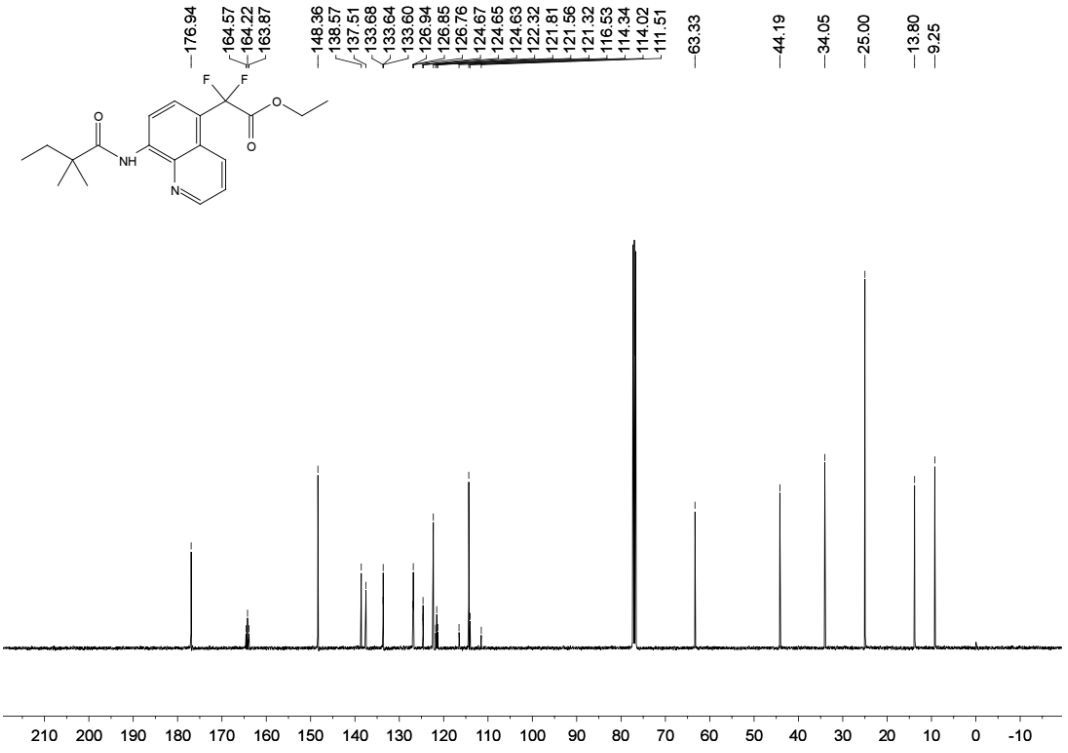
^{1}H NMR for ethyl 2-(8-(2,2-dimethylbutanamido)quinolin-5-yl)-2,2-difluoroacetate (**4ae**)



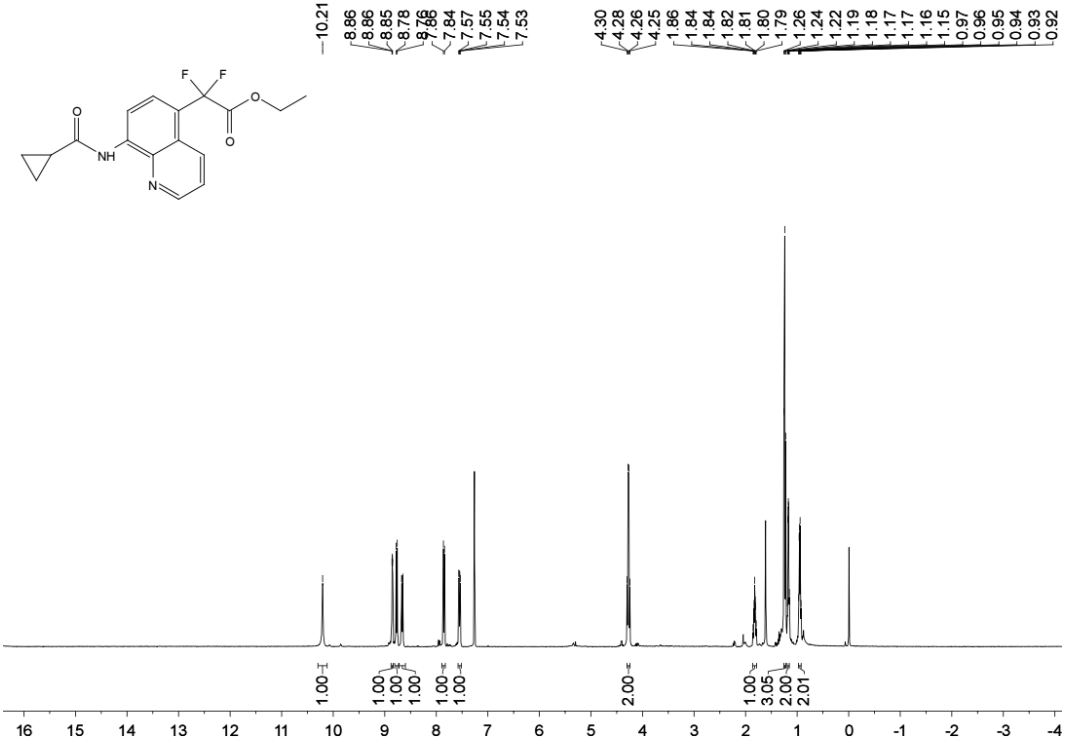
^{19}F NMR for ethyl 2-(8-(2,2-dimethylbutanamido)quinolin-5-yl)-2,2-difluoroacetate (**4ae**)



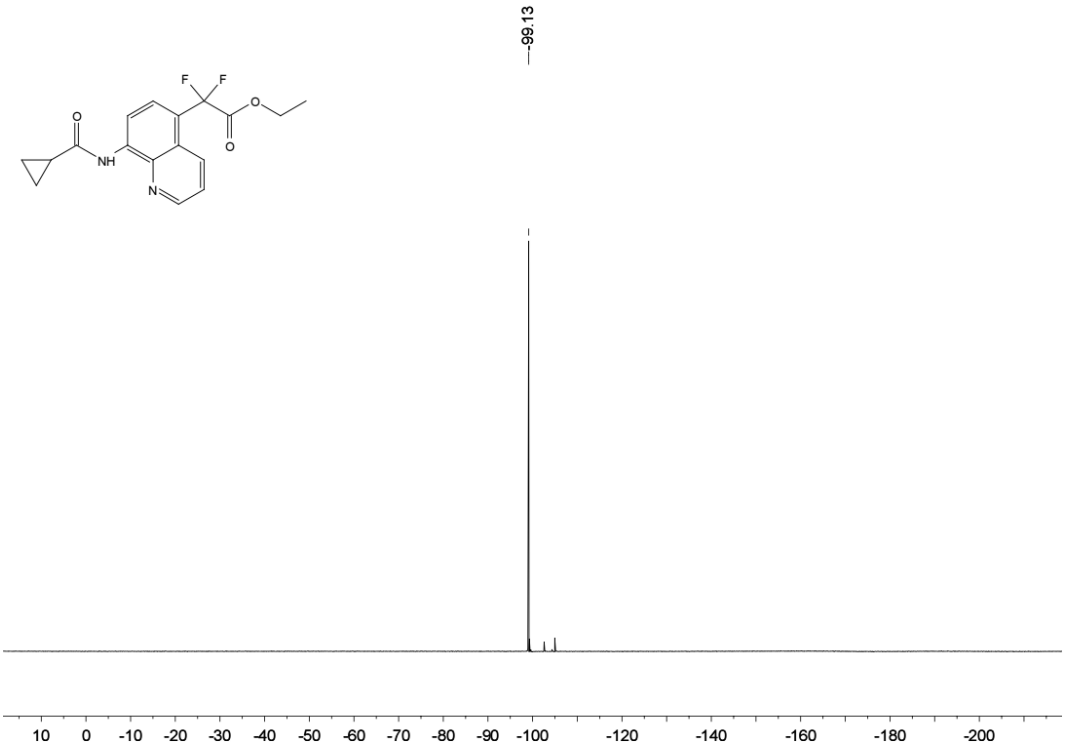
^{13}C NMR for ethyl 2-(8-(2,2-dimethylbutanamido)quinolin-5-yl)-2,2-difluoroacetate (**4ae**)



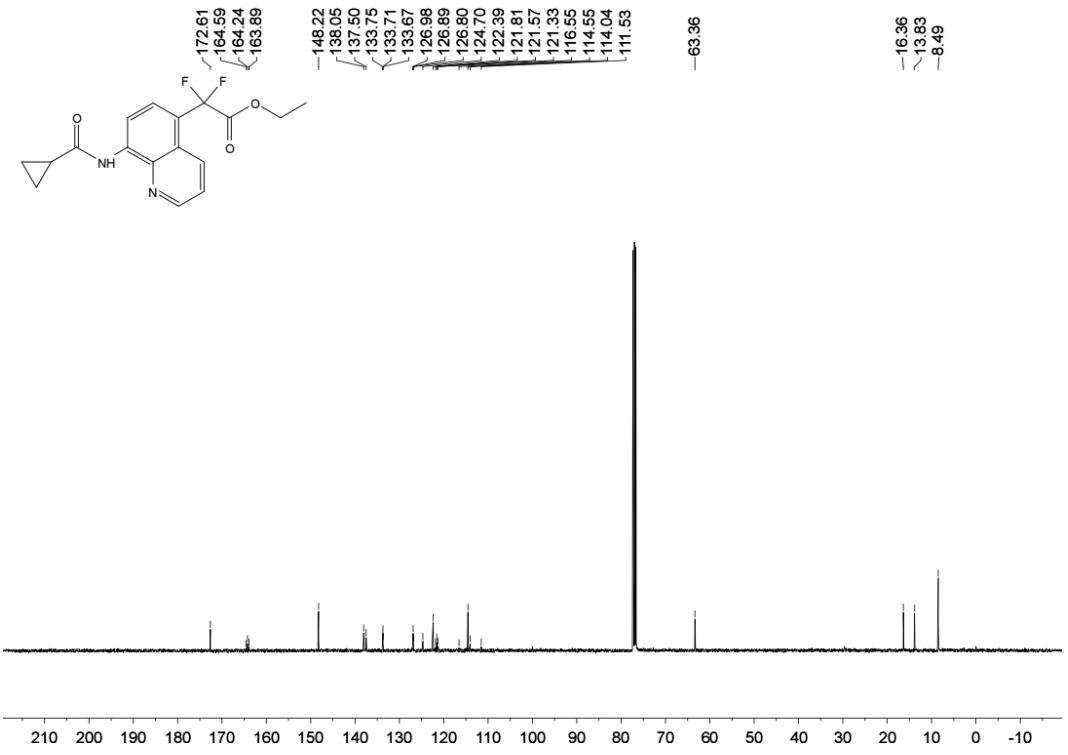
^{1}H NMR for ethyl 2-(8-(cyclopropanecarboxamido)quinolin-5-yl)-2,2-difluoroacetate (**4af**)



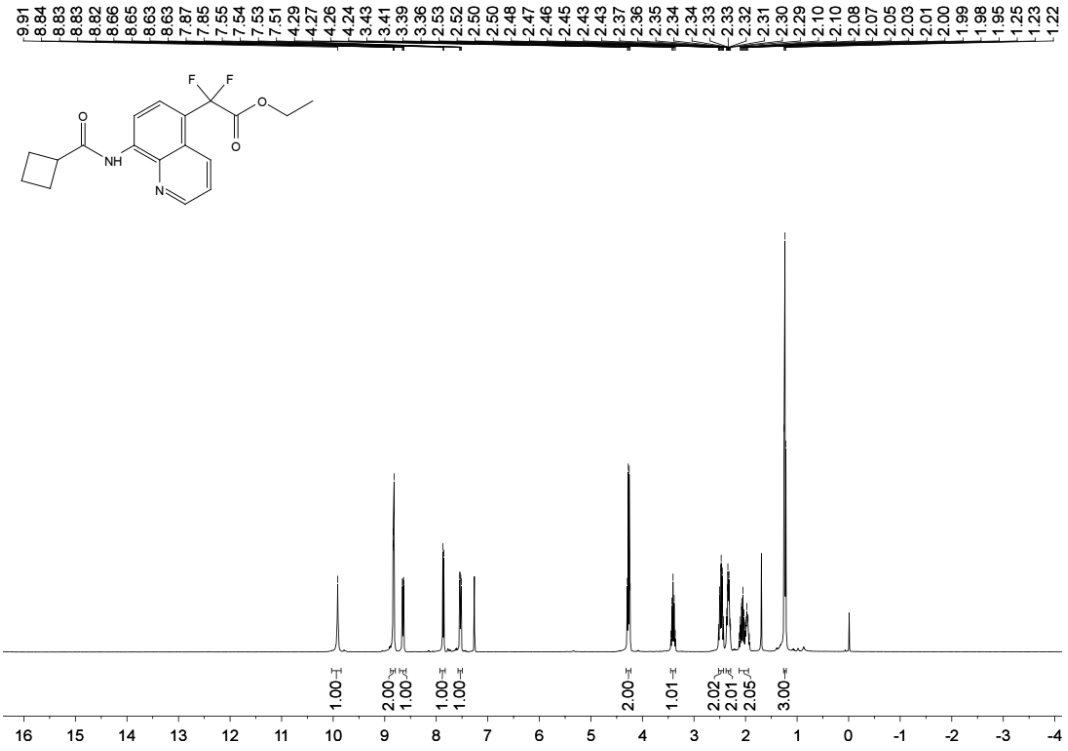
^{19}F NMR for ethyl 2-(8-(cyclopropanecarboxamido)quinolin-5-yl)-2,2-difluoroacetate (**4af**)



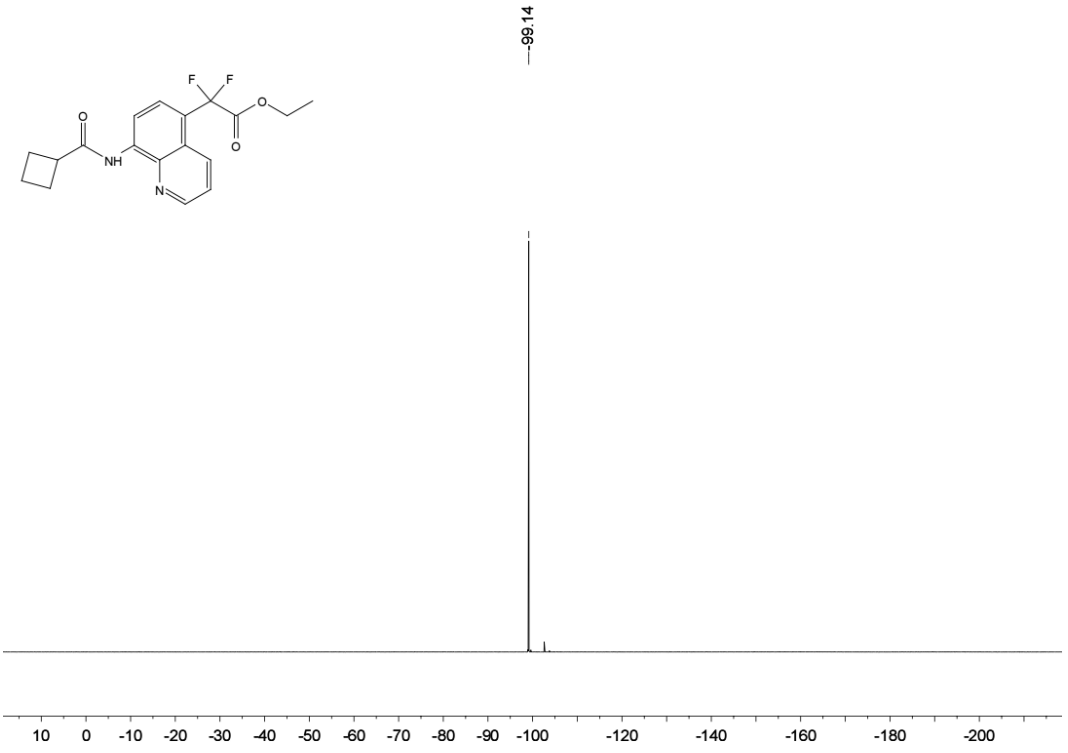
^{13}C NMR for ethyl 2-(8-(cyclopropanecarboxamido)quinolin-5-yl)-2,2-difluoroacetate (**4af**)



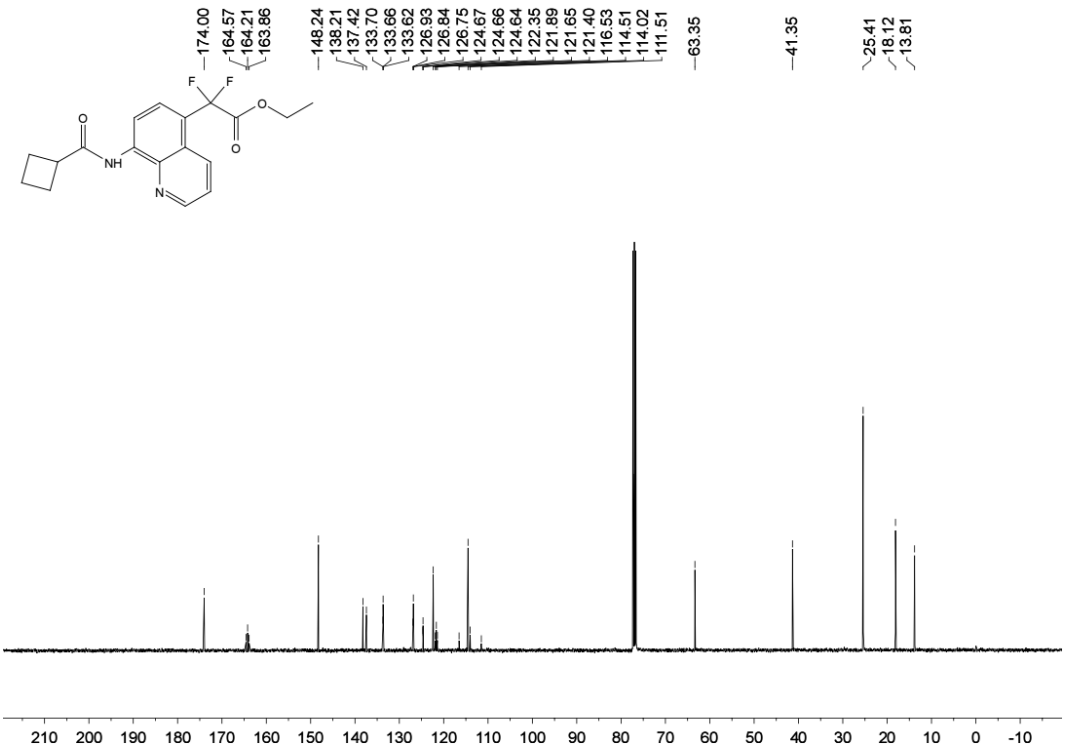
^{1}H NMR for ethyl 2-(8-(cyclobutanecarboxamido)quinolin-5-yl)-2,2-difluoroacetate (**4ag**)



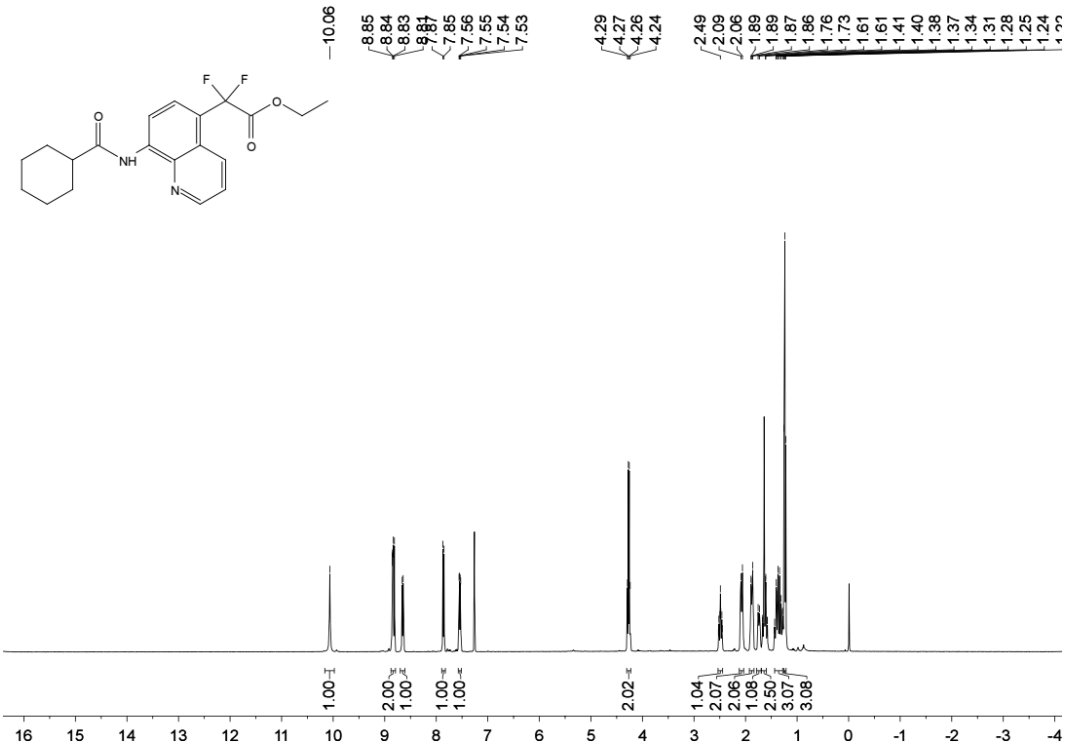
^{19}F NMR for ethyl 2-(8-(cyclobutanecarboxamido)quinolin-5-yl)-2,2-difluoroacetate (**4ag**)



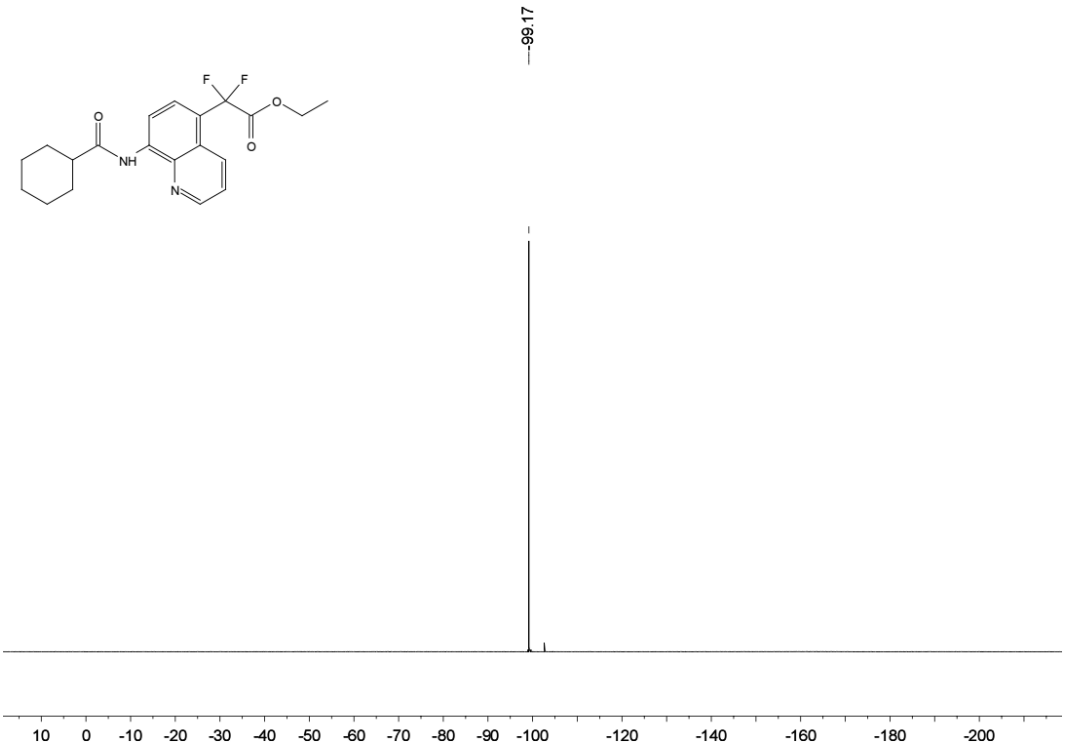
^{13}C NMR for ethyl 2-(8-(cyclobutanecarboxamido)quinolin-5-yl)-2,2-difluoroacetate (**4ag**)



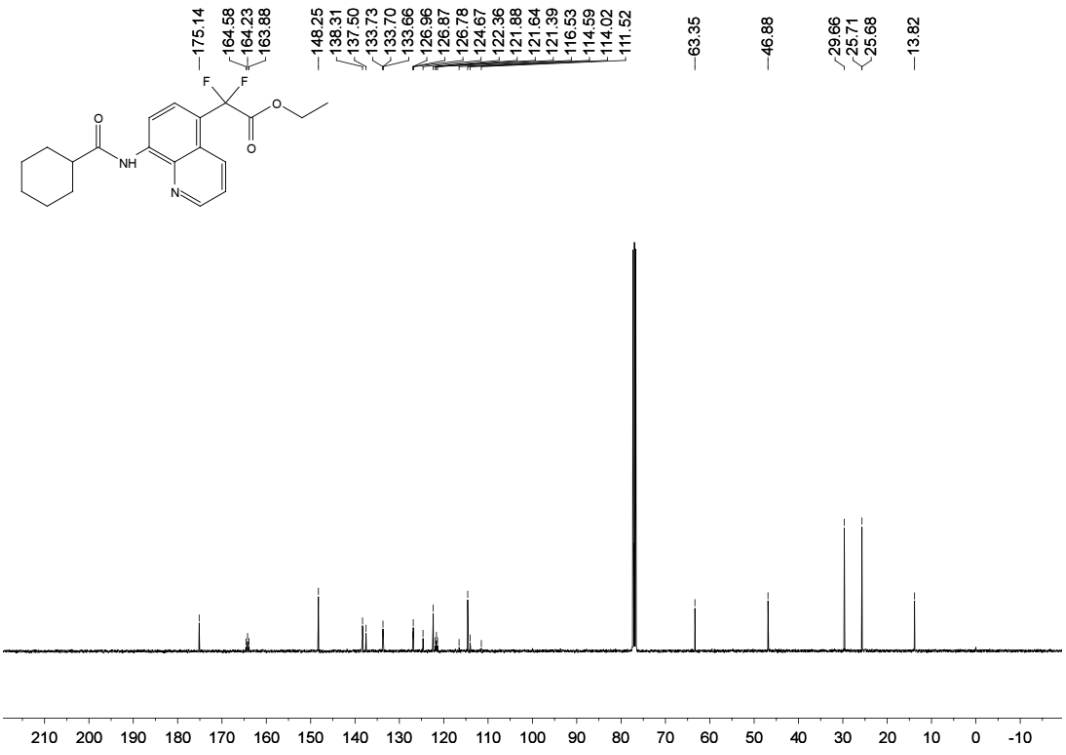
^{1}H NMR for ethyl 2-(8-(cyclohexanecarboxamido)quinolin-5-yl)-2,2-difluoroacetate (**4ah**)



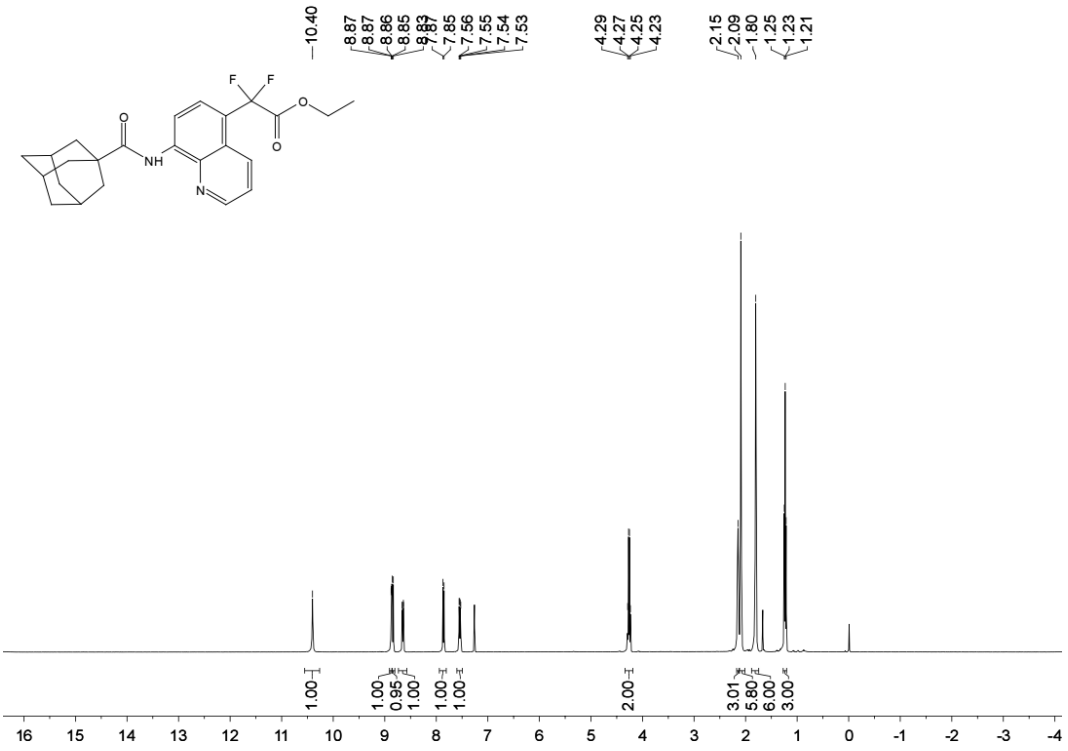
^{19}F NMR for ethyl 2-(8-(cyclohexanecarboxamido)quinolin-5-yl)-2,2-difluoroacetate (**4ah**)



^{13}C NMR for ethyl 2-(8-(cyclohexanecarboxamido)quinolin-5-yl)-2,2-difluoroacetate (**4ah**)

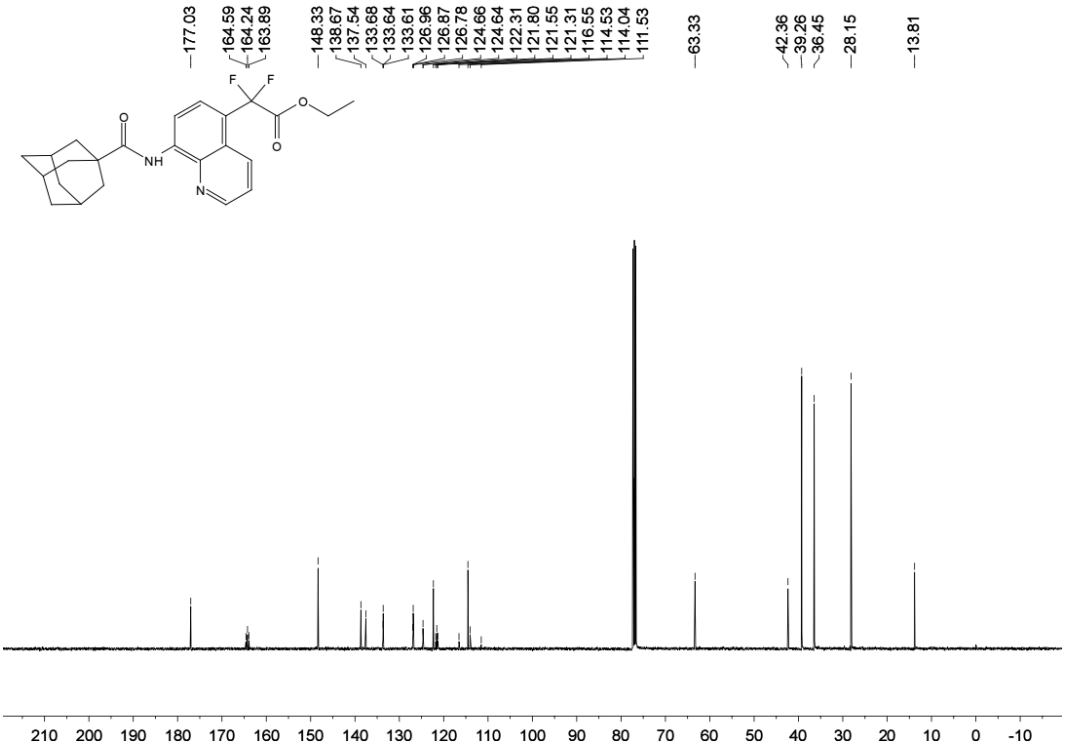


^{1}H NMR for ethyl 2-((8-adamantane-1-carboxamido)quinolin-5-yl)-2,2-difluoroacetate (**4ai**)

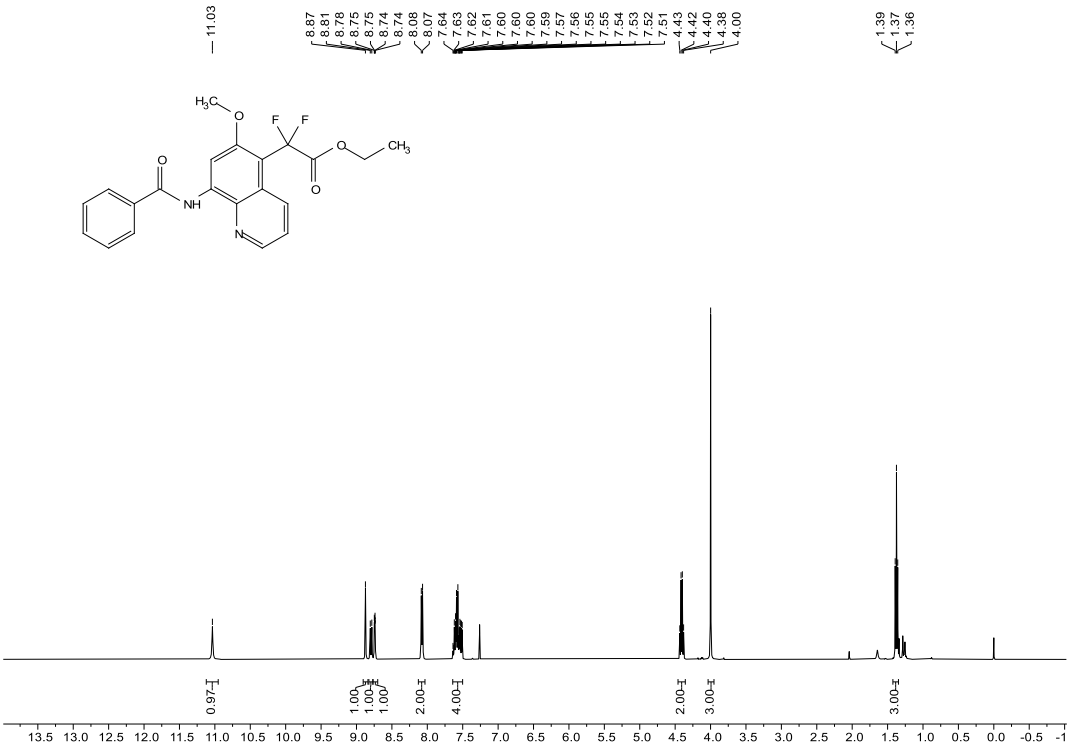


^{19}F NMR for ethyl 2-((8-adamantane-1-carboxamido)quinolin-5-yl)-2,2-difluoroacetate (**4ai**)

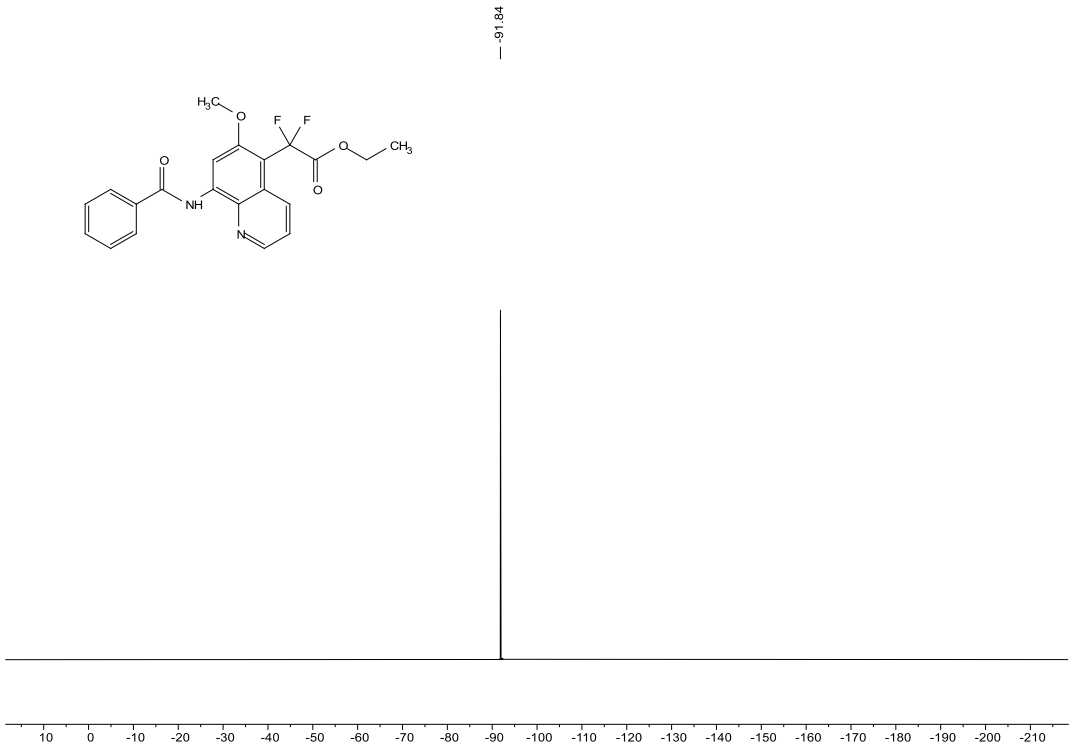
^{13}C NMR for ethyl 2-((8-adamantane-1-carboxamido)quinolin-5-yl)-2,2-difluoroacetate (**4ai**)



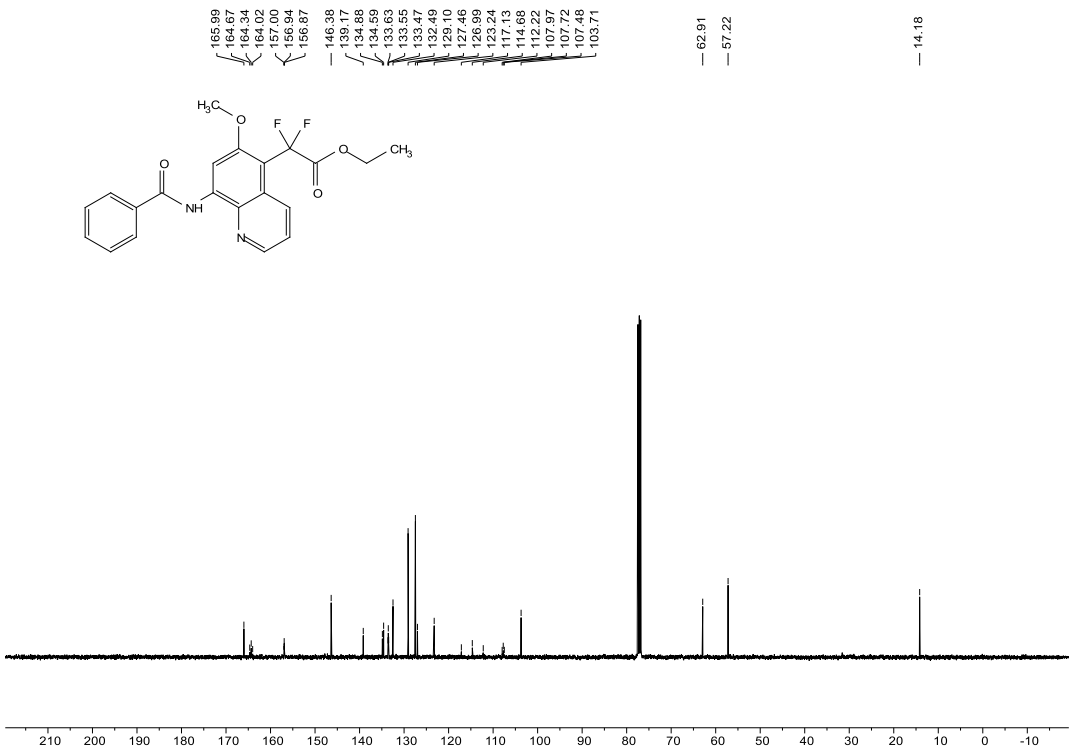
^{1}H NMR for ethyl 2-(8-benzamido-6-methoxyquinolin-5-yl)-2,2-difluoroacetate (**4aj**)



^{19}F NMR for for ethyl 2-(8-benzamido-6-methoxyquinolin-5-yl)-2,2-difluoroacetate (**4aj**)



^{13}C NMR for for ethyl 2-(8-benzamido-6-methoxyquinolin-5-yl)-2,2-difluoroacetate (**4aj**)



7. References

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