Electronic Supplementary Material (ESI) for New Journal of Chemistry.

~Supporting Information~

Photoredox–Catalyzed Direct C–H Monofluoromethylation of Heteroarenes

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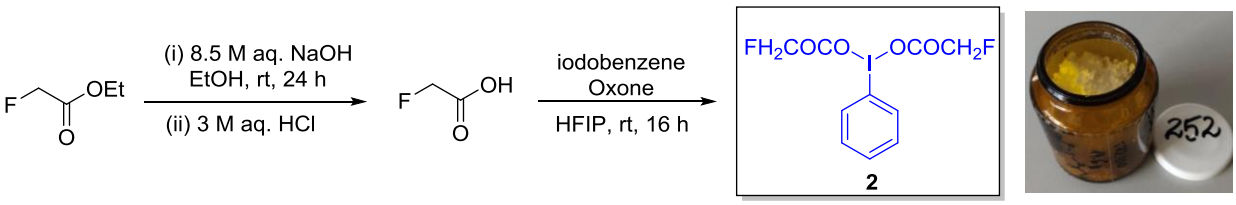
1. General Information

All commercially available substrates were purchased from commercial suppliers or otherwise synthesized according to literature. All solvents were used as received without further purification. All the compounds were purified by using Flash column chromatography on silica gel (35–70 and 60–200 μm). Thin layer chromatography (TLC) was performed on silica gel using Merck TLC Silica gel 60 F254 Aluminium sheets and was visualized by UV lamp, staining with $KMnO_4$. Melting points were recorded on Stanford Research Systems OptiMelt MPA 100 Automated melting point system. ^{1}H and ^{13}C NMR spectral data are reported as chemical shifts (δ) in parts per million (ppm) relative to the solvent peak using the Bruker internal referencing procedure (edlock). ^{19}F NMR spectra are referenced relative to $CFCl_3$ in $CDCl_3$. Coupling constants (*J*) are measured in hertz (Hz). The following abbreviations are used to describe multiplicities s=singlet, d=doublet, t=triplet, q=quartet, quint=quintet, m=multiplet, dd=doublet of doublets, dt=doublet of triplets, td=triplet of doublets, tt=triplet of triplets. NMR spectra were processed with MestReNova 11.0 or higher. All capillary tubing and microfluidic fittings were purchased from IDEX Health & Science. Syringe pumps used: Chemix Inc. Fusion 200 Touch. HRMS analyses were performed on a hybrid quadrupole time-of-flight mass spectrometer equipped with an electron-spray ion source.

Light Source: Reactions were performed in 4 mL vials using an Aldrich® Micro Photochemical Reactor (ALDKIT001), blue LED lights (435–445 nm spectral range).

2. Synthesis of phenyl-λ^3-iodanediyl bis(2-fluoroacetate)



A solution of ethyl fluoroacetate (27 mL, 278.9 mmol) in EtOH (360 mL) was treated with 40 mL of aqueous NaOH (8.5 M) and stirred at room temperature for 24 h. The solvent was rotary evaporated to dryness. The sodium fluoroacetate thus obtained was redissolved in 240 mL of aqueous HCl (3 M), and then the solution was saturated with solid NaCl and extracted with Et_2O (3 × 100 mL). The organic extract was dried over anhydrous Na_2SO_4, filtered, and evaporated to give 2-fluoroacetic acid as slightly yellowish oil (14.2 g, 65%). Spectral data obtained was consistent with previously reported in literature.[1]

Precaution! Extreme caution should be exercised when handling sodium fluoroacetate and fluoroacetic acid. Both compounds are highly toxic to animals and humans and advised to wear protective equipment (e.g. gloves) when handling these toxic intermediates.

Oxone (29.4 g, 96.0 mmol) was added to a stirred solution of iodobenzene (12.8 g, 62.7 mmol) in 130 mL of hexafluoropropanol (HFIP). Then, 2-fluoroacetic acid (14.7 g, 182.2 mmol) was added and the resulting suspension was stirred at room temperature for 16 h. The solvent was removed by rotary evaporation. The dry residue was redissolved in $CHCl_3$, filtered to remove the salts; the filtrate thus obtained was evaporated to dryness. This residue was washed with 3 × 100 mL portions of Et_2O, each time stirring the suspension of the solid product in Et_2O, allowing the solid to settle and discarding the supernatant by decantation. The flask with the resulting wet product was then placed on rotary evaporator to remove the residual solvent. Product was obtained as a white fluffy solid and used without further purification. Spectral data obtained was consistent with previously reported in literature.[2]

Yield: 17.5 g, 78%; Mp 124–126 ^{o}C; **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.23 – 8.04 (m, 2H), 7.72 – 7.58 (m, 1H), 7.57 – 7.47 (m, 2H), 4.76 (d, *J* = 47.5 Hz, 4H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -224.34 (t, *J* = 47.6 Hz, 2F). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.4 (d, *J* = 21.1 Hz), 135.2, 132.7, 131.5, 122.5, 76.7 (d, *J* = 185.5 Hz). **HRMS:** Unstable under HRMS conditions.

2.1 Differential scanning calorimetry and Thermogravimetric analysis of reagent (2)

The differential scanning calorimetry/thermogravimetry analysis (DSC/TGA) was performed with TGA/DSC_2 (Mettler Toledo). Open 100 µL aluminum pans were used. Heating of the samples from 25 °C to 120 °C or 210 °C was performed at a 10 °C·min^{-1} heating rate. Samples of 4–7 mg mass were used, and the nitrogen flow rate was 100±10 mL·min^{-1}.

DSC and TGA studies revealed that reagent **2** started to evaporate or slowly decompose above 100 °C.

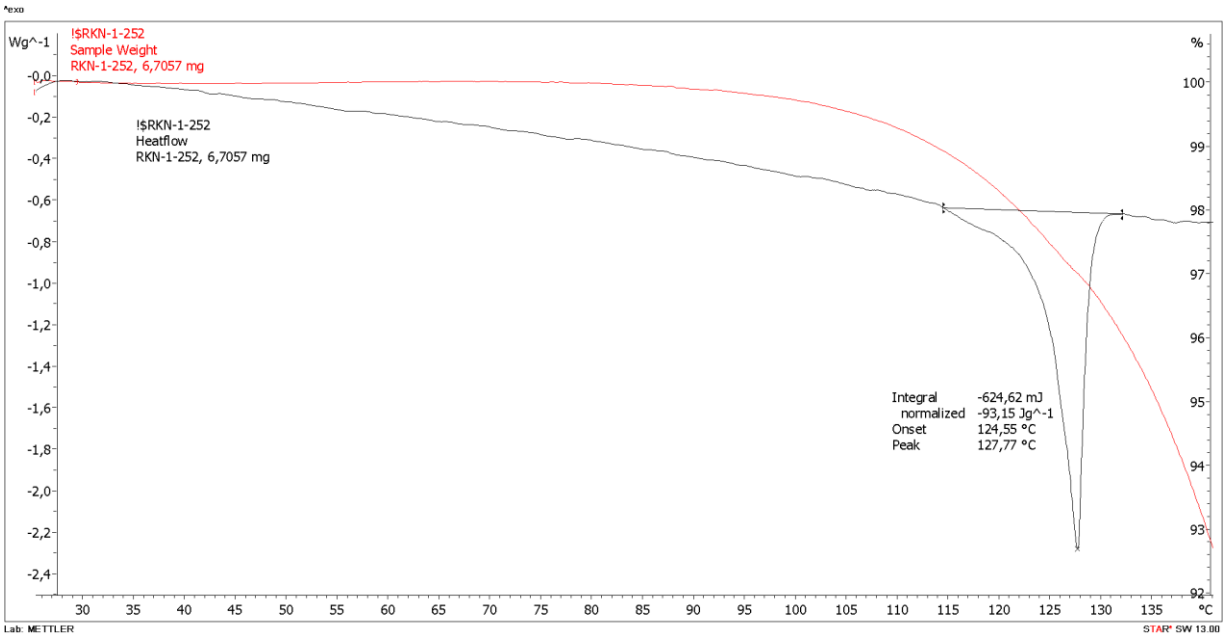


Figure S1. DSC and TGA analysis of phenyl-λ^3-iodanediyl bis(2-fluoroacetate) **(2)**.

2.2 Cyclic voltammetry

The experiments were carried out in a three-electrode glass cell using a PalmSens*4* Potentiostat. A glassy carbon disk (diameter: 1.6 mm) served as the working electrode, and a platinum wire as the counter electrode. The glassy carbon disk was polished using polishing alumina suspension (0.05 µm) prior to each experiment. As reference, a $Ag/AgNO_3$ electrode (silver wire in 0.1 M NBu_4BF_4/CH_3CN solution; $c(AgNO_3)$ = 0.01 M; E_0 = −87 mV vs Fc/Fc^+ couple[3] was used, and this compartment was separated from the rest of the cell with a Vycor frit. Unless stated otherwise, NBu_4BF_4 (0.1 M, electrochemical grade) was employed as the supporting electrolyte in CH_3CN (Acros Organics, HPLC grade) solution. The electrolyte was purged with Ar for at least 2 min prior to recording. Compound **2** was analyzed at a concentration of 2 mM and a scan rate of 100 mV s^{-1}. The peak potentials (E_p) were extracted from voltammograms without background-corrections.

Phenyl-λ^3-iodanediyl bis(2-fluoroacetate) **(2):** E_p (V *vs.* Ag/AgCl) = -0.927 V

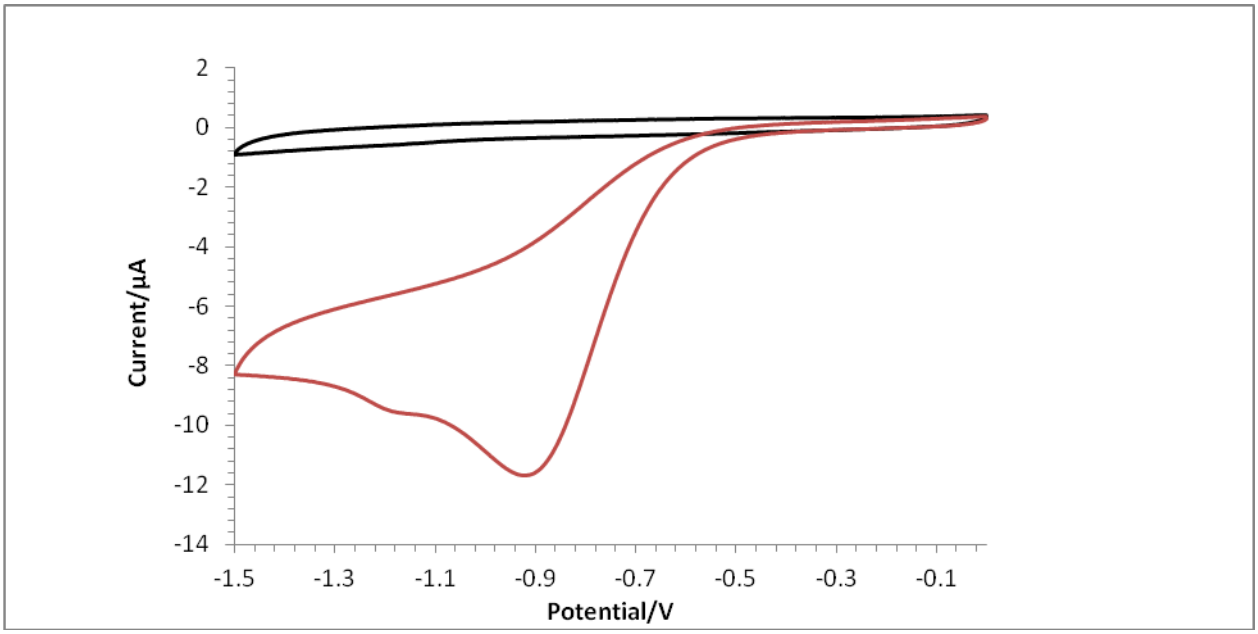
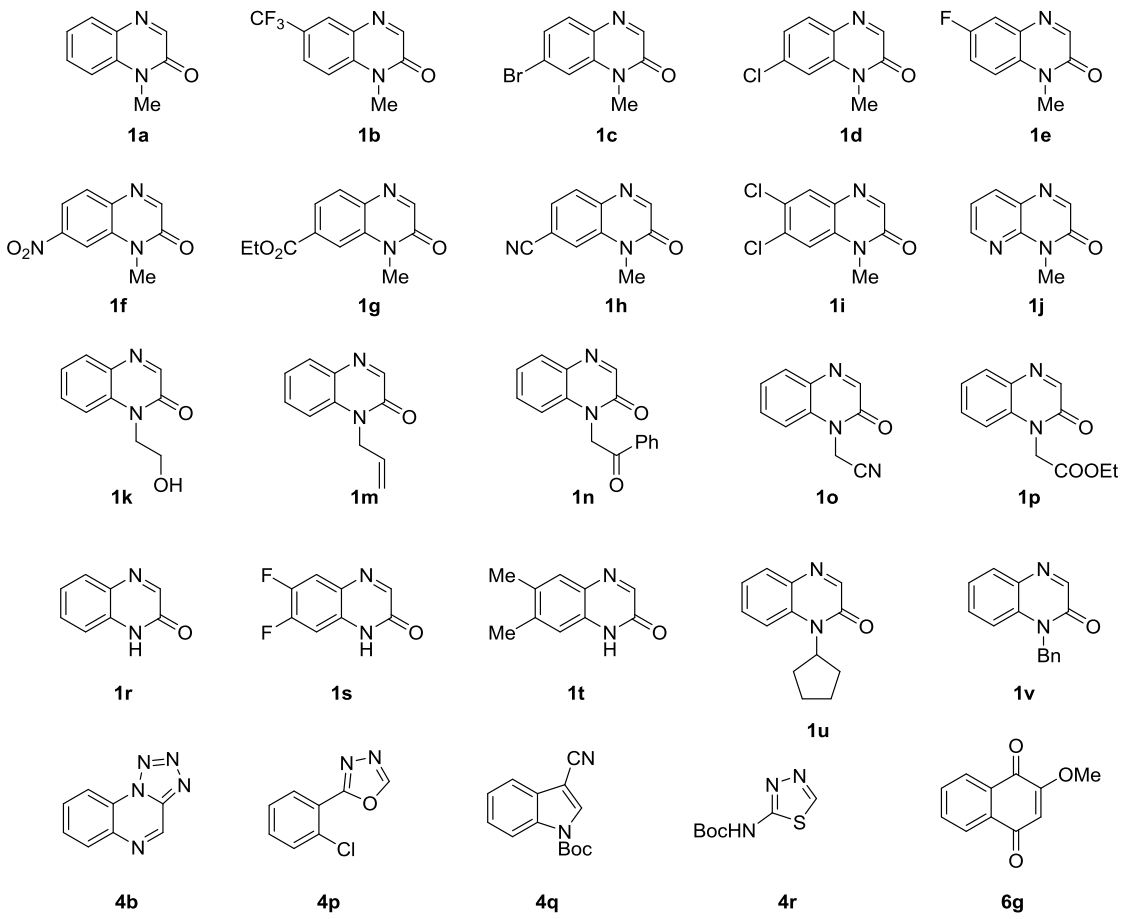


Figure S2. Voltammetric response of phenyl-λ^3-iodanediyl bis(2-fluoroacetate) **(2)**.

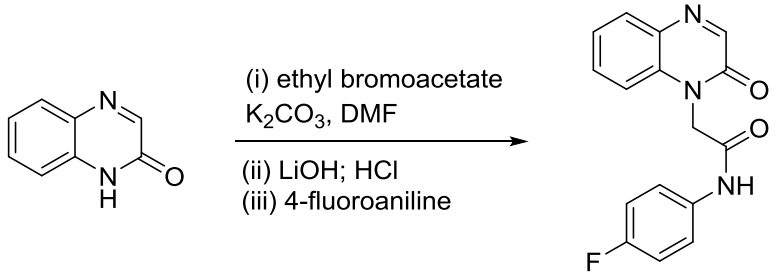
3. General procedures for the synthesis of starting materials

The quinoxalin-2(1*H*)-ones derivatives **1a–k**, **1m–v**[4–9] and the substrates **4b**,[10] **4p–r**[11] and **6g**[12] were synthesized according to previously reported procedures.

In a 100 mL round bottom flask, a mixture of 1,2-phenylenediamine derivatives (12 mmol, 1.0 equiv) and ethyl glyoxalate (~50% in toluene, 1.2 equiv) in ethanol (40 mL) with a magnetic stirring bead was stirred at 100 °C until the raw material was consumed. Then, the mixture was filtered and washed with distilled water (3 × 15 mL). After that, the solid product was dried under reduced pressure to obtain the quinoxalin-2(1*H*)-one derivative **1**. For the alkylation of quinoxalin-2(1*H*)-ones, a solution of quinoxalin-2(1*H*)-one derivatives **1** (1.0 mmol, 1.0 equiv) and potassium carbonate (1.2 equiv) in DMF (0.2 M) was added to a 50 mL round-bottomed flask followed by the addition of the corresponding alkyl halides (1.2 equiv). The resultant solution was stirred overnight at room temperature. After the completion, the reaction mixture was extracted three times with saturated brine solution and EtOAc. Then, the organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated in rotary evaporation. The resultant residue was purified by column chromatography to achieve the desired *N*-alkylation of quinoxalin-2(1*H*)-ones **1a–k, 1m–p** and **1u–v**.



Synthesis of *N*-(4-fluorophenyl)-2-(2-oxoquinoxalin-1(2*H*)-yl)acetamide (1l)

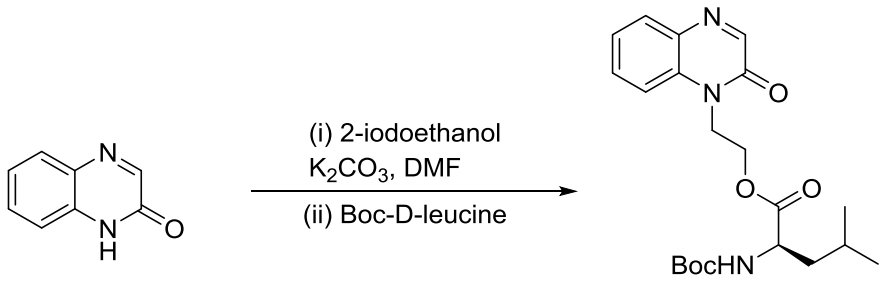


1r **1l**

Substrate **1l** was prepared according to previous literature report.[13] To a 50 mL round-bottom flask was charged with quinoxalin-2(1*H*)-one **1r** (1.0 g, 6.84 mmol), K_2CO_3 (1.42 g, 10.2 mmol), ethyl bromoacetate (1.37 g, 8.2 mmol), and DMF (20 mL). After stirring at room temperature for overnight, the reaction mixture was poured into water (50 mL) and extracted with ethyl acetate (2 × 50 mL). The organic layer was washed with saturated aqueous NH_4Cl solution (50 mL) followed by brine (50 mL) and dried over anhydrous Na_2SO_4. The organic layer was then filtered off, evaporated in vacuo and purified by flash column chromatography (SiO_2, petroleum ether/ethyl acetate, 4:1) to afford ethyl 2-(2-oxoquinoxalin-1(2*H*)-yl) acetate as a pale yellow solid (1.25 g, 79%). Then, in a 50 mL round-bottom flask, ethyl 2-(2-oxoquinoxalin-1(2*H*)-yl)acetate (1.0 g, 4.3 mmol) and LiOH (155 mg, 6.45 mmol) were suspended in THF (30 mL) and water (10 mL). After stirring at room temperature for 3 h, the mixed solvents were removed in vacuo. The obtained solid was dissolved into 20 mL water, and then the resulting solution was acidified by 1 M HCl until light red solid was precipitated. The obtained solid was washed with water (3 × 10 mL), recrystallized with 70% methanol to afford pure 2-(2-oxoquinoxalin-1(2*H*)-yl)acetic acid as a pale yellow solid (760 mg, 86%). Finally, a mixture of 2-(2-oxoquinoxalin-1(2*H*)-yl)acetic acid (350 mg, 1.7 mmol), 4-fluoroaniline (210 mg, 1.89 mmol), EDC·HCl (394 mg, 2.05 mmol), DMAP (21 mg, 0.17 mmol), Et_3N (358 μL, 2.57 mmol,) and DCM (10 mL) was stirred at room temperature for overnight. After then, the reaction mixture was poured into 50 mL water and extracted with DCM (3 × 20 mL). The organic solvent was washed with brine (50 mL) and dried over anhydrous Na_2SO_4. After filtration and concentration in vacuo, the obtained residue was further purified by flash column chromatography (SiO_2, petroleum ether/ethyl acetate, 4:1) to afford the desired product **1l** as a white fluffy solid (425 mg, 83%).

Mp 217–219 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.53 (s, 1H), 8.33 (s, 1H), 7.88 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.65 (ddd, *J* = 8.6, 7.2, 1.5 Hz, 1H), 7.63 – 7.51 (m, 3H), 7.41 (ddd, *J* = 8.2, 7.1, 1.2 Hz, 1H), 7.26 – 7.11 (m, 2H), 5.12 (s, 2H). **^{19}F NMR** (376 MHz, DMSO-d_6) δ -118.85 (tt, *J* = 9.0, 4.9 Hz). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 165.0, 158.6 (d, *J* = 240.0 Hz), 154.7, 150.3, 135.4 (d, *J* = 2.6 Hz), 133.4, 133.1, 131.6, 130.2, 124.1, 121.4 (d, *J* = 8.0 Hz), 115.9 (d, *J* = 22.3 Hz), 115.3, 45.2. **HRMS** (ESI(+)) m/z: Calculated for $C_{16}H_{12}FN_3O_2$ $[M+H]^+$ 298.0992, found 298.1001.

Synthesis of 2-(2-oxoquinoxalin-1(2*H*)-yl)ethyl (*tert*-butoxycarbonyl)-D-leucinate (1q)

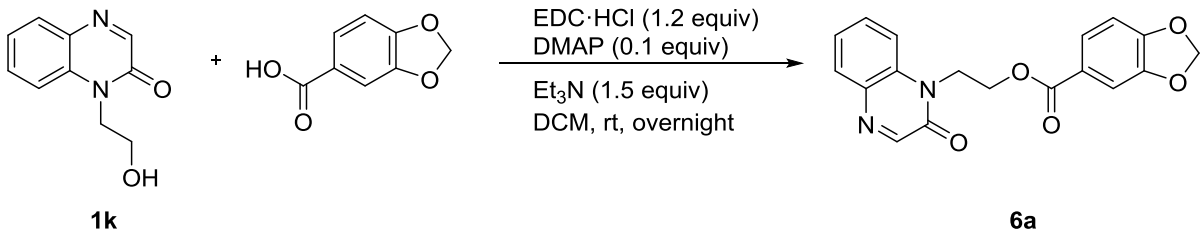


1r **1q**

To a 50 mL round-bottom flask was charged with quinoxalin-2(1*H*)-one **1r** (1.0 g, 6.84 mmol), K_2CO_3 (1.42 g, 10.2 mmol), 2-iodoethanol (1.41 g, 8.2 mmol), and DMF (20 mL). After stirring at room temperature for overnight, the reaction mixture was poured into water (50 mL) and extracted with ethyl acetate (2 × 50 mL). The organic layer was washed with saturated aqueous NH_4Cl solution (50 mL) followed by brine (50 mL) and dried over anhydrous Na_2SO_4. The organic layer was then filtered off, evaporated in vacuo and purified by flash column chromatography (SiO_2, petroleum ether/ethyl acetate, 1:1) to afford 1-(2-hydroxyethyl)quinoxalin-2(1*H*)-one as a white solid (630 mg, 48%). Finally, a mixture of 1-(2-hydroxyethyl)quinoxalin-2(1*H*)-one (200 mg, 1.05 mmol), Boc-*D*-leucine (243 mg, 1.05 mmol), EDC·HCl (242 mg, 2.05 mmol), DMAP (13 mg, 0.11 mmol), Et_3N (220 µL, 1.57 mmol) and DCM (5 mL) was stirred at room temperature for overnight. After then, the reaction mixture was poured into 20 mL water and extracted with DCM (3 × 10 mL). The organic solvent was washed with brine (30 mL) and dried over anhydrous Na_2SO_4. After filtration and concentration in vacuo, the obtained residue was further purified by flash column chromatography (SiO_2, petroleum ether/ethyl acetate, 4:1) to afford the desired product **1q** as a colourless oil (228 mg, 54%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.29 (s, 1H), 7.88 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.61 (ddd, *J* = 8.6, 7.2, 1.6 Hz, 1H), 7.51 (dd, *J* = 8.6, 1.3 Hz, 1H), 7.36 (ddd, *J* = 8.3, 7.2, 1.2 Hz, 1H), 4.82 (d, *J* = 8.6 Hz, 1H), 4.63 – 4.38 (m, 4H), 4.21 (td, *J* = 9.0, 5.2 Hz, 1H), 1.59 (ddq, *J* = 12.9, 8.3, 6.5 Hz, 1H), 1.42 (s, 9H), 1.40 – 1.30 (m, 2H), 0.83 (dd, *J* = 6.6, 5.1 Hz, 6H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 173.3, 155.4, 154.8, 149.9, 133.5, 132.6, 131.2, 130.8, 123.9, 114.0, 79.9, 61.4, 52.0, 41.3, 40.5, 28.3, 24.6, 22.8, 21.6. **HRMS** (ESI(+)) m/z: Calculated for $C_{21}H_{29}N_3O_5$ $[M+Na]^+$ 426.2005, found 426.2013.

Synthesis of 2-(2-oxoquinoxalin-1(2*H*)-yl)ethyl benzo[*d*][1,3]dioxole-5-carboxylate (6a)

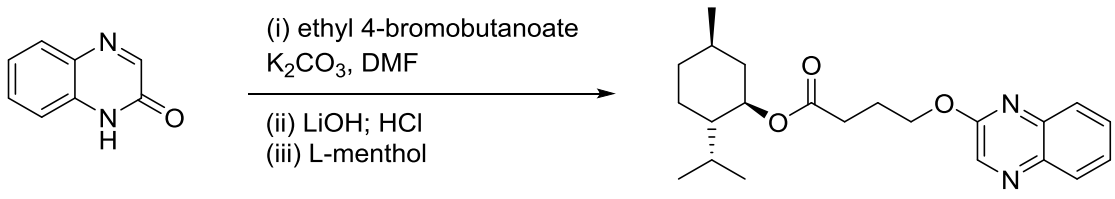


1k **6a**

To a 10 mL round-bottom flask was charged with 1-(2-hydroxyethyl)quinoxalin-2(1*H*)-one **1k** (97.3 mg, 0.51 mmol), piperonylic acid (85 mg, 0.51 mmol), EDC·HCl (118 mg, 0.61 mmol), DMAP (6.25 mg, 0.05 mmol), Et_3N (107 μL, 0.77 mmol) and DCM (3 mL). After stirring at room temperature for overnight, the reaction mixture was poured into 10 mL water and extracted with DCM (3 × 10 mL). The organic solvent was washed with brine (30 mL) and dried over anhydrous Na_2SO_4. After filtration and concentration in vacuo, the obtained residue was further purified by flash column chromatography (SiO_2, petroleum ether/ethyl acetate, 1:1) to afford the desired product **6a** as a white solid (153 mg, 88%).

Mp 166–168 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.31 (s, 1H), 7.94 – 7.84 (m, 1H), 7.65 – 7.52 (m, 2H), 7.51 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.35 (ddd, *J* = 8.3, 5.6, 2.9 Hz, 1H), 7.31 (d, *J* = 1.7 Hz, 1H), 6.77 (d, *J* = 8.2 Hz, 1H), 6.01 (s, 2H), 4.68 – 4.58 (m, 4H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 165.8, 154.9, 151.9, 150.0, 147.7, 133.5, 132.7, 131.1, 130.8, 125.6, 123.9, 123.2, 113.9, 109.5, 108.0, 101.8, 61.1, 40.6. **HRMS** (ESI(+)) m/z: Calculated for $C_{18}H_{14}N_2O_5$ $[M+H]^+$ 339.0981, found 339.0995.

Synthesis of (1*R*,2*R*,5*R*)-2-isopropyl-5-methylcyclohexyl 4-(quinoxalin-2-yloxy)butanoate (6b)



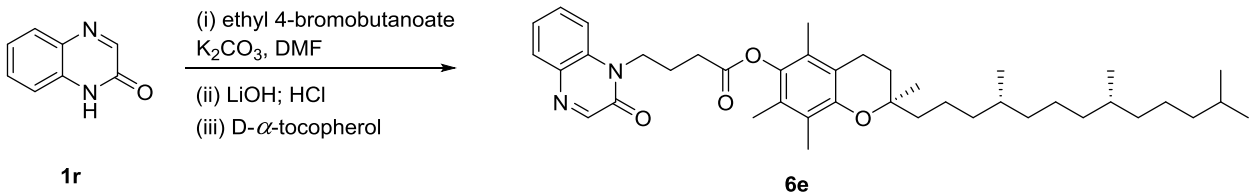
1r **6b**

To a 50 mL round-bottom flask was charged with quinoxalin-2(1*H*)-one **1r** (1.5 g, 10.26 mmol), K_2CO_3 (2.13 g, 10.2 mmol), ethyl 4-bromobutyrate (1.76 mL, 12.3 mmol), and DMF (30 mL). After stirring at room temperature for overnight, the reaction mixture was poured into water (50 mL) and extracted with ethyl acetate (2 × 50 mL). The organic layer was washed with saturated aqueous NH_4Cl solution (50 mL) followed by brine (50 mL) and dried over anhydrous Na_2SO_4. The organic layer was then filtered off, evaporated in vacuo and purified by flash column chromatography (SiO_2,

petroleum ether/ethyl acetate, 9:1) to afford ethyl 4-(quinoxalin-2-yloxy)butanoate as a white solid (950 mg, 36%). Then, in a 50 mL round-bottom flask, ethyl 4-(quinoxalin-2-yloxy)butanoate (500 mg, 1.92 mmol) and LiOH (92 mg, 3.8 mmol) were suspended in THF (10 mL) and water (5 mL). After stirring at room temperature for 4 h, the mixed solvents were removed in vacuo. The obtained solid was dissolved into 20 mL water, and then the resulting solution was acidified by 1 M HCl until pale yellow solid was precipitated. The obtained solid was filtered off and washed with water (3 × 10 mL), recrystallized with 70% methanol to afford pure 4-(quinoxalin-2-yloxy)butanoic acid as a white solid (406 mg, 91%). Finally, a mixture of 4-(quinoxalin-2-yloxy)butanoic acid (350 mg, 1.51 mmol), L-menthol (236 mg, 1.51 mmol), EDC·HCl (318 mg, 1.81 mmol), DMAP (18.4 mg, 0.15 mmol), DIPEA (391 μL, 2.26 mmol) and DCM (10 mL) was stirred at room temperature for overnight. After then, the reaction mixture was poured into 50 mL water and extracted with DCM (3 × 20 mL). The organic solvent was washed with brine (50 mL) and dried over anhydrous Na_2SO_4. After filtration and concentration in vacuo, the obtained residue was further purified by flash column chromatography (SiO_2, petroleum ether/ethyl acetate, 9:1) to afford the desired product **6b** as a white solid (458 mg, 82%).

Mp 48–50 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.46 (s, 1H), 8.01 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.82 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.66 (ddd, *J* = 8.4, 7.0, 1.5 Hz, 1H), 7.56 (ddd, *J* = 8.3, 7.0, 1.4 Hz, 1H), 4.71 (td, *J* = 10.9, 4.4 Hz, 1H), 4.53 (td, *J* = 6.4, 0.9 Hz, 2H), 2.61 – 2.45 (m, 2H), 2.25 – 2.13 (m, 2H), 2.04 – 1.94 (m, 1H), 1.85 (heptd, *J* = 7.0, 2.7 Hz, 1H), 1.66 (ddq, *J* = 12.8, 6.5, 3.4 Hz, 2H), 1.49 (ttd, *J* = 15.1, 6.5, 3.1 Hz, 1H), 1.36 (ddt, *J* = 12.4, 10.8, 3.2 Hz, 1H), 1.12 – 0.79 (m, 3H), 0.89 (d, *J* = 6.5 Hz, 3H), 0.86 (d, *J* = 7.0 Hz, 3H), 0.75 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 172.6, 157.2, 140.3, 139.6, 138.9, 130.1, 128.9, 127.2, 126.5, 74.3, 65.4, 47.0, 40.9, 34.2, 31.3, 31.2, 26.3, 24.3, 23.4, 22.0, 20.7, 16.3. **HRMS** (ESI(+)) m/z: Calculated for $C_{22}H_{30}N_2O_3$ $[M+H]^+$ 371.2335, found 371.2332.

Synthesis of (*R*)-2,5,7,8-tetramethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)chroman-6-yl 4-(2-oxoquinoxalin-1(2*H*)-yl)butanoate (6e)

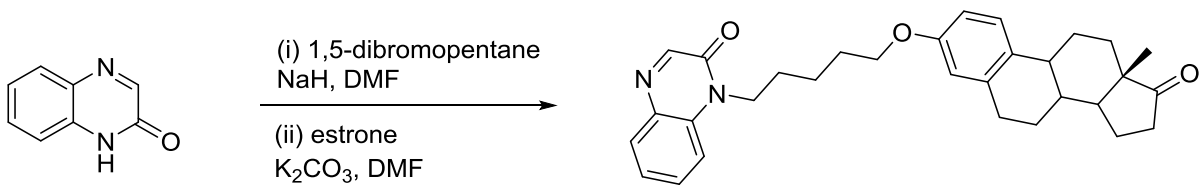


To a 50 mL round-bottom flask was charged with quinoxalin-2(1*H*)-one **1r** (1.5 g, 10.26 mmol), K_2CO_3 (2.13 g, 10.2 mmol), ethyl 4-bromobutyrate (1.76 mL, 12.3 mmol), and DMF (30 mL). After stirring at room temperature for overnight, the reaction mixture was poured into water (50 mL) and extracted with ethyl acetate (2 × 50 mL). The organic layer was washed with saturated aqueous

NH_4Cl solution (50 mL) followed by brine (50 mL) and dried over anhydrous Na_2SO_4. The organic layer was then filtered off, evaporated in vacuo and purified by flash column chromatography (SiO_2, petroleum ether/ethyl acetate, 4:1) to afford ethyl 4-(2-oxoquinoxalin-1(2*H*)-yl)butanoate as a pale yellow solid (1.5 g, 56%). Then, in a 50 mL round-bottom flask, ethyl 4-(2-oxoquinoxalin-1(2*H*)-yl)butanoate (1.0 g, 3.84 mmol) and LiOH (184 mg, 7.68 mmol) were suspended in THF (20 mL) and water (10 mL). After stirring at room temperature for 4 h, the mixed solvents were removed in vacuo. The obtained solid was dissolved into 20 mL water, and then the resulting solution was acidified by 1 M HCl until pale yellow solid was precipitated. The obtained solid was filtered off and washed with water (3 × 10 mL), recrystallized with 70% methanol to afford pure 4-(2-oxoquinoxalin-1(2*H*)-yl)butanoic acid as a pale yellow solid (852 mg, 96%). Finally, a mixture of 4-(2-oxoquinoxalin-1(2*H*)-yl)butanoic acid (705 mg, 1.63 mmol), D-α-tocopherol (380 mg, 1.63 mmol), EDC·HCl (376 mg, 1.96 mmol), DMAP (20 mg, 0.16 mmol), DIPEA (425 μL, 2.45 mmol) and DCM (20 mL) was stirred at room temperature for overnight. After then, the reaction mixture was poured into 50 mL water and extracted with DCM (3 × 20 mL). The organic solvent was washed with brine (50 mL) and dried over anhydrous Na_2SO_4. After filtration and concentration in vacuo, the obtained residue was further purified by flash column chromatography (SiO_2, petroleum ether/ethyl acetate, 4:1) to afford the desired product **6e** as a yellow oil (786 mg, 74%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.32 (s, 1H), 7.89 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.64 (dd, *J* = 8.6, 1.4 Hz, 1H), 7.58 (ddd, *J* = 8.5, 7.0, 1.5 Hz, 1H), 7.35 (ddd, *J* = 8.3, 7.1, 1.3 Hz, 1H), 4.44 – 4.35 (m, 2H), 2.85 (t, *J* = 6.6 Hz, 2H), 2.60 (t, *J* = 6.8 Hz, 2H), 2.25 – 2.14 (m, 2H), 2.10 (s, 3H), 2.03 (s, 3H), 1.99 (s, 3H), 1.80 (ddp, *J* = 20.0, 13.3, 6.1 Hz, 2H), 1.63 – 1.47 (m, 5H), 1.48 – 1.34 (m, 4H), 1.33 – 1.17 (m, 8H), 1.18 – 1.00 (m, 7H), 0.89 – 0.81 (m, 12H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 171.9, 154.9, 150.0, 149.6, 140.3, 133.6, 132.3, 131.4, 130.6, 126.5, 124.8, 123.7, 123.2, 117.5, 114.2, 75.1, 41.2, 39.3, 37.46, 37.43, 37.3, 32.8, 32.7, 30.6, 28.0, 24.8, 24.4, 22.7, 22.6, 22.1, 21.0, 20.6, 19.7, 19.6, 13.0, 12.2, 11.8. **HRMS** (ESI(+)) m/z: Calculated for $C_{41}H_{60}N_2O_4$ $[M+H]^+$ 645.4631, found 645.4644.

Synthesis of 1-(5-(((13*S*)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl)oxy)pentyl)quinoxalin-2(1*H*)-one (6f)

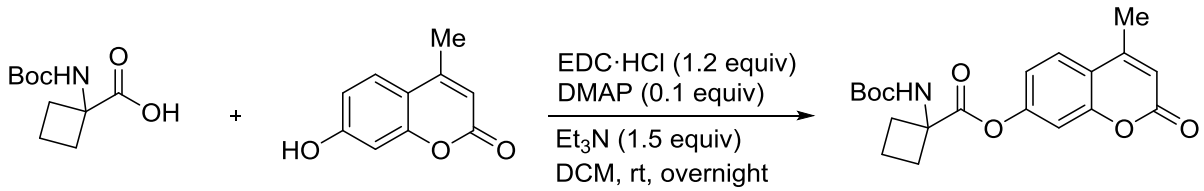


1r **6f**

To a 50 mL round-bottom flask was charged with NaH (60% dispersed in mineral oil) (356 mg, 8.89 mmol), in dry DMF (20 mL), was added quinoxalin-2(1*H*)-one **1r** (1.0 g, 6.84 mmol) portionwise. After stirring at room temperature for 30 min, 1,5-dibromopentane (1.12 mL, 8.2 mmol) was added in a drop-wise manner and the resulting solution was further stirred at room temperature for overnight. The reaction mixture was quenched with water (50 mL) and extracted with ethyl acetate (2 × 50 mL). The organic layer was washed with saturated aqueous NH_4Cl solution (50 mL) followed by brine (50 mL) and dried over anhydrous Na_2SO_4. The organic layer was then filtered off, evaporated in vacuo and purified by flash column chromatography (SiO_2, petroleum ether/ethyl acetate, 1:1) to afford 1-(5-bromopentyl)quinoxalin-2(1*H*)-one as a brown oil (1.35 g, 67%). Finally, a mixture of estrone (230 mg, 0.85 mmol), 1-(5-bromopentyl)quinoxalin-2(1*H*)-one (276 mg, 0.94 mmol), K_2CO_3 (176 mg, 1.28 mmol) in DMF (5 mL), was stirred at room temperature for overnight. The reaction mixture was then poured into 20 mL water and extracted with EtOAc (3 × 10 mL). The organic solvent was washed with brine (30 mL) and dried over anhydrous Na_2SO_4. After filtration and concentration in vacuo, the obtained residue was further purified by flash column chromatography (SiO_2, petroleum ether/ethyl acetate, 4:1) to afford the desired product **6f** as a yellow sticky gum (310 mg, 75%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.29 (s, 1H), 7.89 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.58 (ddd, *J* = 8.7, 7.3, 1.6 Hz, 1H), 7.41 – 7.31 (m, 2H), 7.18 (dd, *J* = 8.7, 1.1 Hz, 1H), 6.69 (dd, *J* = 8.6, 2.8 Hz, 1H), 6.63 (d, *J* = 2.7 Hz, 1H), 4.36 – 4.16 (m, 2H), 3.95 (t, *J* = 6.2 Hz, 2H), 3.00 – 2.81 (m, 2H), 2.50 (dd, *J* = 18.9, 8.4 Hz, 1H), 2.39 (dq, *J* = 11.7, 3.4 Hz, 1H), 2.24 (td, *J* = 10.5, 3.9 Hz, 1H), 2.19 – 1.91 (m, 4H), 1.91 – 1.79 (m, 4H), 1.72 – 1.33 (m, 7H), 0.90 (s, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 220.9, 156.9, 154.8, 150.2, 137.7, 133.6, 132.4, 132.0, 131.0, 130.8, 126.3, 123.6, 114.5, 113.8, 112.1, 67.4, 50.4, 48.0, 43.9, 41.9, 38.3, 35.8, 31.6, 29.6, 29.0, 27.0, 26.5, 25.9, 23.6, 21.6, 13.8. **HRMS** (ESI(+)) m/z: Calculated for $C_{31}H_{36}N_2O_3$ $[M+H]^+$ 485.2804, found 485.2807.

Synthesis of 4-methyl-2-oxo-2*H*-chromen-7-yl 1-((*tert*-butoxycarbonyl)amino)cyclobutane-1-carboxylate (6i)



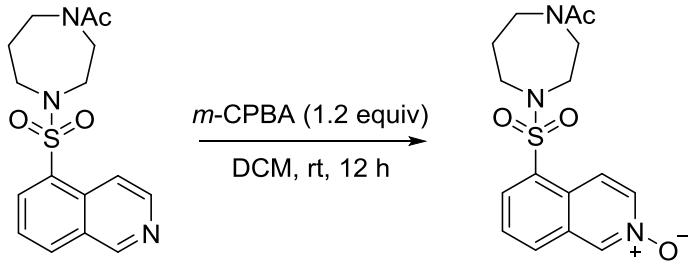
6i

To a 50 mL round-bottom flask was charged with 4-methylumbelliferone (400 mg, 2.27 mmol), 1-*N*-Boc-amino-cyclobutane carboxylic acid (538 mg, 2.5 mmol), EDC·HCl (522 mg, 2.72 mmol), DMAP (28 mg, 0.23 mmol), DIPEA (589 µL, 3.41 mmol) and DCM (20 mL). After stirring at room temperature for overnight, the reaction mixture was poured into 20 mL water and extracted with DCM (3 × 20 mL). The organic solvent was washed with brine (50 mL) and dried over anhydrous Na_2SO_4.

After filtration and concentration in vacuo, the obtained residue was further purified by flash column chromatography (SiO_2, petroleum ether/ethyl acetate, 3:2) to afford the desired product **6i** as a white fluffy solid (708 mg, 83%).

Mp 124–126 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.61 (d, *J* = 8.6 Hz, 1H), 7.14 – 7.02 (m, 2H), 6.27 (d, *J* = 1.3 Hz, 1H), 5.27 (s, 1H), 2.90 – 2.72 (m, 2H), 2.43 (d, *J* = 1.3 Hz, 3H), 2.37 – 2.21 (m, 2H), 2.20 – 2.05 (m, 2H), 1.45 (s, 9H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 171.9, 160.5, 154.8, 154.2, 153.6, 151.9, 125.4, 118.0, 117.8, 114.5, 110.3, 80.4, 58.5, 31.6, 28.3, 18.7, 15.2. **HRMS** (ESI(+)) m/z: Calculated for $C_{20}H_{23}NO_6$ $[M+Na]^+$ 396.1423, found 396.1415.

Synthesis of 5-((4-acetyl-1,4-diazepan-1-yl)sulfonyl)isoquinoline 2-oxide (6j)



6j

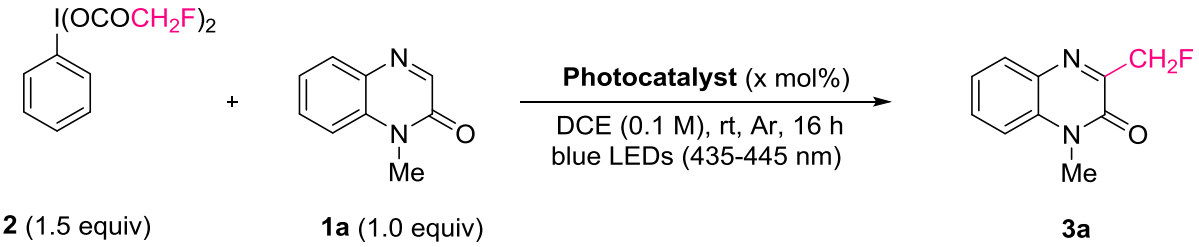
Fasudil (5-((1,4-diazepan-1-yl)sulfonyl)isoquinoline) and its *N*-acetyl derivative were prepared according to literature procedures.[14,15] To a solution of 1-(4-(isoquinolin-5-ylsulfonyl)-1,4-diazepan-1-yl)ethan-1-one (*N*-acetyl-fasudil, 375 mg, 1.12 mmol) in dry DCM (10 mL), *m*-CPBA (77%, 298 mg, 1.29 mmol) was added. The reaction mixture was then stirred at room temperature for overnight. After consumption of starting material, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (10 mL) and extracted with DCM (2 × 10 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered off and evaporated to dryness. The crude material was purified via flash column chromatography (SiO_2, DCM/MeOH, 4:1) to afford *N*-acetyl-fasudil *N*-oxide **6j** as a pale yellow solid (333 mg, 85%).

Mp 210–212 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.79 (d, *J* = 1.9 Hz, 1H), 8.57 – 8.41 (m, 1H), 8.23 (dt, *J* = 7.5, 1.8 Hz, 1H), 8.06 (ddd, *J* = 7.4, 2.6, 1.1 Hz, 1H), 7.95 – 7.82 (m, 1H), 7.78 – 7.57 (m, 1H), 3.80 – 3.57 (m, 4H), 3.54 – 3.29 (m, 4H), 2.06 (d, *J* = 9.2 Hz, 3H), 2.03 – 1.92 (m, 2H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 170.2, 170.0, 138.6, 138.5, 136.2, 135.5, 135.4, 131.2, 131.2, 130.3, 130.1, 130.1, 128.4, 128.3, 124.1, 124.0, 121.6, 121.6, 50.7, 50.2, 49.2, 48.5, 47.7, 47.6, 47.0, 44.5, 29.0, 27.7, 21.5, 21.0. The complex NMR spectra obtained at room temperature due to the amide units which attribute dynamic conformational behaviour of the compound. **HRMS** (ESI(+)) m/z: Calculated for $C_{16}H_{19}N_3O_4S$ $[M+H]^+$ 350.1175, found 350.1176.

4. Optimization of the reaction conditions

Procedure for the optimization studies:

To a 4 mL vial equipped with a stir bar was added photocatalyst (given equivalents), solvent (1 mL), 1-methylquinoxalin-2(1*H*)-one (**1a**) (16 mg, 0.1 mmol, 1.0 equiv), and phenyl-λ^3-iodanediyl bis(2-fluoroacetate**)** (**2**) (given equivalents). The vial was sealed with an open-top cap (PTFE/silicone), degassed with Argon bubbling for 10 seconds and wrapped with parafilm. The reaction mixture was stirred and irradiated by Aldrich® Micro Photochemical Reactor with blue LED lights (435–445 nm spectral range) at room temperature (with air flow cooling) for 16 hours. To the reaction mixture was concentrated in vacuo, 3,4,5-trimethoxybenzaldehyde (19.6 mg, 0.1 mmol) was added and analyzed by quantitative ^{1}H NMR.

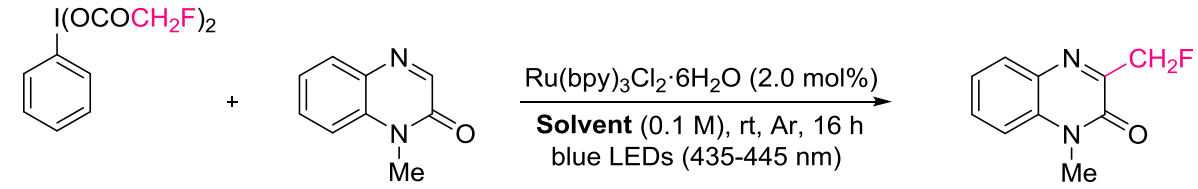


2 (1.5 equiv) **1a** (1.0 equiv) **3a**

Table S1: Screening of photocatalysts:

Entry	Photocatalyst (x mol%)	Yield (3a)
1	$Cu(dap)_2Cl$ (2.0)	50%
2	*fac*-$Ir(ppy)_3$ (2.0)	30%
3	4-CzlPN (2.0)	44%
4	Perylene (2.0)	33%
5	$Ru(bpy)_3Cl_2 \cdot 6H_2O$ (2.0)	89%
6	$Ru(bpy)_3Cl_2 \cdot 6H_2O$ (1.0)	58%
7	$Ru(bpy)_3Cl_2 \cdot 6H_2O$ (5.0)	86%
8	Rhodamine B (2.0)	16%
9	Thioxanthone (2.0)	23%
10	MesAcr (2.0)	48%
11	Triphenylamine (2.0)	12%
12	*N*-phenylthiazine (2.0)	traces

We initially investigated our C–H fluoromethylation protocol of (**1a**) with hypervalent iodine(III) reagent **2** employing $Cu(dap)_2Cl$ as the photocatalyst, DCE as the solvent, the desired product **3a** was obtained in 50% yield. Alternative photo-catalysts such as 4-CzlPN and MesAcr resulted in moderate yields. $Ru(bpy)_3Cl_2 \cdot 6H_2O$ was found a suitable and an efficient photocatalyst for this reaction.



2 (1.5 equiv.) **1a** (1.0 equiv.) **3a**

Table S2: Screening of solvents:

Entry	Solvent	Yield (3a)
1	DCM	82%
2	$CHCl_3$	26%
3	$CDCl_3$	41%
4	DCE	89%
5	DCE (0.05 M)	86%
6	DCE (0.2 M)	81%
7	EtOAc	84%
8	DME	trace
9	dioxane	NP
10	THF	33%
11	MeCN	53%
12	DMSO	24%
13	DMF	trace
14	MeOH	NP
15	acetone	45%
16	dimethyl carbonate	54%
17	toluene	17%

The reaction was successful in other polar and non-polar aprotic solvents, such as acetonitrile dimethyl carbonate, acetone or tetrahydrofuran (THF), but in all cases, lower yields were obtained compared to DCE. The use of dimethyl sulfoxide (DMSO), dimethyl formamide (DMF), dimethoxyethane (DME), toluene, methanol or dioxane resulted in low to no conversion towards the desired product. DCE was chosen as the optimum solvent for this transformation, with DCM and ethyl acetate (EtOAc) being viable alternative solvents.

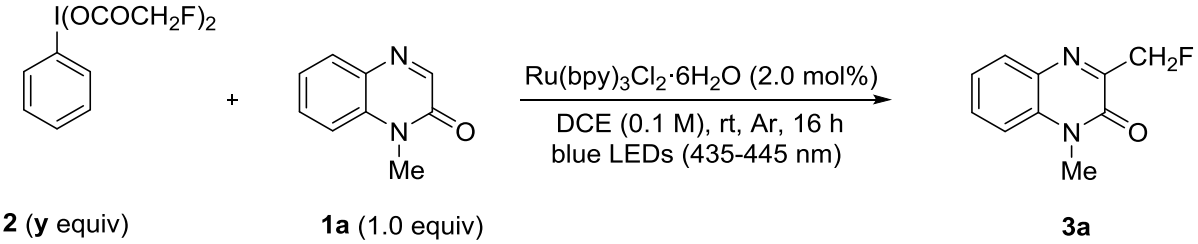


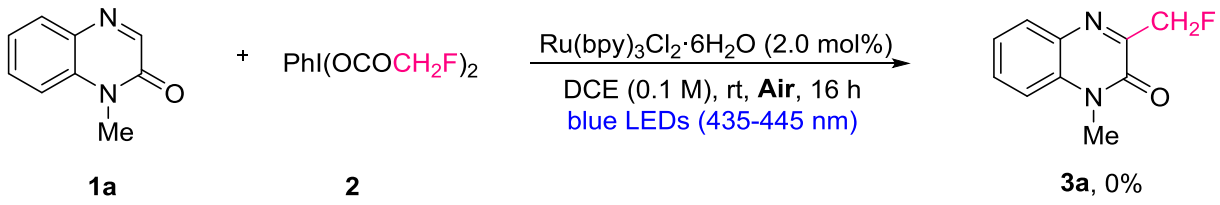
Table S3: Screening of iodine(III) reagent equivalents:

Entry	Reagent (2) (y equiv)	Yield (3a)
1	1.0	54%
2	1.2	71%
3	1.5	89%
4	2.0	88%

1.5 equivalents of hypervalent iodine(III) reagent (**1**) was shown to be optimal for the C-H fluoromethylation protocol.

5. Mechanistic investigations

a. Investigation on the effect of Oxygen:



1a **2** **3a**, 0%

$Ru(bpy)_3Cl_2·6H_2O$ (1.5 mg, 2.0 mol%), 1,2-dichloroethane (DCE) (1.0 mL), 1-methylquinoxalin-2(1*H*)-one (**1a**) (16 mg, 0.1 mmol) and phenyl-λ^3-iodanediyl bis(2-fluoroacetate) (**2**) (53.7 mg, 0.15 mmol) were added to a 4-mL vial equipped with a stir bar. Then, the reaction mixture was stirred in an Aldrich® Micro Photochemical Reactor (ALDKIT001) with blue LED lights (435–445 nm spectral range) at room temperature (with air flow cooling) for 16 h under open air. The reaction mixture was concentrated in vacuum and no formation of desired product **3a** was observed by ^{1}H NMR analysis using 3,4,5-trimethoxybenzaldehyde as an internal standard.

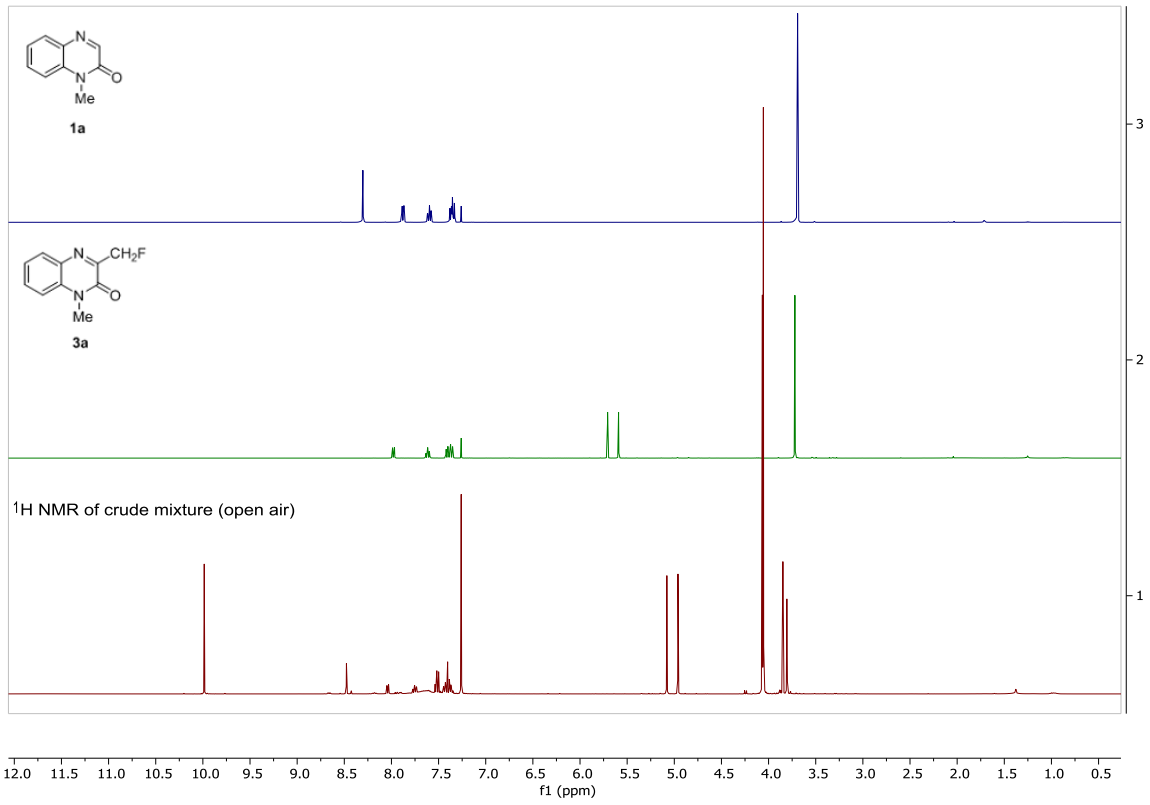
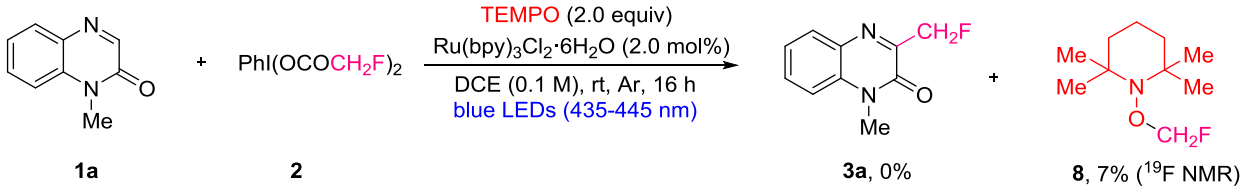


Figure S3. ^{1}H NMR comparison of **1a, 3a** and crude mixture of the reaction in air.

b. Radical trapping experiment with TEMPO:



$Ru(bpy)_3Cl_2·6H_2O$ (1.5 mg, 2.0 mol%), 1,2-dichloroethane (DCE) (1.0 mL), 1-methylquinoxalin-2(1*H*)-one (**1a**) (16 mg, 0.1 mmol), 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) (15.6 mg, 2.0 equiv) and phenyl-λ^3-iodanediyl bis(2-fluoroacetate**)** (**2**) (53.7 mg, 0.15 mmol) were added to a 4-mL vial equipped with a stir bar. Then, the vial was sealed with an open-top cap (PTFE/silicone), degassed via argon bubbling for 30 s, and wrapped using parafilm. Then, the reaction mixture was stirred in an Aldrich® Micro Photochemical Reactor (ALDKIT001) with blue LED lights (435–445 nm spectral range) at room temperature (with air flow cooling) for 16 h. The reaction mixture was concentrated in vacuo and analyzed by quantitative ^{19}F NMR (*α,α,α*-trifluorotoluene as an internal standard) and GC-MS.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -138.69 (t, *J* = 57.5 Hz).

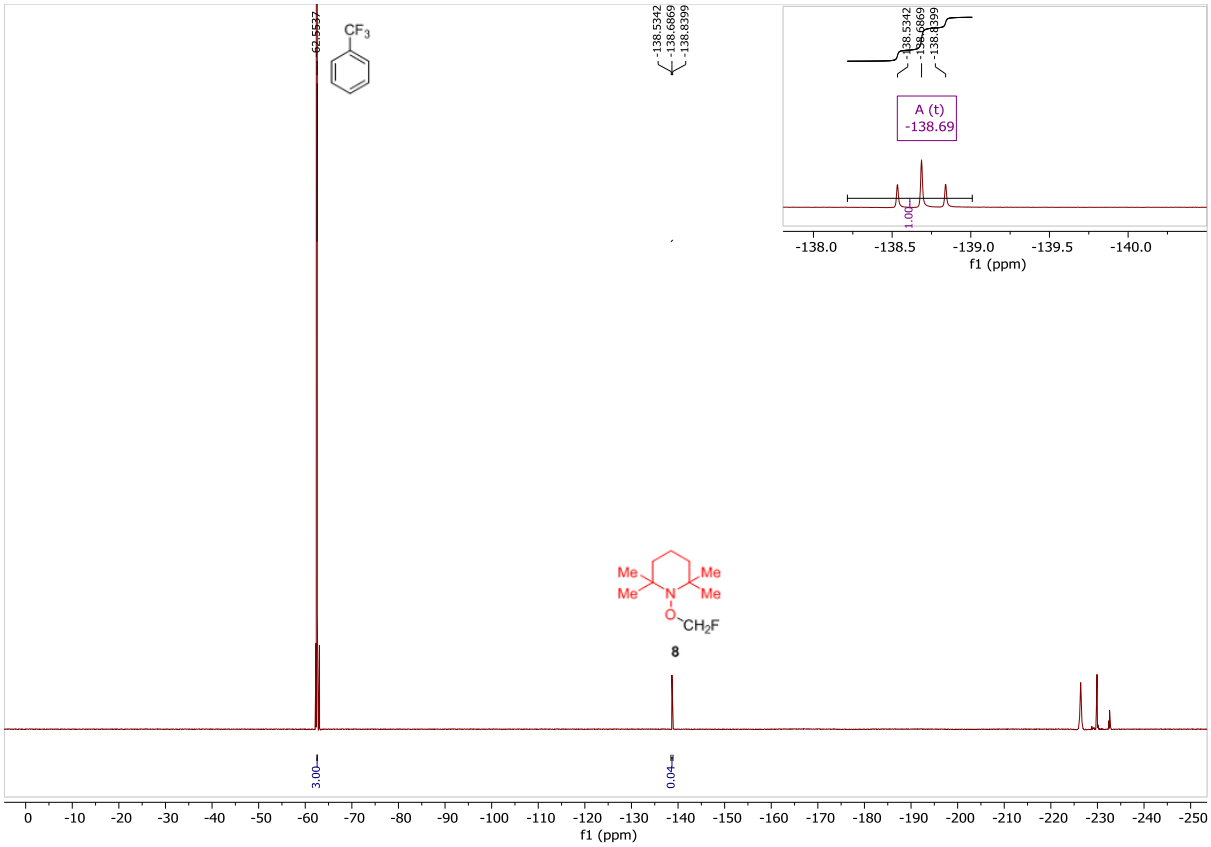


Figure S4. Quantitative ^{19}F NMR of TEMPO experiment.

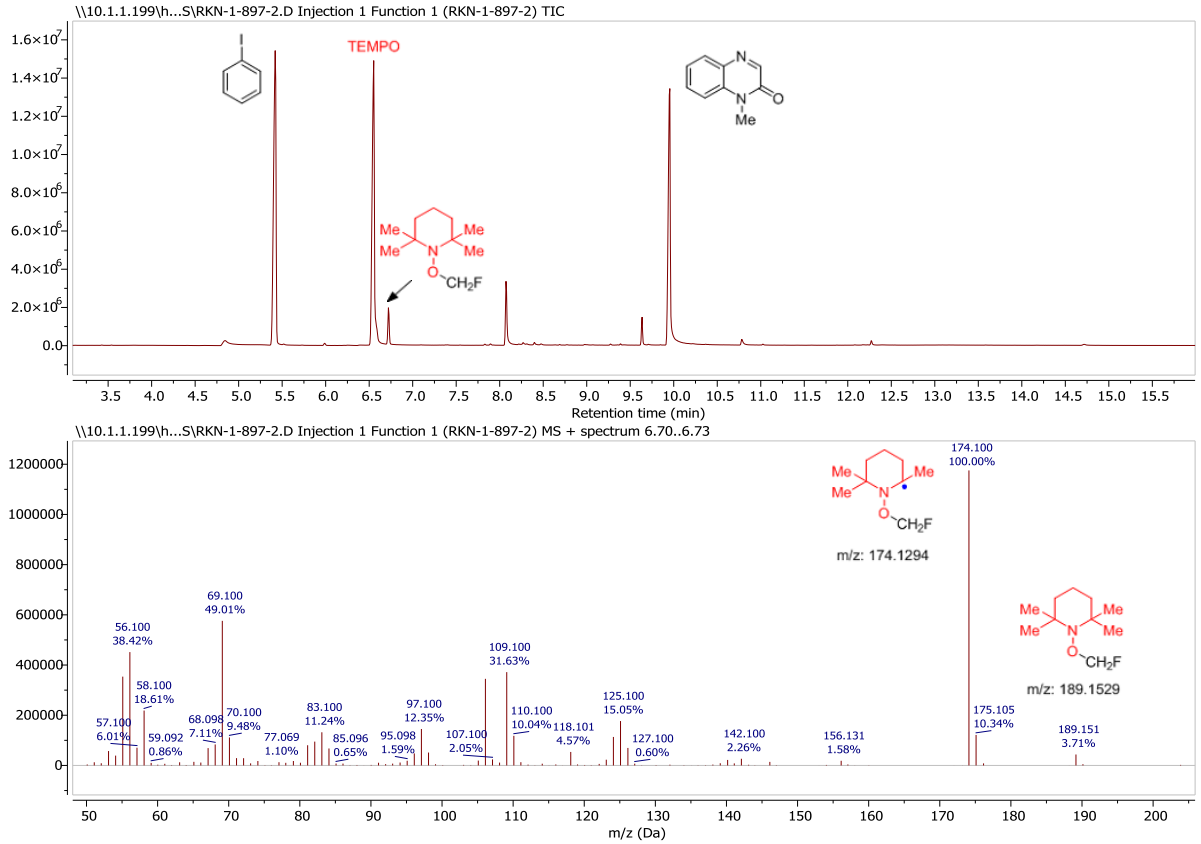
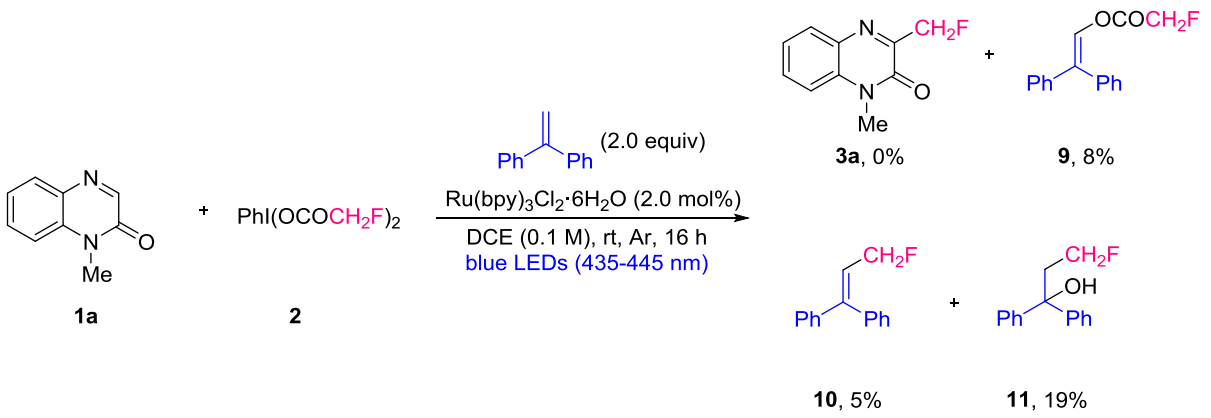


Figure S5. GC-MS detection of TEMPO-CH_2F adducts.

c. Radical trapping experiment with 1,1-diphenylethene:



$Ru(bpy)_3Cl_2·6H_2O$ (1.5 mg, 2.0 mol%), 1,2-dichloroethane (DCE) (1.0 mL), 1-methylquinoxalin-2(1*H*)-one (**1a**) (16 mg, 0.1 mmol), 1,1-diphenylethene (36 mg, 2.0 equiv) and phenyl-λ^3-iodanediyl bis(2-fluoroacetate**)** (**2**) (53.7 mg, 0.15 mmol) were added to a 4-mL vial equipped with a stir bar. Then, the vial was sealed with an open-top cap (PTFE/silicone), degassed via argon bubbling for 30 s, and wrapped using parafilm. Then, the reaction mixture was stirred in an Aldrich® Micro Photochemical Reactor (ALDKIT001) with blue LED lights (435–445 nm spectral range) at room

temperature (with air flow cooling) for 16 h. The reaction mixture was concentrated in vacuo and analyzed by quantitative ^{19}F NMR (*α,α,α*-trifluorotoluene as an internal standard).

9: ^{19}F NMR (376 MHz, Chloroform-*d*) δ -229.67 (t, *J* = 47.0 Hz).

10: ^{19}F NMR (376 MHz, Chloroform-*d*) δ -206.17 (td, *J* = 47.0, 10.7 Hz).[16]

11: ^{19}F NMR (376 MHz, Chloroform-*d*) δ -222.09 (tt, *J* = 47.2, 23.8 Hz).[17]

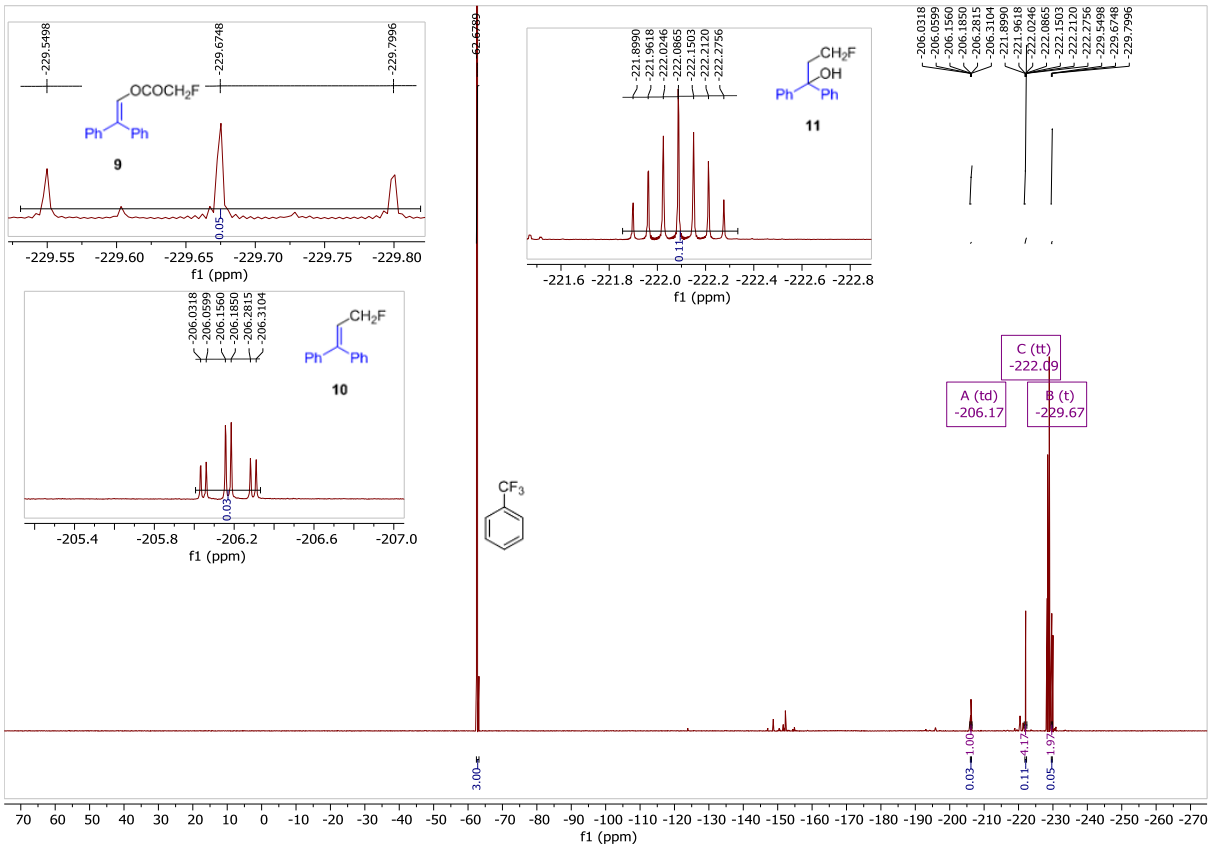
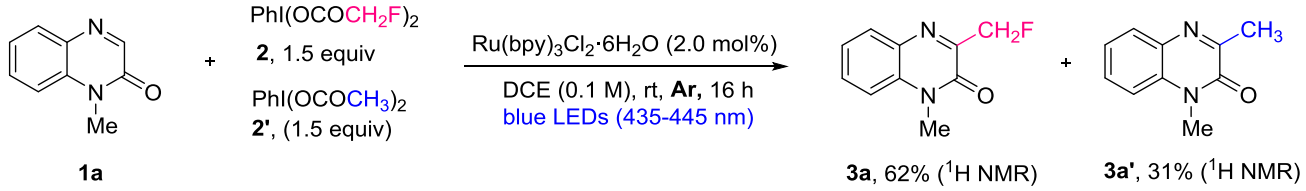


Figure S6. Quantitative ^{19}F NMR analysis of the reaction with 1,1-diphenylethene.

d. Cross-over experiment:



Regarding to the possible reaction mechanism, the cross-over experiments between two different hypervalent iodine(III) reagents **2** and **2'** were examined. It turned out that two products were obtained with inseparable mixture when equimolar amount of **2** and **2'** was treated with **1a**. This result indicated that a separate competing radical C–H monofluoromethylation and methylation might occur in the reaction.

$Ru(bpy)_3Cl_2 \cdot 6H_2O$ (1.5 mg, 2.0 mol%), 1,2-dichloroethane (DCE) (1.0 mL), 1-methylquinoxalin-2(1*H*)-one (**1a**) (16 mg, 0.1 mmol), phenyl-λ^3-iodanediyl bis(2-fluoroacetate) **2** (53.7 mg, 0.15 mmol) and (diacetoxyiodo)benzene (PIDA) (48.3 mg, 0.15 mmol) were added to a 4-mL vial equipped with a stir bar. Then, the vial was sealed with an open-top cap (PTFE/silicone), degassed via argon bubbling for 30 s, and wrapped using parafilm. Then, the reaction mixture was stirred in an Aldrich® Micro Photochemical Reactor (ALDKIT001) with blue LED lights (435–445 nm spectral range) at room temperature (with air flow cooling) for 16 h. The reaction mixture was concentrated in vacuo and analyzed by quantitative ^{1}H NMR (3,4,5-trimethoxybenzaldehyde as an internal standard) and GC-MS.

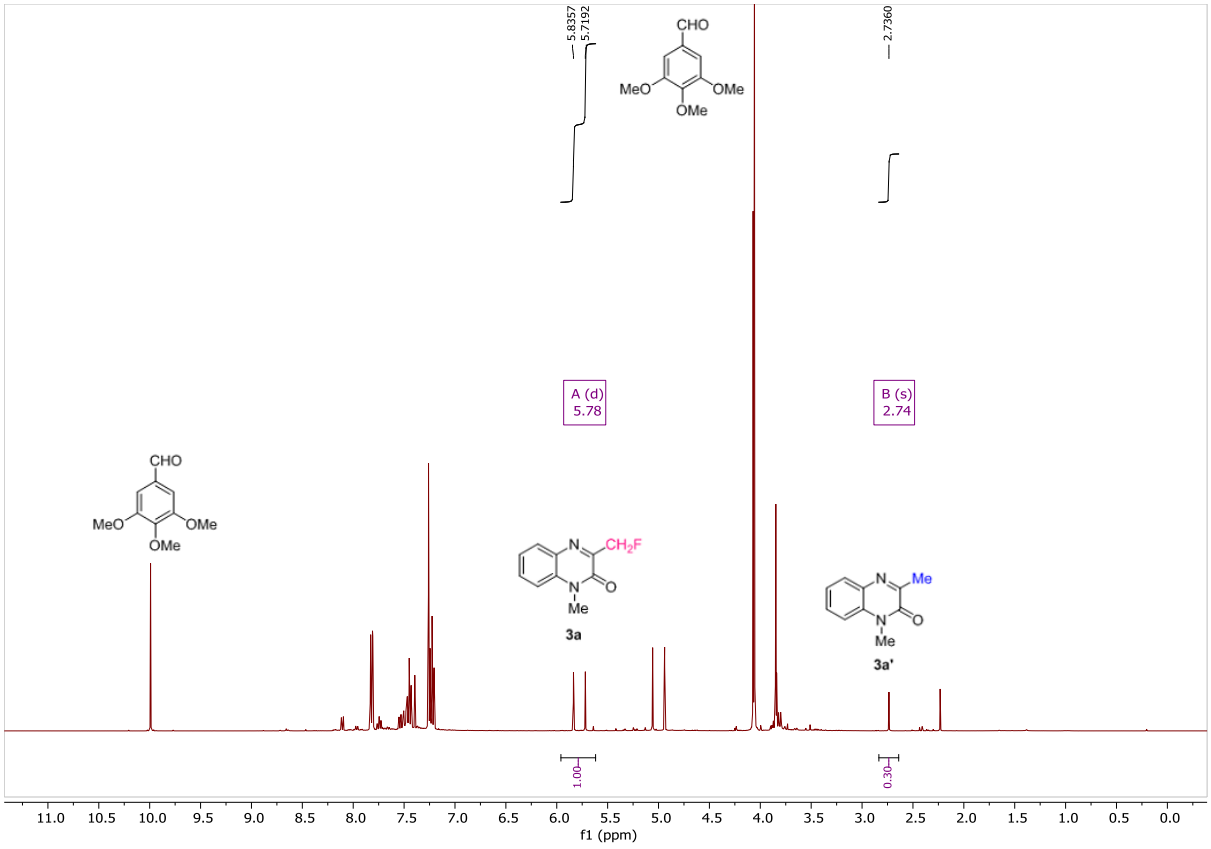


Figure S7. Quantitative ^{1}H NMR analysis of the cross-over experiment.

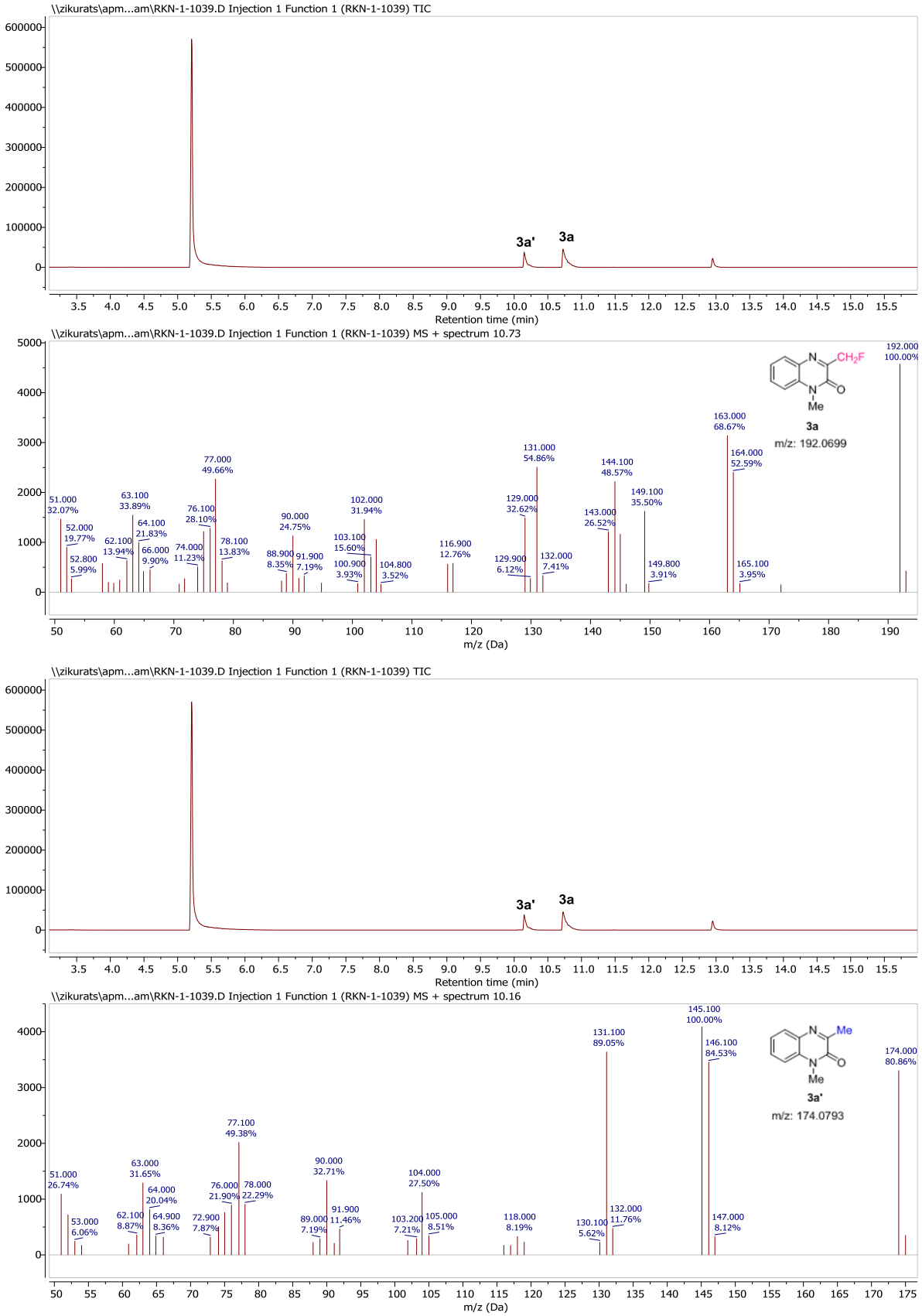
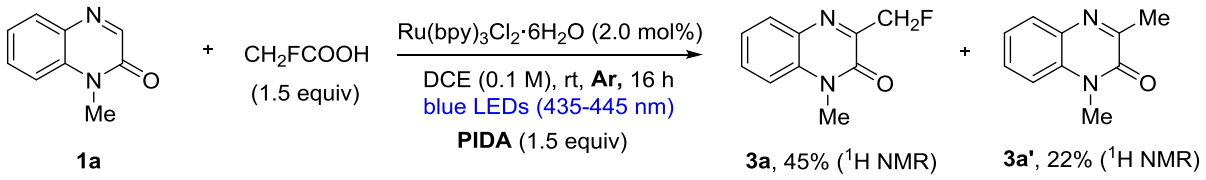


Figure S8. GC-MS analysis of the cross-over experiment.

e. Ligand exchange experiment with PIDA (*in situ* generated reagent 2):



$Ru(bpy)_3Cl_2·6H_2O$ (1.5 mg, 2.0 mol%), 1,2-dichloroethane (DCE) (1.0 mL), 1-methylquinoxalin-2(1*H*)-one (**1a**) (16 mg, 0.1 mmol), 2-fluoroacetic acid (11.7 mg, 0.15 mmol) and (diacetoxyiodo)benzene (PIDA) (48.3 mg, 0.15 mmol) were added to a 4-mL vial equipped with a stir bar. Then, the vial was sealed with an open-top cap (PTFE/silicone), degassed via argon bubbling for 30 s, and wrapped using parafilm. Then, the reaction mixture was stirred in an Aldrich® Micro Photochemical Reactor (ALDKIT001) with blue LED lights (435–445 nm spectral range) at room temperature (with air flow cooling) for 16 h. The reaction mixture was concentrated in vacuo and analyzed by quantitative ^{1}H NMR (3,4,5-trimethoxybenzaldehyde as an internal standard) and GC-MS. This result revealed that <u>inseparable products **3a** and **3a'** were formed and found that the direct use of the reagent **2** was the best for radical C–H monofluoromethylation of heteroarenes</u>.

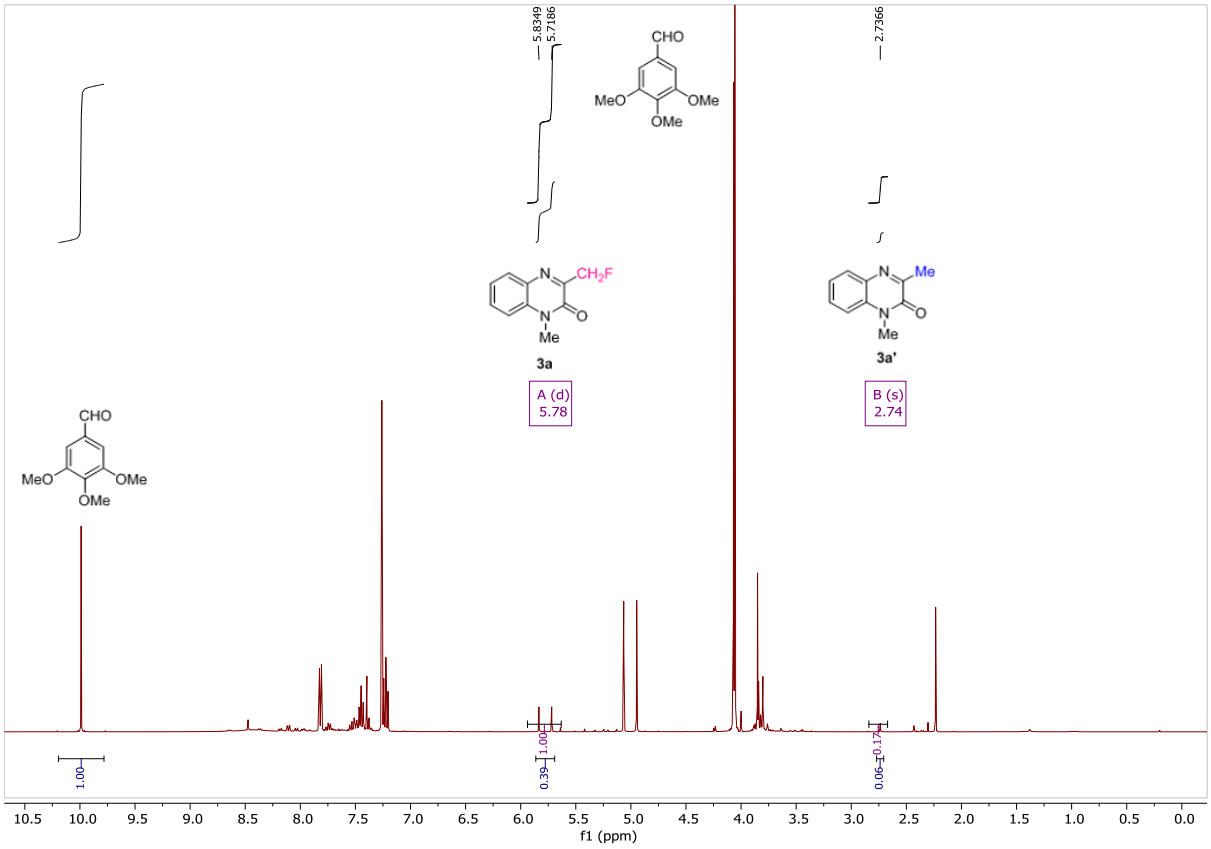


Figure S9. Quantitative ^{1}H NMR analysis of the reaction with *in situ* generated **2**.

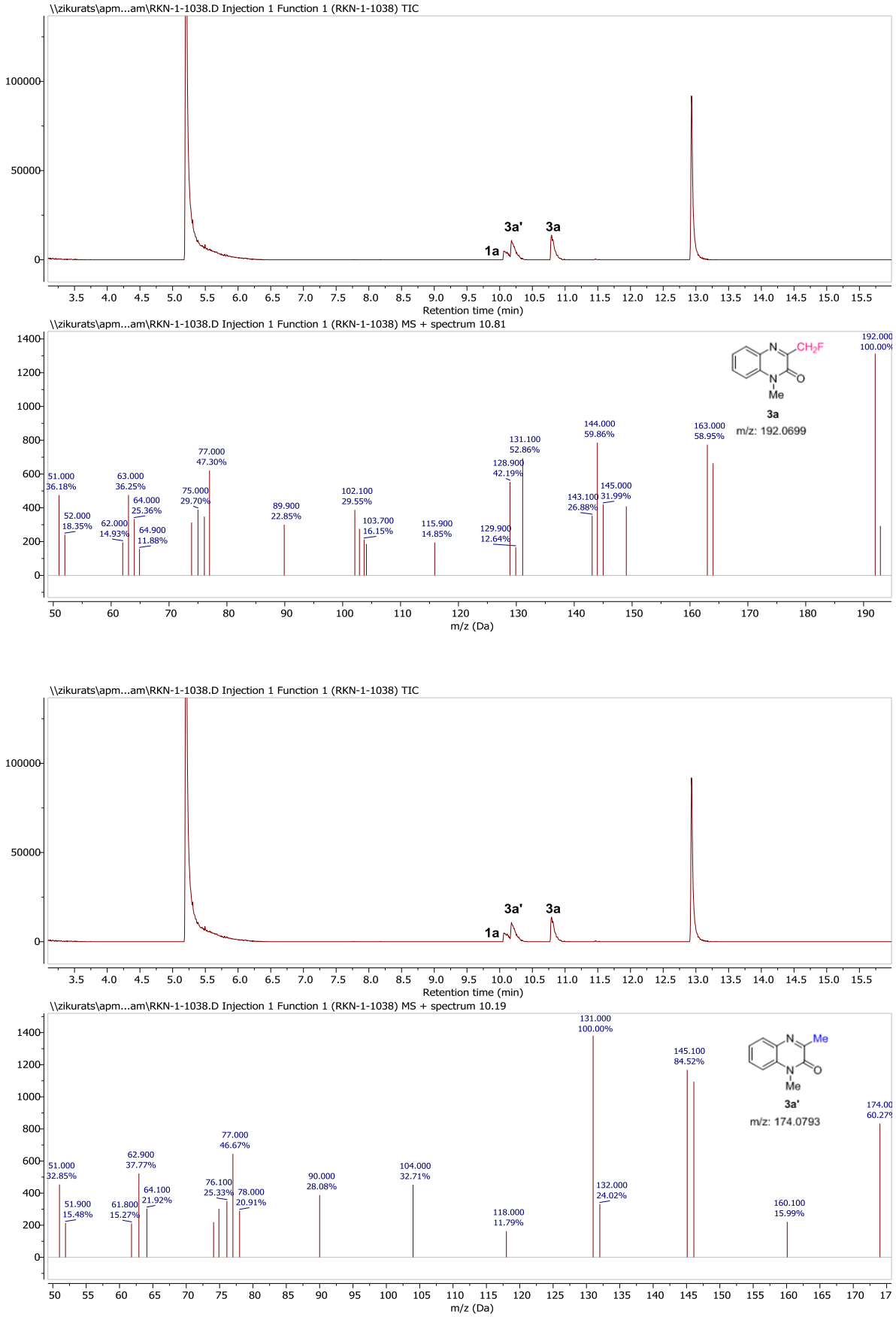


Figure S10. GC-MS analysis of the reaction with *in situ* generated **2**.

e. Light ON-OFF experiment:

Seven standard reaction mixtures in 4 mL vial were equipped with a magnetic stir bar, added 1-methylquinoxalin-2(1*H*)-one (**1a**) (16 mg, 0.1 mmol), phenyl-λ^3-iodanediyl bis(2-fluoroacetate**)** (**2**) (53.7 mg, 0.15 mmol) and $Ru(bpy)_3Cl_2 \cdot 6H_2O$ (1.5 mg, 2.0 mol%) in DCE (1.0 mL). Then, the vial was sealed with an open-top cap (PTFE/silicone), degassed via argon bubbling for 30 s, and wrapped using parafilm. Then, the reaction mixture was stirred in an Aldrich® Micro Photochemical Reactor (ALDKIT001) with blue LED lights (435–445 nm spectral range) at room temperature (with air flow). After 2 h, the blue LEDs were turned off, and one vial was removed from the irradiation setup for analysis. The remaining six vials were stirred in the absence of light for an additional 2 h. Then, one vial was removed for analysis, and the blue LEDs were turned back on to irradiate the remaining five reaction mixtures. After an additional 2 h of irradiation, the blue LEDs were turned off, and one vial was removed for analysis. The remaining four vials were stirred in the absence of light for an additional 2 h. Then, one vial was removed for analysis, and the blue LEDs were turned back on to irradiate the remaining three reaction mixtures. After 2 h, the blue LEDs were turned off, and one vial was removed for analysis. The remaining two vials were stirred in the absence of light for an additional 2 h, then, a vial was removed for analysis and the blue LEDs were turned back on and irradiate the remaining last one reaction mixture for 4 h. The yield was determined by ^{1}H NMR spectroscopy using 3,4,5-trimethoxybenzaldehyde as the internal standard.

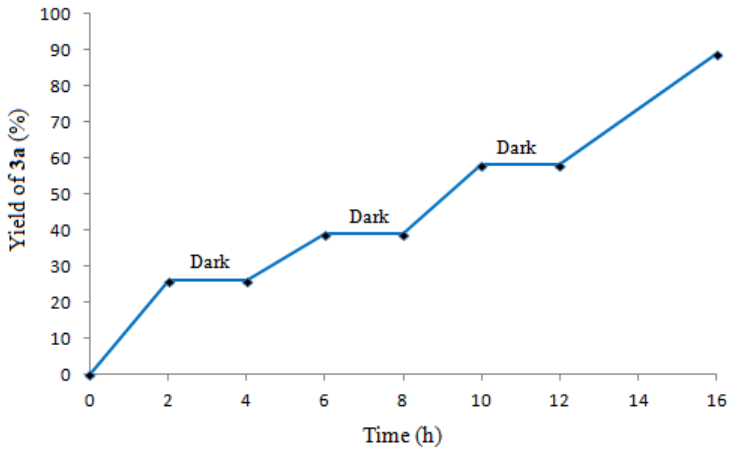
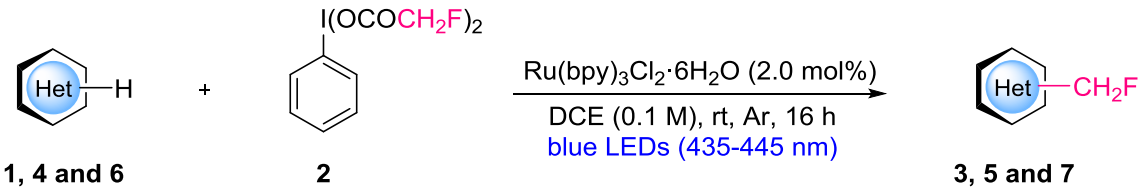


Figure S11. Light ON-OFF experiment.

6. General procedure for C–H radical monofluoromethylation of heteroarenes



1, 4 and 6 **2** **3, 5 and 7**

To a 4 mL vial equipped with a stir bar was added $Ru(bpy)_3Cl_2·6H_2O$ (2 mol%), DCE (0.1 M), respective heteroarene (1.0 equiv), and phenyl-λ^3-iodanediyl bis(2-fluoroacetate) **2** (1.5 equiv). The vial was sealed with an open-top cap (PTFE/silicone), degassed with Argon bubbling for 10 seconds and wrapped with parafilm. The reaction mixture was stirred and irradiated by an Aldrich® Micro Photochemical Reactor with blue LED lights (435–445 nm spectral range) at room temperature (with air flow cooling) for 16 h. The solvent was evaporated under reduced pressure. The crude reaction mixture was re-dissolved in DCM (20 mL) and washed saturated aqueous $NaHCO_3$ solution (2 × 20 mL) and extracted. The organic layer was dried over anhydrous Na_2SO_4 and evaporated to dryness. The crude mixture was purified by flash column chromatography (SiO_2, petroleum ether/EtOAc) to afford the corresponding fluoromethylated heteroarene.

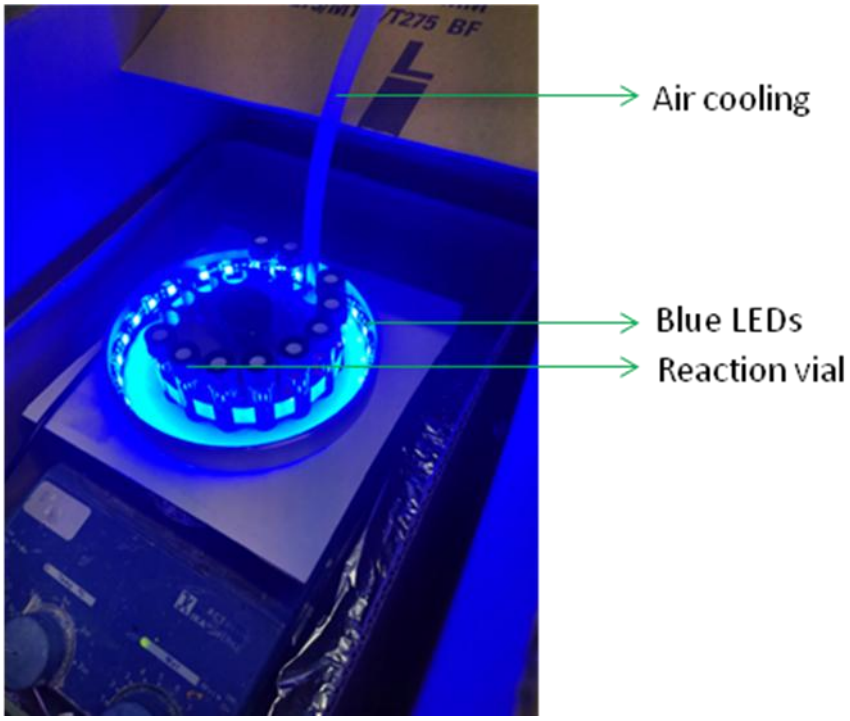
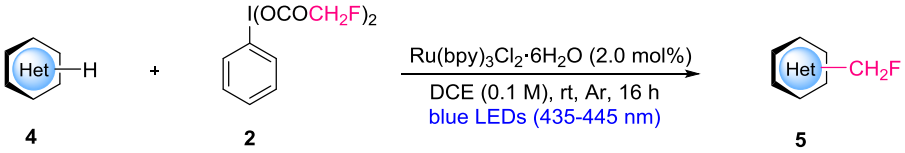


Figure S12. Experimental set-up for the C–H radical monofluoromethylation of heteroarenes.

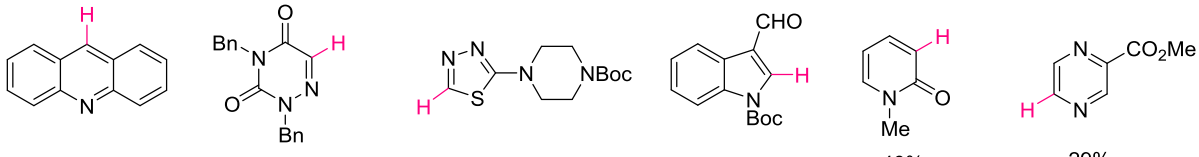


4 **2** **5**

Successful substrates

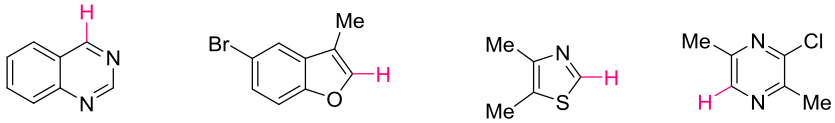
a. desired product formed but inseparable from unreacted starting heteroarene

Yield determined by ^{1}H NMR analysis of the crude reaction mixture using 3,4,5-trimethoxybenzaldehyde as the internal standard



90% 67% 31% 79% 40% 29%

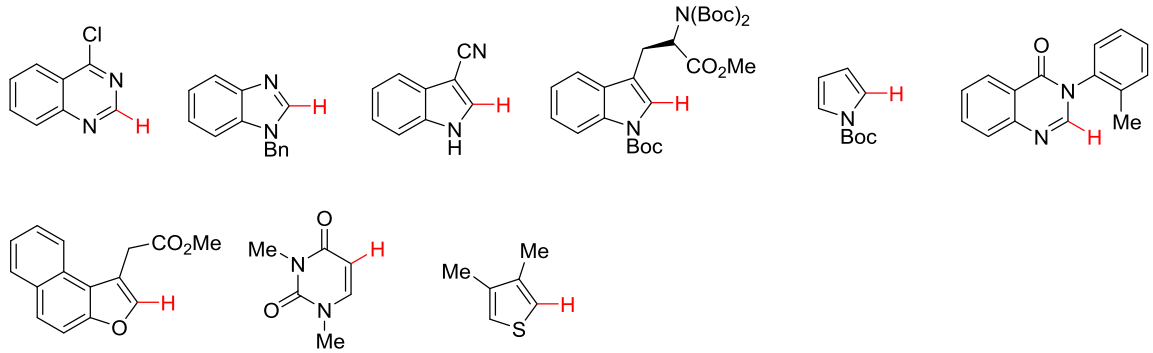
b. desired product formed but volatile or unstable



30% 46% 63% 23%

Unsuccessful substrates

a. no reaction



b. traces amount of product formed

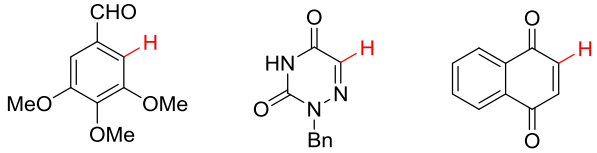
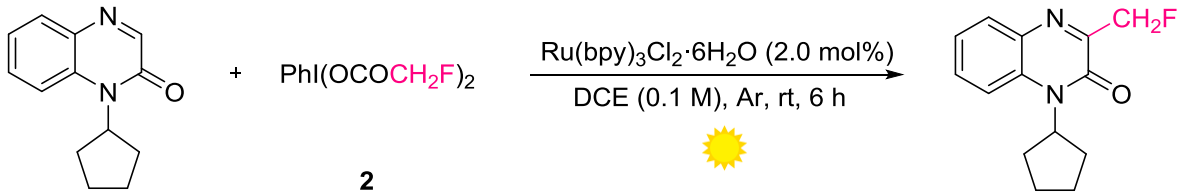


Figure S13. Other successful and unsuccessful substrates.

7. Synthetic applications

7.1 Sun-light driven reaction



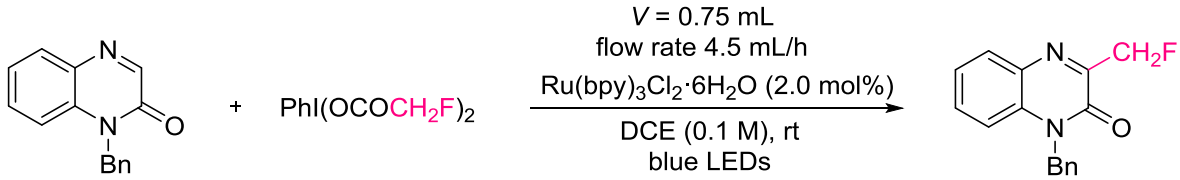
1u **2** **3u**

To a 4 mL vial equipped with a stir bar was added $Ru(bpy)_3Cl_2·6H_2O$ (3 mg, 2 mol%), DCE (2 mL), 1-cyclopentylquinoxalin-2(1*H*)-one (**1u**) (43 mg, 0.2 mmol, 1.0 equiv), and phenyl-λ^3-iodanediyl bis(2-fluoroacetate**)** (**2**) (107.4 mg, 0.3 mmol). The vial was sealed with an open-top cap (PTFE/silicone), degassed with Argon bubbling for 10 seconds and wrapped with parafilm. The reaction mixture was stirred and irradiated by sun light at room temperature for 6 h. The solvent was evaporated under reduced pressure. The crude reaction mixture was re-dissolved in DCM (20 mL) and washed with saturated aqueous $NaHCO_3$ solution (2 × 20 mL) and extracted. The organic layer was dried over anhydrous Na_2SO_4 and evaporated to dryness. The crude mixture was purified by flash column chromatography (SiO_2, petroleum ether/EtOAc, 30:1) to afford the product **3v** as colourless oil (32 mg, 65%).

Figure S14. Sun-light promoted C–H radical monofluoromethylation reaction.

7.2 Procedure for the Scale-up experiment in Continuous flow

The scale-up experiment was performed for the synthesis of 1-benzyl-3-(fluoromethyl)quinoxalin-2(1*H*)-one (**3v**).



1v **2** **3v**

An oven-dried 50 mL glass vial was charged with 1-benzylquinoxalin-2(1*H*)-one (**1v**) (1 g, 4.23 mmol, 1.0 equiv), phenyl-λ^3-iodanediyl bis(2-fluoroacetate) (**2**) (2.27 g, 6.34 mmol) and $Ru(bpy)_3Cl_2·6H_2O$ (63.37 mg, 0.0846 mmol, 0.02 equiv). 1,2-dichloroethane (DCE) (42 mL, 0.1 M) was added to the mixture. Next, the vial was closed with a screw-cap septum. The vial was degassed via bubbling argon gas using balloon. The mixture was sonicated for 10 minutes in the absence of light to make the reaction solution homogeneous. Next, the solution was transferred into a 50 mL syringe and pumped continuously using a syringe pump (4.5 $mL·h^{-1}$, t_R = 10 min) through a self-made flow reactor (materials: FEP tubing (ϕ 0.8 × ϕ1.6 mm); wall thickness: 0.4 mm; loop volume: 0.75 mL; distance between LEDs and tubing: 1.5 cm) as shown below. The reactor active zone was kept at room temperature with compressed air. The outlet of the reactor was put into a round bottom flask and the product was collected for 9 h 40 minutes. The solvent was evaporated under reduced pressure. The crude reaction mixture was re-dissolved in DCM (50 mL), washed with saturated aqueous $NaHCO_3$ solution (2 × 50 mL) and extracted. The organic layer was dried over anhydrous Na_2SO_4 and evaporated to dryness. The crude mixture was purified by flash column chromatography (SiO_2, petroleum ether/EtOAc, 9:1) to afford the product **3v** as a pale yellow solid (880 mg, 3.28 mmol, 78%).

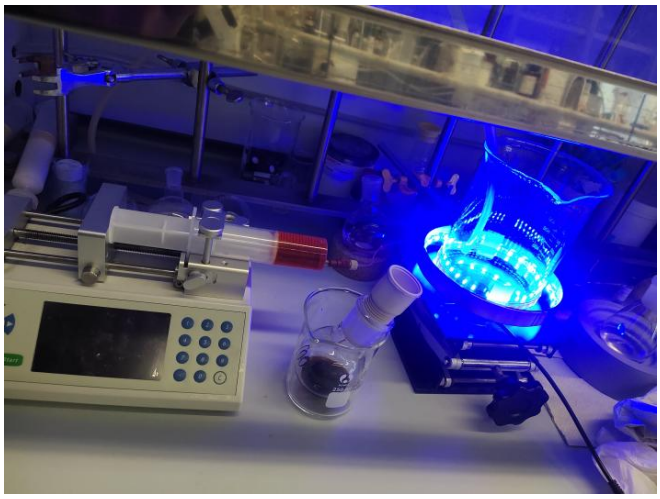


Figure S15. The C–H monofluoromethylation reaction in continuous flow mode.

8. Evaluation of anti-microbial activity

Antimicrobial activity was assessed according to Wiegand et al. method with minor modifications.[18] Several reference microbial strains from the Microbial Strain Collection of Latvia (MSCL) were used to determine antimicrobial activity: *Staphylococcus aureus* MSCL 330, *Escherichia coli* MSCL 332 and *Candida albicans* MSCL 378. The inoculum of microorganisms was prepared in sterile water at a density of 0.08-0.10 at 625 nm and diluted 100-fold in the appropriate broth. The Mueller-Hinton broth for bacteria and Malt Extract broth for *C. albicans* was used for susceptibility testing using a twofold serial broth micro dilution test which allowed the determination of minimum inhibitory concentration (MIC) and minimum bactericidal/fungicidal concentration (MBC/MFC). The 96-well plates were incubated at 37 °C for 24 h. The MIC was defined as the lowest concentration of the test material at which no visible growth was observed. From the wells of the 96-well plate where no microbial growth was detected, 4 µl of well broth was plated on Malt Extract Agar for *C. albicans* or R2A medium for bacteria to determine the MBC/MFC.[19]

Table S4. Minimum inhibitory concentration (MIC) and minimum bactericidal/fungicidal concentration (MBC/MFC) of substances, **µg/ml**. Dissolved in DMSO.

Compounds		*Escherichia coli* MSCL 332		*Staphylococcus aureus* MSCL 330		*Candida albicans* MSCL 378	
		MIC	MBC	MIC	MBC	MIC	MFC
1	**3a**	512	512	512	1024	**128**	256
2	**3b**	512	1024	512	1024	**128**	256
3	**3c**	512	512	512	1024	**128**	256
4	**3d**	512	1024	512	1024	**128**	256
5	**3e**	512	512	512	512	**128**	256
6	**3j**	512	512	512	512	256	256
7	**3l**	512	1024	512	1024	**128**	**128**
8	**3n**	512	512	512	1024	**128**	256
9	**3o**	512	1024	512	1024	256	256
10	**3p**	512	1024	512	1024	256	256
11	**3r**	512	512	512	1024	**128**	256
12	**3s**	512	512	512	1024	256	256
13	**3t**	512	512	512	1024	256	256
14	**3u**	**128**	**128**	**128**	1024	**32**	**32**
15	**3v**	512	512	256	512	**64**	**64**
16	**3va**	512	512	512	1024	**8**	**128**
17	**3vb**	512	512	512	512	**1**	**128**
18	**3vb'**	512	512	512	1024	**2**	**4**
19	**3vc**	512	512	512	1024	**4**	256
20	**3vd**	512	512	256	1024	256	256
21	**3ve**	512	512	512	512	**128**	512
22	**3vf**	512	512	512	512	**128**	512
23	**3vg**	512	512	512	1024	256	256
24	**5d**	**128**	**128**	256	512	**4**	**16**

25	**5e**	**128**	**512**	**8**	**64**	**16**	**512**
26	**5ea**	**32**	**32**	**4**	**16**	**0.5**	**2**
27	**5eb**	**128**	512	**8**	**16**	**4**	**32**
28	**5ec**	**32**	**64**	**8**	**32**	**128**	256
29	**5ed**	**256**	512	**8**	**64**	**32**	**32**
30	**5h**	512	512	512	1024	**64**	**64**
31	**5i**	256	512	512	512	**128**	512
32	**5j**	512	512	512	512	**64**	**128**
33	**5m**	512	512	512	512	**128**	512
34	Osthol	512	512	**32**	1024	**16**	**128**
35	**7h**	512	512	256	1024	**128**	**128**
	Gentamicin	1	4	0.25	4	-	-
	Fluconazole	-	-	-	-	32	>256
	DMSO	512	1024	512	1024	256	256

9. Evaluation of anti-cancer activity

Cell cytotoxicity assay

For the cell cytotoxicity assay, Hep G2, MCF7, HeLa, HCT 116 and Hek 293 cell lines were used. Each cell line was seeded in a 96-well plate at a density of $1x10^5$ cells per milliliter, total volume of 100 µl in each well. After seeding, cells were left to rest for 6 hours. Various concentrations of test compounds dissolved in DMSO were added to cell media and incubated for 48 h, vehicle solution was added to control cells to ensure the same DMSO end concentration of 1% in all wells. After the incubation, cell viability was assessed by MTT assay. Briefly, 100 µL of MTT solution was added to all wells (end concentration 1 mg/mL) and incubated for 2 h at +37 °C. After incubation, the MTT solution was discarded and 100 µL of isopropanol was added to dissolve the sediment. Absorption was measured at 570 and 650 nm using a Hidex Sense microplate reader.

Table S5. The IC_{50} values of Osthol and **7h** against various cell lines

Tumor types	Cell line	IC_{50} ± SD (µM)	
		Osthol	**7h**
Breast cancer	**MCF-7**	108.3 ± 29.4	**12.4 ± 2.7**
Hepatocellular carcinoma	**HepG-2**	96.3 ± 28.3	**8.9 ± 1.3**
Cervical carcinoma	**Hela**	61 ± 13.8	**8.7 ± 1.3**
Colon cancer	**HCT-116**	78.3 ± 22.8	**4.7 ± 0.4**
Human embryonic kidney	**Hek 293**	111.0 ± 37.7	**3.0 ± 0.4**

The data are presented as mean value ± SD. The experiments were performed in triplicate with 3 technical replicates in each experiment.

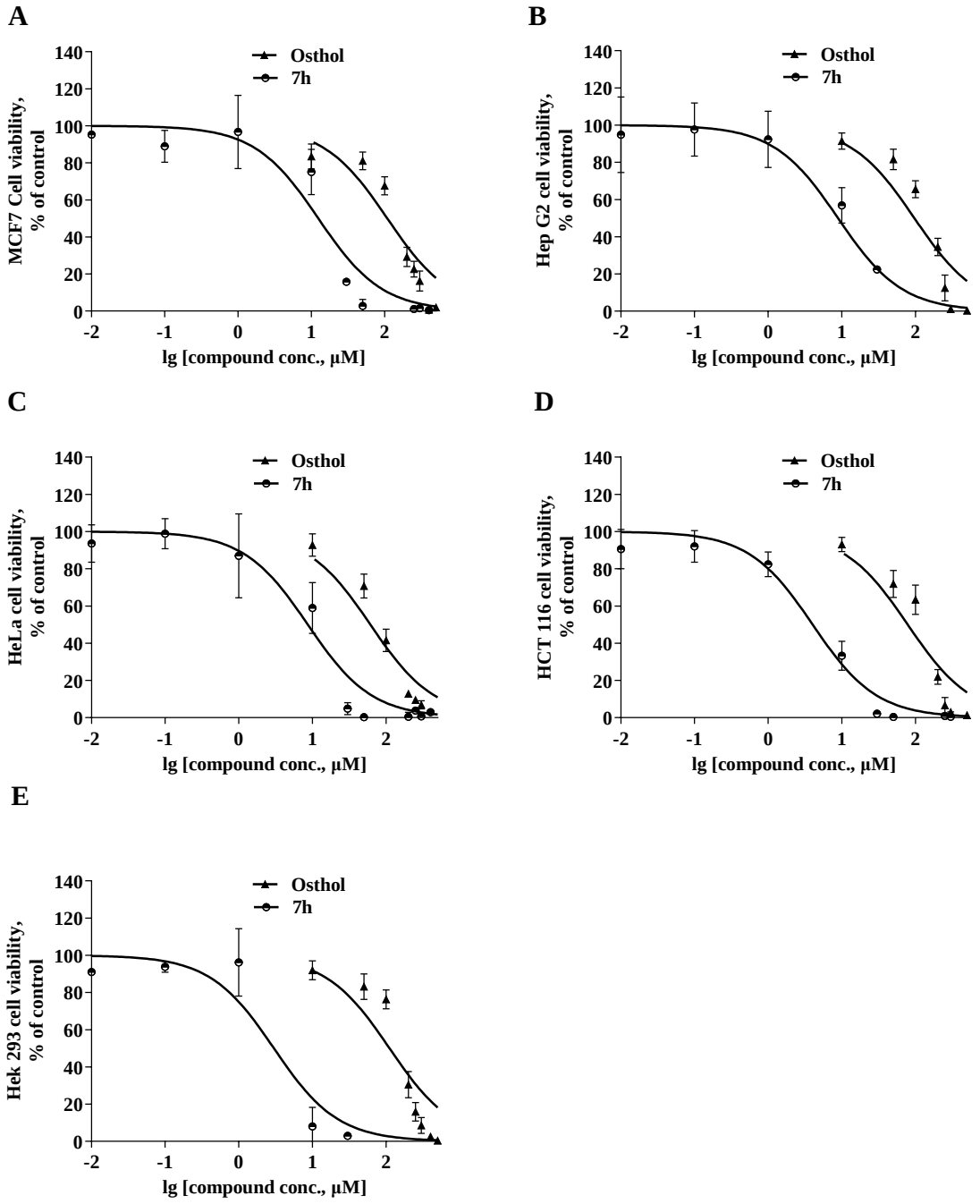
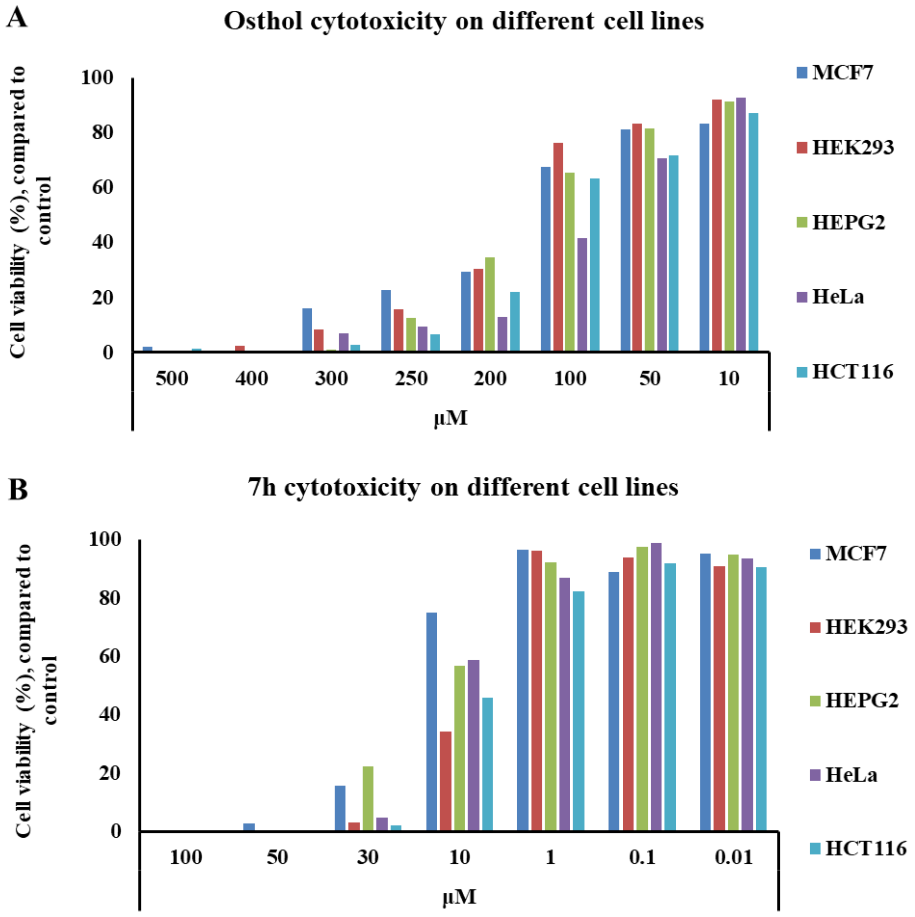


Figure S16. The IC_{50} curves of Osthol and **7h** on various cell lines. The effects on MCF7 cell line (**A**), Hep G2 cell line (**B**), HeLa cell line (**C**), HCT 116 cell line (**D**), Hek 293 cell line (**E**).


A
Osthol cytotoxicity on different cell lines
Cell viability (%), compared to control
100
80
60
40
20
0
500
400
300
250
200
100
50
10
μM
MCF7
HEK293
HEPG2
HeLa
HCT116
B
7h cytotoxicity on different cell lines
Cell viability (%), compared to control
100
80
60
40
20
0
100
50
30
10
1
0.1
0.01
μM
MCF7
HEK293
HEPG2
HeLa
HCT116

10. X-ray crystal structures of products

X-ray single crystal structure of (**3b**): Pale yellow crystals were obtained by slow evaporation from saturated solution in chloroform.

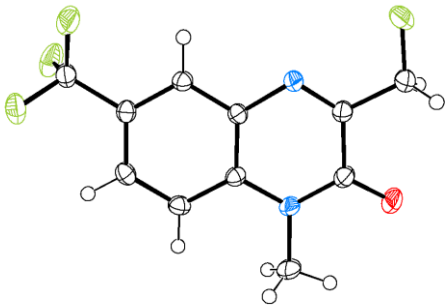


Table S6. Crystal data and refinement of **3b**

Chemical formula	$C_{11}H_8F_4N_2O$
M_r	260.19
Crystal system, space group	Orthorhombic, *Pbca*
Temperature (K)	150
a, *b*, *c* (Å)	14.4989 (2), 7.0904 (1), 20.0236 (3)
V (Å^3)	2058.49 (5)
Z	8
Radiation type	Cu *K*α
μ (mm^{-1})	1.41
Crystal size (mm)	0.20 × 0.12 × 0.05
Data collection	
Diffractometer	XtaLAB Synergy, Dualflex, HyPix
Absorption correction	Multi-scan *CrysAlis PRO* 1.171.41.112a (Rigaku Oxford Diffraction, 2021) Empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm.
T_{min}, T_{max}	0.761, 1.000
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	10196, 2078, 1840
R_{int}	0.031
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.631
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.035, 0.102, 1.07
No. of reflections	2078
No. of parameters	164

H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.30, -0.25
CCDC	2277851

X-ray single crystal structure of (**3l**): Colourless crystals were obtained by slow evaporation from saturated solution in methanol.

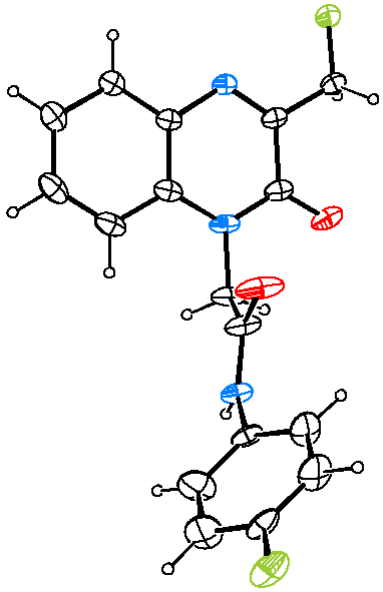


Table S7. Crystal data and refinement of **3l**

Chemical formula	$C_{17}H_{13}F_2N_3O_2$
M_r	329.30
Crystal system, space group	Monoclinic, $P2_1/c$
Temperature (K)	150
a, *b*, *c* (Å)	16.6303 (5), 4.6620 (2), 18.9217 (6)
β (°)	102.227 (3)
V (Å^3)	1433.73 (9)
Z	4
Radiation type	Cu *K*α
μ (mm^{-1})	1.02
Crystal size (mm)	0.30 × 0.05 × 0.04
Data collection	
Diffractometer	XtaLAB Synergy, Dualflex, HyPix
Absorption correction	Multi-scan *CrysAlis PRO* 1.171.41.123a (Rigaku Oxford Diffraction, 2022) Empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm.

T_{min}, T_{max}	0.608, 1.000
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	13626, 2827, 2260
R_{int}	0.035
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.631
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.060, 0.167, 1.07
No. of reflections	2827
No. of parameters	218
H-atom treatment	H-atom parameters constrained
$\Delta\rangle_{max}$, $\Delta\rangle_{min}$ (e Å^{-3})	0.35, -0.36
CCDC	2277848

X-ray single crystal structure of (**3r**): Yellow crystals were obtained by slow evaporation from saturated solution in methanol.

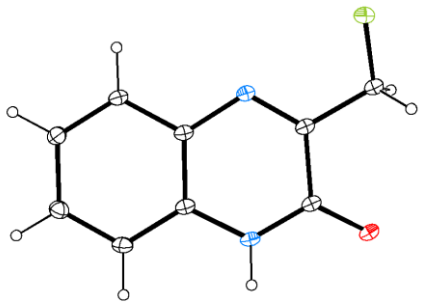


Table S8. Crystal data and refinement of **3r**

Chemical formula	$C_9H_7FN_2O$
M_r	178.17
Crystal system, space group	Triclinic, $P\bar{1}$
Temperature (K)	150
a, b, c (Å)	4.2581 (1), 8.4237 (2), 10.9697 (3)
α, β, γ (°)	94.118 (2), 98.142 (2), 94.746 (2)
V (Å^3)	386.78 (2)
Z	2
Radiation type	Cu $K\alpha$
μ (mm^{-1})	1.01
Crystal size (mm)	0.32 × 0.05 × 0.04
Data collection	
Diffractometer	XtaLAB Synergy, Dualflex, HyPix

Absorption correction	Multi-scan *CrysAlis PRO* 1.171.41.123a (Rigaku Oxford Diffraction, 2022) Empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm.
T_{min}, T_{max}	0.637, 1.000
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	7180, 1532, 1366
R_{int}	0.036
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.630
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.038, 0.114, 1.09
No. of reflections	1532
No. of parameters	118
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.16, -0.26
CCDC	2277848

X-ray single crystal structure of (**5h**): Pale yellow crystals were obtained by slow evaporation from saturated solution in chloroform.

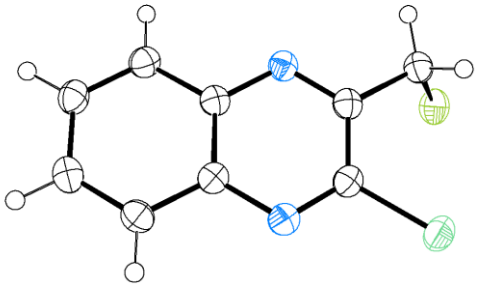


Table S9. Crystal data and refinement of **5h**

Chemical formula	$C_9H_6ClFN_2$
M_r	196.61
Crystal system, space group	Triclinic, $P\bar{1}$
Temperature (K)	150
a, b, c (Å)	6.7276 (4), 7.3697 (4), 9.4118 (5)
α, β, γ (°)	72.213 (5), 73.348 (5), 69.557 (5)
V (Å^3)	407.80 (4)
Z	2
Radiation type	Cu $K\alpha$
μ (mm^{-1})	3.87

Crystal size (mm)	0.24 × 0.12 × 0.07
Data collection	
Diffractometer	XtaLAB Synergy, Dualflex, HyPix
Absorption correction	Multi-scan *CrysAlis PRO* 1.171.41.123a (Rigaku Oxford Diffraction, 2022) Empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm.
T_{min}, T_{max}	0.317, 1.000
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	7362, 1599, 1454
R_{int}	0.063
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.628
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.054, 0.162, 1.08
No. of reflections	1599
No. of parameters	118
H-atom treatment	H-atom parameters constrained
$\Delta\chi_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.72, -0.59
CCDC	2277849

X-ray single crystal structure of (**5o**): Yellow crystals were obtained by slow evaporation from saturated solution in chloroform.

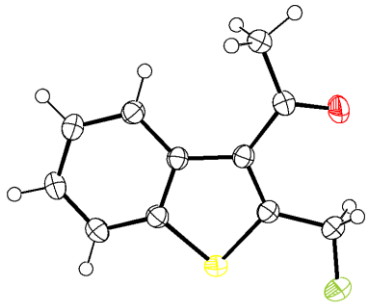


Table S10. Crystal data and refinement of **5o**

Chemical formula	$C_{11}H_9FOS$
M_r	208.24
Crystal system, space group	Monoclinic, $P2_1/n$
Temperature (K)	150
a, b, c (Å)	7.3460 (3), 13.5411 (6), 9.8815 (4)
β (°)	109.134 (5)
V (Å^3)	928.64 (7)

Z	4
Radiation type	Cu $K\alpha$
μ (mm^{-1})	2.92
Crystal size (mm)	0.15 × 0.10 × 0.08
Data collection	
Diffractometer	XtaLAB Synergy, Dualflex, HyPix
Absorption correction	Multi-scan *CrysAlis PRO* 1.171.41.112a (Rigaku Oxford Diffraction, 2021) Empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm.
T_{min}, T_{max}	0.339, 1.000
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	7838, 1779, 1631
R_{int}	0.067
$(\sin\theta/\lambda)_{max}$ ($Å^{-1}$)	0.629
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.053, 0.145, 1.08
No. of reflections	1779
No. of parameters	128
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e $Å^{-3}$)	0.50, -0.51
CCDC	2277847

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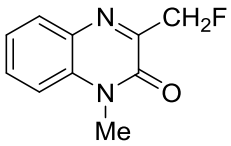
12. Characterization data

3-(Fluoromethyl)-1-methylquinoxalin-2(1*H*)-one (3a)[21]

Following the general procedure (GP), compound **3a** was obtained from 1-methylquinoxalin-2(1*H*)-one **1a** (0.2 mmol scale).



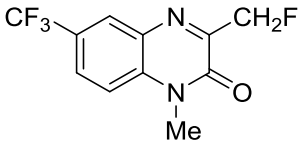
3a

Eluent: Petroleum ether/EtOAc (20:1 to 4:1). Yield: 31 mg, 81%; pale yellow solid; mp 103–105 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.98 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.62 (ddd, *J* = 8.6, 7.3, 1.5 Hz, 1H), 7.46 – 7.33 (m, 2H), 5.65 (d, *J* = 46.5 Hz, 2H), 3.72 (s, 3H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -230.28 (t, *J* = 46.7 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 153.6 (d, *J* = 14.1 Hz), 153.5 (d, *J* = 2.3 Hz), 133.2, 132.5, 131.0, 130.6, 124.1, 113.8, 81.0 (d, *J* = 174.5 Hz), 28.8. **HRMS** (ESI(+)) m/z: Calculated for $C_{10}H_9FN_2O$ $[M+H]^+$ 193.0777, found 193.0781.

3-(Fluoromethyl)-1-methyl-6-(trifluoromethyl)quinoxalin-2(1*H*)-one (3b)

Following GP, compound **3b** was obtained from 1-methyl-6-(trifluoromethyl)quinoxalin-2(1*H*)-one **1b** (0.2 mmol scale).



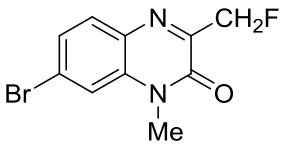
3b

Eluent: Petroleum ether/EtOAc (20:1 to 4:1). Yield: 40.5 mg, 78%; off-white solid; mp 154–156 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.26 (d, *J* = 2.1 Hz, 1H), 7.82 (dd, *J* = 8.8, 2.1 Hz, 1H), 7.46 (d, *J* = 8.7 Hz, 1H), 5.65 (d, *J* = 46.4 Hz, 2H), 3.74 (s, 3H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -62.13 (s, 3F), -231.21 (t, *J* = 46.4 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 155.4 (d, *J* = 14.3 Hz), 153.3 (d, *J* = 2.6 Hz), 135.5, 131.8, 128.0 (q, *J* = 3.9 Hz), 127.3 (q, *J* = 3.5 Hz), 126.4 (q, *J* = 33.9 Hz), 123.5 (q, *J* = 272.0 Hz), 114.5, 80.7 (d, *J* = 176.0 Hz), 29.0. **HRMS** (ESI(+)) m/z: Calculated for $C_{11}H_8F_4N_2O$ $[M+H]^+$ 261.0651, found 261.0659.

7-Bromo-3-(fluoromethyl)-1-methylquinoxalin-2(1*H*)-one (3c)

Following GP, compound **3c** was obtained from 7-bromo-1-methylquinoxalin-2(1*H*)-one **1c** (0.2 mmol scale).



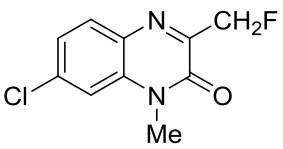
3c

Eluent: Petroleum ether/EtOAc (20:1 to 4:1). Yield: 40 mg, 74%; pale yellow solid; mp 193–195 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.92 – 7.71 (m, 1H), 7.50 (m, 2H), 5.61 (d, *J* = 46.5 Hz, 2H), 3.68 (s, 3H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -230.63 (t, *J* = 46.5 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 153.9 (d, *J* = 14.3 Hz), 153.2 (d, *J* = 2.5 Hz), 134.2, 131.7, 131.3, 127.4, 125.2, 116.9, 80.9 (d, *J* = 175.1 Hz), 28.9. **HRMS** (ESI(+)) m/z: Calculated for $C_{10}H_8BrFN_2O$ $[M+H]^+$ 270.9882, found 270.9884.

7-Chloro-3-(fluoromethyl)-1-methylquinoxalin-2(1*H*)-one (3d)

Following GP, compound **3d** was obtained from 7-chloro-1-methylquinoxalin-2(1*H*)-one **1d** (0.2 mmol scale).



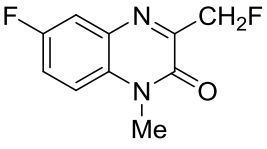
3d

Eluent: Petroleum ether/EtOAc (20:1 to 4:1). Yield: 36 mg, 79%; pale yellow solid; mp 189–191 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.93 – 7.86 (m, 1H), 7.41 – 7.32 (m, 2H), 5.62 (d, *J* = 46.5 Hz, 2H), 3.68 (s, 3H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -230.52 (t, *J* = 46.6 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 153.7 (d, *J* = 14.2 Hz), 153.2 (d, *J* = 2.5 Hz), 137.1, 134.1, 131.6, 131.0, 124.5, 113.9, 80.9 (d, *J* = 175.0 Hz), 28.9. **HRMS** (ESI(+)) m/z: Calculated for $C_{10}H_8ClFN_2O$ $[M+H]^+$ 227.0387, found 227.0393.

6-Fluoro-3-(fluoromethyl)-1-methylquinoxalin-2(1*H*)-one (3e)

Following GP, compound **3e** was obtained from 6-fluoro-1-methylquinoxalin-2(1*H*)-one **1e** (0.2 mmol scale).



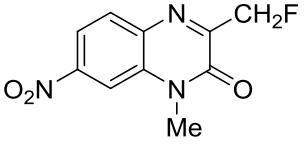
3e

Eluent: Petroleum ether/EtOAc (20:1 to 4:1). Yield: 30 mg, 72%; yellow solid; mp 112–114 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.67 (dd, *J* = 8.6, 2.7 Hz, 1H), 7.41 – 7.28 (m, 2H), 5.64 (d, *J* = 46.5 Hz, 2H), 3.71 (s, 3H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -117.94 (td, *J* = 8.1, 5.0 Hz, 1F), -231.07 (t, *J* = 46.6 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 158.8 (d, *J* = 244.7 Hz), 155.2 (d, *J* = 14.1 Hz), 153.1 (d, *J* = 2.6 Hz), 133.0 (d, *J* = 11.4 Hz), 129.8, 118.8 (d, *J* = 24.0 Hz), 115.9 (d, *J* = 22.6 Hz), 114.9 (d, *J* = 8.7 Hz), 80.9 (d, *J* = 175.5 Hz), 29.0. **HRMS** (ESI(+)) m/z: Calculated for $C_{10}H_8F_2N_2O$ $[M+H]^+$ 211.0683, found 211.0688.

3-(Fluoromethyl)-1-methyl-7-nitroquinoxalin-2(1*H*)-one (3f)

Following GP, compound **3f** was obtained from 1-methyl-7-nitroquinoxalin-2(1*H*)-one **1f** (0.2 mmol scale).



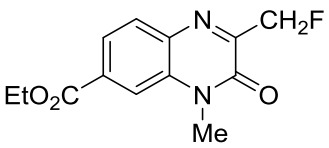
3f

Eluent: Petroleum ether/EtOAc (20:1 to 4:1). Yield: 32 mg, 67%; yellow solid; mp 139–141 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.26 (d, *J* = 2.2 Hz, 1H), 8.23 (dd, *J* = 8.7, 2.3 Hz, 1H), 8.14 (d, *J* = 8.7 Hz, 1H), 5.69 (d, *J* = 46.3 Hz, 2H), 3.79 (s, 3H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -232.21 (t, *J* = 46.2 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 157.7 (d, *J* = 14.0 Hz), 152.9 (d, *J* = 2.7 Hz), 148.2, 135.6, 133.5, 131.7, 118.6, 109.7, 80.7 (d, *J* = 177.5 Hz), 29.3. **HRMS** (ESI(+)) m/z: Calculated for $C_{10}H_8FN_3O_3$ $[M+H]^+$ 238.0628, found 238.0639.

Ethyl 2-(fluoromethyl)-4-methyl-3-oxo-3,4-dihydroquinoxaline-6-carboxylate (3g)

Following GP, compound **3g** was obtained from ethyl 4-methyl-3-oxo-3,4-dihydroquinoxaline-6-carboxylate **1g** (0.2 mmol scale).



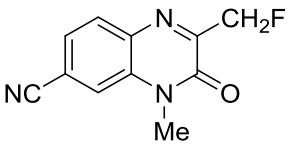
3g

Eluent: Petroleum ether/EtOAc (20:1 to 4:1). Yield: 33 mg, 62%; pale yellow solid; mp 128–130 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.06 (s, 1H), 8.04 (d, *J* = 1.5 Hz, 1H), 5.67 (d, *J* = 46.5 Hz, 2H), 4.46 (q, *J* = 7.1 Hz, 2H), 3.77 (s, 3H), 1.44 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -231.49 (t, *J* = 46.2 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 165.4, 156.0 (d, *J* = 13.9 Hz), 153.3 (d, *J* = 2.6 Hz), 134.9, 133.0, 132.2, 130.6, 124.7, 115.5, 80.9 (d, *J* = 175.9 Hz), 61.8, 29.0, 14.3. **HRMS** (ESI(+)) m/z: Calculated for $C_{13}H_{13}FN_2O_3$ $[M+H]^+$ 265.0988, found 265.0995.

2-(Fluoromethyl)-4-methyl-3-oxo-3,4-dihydroquinoxaline-6-carbonitrile (3h)

Following GP, compound **3h** was obtained from 2-(fluoromethyl)-4-methyl-3-oxo-3,4-dihydroquinoxaline-6-carbonitrile **1h** (0.2 mmol scale).



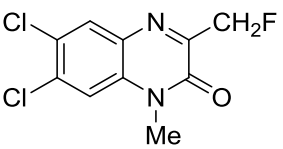
3h

Eluent: Petroleum ether/EtOAc (20:1 to 4:1). Yield: 24 mg, 55%; yellow solid; mp 112–114 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.08 (d, *J* = 8.7 Hz, 1H), 7.71 – 7.59 (m, 2H), 5.67 (d, *J* = 46.4 Hz, 2H), 3.73 (s, 3H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -231.98 (t, *J* = 46.6 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 157.1 (d, *J* = 14.0 Hz), 152.8 (d, *J* = 2.9 Hz), 134.5, 133.5, 131.5, 126.9, 118.0, 117.8, 114.1, 80.7 (d, *J* = 177.2 Hz), 29.0. **HRMS** (ESI(+)) m/z: Calculated for $C_{11}H_8FN_3O$ $[M+H]^+$ 218.0730, found 218.0740.

6,7-Dichloro-3-(fluoromethyl)-1-methylquinoxalin-2(1*H*)-one (3i)

Following GP, compound **3i** was obtained from 6,7-dichloro-1-methylquinoxalin-2(1*H*)-one **1i** (0.2 mmol scale).



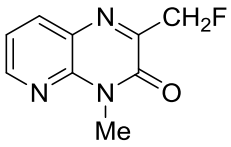
3i

Eluent: Petroleum ether/EtOAc (20:1 to 4:1). Yield: 36 mg, 69%; pale yellow solid; mp_{dec} 180–182 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.06 (s, 1H), 7.45 (s, 1H), 5.62 (d, *J* = 46.4 Hz, 2H), 3.68 (s, 3H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -231.03 (t, *J* = 46.2 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 155.1 (d, *J* = 14.2 Hz), 152.9 (d, *J* = 2.6 Hz), 135.3, 132.5, 131.5, 131.3, 128.1, 115.3, 80.7 (d, *J* = 176.0 Hz), 29.0. **HRMS** (ESI(+)) m/z: Calculated for $C_{10}H_7Cl_2FN_2O$ $[M]^+$ 260.9998, found 261.0007.

2-(Fluoromethyl)-4-methylpyrido[2,3-*b*]pyrazin-3(4*H*)-one (3j)

Following GP, compound **3j** was obtained from 4-methylpyrido[2,3-*b*]pyrazin-3(4*H*)-one **1j** (0.2 mmol scale).



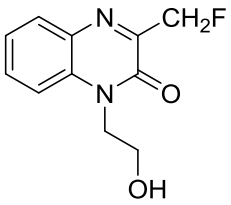
3j

Eluent: Petroleum ether/EtOAc (20:1 to 4:1). Yield: 24 mg, 62%; pale yellow solid; mp 113–115 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.63 (dd, *J* = 4.7, 1.8 Hz, 1H), 8.28 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.37 (dd, *J* = 7.9, 4.7 Hz, 1H), 5.68 (d, *J* = 46.4 Hz, 2H), 3.84 (s, 3H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -231.78 (t, *J* = 46.6 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 155.0 (d, *J* = 14.1 Hz), 154.7, 150.1, 143.9, 137.8, 127.9, 120.0, 80.8 (d, *J* = 175.7 Hz), 27.6. **HRMS** (ESI(+)) m/z: Calculated for $C_9H_8FN_3O$ $[M+H]^+$ 194.0730, found 194.0730.

3-(Fluoromethyl)-1-(2-hydroxyethyl)quinoxalin-2(1*H*)-one (3k)

Following GP, compound **3k** was obtained from 1-(2-hydroxyethyl)quinoxalin-2(1*H*)-one **1k** (0.2 mmol scale).



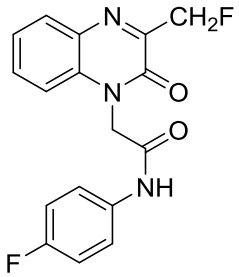
3k

Eluent: Petroleum ether/EtOAc (9:1 to 1:1). Yield: 34 mg, 77%; yellow solid; mp 167–169 °C.

^{1}H NMR (400 MHz, Methanol-d_4) δ 7.91 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.72 (dd, *J* = 8.6, 1.4 Hz, 1H), 7.66 (ddd, *J* = 8.6, 7.0, 1.5 Hz, 1H), 7.42 (ddd, *J* = 8.2, 7.0, 1.4 Hz, 1H), 5.58 (d, *J* = 46.7 Hz, 2H), 4.47 (t, *J* = 5.9 Hz, 2H), 3.90 (t, *J* = 5.9 Hz, 2H). **Note:** -O*H* not observed. **^{19}F NMR** (376 MHz, Methanol-d_4) δ -231.19 (t, *J* = 46.7 Hz, 1F). **^{13}C NMR** (101 MHz, Methanol-d_4) δ 155.4 (d, *J* = 2.0 Hz), 154.9 (d, *J* = 14.3 Hz), 134.6, 133.9, 132.1, 130.9, 125.1, 116.2, 82.1 (d, *J* = 172.1 Hz), 59.7, 45.4. **HRMS** (ESI(+)) m/z: Calculated for $C_{11}H_{11}FN_2O_2$ $[M+H]^+$ 223.0883, found 223.0885.

2-(3-(Fluoromethyl)-2-oxoquinoxalin-1(2*H*)-yl)-*N*-(4-fluorophenyl)acetamide (3l)

Following GP, compound **3l** was obtained from *N*-(4-fluorophenyl)-2-(2-oxoquinoxalin-1(2*H*)-yl)acetamide **1l** (0.2 mmol scale).



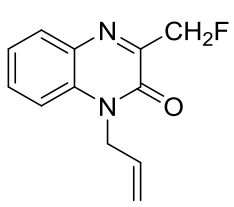
3l

Eluent: Petroleum ether/EtOAc (9:1 to 3:1). Yield: 44 mg, 67%; yellow solid; mp 249–251 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.52 (s, 1H), 7.92 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.66 (ddd, *J* = 8.6, 7.1, 1.6 Hz, 1H), 7.57 (ddd, *J* = 8.5, 5.5, 3.1 Hz, 3H), 7.43 (ddd, *J* = 8.2, 7.2, 1.2 Hz, 1H), 7.21 – 7.10 (m, 2H), 5.59 (d, *J* = 46.5 Hz, 2H), 5.14 (s, 2H). **^{19}F NMR** (376 MHz, DMSO-d_6) δ -118.83 (tt, *J* = 8.9, 5.0 Hz, 1F), -226.95 (t, *J* = 46.5 Hz, 1F). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 164.9, 158.6 (d, *J* = 240.2 Hz), 153.74 (d, *J* = 13.9 Hz), 153.5 (d, *J* = 2.5 Hz), 135.3 (d, *J* = 2.5 Hz), 133.6, 132.2, 131.6, 130.1, 124.3, 121.4 (d, *J* = 8.0 Hz), 115.9 (d, *J* = 22.2 Hz), 115.4, 81.4 (d, *J* = 170.2 Hz), 45.3. **HRMS** (ESI(+)) m/z: Calculated for $C_{17}H_{13}F_2N_3O_2$ $[M+H]^+$ 330.1054, found 330.1053.

1-Allyl-3-(fluoromethyl)quinoxalin-2(1*H*)-one (3m)

Following GP, compound **3m** was obtained from 1-allylquinoxalin-2(1*H*)-one **1m** (0.2 mmol scale).



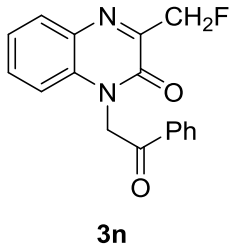
3m

Eluent: Petroleum ether/EtOAc (20:1 to 9:1). Yield: 27 mg, 62%; yellowish brown solid; mp 66–68 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.99 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.58 (ddd, *J* = 8.7, 7.3, 1.6 Hz, 1H), 7.39 (ddd, *J* = 8.0, 7.3, 1.2 Hz, 1H), 7.34 (dd, *J* = 8.5, 1.2 Hz, 1H), 5.93 (ddt, *J* = 17.2, 10.4, 5.1 Hz, 1H), 5.66 (d, *J* = 46.6 Hz, 2H), 5.29 (dtd, *J* = 10.4, 1.6, 0.7 Hz, 1H), 5.18 (dtd, *J* = 17.2, 1.8, 0.8 Hz, 1H), 4.99 – 4.85 (m, 2H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -230.31 (t, *J* = 46.9 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 153.6 (d, *J* = 14.2 Hz), 153.2 (d, *J* = 2.6 Hz), 132.7, 132.4, 130.9, 130.6, 130.2, 124.1, 118.4, 114.4, 80.9 (d, *J* = 174.5 Hz), 44.2. **HRMS** (ESI(+)) m/z: Calculated for $C_{12}H_{11}FN_2O$ $[M+H]^+$ 219.0934, found 219.0943.

3-(Fluoromethyl)-1-(2-oxo-2-phenylethyl)quinoxalin-2(1*H*)-one (3n)

Following GP, compound **3n** was obtained from 1-(2-oxo-2-phenylethyl)quinoxalin-2(1*H*)-one **1n** (0.2 mmol scale).



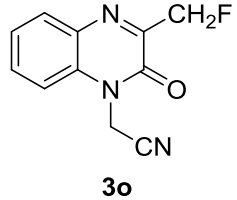
3n

Eluent: Petroleum ether/EtOAc (20:1 to 9:1). Yield: 43 mg, 73%; yellow solid; mp 175–177 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.11 – 8.04 (m, 2H), 8.01 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.73 – 7.64 (m, 1H), 7.62 – 7.52 (m, 2H), 7.50 (ddd, *J* = 8.6, 7.3, 1.5 Hz, 1H), 7.38 (ddd, *J* = 8.3, 7.3, 1.2 Hz, 1H), 6.99 (dd, *J* = 8.4, 1.2 Hz, 1H), 5.74 (s, 2H), 5.66 (d, *J* = 46.5 Hz, 2H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -230.17 (t, *J* = 46.6 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 190.6, 153.4, 153.3 (d, *J* = 11.7 Hz), 134.5, 134.3, 132.7, 131.1, 130.8, 129.1, 128.2, 124.2, 113.6, 80.9 (d, *J* = 174.5 Hz), 48.1. **HRMS** (ESI(+)) m/z: Calculated for $C_{17}H_{13}FN_2O_2$ $[M+H]^+$ 297.1039, found 297.1044.

2-(3-(Fluoromethyl)-2-oxoquinoxalin-1(2*H*)-yl)acetonitrile (3o)

Following GP, compound **3o** was obtained from 2-(2-oxoquinoxalin-1(2*H*)-yl)acetonitrile **1o** (0.2 mmol scale).



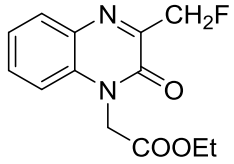
3o

Eluent: Petroleum ether/EtOAc (10:1 to 3:1). Yield: 36 mg, 82%; pale yellow solid; mp 172–174 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.03 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.71 (ddd, *J* = 8.7, 7.4, 1.5 Hz, 1H), 7.50 (ddd, *J* = 8.0, 7.4, 1.2 Hz, 1H), 7.37 (dd, *J* = 8.3, 1.1 Hz, 1H), 5.63 (d, *J* = 46.4 Hz, 2H), 5.21 (s, 2H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -229.65 (t, *J* = 46.2 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 153.2 (d, *J* = 14.5 Hz), 152.3 (d, *J* = 2.3 Hz), 132.6, 131.9, 131.4, 131.0, 125.3, 113.2, 113.1, 80.7 (d, *J* = 175.3 Hz), 29.0. **HRMS** (ESI(+)) m/z: Calculated for $C_{11}H_8FN_3O$ $[M+H]^+$ 218.0730, found 218.0737.

Ethyl 2-(3-(fluoromethyl)-2-oxoquinoxalin-1(2*H*)-yl)acetate (3p)

Following GP, compound **3p** was obtained from ethyl 2-(2-oxoquinoxalin-1(2*H*)-yl)acetate **1p** (0.2 mmol scale).



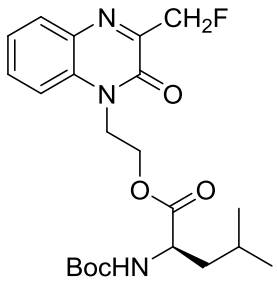
3p

Eluent: Petroleum ether/EtOAc (10:1 to 3:1). Yield: 43 mg, 81%; pale yellow solid; mp 110–112 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.99 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.57 (ddd, *J* = 8.6, 7.3, 1.5 Hz, 1H), 7.40 (ddd, *J* = 8.3, 7.3, 1.2 Hz, 1H), 7.11 (dd, *J* = 8.5, 1.2 Hz, 1H), 5.65 (d, *J* = 46.6 Hz, 2H), 5.03 (s, 2H), 4.25 (q, *J* = 7.1 Hz, 2H), 1.27 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -230.35 (t, *J* = 46.6 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 166.7, 153.4 (d, *J* = 14.3 Hz), 153.1 (d, *J* = 2.6 Hz), 132.5, 132.4, 131.2, 130.9, 124.4, 113.2, 80.8 (d, *J* = 174.8 Hz), 62.2, 43.2, 14.1. **HRMS** (ESI(+)) m/z: Calculated for $C_{13}H_{13}FN_2O_3$ $[M+H]^+$ 265.0988, found 265.0999.

2-(3-(Fluoromethyl)-2-oxoquinoxalin-1(2*H*)-yl)ethyl (tert-butoxycarbonyl)-*D*-leucinate (3q)

Following GP, compound **3q** was obtained from 2-(2-oxoquinoxalin-1(2*H*)-yl)ethyl (*tert*-butoxycarbonyl)-*D*-leucinate **1q** (0.2 mmol scale).



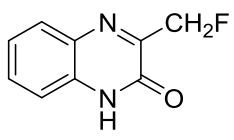
3q

Eluent: Petroleum ether/EtOAc (10:1 to 3:1). Yield: 62 mg, 71%; yellow oil.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.99 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.63 (ddd, *J* = 8.7, 7.2, 1.5 Hz, 1H), 7.57 – 7.47 (m, 1H), 7.40 (ddd, *J* = 8.2, 7.2, 1.2 Hz, 1H), 5.64 (d, *J* = 46.5 Hz, 2H), 4.77 (d, *J* = 8.7 Hz, 1H), 4.63 – 4.51 (m, 2H), 4.54 – 4.41 (m, 1H), 4.21 (td, *J* = 8.9, 5.1 Hz, 1H), 1.70 – 1.52 (m, 1H), 1.42 (s, 9H), 1.40 – 1.28 (m, 2H), 0.84 (dd, *J* = 6.6, 3.9 Hz, 6H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -230.18 (t, *J* = 46.5 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 173.3, 155.4, 153.49 (d, *J* = 2.7 Hz), 153.45 (d, *J* = 14.2 Hz), 132.73, 132.70, 131.2, 130.9, 124.3, 113.9, 80.9 (d, *J* = 174.7 Hz), 80.0, 61.3, 52.0, 41.3, 40.6, 28.3, 24.6, 22.8, 21.5. **HRMS** (ESI(+)) m/z: Calculated for $C_{22}H_{30}FN_3O_5$ $[M+Na]^+$ 458.2067, found 458.2083.

3-(Fluoromethyl)quinoxalin-2(1*H*)-one (3r)

Following GP, compound **3r** was obtained from quinoxalin-2(1*H*)-one **1r** (0.2 mmol scale).



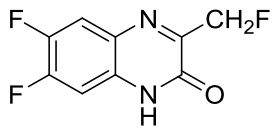
3r

Eluent: Petroleum ether/EtOAc (9:1 to 1:1). Yield: 22 mg, 62%; off-white solid; mp 218–220 °C.

^{1}H NMR (400 MHz, Methanol-d_4) δ 7.86 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.57 (ddd, *J* = 8.5, 7.3, 1.4 Hz, 1H), 7.37 (ddd, *J* = 8.4, 7.3, 1.3 Hz, 1H), 7.33 (dd, *J* = 8.2, 1.3 Hz, 1H), 5.56 (d, *J* = 46.7 Hz, 2H). **Note**: N*H* not observed. **^{19}F NMR** (376 MHz, Methanol-d_4) δ -231.07 (t, *J* = 46.7 Hz, 1F). **^{13}C NMR** (101 MHz, Methanol-d_4) δ 154.7 (d, *J* = 14.0 Hz), 154.4 (d, *J* = 2.3 Hz), 132.0, 131.9, 130.7, 128.6, 123.8, 115.3, 80.5 (d, *J* = 171.6 Hz). **HRMS** (ESI(+)) m/z: Calculated for $C_9H_7FN_2O$ $[M+H]^+$ 179.0621, found 179.0625.

6,7-Difluoro-3-(fluoromethyl)quinoxalin-2(1*H*)-one (3s)

Following GP, compound **3s** was obtained from 6,7-difluoroquinoxalin-2(1*H*)-one **1s** (0.2 mmol scale).



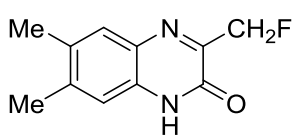
3s

Eluent: Petroleum ether/EtOAc (9:1 to 1:1). Yield: 15 mg, 35%; red solid; mp_{dec} 238–240 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.69 (s, 1H), 7.97 (dd, *J* = 11.0, 8.2 Hz, 1H), 7.26 (dd, *J* = 11.1, 7.6 Hz, 1H), 5.53 (d, *J* = 46.5 Hz, 2H). **^{19}F NMR** (376 MHz, DMSO-d_6) δ -132.47 (dt, *J* = 23.3, 9.8 Hz), -143.05 (dt, *J* = 23.9, 9.1 Hz), -228.80 (t, *J* = 46.5 Hz). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 155.7 (d, *J* = 13.4 Hz), 153.3 (d, *J* = 2.8 Hz), 150.6 (dd, *J* = 250.6, 14.8 Hz), 145.8 (dd, *J* = 242.6, 14.3 Hz), 129.6 (d, *J* = 9.2 Hz), 127.7 (dd, *J* = 10.0, 2.0 Hz), 116.5 (d, *J* = 18.3 Hz), 103.4 (d, *J* = 22.0 Hz), 80.6 (d, *J* = 170.6 Hz). **HRMS** (ESI(+)) m/z: Calculated for $C_9H_5F_3N_2O$ $[M+H]^+$ 215.0432, found 215.0441.

3-(Fluoromethyl)-6,7-dimethylquinoxalin-2(1*H*)-one (3t)

Following GP, compound **3t** was obtained from 6,7-dimethylquinoxalin-2(1*H*)-one **1t** (0.2 mmol scale).



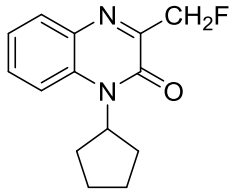
3t

Eluent: Petroleum ether/EtOAc (9:1 to 1:1). Yield: 26 mg, 63%; off-white solid; mp_{dec} > 250 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.46 (s, 1H), 7.60 (s, 1H), 7.10 (s, 1H), 5.49 (d, *J* = 46.7 Hz, 2H), 2.32 (s, 3H), 2.30 (s, 3H). **^{19}F NMR** (376 MHz, DMSO-d_6) δ -225.83 (t, *J* = 46.7 Hz, 1F). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 153.8 (d, *J* = 2.3 Hz), 153.4 (d, *J* = 13.4 Hz), 140.5, 132.2, 130.2, 129.9, 128.6, 115.5, 80.9 (d, *J* = 168.5 Hz), 19.8, 18.9. **HRMS** (ESI(+)) m/z: Calculated for $C_{11}H_{11}FN_2O$ $[M+H]^+$ 207.0934, found 207.0938.

1-Cyclopentyl-3-(fluoromethyl)quinoxalin-2(1*H*)-one (3u)

Following GP, compound **3u** was obtained from 1-cyclopentylquinoxalin-2(1*H*)-one **1u** (0.2 mmol scale).



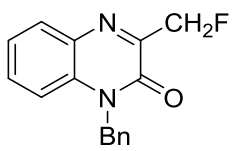
3u

Eluent: Petroleum ether/EtOAc (100% PE to 30:1). Yield: 32 mg, 65%; colourless oil.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.05 (tt, *J* = 14.1, 8.2, 1.5 Hz, 1H), 7.83 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.67 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H), 7.56 (ddd, *J* = 8.3, 7.0, 1.4 Hz, 1H), 5.68 (tt, *J* = 5.9, 3.0 Hz, 1H), 5.62 (d, *J* = 46.8 Hz, 2H), 2.16 – 1.98 (m, 2H), 1.98 – 1.76 (m, 4H), 1.76 – 1.63 (m, 2H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -225.59 (t, *J* = 46.8 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 155.0 (d, *J* = 0.8 Hz), 144.0 (d, *J* = 14.9 Hz), 140.8 (d, *J* = 2.1 Hz), 138.0, 130.2, 129.0, 127.0, 126.6, 80.9 (d, *J* = 172.5 Hz), 79.27, 32.7, 23.9. **HRMS** (ESI(+)) m/z: Calculated for $C_{14}H_{15}FN_2O$ $[M+H]^+$ 247.1247, found 247.1251.

1-Benzyl-3-(fluoromethyl)quinoxalin-2(1*H*)-one (3v)

Following GP, compound **3v** was obtained from 1-benzylquinoxalin-2(1*H*)-one **1v** (0.2 mmol scale).



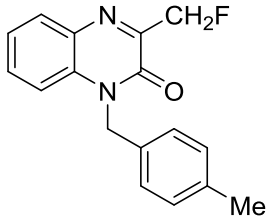
3v

Eluent: Petroleum ether/EtOAc (20:1 to 9:1). Yield: 32 mg, 85%; white solid; mp 95–97 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.99 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.49 (ddd, *J* = 8.6, 7.3, 1.6 Hz, 1H), 7.33 (dddt, *J* = 14.4, 8.1, 4.4, 1.4 Hz, 5H), 7.29 – 7.21 (m, 2H), 5.71 (d, *J* = 46.5 Hz, 2H), 5.51 (s, 2H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -230.13 (t, *J* = 46.5 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 153.8, 153.7 (d, *J* = 2.1 Hz), 134.8, 132.8, 132.6, 131.0, 130.7, 129.0, 127.9, 126.9, 124.1, 81.0 (d, *J* = 174.7 Hz), 45.6. **HRMS** (ESI(+)) m/z: Calculated for $C_{16}H_{13}FN_2O$ $[M+H]^+$ 269.1090, found 269.1097.

3-(Fluoromethyl)-1-(4-methylbenzyl)quinoxalin-2(1*H*)-one (3va)

Following GP, compound **3va** was obtained from 1-(4-methylbenzyl)quinoxalin-2(1*H*)-one **1va** (0.2 mmol scale).



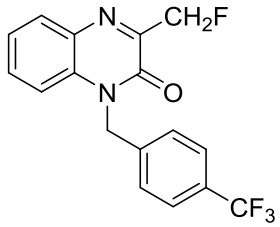
3va

Eluent: Petroleum ether/EtOAc (20:1 to 9:1). Yield: 39 mg, 69%; pale yellow solid; mp 126–128 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.98 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.54 – 7.44 (m, 1H), 7.42 – 7.29 (m, 2H), 7.21 – 7.08 (m, 4H), 5.71 (d, *J* = 46.6 Hz, 2H), 5.46 (s, 2H), 2.30 (s, 3H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -230.14 (t, *J* = 46.6 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 153.7 (d, *J* = 16.0 Hz), 153.7, 137.6, 132.8, 132.6, 131.8, 130.9, 130.6, 129.6, 126.9, 124.1, 114.6, 81.0 (d, *J* = 174.5 Hz), 45.4, 21.1. **HRMS** (ESI(+)) m/z: Calculated for $C_{17}H_{15}FN_2O$ $[M+H]^+$ 283.1247, found 283.1252.

3-(Fluoromethyl)-1-(4-(trifluoromethyl)benzyl)quinoxalin-2(1*H*)-one (3vb)

Following GP, compound **3vb** was obtained from 1-(4-(trifluoromethyl)benzyl)quinoxalin-2(1*H*)-one **1vb** (0.2 mmol scale).



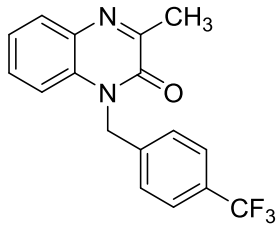
3vb

Eluent: Petroleum ether/EtOAc (20:1 to 9:1). Yield: 49 mg, 73%; pale yellow solid; mp 139–141 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.01 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.59 (d, *J* = 8.1 Hz, 2H), 7.51 (ddd, *J* = 8.6, 7.3, 1.6 Hz, 1H), 7.42 – 7.32 (m, 3H), 7.22 (dd, *J* = 8.4, 1.2 Hz, 1H), 5.70 (d, *J* = 46.5 Hz, 2H), 5.56 (s, 2H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -62.70 (s, 3F), -229.93 (t, *J* = 46.6 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 153.7 (d, *J* = 14.4 Hz), 153.6 (d, *J* = 2.4 Hz), 138.8, 132.8, 132.3, 131.1 (d, *J* = 25.7 Hz), 130.3 (q, *J* = 32.6 Hz), 127.2, 126.0 (q, *J* = 3.7 Hz), 124.4, 123.8 (q, *J* = 272.1 Hz), 114.2, 80.9 (d, *J* = 174.9 Hz), 45.2. **HRMS** (ESI(+)) m/z: Calculated for $C_{17}H_{12}F_4N_2O$ $[M+H]^+$ 337.0964, found 337.0978.

3-Methyl-1-(4-(trifluoromethyl)benzyl)quinoxalin-2(1*H*)-one (3vb')

Following GP, compound **3vb'** was obtained from 1-(4-(trifluoromethyl)benzyl)quinoxalin-2(1*H*)-one **1vb** (0.2 mmol scale) and purified by preparative TLC (petroleum ether/EtOAc, 85:15).



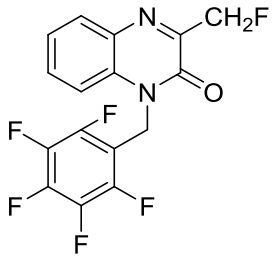
3vb'

Yield: 24 mg, 38%; off-white solid; mp 132–134 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.84 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.58 (d, *J* = 8.1 Hz, 2H), 7.42 (ddd, *J* = 8.5, 7.3, 1.6 Hz, 1H), 7.38 – 7.28 (m, 3H), 7.15 (dd, *J* = 8.5, 1.3 Hz, 1H), 5.54 (s, 2H), 2.66 (s, 3H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -62.65 (s,3F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 158.5, 155.1, 139.3, 132.9, 132.3, 130.1 (q, *J* = 32.7 Hz), 129.8 (d, *J* = 6.1 Hz), 127.2, 125.9 (q, *J* = 3.7 Hz), 123.9, 123.9 (q, *J* = 272.1 Hz), 114.0, 45.5, 21.6. **HRMS** (ESI(+)) m/z: Calculated for $C_{17}H_{13}F_3N_2O$ $[M+H]^+$ 319.1058, found 319.1060.

3-(Fluoromethyl)-1-((perfluorophenyl)methyl)quinoxalin-2(1*H*)-one (3vc)

Following GP, compound **3vc** was obtained from 1-((perfluorophenyl)methyl)quinoxalin-2(1*H*)-one **1vc** (0.2 mmol scale).



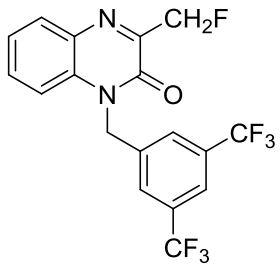
3vc

Eluent: Petroleum ether/EtOAc (10:1 to 4:1). Yield: 62 mg, 87%; pale yellow solid; mp 151–153 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.00 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.57 (ddd, *J* = 8.6, 7.3, 1.6 Hz, 1H), 7.41 (ddd, *J* = 8.3, 7.3, 1.2 Hz, 1H), 7.27 (d, *J* = 8.8 Hz, 1H), 5.66 (d, *J* = 47.7 Hz, 2H), 5.60 (s, 2H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -140.39 – -143.42 (m, 2F), -152.73 (t, *J* = 21.0 Hz, 1F), -158.78 – -161.33 (m, 2F), -230.24 (t, *J* = 46.6 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 153.4 (d, *J* = 14.4 Hz), 153.2 (d, *J* = 2.5 Hz), 146.6 (dp, *J* = 11.7, 4.1 Hz), 144.1 (ddt, *J* = 11.7, 7.8, 4.1 Hz), 142.7 – 142.3 (m), 140.2 – 139.7 (m), 139.3 – 138.6 (m), 136.8 – 136.2 (m), 132.8, 131.8, 131.2 (d, *J* = 2.6 Hz), 124.5, 113.1, 108.7 (td, *J* = 15.6, 3.8 Hz), 80.8 (d, *J* = 175.1 Hz), 34.5. **HRMS** (ESI(+)) m/z: Calculated for $C_{16}H_8F_6N_2O$ $[M+H]^+$ 359.0619, found 359.0628.

1-(3,5-Bis(trifluoromethyl)benzyl)-3-(fluoromethyl)quinoxalin-2(1*H*)-one (3vd)

Following GP, compound **3vd** was obtained from 1-(3,5-bis(trifluoromethyl)benzyl)quinoxalin-2(1*H*)-one **1vd** (0.2 mmol scale).



3vd

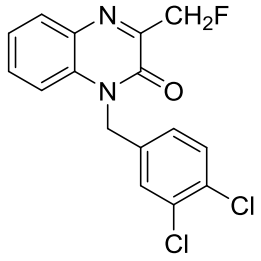
Eluent: Petroleum ether/EtOAc (20:1 to 4:1). Yield: 60 mg, 74%; yellow solid; mp 180–182 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.04 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.82 (s, 1H), 7.70 (d, *J* = 1.7 Hz, 2H), 7.56 (ddd, *J* = 8.7, 7.3, 1.5 Hz, 1H), 7.43 (ddd, *J* = 8.4, 7.4, 1.2 Hz, 1H), 7.20 (dd, *J* = 8.4, 1.2 Hz, 1H), 5.71 (d, *J* = 46.4 Hz, 2H), 5.59 (s, 2H). ^{19}F NMR (564 MHz, Chloroform-*d*) δ -62.89 (s, 6F), -230.00 (t, *J* = 46.9 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 153.7 (d, *J* = 14.5 Hz), 153.5 (d, *J* = 2.5 Hz), 137.6, 132.8, 132.5 (q, *J* = 33.7 Hz), 132.1, 131.3 (d, *J* =

23.9 Hz), 127.2 (d, *J* = 3.8 Hz), 124.7, 122.9 (q, *J* = 272.7 Hz), 122.2 (dt, *J* = 7.5, 3.5 Hz), 113.6, 80.9 (d, *J* = 175.0 Hz), 45.0. **HRMS** (ESI(+)) m/z: Calculated for $C_{18}H_{11}F_7N_2O$ $[M+H]^+$ 405.0838, found 405.0848.

1-(3,4-Dichlorobenzyl)-3-(fluoromethyl)quinoxalin-2(1*H*)-one (3ve)

Following GP, compound **3ve** was obtained from 1-(3,4-dichlorobenzyl)quinoxalin-2(1*H*)-one **1ve** (0.2 mmol scale).



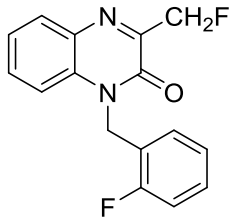
3ve

Eluent: Petroleum ether/EtOAc (20:1 to 4:1). Yield: 64 mg, 76%; white solid; mp 204–206 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.01 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.53 (ddd, *J* = 8.6, 7.3, 1.5 Hz, 1H), 7.43 – 7.36 (m, 2H), 7.35 (d, *J* = 2.0 Hz, 1H), 7.22 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.11 – 7.07 (m, 1H), 5.70 (d, *J* = 46.5 Hz, 2H), 5.44 (s, 2H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -229.95 (t, *J* = 46.2 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 153.7 (d, *J* = 14.2 Hz), 153.5 (d, *J* = 2.5 Hz), 135.0, 133.3, 132.8, 132.2, 131.2, 131.0, 131.0, 128.9, 126.3, 124.5, 114.1, 80.9 (d, *J* = 174.8 Hz), 44.6. **HRMS** (ESI(+)) m/z: Calculated for $C_{16}H_{11}Cl_2FN_2O$ $[M+H]^+$ 337.0311, found 337.0315.

1-(2-Fluorobenzyl)-3-(fluoromethyl)quinoxalin-2(1*H*)-one (3vf)

Following GP, compound **3vf** was obtained from 1-(2-fluorobenzyl)quinoxalin-2(1*H*)-one **1vf** (0.2 mmol scale).

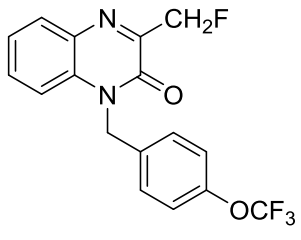


3vf

Eluent: Petroleum ether/EtOAc (10:1 to 4:1). Yield: 47 mg, 82%; white solid; mp 122–124 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.99 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.51 (ddd, *J* = 8.6, 7.3, 1.5 Hz, 1H), 7.37 (ddd, *J* = 8.3, 7.3, 1.2 Hz, 1H), 7.34 – 7.20 (m, 2H), 7.18 – 7.07 (m, 1H), 7.08 – 6.94 (m, 2H), 5.71 (d, *J* = 46.5 Hz, 2H), 5.56 (s, 2H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -118.11 – -118.26 (m, 1F), -230.03 (t, *J* = 46.3 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 160.3 (d, *J* = 246.0 Hz), 153.8 (d, *J* = 2.5 Hz), 153.6 (d, *J* = 14.4 Hz), 132.7, 132.3, 131.2, 130.7, 129.7 (d, *J* = 8.3 Hz), 128.5 (d, *J* = 3.5 Hz), 124.7 (d, *J* = 3.6 Hz), 124.3, 121.9 (d, *J* = 13.9 Hz), 115.6 (d, *J* = 21.4 Hz), 114.2 (d, *J* = 2.5 Hz), 81.0 (d, *J* = 174.6 Hz), 39.1 (d, *J* = 5.2 Hz). **HRMS** (ESI(+)) m/z: Calculated for $C_{16}H_{12}F_2N_2O$ $[M+H]^+$ 287.0996, found 287.1007.

3-(Fluoromethyl)-1-(4-(trifluoromethoxy)benzyl)quinoxalin-2(1*H*)-one (3vg)



3vg

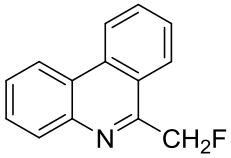
Following GP, compound **3vg** was obtained from 1-(4-(trifluoromethoxy)benzyl)quinoxalin-2(1*H*)-one **1vg** (0.2 mmol scale).

Eluent: Petroleum ether/EtOAc (20:1 to 4:1). Yield: 58 mg, 82%; pale yellow solid; mp 116–118 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.98 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.50 (ddd, *J* = 8.6, 7.3, 1.6 Hz, 1H), 7.36 (ddd, *J* = 8.3, 7.3, 1.2 Hz, 1H), 7.31 – 7.22 (m, 3H), 7.15 (dd, *J* = 8.6, 1.3 Hz, 2H), 5.68 (d, *J* = 46.5 Hz, 2H), 5.48 (s, 2H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -57.91 (s, 3F), -229.92 (t, *J* = 46.6 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 153.7 (d, *J* = 14.2 Hz), 153.6 (d, *J* = 2.4 Hz), 148.8 (q, *J* = 1.8 Hz), 133.4, 132.8, 132.4, 131.0 (d, *J* = 26.8 Hz), 128.5, 124.3, 121.5, 120.3 (q, *J* = 257.5 Hz), 114.2, 81.0 (d, *J* = 174.7 Hz), 45.0. **HRMS** (ESI(+)) m/z: Calculated for $C_{17}H_{12}F_4N_2O_2$ $[M+H]^+$ 353.0913, found 353.0920.

6-(Fluoromethyl)phenanthridine (5a)[17]

Following GP, compound **5a** was obtained from phenanthridine **4a** (0.1 mmol scale).



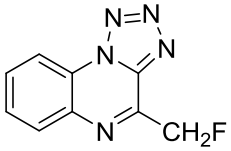
5a

Eluent: Petroleum ether/EtOAc (20:1 to 9:1). Yield: 14.3 mg, 68%; white solid; mp 120–122 °C

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.71 – 8.65 (m, 1H), 8.60 (dd, *J* = 8.0, 1.6 Hz, 1H), 8.36 (dddd, *J* = 8.3, 2.2, 1.3, 0.7 Hz, 1H), 8.22 – 8.18 (m, 1H), 7.89 (ddd, *J* = 8.3, 7.0, 1.3 Hz, 1H), 7.82 – 7.68 (m, 3H), 6.02 (d, *J* = 47.3 Hz, 2H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -212.87 (td, *J* = 47.1, 2.8 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 154.8 (d, *J* = 16.8 Hz), 143.1, 133.2, 130.9, 130.3, 128.9, 127.7 (d, *J* = 6.2 Hz), 126.2 (d, *J* = 4.2 Hz), 124.7, 124.5 (d, *J* = 1.6 Hz), 122.4, 122.0, 85.5 (d, *J* = 169.5 Hz). **HRMS** (ESI(+)) m/z: Calculated for $C_{14}H_{10}FN$ $[M+H]^+$ 212.0876, found 212.0879.

4-(Fluoromethyl)tetrazolo[1,5-*a*]quinoxaline (5b)

Following GP, compound **5b** was obtained from tetrazolo[1,5-*a*]quinoxaline **4b** (0.1 mmol scale).



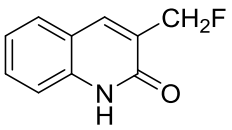
5b

Eluent: Petroleum ether/EtOAc (20:1 to 9:1). Yield: 12.5 mg, 61%; white solid; mp 168–170 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.70 – 8.63 (m, 1H), 8.36 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.99 – 7.94 (m, 1H), 7.93 – 7.87 (m, 1H), 6.06 (d, *J* = 46.2 Hz, 2H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -225.00 (t, *J* = 46.2 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 147.2 (d, *J* = 18.2 Hz), 141.2, 136.2, 131.9, 130.8, 130.1, 116.4, 81.0 (d, *J* = 176.5 Hz). **Note:** NMR spectra ^{1}H and ^{13}C contain starting material as an impurity ~ 15%. **HRMS** (ESI(+)) m/z: Calculated for $C_9H_6FN_5$ $[M+H]^+$ 204.0685, found 204.0688.

3-(Fluoromethyl)quinolin-2(1*H*)-one (5c)

Following GP, compound **5c** was obtained from quinolin-2(1*H*)-one **4c** (0.1 mmol scale).



5c

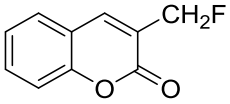
Eluent: Petroleum ether/EtOAc (20:1 to 9:1). Yield: 13.7 mg, 77%; white solid; mp_{dec} 180–182 °C.

^{1}H NMR (400 MHz, Methanol-d_4) δ 8.02 (d, *J* = 0.9 Hz, 2H), 7.69 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.55 (ddd, *J* = 8.5, 7.1, 1.4 Hz, 1H), 7.35 (dd, *J* = 8.3, 1.0 Hz, 1H), 7.27 (ddd, *J* = 8.1, 7.2, 1.1 Hz, 1H), 5.38 (dd, *J* = 47.3, 1.1 Hz, 2H). **^{19}F NMR** (376 MHz, Methanol-d_4) δ -222.26 (t, *J* = 47.2 Hz, 1F). **^{13}C NMR** (101 MHz, Methanol-d_4) δ 161.8

(d, *J* = 4.5 Hz), 138.2 (d, *J* = 1.3 Hz), 130.6, 128.0, 127.9, 127.8, 122.6, 119.5, 115.0, 79.6 (d, *J* = 166.3 Hz). **HRMS** (ESI(+)) m/z: Calculated for $C_{10}H_8FNO$ $[M+H]^+$ 178.0668, found 178.0667.

3-(Fluoromethyl)-2*H*-chromen-2-one (5d)[1]

Following GP, compound **5d** was obtained from 2*H*-chromen-2-one **4d** (0.1 mmol scale).



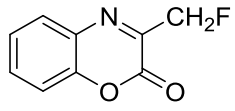
5d

Eluent: Petroleum ether/EtOAc (20:1 to 9:1). Yield: 13 mg, 73%; white solid; mp 83–85 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.81 (s, 1H), 7.55 (dd, *J* = 8.9, 6.6 Hz, 2H), 7.44 – 7.28 (m, 2H), 5.37 (dd, *J* = 46.5, 1.5 Hz, 2H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -225.58 (t, *J* = 46.6 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 159.5 (d, *J* = 6.0 Hz), 153.4, 139.0 (d, *J* = 9.4 Hz), 131.8, 128.0, 124.7, 124.3 (d, *J* = 18.9 Hz), 118.6, 116.7, 79.5 (d, *J* = 170.8 Hz). **HRMS** (ESI(+)) m/z: Calculated for $C_{10}H_7FO_2$ $[M+H]^+$ 179.0508, found 179.0506.

3-(Fluoromethyl)-2*H*-benzo[*b*][1,4]oxazin-2-one (5e)

Following GP, compound **5e** was obtained from 2*H*-benzo[*b*][1,4]oxazin-2-one **4e** (0.1 mmol scale).



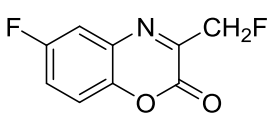
5e

Eluent: Petroleum ether/EtOAc (99:1 to 20:1). Yield: 13.2 mg, 74%; white solid; mp 113–115 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.88 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.57 (ddd, *J* = 8.7, 7.4, 1.6 Hz, 1H), 7.42 (td, *J* = 7.7, 1.3 Hz, 1H), 7.34 (dd, *J* = 8.2, 1.3 Hz, 1H), 5.56 (d, *J* = 46.1 Hz, 2H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -229.47 (t, *J* = 46.0 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 151.5 (d, *J* = 2.4 Hz), 150.8 (d, *J* = 15.2 Hz), 146.4 (d, *J* = 1.6 Hz), 132.1, 130.7, 129.7, 125.9, 116.6, 80.3 (d, *J* = 176.8 Hz). **HRMS** (ESI(+)) m/z: Calculated for $C_9H_6FNO_2$ $[M+H]^+$ 180.0461, found 180.0462.

6-Fluoro-3-(fluoromethyl)-2*H*-benzo[*b*][1,4]oxazin-2-one (5ea)

Following GP, compound **5ea** was obtained from 6-fluoro-2*H*-benzo[*b*][1,4]oxazin-2-one **4ea** (0.2 mmol scale).



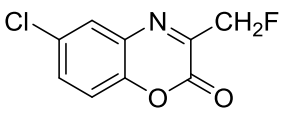
5ea

Eluent: Petroleum ether/EtOAc (20:1 to 9:1). Yield: 31 mg, 74%; yellow solid; mp 124–126 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.57 (dd, *J* = 8.0, 2.6 Hz, 1H), 7.37 – 7.25 (m, 2H), 5.56 (d, *J* = 46.0 Hz, 2H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -114.72 (td, *J* = 7.7, 5.0 Hz, 1F), -230.20 (t, *J* = 46.0 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 159.4 (d, *J* = 246.3 Hz), 152.1 (d, *J* = 14.9 Hz), 151.0 (d, *J* = 2.4 Hz), 142.7 (d, *J* = 2.3 Hz), 131.1 (d, *J* = 11.5 Hz), 119.5 (d, *J* = 24.7 Hz), 117.7 (d, *J* = 8.9 Hz), 115.4 (d, *J* = 24.1 Hz), 80.2 (d, *J* = 178.1 Hz). **HRMS** (ESI(–)) m/z: Calculated for $C_9H_5F_2NO_2$ $[M–H]^+$ 196.0210, found 196.0214.

6-Chloro-3-(fluoromethyl)-2*H*-benzo[*b*][1,4]oxazin-2-one (5eb)

Following GP, compound **5eb** was obtained from 6-chloro-2*H*-benzo[*b*][1,4]oxazin-2-one **4eb** (0.2 mmol scale).



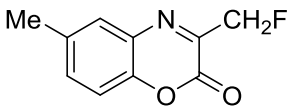
5eb

Eluent: Petroleum ether/EtOAc (20:1 to 9:1). Yield: 33 mg, 77%; yellow solid; mp 144–146 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.86 (d, *J* = 2.5 Hz, 1H), 7.52 (dd, *J* = 8.8, 2.5 Hz, 1H), 7.29 (d, *J* = 8.8 Hz, 1H), 5.55 (d, *J* = 46.0 Hz, 2H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -229.98 (t, *J* = 46.1 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 152.1, 152.0, 150.8 (d, *J* = 2.4 Hz), 145.0 (d, *J* = 1.5 Hz), 132.0, 131.1, 129.1, 117.7, 80.1 (d, *J* = 178.1 Hz). **HRMS** (ESI(–)) m/z: Calculated for $C_9H_5ClFNO_2$ $[M–H]^+$ 211.9915, found 211.9918.

3-(Fluoromethyl)-6-methyl-2*H*-benzo[*b*][1,4]oxazin-2-one (5ec)

Following GP, compound **5ec** was obtained from 6-methyl-2*H*-benzo[*b*][1,4]oxazin-2-one **4ec** (0.2 mmol scale).



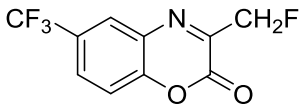
5ec

Eluent: Petroleum ether/EtOAc (20:1 to 9:1). Yield: 30.5 mg, 79%; yellow solid; mp 138–140 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.80 – 7.58 (m, 1H), 7.36 (dd, *J* = 8.5, 2.1 Hz, 1H), 7.21 (d, *J* = 8.4 Hz, 1H), 5.54 (d, *J* = 46.2 Hz, 2H), 2.45 (s, 3H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -229.18 (t, *J* = 46.2 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 151.7 (d, *J* = 2.4 Hz), 150.6 (d, *J* = 15.1 Hz), 144.4 (d, *J* = 1.6 Hz), 136.0, 133.0, 130.4, 129.5, 116.1, 80.4 (d, *J* = 176.6 Hz), 20.8. **HRMS** (ESI(+)) m/z: Calculated for $C_{10}H_8FNO_2$ $[M+H]^+$ 194.0617, found 194.0613.

3-(Fluoromethyl)-6-(trifluoromethyl)-2*H*-benzo[*b*][1,4]oxazin-2-one (5ed)

Following GP, compound **5ed** was obtained from 6-(trifluoromethyl)-2*H*-benzo[*b*][1,4]oxazin-2-one **4ed** (0.2 mmol scale).



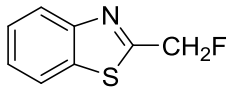
5ed

Eluent: Petroleum ether/EtOAc (20:1 to 9:1). Yield: 35 mg, 71%; yellow solid; mp 112–114 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.18 (d, *J* = 2.1 Hz, 1H), 7.82 (dd, *J* = 8.6, 2.2 Hz, 1H), 7.47 (d, *J* = 8.7 Hz, 1H), 5.58 (d, *J* = 46.0 Hz, 2H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -62.34 (s, 3F), -230.22 (t, *J* = 46.1 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 152.5 (d, *J* = 15.2 Hz), 150.4 (d, *J* = 2.4 Hz), 148.4, 130.3, 128.6 (q, *J* = 3.6 Hz), 128.6 (q, *J* = 34.0 Hz), 127.3 (q, *J* = 3.9 Hz), 123.1 (q, *J* = 272.4 Hz), 117.5, 80.1 (d, *J* = 178.6 Hz). **HRMS** (ESI(+)) m/z: Calculated for $C_{10}H_5F_4NO_2$ $[M+H]^+$ 248.0335, found 248.0331.

2-(Fluoromethyl)benzo[*d*]thiazole (5f)

Following GP, compound **5f** was obtained from benzo[*d*]thiazole **4f** (0.1 mmol scale).

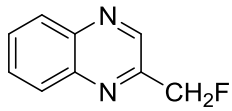


5f

Eluent: Petroleum ether/EtOAc (20:1 to 9:1). Yield: 7 mg, 42%; pale yellow oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.05 (dt, *J* = 8.2, 0.9 Hz, 1H), 7.94 (ddd, *J* = 8.0, 1.4, 0.7 Hz, 1H), 7.52 (ddd, *J* = 8.2, 7.2, 1.3 Hz, 1H), 7.44 (ddd, *J* = 8.3, 7.2, 1.2 Hz, 1H), 5.75 (d, *J* = 46.7 Hz, 2H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -213.75 (t, *J* = 46.7 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 165.9 (d, *J* = 24.4 Hz), 152.8, 135.0, 126.4, 125.6, 123.4, 121.9, 81.4 (d, *J* = 170.6 Hz). **HRMS** (ESI(+)) m/z: Calculated for C_8H_6FNS $[M+H]^+$ 168.0283, found 168.0283.

2-(Fluoromethyl)quinoxaline (5g)[1]

Following GP, compounds **5g** and **5g'** were obtained from quinoxaline **4g** (0.1 mmol scale).

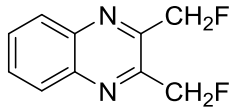


5g

Eluent: Petroleum ether/EtOAc (20:1 to 9:1). Yield: 2.5 mg, 13%; colourless oil.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.05 (s, 1H), 8.23 – 8.11 (m, 1H), 8.11 – 8.03 (m, 1H), 7.85 – 7.73 (m, 2H), 5.73 (d, *J* = 46.7 Hz, 2H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -222.95 (t, *J* = 46.7 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 151.0 (d, *J* = 21.0 Hz), 144.7 (d, *J* = 94.2 Hz), 143.2 (d, *J* = 5.4 Hz), 141.9 (d, *J* = 87.3 Hz), 130.5, 130.3, 129.4, 129.1, 83.6 (d, *J* = 170.2 Hz). **HRMS** (ESI(+)) m/z: Calculated for $C_9H_7FN_2$ $[M+H]^+$ 163.0672, found 163.0670.

2,3-Bis(fluoromethyl)quinoxaline (5g')[1]



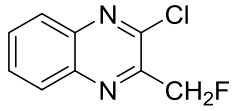
5g'

Eluent: Petroleum ether/EtOAc (50:1 to 20:1). Yield: 5.5 mg, 32%; white solid; mp_{dec} 95–97 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.14 (dt, *J* = 6.6, 3.3 Hz, 2H), 7.84 (dt, *J* = 6.3, 3.1 Hz, 2H), 5.82 (dd, *J* = 43.6, 2.2 Hz, 1H), 5.82 (d, *J* = 48.1 Hz, 2H), 5.73 (dd, *J* = 46.7, 3.7 Hz, 1H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -218.39 – -218.70 (m, 2F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 149.2 (d, *J* = 19.0 Hz), 141.3, 131.0, 129.3, 83.7 (dd, *J* = 169.1, 3.6 Hz). **HRMS** (ESI(+)) m/z: Calculated for $C_{10}H_8F_2N_2$ $[M+H]^+$ 195.0734, found 195.0735.

2-Chloro-3-(fluoromethyl)quinoxaline (5h)

Following GP, compound **5h** was obtained from 2-chloroquinoxaline **4h** (0.1 mmol scale).



5h

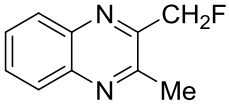
Eluent: Petroleum ether/EtOAc (20:1 to 9:1). Yield: 10 mg, 13%; white solid; mp 77–79 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.23 – 8.12 (m, 1H), 8.12 – 8.01 (m, 1H), 7.92 – 7.77 (m, 2H), 5.78 (d, *J* = 46.6 Hz, 2H). **^{19}F NMR** (376 MHz,

Chloroform-*d*) δ -221.27 (t, *J* = 46.7 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 148.3 (d, *J* = 15.8 Hz), 145.7, 141.9 (d, *J* = 1.9 Hz), 140.5, 131.6, 130.7, 129.3, 128.3, 82.0 (d, *J* = 174.7 Hz). **HRMS** (ESI(+)) m/z: Calculated for $C_9H_6ClFN_2$ $[M+H]^+$ 197.0282, found 197.0289.

2-(Fluoromethyl)-3-methylquinoxaline (5i)[1]

Following GP, compound **5i** was obtained from 2-methylquinoxaline **4i** (0.1 mmol scale).



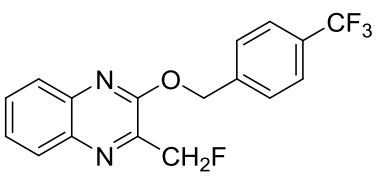
5i

Eluent: Petroleum ether/EtOAc (20:1 to 9:1). Yield: 17.5 mg, 50%; yellow oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.18 – 7.91 (m, 2H), 7.87 – 7.62 (m, 2H), 5.70 (d, *J* = 47.1 Hz, 2H), 2.84 (d, *J* = 2.0 Hz, 3H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -217.48 (td, *J* = 47.1, 1.8 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 153.3, 149.2 (d, *J* = 17.2 Hz), 142.1 (d, *J* = 2.2 Hz), 140.4, 130.5 (d, *J* = 1.5 Hz), 129.4, 129.2, 128.4 (d, *J* = 1.5 Hz), 84.3 (d, *J* = 169.6 Hz), 22.0 (d, *J* = 2.6 Hz).

HRMS (ESI(+)) m/z: Calculated for $C_{10}H_9FN_2$ $[M+H]^+$ 177.0828, found 177.0830.

2-(Fluoromethyl)-3-((4-(trifluoromethyl)benzyl)oxy)quinoxaline (5j)

Following GP, compound **5j** was obtained from 2-((4-(trifluoromethyl)benzyl)oxy)quinoxaline **4j** (0.1 mmol scale).



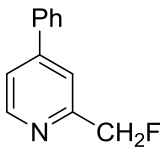
5j

Eluent: Petroleum ether/EtOAc (100% PE to 49:1). Yield: 24 mg, 71%; off-white solid; mp 91–93 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.09 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.87 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.71 (ddd, *J* = 8.5, 6.9, 1.5 Hz, 1H), 7.70 – 7.56 (m, 5H), 5.70 (d, *J* = 46.7 Hz, 2H), 5.67 (s, 2H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -62.60 (s, 3F), -223.75 (t, *J* = 46.7 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 154.8, 143.3 (d, *J* = 15.8 Hz), 140.5 (d, *J* = 2.1 Hz), 140.2, 138.5, 130.7, 130.3 (q, *J* = 32.4 Hz), 129.2, 128.0, 127.3, 126.9, 125.5 (q, *J* = 3.8 Hz), 123.9 (d, *J* = 271.8 Hz), 81.18(d, *J* = 172.0 Hz), 67.2. **HRMS** (ESI(+)) m/z: Calculated for $C_{17}H_{12}F_4N_2O$ $[M+H]^+$ 337.0964, found 337.0981.

2-(Fluoromethyl)-4-phenylpyridine (5k)[1]

Following GP, compound **5k** was obtained from 4-phenylpyridine **4k** (0.1 mmol scale).

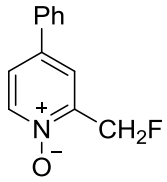


5k

Eluent: Petroleum ether/EtOAc (20:1 to 4:1). Yield: 5 mg, 27%; colourless oil. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.78 – 8.44 (m, 1H), 7.85 – 7.58 (m, 3H), 7.57 – 7.36 (m, 4H), 5.56 (dd, *J* = 46.9, 0.7 Hz, 2H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -221.29 (t, *J* = 46.8 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 156.9 (d, *J* = 21.2 Hz), 149.7 (d, *J* = 1.7 Hz), 149.4, 137.9, 129.2, 129.1, 127.0, 121.0, 118.4 (d, *J* = 5.9 Hz), 84.4 (d, *J* = 170.1 Hz). **HRMS** (ESI(+)) m/z: Calculated for $C_{12}H_{10}FN$ $[M+H]^+$ 188.0876, found 188.0883.

2-(Fluoromethyl)-4-phenylpyridine 1-oxide (5l)

Following GP, compound **5l** was obtained from 4-phenylpyridine 1-oxide **4l** (0.1 mmol scale) and purified by preparative TLC (acetone/petroleum ether, 1:1).



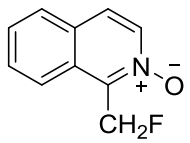
5l

Yield: 9 mg, 44%; white solid; mp_{dec} 132−134 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.62 (d, *J* = 5.2 Hz, 1H), 7.84 – 7.60 (m, 3H), 7.58 – 7.41 (m, 5H), 5.56 (d, *J* = 46.9 Hz, 2H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -221.29 (t, *J* = 46.8 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 156.9 (d, *J* = 21.0 Hz), 149.7 (d, *J* = 2.1 Hz), 149.4, 137.9, 129.2, 129.1, 127.0, 121.0, 118.4 (d, *J* = 5.8 Hz), 84.4 (d, *J* = 170.2 Hz). **HRMS** (ESI(+)) m/z: Calculated for $C_{12}H_{10}FNO$ $[M+H–O]^+$ 188.0876, found 188.0882.

1-(Fluoromethyl)isoquinoline 2-oxide (5m)

Following GP, compound **5m** was obtained from isoquinoline 2-oxide **4m** (0.1 mmol scale).



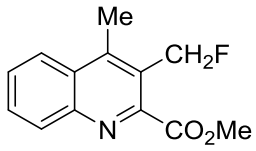
5m

Eluent: Petroleum ether/acetone (9:1 to 3:2). Yield: 10.5 mg, 59%; yellowish brown solid; mp_{dec} 96–98 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.19 (d, *J* = 7.1 Hz, 1H), 8.14 (d, *J* = 8.5 Hz, 1H), 7.80 (d, *J* = 8.1 Hz, 1H), 7.74 – 7.64 (m, 2H), 7.61 (t, *J* = 7.5 Hz, 1H), 6.20 (d, *J* = 47.4 Hz, 2H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -221.09 (t, *J* = 47.4 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 141.3, 136.7, 129.9 (d, *J* = 2.1 Hz), 128.9, 128.8 (d, *J* = 1.9 Hz), 128.7, 127.4, 124.76 (d, *J* = 2.6 Hz), 123.3 (d, *J* = 5.1 Hz), 75.3 (d, *J* = 167.3 Hz). **HRMS** (ESI(+)) m/z: Calculated for $C_{10}H_8FNO$ $[M+H]^+$ 178.0668, found 178.0673.

Methyl 3-(fluoromethyl)-4-methylquinoline-2-carboxylate (5n)

Following GP, compound **5n** was obtained from methyl 4-methylquinoline-2-carboxylate **4n** (0.1 mmol scale).



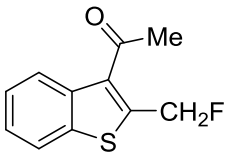
5n

Eluent: Petroleum ether/EtOAc (20:1 to 9:1). Yield: 10.5 mg, 60%; white solid; mp 97–99 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.11 – 8.02 (m, 1H), 7.82 – 7.71 (m, 2H), 7.56 (td, *J* = 7.4, 6.9, 1.2 Hz, 1H), 5.60 (d, *J* = 47.3 Hz, 2H), 4.09 (s, 3H), 2.84 (d, *J* = 1.5 Hz, 3H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -209.47 (t, *J* = 47.2 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 167.5, 158.1, 147.7 (d, *J* = 2.3 Hz), 139.6 (d, *J* = 5.4 Hz), 130.6, 129.0, 127.2, 125.0 (d, *J* = 1.7 Hz), 123.7 (d, *J* = 15.7 Hz), 122.5 (d, *J* = 2.2 Hz), 79.7 (d, *J* = 167.8 Hz), 52.9, 23.3. **HRMS** (ESI(+)) m/z: Calculated for $C_{13}H_{12}FNO_2$ $[M+H]^+$ 234.0930, found 234.0938.

1-(2-(Fluoromethyl)benzo[*b*]thiophen-3-yl)ethan-1-one (5o)

Following GP, compound **5o** was obtained from 1-(benzo[*b*]thiophen-3-yl)ethan-1-one **4o** (0.1 mmol scale).



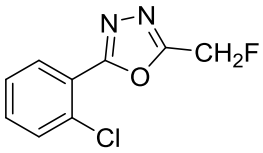
5o

Eluent: Petroleum ether/EtOAc (100% PE to 49:1). Yield: 12 mg, 58%; pale yellow solid; mp 98–100 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.12 (dt, *J* = 8.3, 1.0 Hz, 1H), 7.89 (dt, *J* = 8.0, 1.1 Hz, 1H), 7.50 (ddd, *J* = 8.3, 7.1, 1.2 Hz, 1H), 7.41 (ddd, *J* = 8.2, 7.1, 1.2 Hz, 1H), 5.92 (d, *J* = 47.9 Hz, 2H), 2.75 (s, 3H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -203.62 (t, *J* = 48.2 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 194.6 (d, *J* = 1.7 Hz), 152.3 (d, *J* = 18.9 Hz), 138.6 (d, *J* = 2.2 Hz), 136.9, 131.9 (d, *J* = 2.2 Hz), 125.5, 124.7, 123.3 (d, *J* = 1.7 Hz), 122.8, 81.6 (d, *J* = 166.8 Hz), 31.4 (d, *J* = 1.5 Hz). **HRMS** (ESI(+)) m/z: Calculated for $C_{11}H_9FOS$ $[M–F]^+$ 189.0374, found 189.0381.

2-(2-Chlorophenyl)-5-(fluoromethyl)-1,3,4-oxadiazole (5p)

Following GP, compound **5p** was obtained from 2-(2-chlorophenyl)-1,3,4-oxadiazole **4p** (0.1 mmol scale).



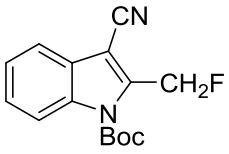
5p

Eluent: Petroleum ether/EtOAc (20:1 to 4:1). Yield: 8 mg, 38%; white sticky gum.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.01 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.63 – 7.52 (m, 1H), 7.50 (td, *J* = 7.7, 1.7 Hz, 1H), 7.43 (td, *J* = 7.6, 1.4 Hz, 1H), 5.62 (d, *J* = 47.0 Hz, 2H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -221.94 (t, *J* = 47.1 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 164.5, 161.4 (d, *J* = 20.2 Hz), 133.4, 132.9, 131.3, 127.1, 122.6, 73.1 (d, *J* = 173.4 Hz). **HRMS** (ESI(+)) m/z: Calculated for $C_9H_6ClFN_2O$ $[M+H]^+$ 213.0231, found 213.0232.

***tert*-Butyl 3-cyano-2-(fluoromethyl)-1*H*-indole-1-carboxylate (5q)**

Following GP, compound **5q** was obtained from *tert*-butyl 3-cyano-1*H*-indole-1-carboxylate **4q** (0.1 mmol scale).



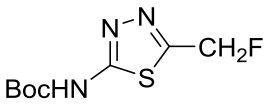
5q

Eluent: Petroleum ether/EtOAc (100% PE to 20:1). Yield: 19.5 mg, 71%; white solid; mp 148–150 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.18 (dt, *J* = 8.6, 1.0 Hz, 1H), 7.75 – 7.68 (m, 1H), 7.50 – 7.41 (m, 1H), 7.43 – 7.35 (m, 1H), 5.83 (d, *J* = 46.8 Hz, 2H), 1.72 (s, 9H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -209.54 (t, *J* = 46.7 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 148.6, 141.6 (d, *J* = 18.3 Hz), 135.6 (d, *J* = 1.4 Hz), 127.0 (d, *J* = 1.3 Hz), 126.6 (d, *J* = 2.1 Hz), 124.6, 119.7, 116.1, 113.4 (d, *J* = 2.1 Hz), 95.5 (d, *J* = 6.3 Hz), 86.8, 76.3 (d, *J* = 172.2 Hz), 27.9. **HRMS** (ESI(+)) m/z: Calculated for $C_{15}H_{15}FN_2O_2$ $[M–Boc]^+$ 173.0515, found 173.0521.

***tert*-Butyl (5-(fluoromethyl)-1,3,4-thiadiazol-2-yl)carbamate (5r)**

Following GP, compound **5r** was obtained from *tert*-butyl (1,3,4-thiadiazol-2-yl)carbamate **4r** (0.1 mmol scale).



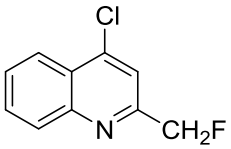
5r

Eluent: Petroleum ether/EtOAc (9:1 to 3:2). Yield: 5 mg, 22%; white solid; mp_{dec} > 120 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.48 (s, 1H), 5.65 (d, *J* = 47.3 Hz, 2H), 1.57 (s, 9H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -209.76 (t, *J* = 47.4 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 162.9, 159.0 (d, *J* = 24.2 Hz), 151.8 (d, *J* = 2.0 Hz), 83.9, 78.2 (d, *J* = 170.0 Hz), 28.0. **HRMS** (ESI(–)) m/z: Calculated for $C_8H_{12}FN_3O_2S$ $[M–H]^+$ 232.0556, found 232.0560.

4-Chloro-2-(fluoromethyl)quinoline (5s)

Following GP, compound **5s** was obtained from 4-chloroquinoline **4s** (0.1 mmol scale).



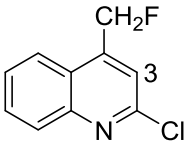
5s

Eluent: Petroleum ether/EtOAc (20:1 to 9:1). Yield: 7.6 mg, 39%; white solid; mp 81–83 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.25 (dd, *J* = 9.4, 0.9 Hz, 1H), 8.07 (ddd, *J* = 8.4, 1.2, 0.6 Hz, 1H), 7.79 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.71 (d, *J* = 1.3 Hz, 1H), 7.66 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 5.63 (d, *J* = 46.8 Hz, 2H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -222.36 (t, *J* = 46.7 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 156.8 (d, *J* = 22.4 Hz), 148.2 (d, *J* = 1.9 Hz), 143.7, 130.8, 129.4, 127.7, 125.9, 124.2, 118.3 (d, *J* = 6.0 Hz), 84.3 (d, *J* = 171.7 Hz). **HRMS** (ESI(+)) m/z: Calculated for $C_{10}H_7ClFN$ $[M+H]^+$ 196.0329, found 196.0335.

Mixture of 2-Chloro-4-(fluoromethyl)quinoline and 2-chloro-3-(fluoromethyl)quinoline (5t)

Following GP, compound **5t** was isolated as a mixture of regioisomers and obtained from 2-chloroquinoline **4t** (0.1 mmol scale). Purification by preparative TLC using Petroleum ether/EtOAc (1:1).



5t

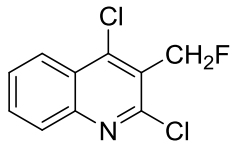
C3/C4 = 1:1.1

Yield: 8.5 mg, 21%; white solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.38 (ddd, *J* = 8.8, 1.8, 0.8 Hz, 1H), 8.07 (ddt, *J* = 8.6, 4.8, 1.0 Hz, 2H), 7.84 – 7.76 (m, 2H), 7.77 – 7.68 (m, 1H), 7.65 – 7.55 (m, 2H), 7.54 – 7.42 (m, 2H), 5.89 (dd, *J* = 46.5, 1.1 Hz, 2H), 5.80 (d, *J* = 47.8 Hz, 2H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ **C3-CH_2F**: -204.83 (t, *J* = 47.7 Hz, 1F), **C4-CH_2F**: -223.25 (t, *J* = 46.7 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 150.9 (d, *J* = 23.6 Hz), 148.3 (d, *J* = 1.9 Hz), 147.7, 144.6 (d, *J* = 16.8 Hz), 135.2, 132.2 (d, *J* = 15.9 Hz), 130.7, 130.4 (d, *J* = 3.2 Hz), 130.0 (d, *J* = 1.7 Hz), 129.5, 127.7 (d, *J* = 7.6 Hz), 127.4, 125.3, 123.6, 122.8, 122.5, 119.4 (d, *J* = 11.7 Hz), 82.5 (d, *J* = 167.0 Hz), 80.7 (d, *J* = 173.2 Hz). **HRMS** (ESI(+)) m/z: Calculated for $C_{10}H_7ClFN$ $[M+H]^+$ 196.0329, found 196.0335.

2,4-Dichloro-3-(fluoromethyl)quinoline (5u)

Following GP, compound **5u** was obtained from 2,4-dichloroquinoline **4u** (0.1 mmol scale).



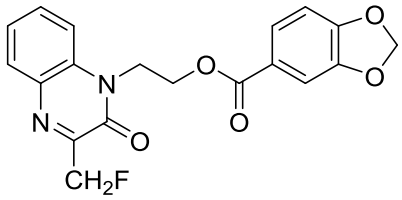
5u

Eluent: Petroleum ether/EtOAc (20:1 to 9:1). Yield: 8 mg, 35%; pale yellow solid; mp 76–78 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.27 (ddd, *J* = 8.5, 1.5, 0.8 Hz, 1H), 8.05 (dd, *J* = 8.5, 1.2 Hz, 1H), 7.84 (ddt, *J* = 8.3, 7.0, 1.2 Hz, 1H), 7.70 (ddd, *J* = 8.3, 6.9, 1.2 Hz, 1H), 5.88 (d, *J* = 47.3 Hz, 2H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -211.75 (t, *J* = 47.4 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 151.1 (d, *J* = 1.9 Hz), 147.8 (d, *J* = 2.4 Hz), 146.6 (d, *J* = 4.9 Hz), 132.3 (d, *J* = 1.8 Hz), 128.9 (d, *J* = 1.8 Hz), 128.4, 125.4 (d, *J* = 2.6 Hz), 125.2 (d, *J* = 1.9 Hz), 125.0 (d, *J* = 15.4 Hz), 79.0 (d, *J* = 168.7 Hz). **HRMS** (ESI(+)) m/z: Calculated for $C_{10}H_6Cl_2FN$ $[M+H]^+$ 229.9940, found 229.9946.

2-(3-(Fluoromethyl)-2-oxoquinoxalin-1(2*H*)-yl)ethyl benzo[*d*][1,3]dioxole-5-carboxylate (7a)

Following GP, compound **7a** was obtained from 2-(2-oxoquinoxalin-1(2*H*)-yl)ethyl benzo[*d*][1,3]dioxole-5-carboxylate **6a** (0.1 mmol scale).



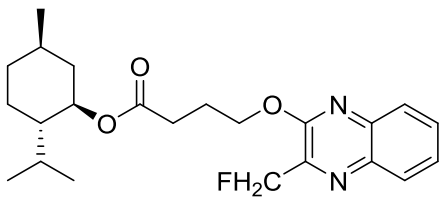
7a

Eluent: Petroleum ether/EtOAc (9:1 to 3:1). Yield: 27 mg, 73%; white solid; mp 168–170 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.99 (dt, *J* = 8.1, 1.1 Hz, 1H), 7.62 – 7.55 (m, 2H), 7.51 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.46 – 7.36 (m, 1H), 7.31 (d, *J* = 1.5 Hz, 1H), 6.78 (dd, *J* = 8.2, 0.4 Hz, 1H), 6.03 (s, 2H), 5.65 (d, *J* = 46.5 Hz, 2H), 4.70 – 4.60 (m, 4H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -230.16 (t, *J* = 46.6 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 165.8, 153.5 (d, *J* = 4.2 Hz), 153.4 (d, *J* = 7.6 Hz), 151.9, 147.7, 132.7, 132.7, 131.1, 130.9, 125.6, 124.2, 123.2, 113.9, 109.5, 108.0, 101.9, 80.9 (d, *J* = 174.5 Hz), 61.0, 40.7. **HRMS** (ESI(+)) m/z: Calculated for $C_{19}H_{15}FN_2O_5$ $[M+H]^+$ 371.1043, found 371.1054.

(1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl 4-((3-(fluoromethyl)quinoxalin-2-yl)oxy)butanoate (7b)

Following GP, compound **7b** was obtained from (1R,2S,5R)-2-isopropyl-5-methylcyclohexyl 4-(quinoxalin-2-yloxy)butanoate **6b** (0.1 mmol scale).



7b

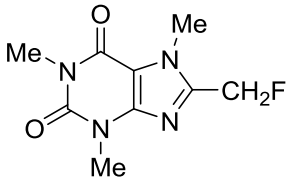
Eluent: Petroleum ether/EtOAc (20:1 to 4:1). Yield: 29 mg, 72%; colourless oil.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.06 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.83 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.68 (ddd, *J* = 8.3, 6.9, 1.5 Hz, 1H), 7.58 (ddd, *J* = 8.4, 7.0, 1.5 Hz, 1H), 5.65 (d, *J* = 46.8 Hz, 2H), 4.70 (td, *J* = 10.9, 4.4 Hz, 1H), 4.64 – 4.47 (m, 2H), 2.52 (t, *J* = 7.4 Hz, 2H), 2.20 (p, *J* = 7.0 Hz, 2H), 2.05 – 1.90 (m, 1H), 1.83 (pd, *J* = 7.0, 2.7 Hz, 1H), 1.75 – 1.57 (m, 2H), 1.48 (ddtd, *J* = 15.1, 12.0, 6.5, 3.2 Hz, 1H), 1.35 (ddt, *J* = 12.4, 10.8,

3.1 Hz, 1H), 1.10 – 0.90 (m, 3H), 0.88 (d, *J* = 6.6 Hz, 3H), 0.85 (d, *J* = 7.0 Hz, 3H), 0.74 (d, *J* = 7.0 Hz, 3H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -224.71 (t, *J* = 46.9 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 172.5, 155.2 (d, *J* = 1.4 Hz), 143.5 (d, *J* = 15.3 Hz), 140.7 (d, *J* = 2.0 Hz), 138.3, 130.4, 129.1, 126.9, 81.0 (d, *J* = 172.4 Hz), 74.4, 65.7, 47.0, 40.9, 34.2, 31.3, 31.1, 26.3, 24.2, 23.4, 22.0, 20.7, 16.3. **HRMS** (ESI(+)) m/z: Calculated for $C_{23}H_{31}FN_2O_3$ $[M+H]^+$ 403.2397, found 403.2403.

8-(Fluoromethyl)-1,3,7-trimethyl-3,7-dihydro-1*H*-purine-2,6-dione (7c)[21]

Following GP, compound **7c** was obtained from 1,3,7-trimethyl-3,7-dihydro-1*H*-purine-2,6-dione **6c** (0.1 mmol scale).



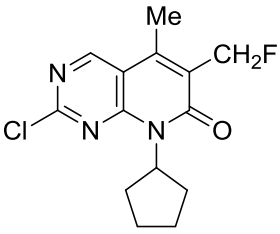
7c

Eluent: Petroleum ether/acetone (20:1 to 4:1). Yield: 10 mg, 43%; white solid; mp 148–150 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.48 (d, *J* = 47.9 Hz, 2H), 4.07 (d, *J* = 1.7 Hz, 3H), 3.57 (s, 3H), 3.41 (s, 3H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -215.60 (t, *J* = 47.9 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 155.5, 151.5, 147.3, 146.4 (d, *J* = 18.9 Hz), 109.0, 75.4 (d, *J* = 168.6 Hz), 32.3 (d, *J* = 1.8 Hz), 29.7, 28.0. **HRMS** (ESI(+)) m/z: Calculated for $C_9H_{11}FN_4O_2$ $[M+H]^+$ 227.0944, found 227.0952.

2-Chloro-8-cyclopentyl-6-(fluoromethyl)-5-methylpyrido[2,3-*d*]pyrimidin-7(8*H*)-one (7d)

Following GP, compound **7d** was obtained from 2-chloro-8-cyclopentyl-5-methylpyrido[2,3-*d*]pyrimidin-7(8*H*)-one **6d** (0.1 mmol scale).



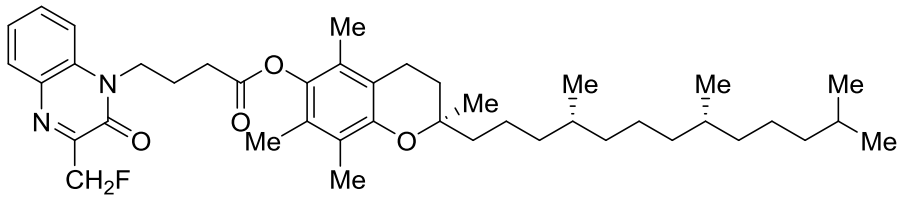
7d

Eluent: Petroleum ether/EtOAc (20:1 to 9:1). Yield: 14.5 mg, 49%; white solid; mp 87–89 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.87 (d, *J* = 0.9 Hz, 1H), 5.89 (tt, *J* = 9.8, 7.7 Hz, 1H), 5.57 (d, *J* = 47.6 Hz, 2H), 2.59 (d, *J* = 3.2 Hz, 3H), 2.28 – 2.14 (m, 2H), 2.18 – 2.06 (m, 2H), 1.98 – 1.86 (m, 2H), 1.76 – 1.61 (m, 2H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -213.50 (tq, *J* = 47.1, 3.2 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 161.8 (d, *J* = 2.1 Hz), 160.3 (d, *J* = 1.7 Hz), 158.0, 156.7 (d, *J* = 2.1 Hz), 155.6 (d, *J* = 1.6 Hz), 144.40(d, *J* = 4.2 Hz), 127.5 (d, *J* = 14.2 Hz), 113.1 (d, *J* = 2.9 Hz), 76.0 (d, *J* = 141.9 Hz), 54.4, 28.7, 26.1, 13.9. **HRMS** (ESI(+)) m/z: Calculated for $C_{14}H_{15}ClFN_3O$ $[M+H]^+$ 296.0966, found 296.0975.

(*R*)-2,5,7,8-Tetramethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)chroman-6-yl 4-(3-(fluoromethyl)-2-oxoquinoxalin-1(2*H*)-yl)butanoate (7e)

Following GP, compound **7e** was obtained from (*R*)-2,5,7,8-tetramethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)chroman-6-yl 4-(2-oxoquinoxalin-1(2*H*)-yl)butanoate **6e** (0.1 mmol scale).



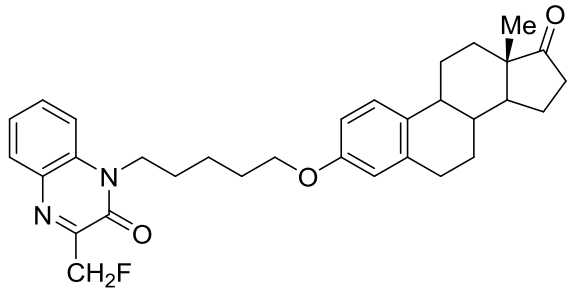
7e

Eluent: Petroleum ether/EtOAc (9:1 to 7:3). Yield: 48 mg, 71%; pale yellow oil.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.98 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.65 (dd, *J* = 8.5, 1.3 Hz, 1H), 7.59 (ddd, *J* = 8.5, 7.1, 1.6 Hz, 1H), 7.38 (ddd, *J* = 8.2, 7.1, 1.3 Hz, 1H), 5.66 (d, *J* = 46.6 Hz, 2H), 4.61 – 4.28 (m, 2H), 2.85 (t, *J* = 6.6 Hz, 2H), 2.60 (t, *J* = 6.8 Hz, 2H), 2.26 – 2.13 (m, 2H), 2.10 (s, 3H), 2.03 (s, 3H), 1.99 (s, 3H), 1.80 (ddt, *J* = 21.0, 13.5, 7.0 Hz, 2H), 1.55 – 1.33 (m, 7H), 1.32 – 1.20 (m, 7H), 1.18 – 0.99 (m, 10H), 0.85 (dd, *J* = 8.2, 6.5 Hz, 12H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -230.03 (t, *J* = 46.6 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 171.8, 153.4 (d, *J* = 6.0 Hz), 153.3 (d, *J* = 6.0 Hz), 149.6, 140.3, 132.7, 132.4, 131.4, 130.7, 126.5, 124.7, 124.1, 123.2, 117.5, 114.1, 81.0 (d, *J* = 174.3 Hz), 75.1, 41.4, 39.3, 37.47, 37.43, 37.3, 32.8, 32.7, 30.6, 28.0, 24.8, 24.4, 22.7, 22.6, 22.1, 21.0, 20.6, 19.7, 19.6, 13.0, 12.2, 11.8. **HRMS** (ESI(+)) m/z: Calculated for $C_{42}H_{61}FN_2O_4$ $[M+H]^+$ 677.4694, found 677.4716.

3-(Fluoromethyl)-1-(5-(((13*S*)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl)oxy)pentyl)quinoxalin-2(1*H*)-one (7f)

Following GP, compound **7f** was obtained from 1-(5-(((13*S*)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl)oxy)pentyl)quinoxalin-2(1*H*)-one **6f** (0.1 mmol scale).



7f

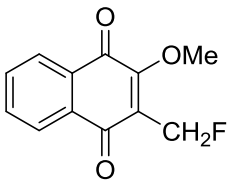
Eluent: Petroleum ether/EtOAc (20:1 to 9:1). Yield: 36 mg, 70%; yellow solid; mp 122–124 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.99 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.60 (ddd, *J* = 8.7, 7.4, 1.6 Hz, 1H), 7.43 – 7.33 (m, 2H), 7.19 (d, *J* = 8.5 Hz, 1H), 6.70 (dd, *J* = 8.6, 2.8 Hz, 1H), 6.63 (d, *J* = 2.6 Hz, 2H), 5.65 (d, *J* = 46.6 Hz, 2H), 4.33 – 4.25 (m, 2H), 3.96 (t, *J* = 6.2 Hz, 2H), 2.89 (dt, *J* = 8.0, 4.4 Hz,

2H), 2.56 – 2.45 (m, 1H), 2.39 (dt, *J* = 11.7, 3.0 Hz, 1H), 2.31 – 2.20 (m, 1H), 2.20 – 1.92 (m, 4H), 1.92 – 1.76 (m, 4H), 1.70 – 1.50 (m, 5H), 1.51 – 1.31 (m, 2H), 0.91 (s, 3H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -230.30 (t, *J* = 46.6 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 220.9, 156.9, 153.6 (d, *J* = 14.2 Hz), 153.3 (d, *J* = 2.2 Hz), 137.7, 132.8, 132.4, 132.0, 130.9, 130.8, 126.3, 123.9, 114.5, 113.7, 112.1, 81.0 (d, *J* = 174.5 Hz), 67.4, 50.4, 48.0, 44.0, 42.0, 38.4, 35.8, 31.6, 29.6, 28.9, 27.0, 26.5, 25.9, 23.7, 21.6, 13.8. **HRMS** (ESI(+)) m/z: Calculated for $C_{32}H_{37}FN_2O_3$ $[M+H]^+$ 517.2866, found 517.2883.

2-(Fluoromethyl)-3-methoxynaphthalene-1,4-dione (7g)

Following GP, compound **7g** was obtained from 2-methoxynaphthalene-1,4-dione **6g** (0.1 mmol scale).



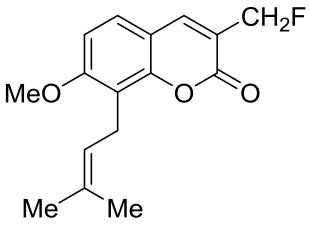
7g

Eluent: Petroleum ether/EtOAc (100% PE to 47:3). Yield: 10 mg, 22%; yellow solid; mp 82–84 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.13 (ddd, *J* = 7.0, 1.9, 0.6 Hz, 1H), 8.08 (ddd, *J* = 7.0, 1.7, 0.6 Hz, 1H), 7.75 (pd, *J* = 7.4, 1.6 Hz, 2H), 5.45 (d, *J* = 47.1 Hz, 2H), 4.30 (d, *J* = 0.7 Hz, 3H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -216.08 (t, *J* = 47.1 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 183.7, 181.8, 159.9 (d, *J* = 5.1 Hz), 134.5, 133.5, 131.5 (d, *J* = 2.9 Hz), 126.5, 126.4, 125.1, 125.0, 73.1 (d, *J* = 163.5 Hz), 62.0. **HRMS** (ESI(+)) m/z: Calculated for $C_{12}H_9FO_3$ $[M+H]^+$ 221.0614, found 221.0612.

3-(Fluoromethyl)-7-methoxy-8-(3-methylbut-2-en-1-yl)-2*H*-chromen-2-one (7h)

Following GP, compound **7h** was obtained from 7-methoxy-8-(3-methylbut-2-en-1-yl)-2*H*-chromen-2-one (Osthol) **6h** (0.1 mmol scale).



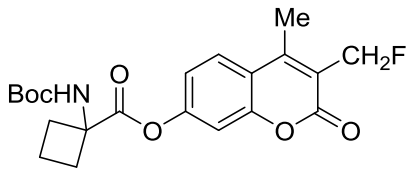
7h

Eluent: Petroleum ether/EtOAc (20:1 to 9:1). Yield: 19 mg, 51%; white solid; mp 105–107 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.72 (q, *J* = 1.3 Hz, 1H), 7.33 (d, *J* = 8.6 Hz, 1H), 6.86 (d, *J* = 8.6 Hz, 1H), 5.33 (dd, *J* = 46.9, 1.3 Hz, 2H), 5.21 (tdt, *J* = 7.3, 2.8, 1.4 Hz, 1H), 3.93 (s, 3H), 3.66 – 3.40 (m, 2H), 1.84 (d, *J* = 1.4 Hz, 3H), 1.66 (d, *J* = 1.4 Hz, 3H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -222.17 (t, *J* = 46.8 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 160.3, 160.1 (d, *J* = 5.5 Hz), 152.4 (d, *J* = 1.0 Hz), 140.3 (d, *J* = 8.7 Hz), 132.7, 126.5, 120.9, 120.2 (d, *J* = 18.7 Hz), 117.9, 112.7, 107.6, 79.8 (d, *J* = 169.2 Hz), 56.0, 25.8, 21.9, 17.9. **HRMS** (ESI(+)) m/z: Calculated for $C_{16}H_{17}FO_3$ $[M+H]^+$ 277.1240, found 277.1245.

3-(Fluoromethyl)-4-methyl-2-oxo-2*H*-chromen-7-yl 1-((*tert*-butoxycarbonyl)amino)cyclobutane-1-carboxylate (7i)

Following GP, compound **7i** was obtained from 4-methyl-2-oxo-2*H*-chromen-7-yl 1-((tert-butoxycarbonyl)amino)cyclobutane-1-carboxylate **6i** (0.1 mmol scale) and purified by preparative TLC (Petroleum ether/EtOAc, 7:3).



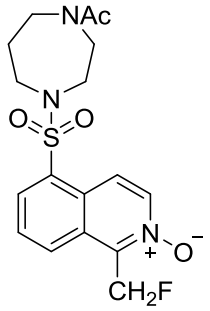
7i

Yield: 25.5 mg, 63%; colourless gum.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.70 (d, *J* = 9.0 Hz, 1H), 7.19 – 7.03 (m, 2H), 5.50 (d, *J* = 47.9 Hz, 2H), 5.29 (s, 1H), 2.80 (dt, *J* = 13.6, 7.8 Hz, 2H), 2.56 (d, *J* = 3.2 Hz, 3H), 2.30 (q, *J* = 9.1, 8.6 Hz, 2H), 2.10 (p, *J* = 7.2 Hz, 2H), 1.45 (s, 9H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -211.77 (t, *J* = 47.7 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 171.8, 160.5 (d, *J* = 2.2 Hz), 154.8, 154.1, 153.7 (d, *J* = 1.9 Hz), 152.8 (d, *J* = 4.1 Hz), 126.2 (d, *J* = 1.9 Hz), 119.6 (d, *J* = 15.4 Hz), 118.3, 117.8 (d, *J* = 2.8 Hz), 110.2, 80.5, 76.4 (d, *J* = 165.5 Hz), 58.5, 31.6, 28.3, 15.2. **HRMS** (ESI(+)) m/z: Calculated for $C_{21}H_{24}FNO_6$ $[M+Na]^+$ 428.1485, found 428.1484.

5-((4-Acetyl-1,4-diazepan-1-yl)sulfonyl)-1-(fluoromethyl)isoquinoline 2-oxide (7j)

Following GP, compound **7j** was obtained from *N*-Ac-fasudil-*N*-oxide **6j** (0.1 mmol scale).

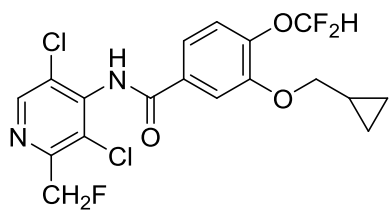


7j

Eluent: EtOAc/MeOH (20:1 to 4:1). Yield: 22.5 mg, 59%; yellow gum.

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.55 – 8.37 (m, 3H), 8.14 (d, *J* = 7.4 Hz, 1H), 7.88 (ddd, *J* = 8.5, 7.4, 2.1 Hz, 1H), 6.13 (d, *J* = 47.2 Hz, 2H), 3.49 (dddt, *J* = 39.1, 15.8, 11.4, 5.6 Hz, 8H), 1.95 (d, *J* = 8.6 Hz, 3H), 1.75 (ddt, *J* = 21.2, 11.8, 6.2 Hz, 2H). **^{19}F NMR** (376 MHz, DMSO-d_6) δ -217.59 (t, *J* = 47.2 Hz, 1F). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 169.7, 141.6 (d, *J* = 4.2 Hz), 141.4 (d, *J* = 4.0 Hz), 138.9 (t, *J* = 3.1 Hz), 135.7 (d, *J* = 21.8 Hz), 130.8, 129.9, 129.6, 129.0 (d, *J* = 4.0 Hz), 123.5 (d, *J* = 2.4 Hz), 123.4 (d, *J* = 2.2 Hz), 122.2 (d, *J* = 3.4 Hz), 74.5 (d, *J* = 161.4 Hz), 49.7, 49.1, 48.0, 47.9, 47.4, 46.9, 46.2, 44.3, 29.5, 28.2, 21.7, 21.5. The complex NMR spectra obtained at room temperature due to the amide units which attribute dynamic conformational behaviour of the compound. **HRMS** (ESI(+)) m/z: Calculated for $C_{17}H_{20}FN_3O_4S$ $[M+H]^+$ 382.1237, found 382.1248.

3-(Cyclopropylmethoxy)-*N*-(3,5-dichloro-2-(fluoromethyl)pyridin-4-yl)-4-(difluoromethoxy)benzamide (7k)



7k

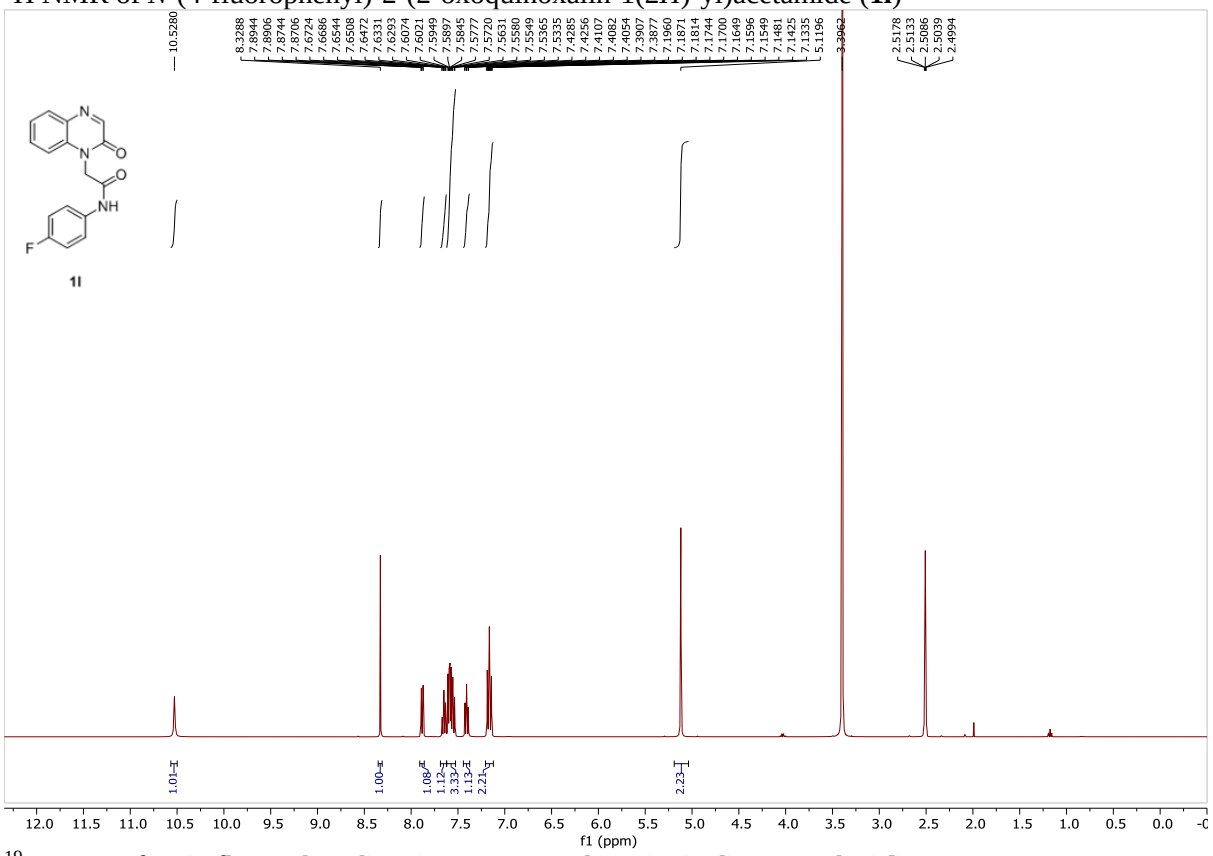
Following GP, compound **7k** was obtained from Roflumilast **6k** (0.1 mmol scale) and purified by preparative TLC (Petroleum ether/EtOAc, 3:2).

Yield: 12 mg, 28%; off-white solid; mp 77–79 °C.

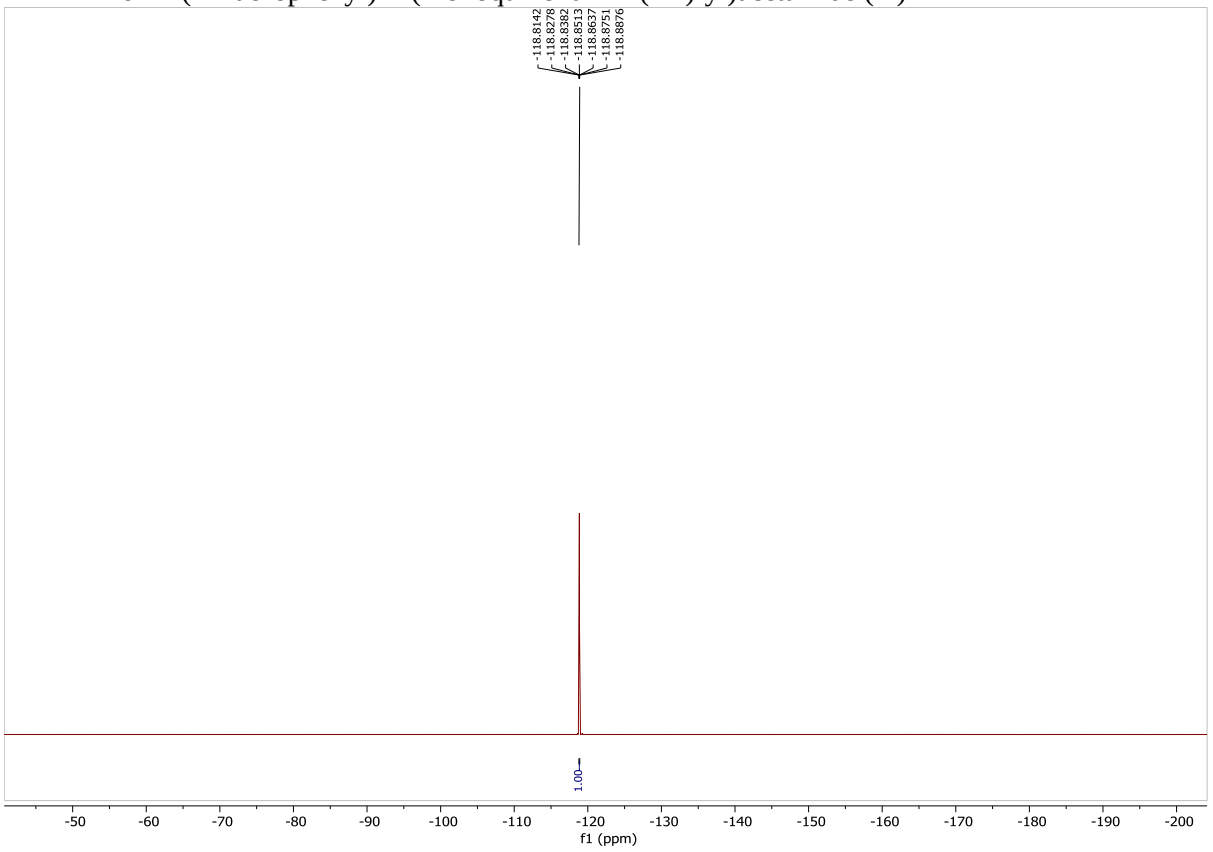
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.62 (s, 1H), 7.72 (s, 1H), 7.59 (d, *J* = 2.1 Hz, 1H), 7.48 (dd, *J* = 8.3, 2.1 Hz, 1H), 7.30 (d, *J* = 8.3 Hz, 1H), 6.75 (t, *J* = 74.8 Hz, 1H), 5.60 (d, *J* = 47.0 Hz, 2H), 3.97 (d, *J* = 7.0 Hz, 2H), 1.39 – 1.29 (m, 1H), 0.73 – 0.64 (m, 2H), 0.46 – 0.30 (m, 2H). **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -82.07 (d, *J* = 74.4 Hz, 2F), -218.16 (t, *J* = 46.7 Hz, 1F). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 163.7, 151.8 (d, *J* = 16.0 Hz), 151.0, 147.6, 143.9 (t, *J* = 3.1 Hz), 140.4, 130.7, 129.3 (d, *J* = 3.1 Hz), 128.3 (d, *J* = 2.0 Hz), 122.3, 119.9, 115.6 (t, *J* = 261.7 Hz), 114.2, 82.2 (d, *J* = 172.3 Hz), 74.2, 10.0, 3.3. **HRMS** (ESI(+)) m/z: Calculated for $C_{18}H_{15}Cl_2F_3N_2O_3$ $[M+H]^+$ 435.0490, found 435.0504.

13. Copies of ^{1}H, ^{19}F and ^{13}C spectra

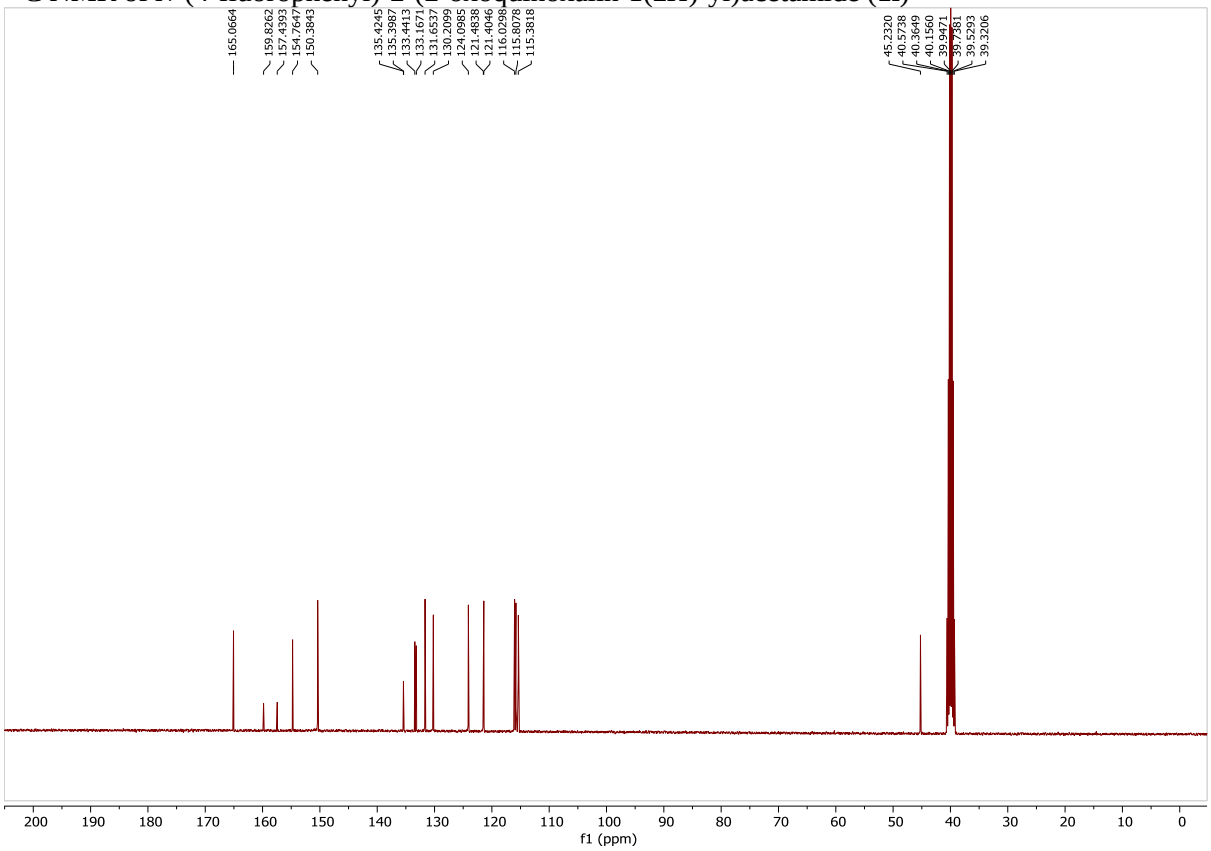
^{1}H NMR of *N*-(4-fluorophenyl)-2-(2-oxoquinoxalin-1(2*H*)-yl)acetamide (**1l**)



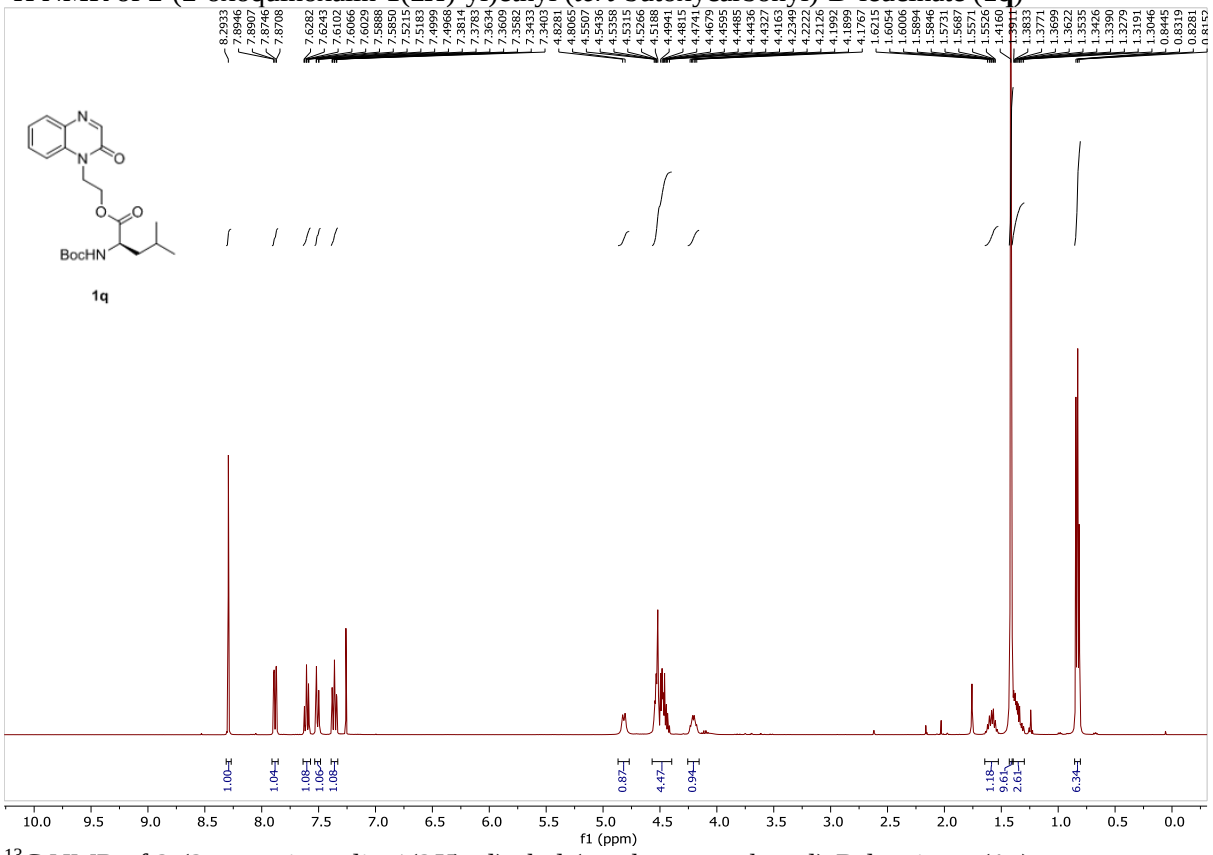
^{19}F NMR of *N*-(4-fluorophenyl)-2-(2-oxoquinoxalin-1(2*H*)-yl)acetamide (**1l**)



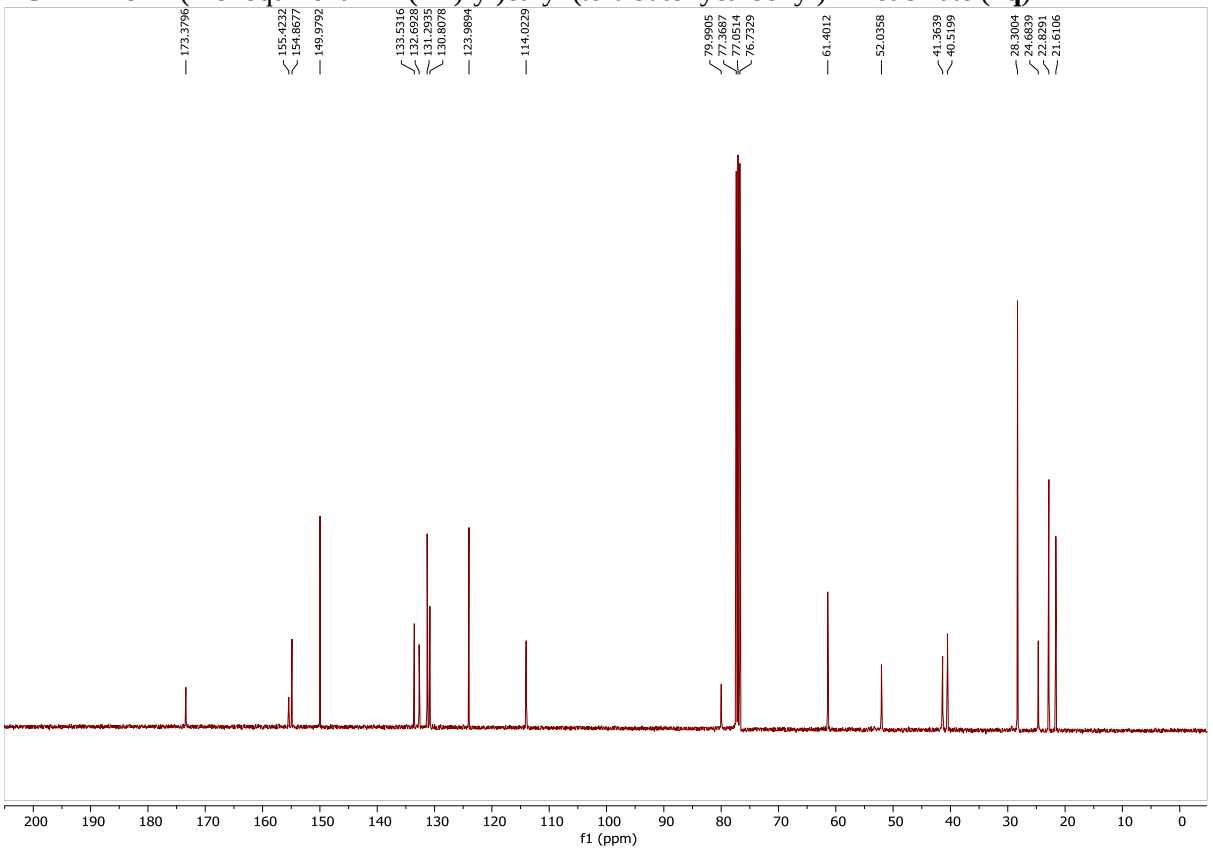
^{13}C NMR of *N*-(4-fluorophenyl)-2-(2-oxoquinoxalin-1(2*H*)-yl)acetamide (**1l**)



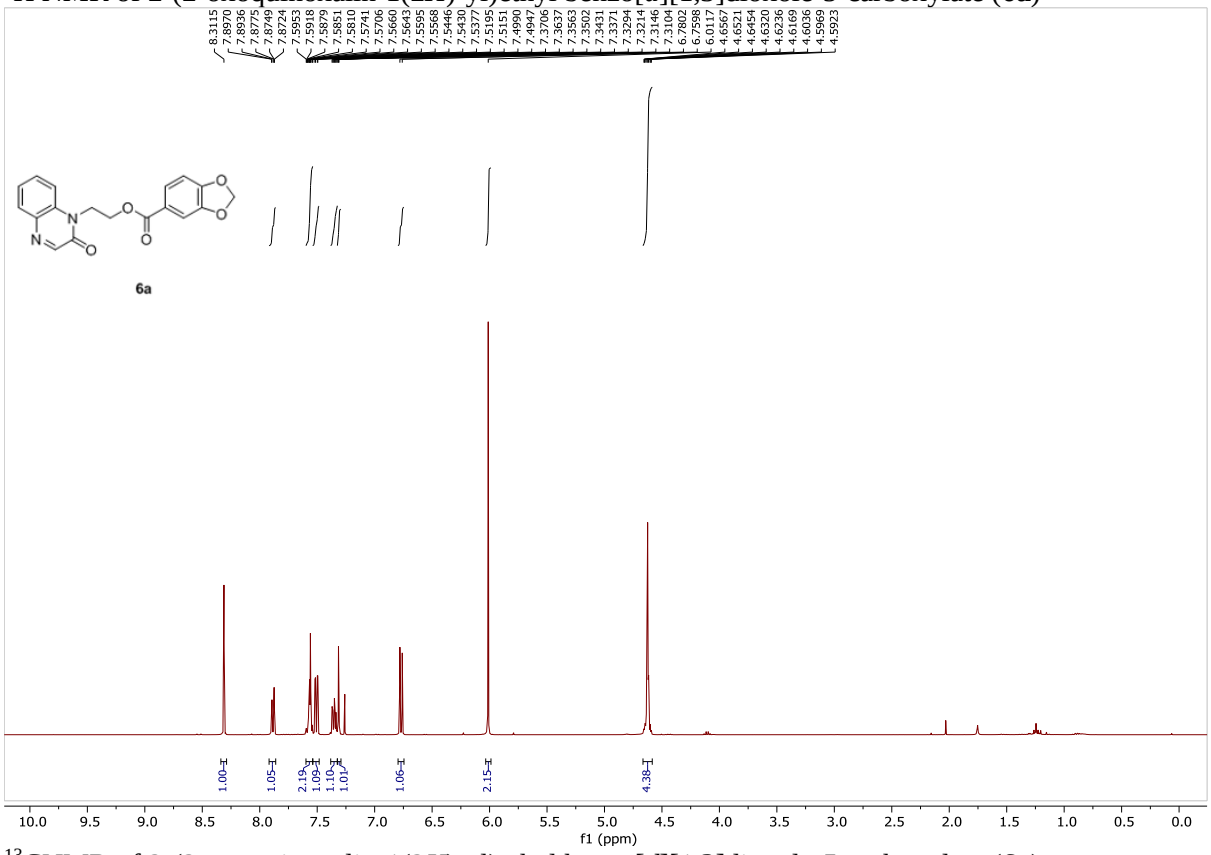
^{1}H NMR of 2-(2-oxoquinoxalin-1(2*H*)-yl)ethyl (*tert*-butoxycarbonyl)-D-leucinate (**1q**)



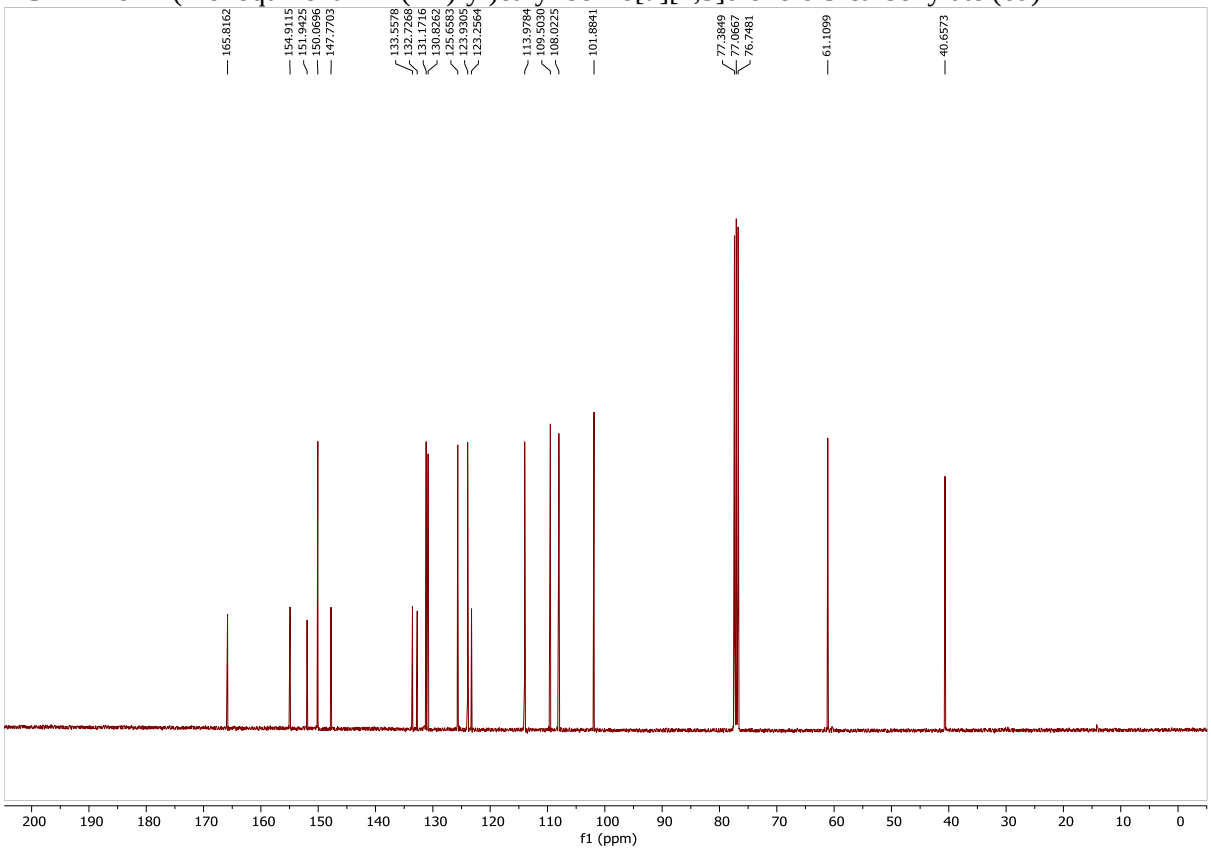
^{13}C NMR of 2-(2-oxoquinoxalin-1(2*H*)-yl)ethyl (*tert*-butoxycarbonyl)-D-leucinate (**1q**)



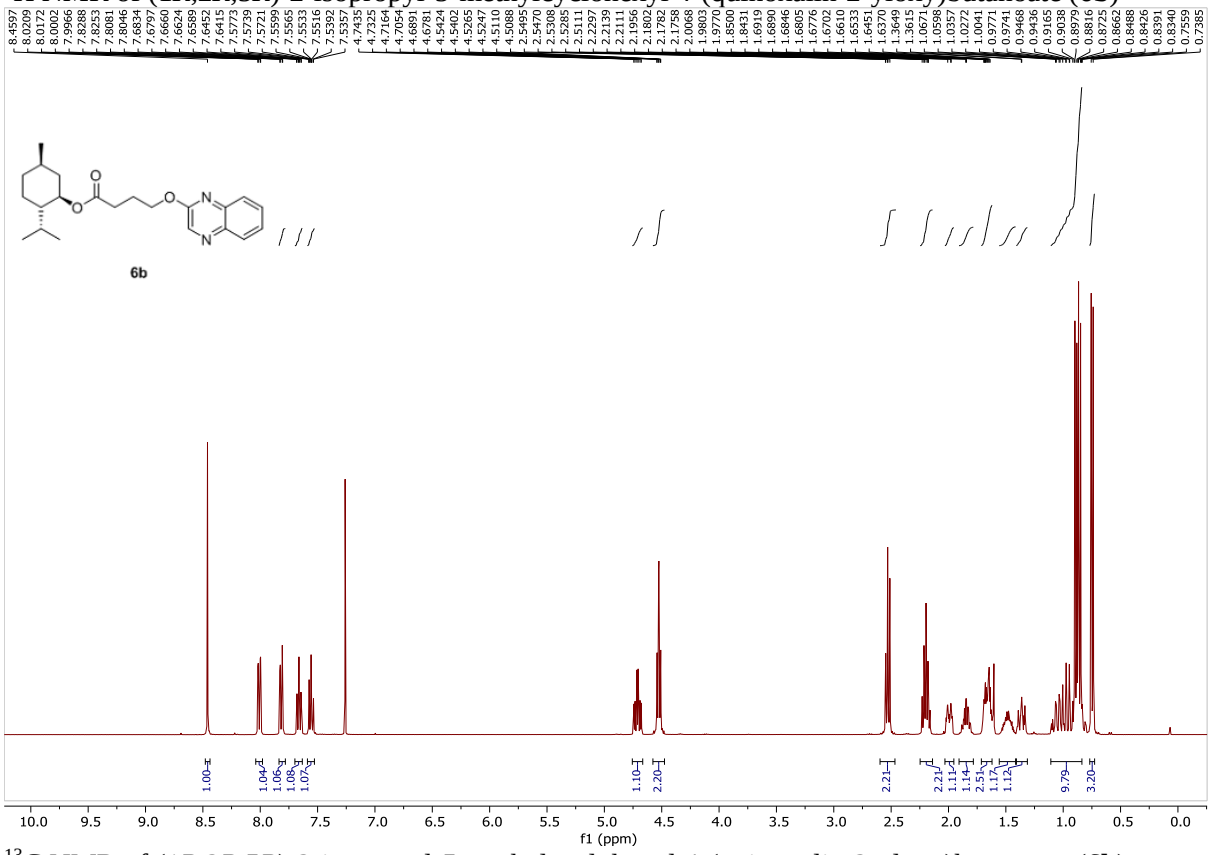
^{1}H NMR of 2-(2-oxoquinoxalin-1(2*H*)-yl)ethyl benzo[*d*][1,3]dioxole-5-carboxylate (**6a**)



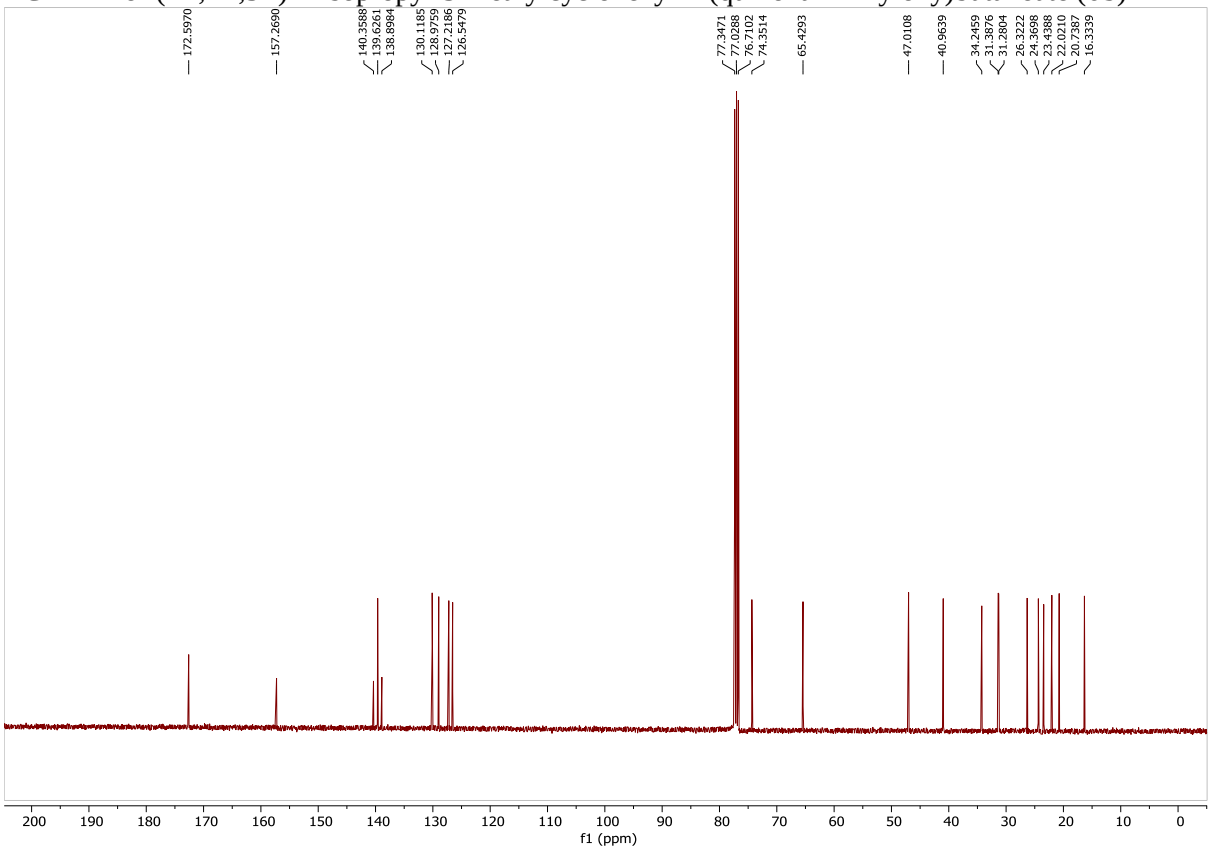
^{13}CNMR of 2-(2-oxoquinoxalin-1(2*H*)-yl)ethyl benzo[*d*][1,3]dioxole-5-carboxylate (**6a**)



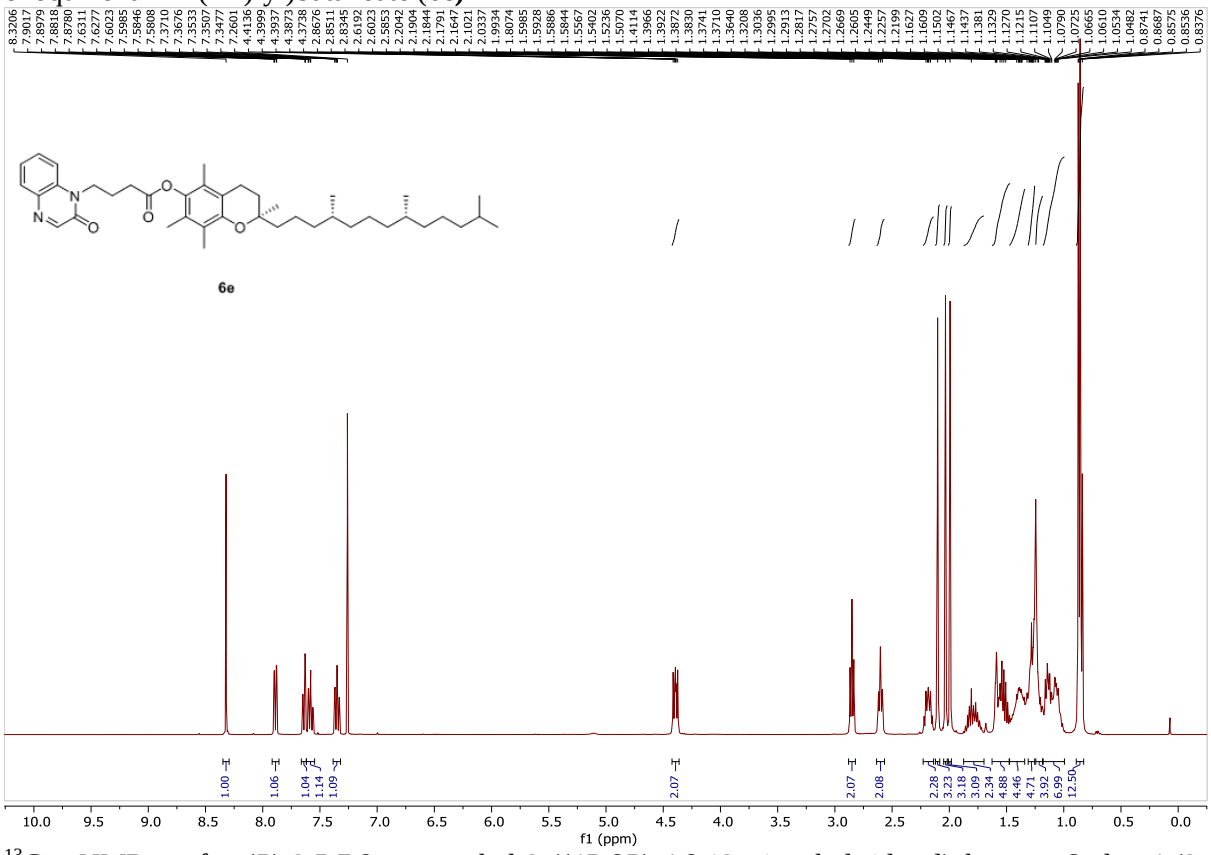
^{1}H NMR of (1*R*,2*R*,5*R*)-2-isopropyl-5-methylcyclohexyl 4-(quinoxalin-2-yloxy)butanoate (**6b**)



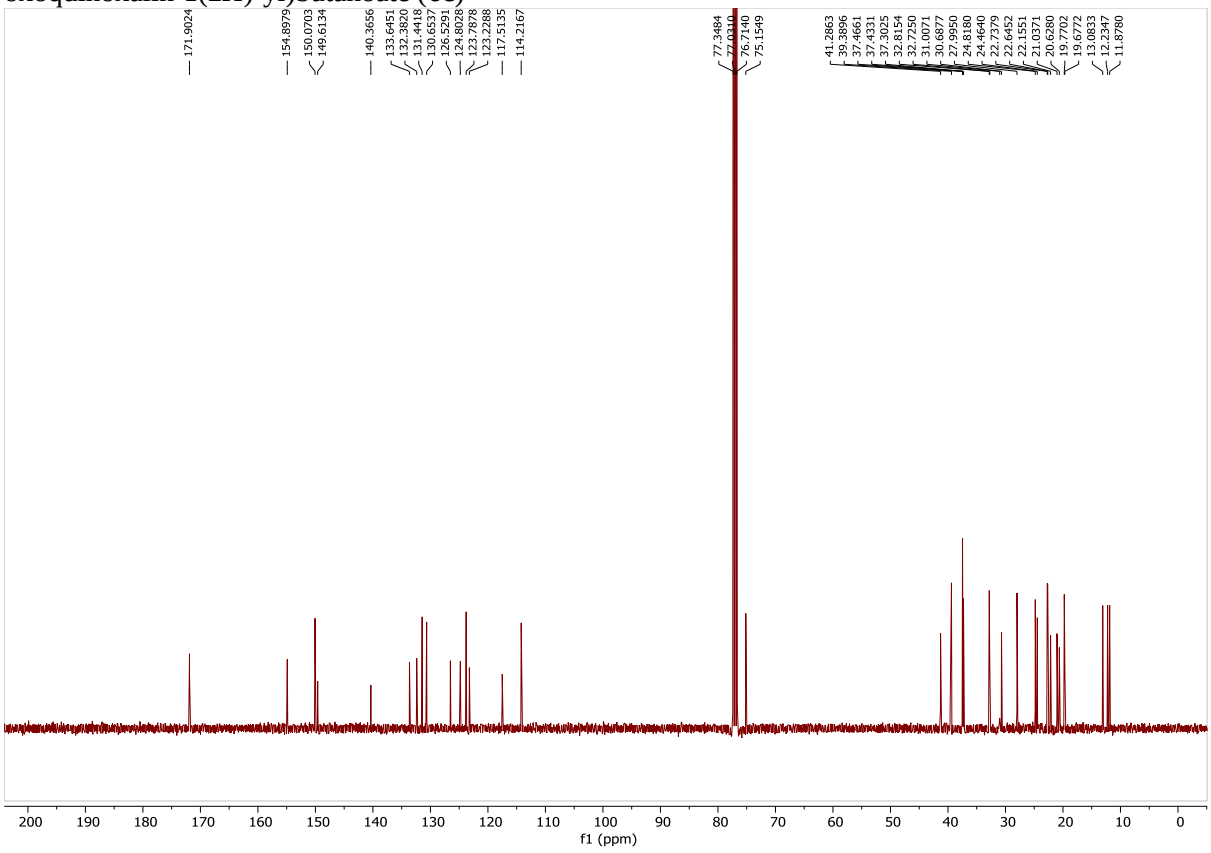
^{13}C NMR of (1*R*,2*R*,5*R*)-2-isopropyl-5-methylcyclohexyl 4-(quinoxalin-2-yloxy)butanoate (**6b**)



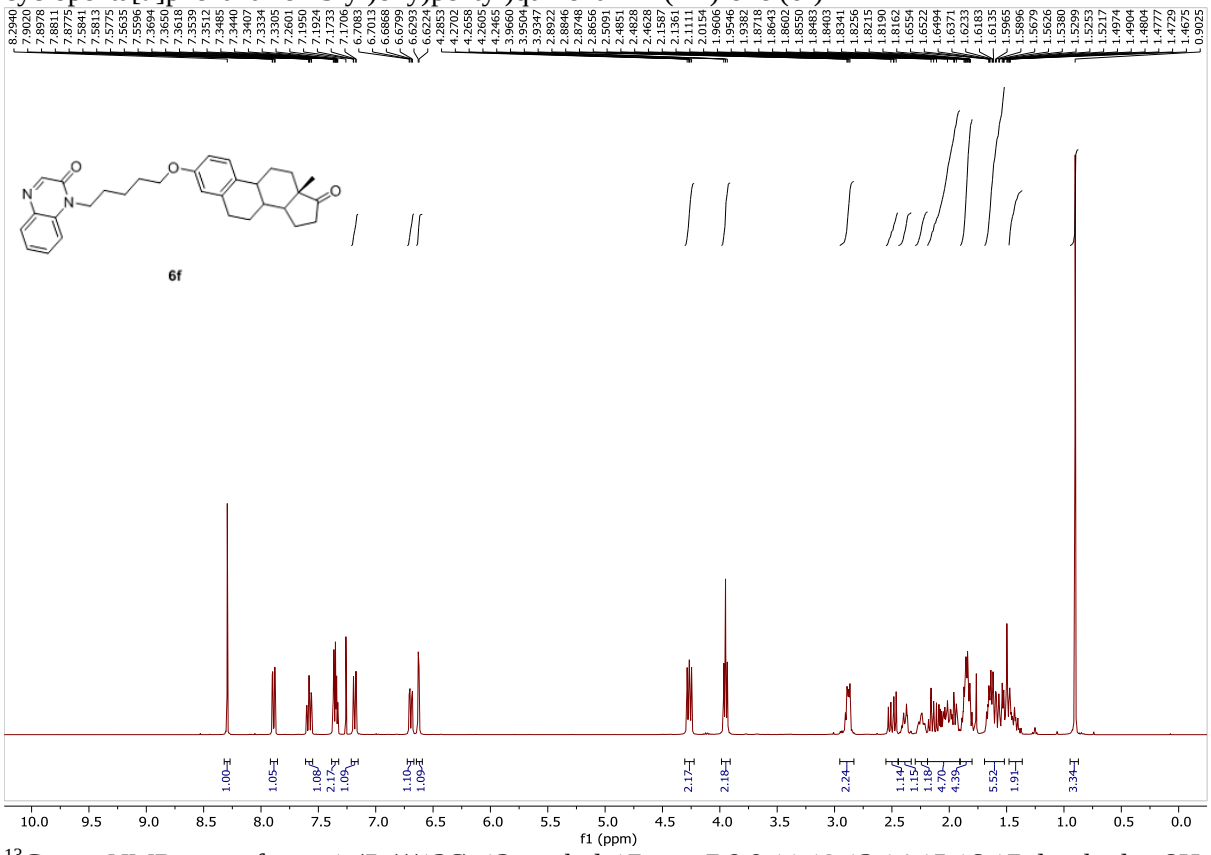
^{1}H NMR of (*R*)-2,5,7,8-tetramethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)chroman-6-yl 4-(2-oxoquinoxalin-1(2*H*)-yl)butanoate (**6e**)



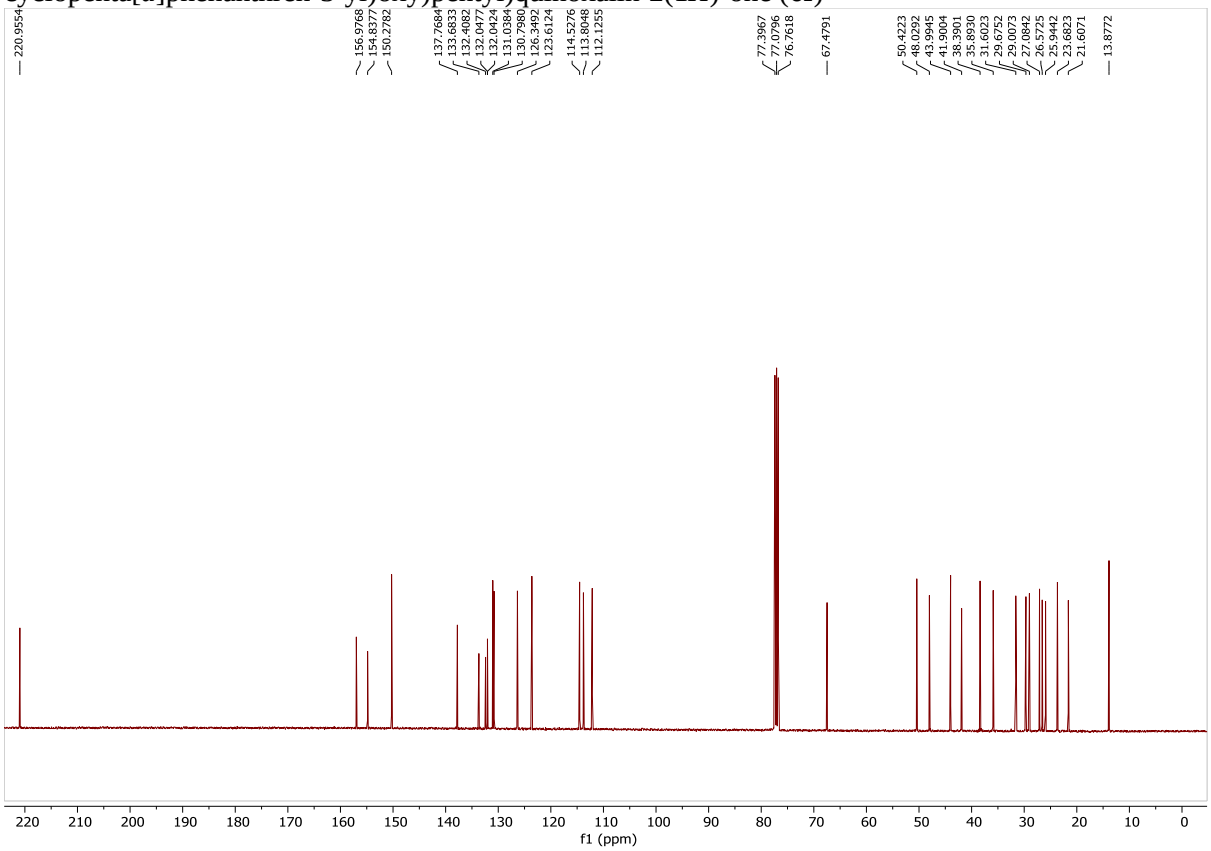
^{13}C NMR of (*R*)-2,5,7,8-tetramethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)chroman-6-yl 4-(2-oxoquinoxalin-1(2*H*)-yl)butanoate (**6e**)



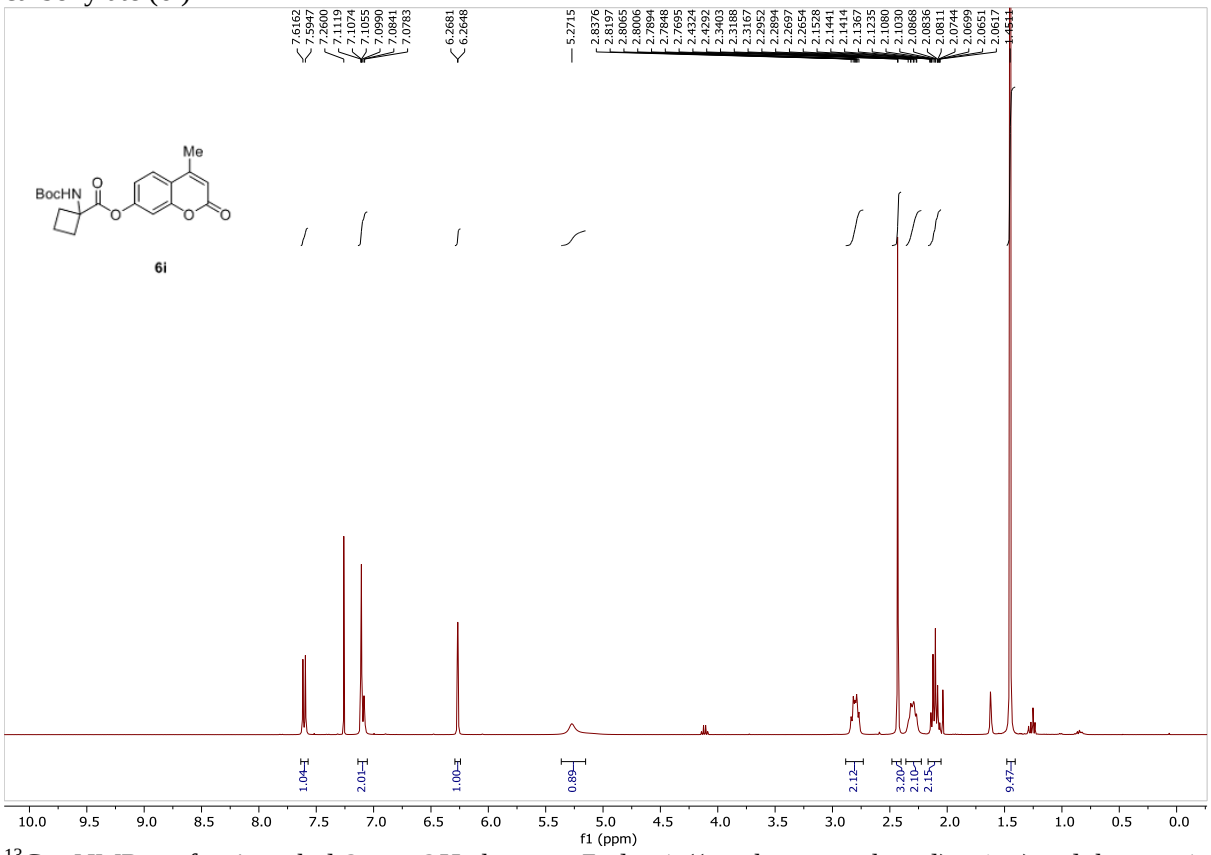
^{1}H NMR of 1-(5-(((13*S*)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl)oxy)pentyl)quinoxalin-2(1*H*)-one (**6f**)



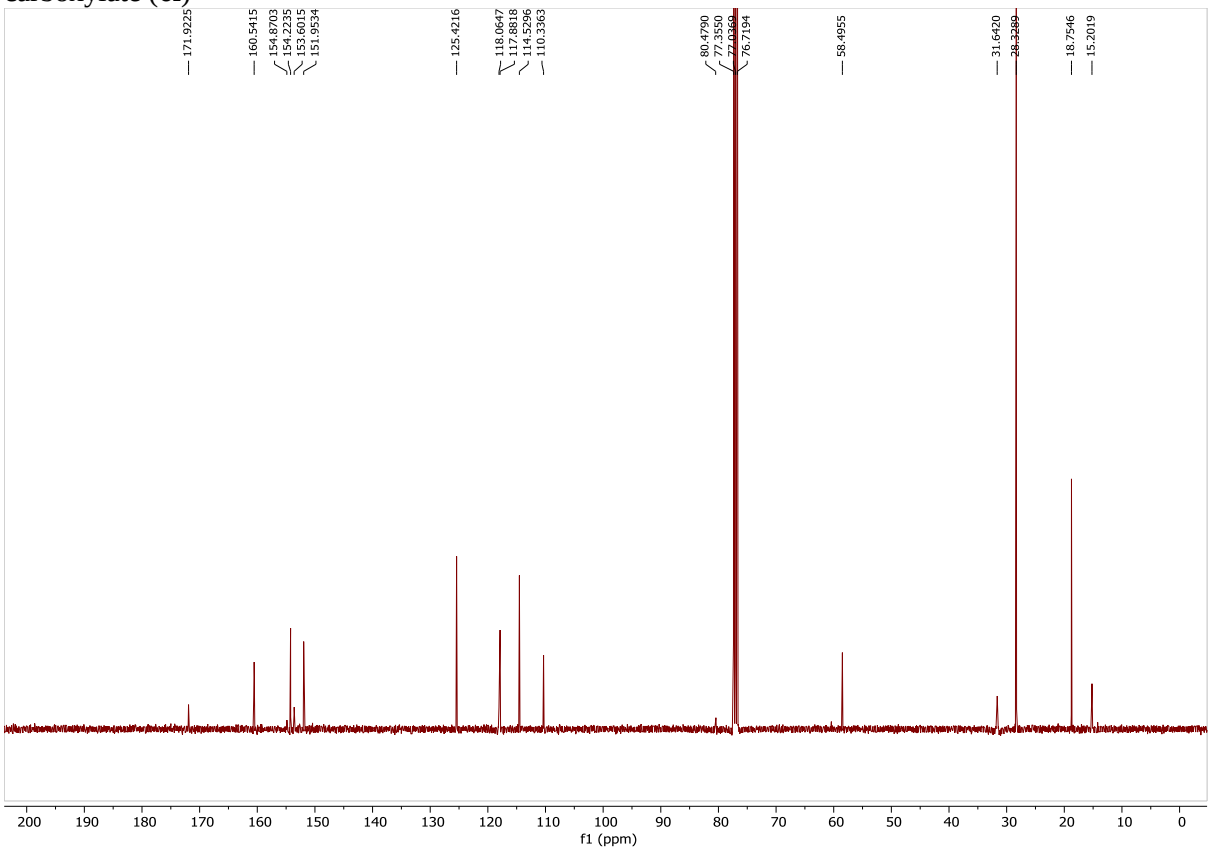
^{13}C NMR of 1-(5-(((13*S*)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl)oxy)pentyl)quinoxalin-2(1*H*)-one (**6f**)



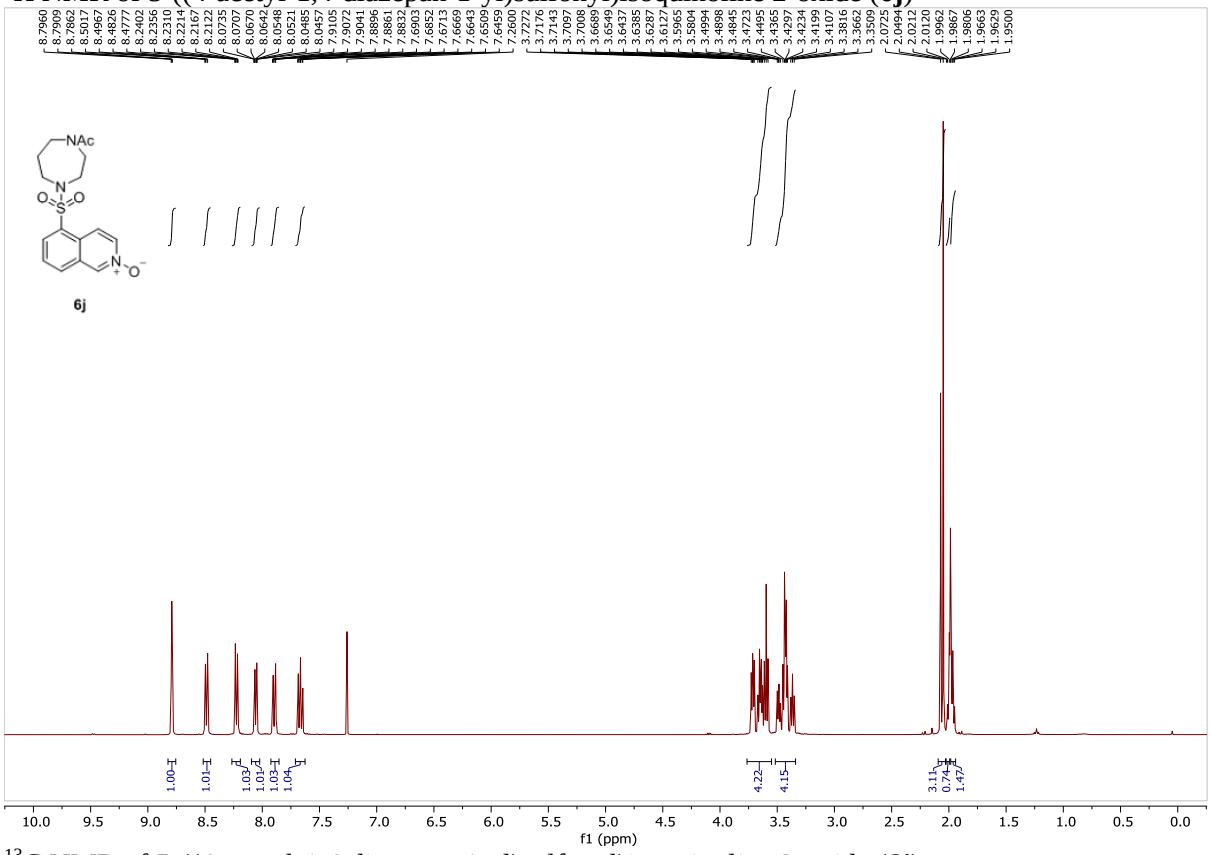
^{1}H NMR of 4-methyl-2-oxo-2*H*-chromen-7-yl 1-((*tert*-butoxycarbonyl)amino)cyclobutane-1-carboxylate (**6i**)



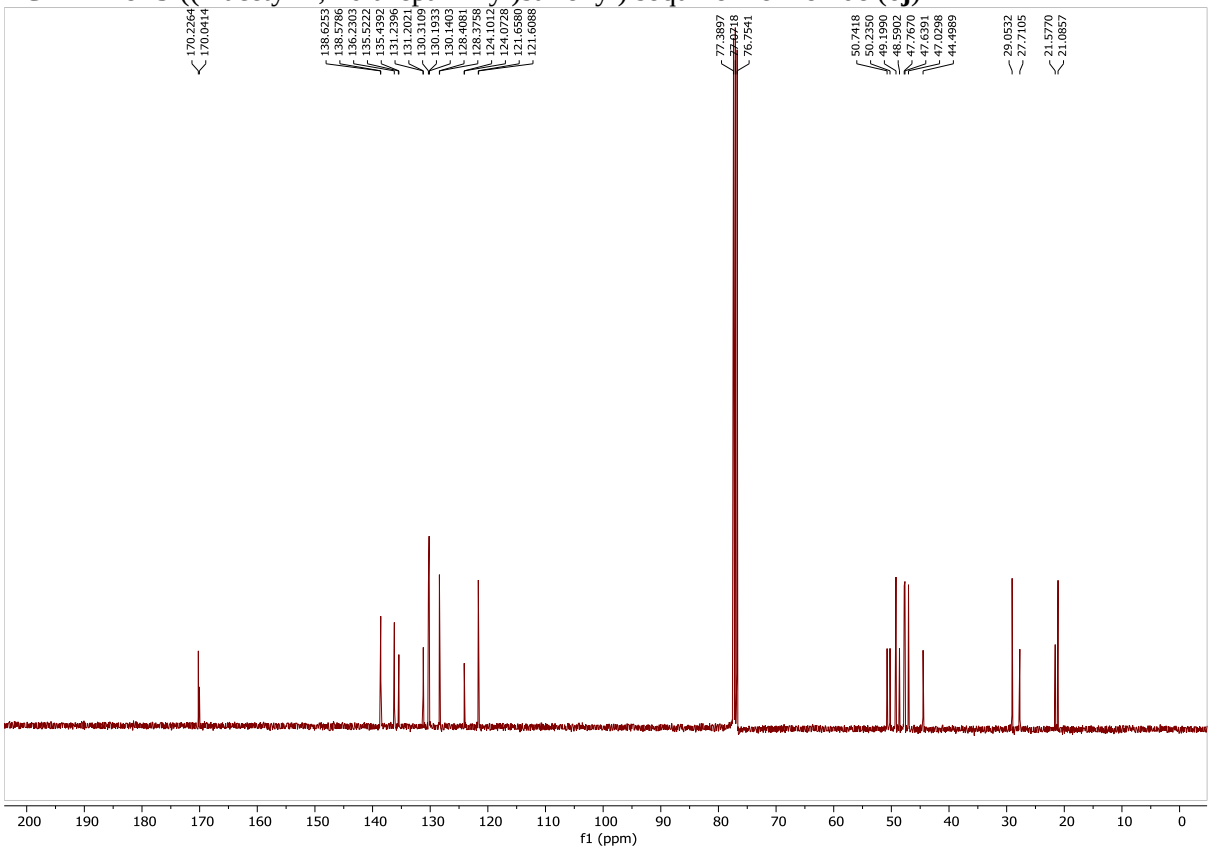
^{13}C NMR of 4-methyl-2-oxo-2*H*-chromen-7-yl 1-((*tert*-butoxycarbonyl)amino)cyclobutane-1-carboxylate (**6i**)



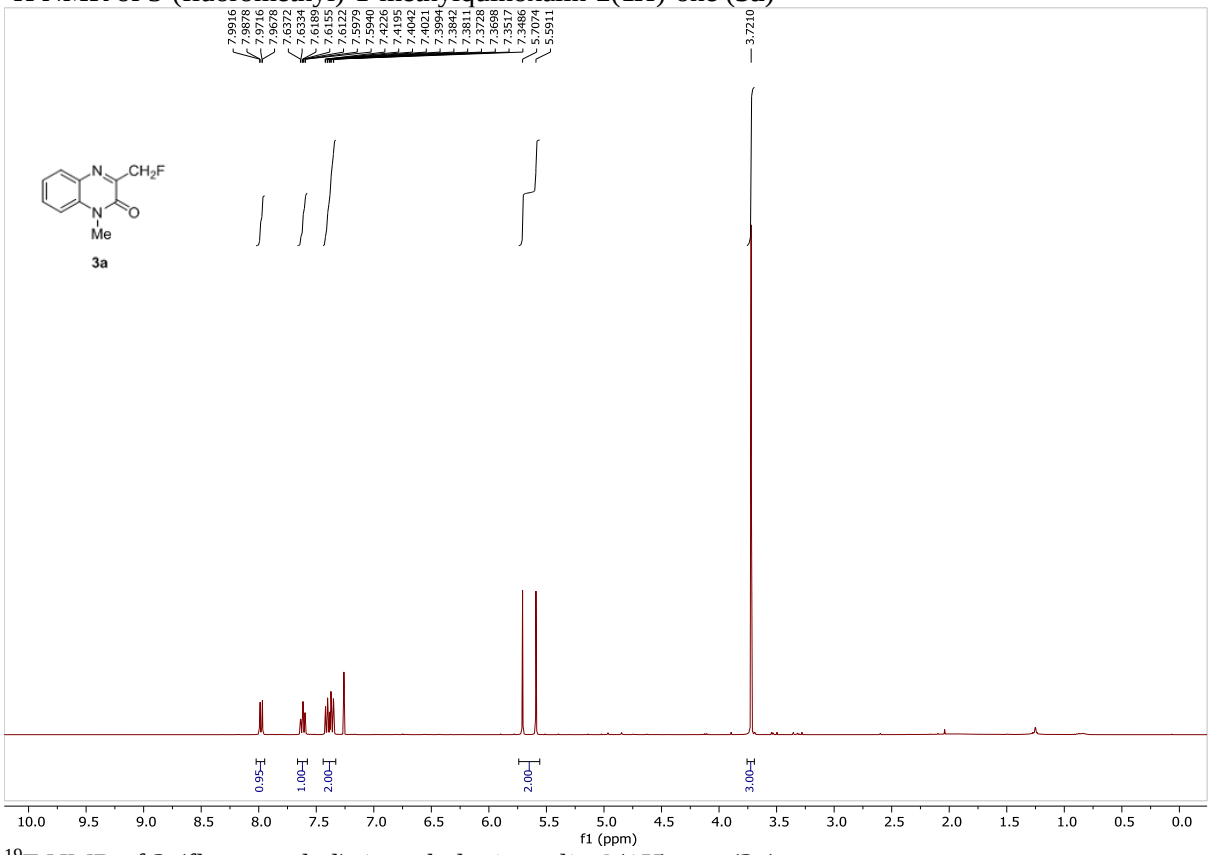
^{1}H NMR of 5-((4-acetyl-1,4-diazepan-1-yl)sulfonyl)isoquinoline 2-oxide (**6j**)



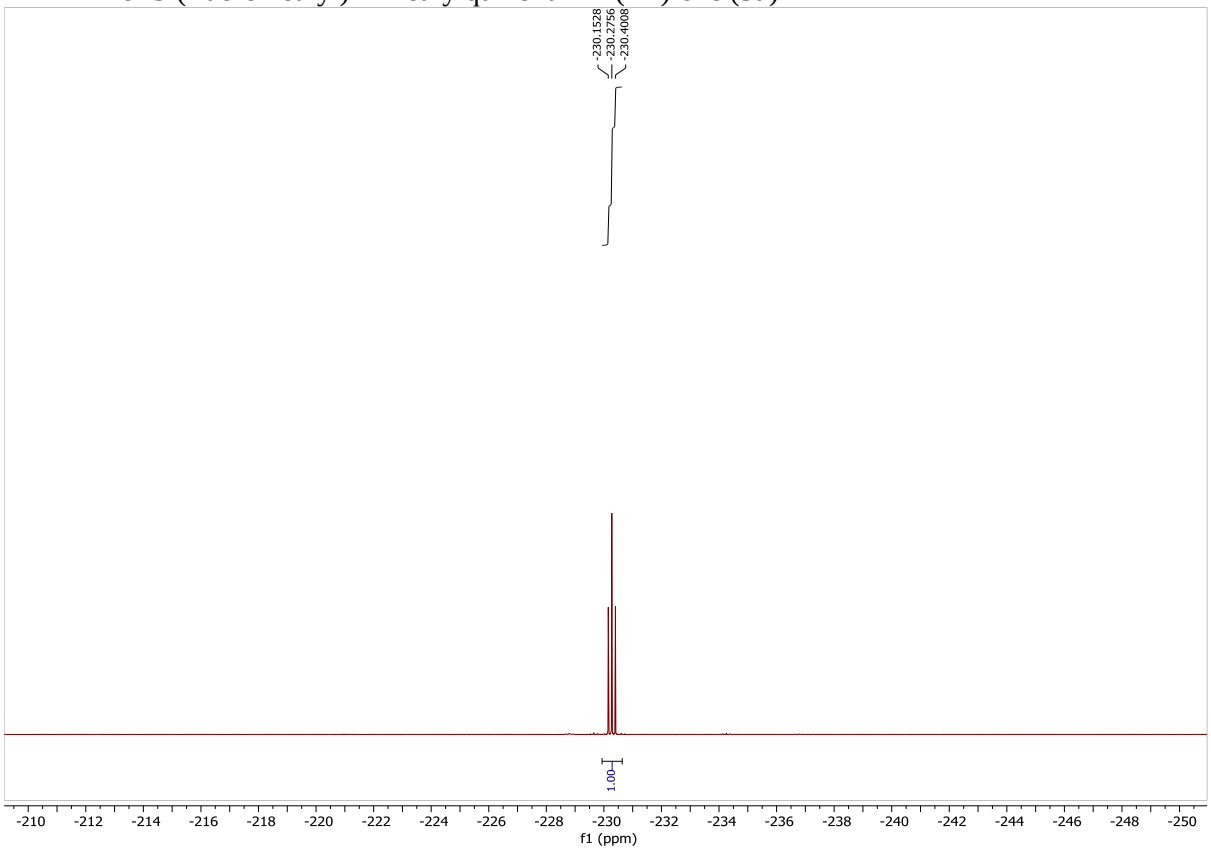
^{13}C NMR of 5-((4-acetyl-1,4-diazepan-1-yl)sulfonyl)isoquinoline 2-oxide (**6j**)



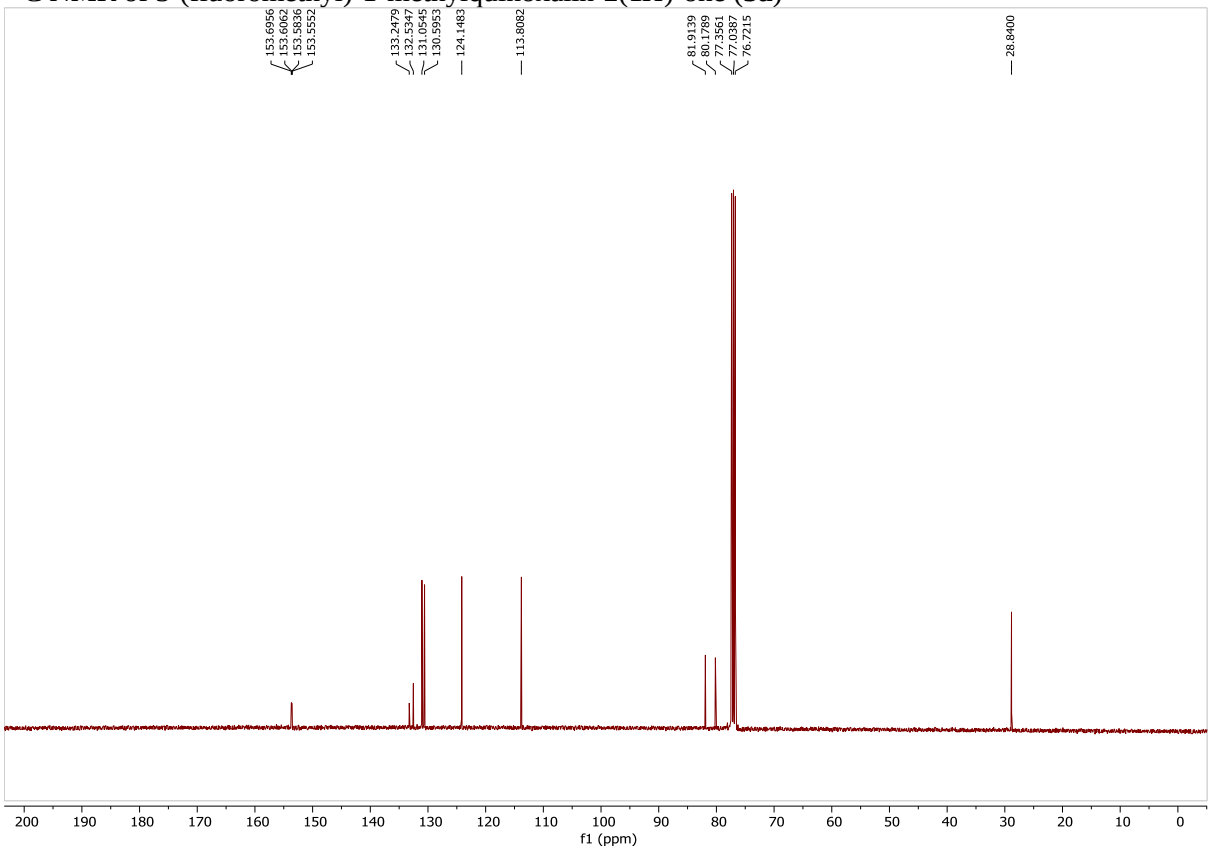
^{1}H NMR of 3-(fluoromethyl)-1-methylquinoxalin-2(1*H*)-one (**3a**)



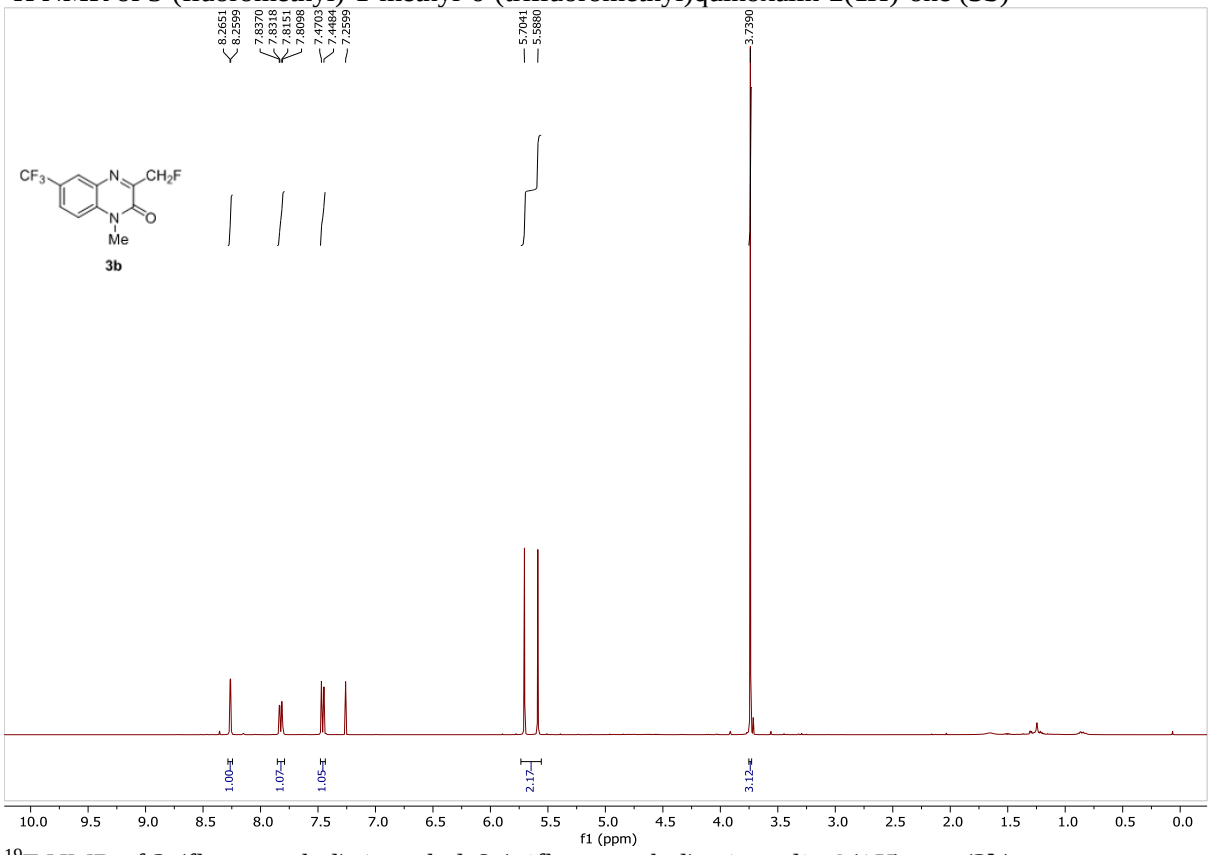
^{19}F NMR of 3-(fluoromethyl)-1-methylquinoxalin-2(1*H*)-one (**3a**)



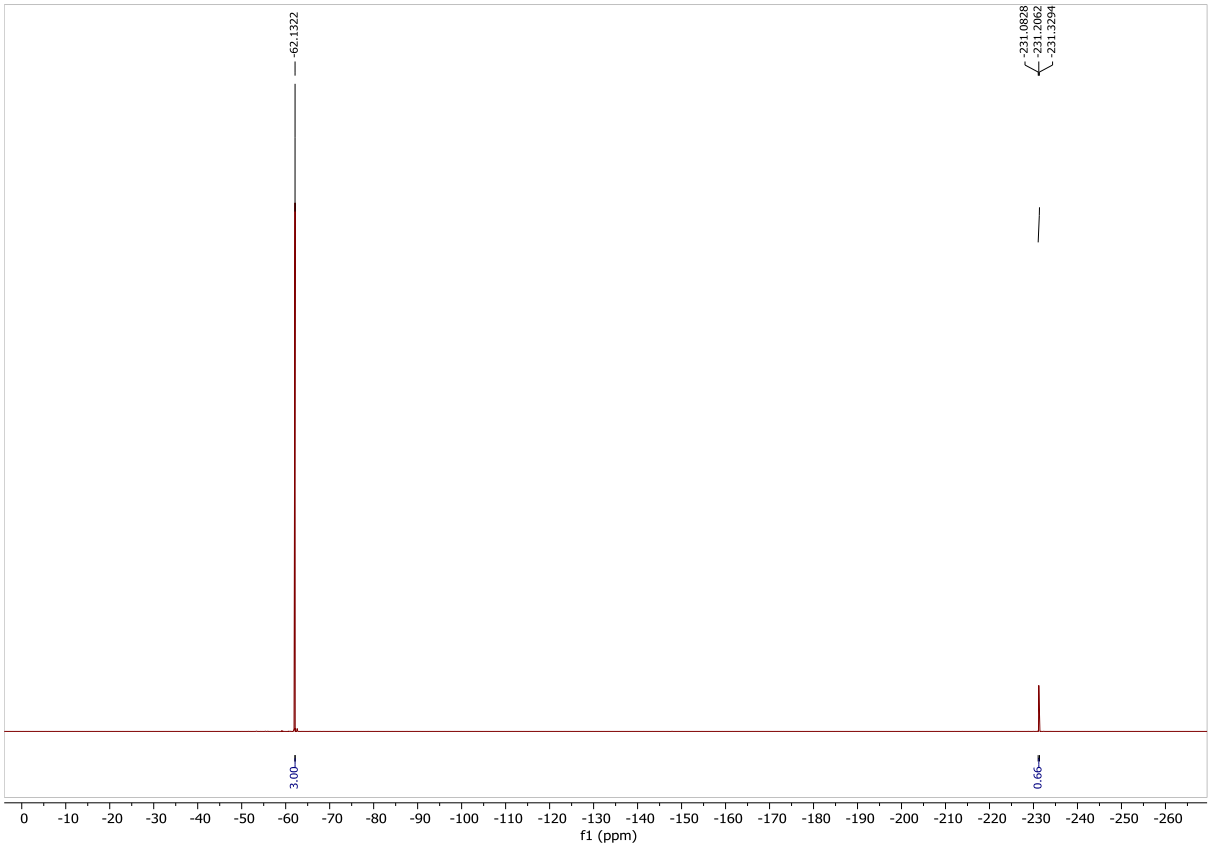
^{13}C NMR of 3-(fluoromethyl)-1-methylquinoxalin-2(1*H*)-one (**3a**)



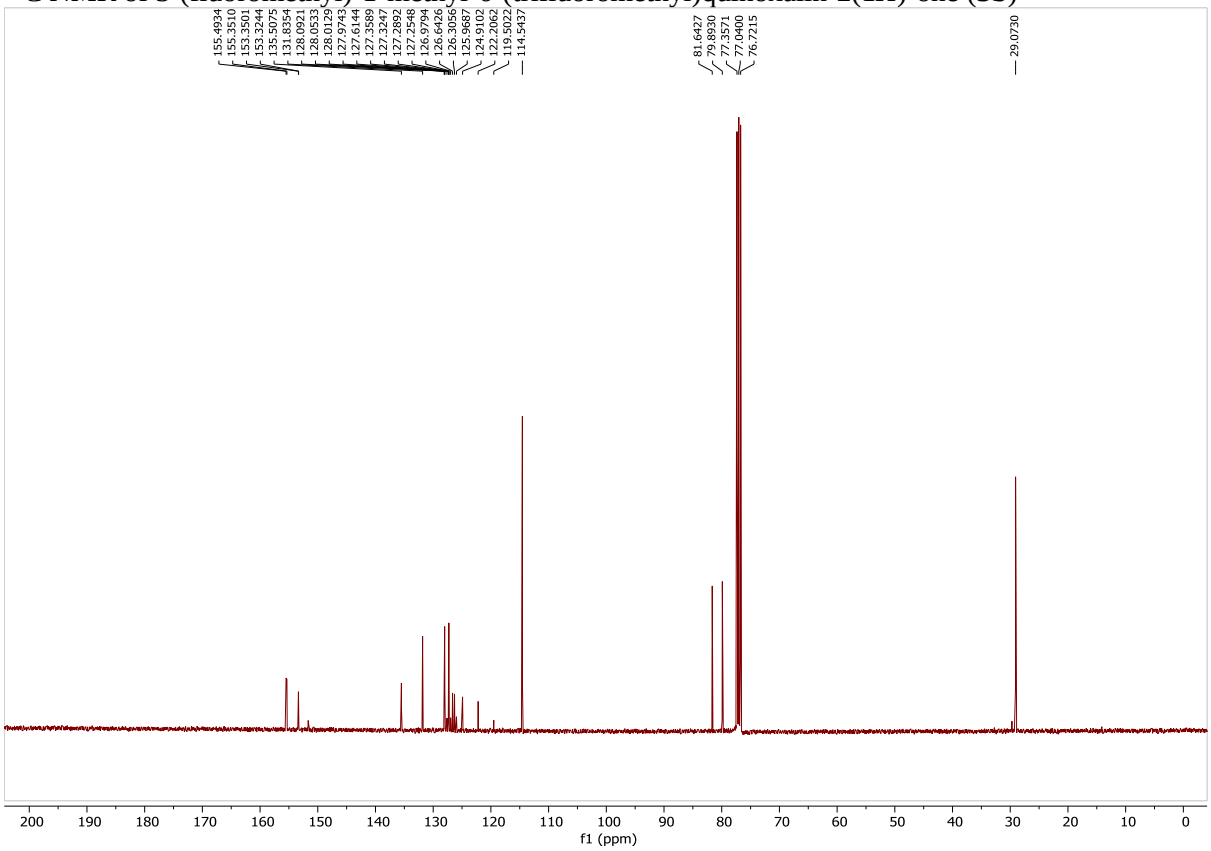
^{1}H NMR of 3-(fluoromethyl)-1-methyl-6-(trifluoromethyl)quinoxalin-2(1*H*)-one (**3b**)



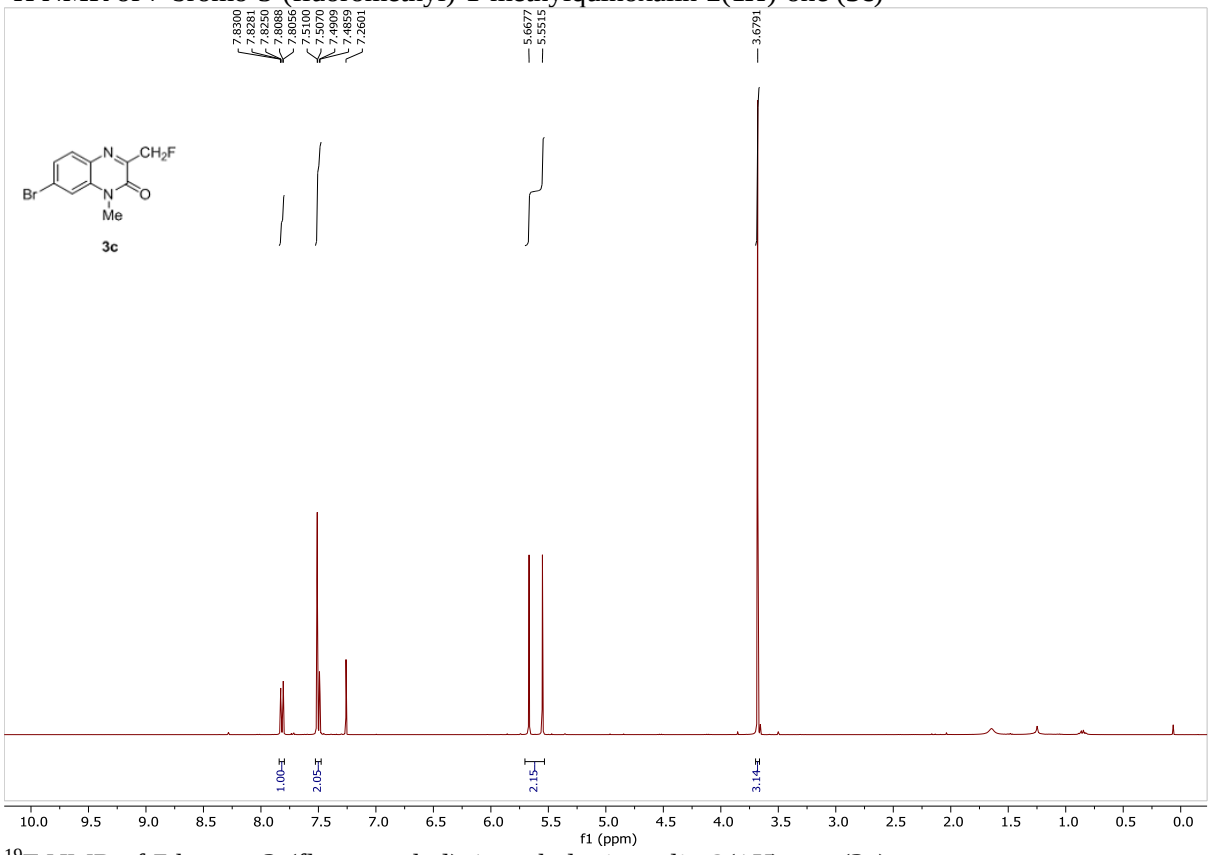
^{19}F NMR of 3-(fluoromethyl)-1-methyl-6-(trifluoromethyl)quinoxalin-2(1*H*)-one (**3b**)



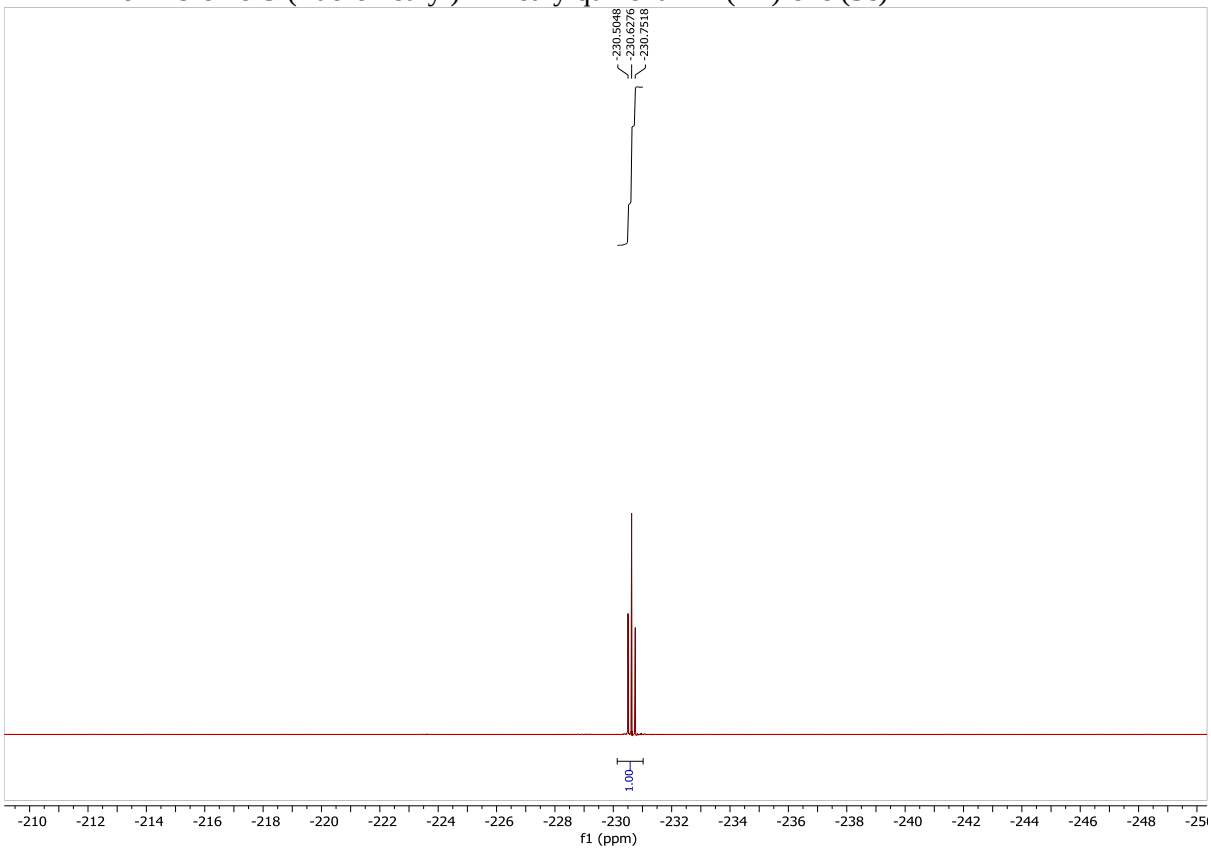
^{13}C NMR of 3-(fluoromethyl)-1-methyl-6-(trifluoromethyl)quinoxalin-2(1*H*)-one (**3b**)



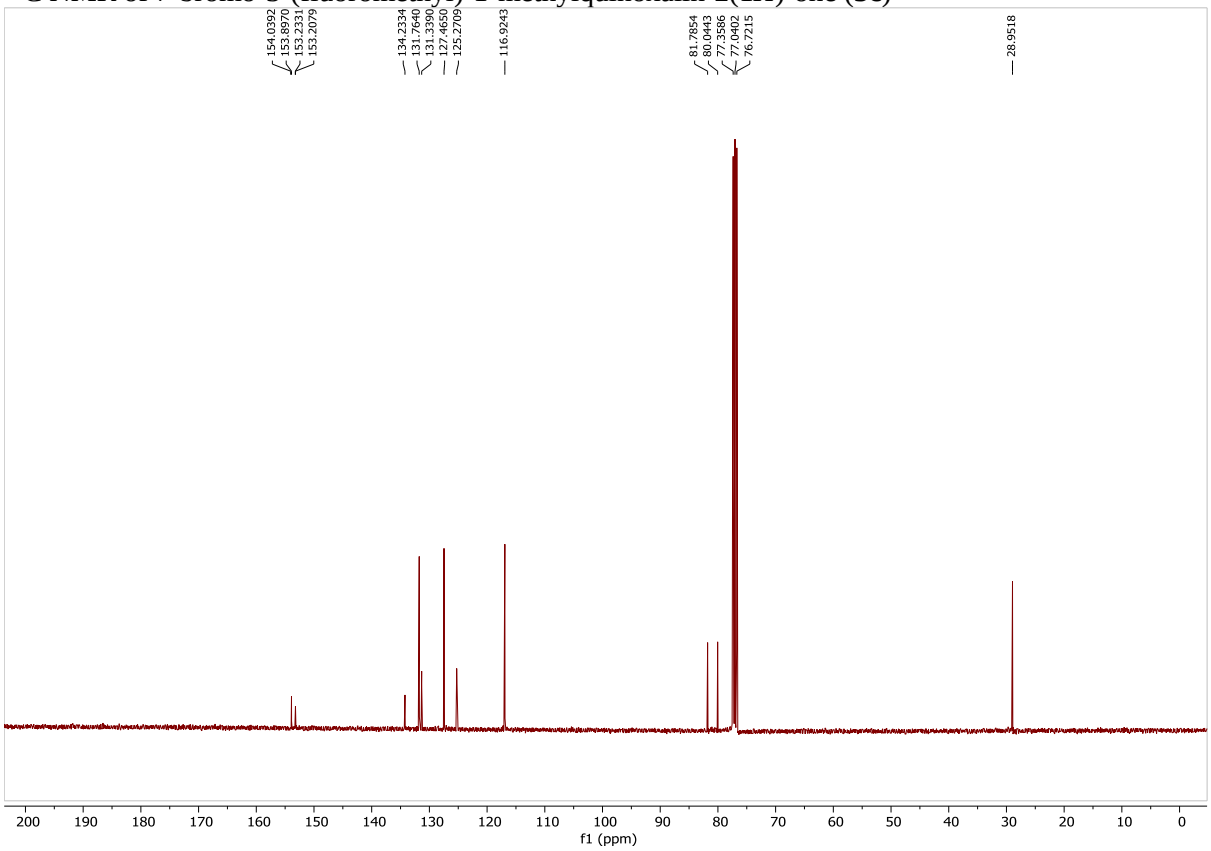
^{1}H NMR of 7-bromo-3-(fluoromethyl)-1-methylquinoxalin-2(1*H*)-one (**3c**)



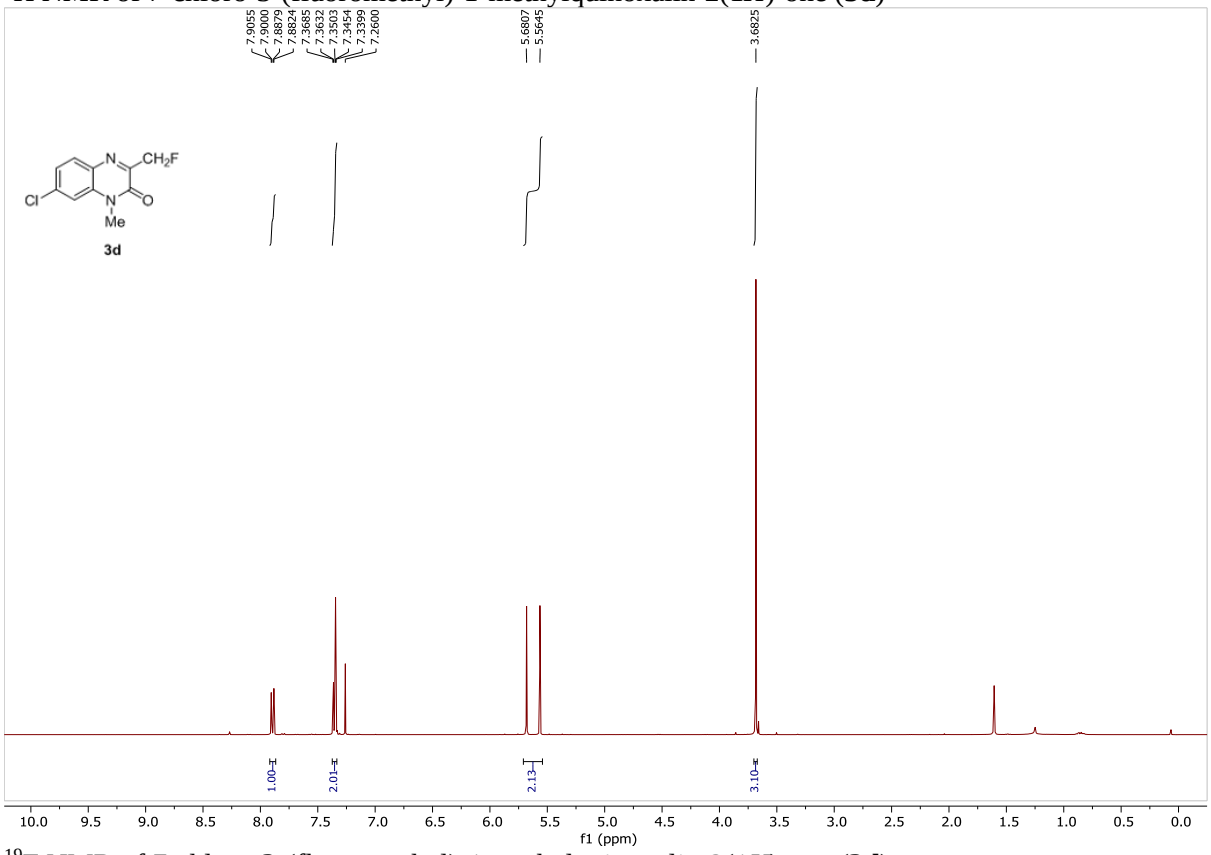
^{19}F NMR of 7-bromo-3-(fluoromethyl)-1-methylquinoxalin-2(1*H*)-one (**3c**)



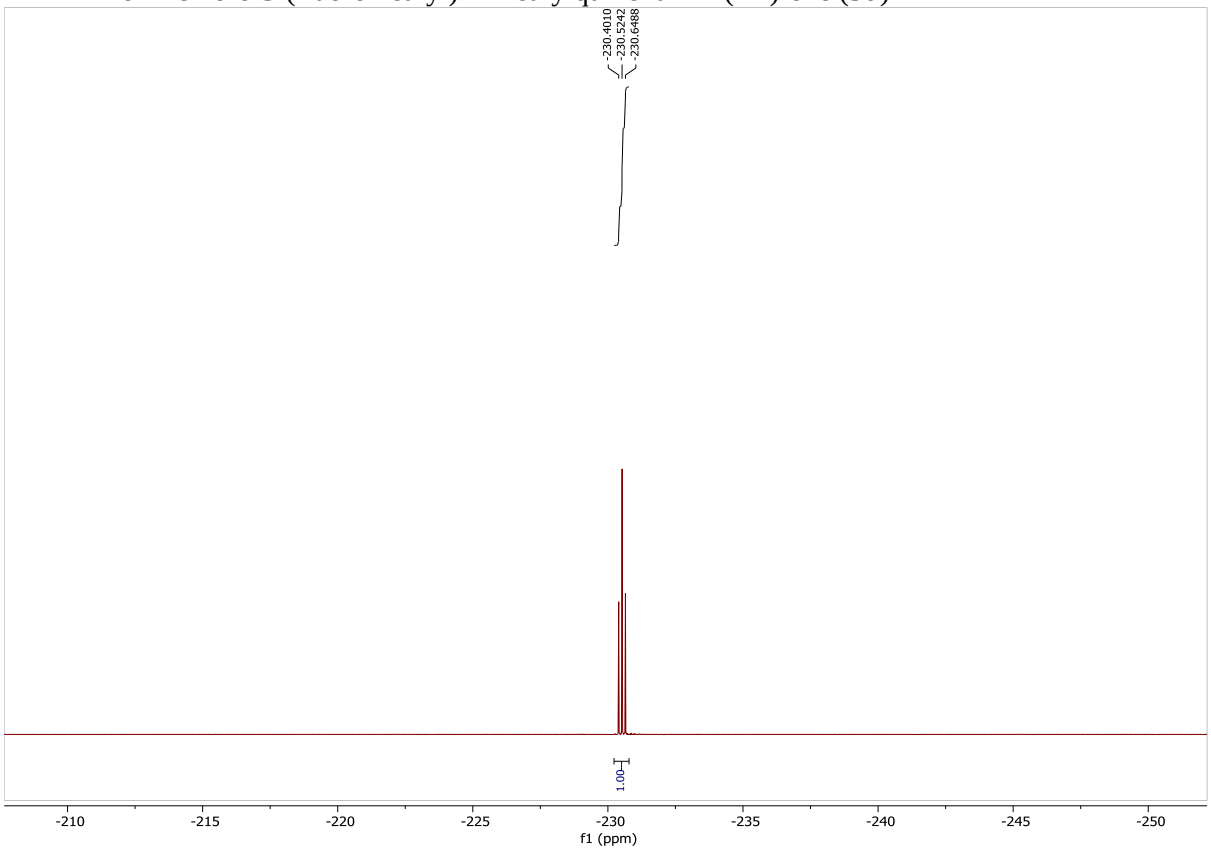
^{13}C NMR of 7-bromo-3-(fluoromethyl)-1-methylquinoxalin-2(1*H*)-one (**3c**)



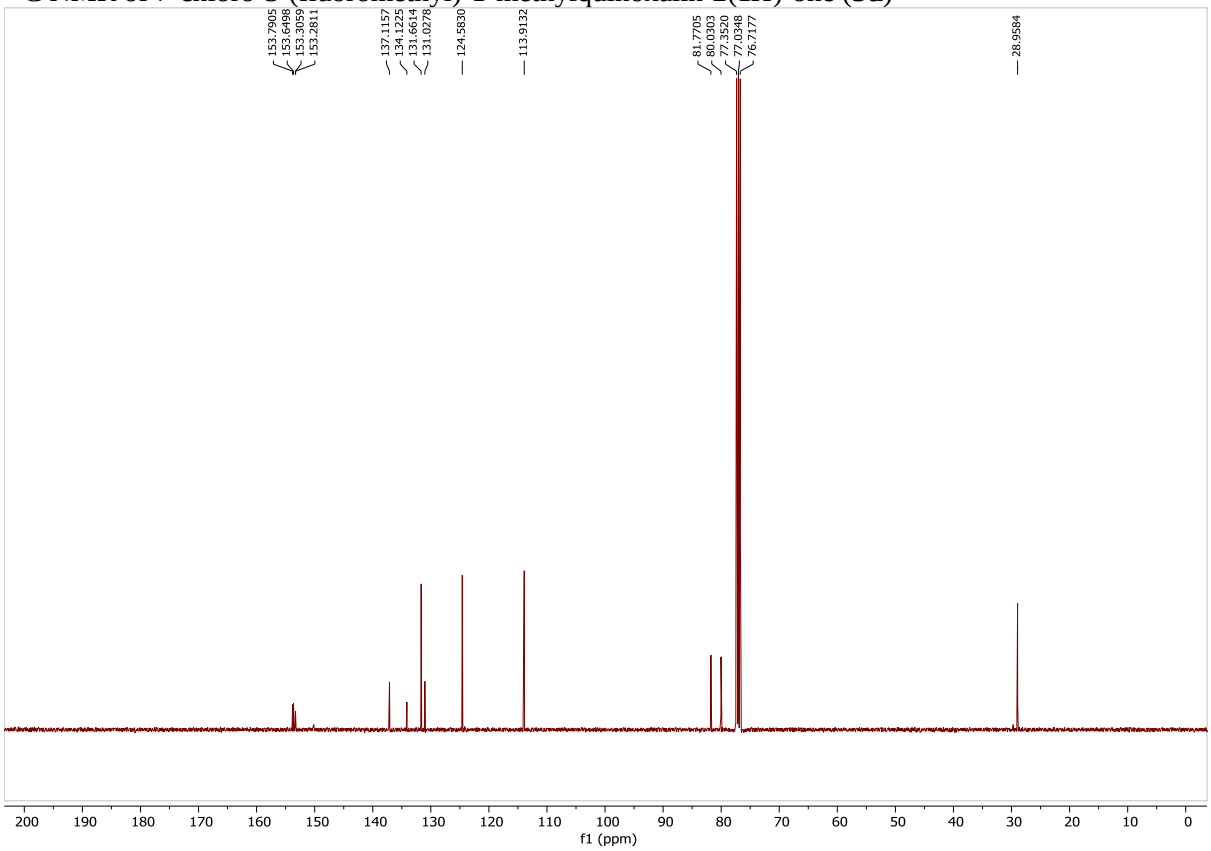
^{1}H NMR of 7-chloro-3-(fluoromethyl)-1-methylquinoxalin-2(1*H*)-one (**3d**)



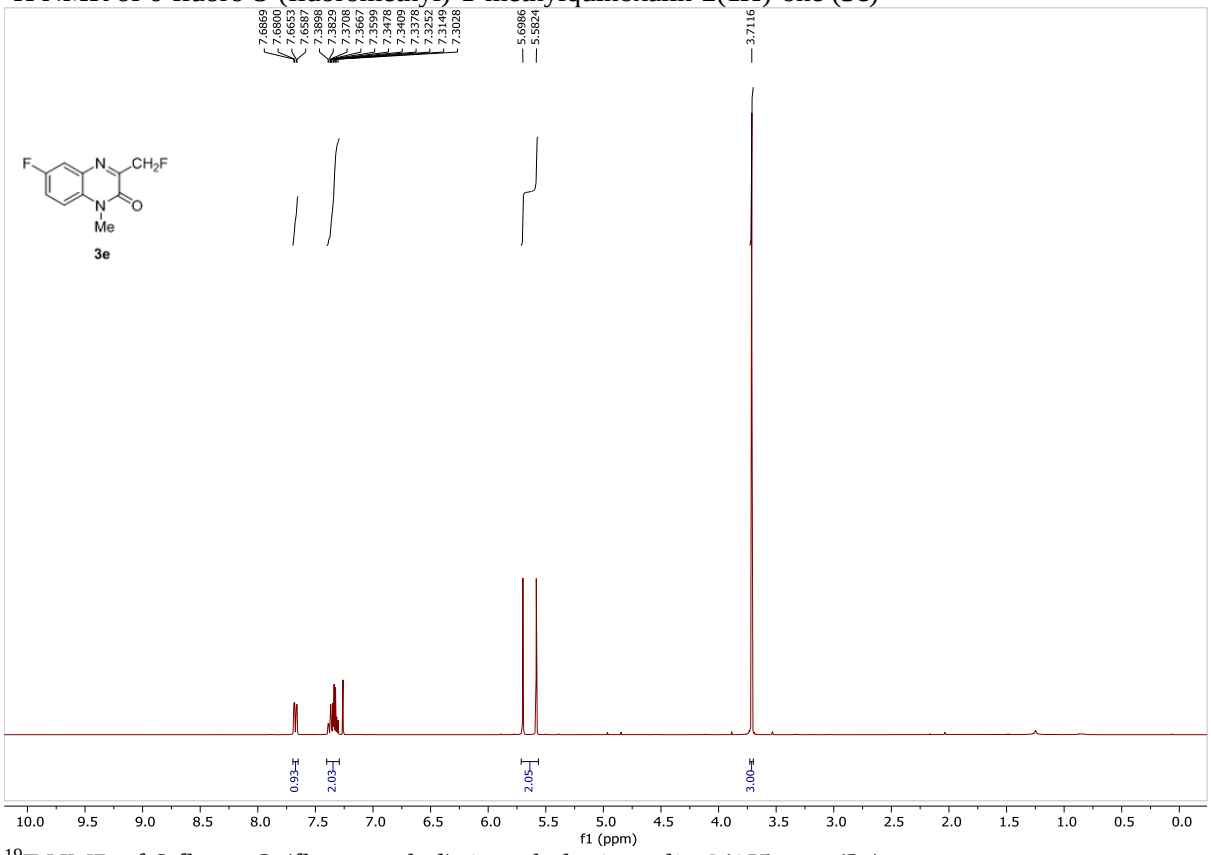
^{19}F NMR of 7-chloro-3-(fluoromethyl)-1-methylquinoxalin-2(1*H*)-one (**3d**)



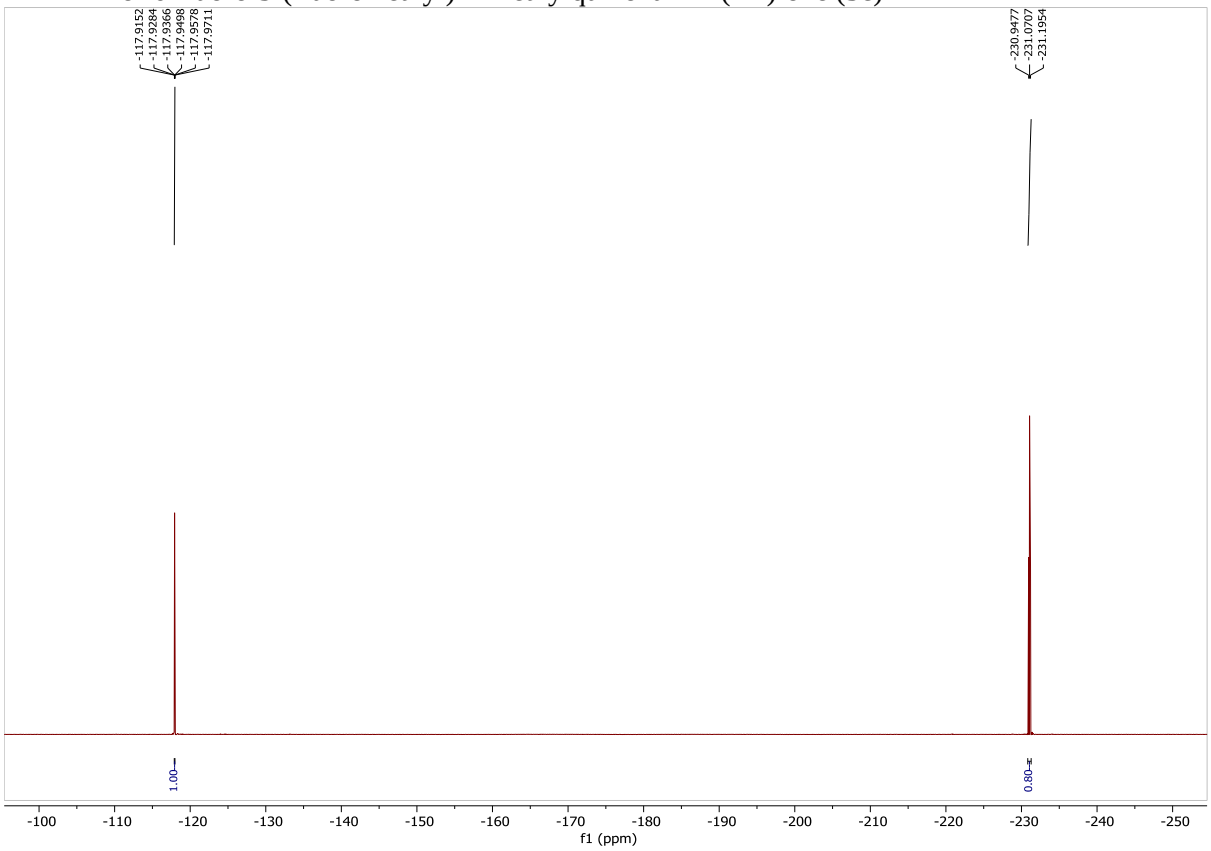
^{13}C NMR of 7-chloro-3-(fluoromethyl)-1-methylquinoxalin-2(1*H*)-one (**3d**)



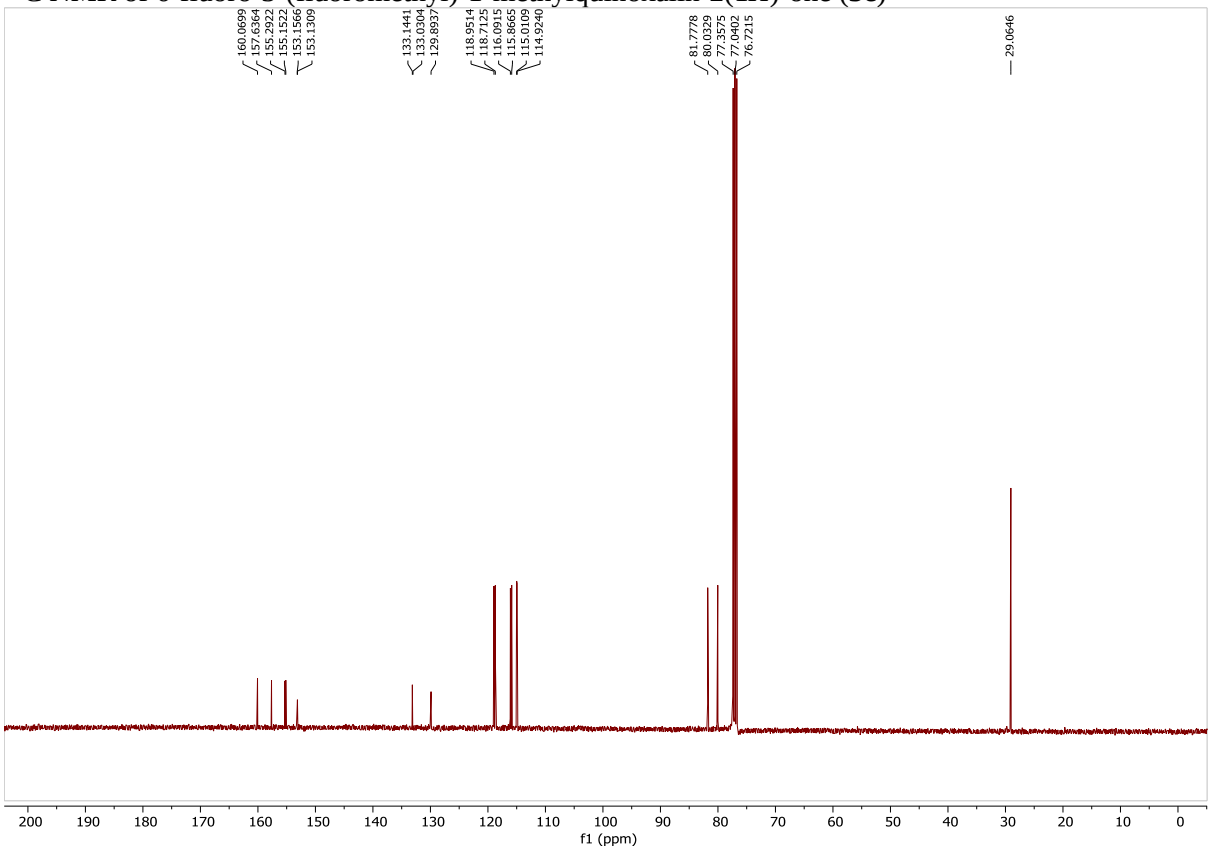
^{1}H NMR of 6-fluoro-3-(fluoromethyl)-1-methylquinoxalin-2(1*H*)-one (**3e**)



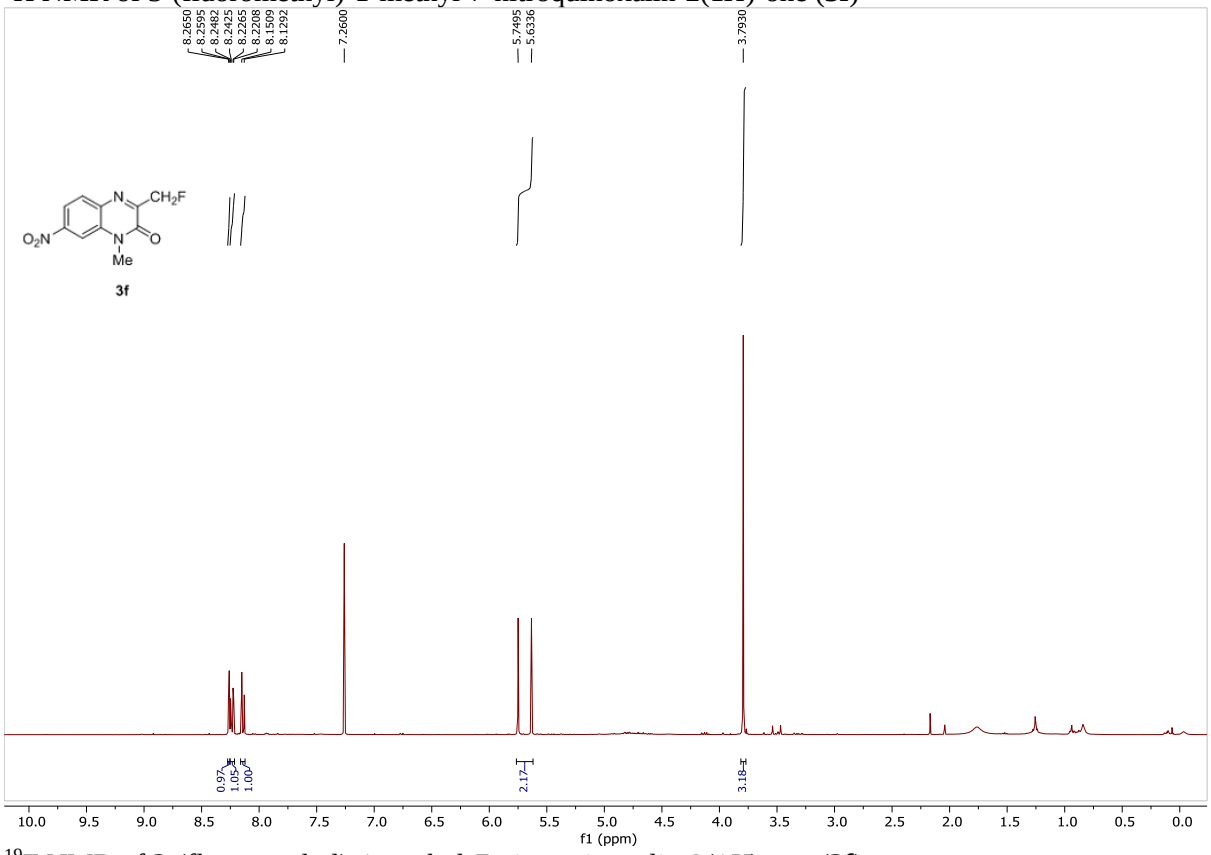
^{19}F NMR of 6-fluoro-3-(fluoromethyl)-1-methylquinoxalin-2(1*H*)-one (**3e**)



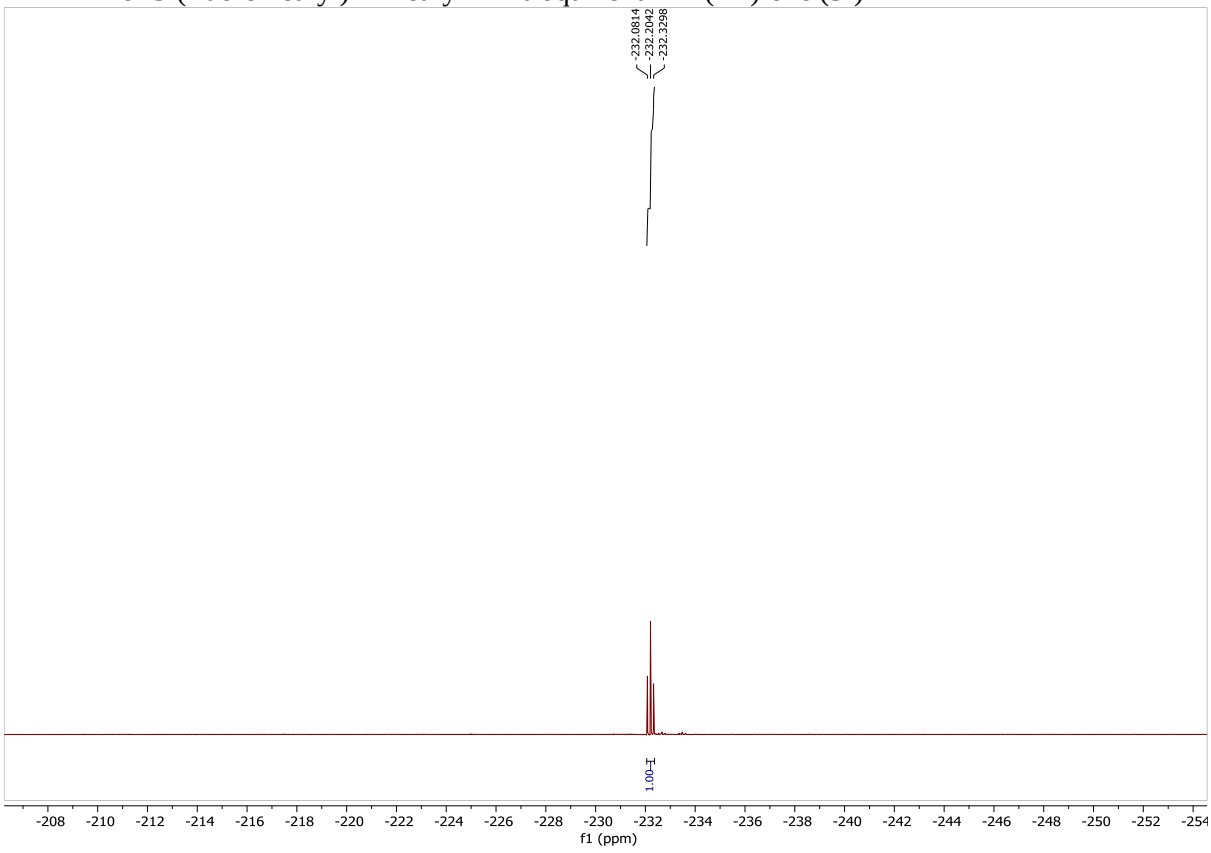
^{13}C NMR of 6-fluoro-3-(fluoromethyl)-1-methylquinoxalin-2(1*H*)-one (**3e**)



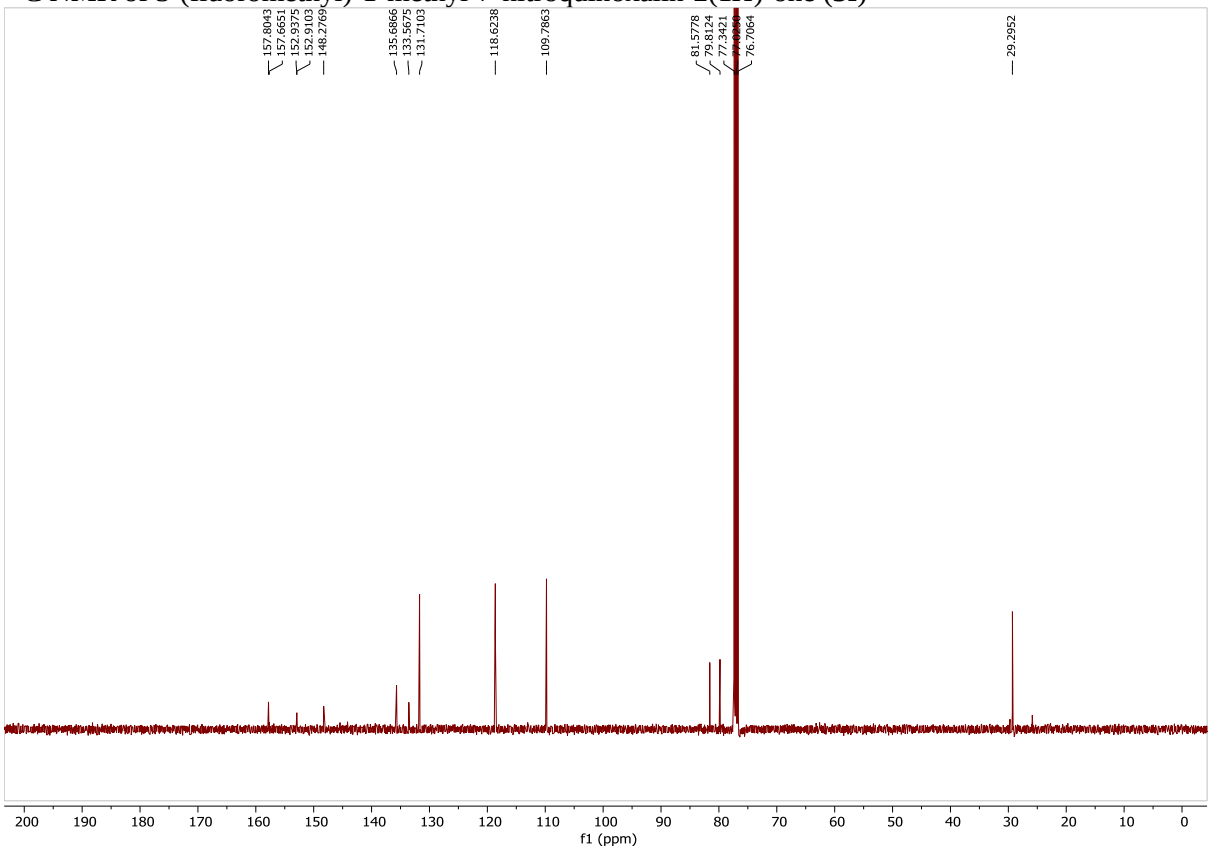
[1]H NMR of 3-(fluoromethyl)-1-methyl-7-nitroquinoxalin-2(1*H*)-one (**3f**)



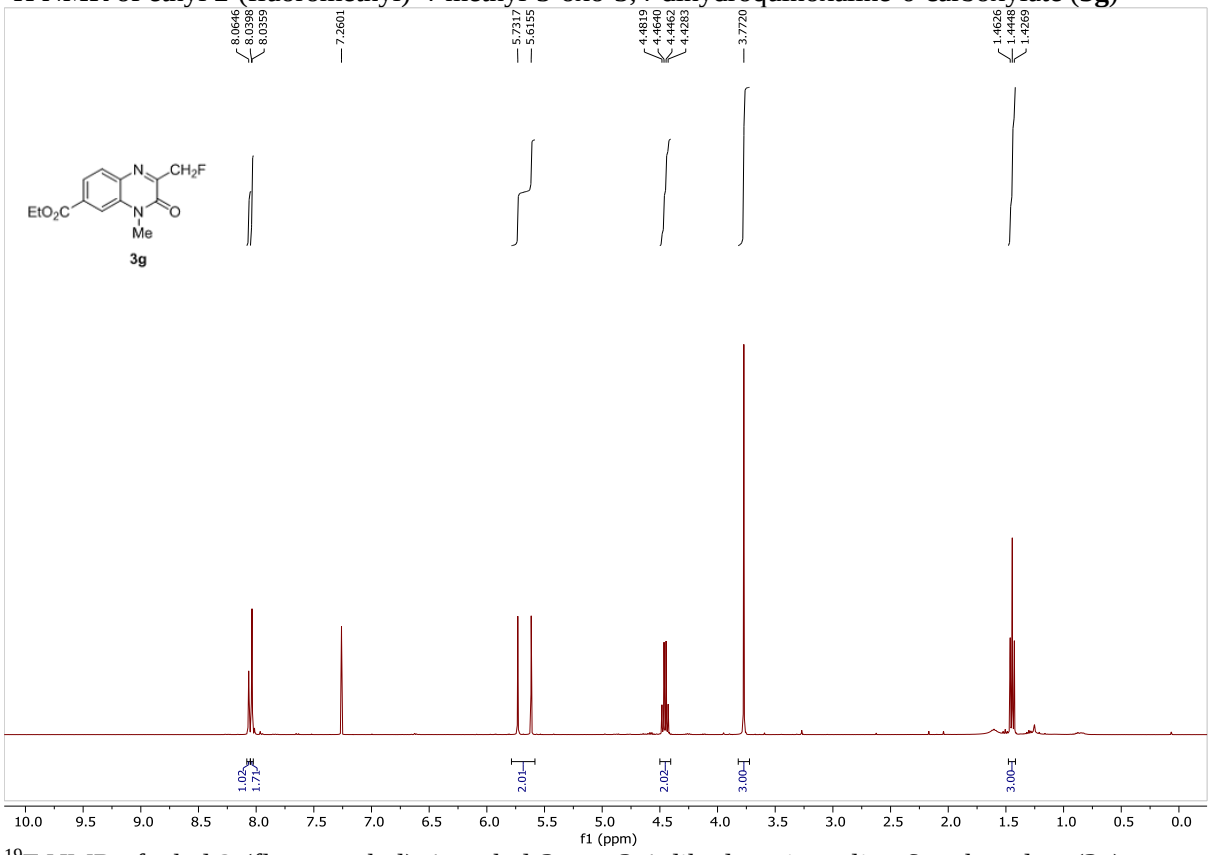
[19]F NMR of 3-(fluoromethyl)-1-methyl-7-nitroquinoxalin-2(1*H*)-one (**3f**)



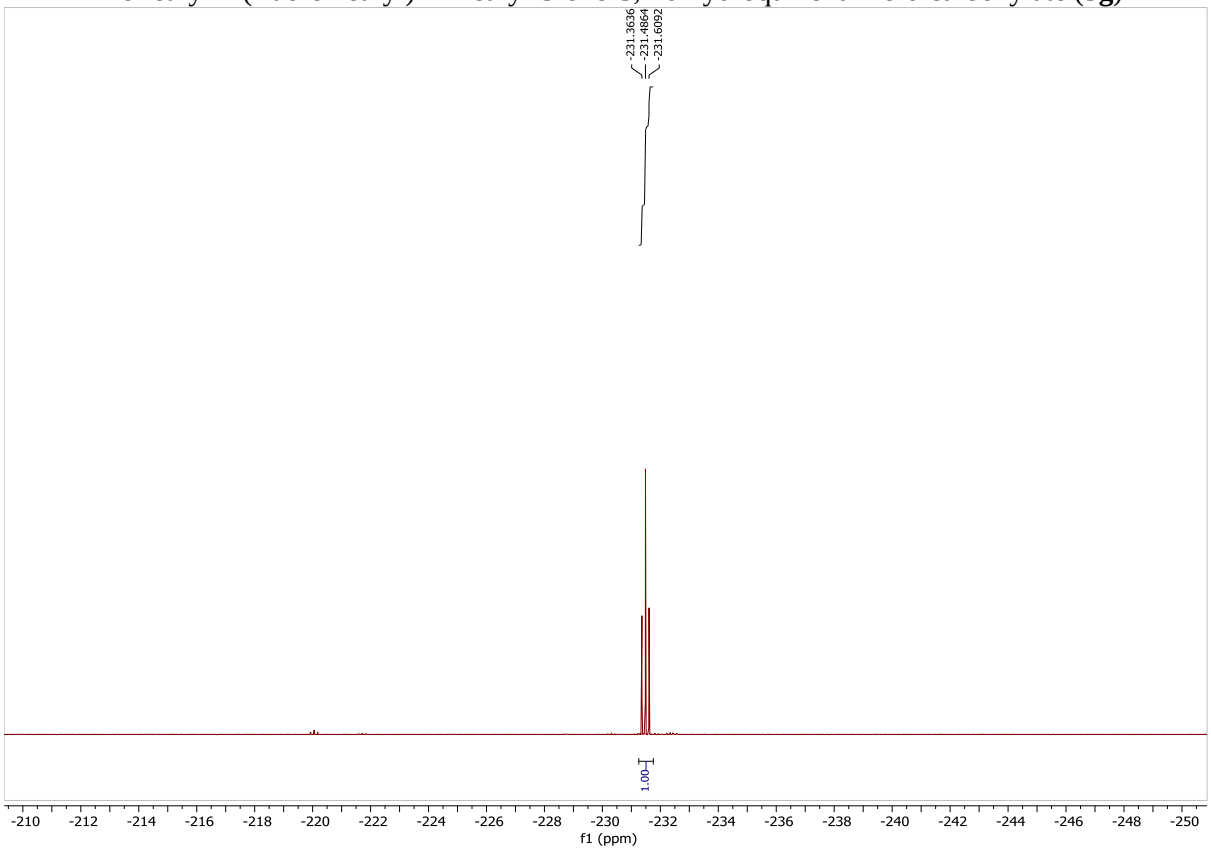
^{13}C NMR of 3-(fluoromethyl)-1-methyl-7-nitroquinoxalin-2(1*H*)-one (**3f**)



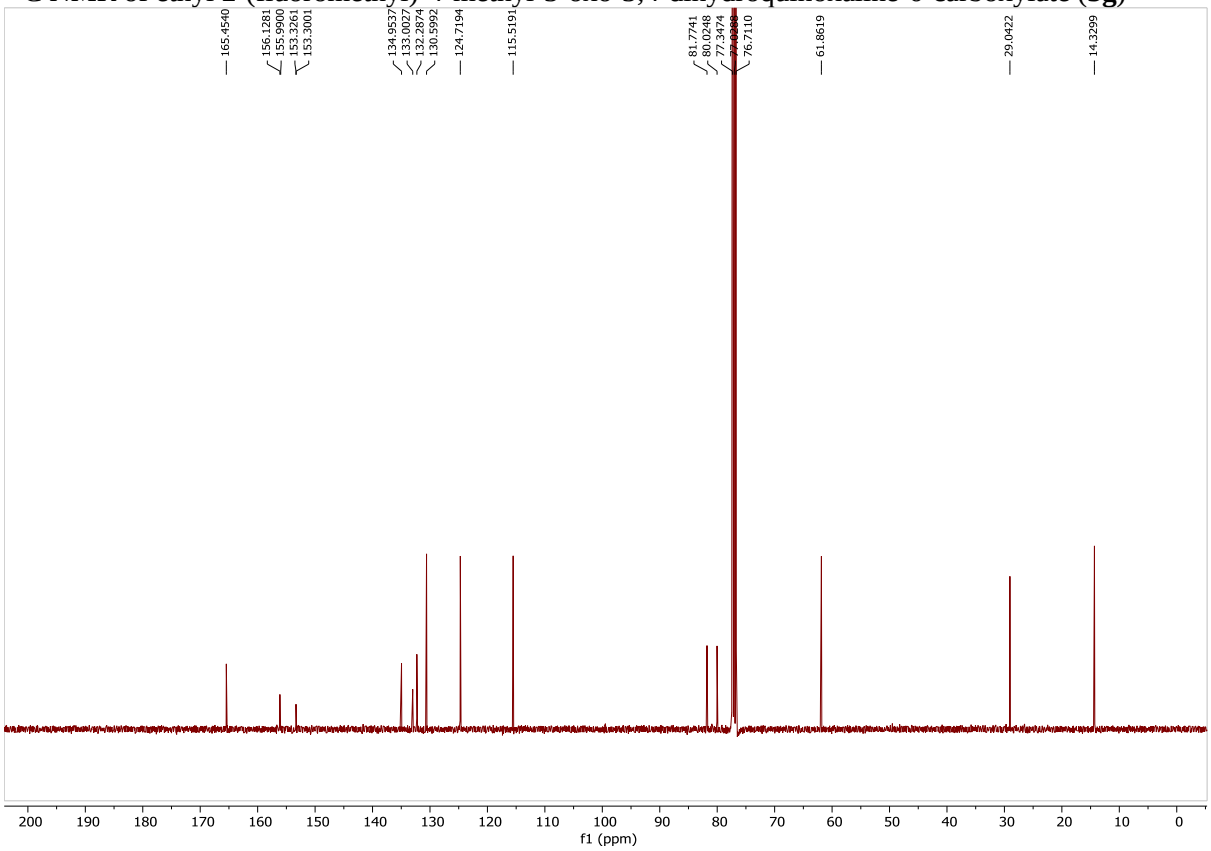
^{1}H NMR of ethyl 2-(fluoromethyl)-4-methyl-3-oxo-3,4-dihydroquinoxaline-6-carboxylate (**3g**)



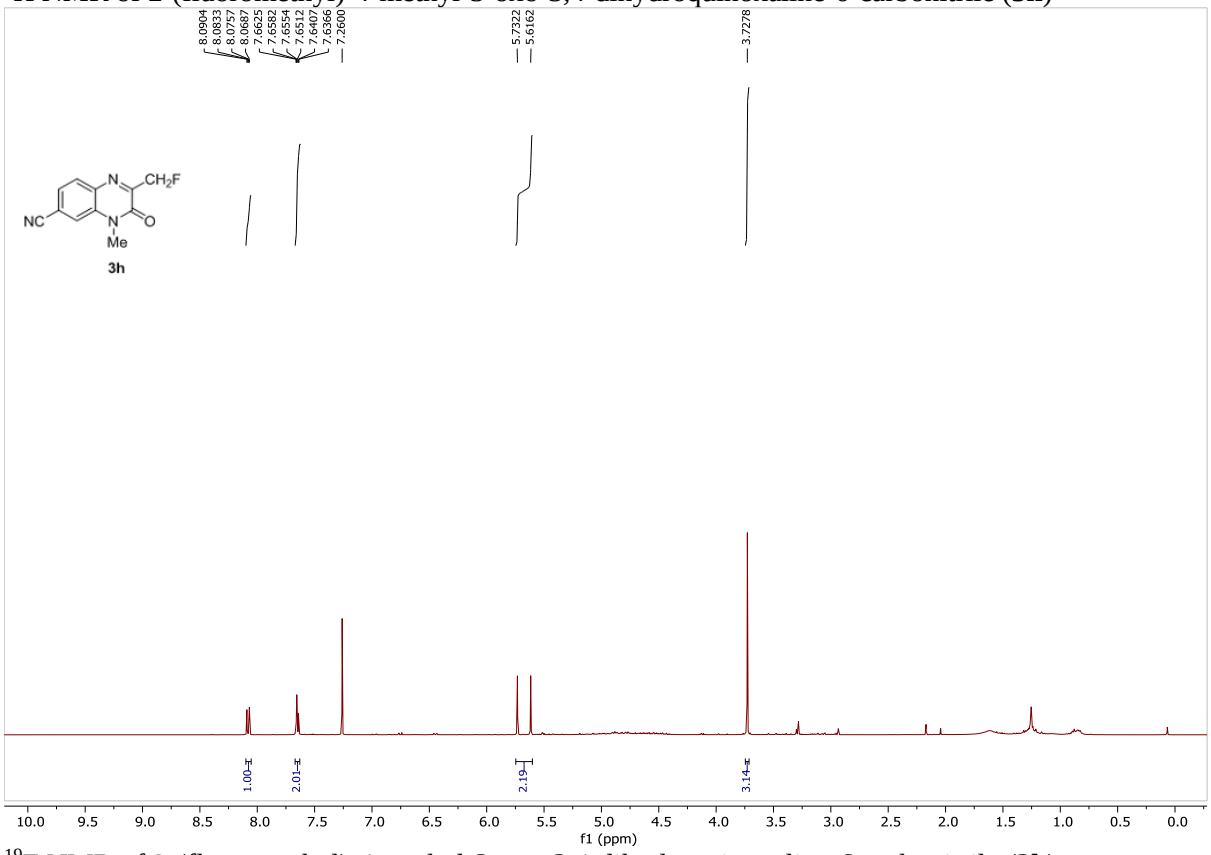
^{19}F NMR of ethyl 2-(fluoromethyl)-4-methyl-3-oxo-3,4-dihydroquinoxaline-6-carboxylate (**3g**)



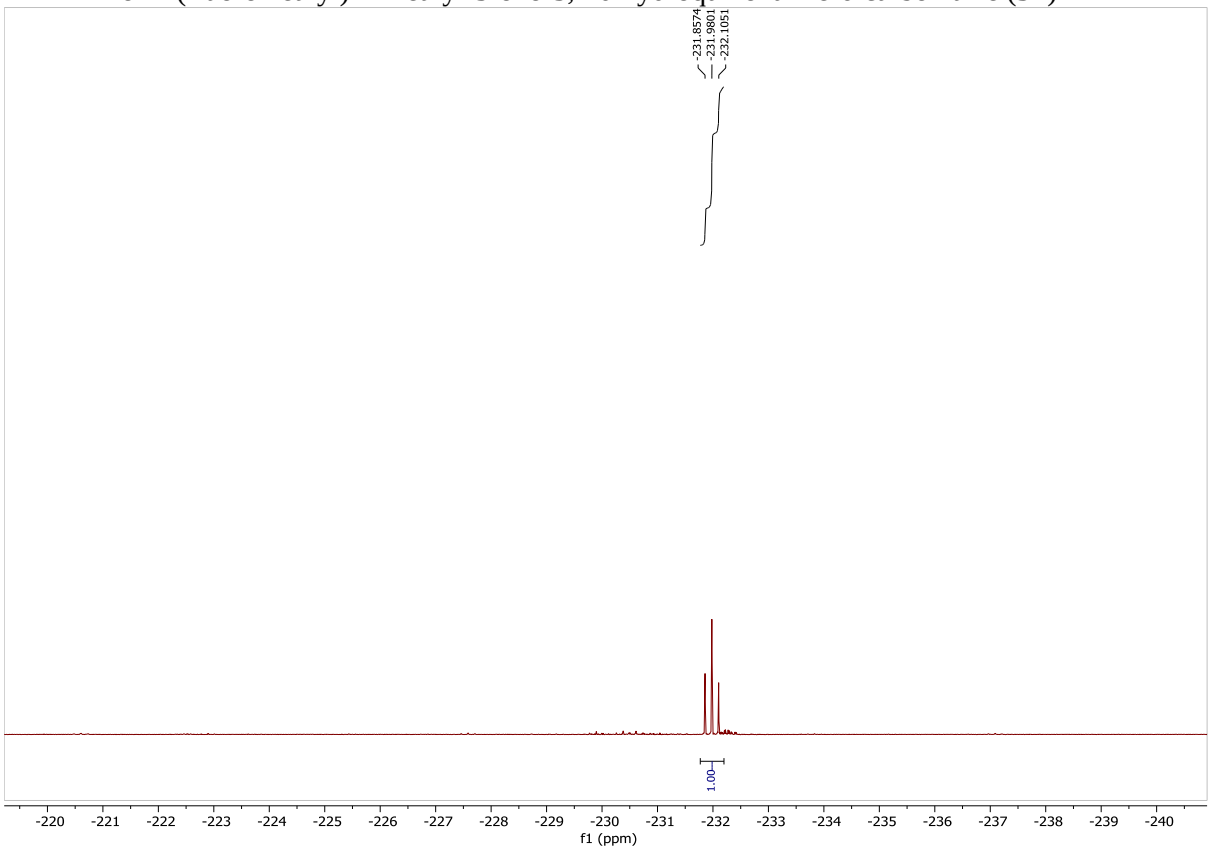
^{13}C NMR of ethyl 2-(fluoromethyl)-4-methyl-3-oxo-3,4-dihydroquinoxaline-6-carboxylate (**3g**)



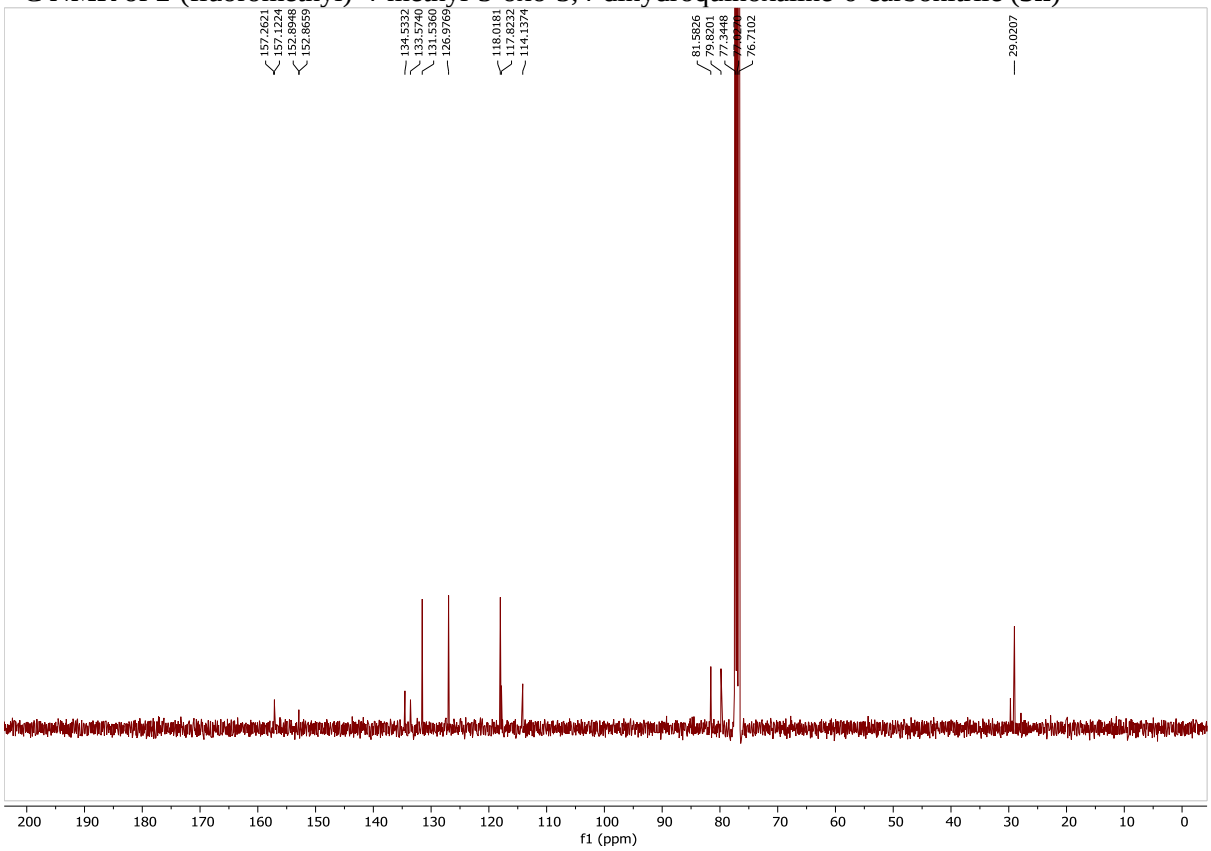
^{1}H NMR of 2-(fluoromethyl)-4-methyl-3-oxo-3,4-dihydroquinoxaline-6-carbonitrile (**3h**)



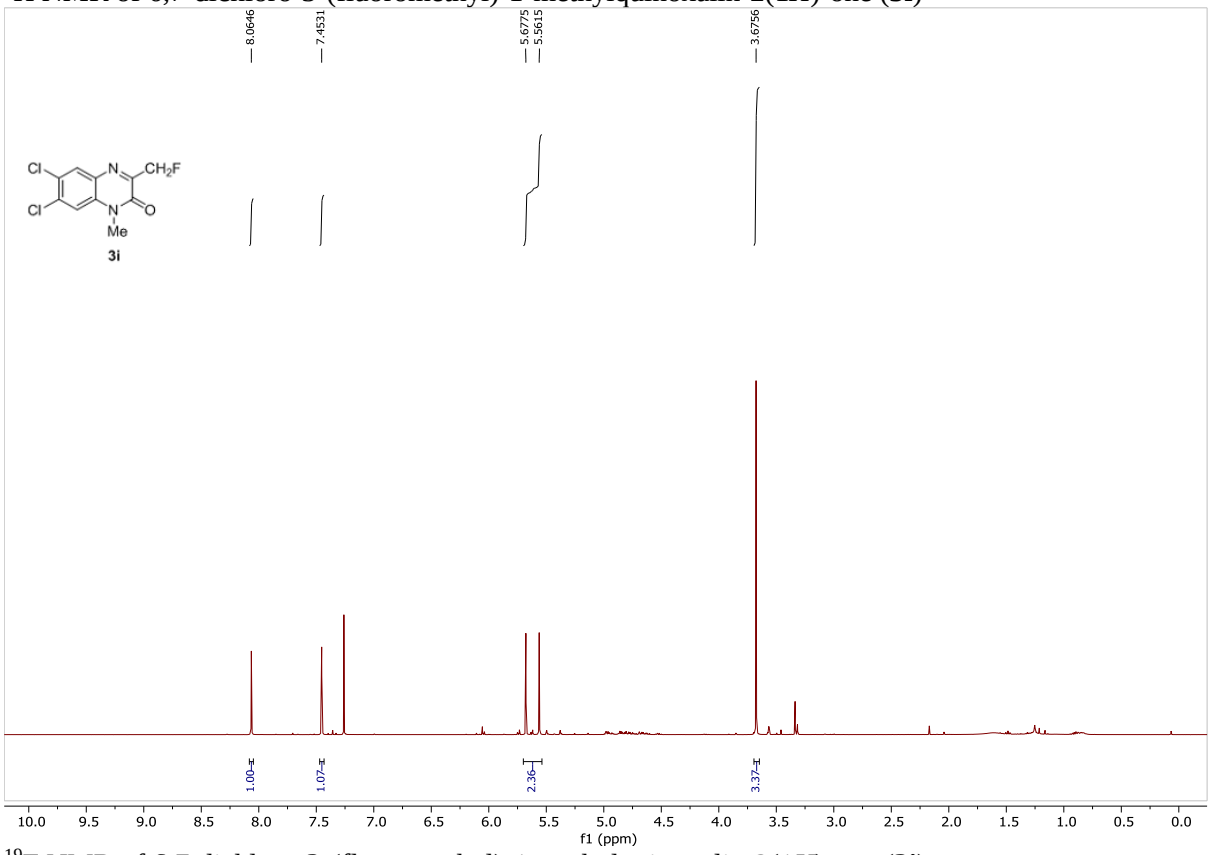
^{19}F NMR of 2-(fluoromethyl)-4-methyl-3-oxo-3,4-dihydroquinoxaline-6-carbonitrile (**3h**)



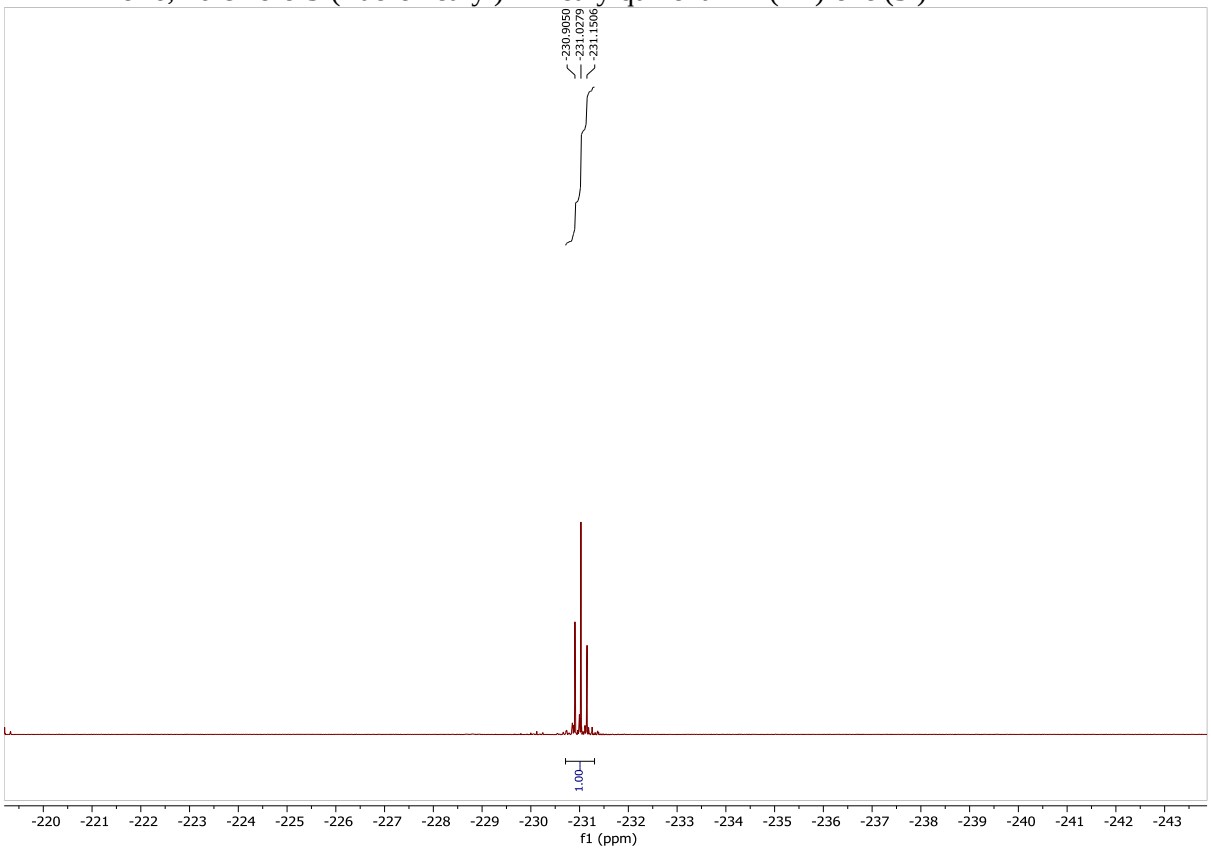
^{13}C NMR of 2-(fluoromethyl)-4-methyl-3-oxo-3,4-dihydroquinoxaline-6-carbonitrile (**3h**)



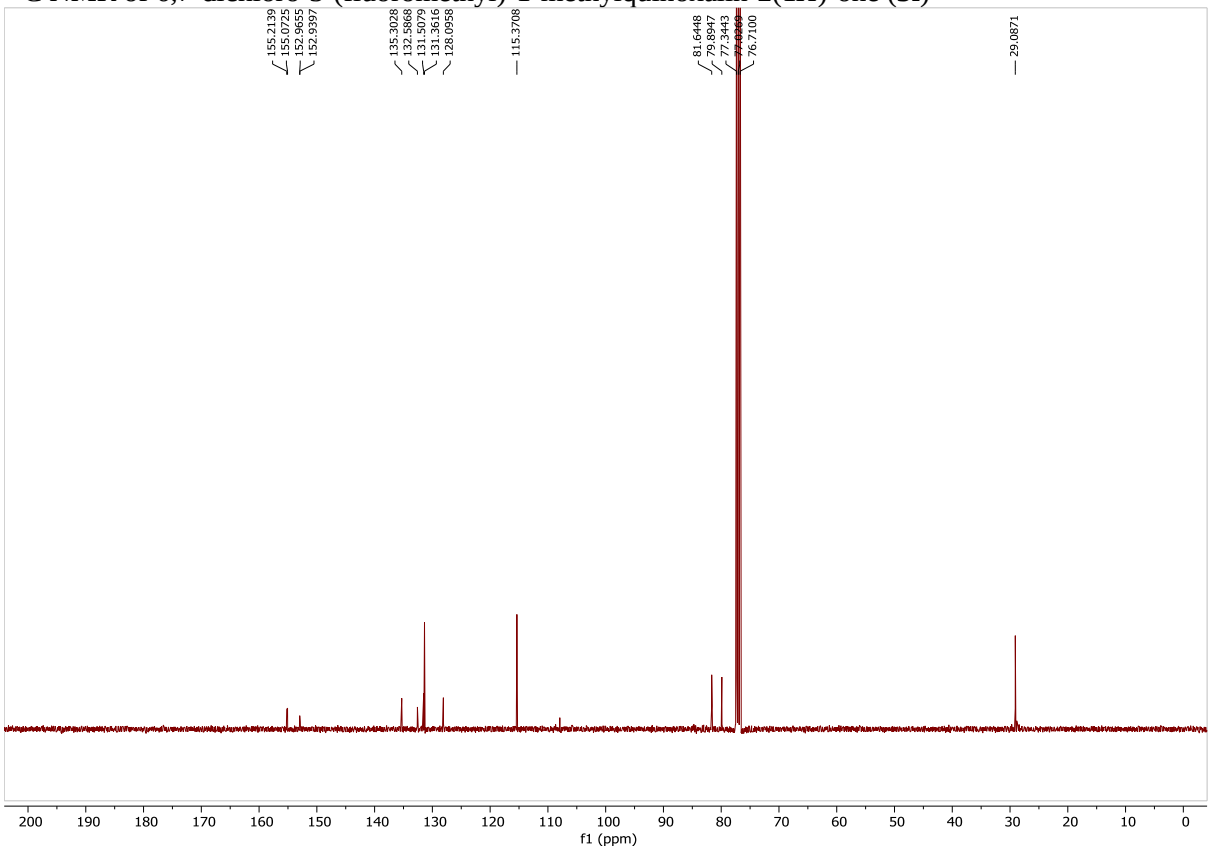
^{1}H NMR of 6,7-dichloro-3-(fluoromethyl)-1-methylquinoxalin-2(1*H*)-one (**3i**)



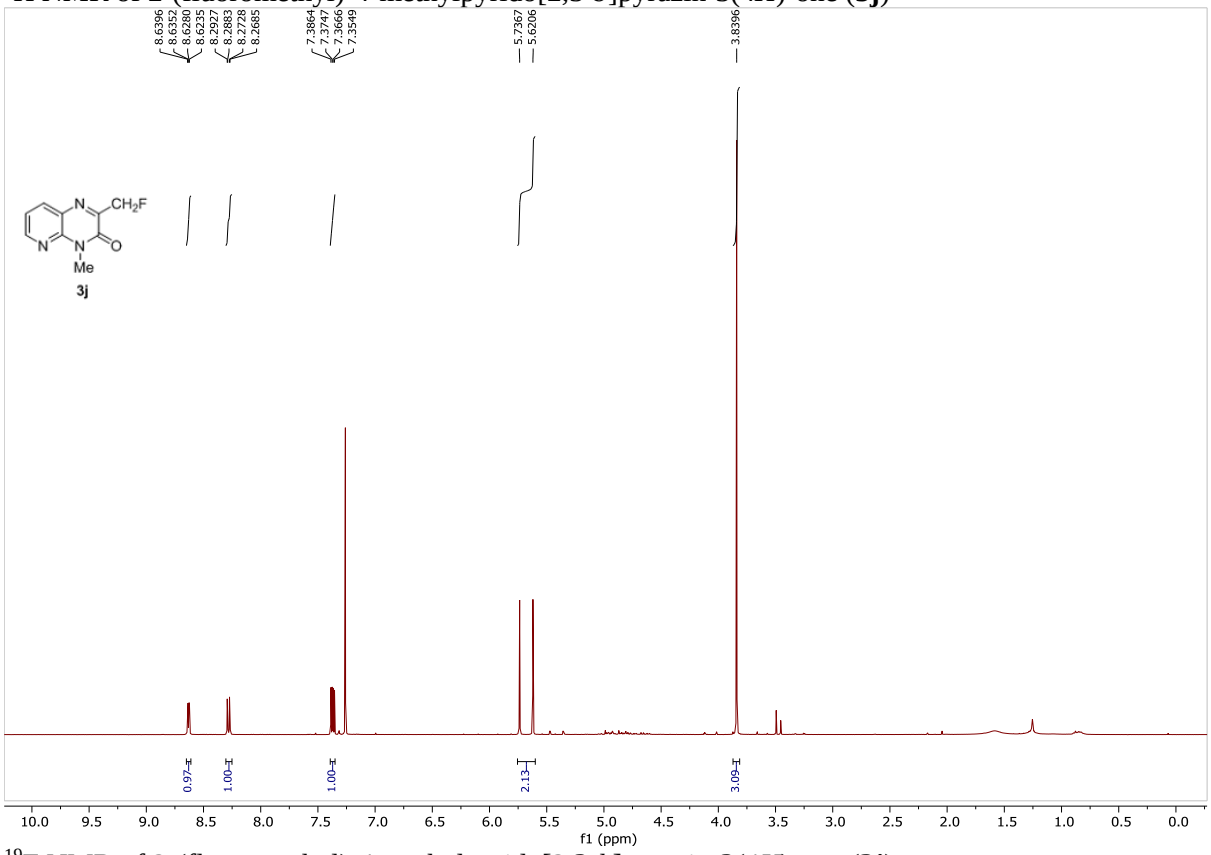
^{19}F NMR of 6,7-dichloro-3-(fluoromethyl)-1-methylquinoxalin-2(1*H*)-one (**3i**)



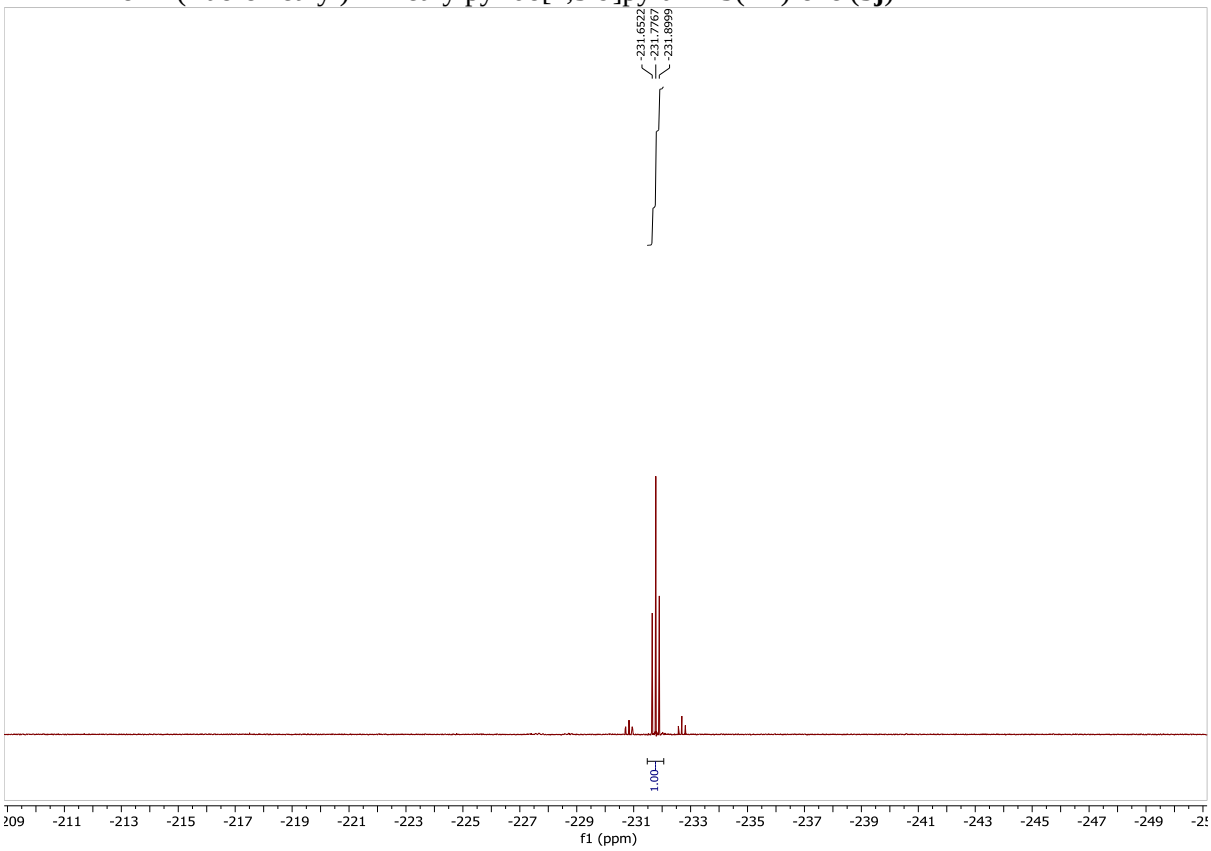
^{13}C NMR of 6,7-dichloro-3-(fluoromethyl)-1-methylquinoxalin-2(1*H*)-one (**3i**)



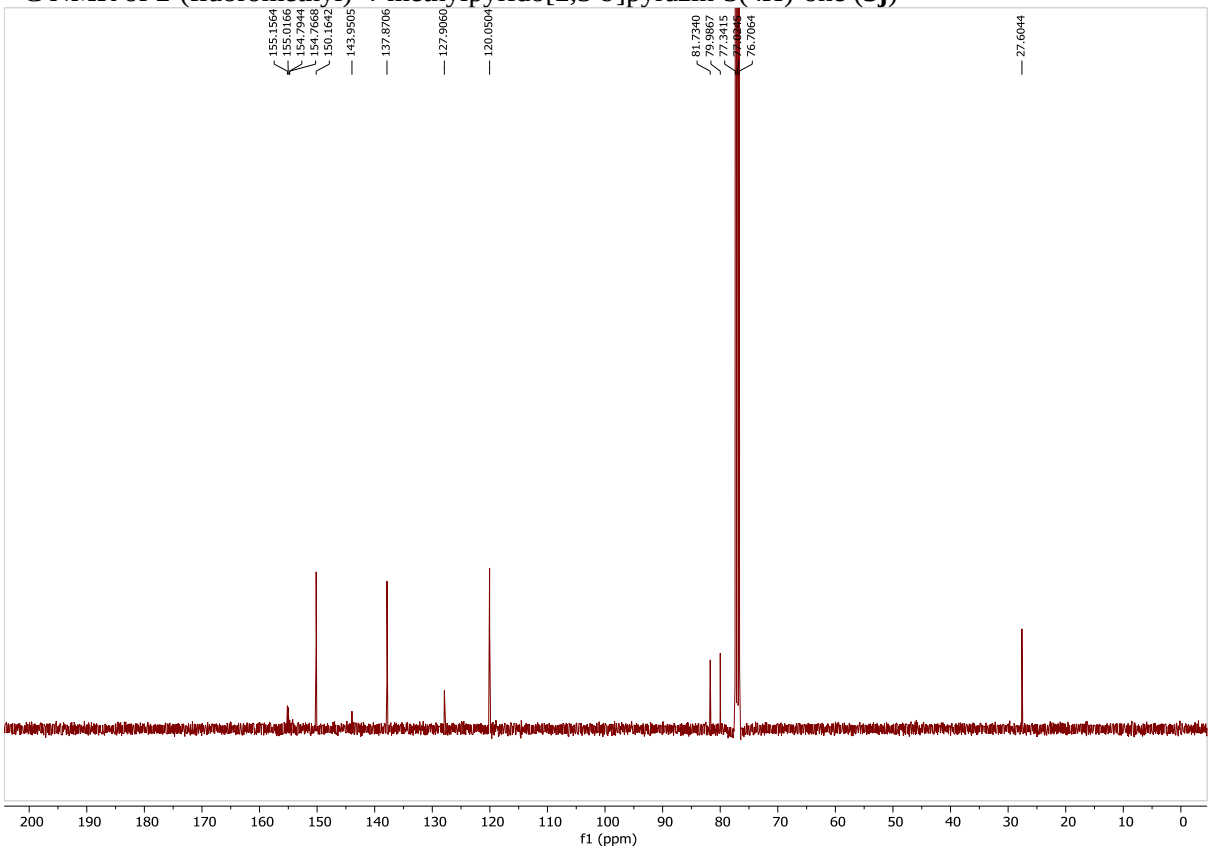
^{1}H NMR of 2-(fluoromethyl)-4-methylpyrido[2,3-*b*]pyrazin-3(4*H*)-one (**3j**)



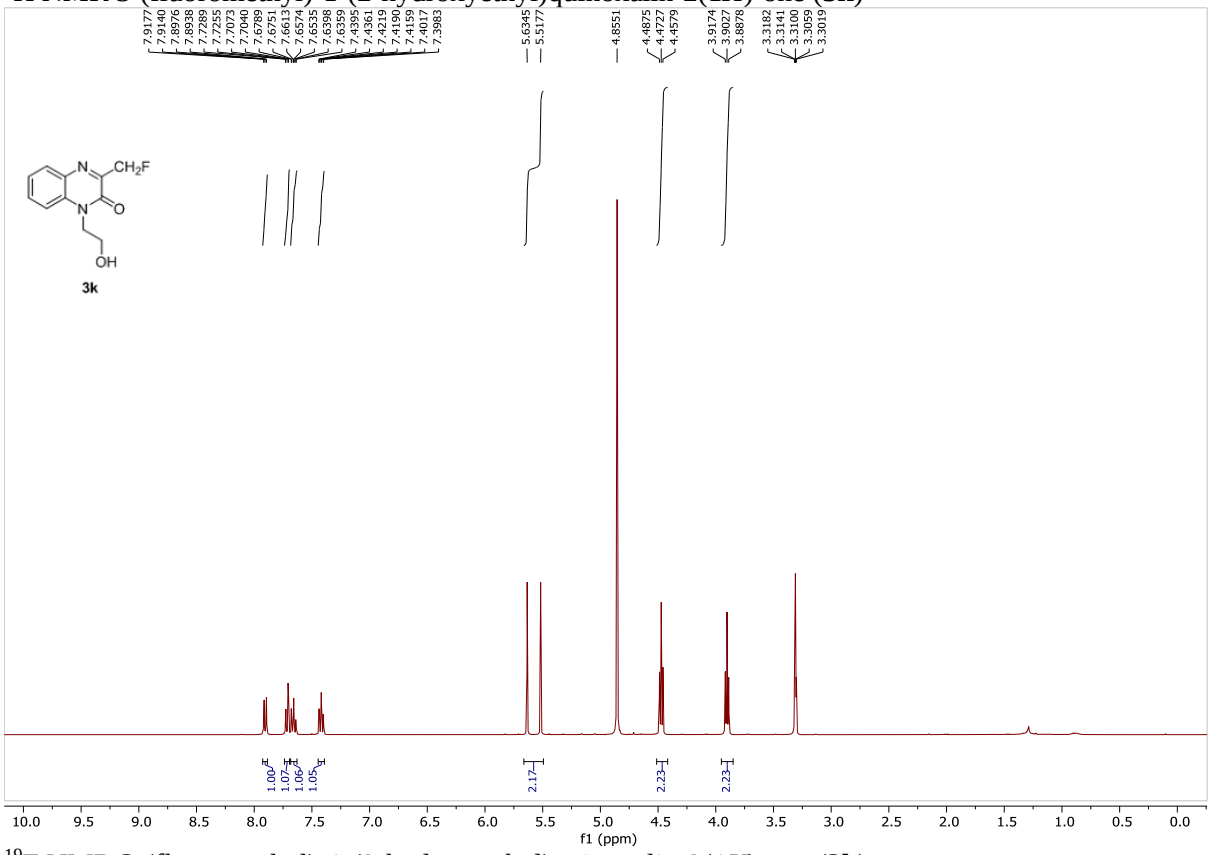
^{19}F NMR of 2-(fluoromethyl)-4-methylpyrido[2,3-*b*]pyrazin-3(4*H*)-one (**3j**)



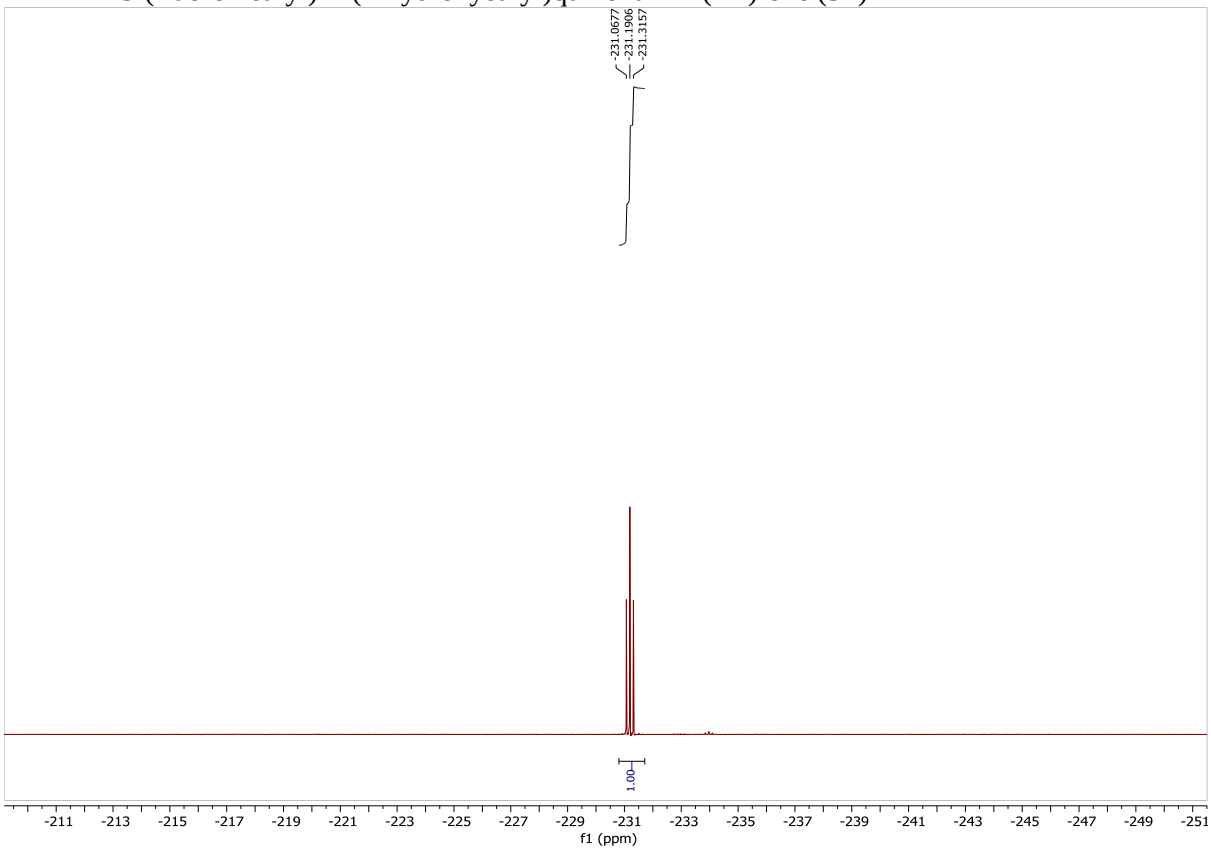
^{13}C NMR of 2-(fluoromethyl)-4-methylpyrido[2,3-*b*]pyrazin-3(4*H*)-one (**3j**)



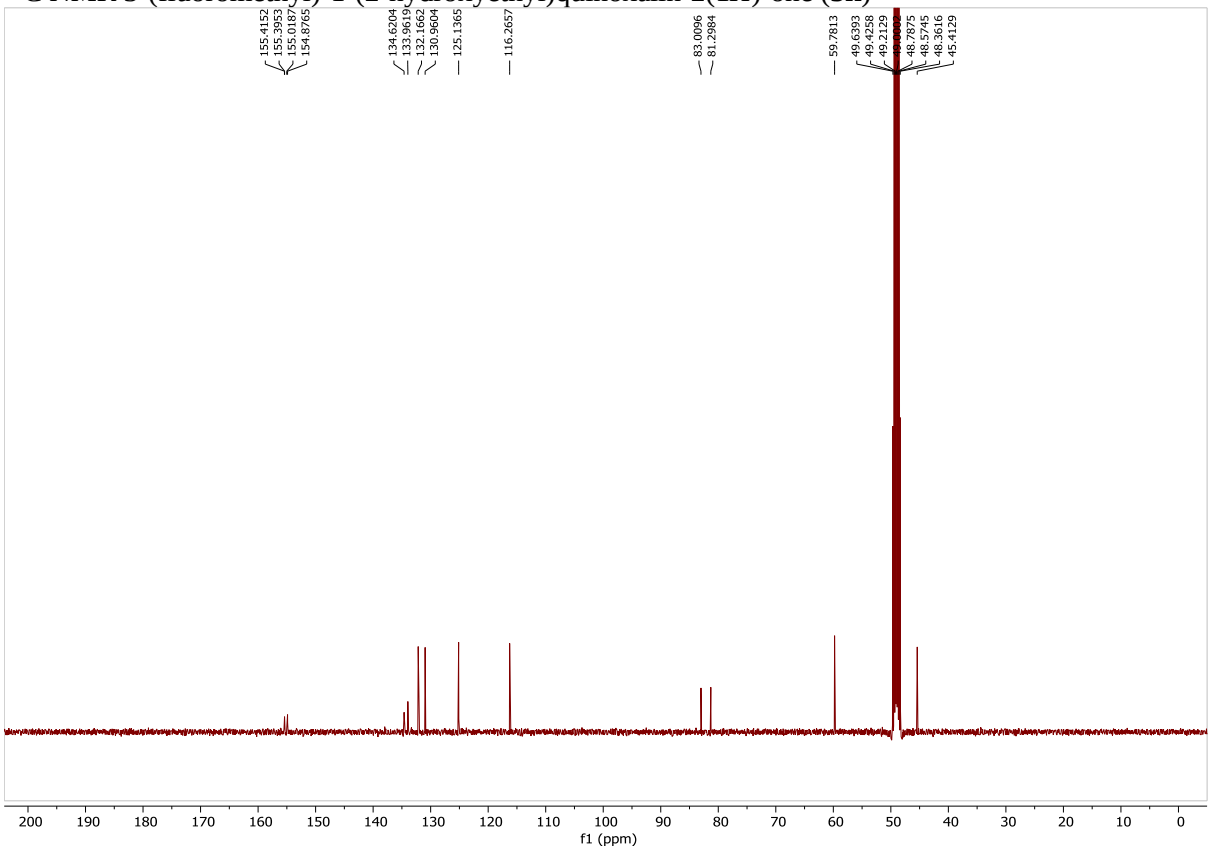
^{1}H NMR 3-(fluoromethyl)-1-(2-hydroxyethyl)quinoxalin-2(1*H*)-one (**3k**)



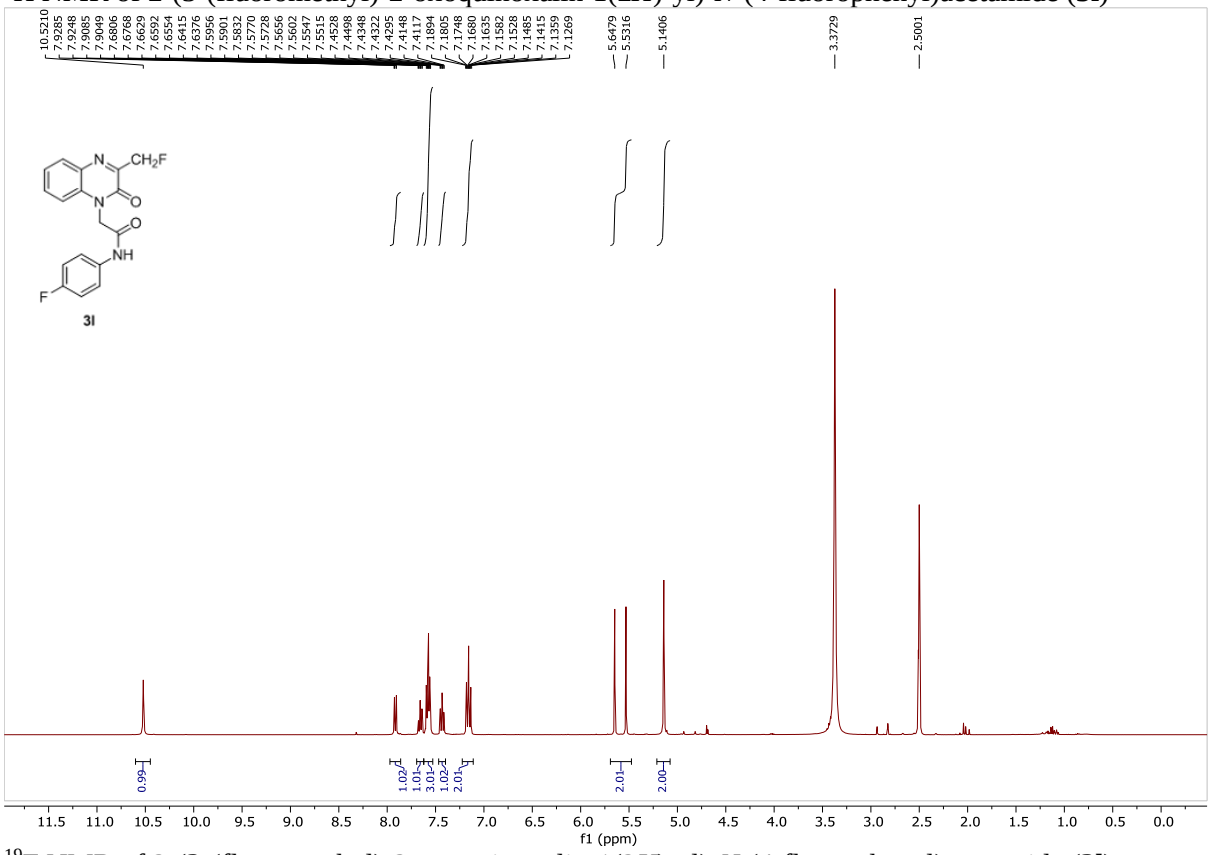
^{19}F NMR 3-(fluoromethyl)-1-(2-hydroxyethyl)quinoxalin-2(1*H*)-one (**3k**)



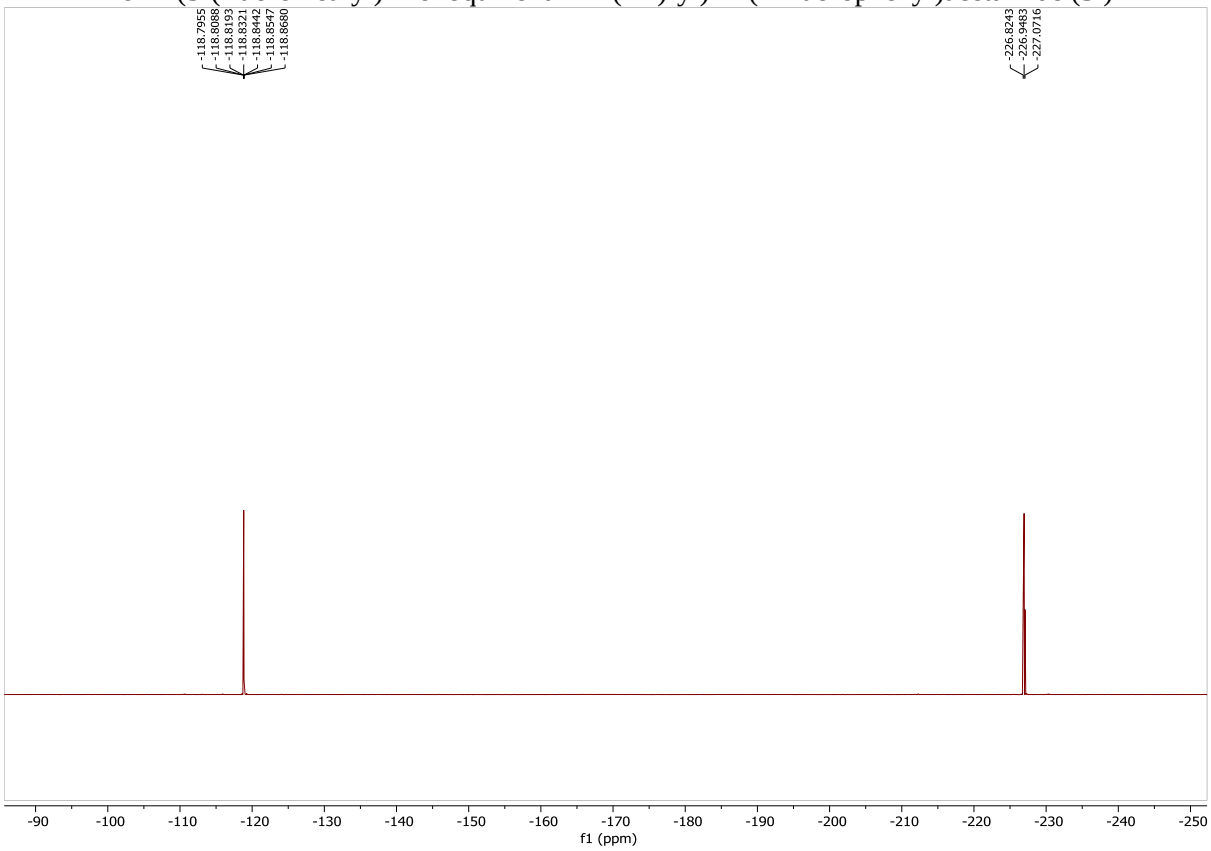
^{13}C NMR 3-(fluoromethyl)-1-(2-hydroxyethyl)quinoxalin-2(1*H*)-one (**3k**)



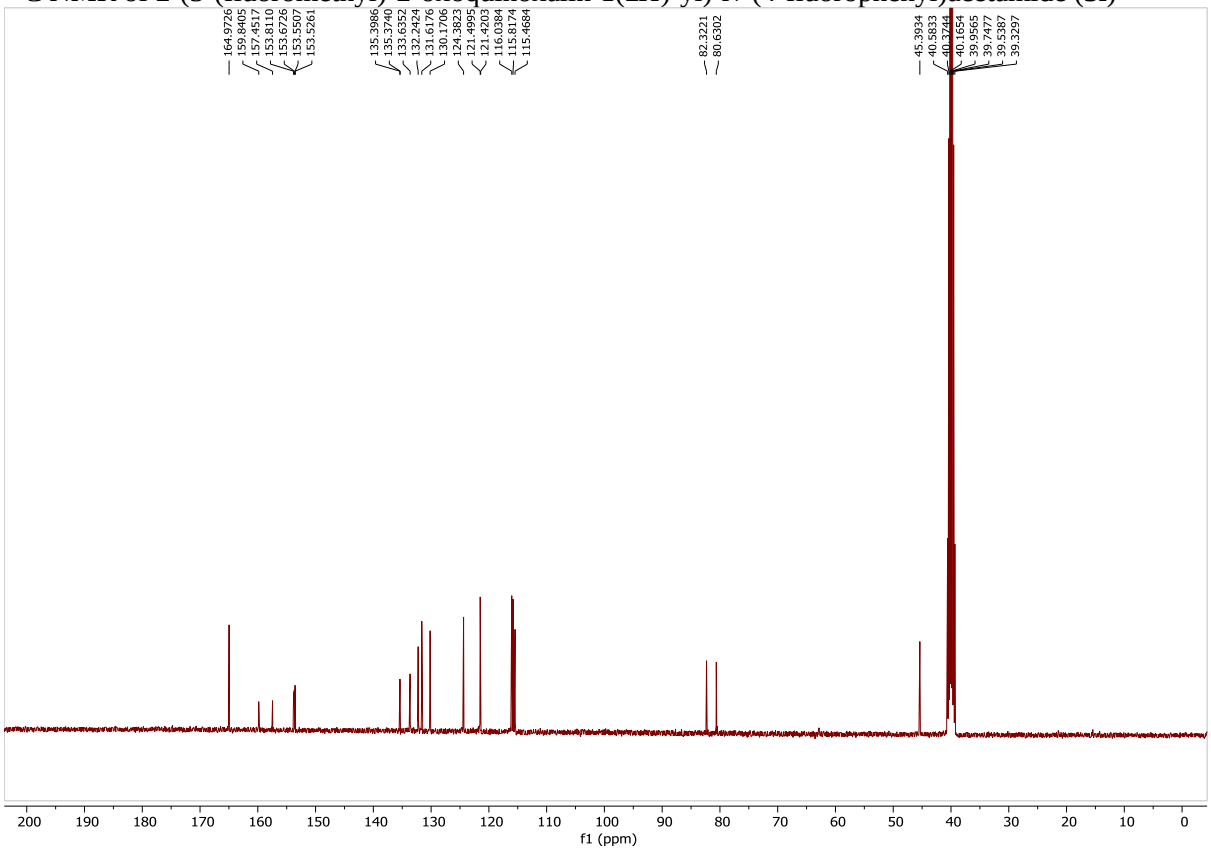
^{1}H NMR of 2-(3-(fluoromethyl)-2-oxoquinoxalin-1(2*H*)-yl)-*N*-(4-fluorophenyl)acetamide (**3l**)



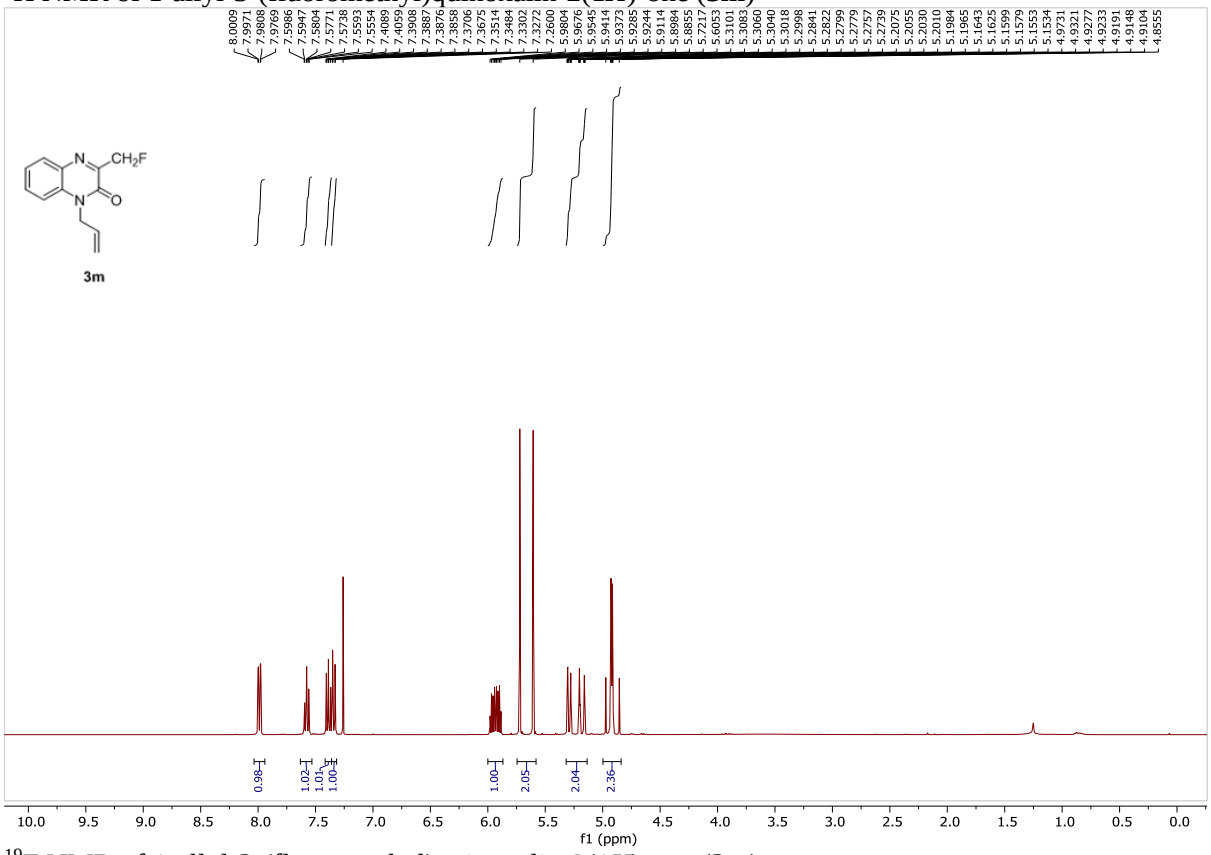
^{19}F NMR of 2-(3-(fluoromethyl)-2-oxoquinoxalin-1(2*H*)-yl)-*N*-(4-fluorophenyl)acetamide (**3l**)



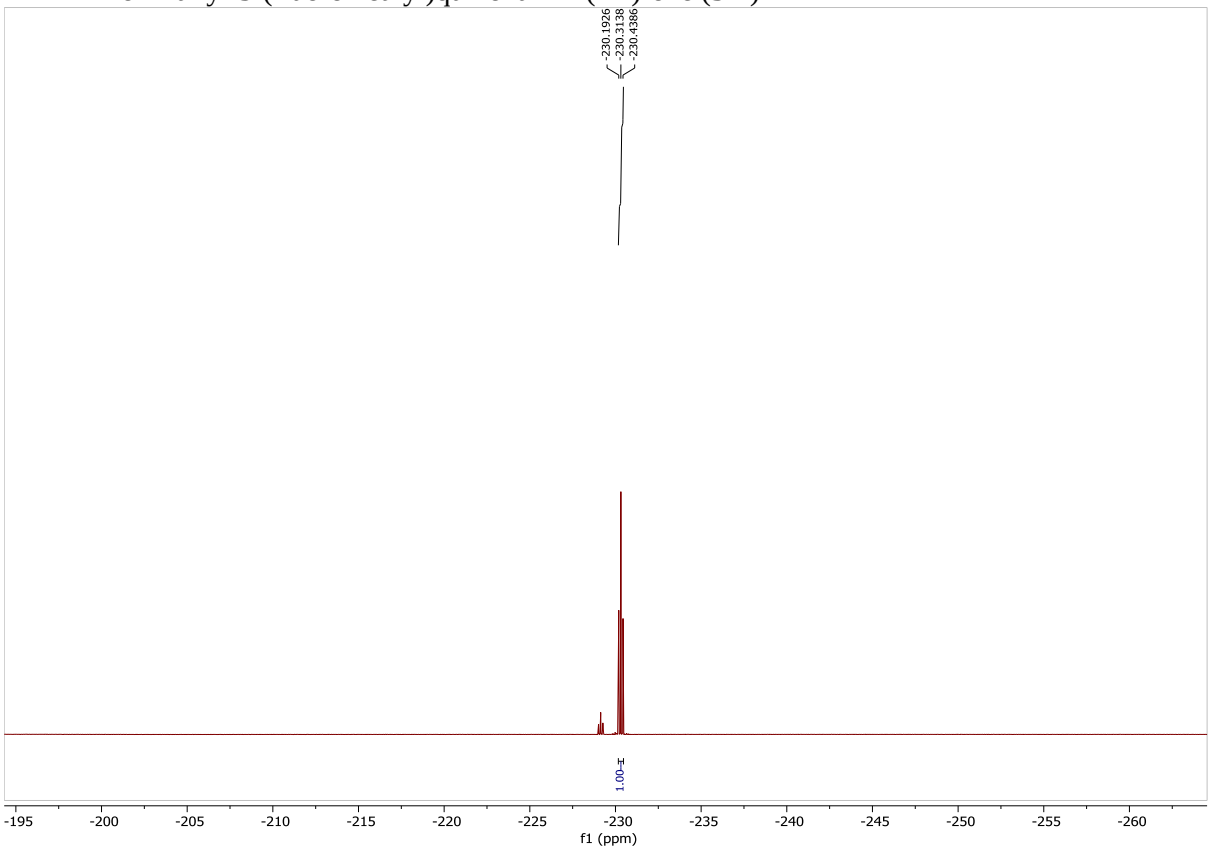
^{13}C NMR of 2-(3-(fluoromethyl)-2-oxoquinoxalin-1(2*H*)-yl)-*N*-(4-fluorophenyl)acetamide (**3l**)



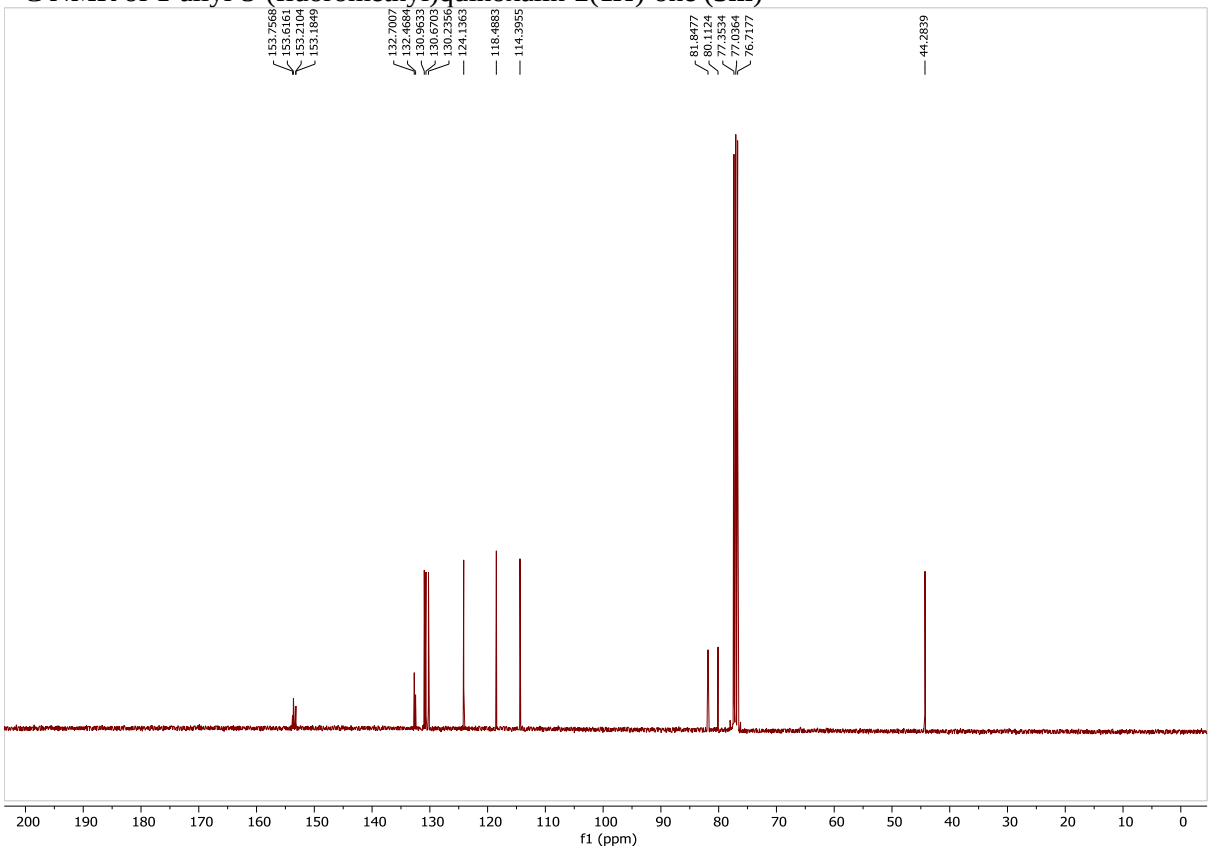
^{1}H NMR of 1-allyl-3-(fluoromethyl)quinoxalin-2(1*H*)-one (**3m**)



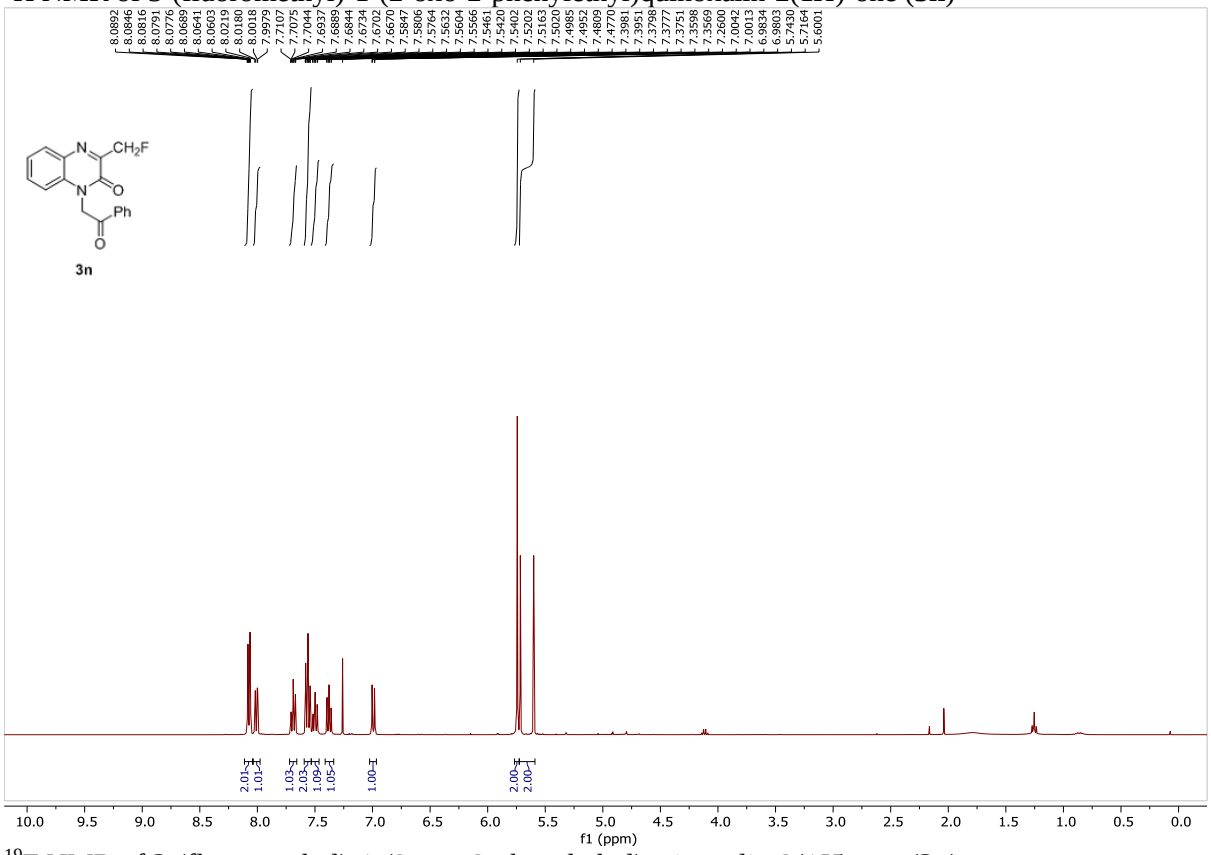
^{19}F NMR of 1-allyl-3-(fluoromethyl)quinoxalin-2(1*H*)-one (**3m**)



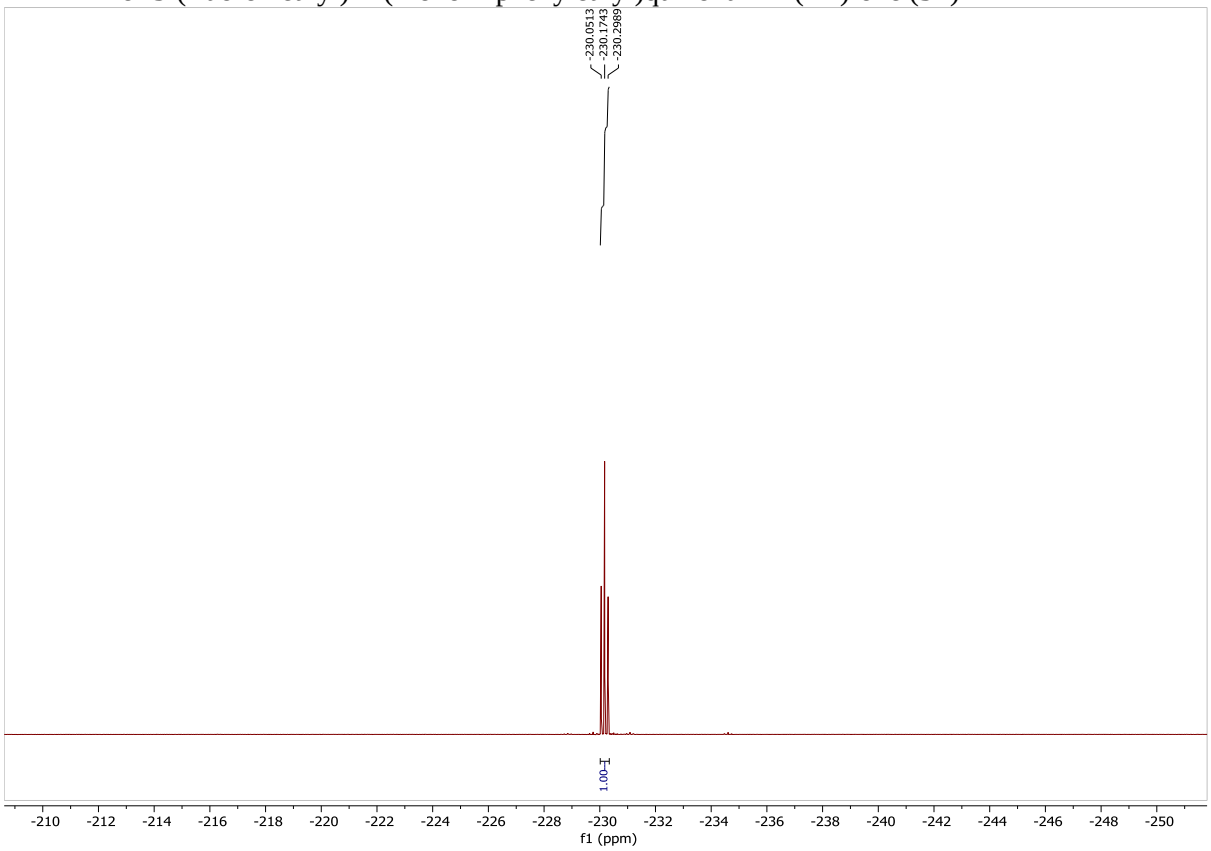
^{13}C NMR of 1-allyl-3-(fluoromethyl)quinoxalin-2(1*H*)-one (**3m**)



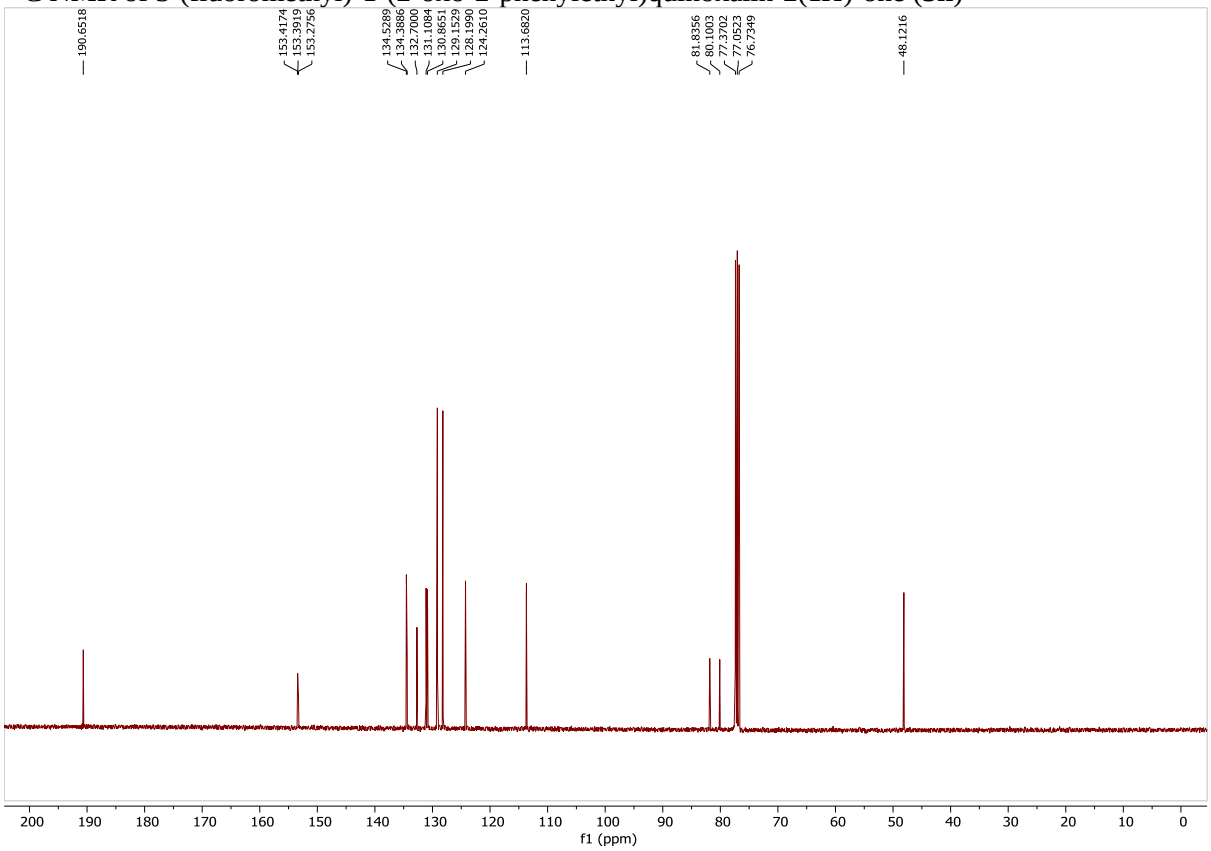
^{1}H NMR of 3-(fluoromethyl)-1-(2-oxo-2-phenylethyl)quinoxalin-2(1*H*)-one (**3n**)



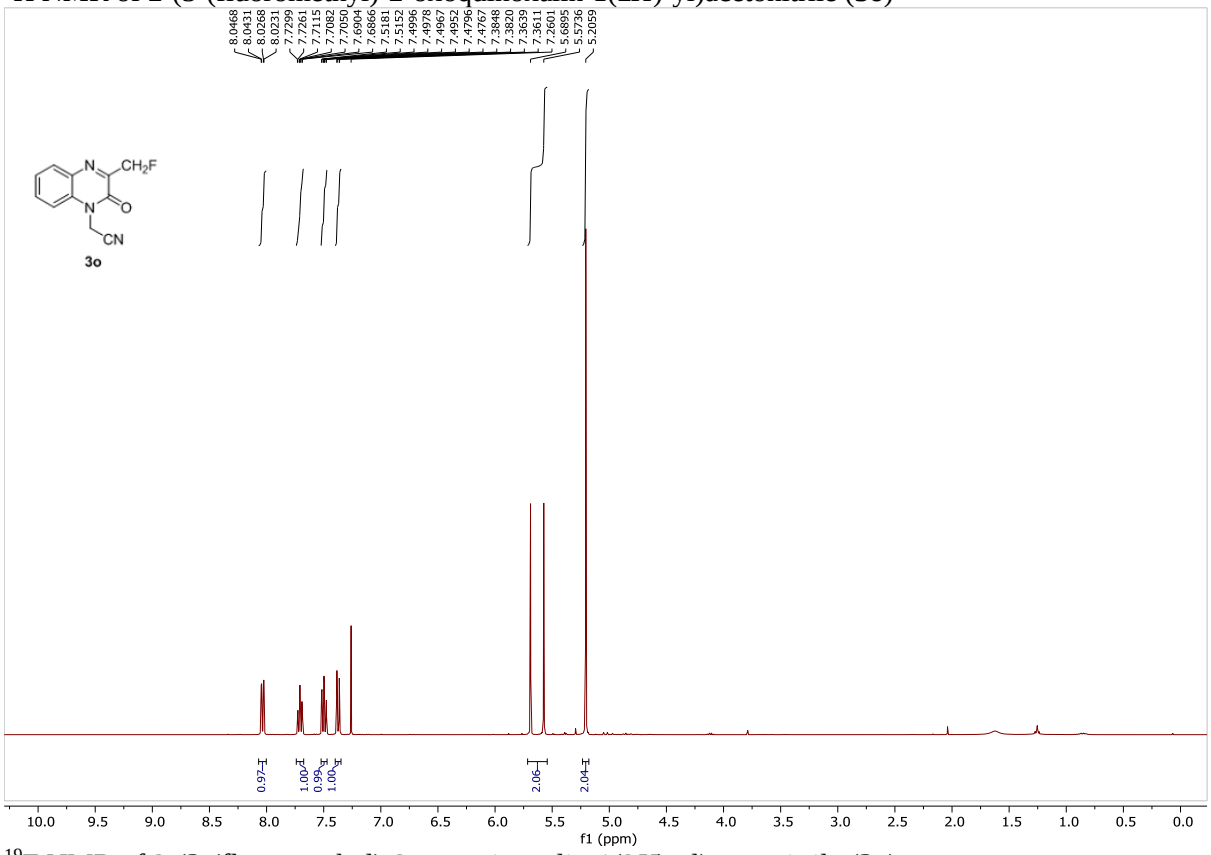
^{19}F NMR of 3-(fluoromethyl)-1-(2-oxo-2-phenylethyl)quinoxalin-2(1*H*)-one (**3n**)



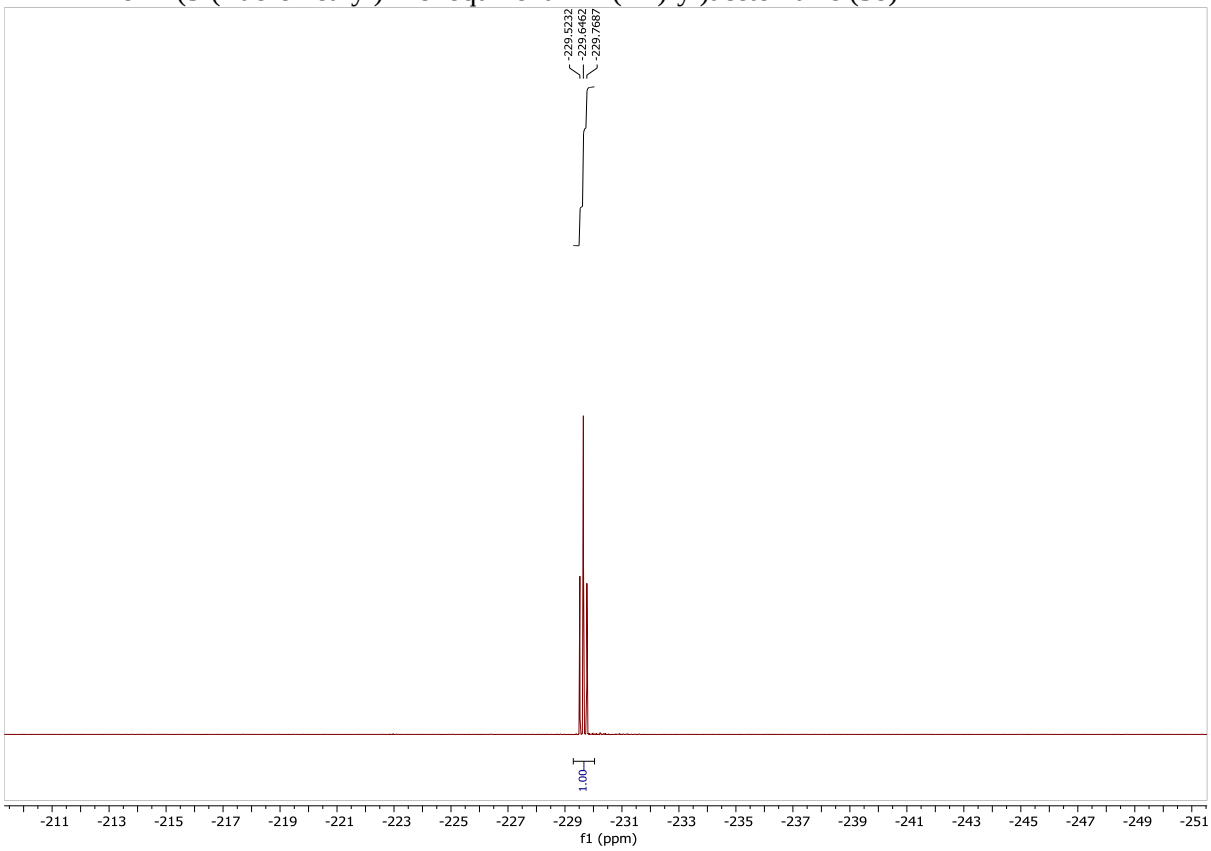
^{13}C NMR of 3-(fluoromethyl)-1-(2-oxo-2-phenylethyl)quinoxalin-2(1*H*)-one (**3n**)



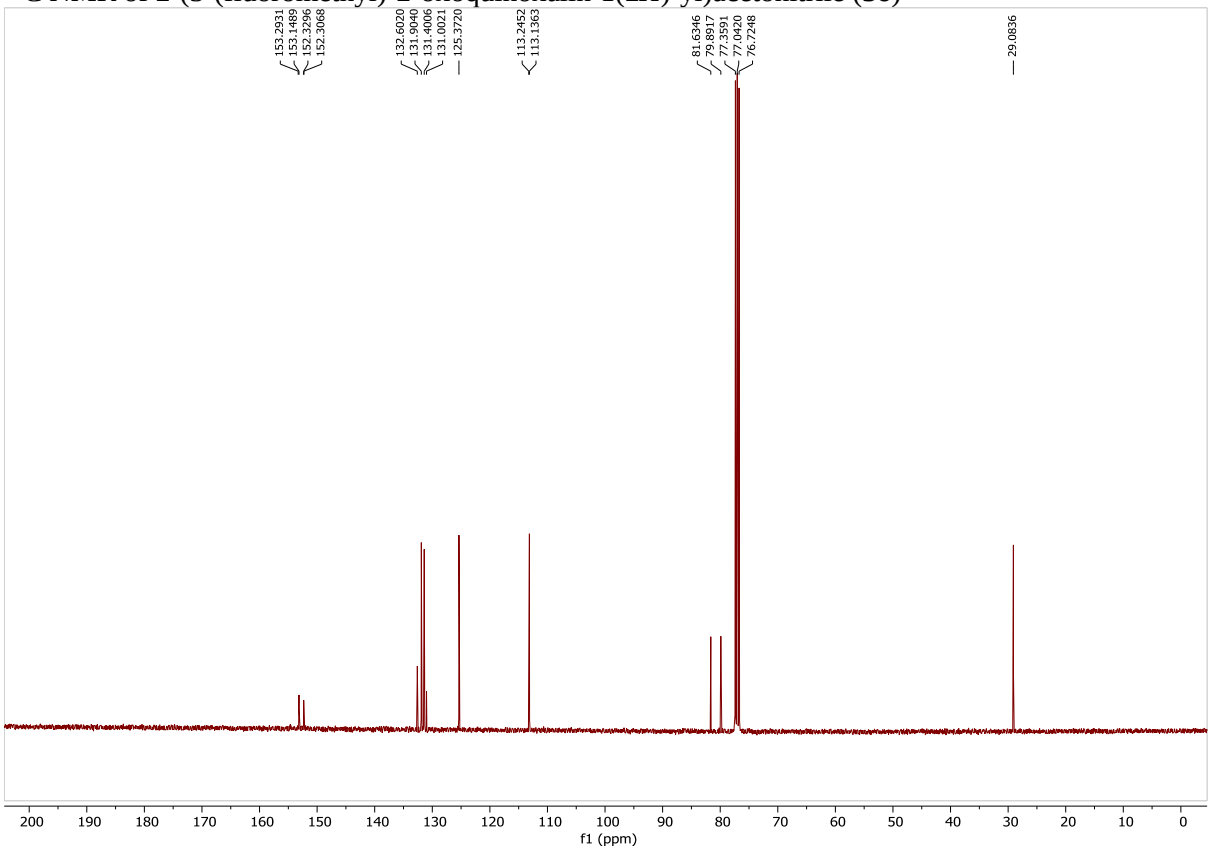
^{1}H NMR of 2-(3-(fluoromethyl)-2-oxoquinoxalin-1(2*H*)-yl)acetonitrile (**3o**)



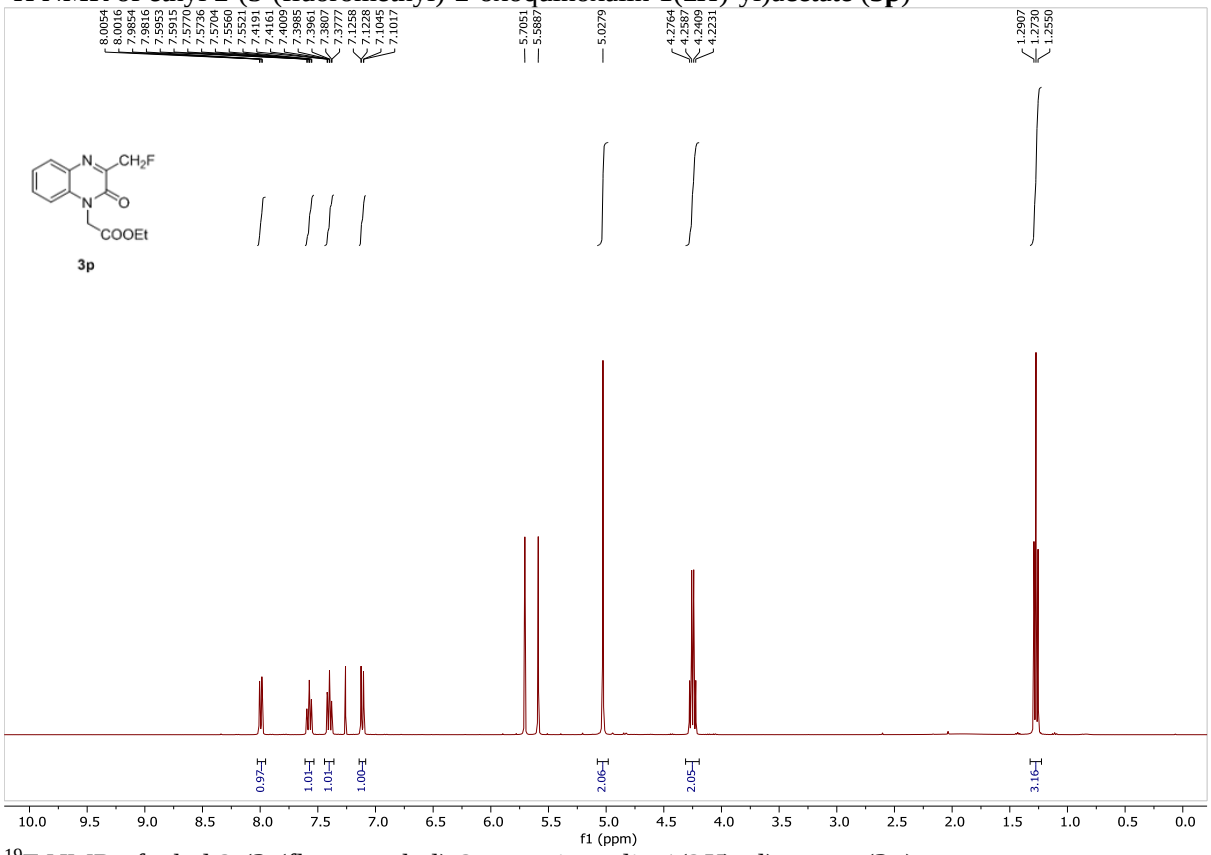
^{19}F NMR of 2-(3-(fluoromethyl)-2-oxoquinoxalin-1(2*H*)-yl)acetonitrile (**3o**)



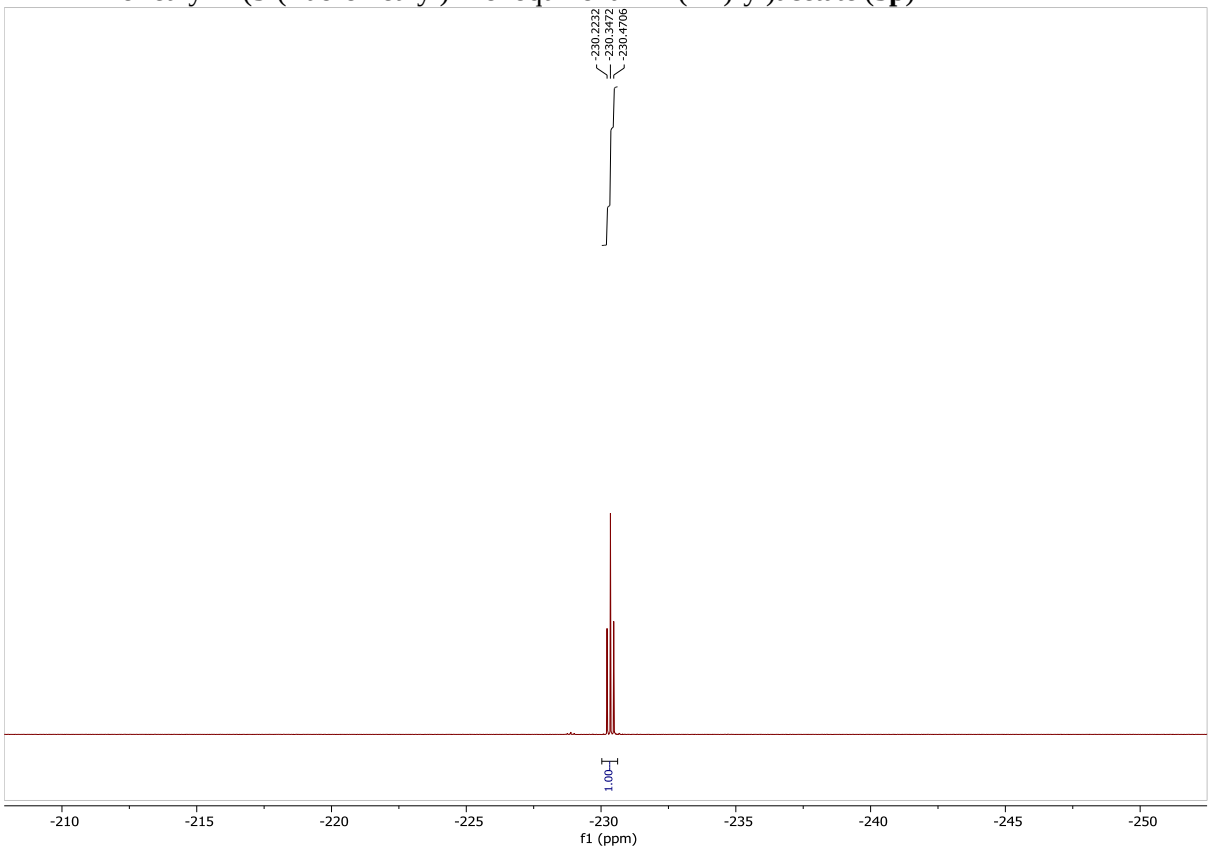
^{13}C NMR of 2-(3-(fluoromethyl)-2-oxoquinoxalin-1(2*H*)-yl)acetonitrile (**3o**)



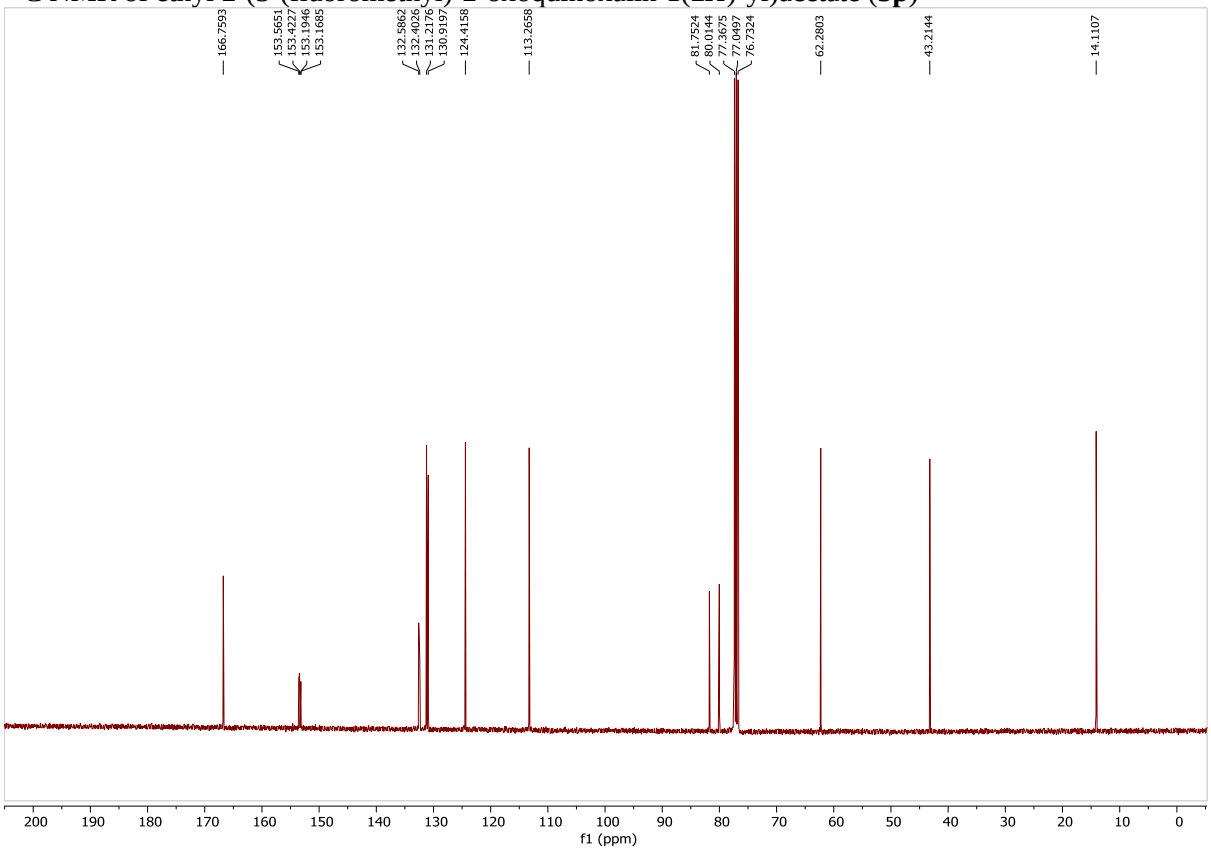
^{1}H NMR of ethyl 2-(3-(fluoromethyl)-2-oxoquinoxalin-1(2*H*)-yl)acetate (**3p**)



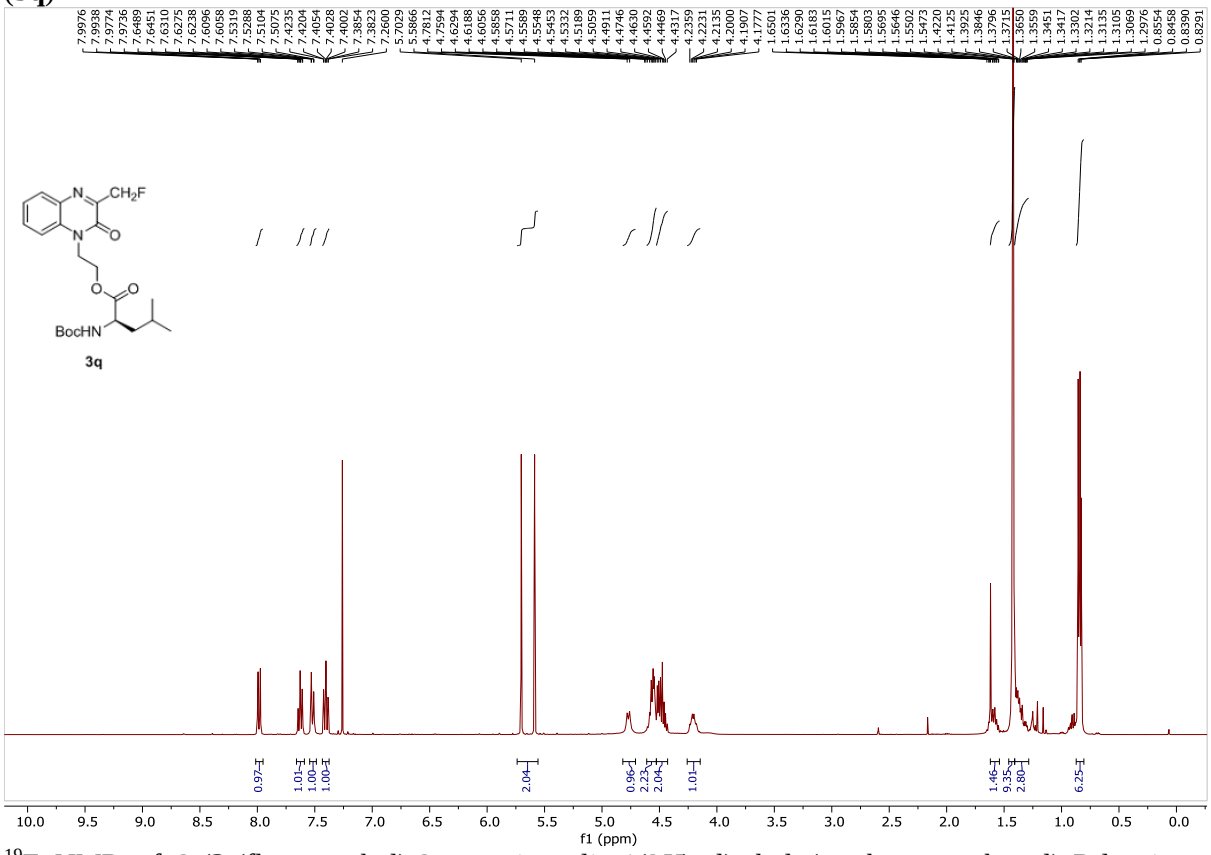
^{19}F NMR of ethyl 2-(3-(fluoromethyl)-2-oxoquinoxalin-1(2*H*)-yl)acetate (**3p**)



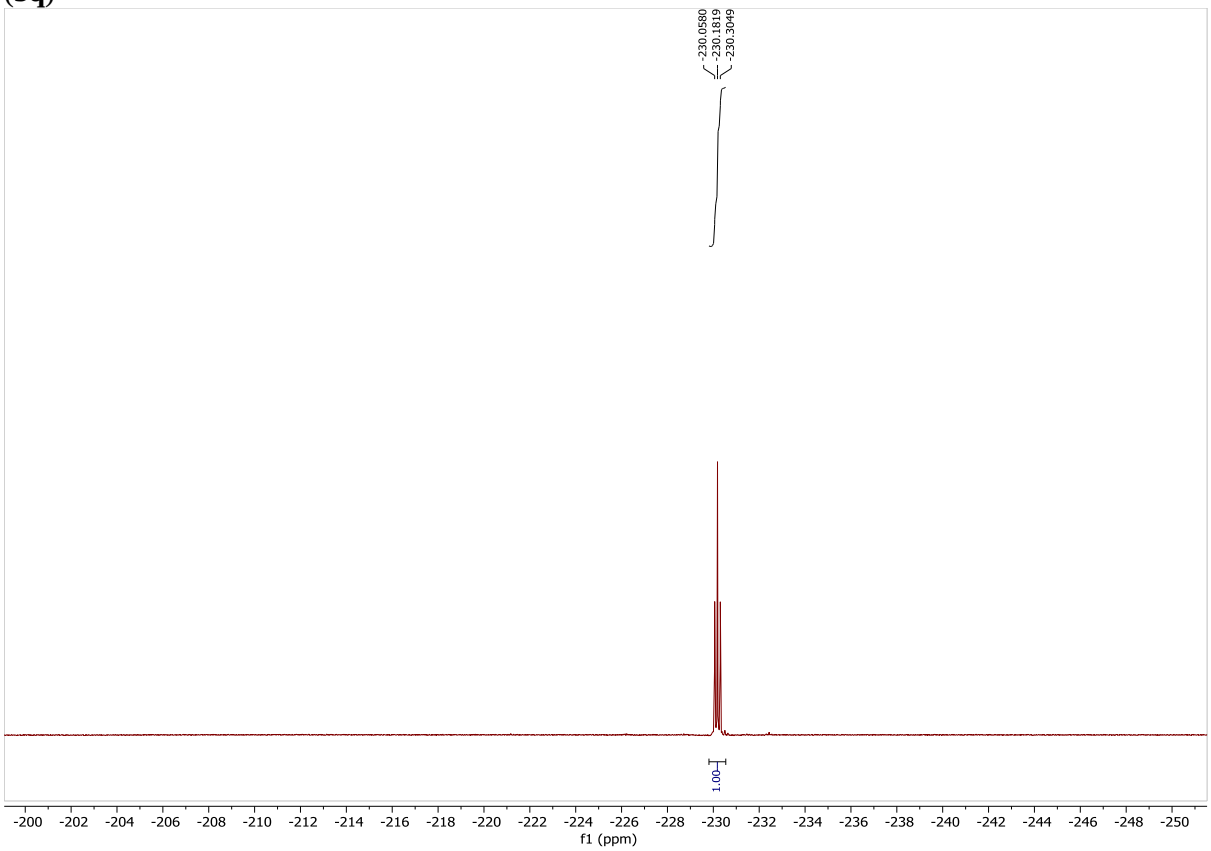
^{13}C NMR of ethyl 2-(3-(fluoromethyl)-2-oxoquinoxalin-1(2*H*)-yl)acetate (**3p**)



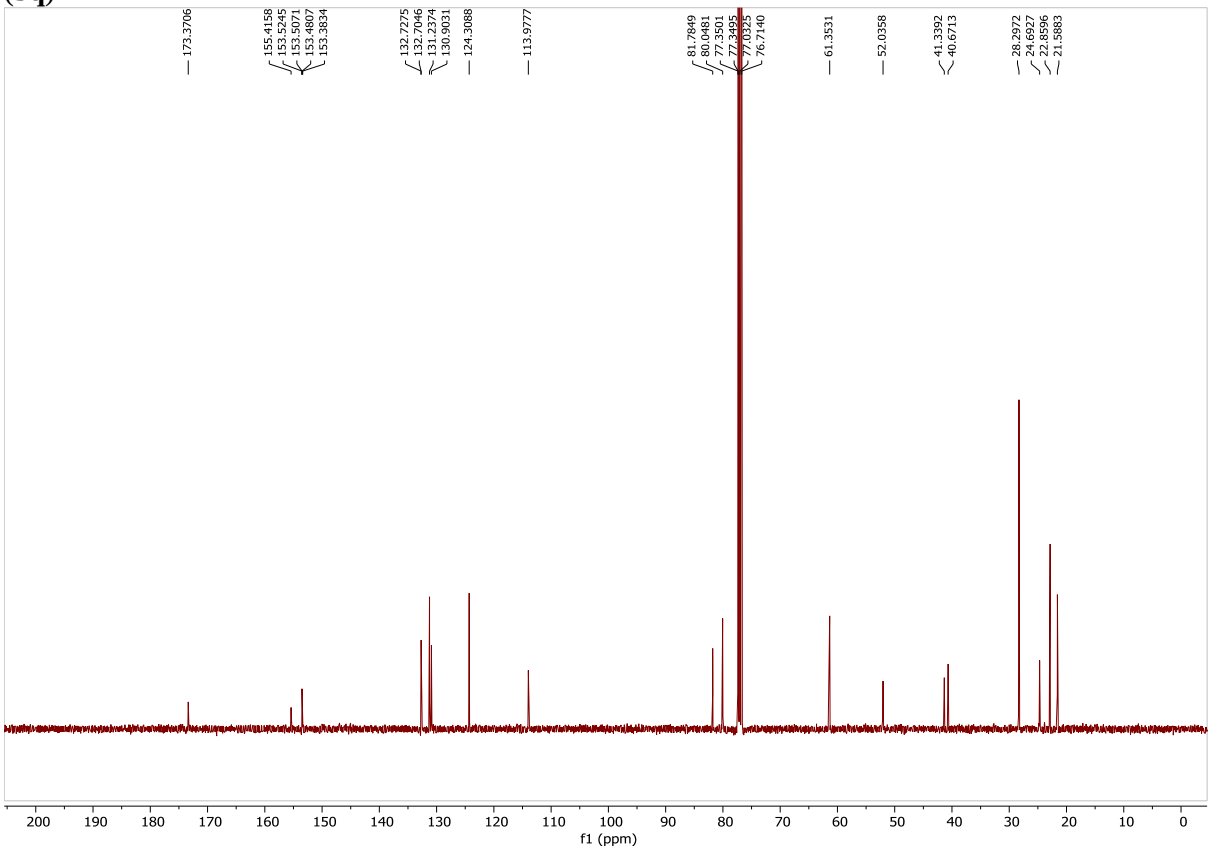
^{1}H NMR of 2-(3-(fluoromethyl)-2-oxoquinoxalin-1(2*H*)-yl)ethyl (tert-butoxycarbonyl)-*D*-leucinate (**3q**)



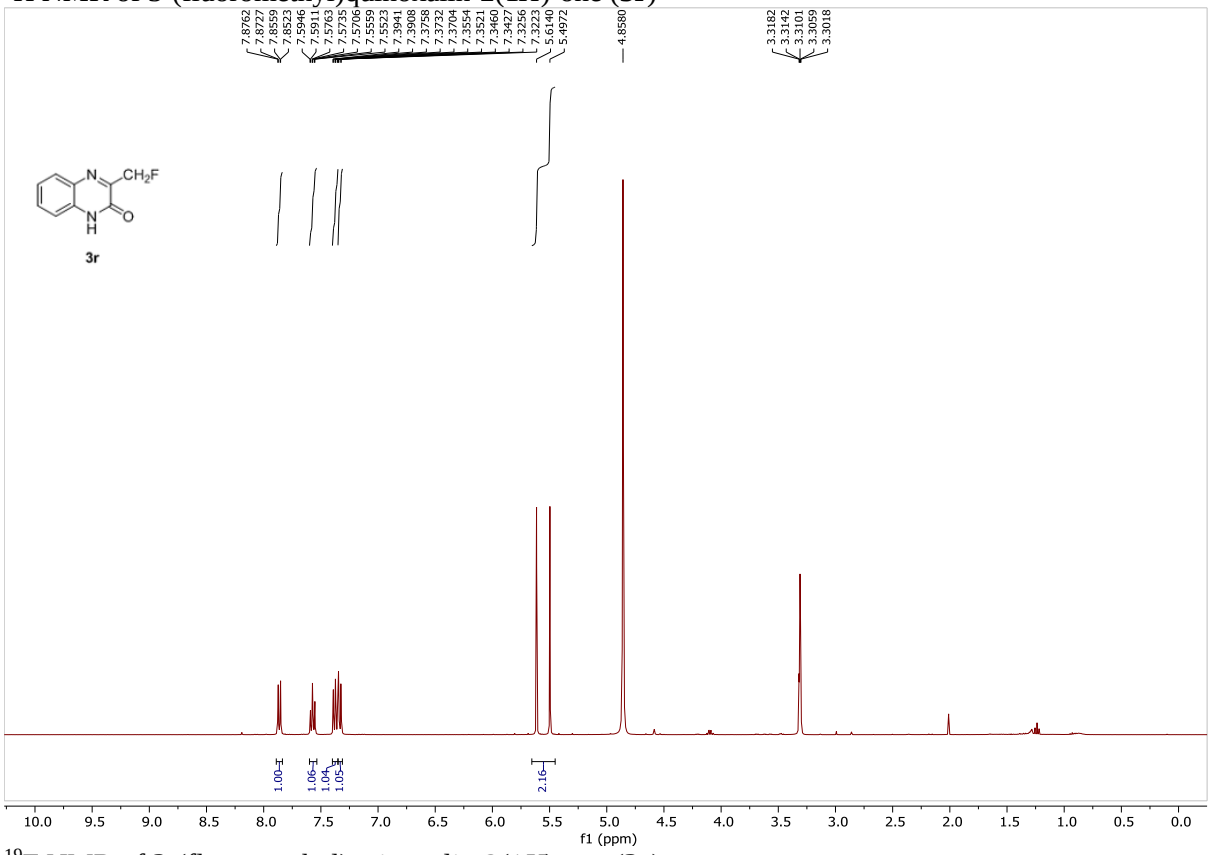
^{19}F NMR of 2-(3-(fluoromethyl)-2-oxoquinoxalin-1(2*H*)-yl)ethyl (tert-butoxycarbonyl)-*D*-leucinate (**3q**)



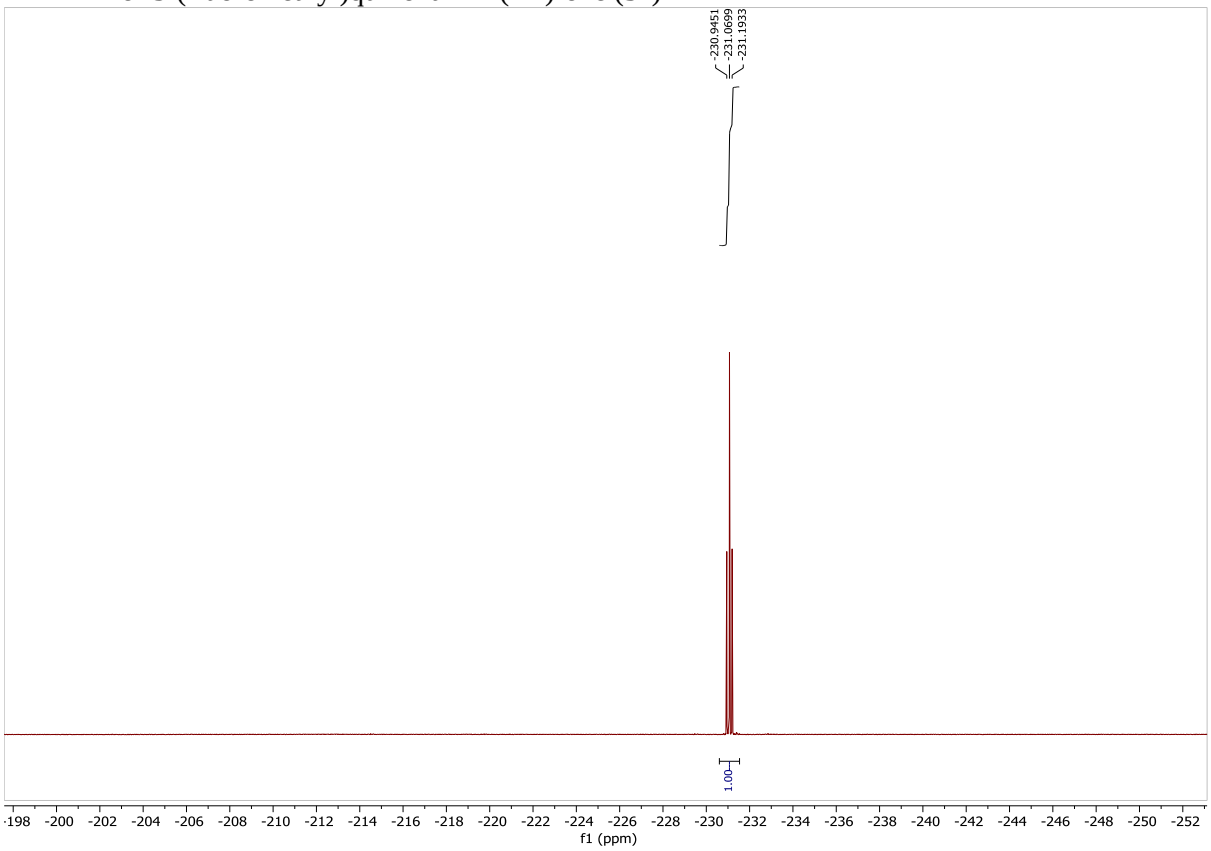
^{13}C NMR of 2-(3-(fluoromethyl)-2-oxoquinoxalin-1(2*H*)-yl)ethyl (tert-butoxycarbonyl)-*D*-leucinate (**3q**)



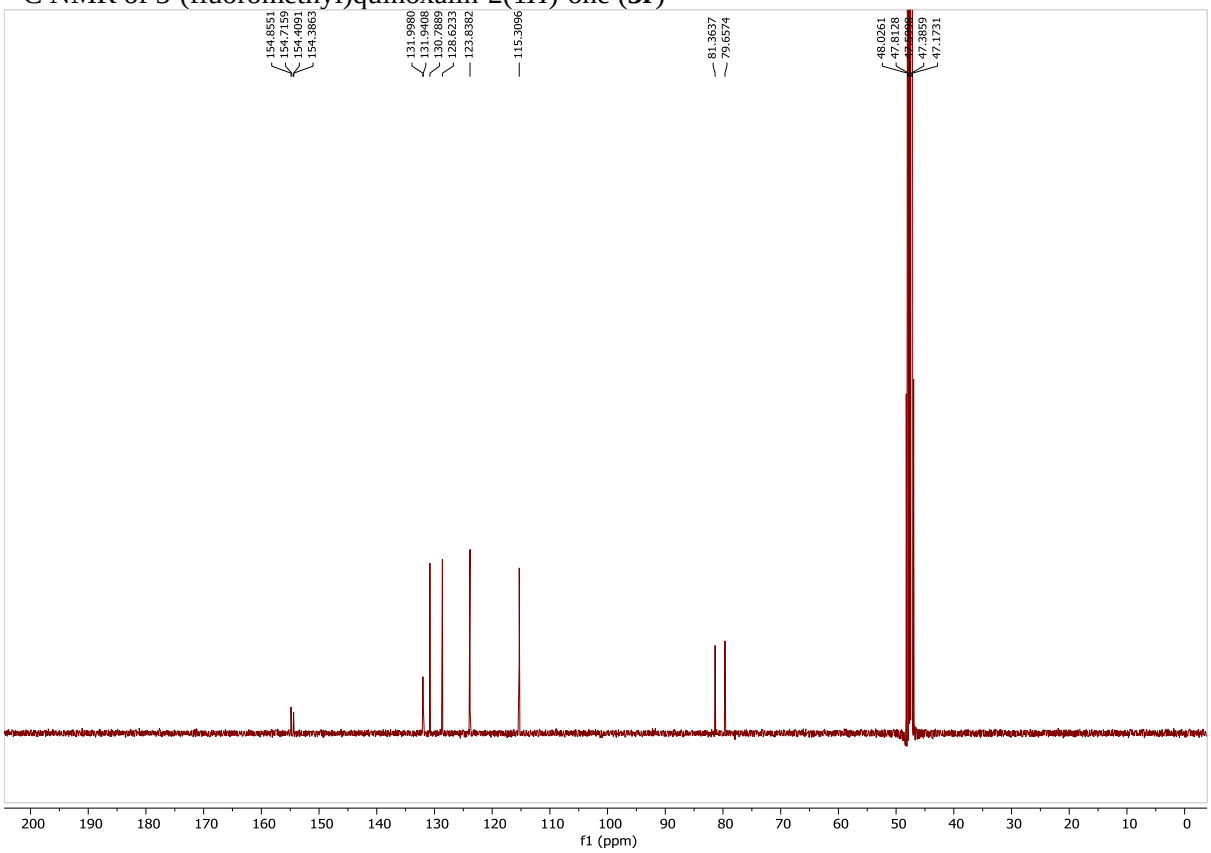
^{1}H NMR of 3-(fluoromethyl)quinoxalin-2(1*H*)-one (**3r**)



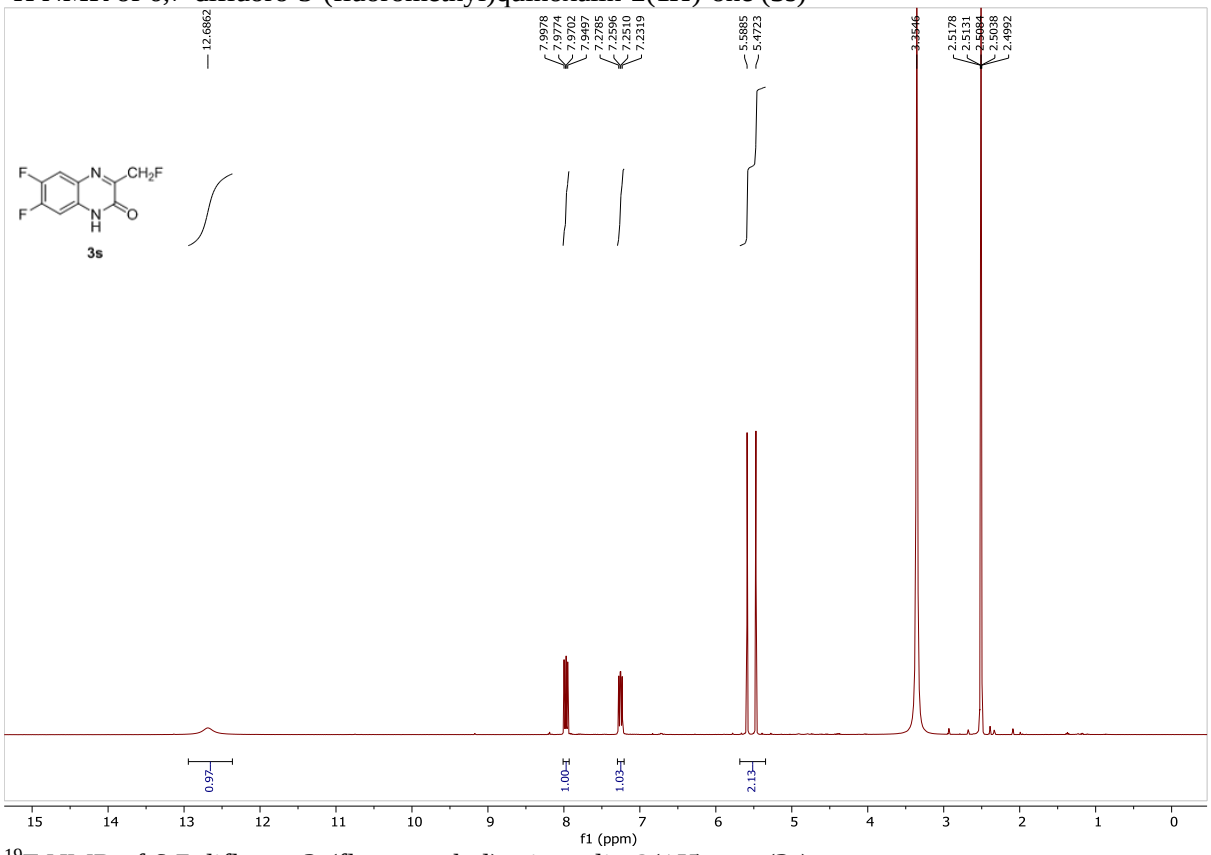
^{19}F NMR of 3-(fluoromethyl)quinoxalin-2(1*H*)-one (**3r**)



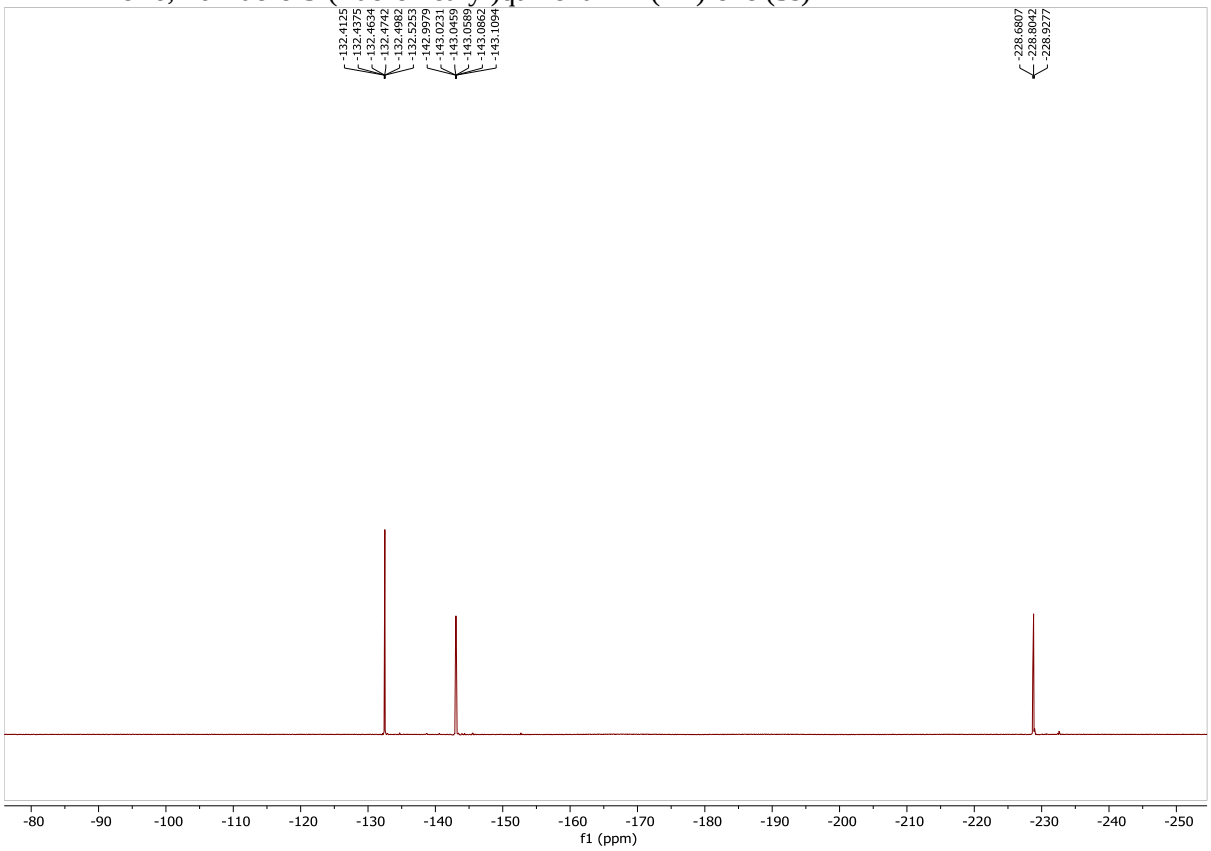
^{13}C NMR of 3-(fluoromethyl)quinoxalin-2(1*H*)-one (**3r**)



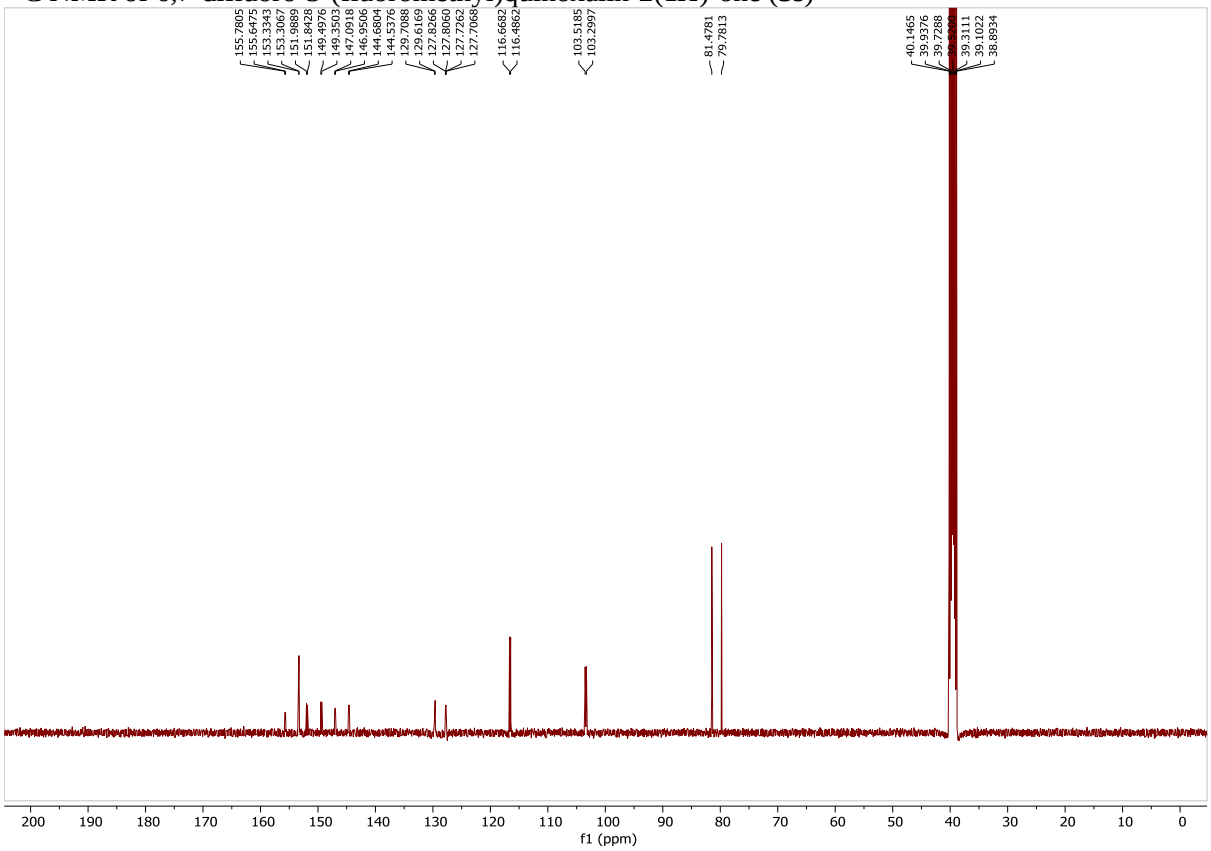
^{1}H NMR of 6,7-difluoro-3-(fluoromethyl)quinoxalin-2(1*H*)-one (**3s**)



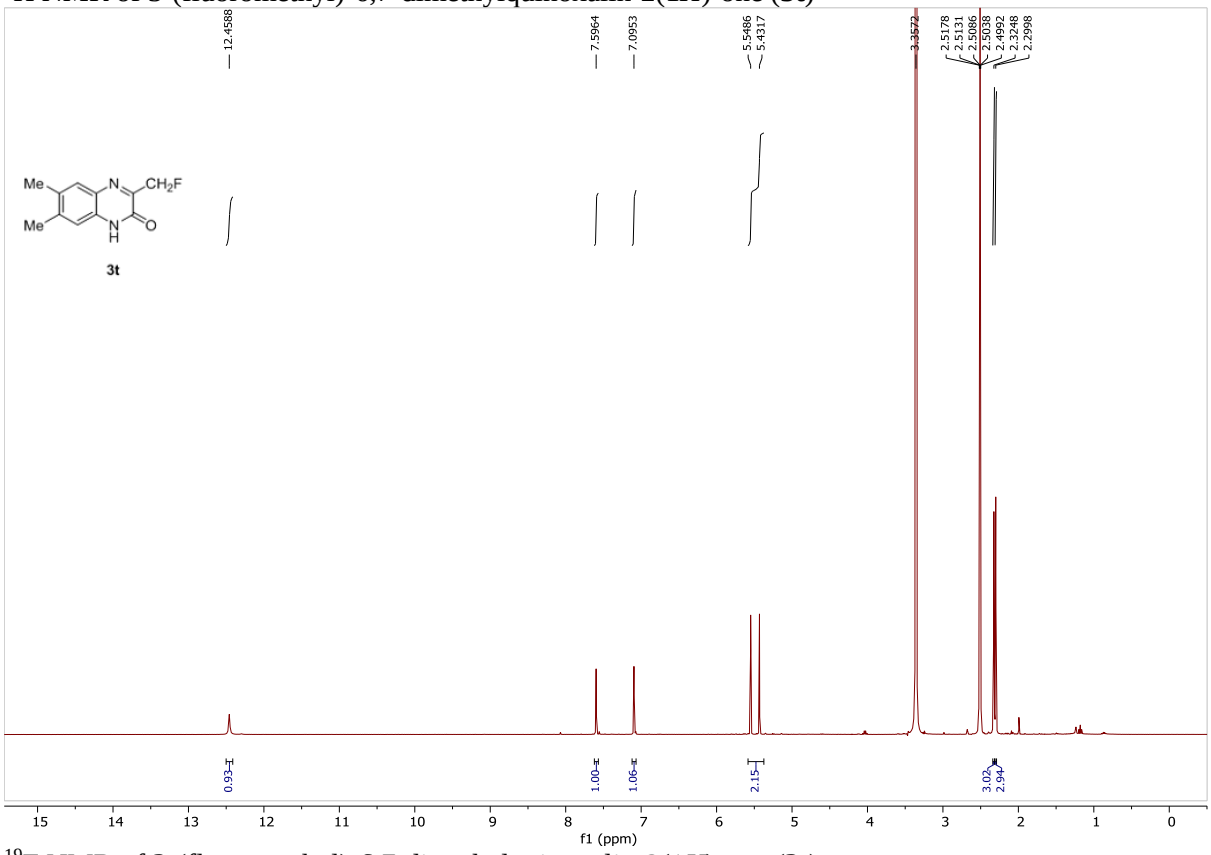
^{19}F NMR of 6,7-difluoro-3-(fluoromethyl)quinoxalin-2(1*H*)-one (**3s**)



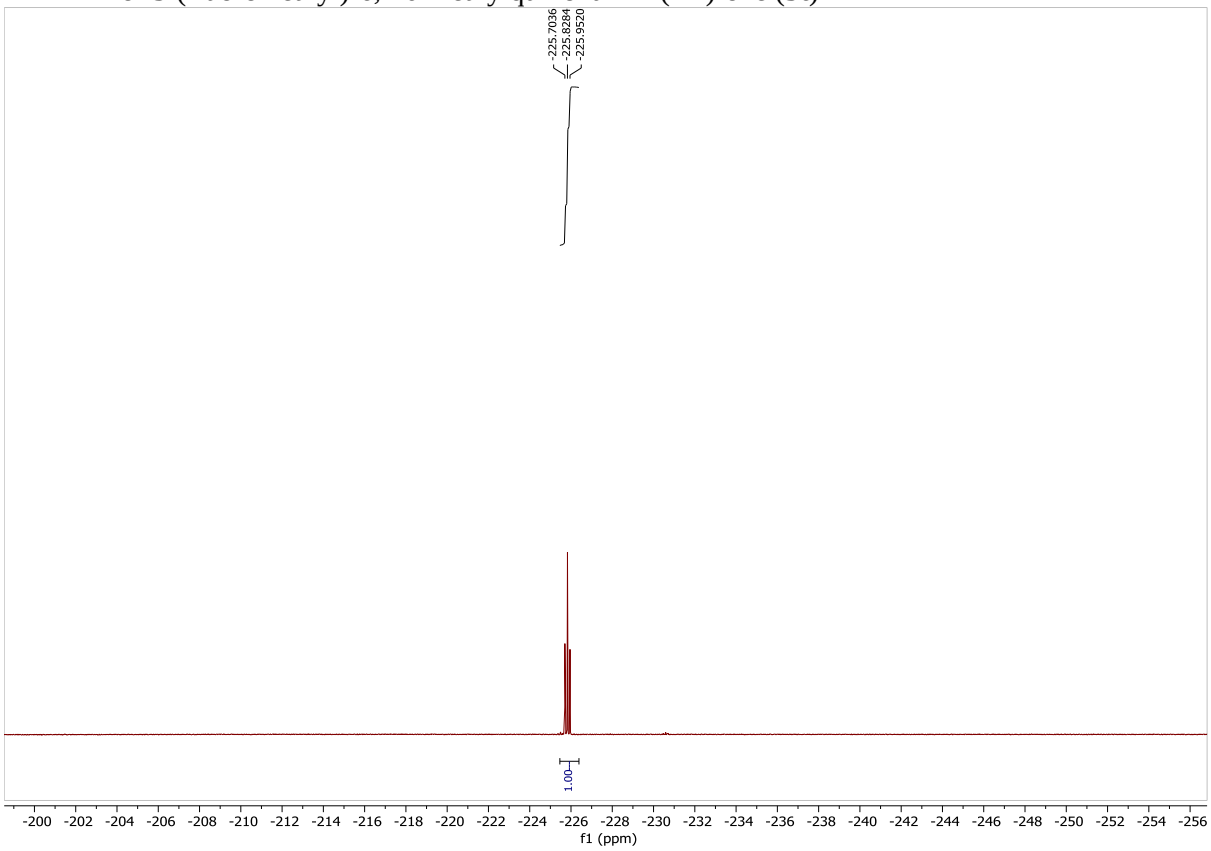
^{13}C NMR of 6,7-difluoro-3-(fluoromethyl)quinoxalin-2(1*H*)-one (**3s**)



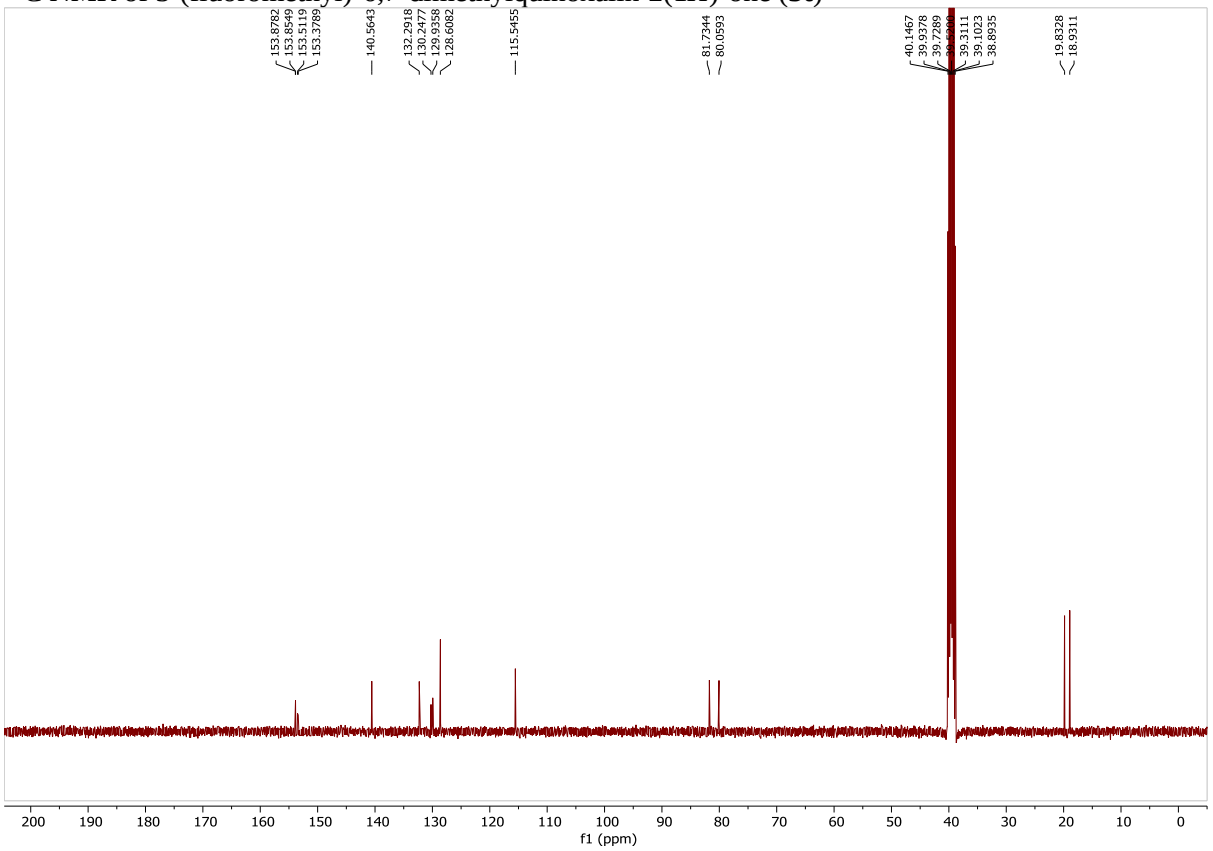
^{1}H NMR of 3-(fluoromethyl)-6,7-dimethylquinoxalin-2(1*H*)-one (**3t**)



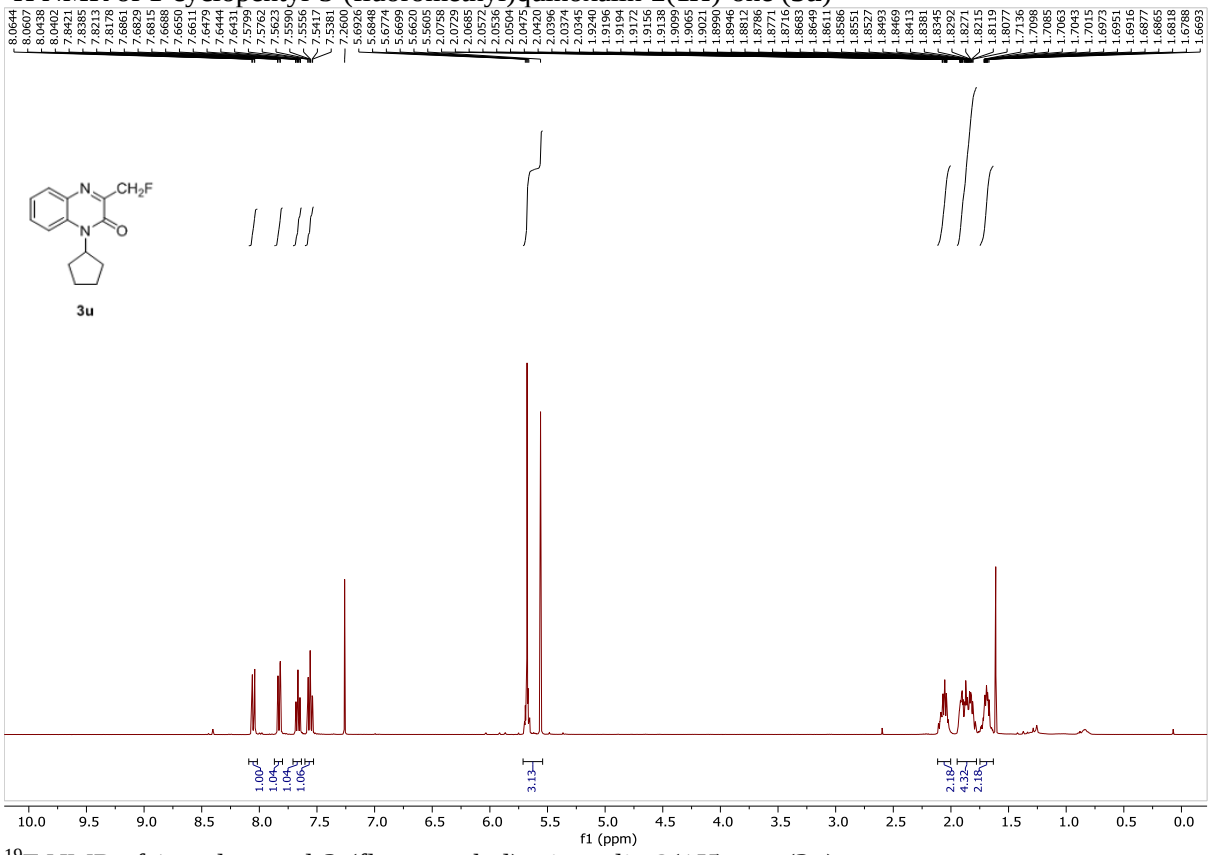
^{19}F NMR of 3-(fluoromethyl)-6,7-dimethylquinoxalin-2(1*H*)-one (**3t**)



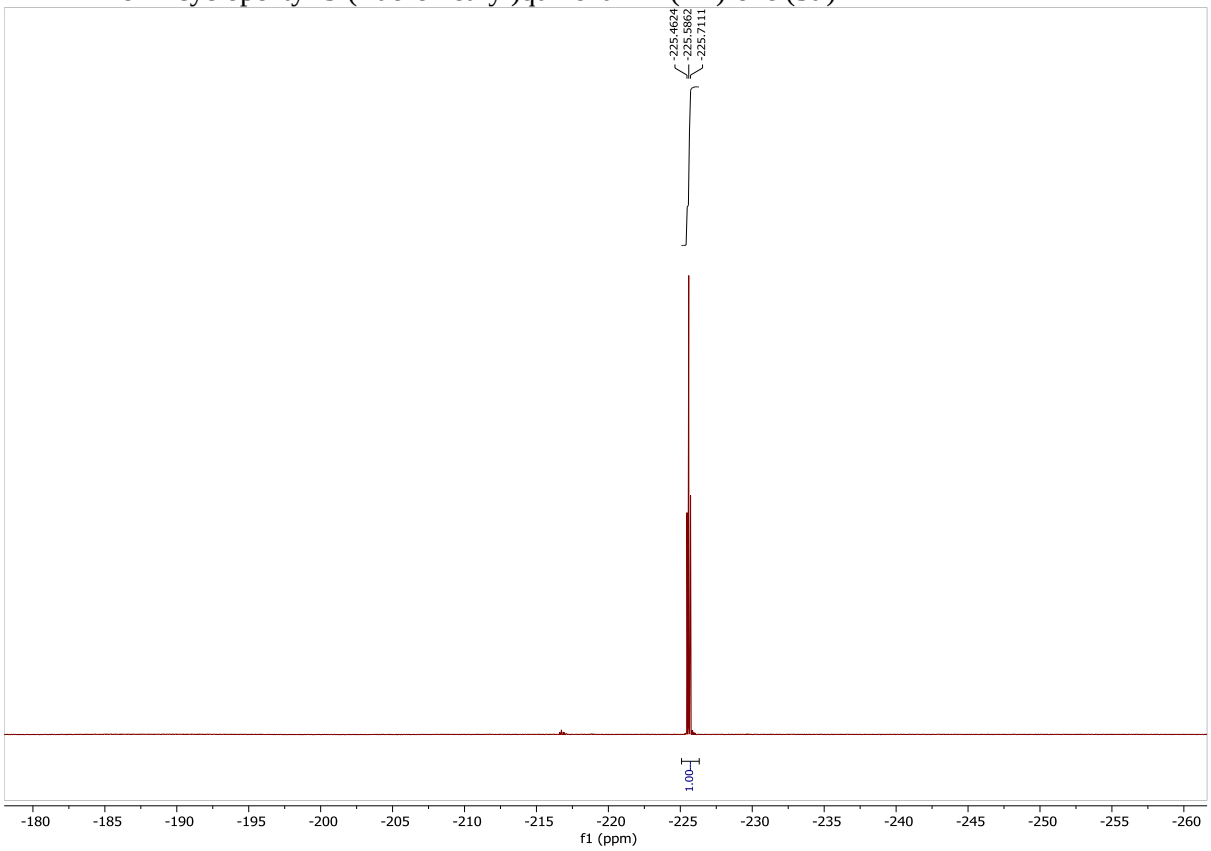
^{13}C NMR of 3-(fluoromethyl)-6,7-dimethylquinoxalin-2(1*H*)-one (**3t**)



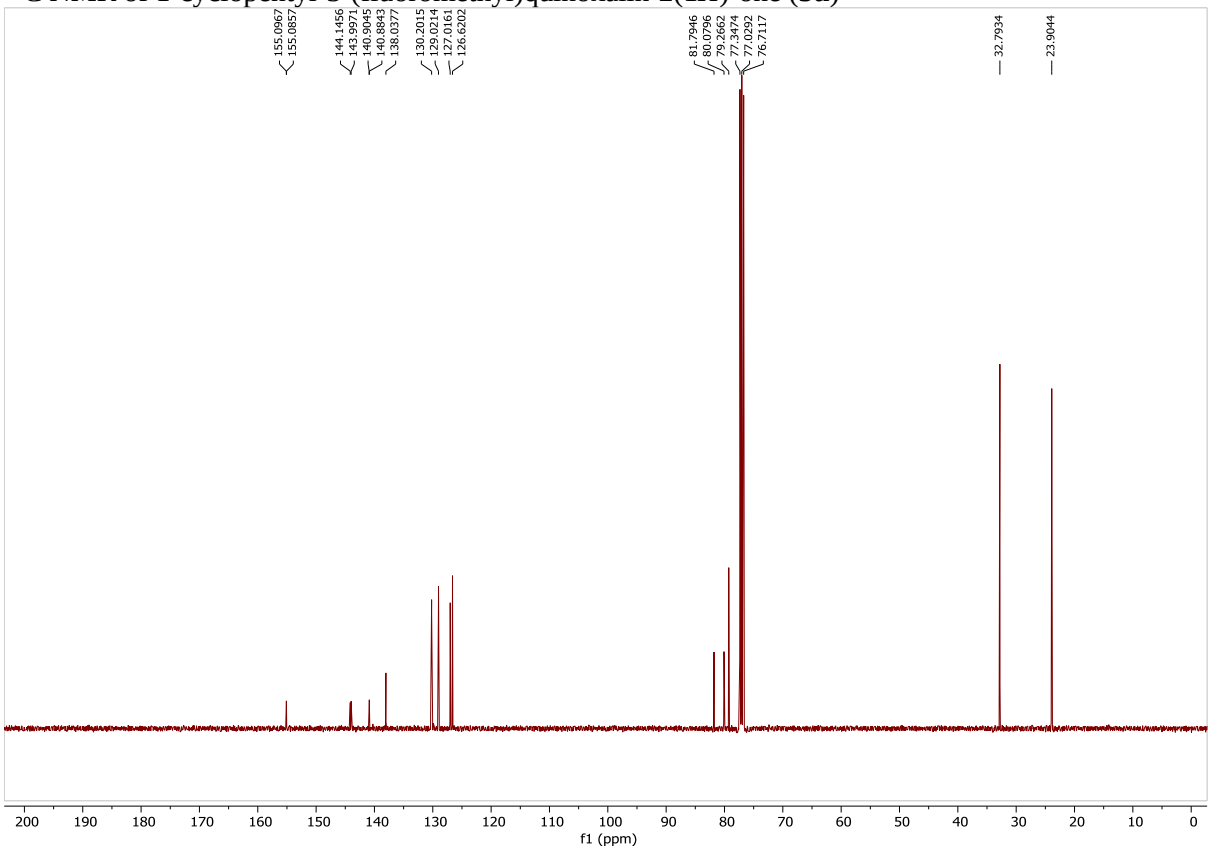
^{1}H NMR of 1-cyclopentyl-3-(fluoromethyl)quinoxalin-2(1*H*)-one (**3u**)



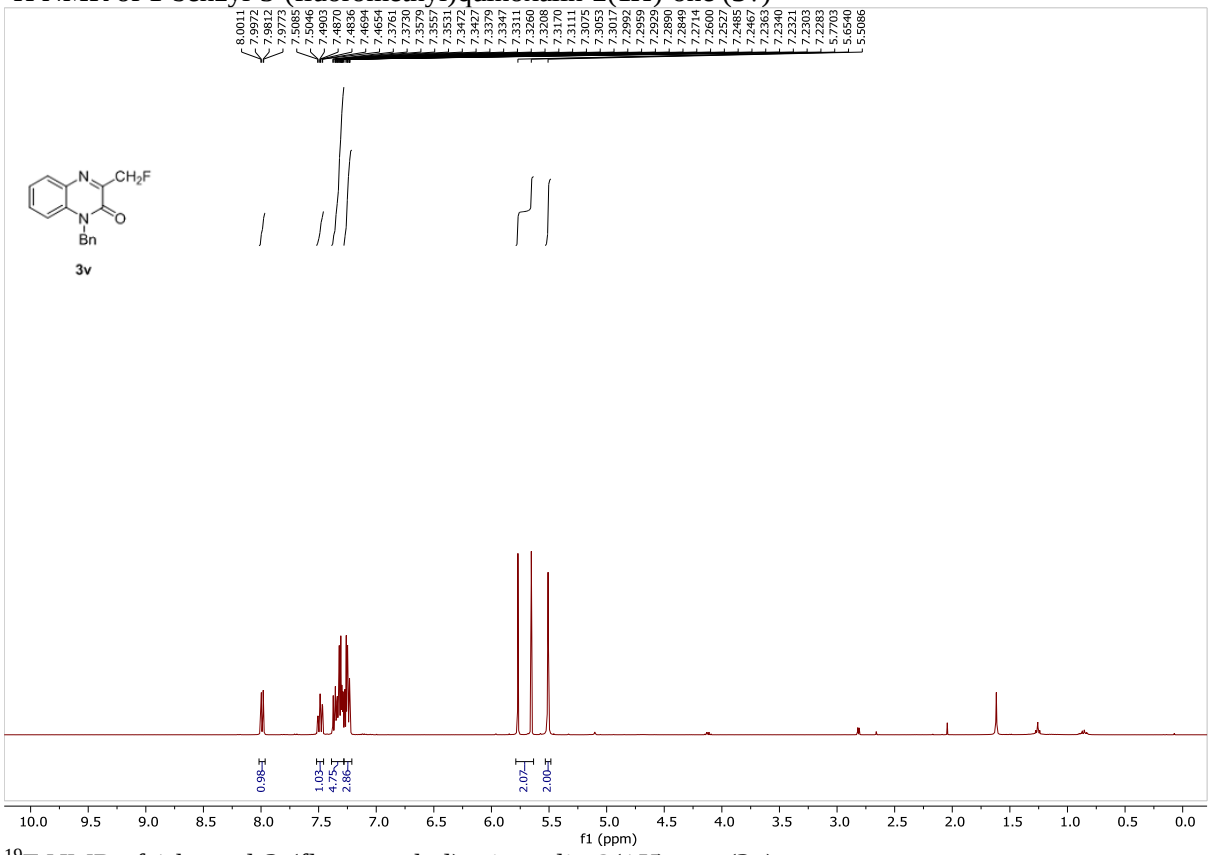
^{19}F NMR of 1-cyclopentyl-3-(fluoromethyl)quinoxalin-2(1*H*)-one (**3u**)



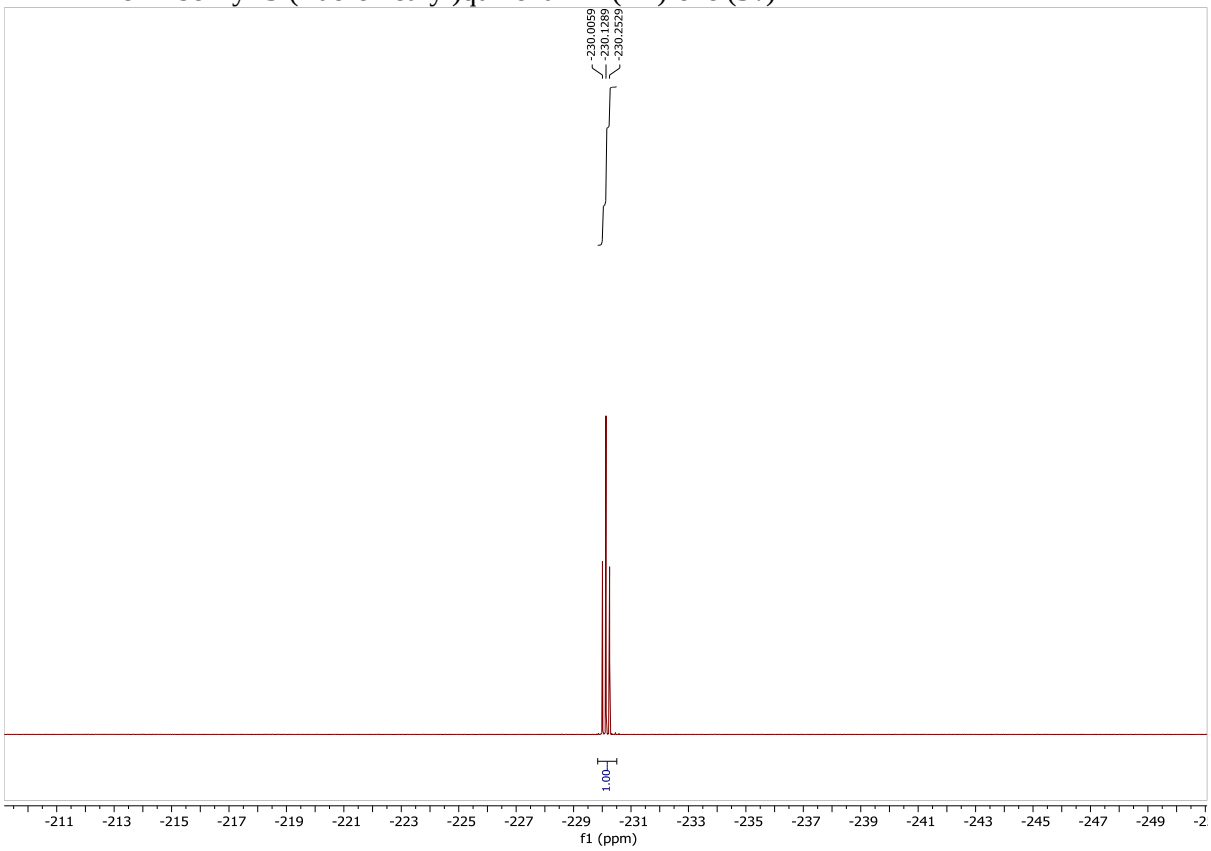
^{13}C NMR of 1-cyclopentyl-3-(fluoromethyl)quinoxalin-2(1*H*)-one (**3u**)



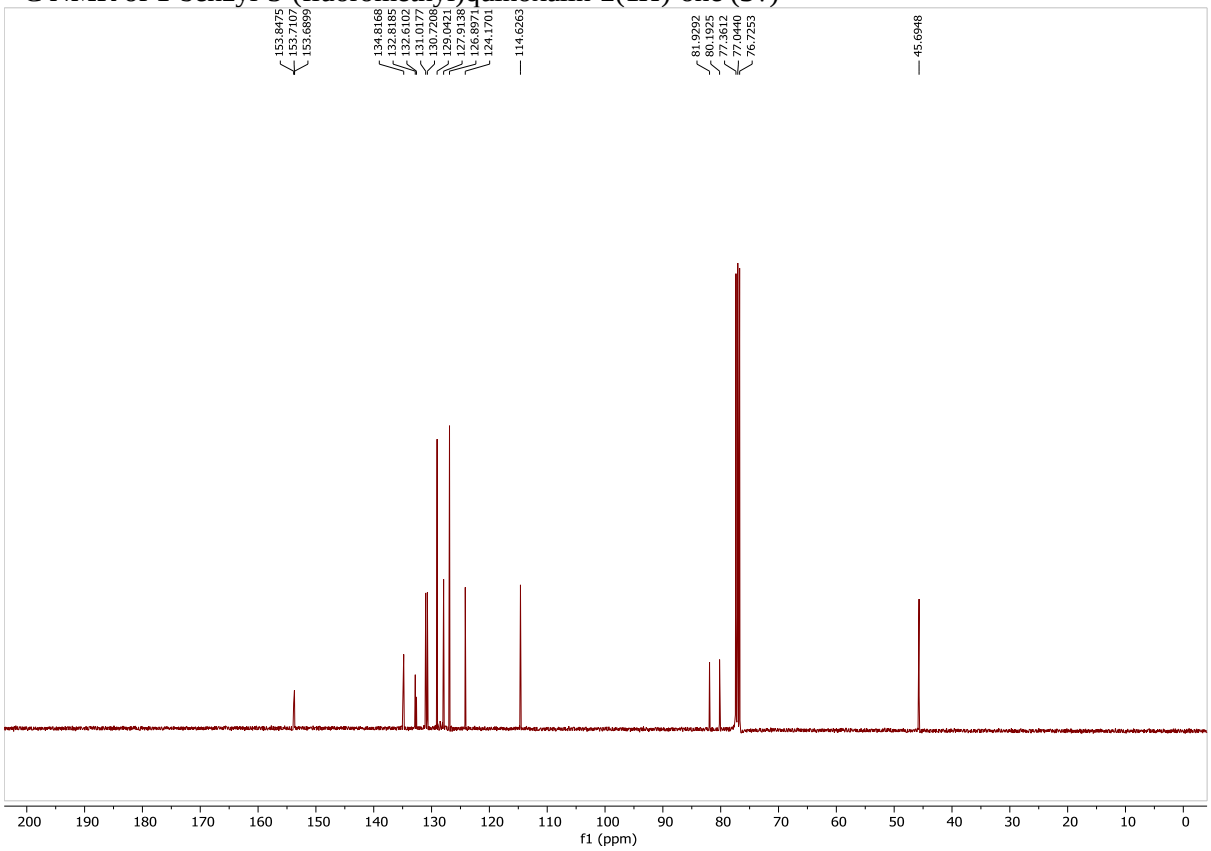
^{1}H NMR of 1-benzyl-3-(fluoromethyl)quinoxalin-2(1*H*)-one (**3v**)



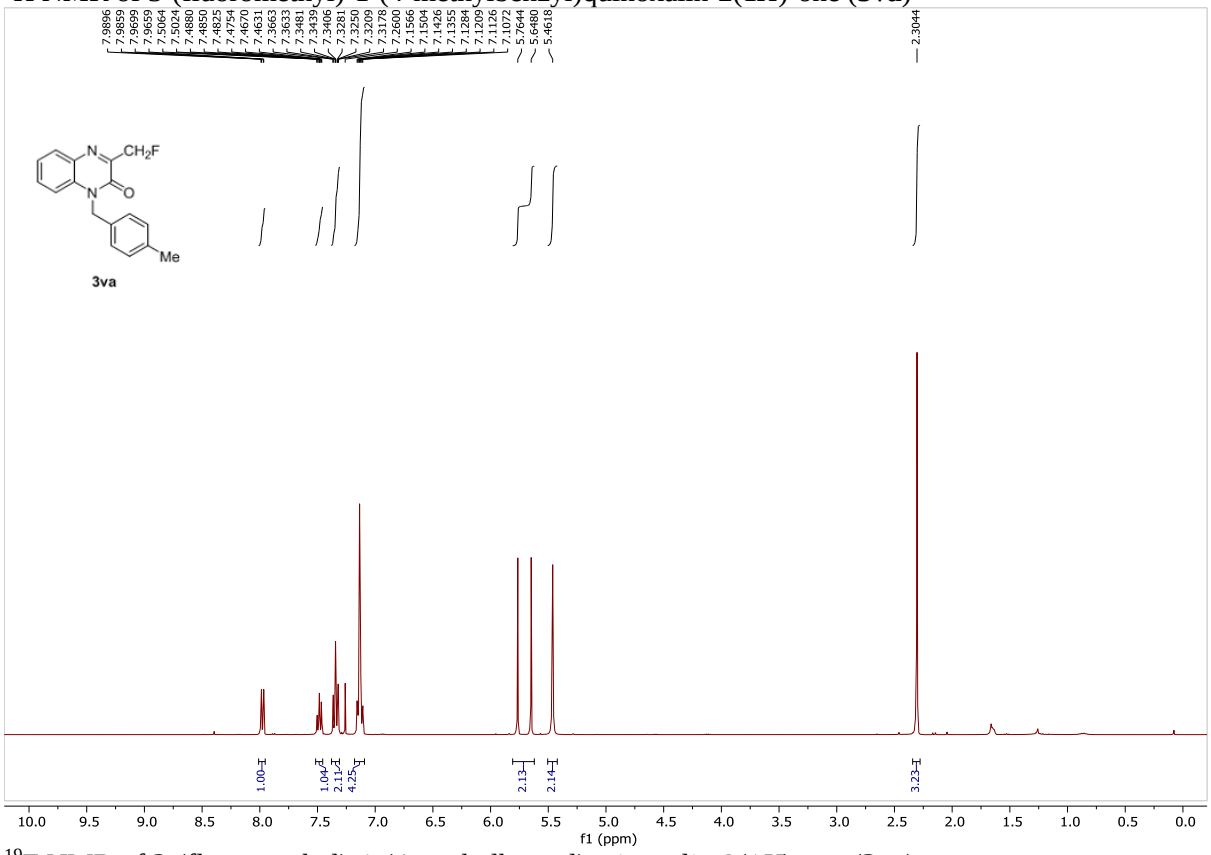
^{19}F NMR of 1-benzyl-3-(fluoromethyl)quinoxalin-2(1*H*)-one (**3v**)



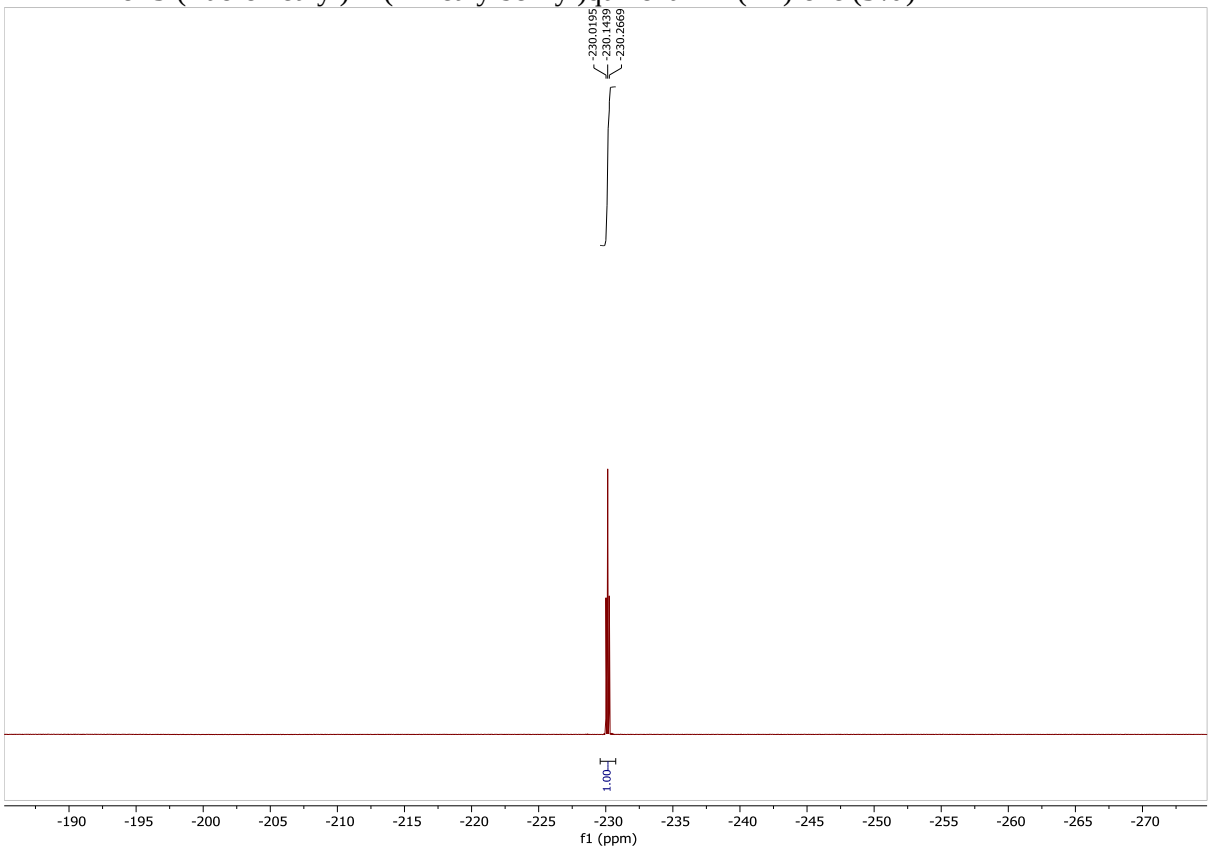
^{13}C NMR of 1-benzyl-3-(fluoromethyl)quinoxalin-2(1*H*)-one (**3v**)



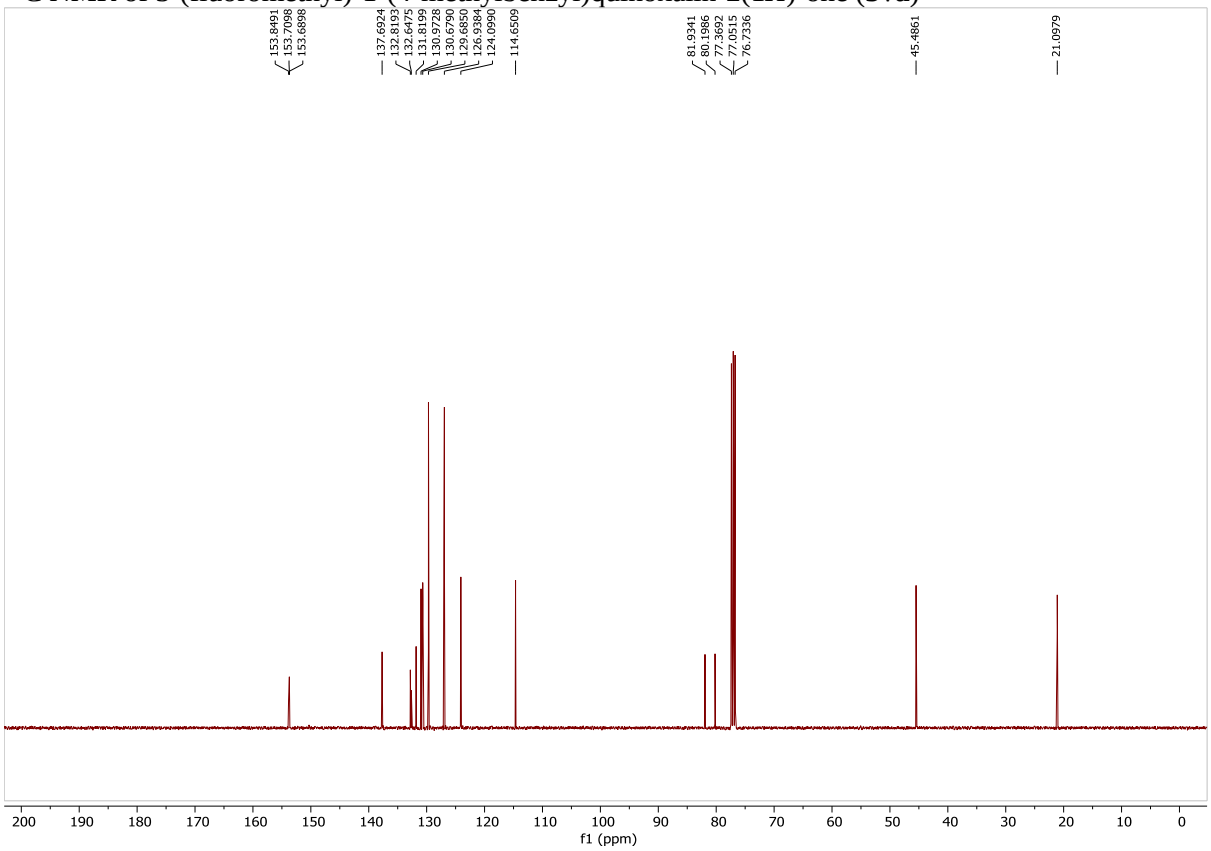
^{1}H NMR of 3-(fluoromethyl)-1-(4-methylbenzyl)quinoxalin-2(1*H*)-one (**3va**)



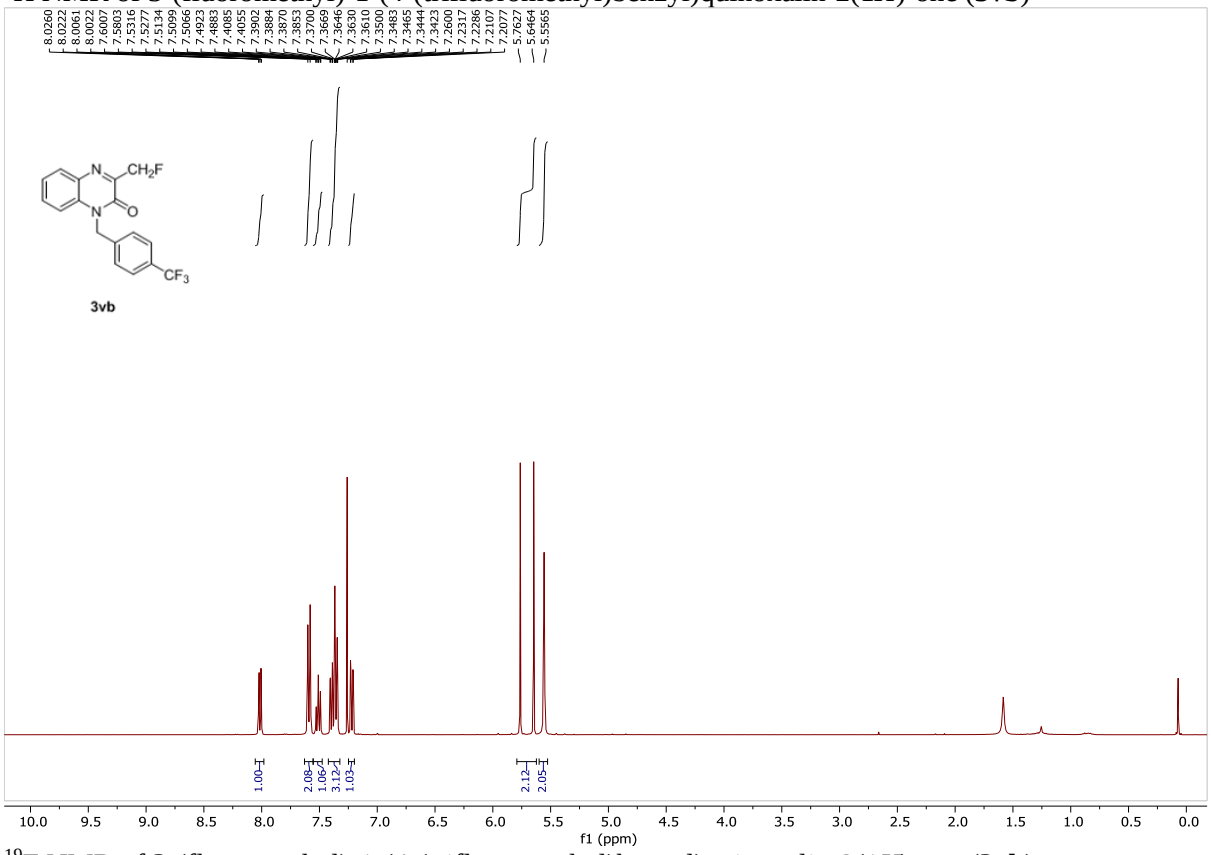
^{19}F NMR of 3-(fluoromethyl)-1-(4-methylbenzyl)quinoxalin-2(1*H*)-one (**3va**)



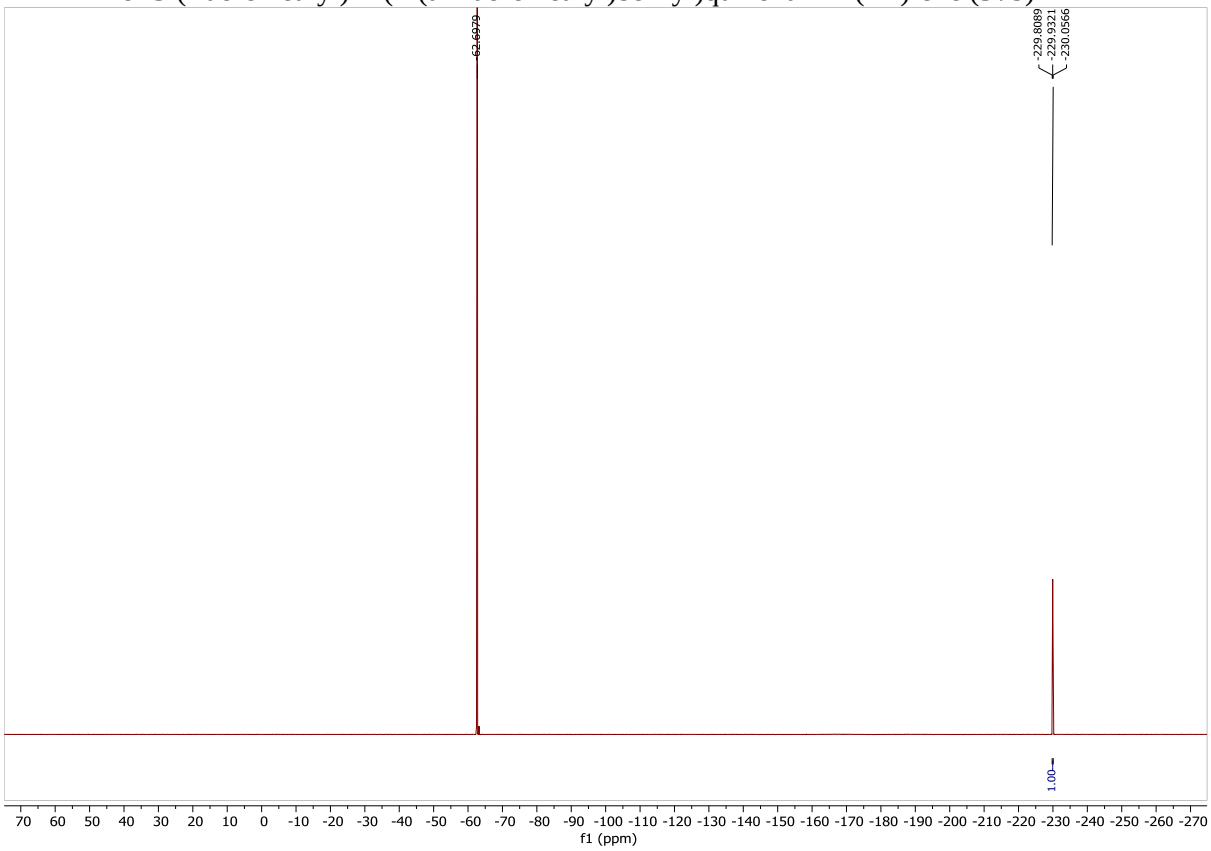
^{13}C NMR of 3-(fluoromethyl)-1-(4-methylbenzyl)quinoxalin-2(1*H*)-one (**3va**)



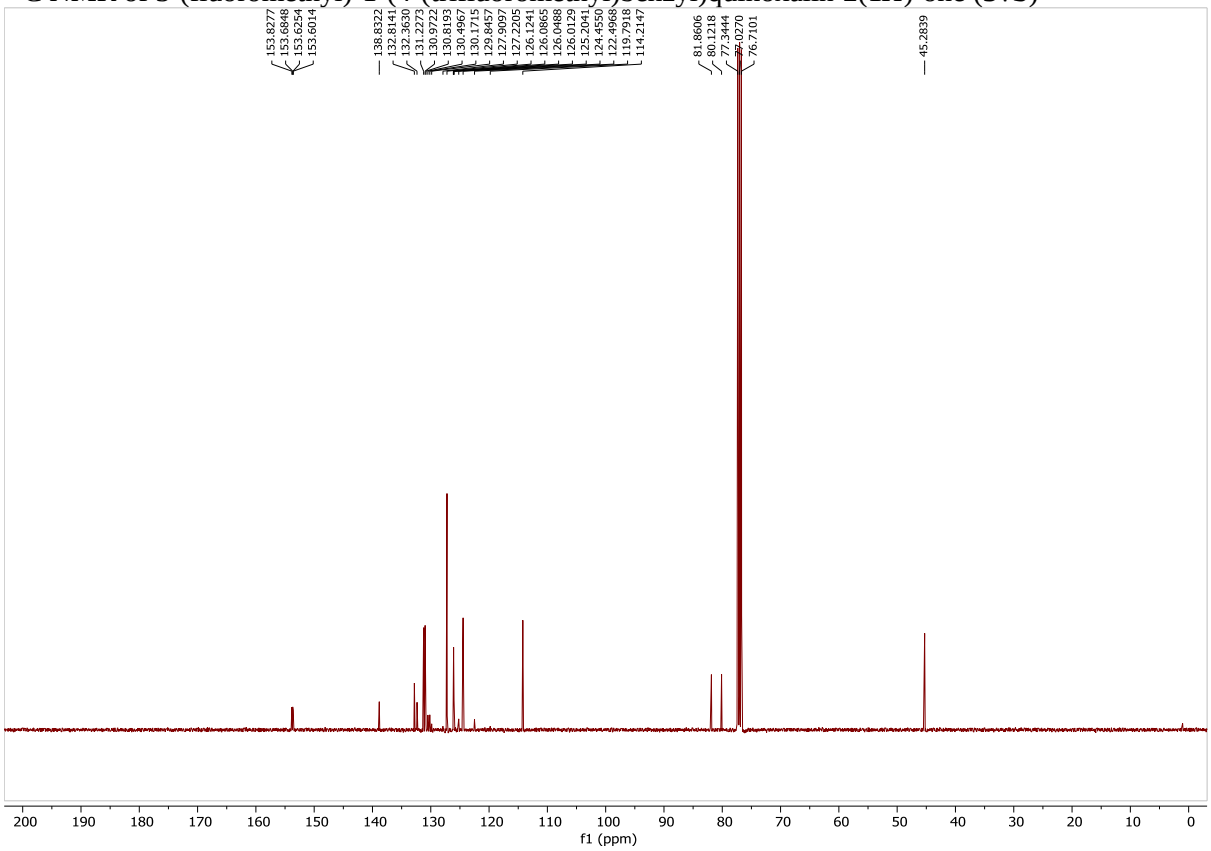
^{1}H NMR of 3-(fluoromethyl)-1-(4-(trifluoromethyl)benzyl)quinoxalin-2(1*H*)-one (**3vb**)



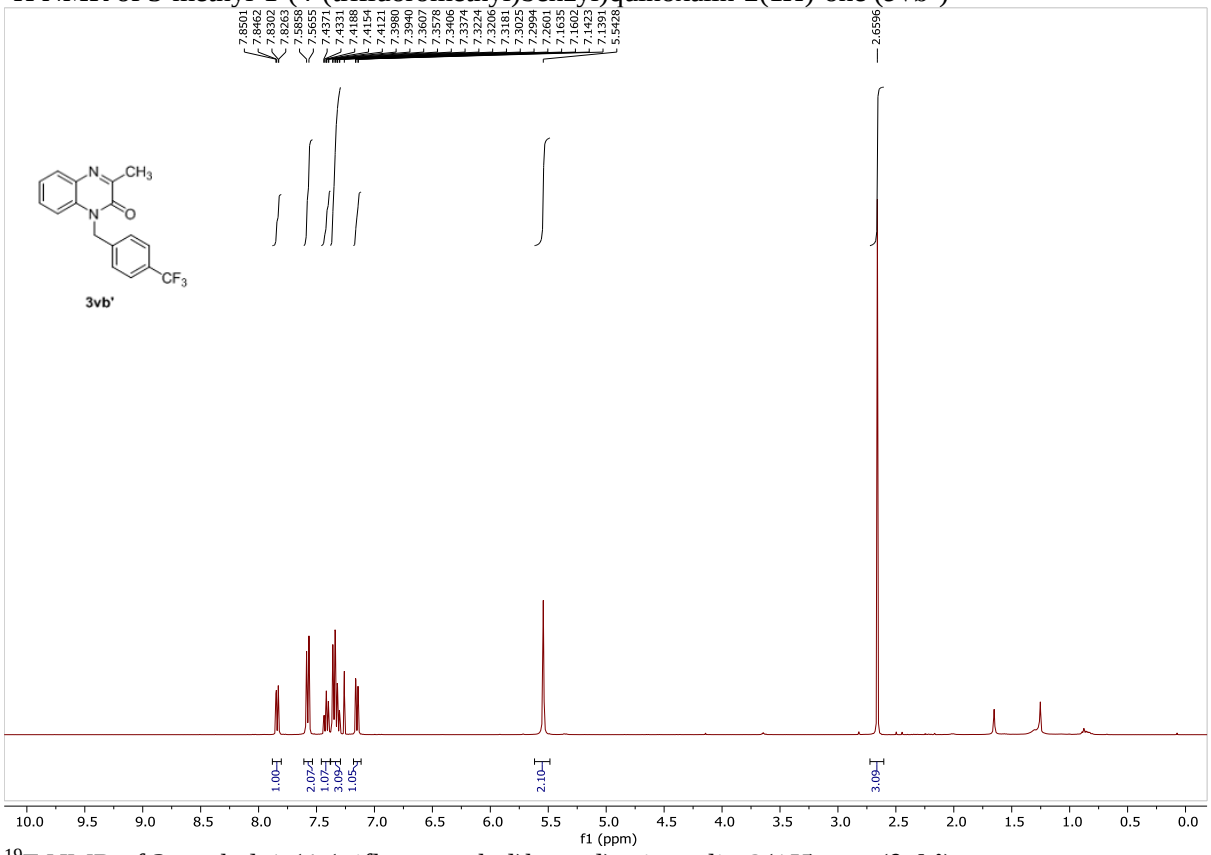
^{19}F NMR of 3-(fluoromethyl)-1-(4-(trifluoromethyl)benzyl)quinoxalin-2(1*H*)-one (**3vb**)



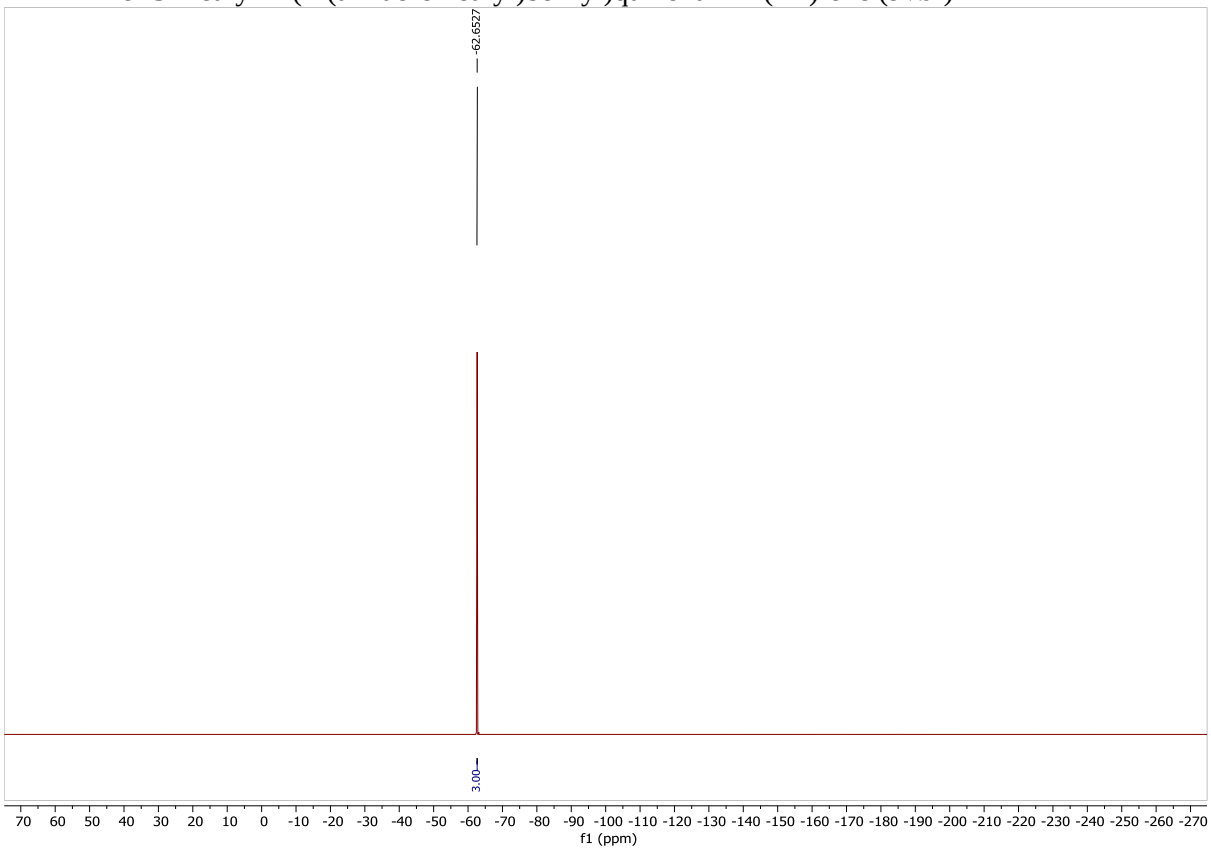
^{13}C NMR of 3-(fluoromethyl)-1-(4-(trifluoromethyl)benzyl)quinoxalin-2(1*H*)-one (**3vb**)



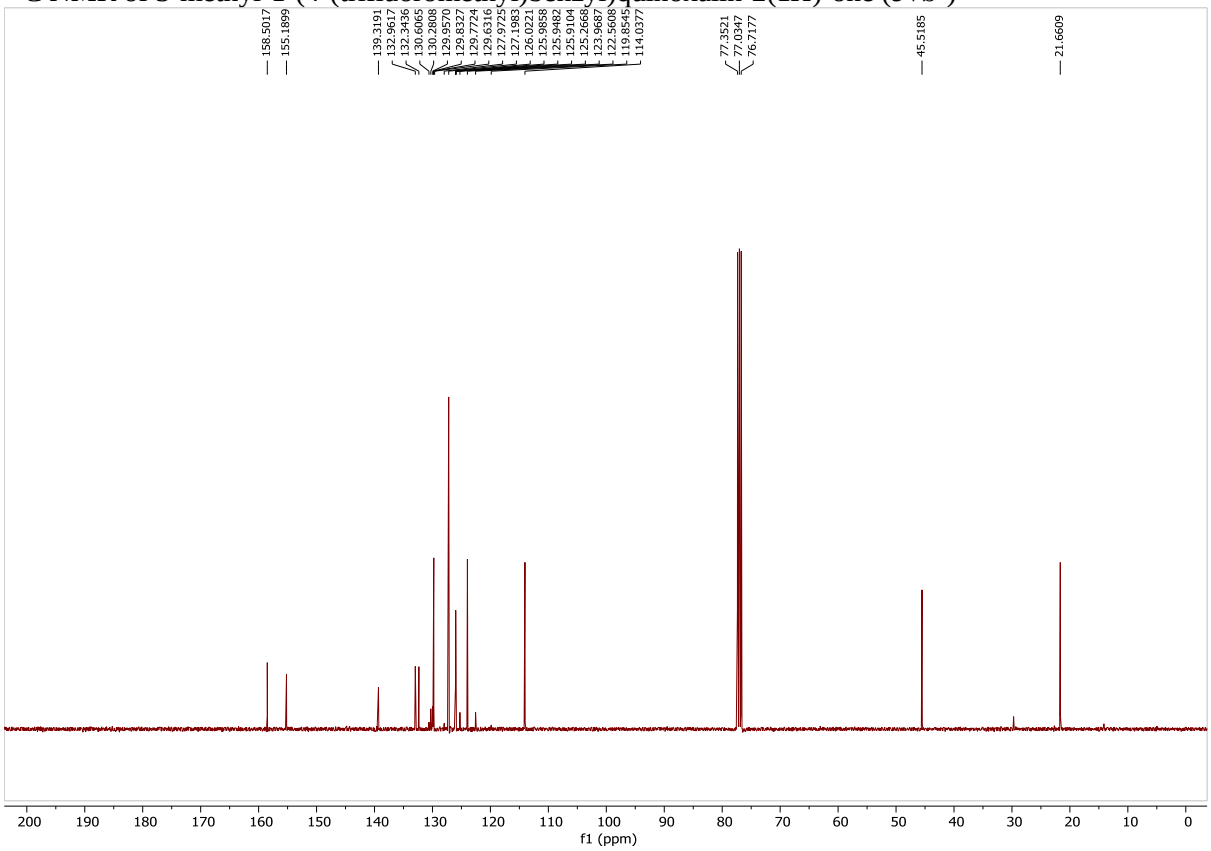
^{1}H NMR of 3-methyl-1-(4-(trifluoromethyl)benzyl)quinoxalin-2(1*H*)-one (**3vb'**)



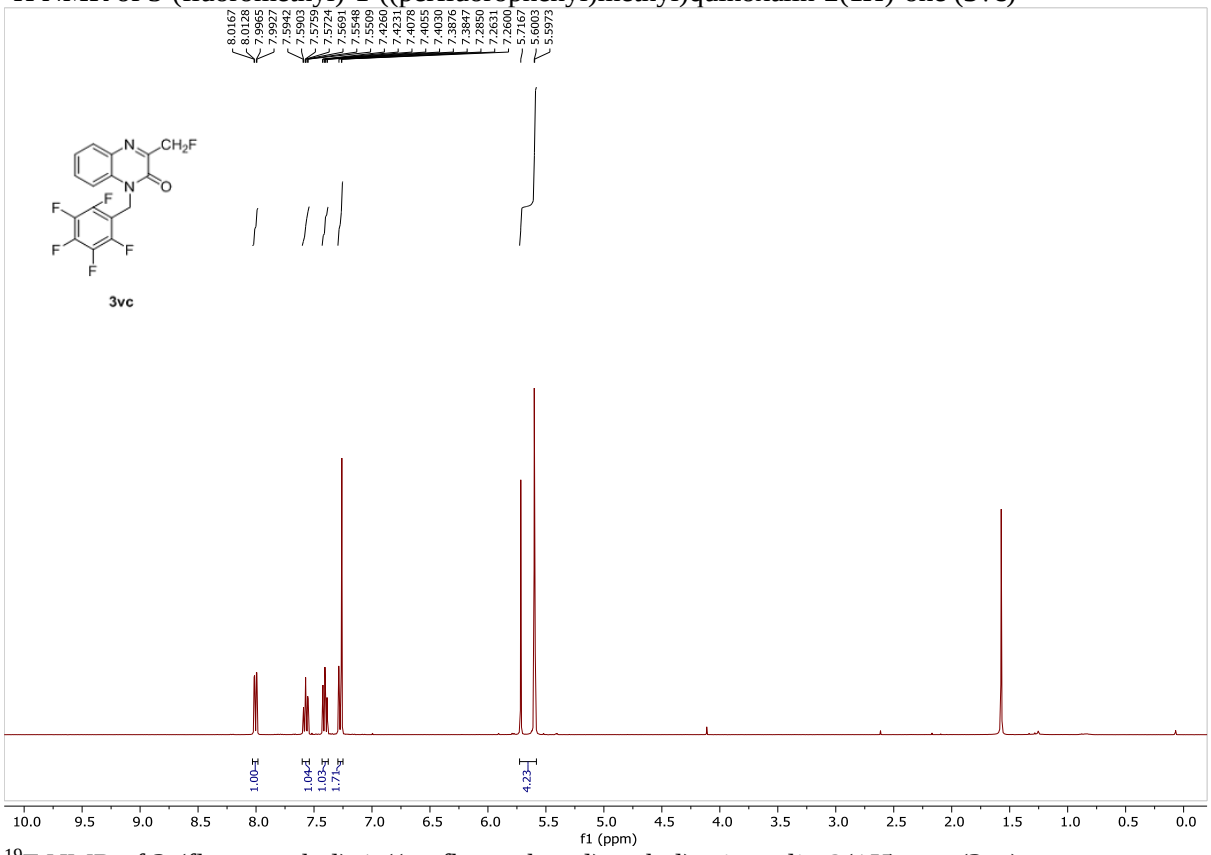
^{19}F NMR of 3-methyl-1-(4-(trifluoromethyl)benzyl)quinoxalin-2(1*H*)-one (**3vb'**)



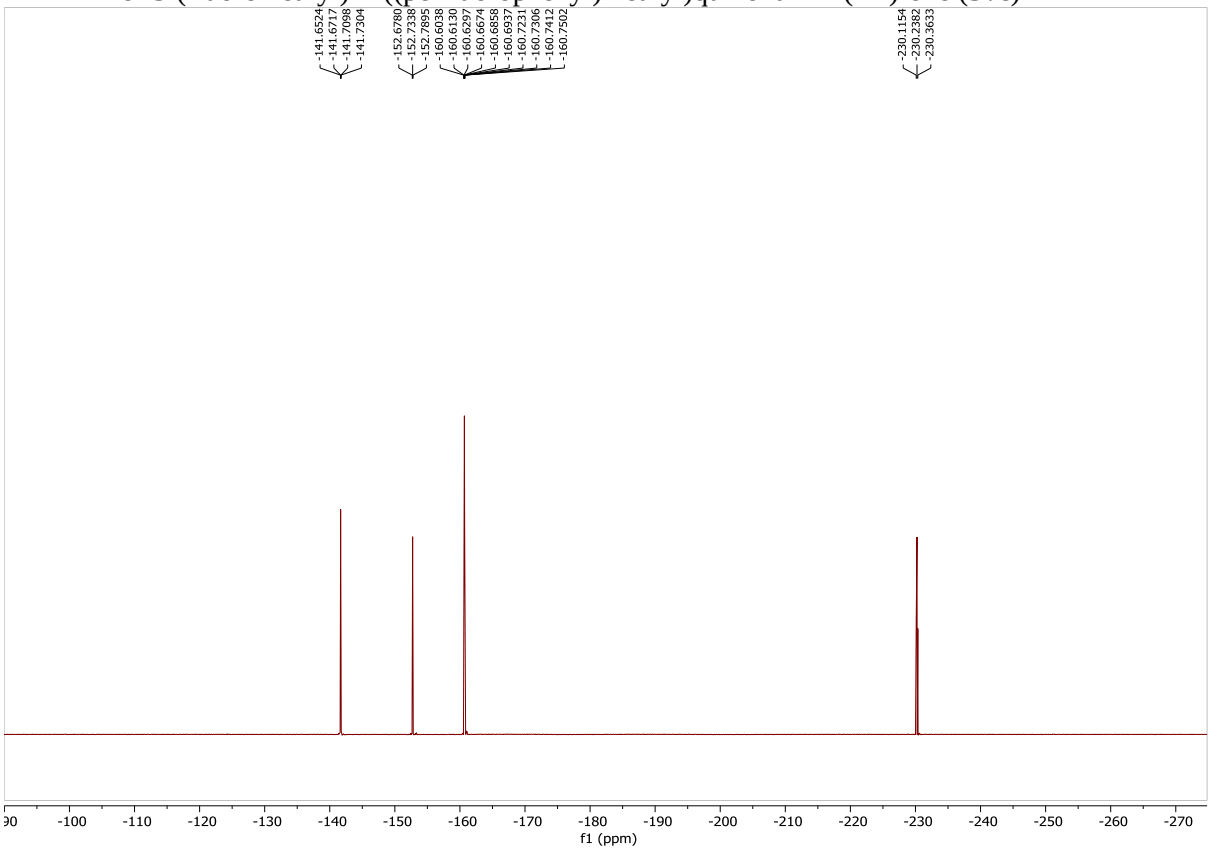
^{19}C NMR of 3-methyl-1-(4-(trifluoromethyl)benzyl)quinoxalin-2(1*H*)-one (**3vb'**)



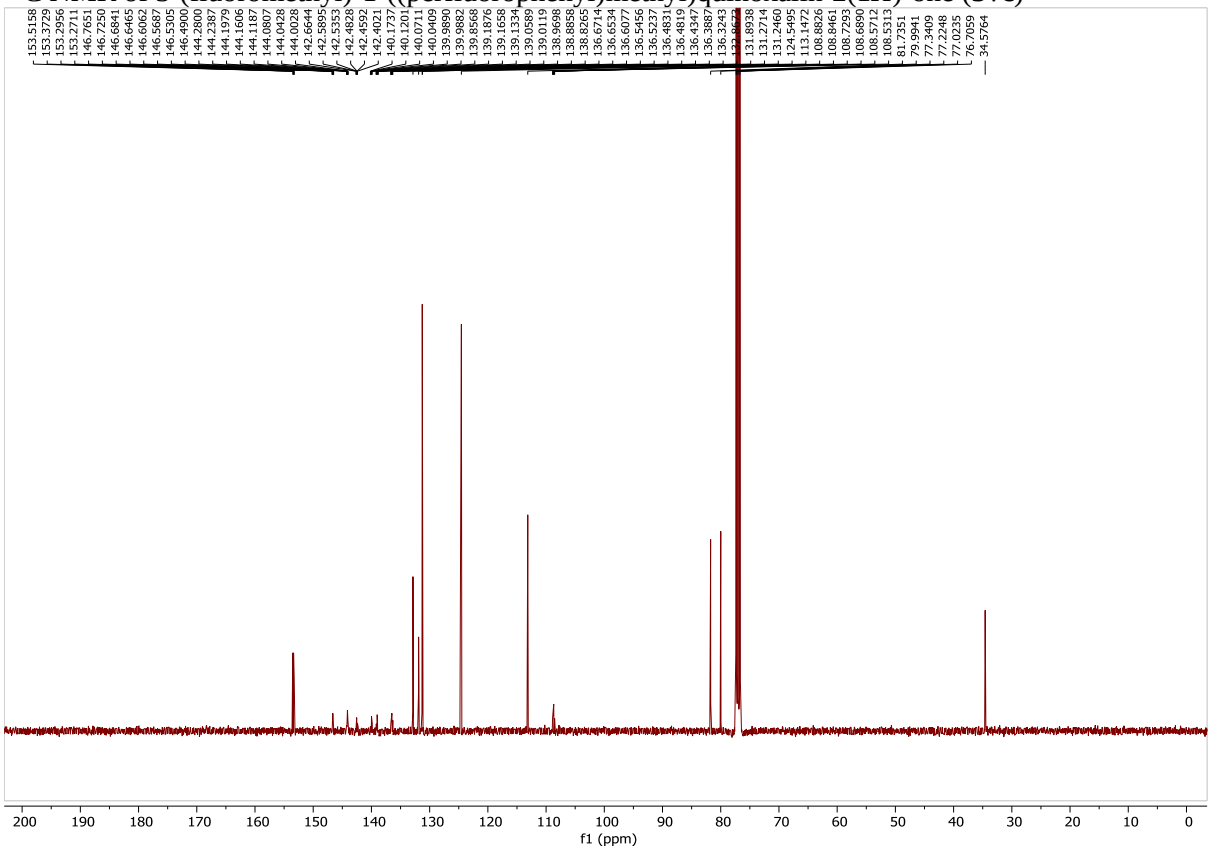
^{1}H NMR of 3-(fluoromethyl)-1-((perfluorophenyl)methyl)quinoxalin-2(1*H*)-one (**3vc**)



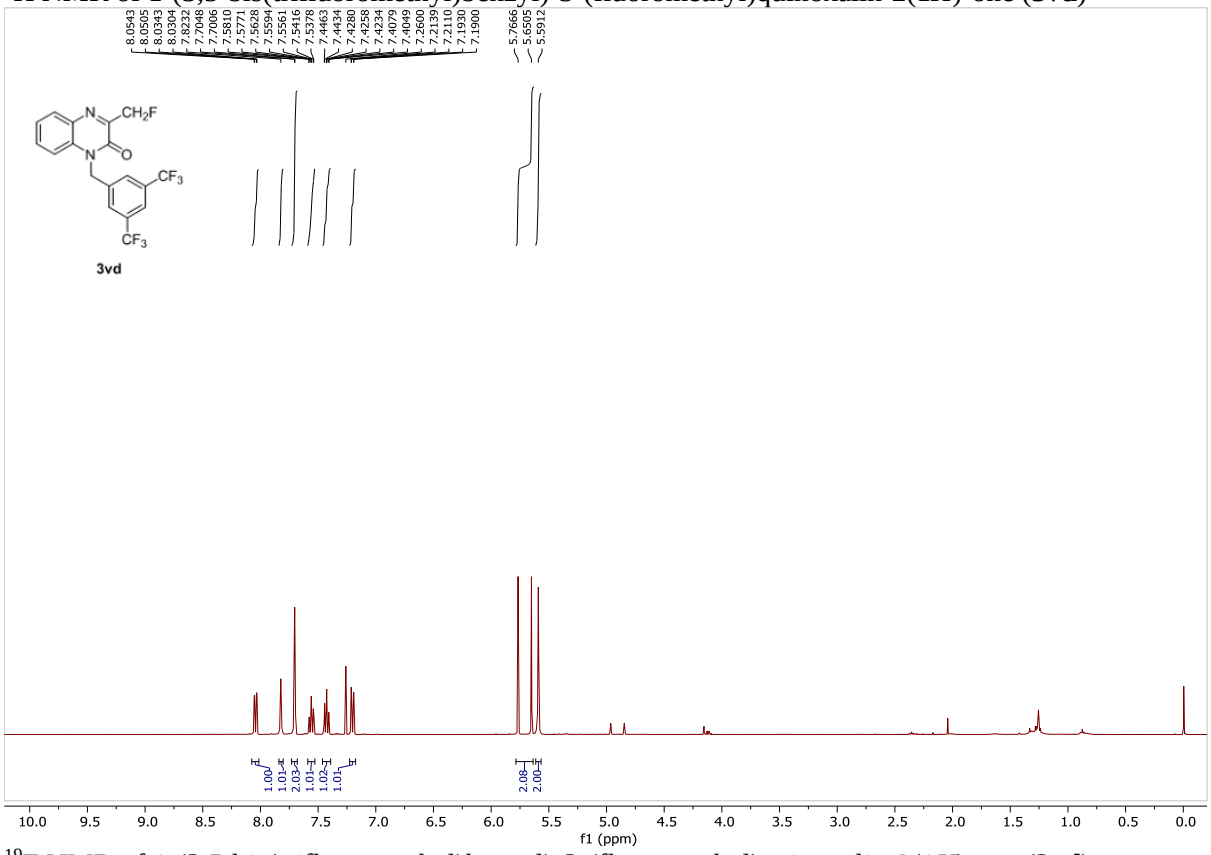
^{19}F NMR of 3-(fluoromethyl)-1-((perfluorophenyl)methyl)quinoxalin-2(1*H*)-one (**3vc**)



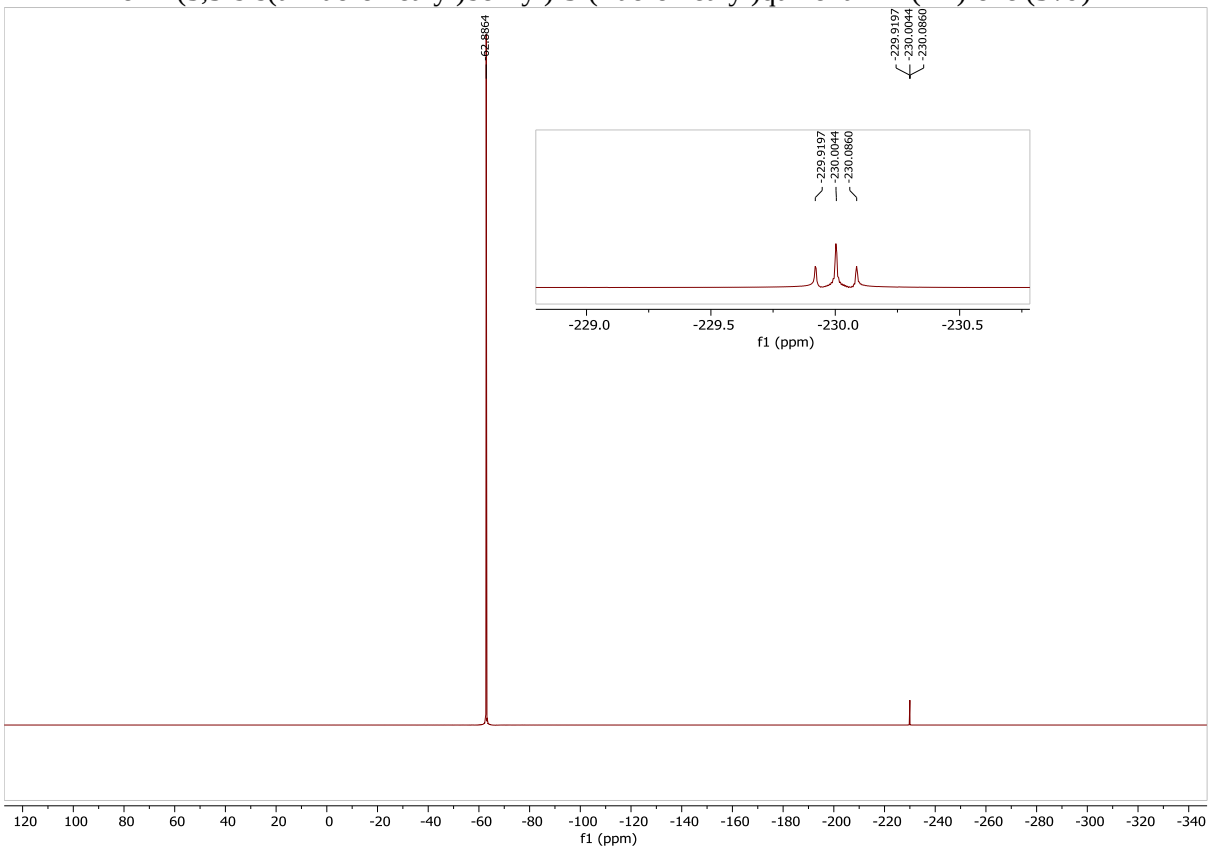
^{13}C NMR of 3-(fluoromethyl)-1-((perfluorophenyl)methyl)quinoxalin-2(1*H*)-one (**3vc**)



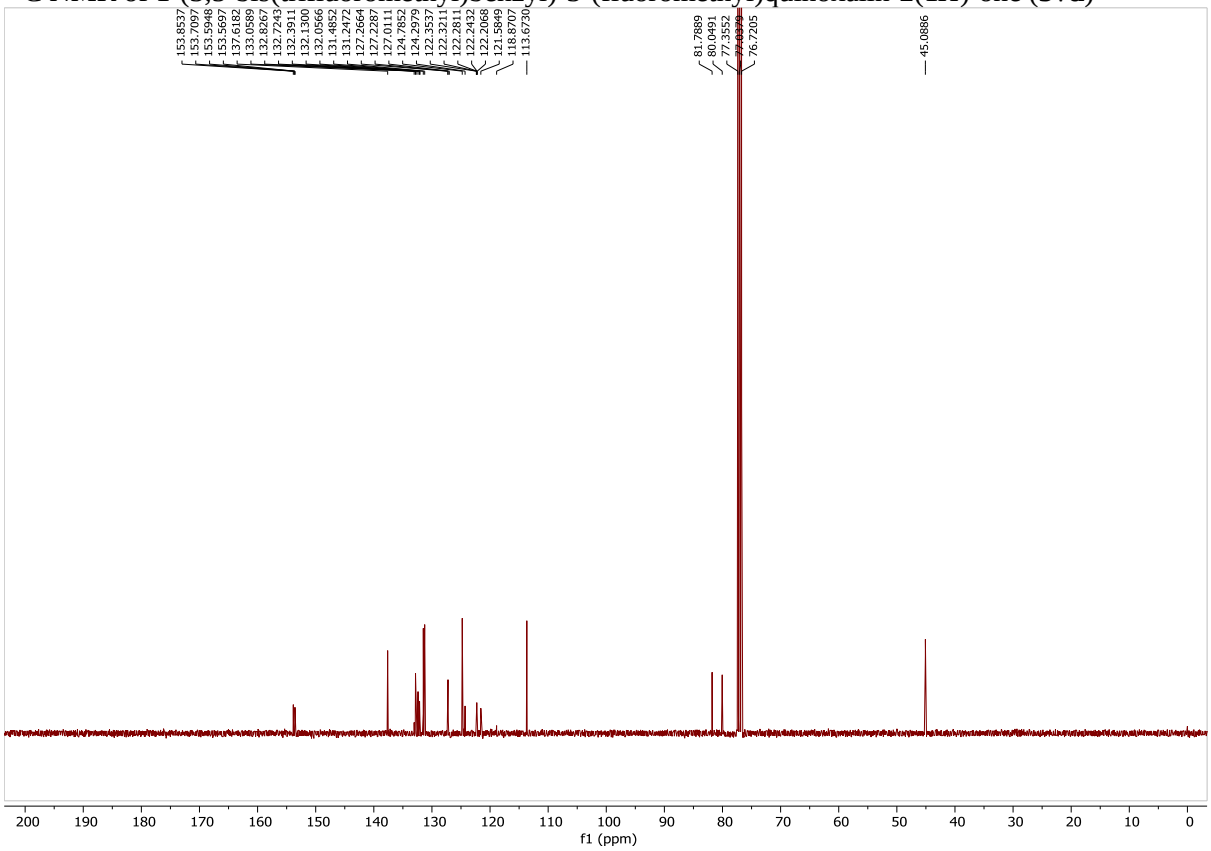
^{1}H NMR of 1-(3,5-bis(trifluoromethyl)benzyl)-3-(fluoromethyl)quinoxalin-2(1*H*)-one (**3vd**)



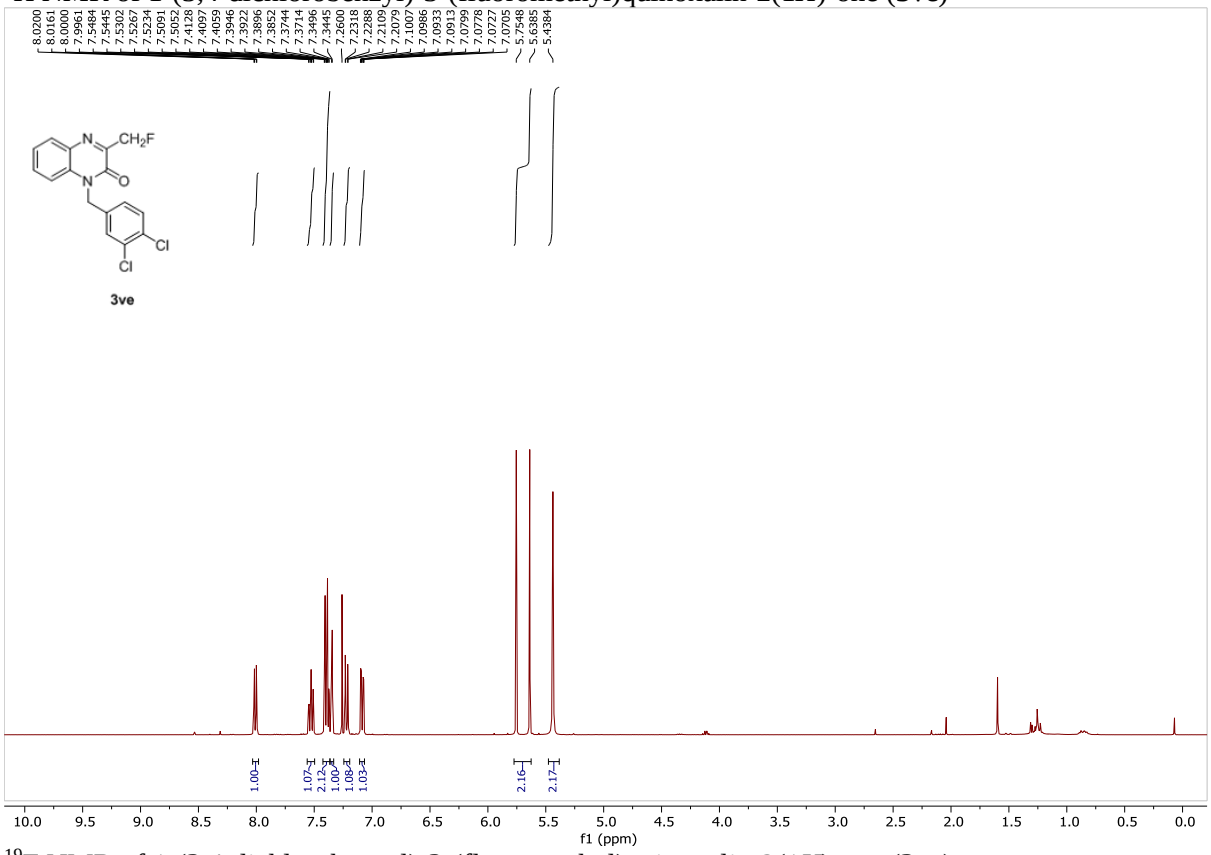
^{19}F NMR of 1-(3,5-bis(trifluoromethyl)benzyl)-3-(fluoromethyl)quinoxalin-2(1*H*)-one (**3vd**)



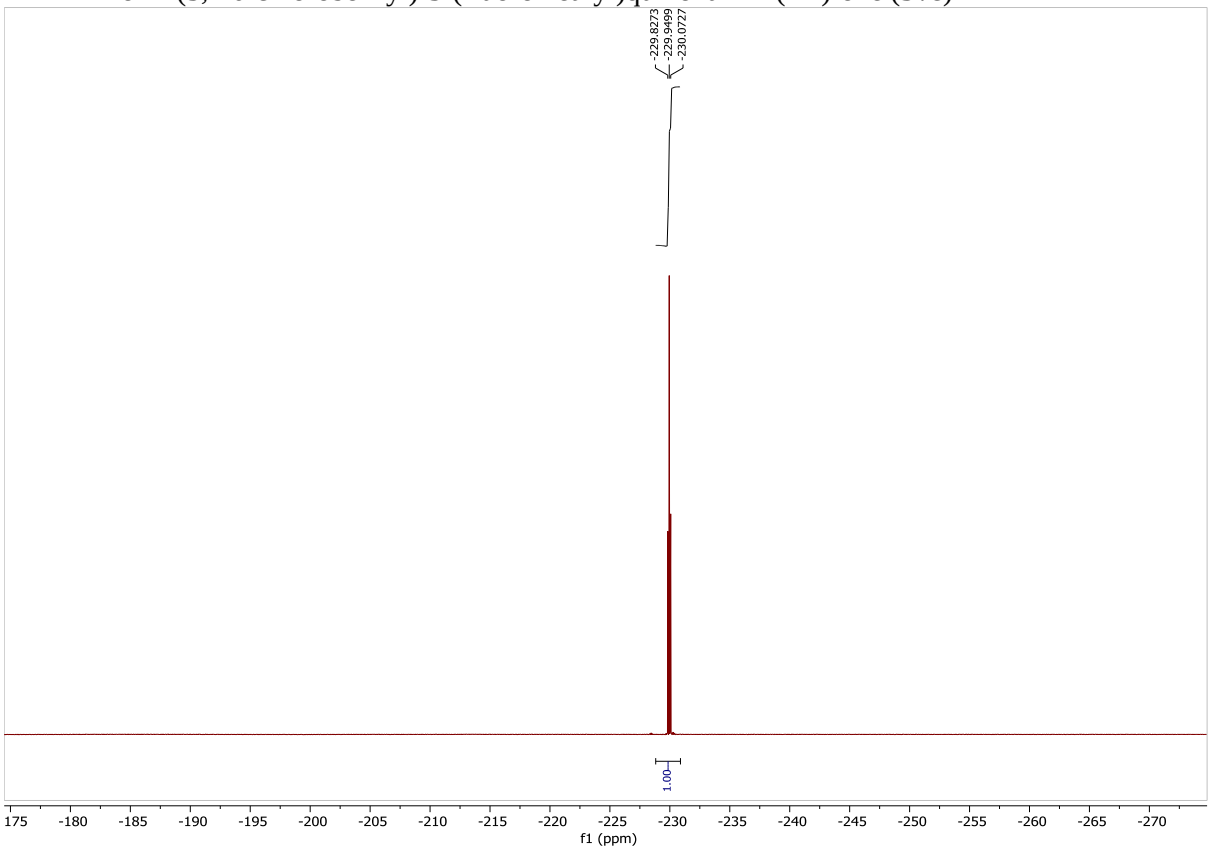
^{13}C NMR of 1-(3,5-bis(trifluoromethyl)benzyl)-3-(fluoromethyl)quinoxalin-2(1*H*)-one (**3vd**)



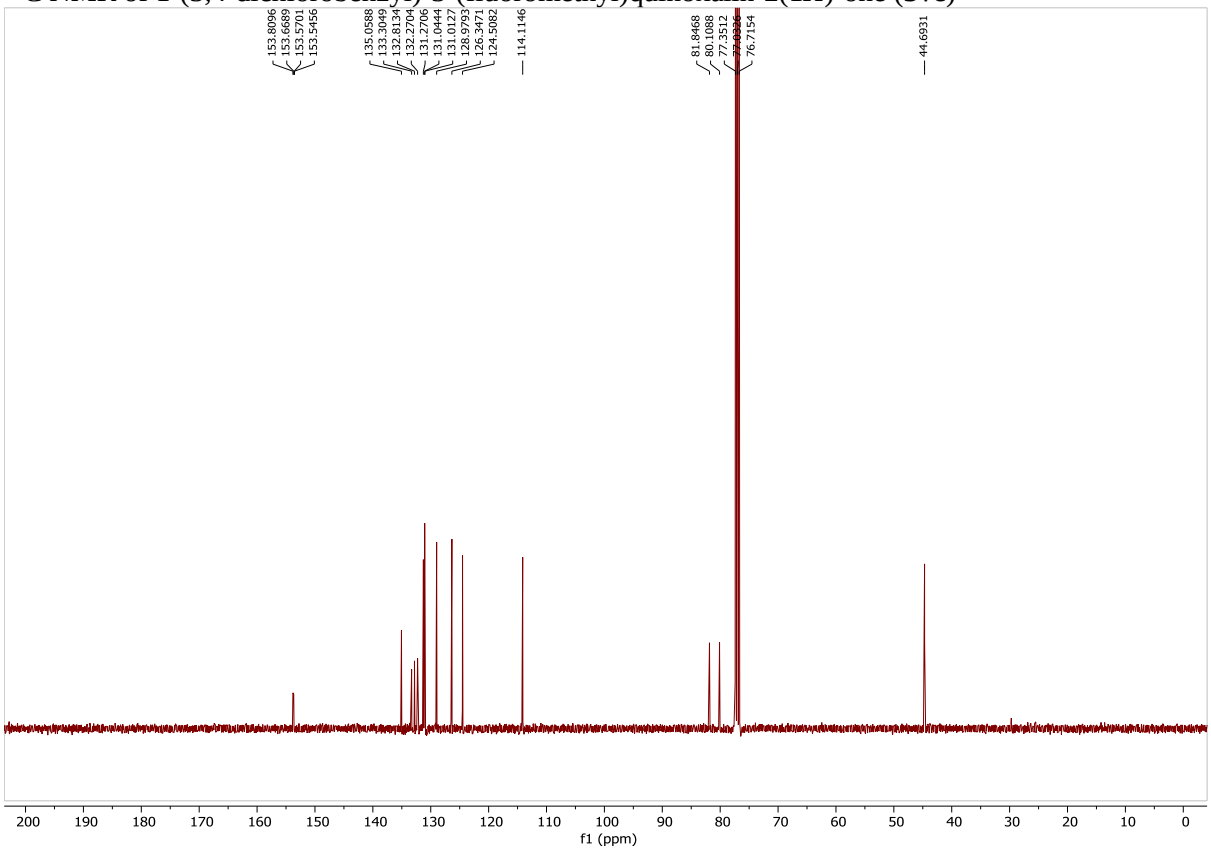
^{1}H NMR of 1-(3,4-dichlorobenzyl)-3-(fluoromethyl)quinoxalin-2(1*H*)-one (**3ve**)



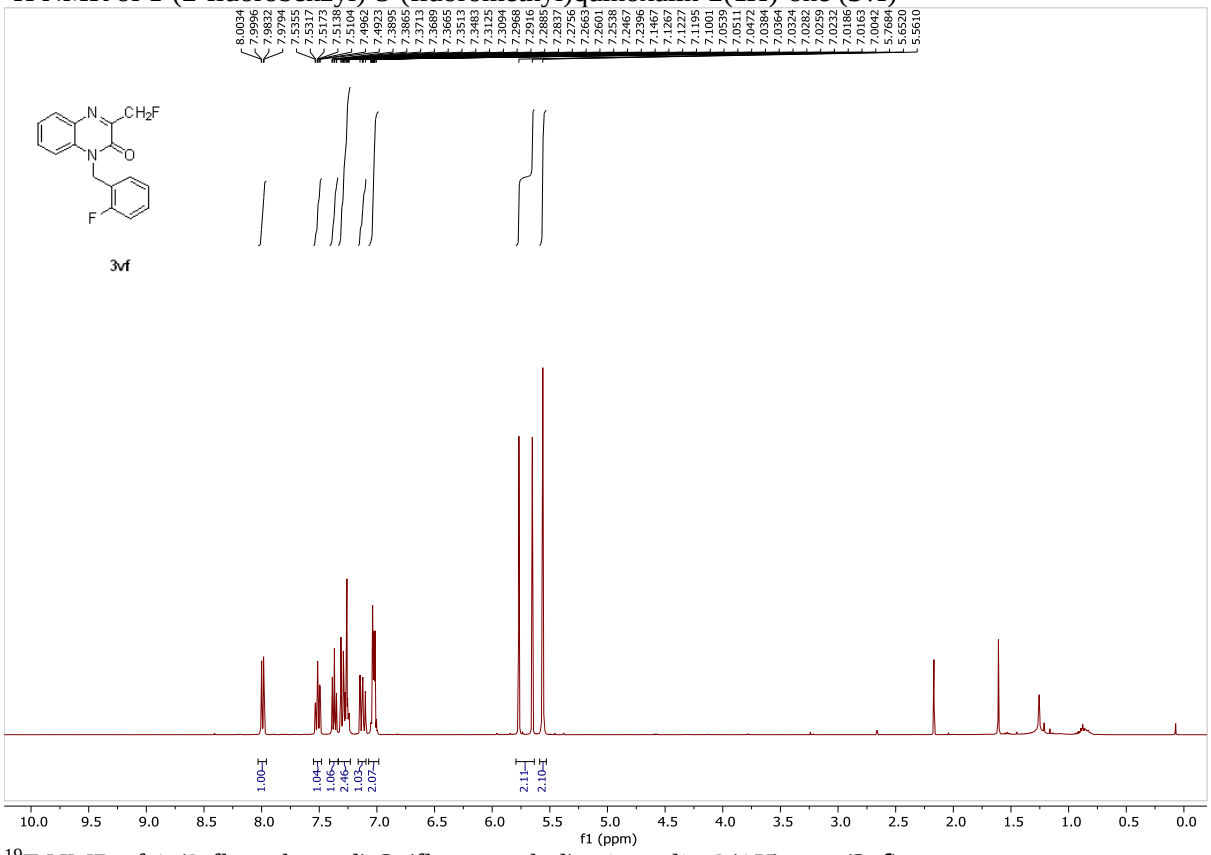
^{19}F NMR of 1-(3,4-dichlorobenzyl)-3-(fluoromethyl)quinoxalin-2(1*H*)-one (**3ve**)



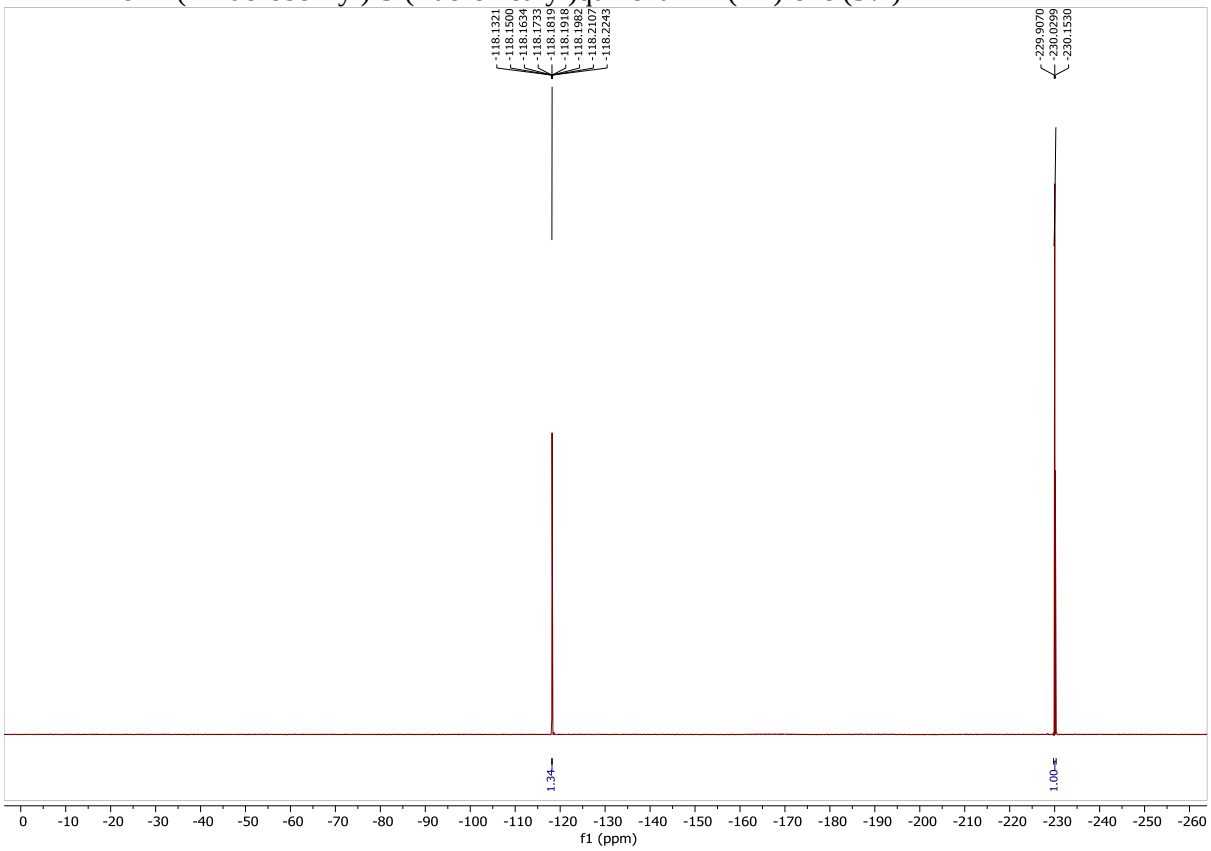
^{13}C NMR of 1-(3,4-dichlorobenzyl)-3-(fluoromethyl)quinoxalin-2(1*H*)-one (**3ve**)



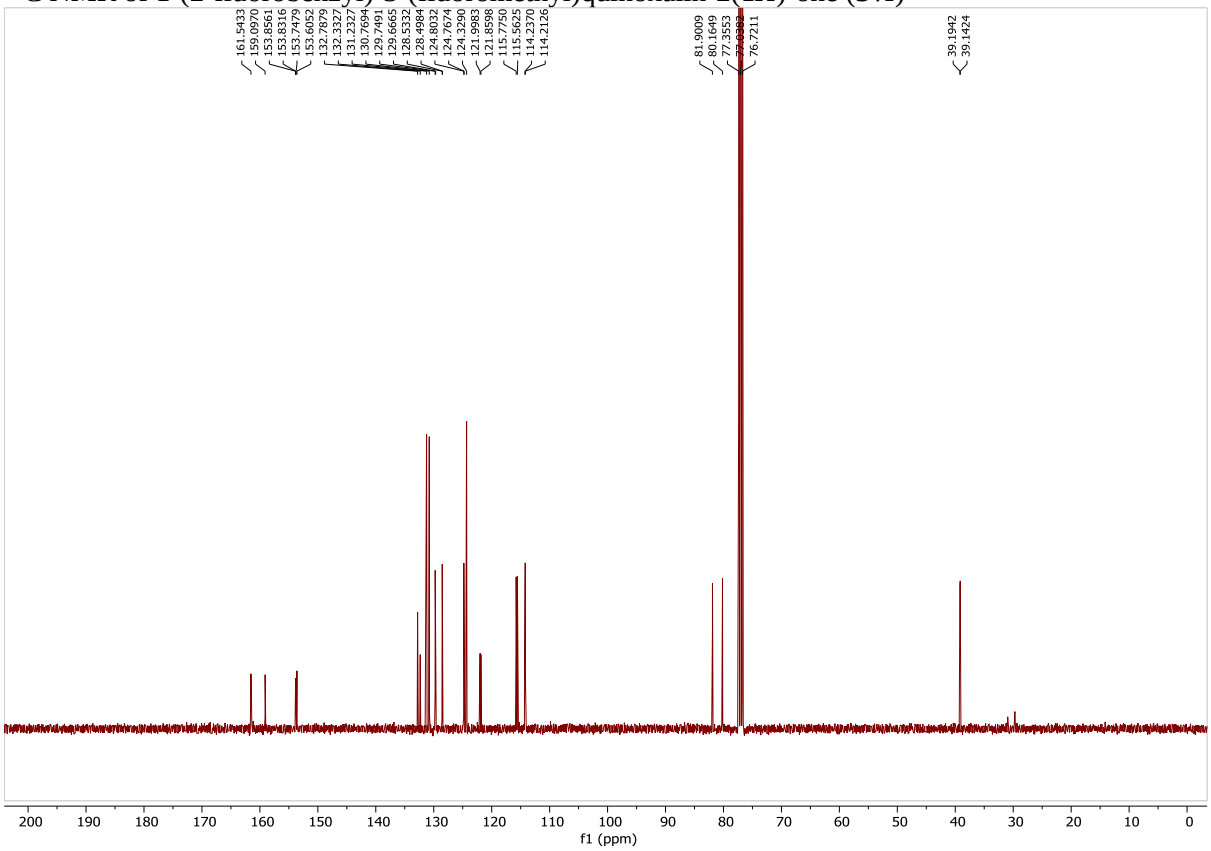
^{1}H NMR of 1-(2-fluorobenzyl)-3-(fluoromethyl)quinoxalin-2(1*H*)-one (**3vf**)



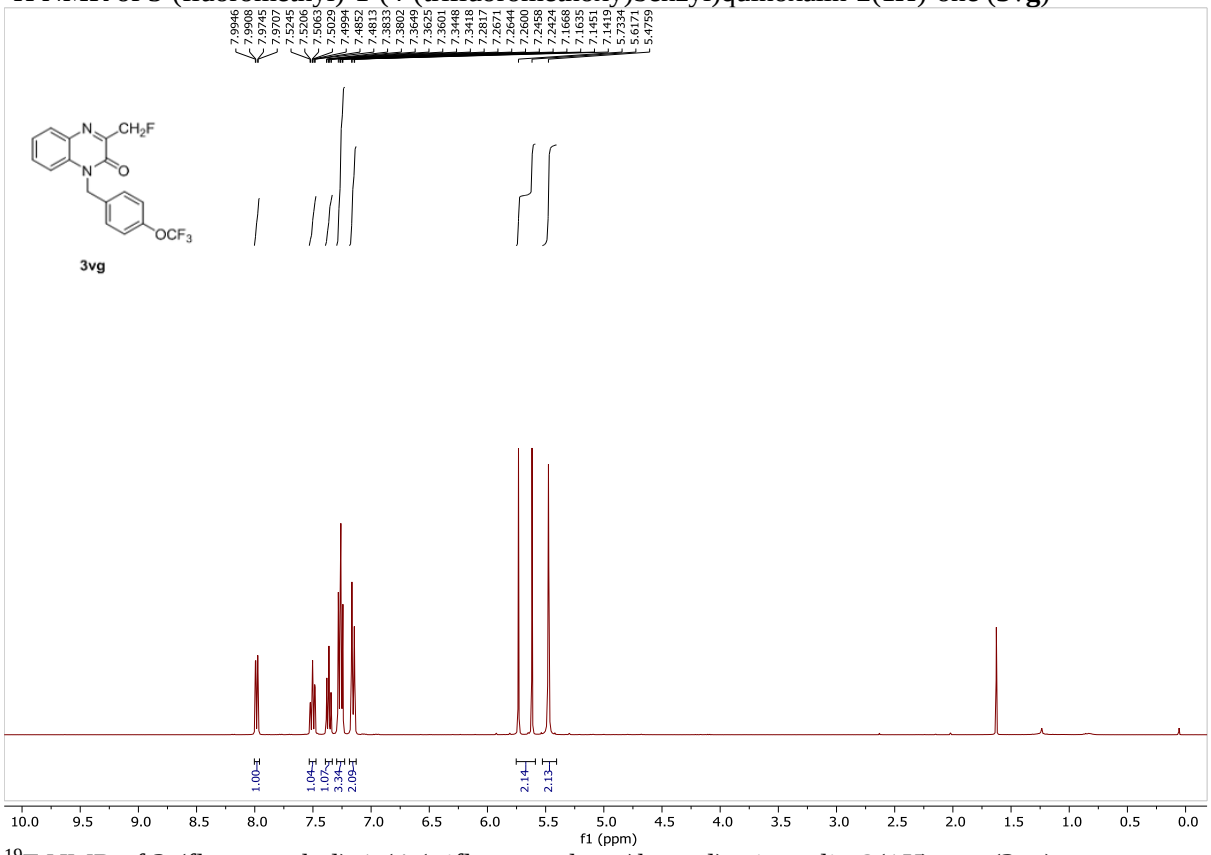
^{19}F NMR of 1-(2-fluorobenzyl)-3-(fluoromethyl)quinoxalin-2(1*H*)-one (**3vf**)



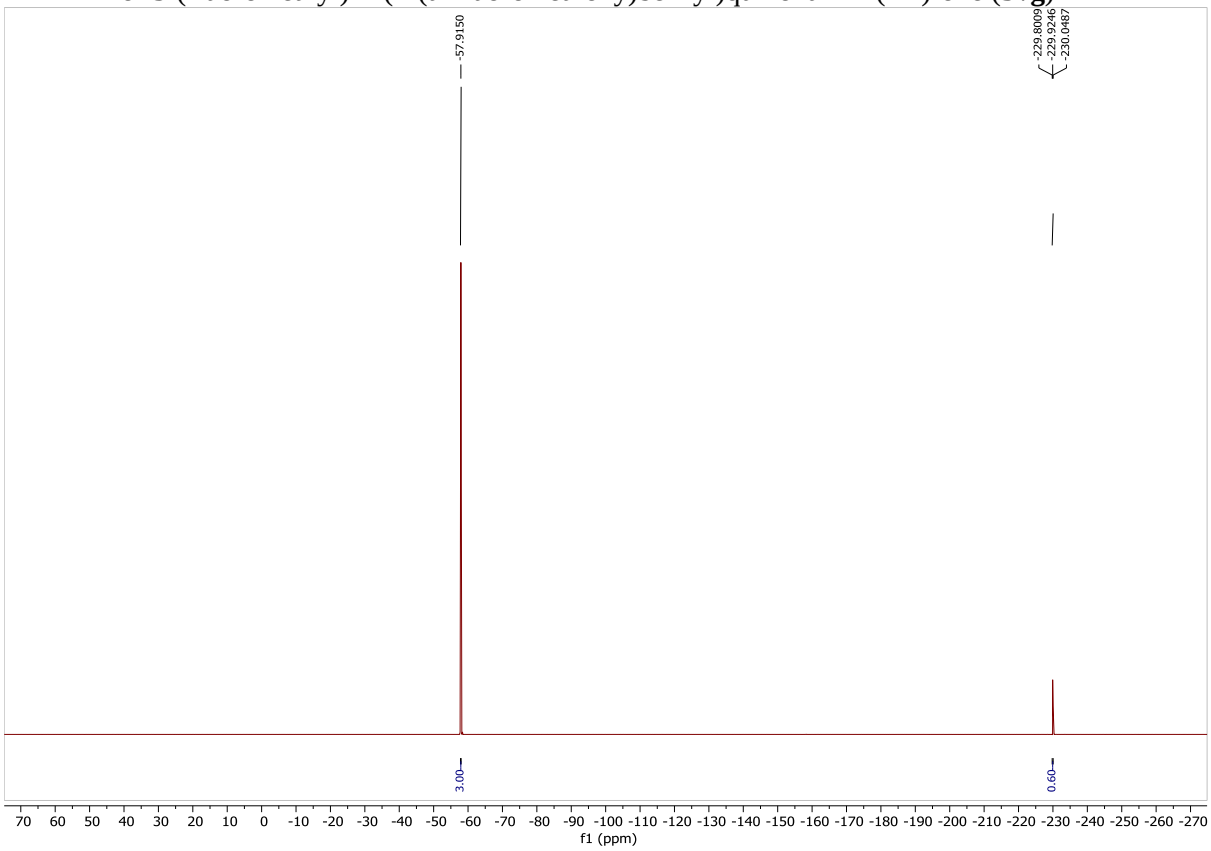
^{13}C NMR of 1-(2-fluorobenzyl)-3-(fluoromethyl)quinoxalin-2(1*H*)-one (**3vf**)



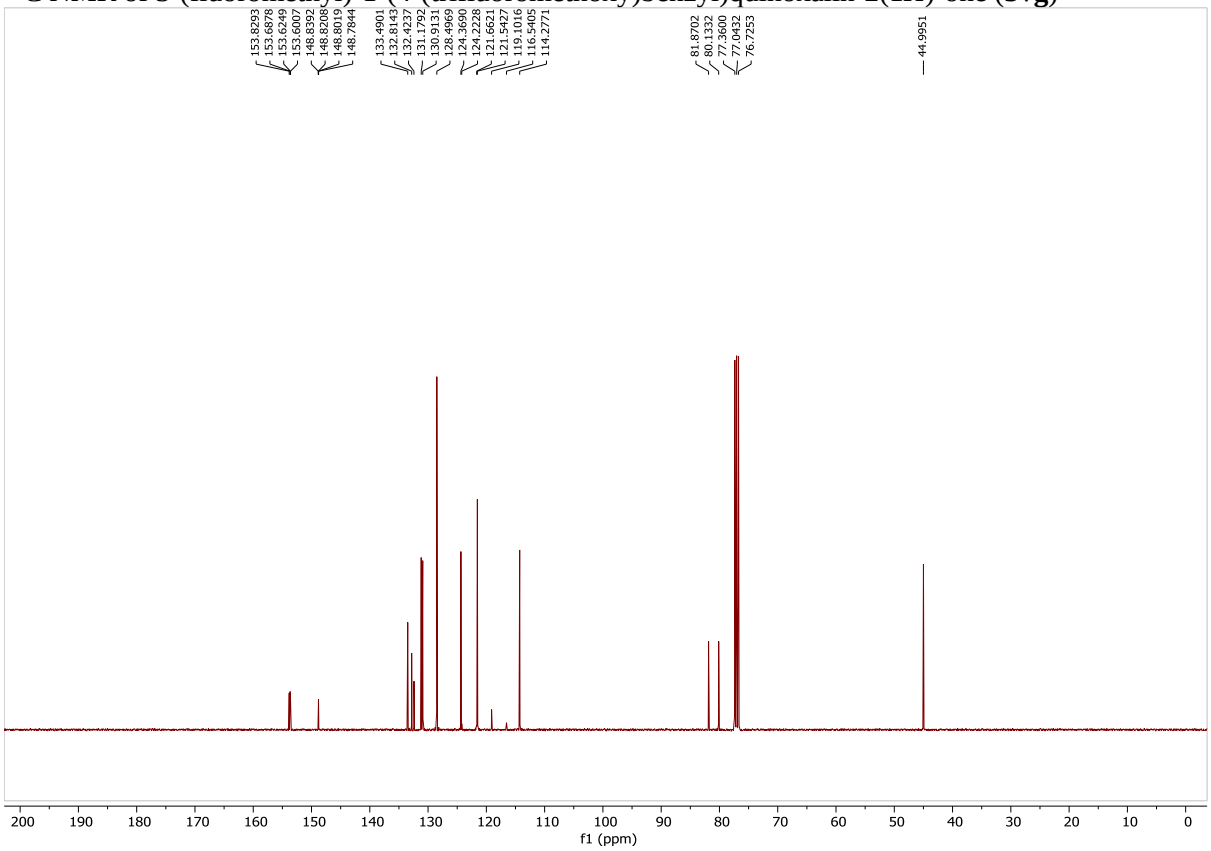
^{1}H NMR of 3-(fluoromethyl)-1-(4-(trifluoromethoxy)benzyl)quinoxalin-2(1*H*)-one (**3vg**)



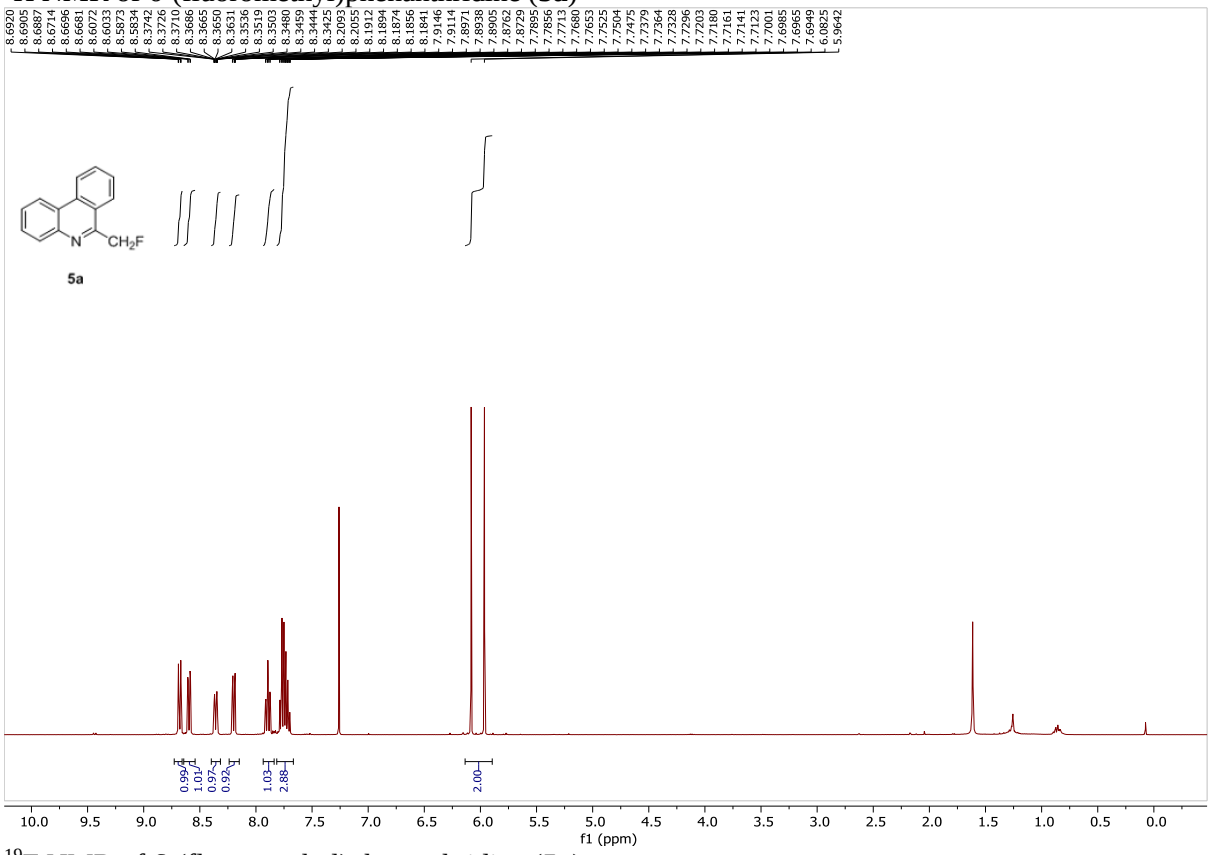
^{19}F NMR of 3-(fluoromethyl)-1-(4-(trifluoromethoxy)benzyl)quinoxalin-2(1*H*)-one (**3vg**)



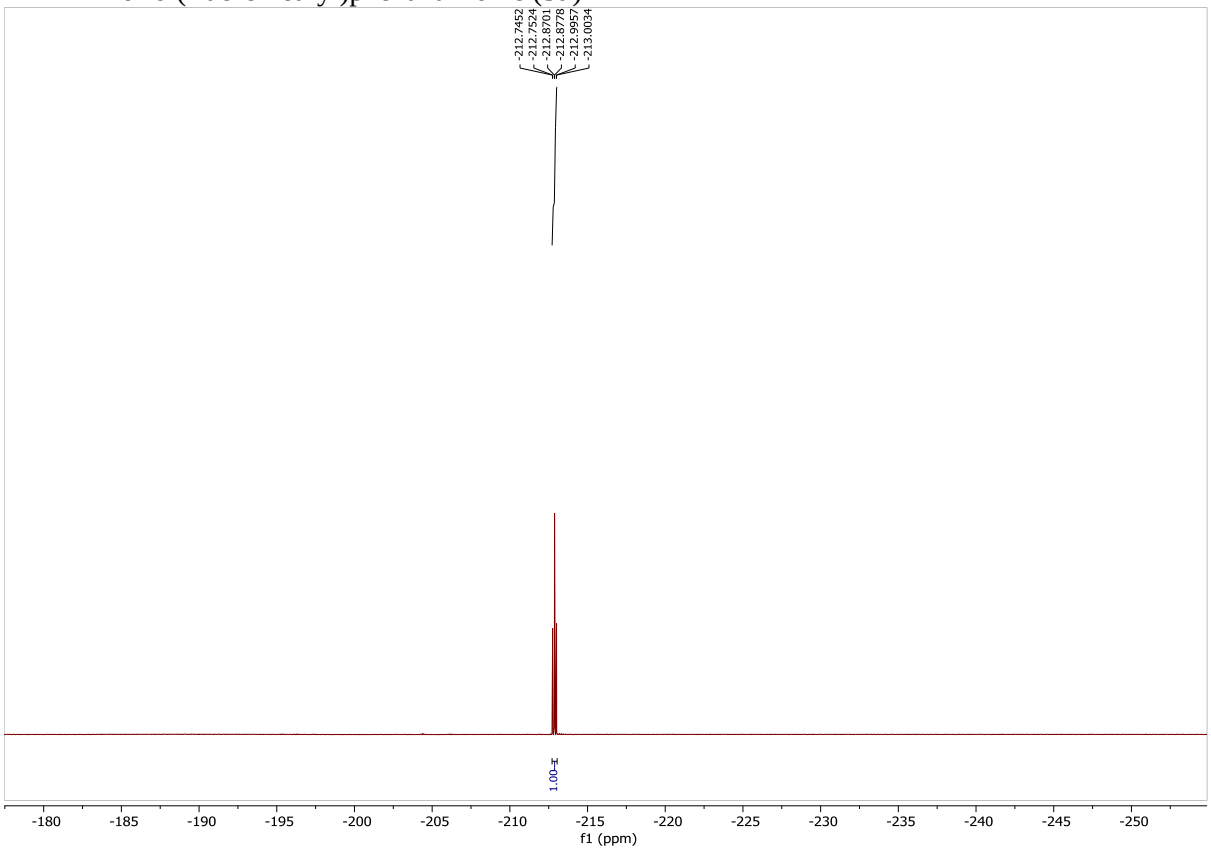
^{13}C NMR of 3-(fluoromethyl)-1-(4-(trifluoromethoxy)benzyl)quinoxalin-2(1*H*)-one (**3vg**)



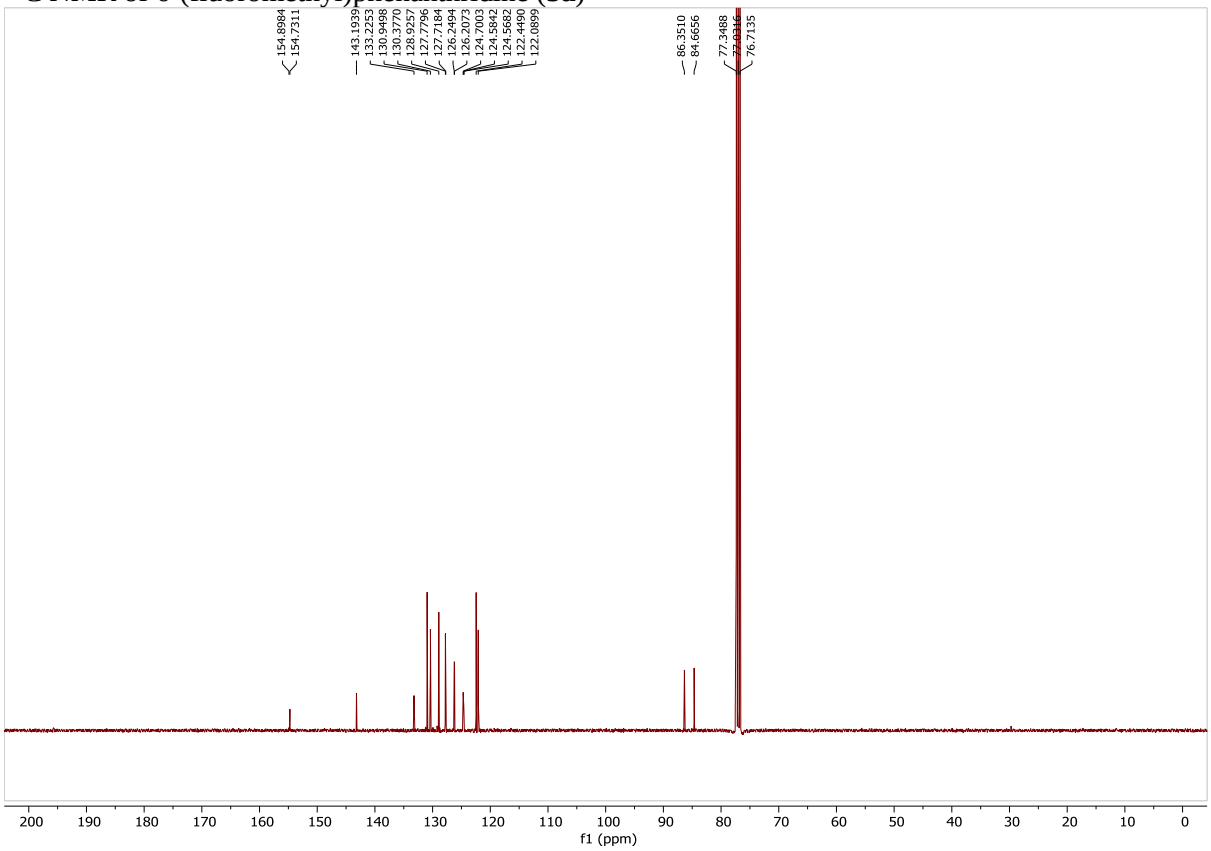
^{1}H NMR of 6-(fluoromethyl)phenanthridine (**5a**)



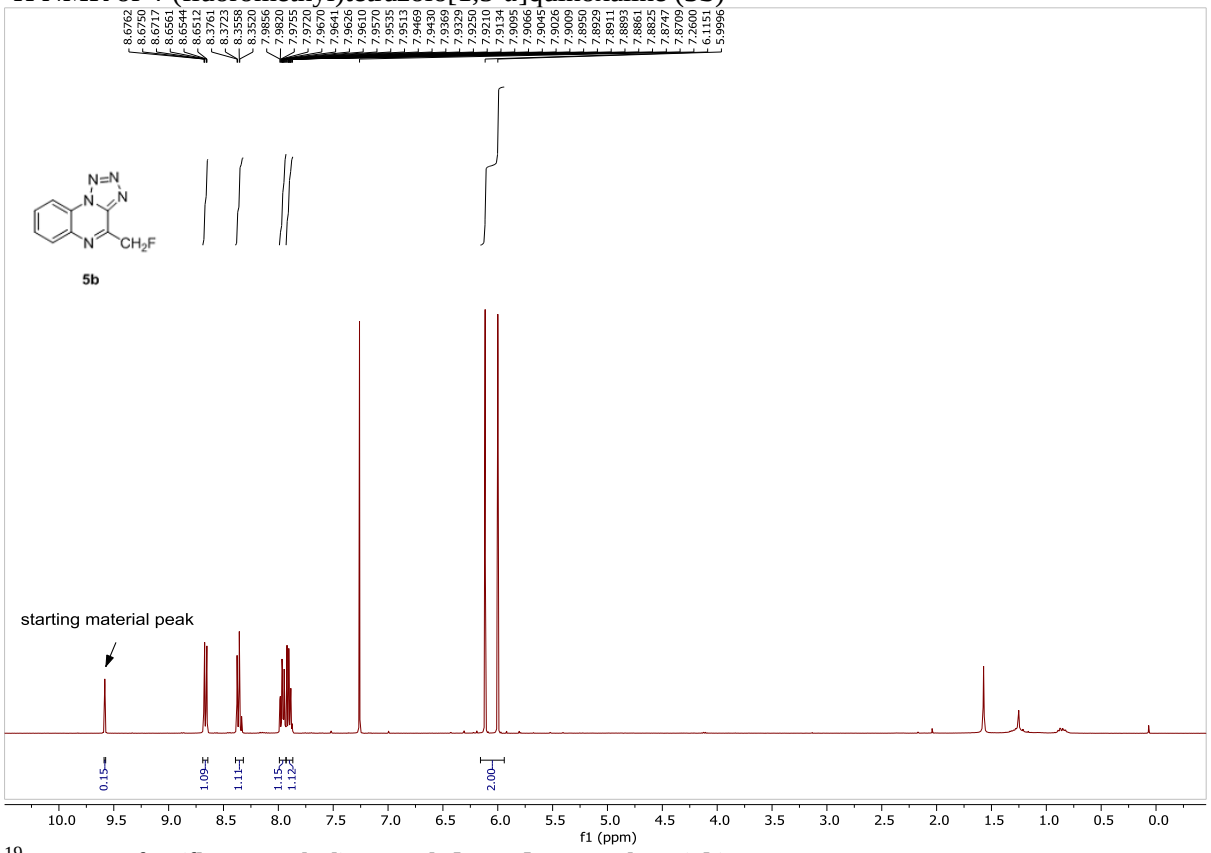
^{19}F NMR of 6-(fluoromethyl)phenanthridine (**5a**)



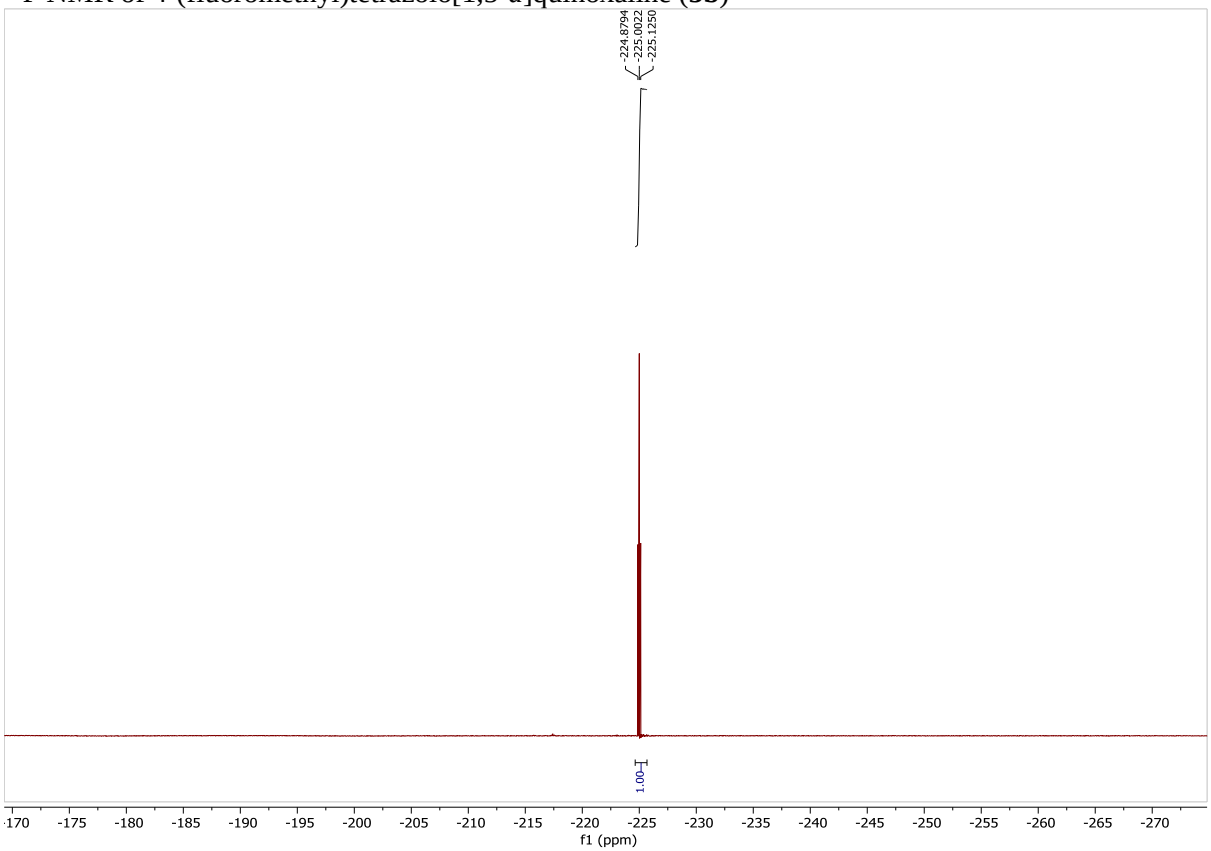
^{13}C NMR of 6-(fluoromethyl)phenanthridine (**5a**)



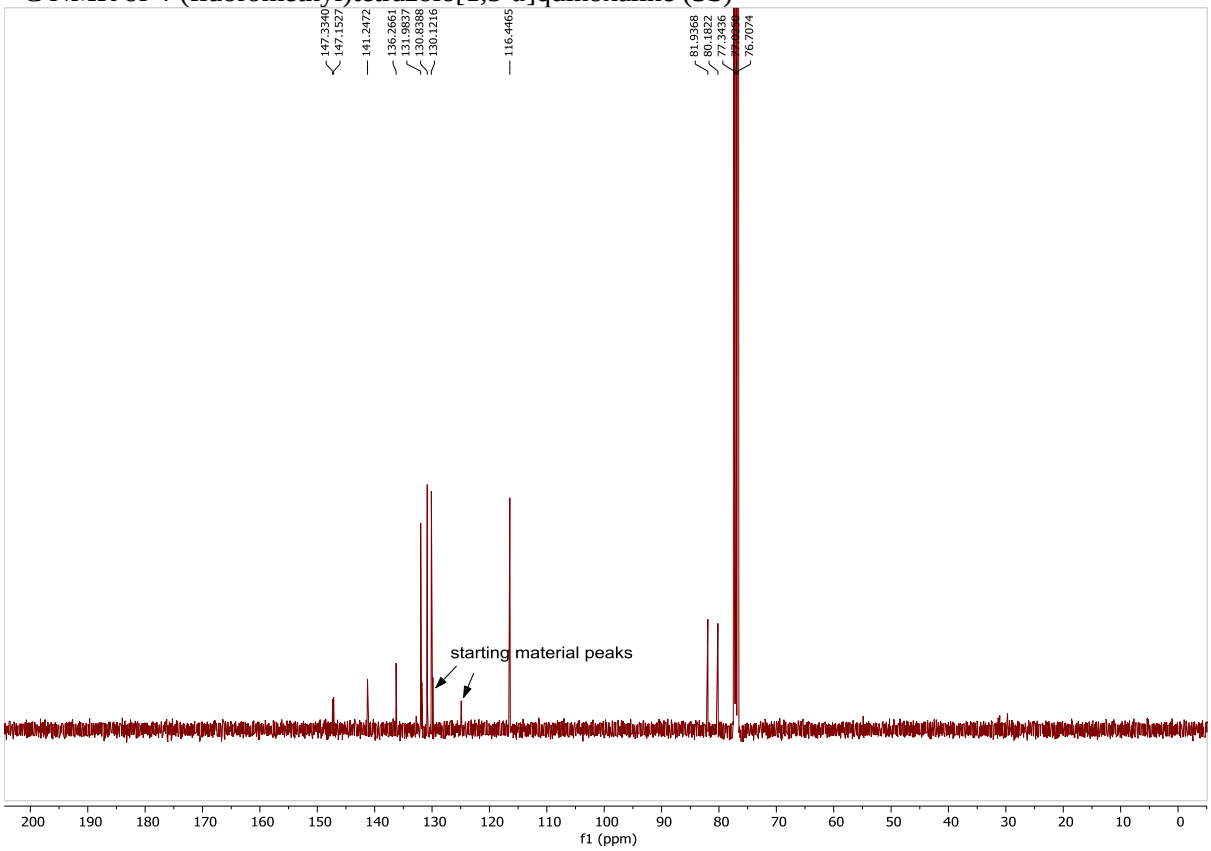
^{1}H NMR of 4-(fluoromethyl)tetrazolo[1,5-*a*]quinoxaline (**5b**)



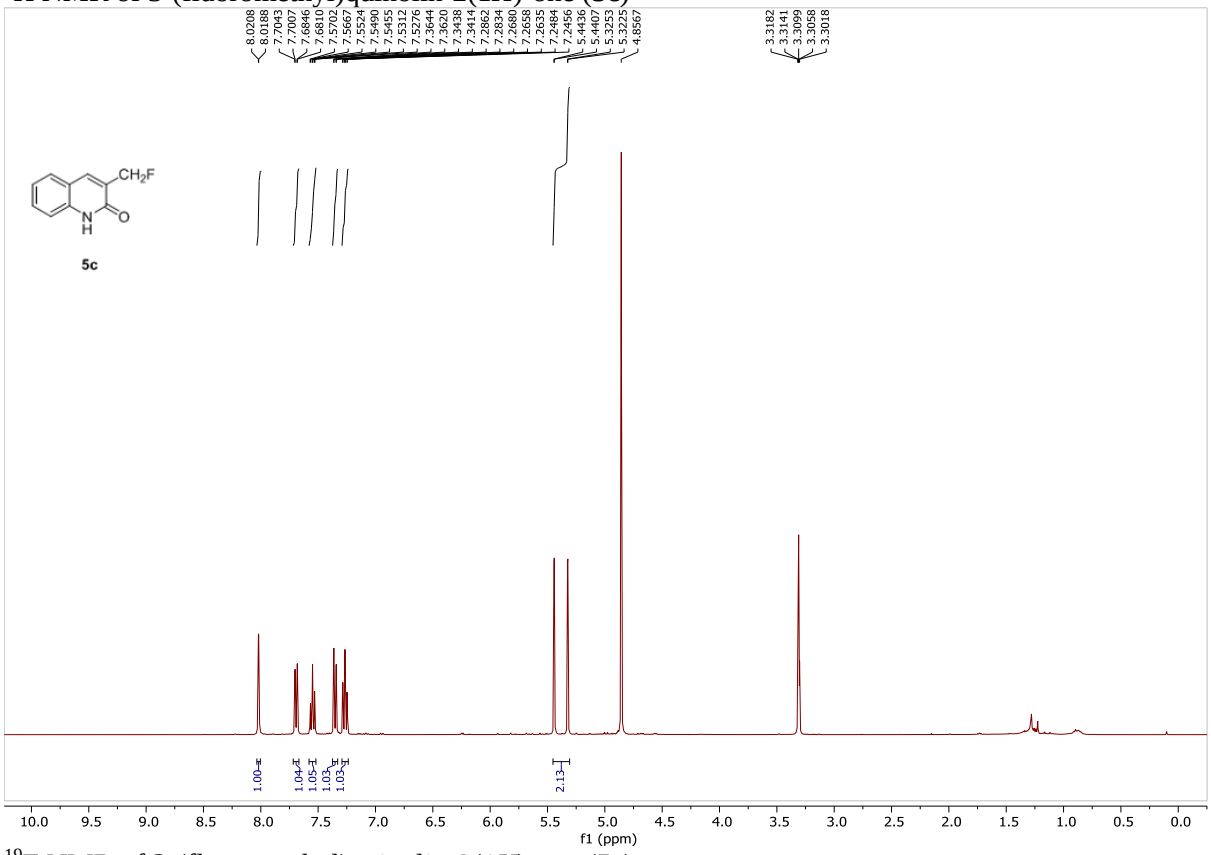
^{19}F NMR of 4-(fluoromethyl)tetrazolo[1,5-*a*]quinoxaline (**5b**)



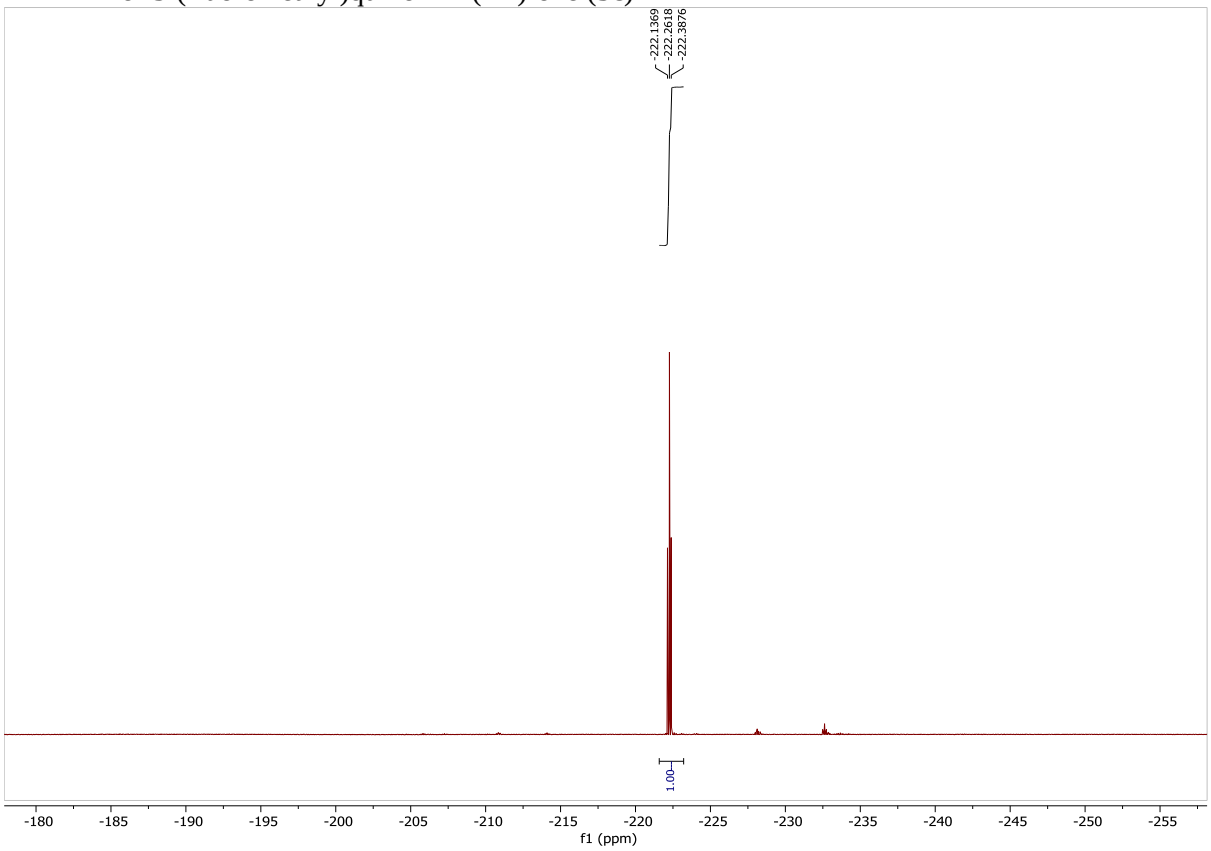
^{13}C NMR of 4-(fluoromethyl)tetrazolo[1,5-*a*]quinoxaline (**5b**)



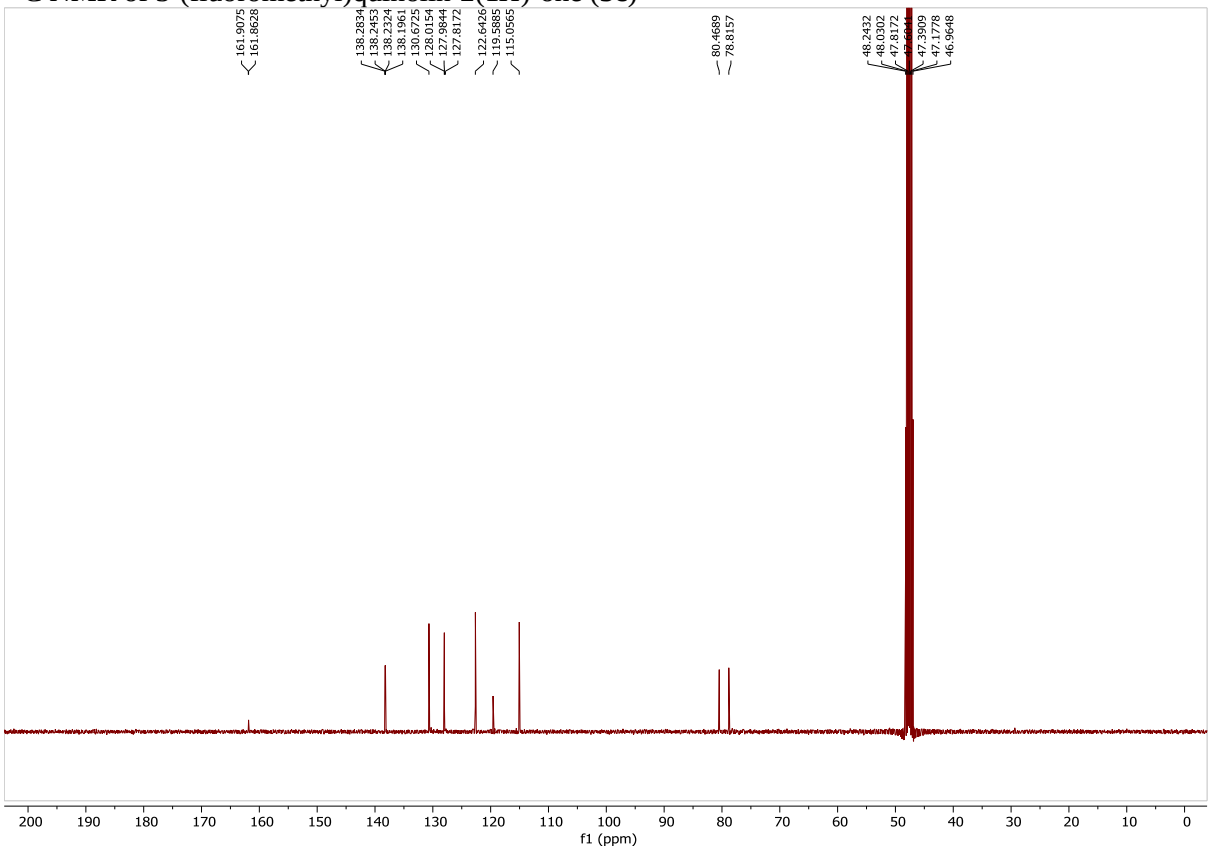
^{1}H NMR of 3-(fluoromethyl)quinolin-2(1*H*)-one (**5c**)



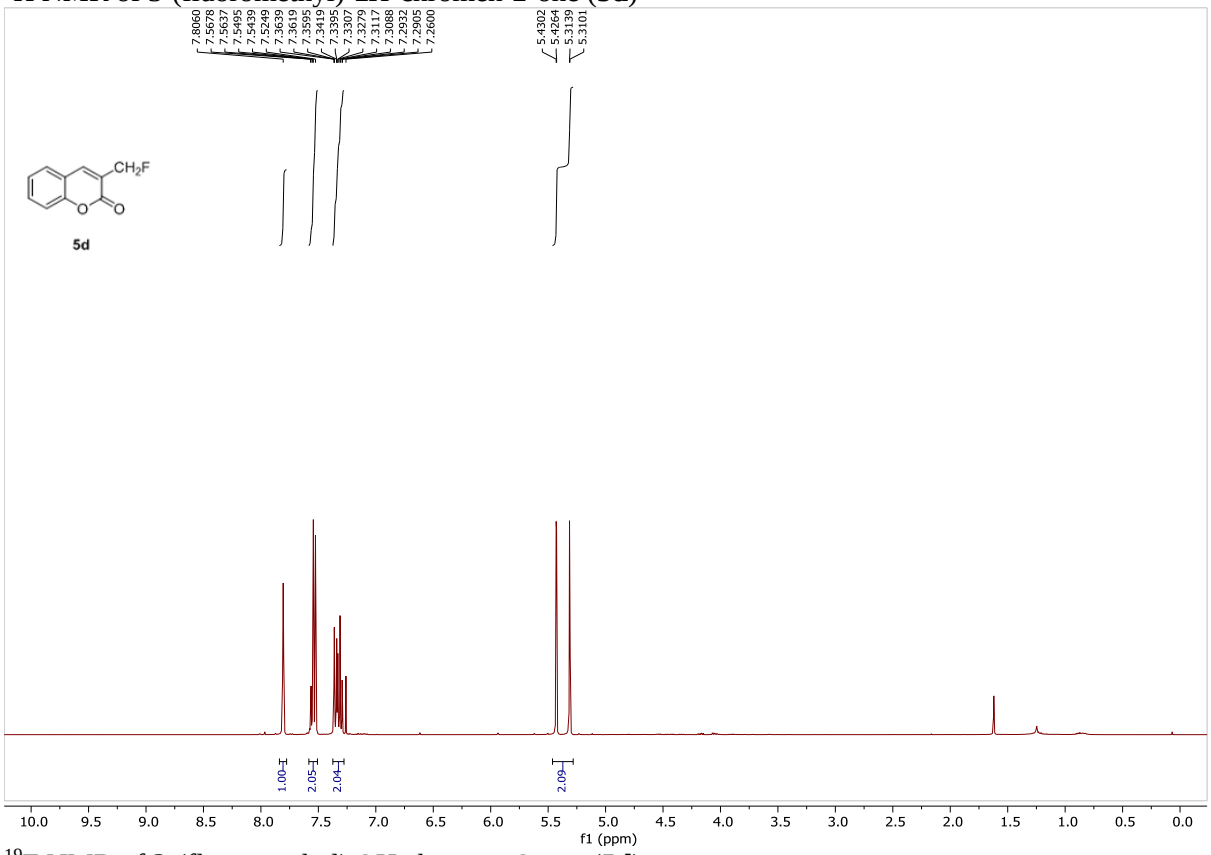
^{19}F NMR of 3-(fluoromethyl)quinolin-2(1*H*)-one (**5c**)



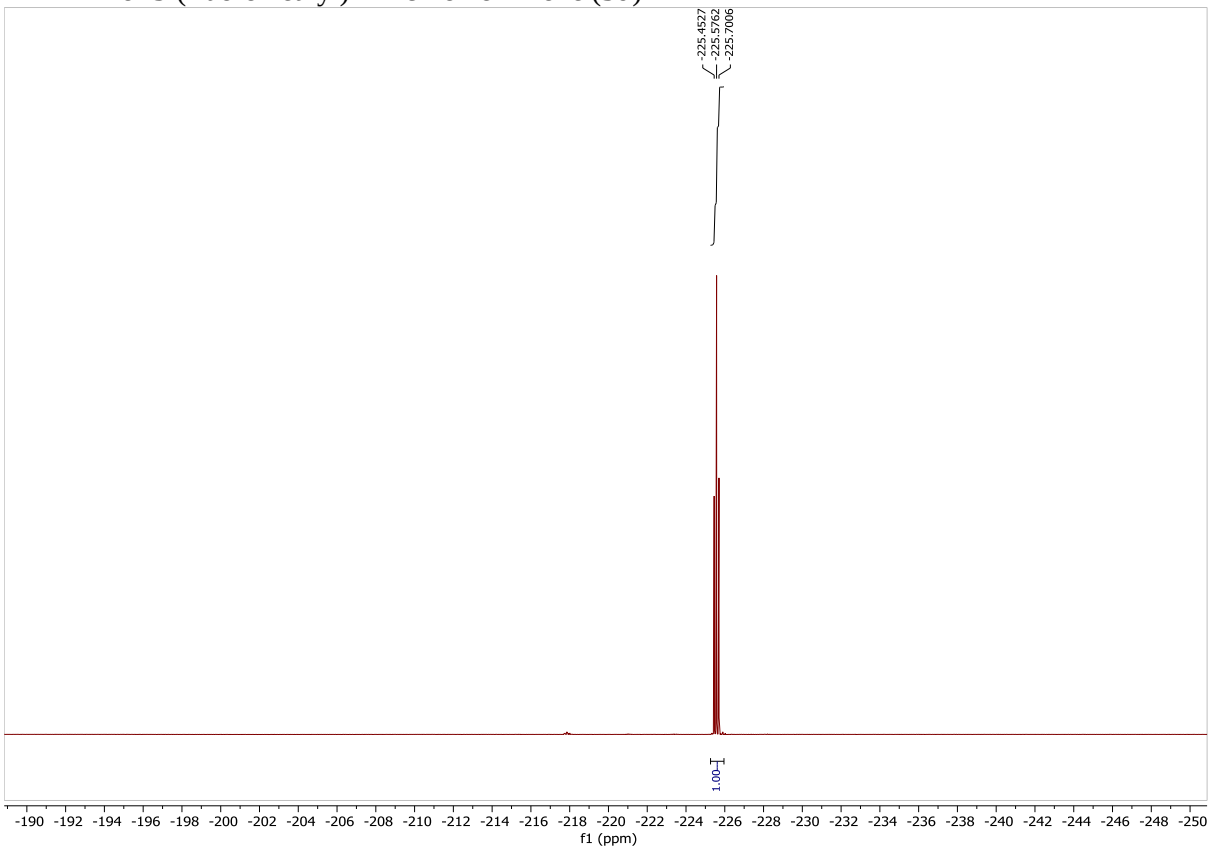
^{13}C NMR of 3-(fluoromethyl)quinolin-2(1*H*)-one (**5c**)



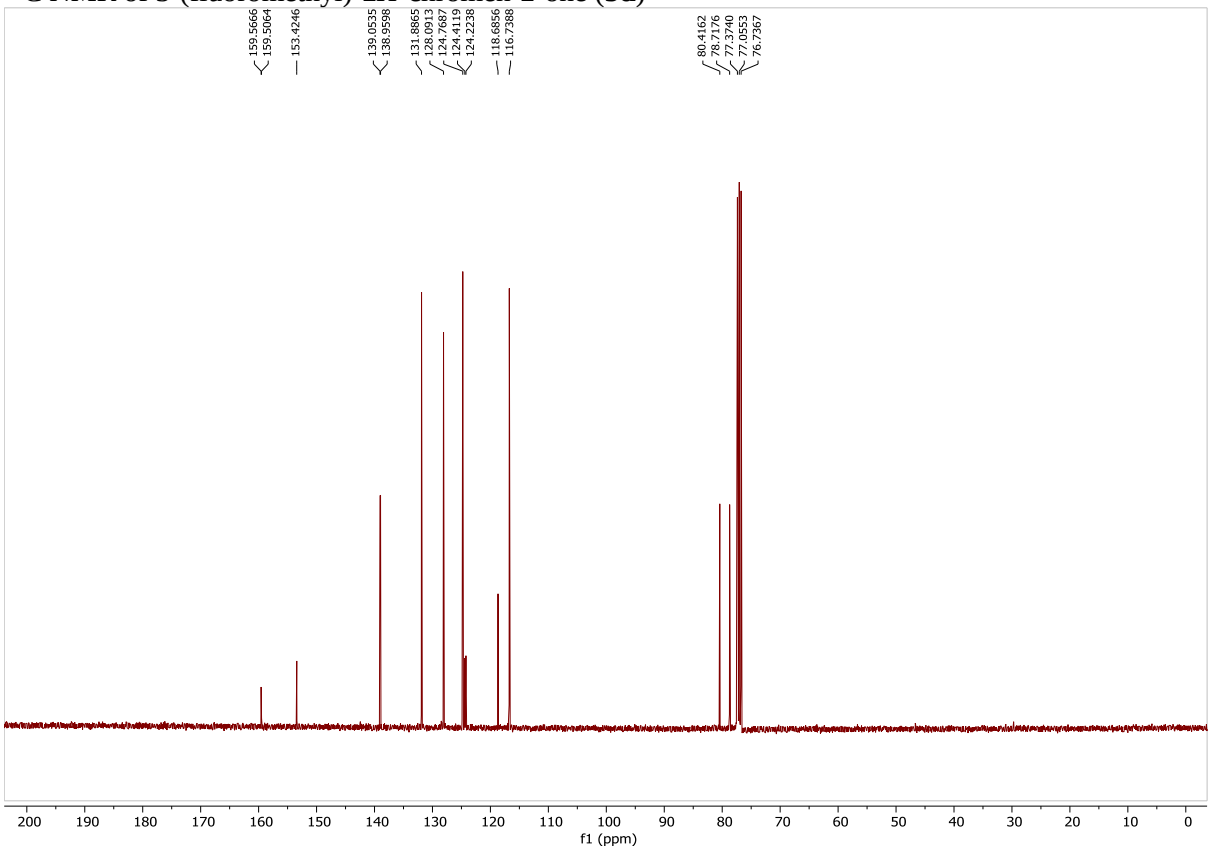
^{1}H NMR of 3-(fluoromethyl)-2*H*-chromen-2-one (**5d**)



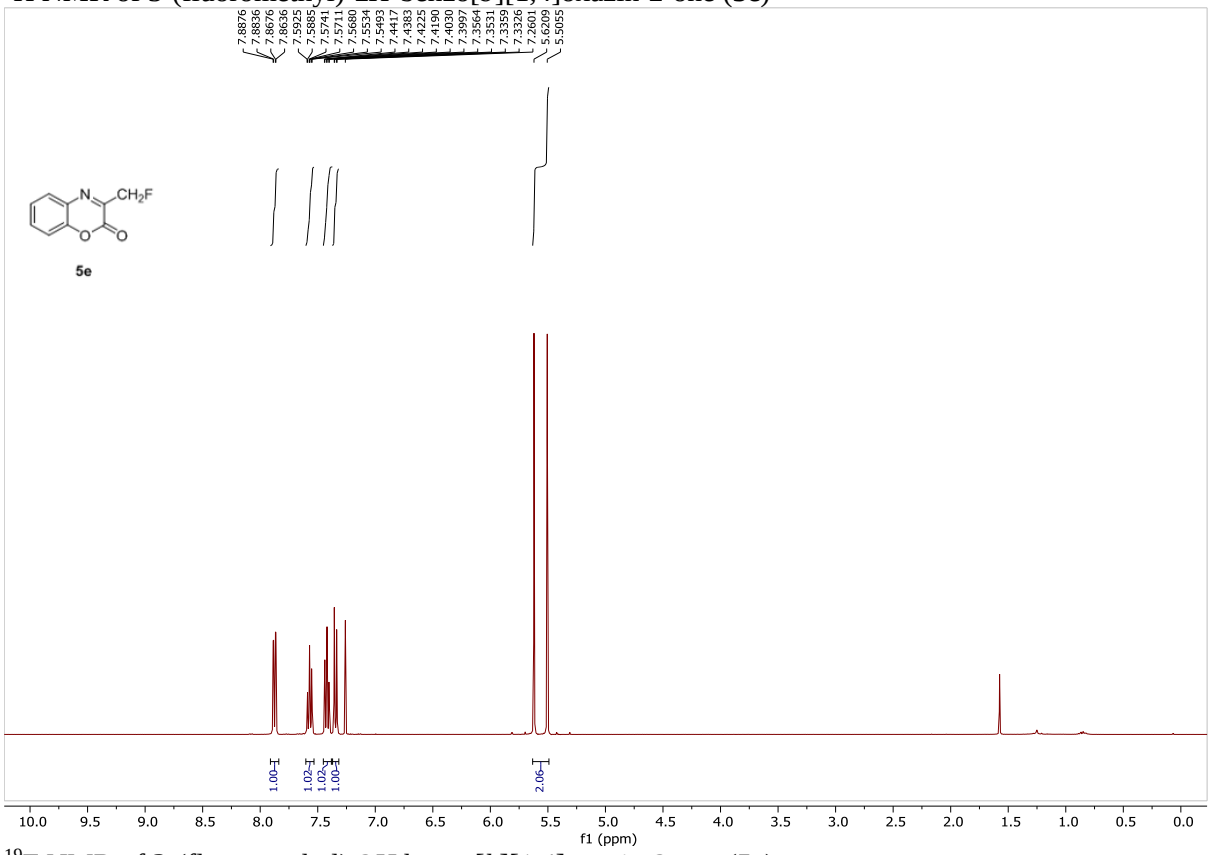
^{19}F NMR of 3-(fluoromethyl)-2*H*-chromen-2-one (**5d**)



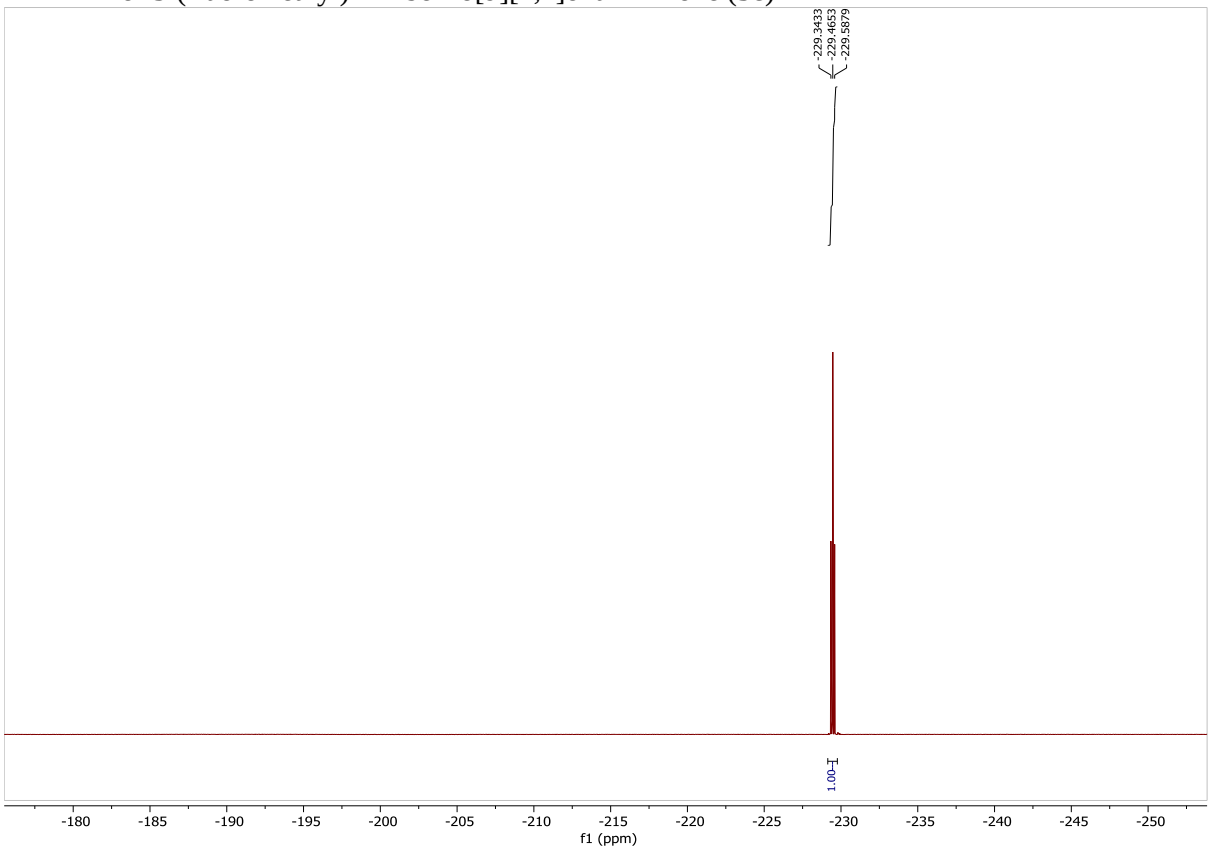
^{13}C NMR of 3-(fluoromethyl)-2*H*-chromen-2-one (**5d**)



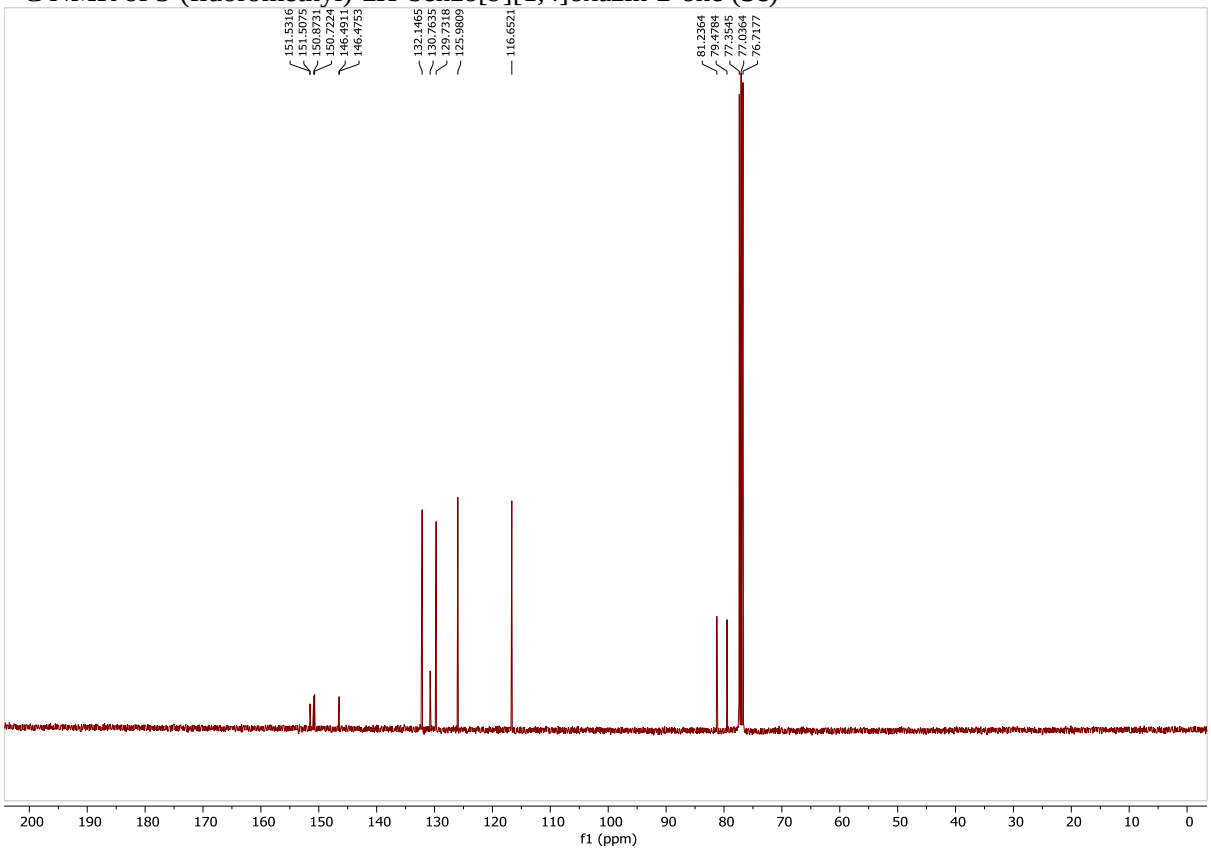
^{1}H NMR of 3-(fluoromethyl)-2*H*-benzo[*b*][1,4]oxazin-2-one (**5e**)



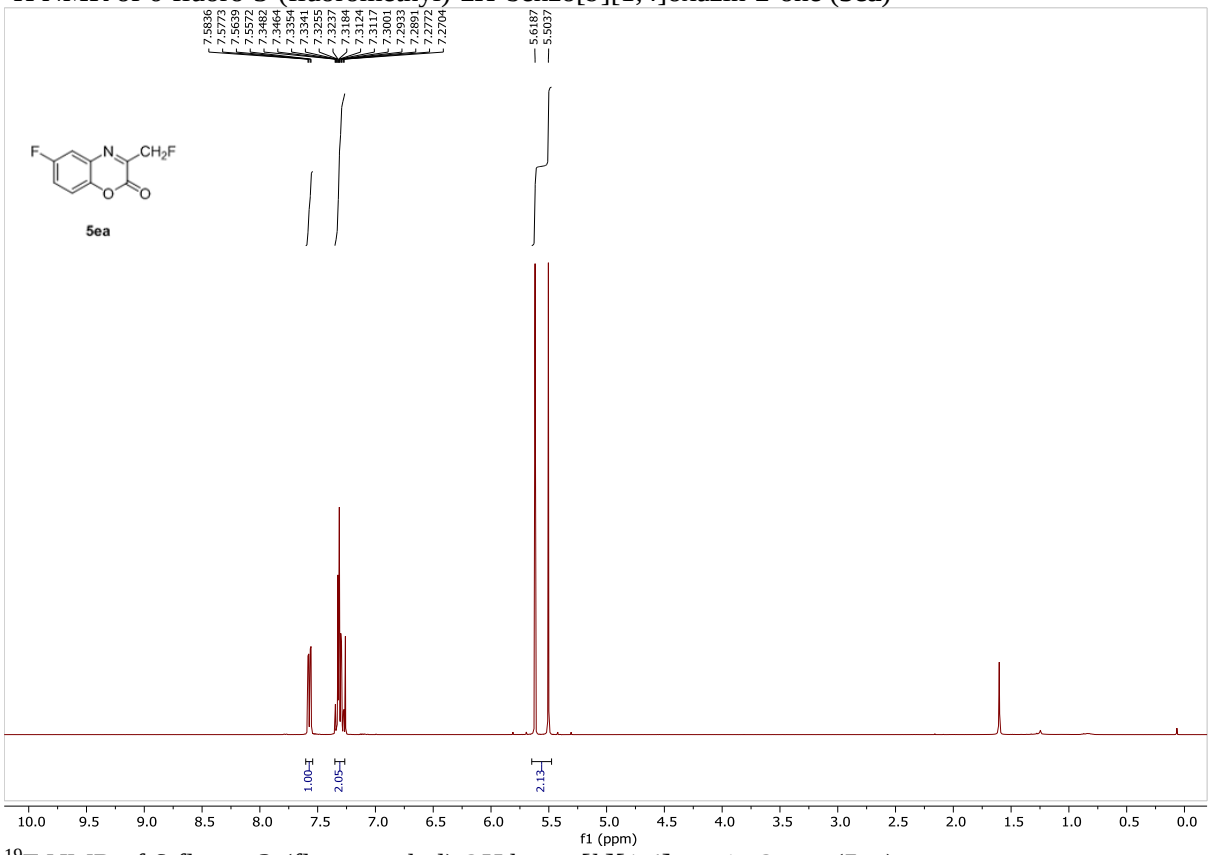
^{19}F NMR of 3-(fluoromethyl)-2*H*-benzo[*b*][1,4]oxazin-2-one (**5e**)



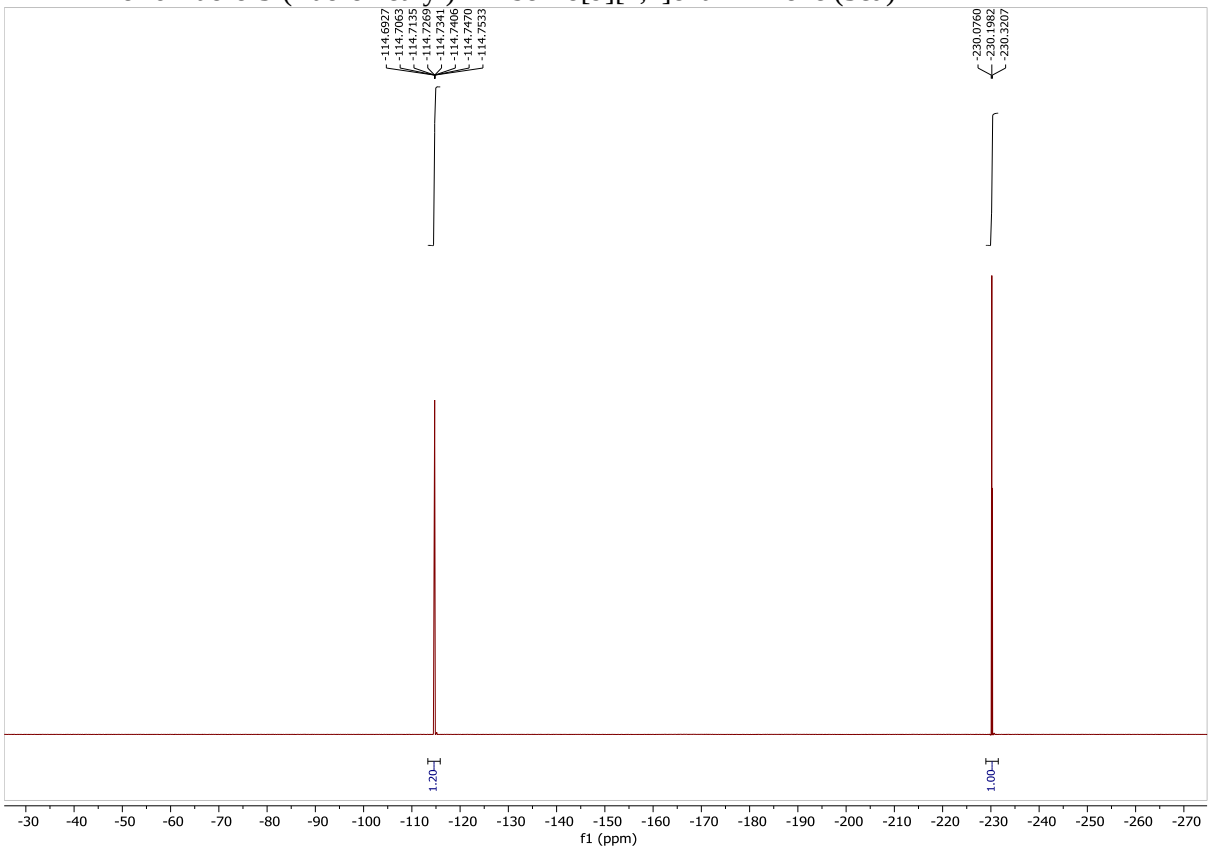
^{13}C NMR of 3-(fluoromethyl)-2*H*-benzo[*b*][1,4]oxazin-2-one (**5e**)



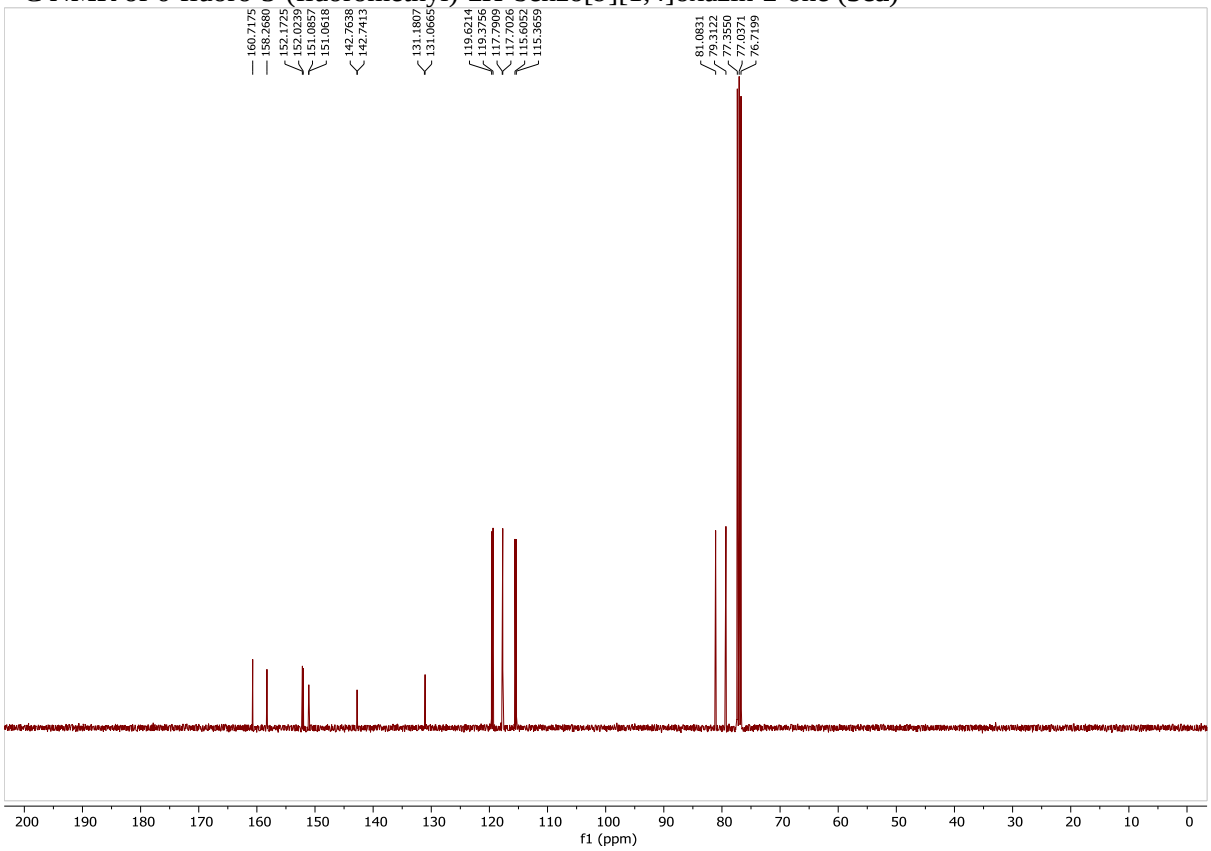
^{1}H NMR of 6-fluoro-3-(fluoromethyl)-2*H*-benzo[*b*][1,4]oxazin-2-one (**5ea**)



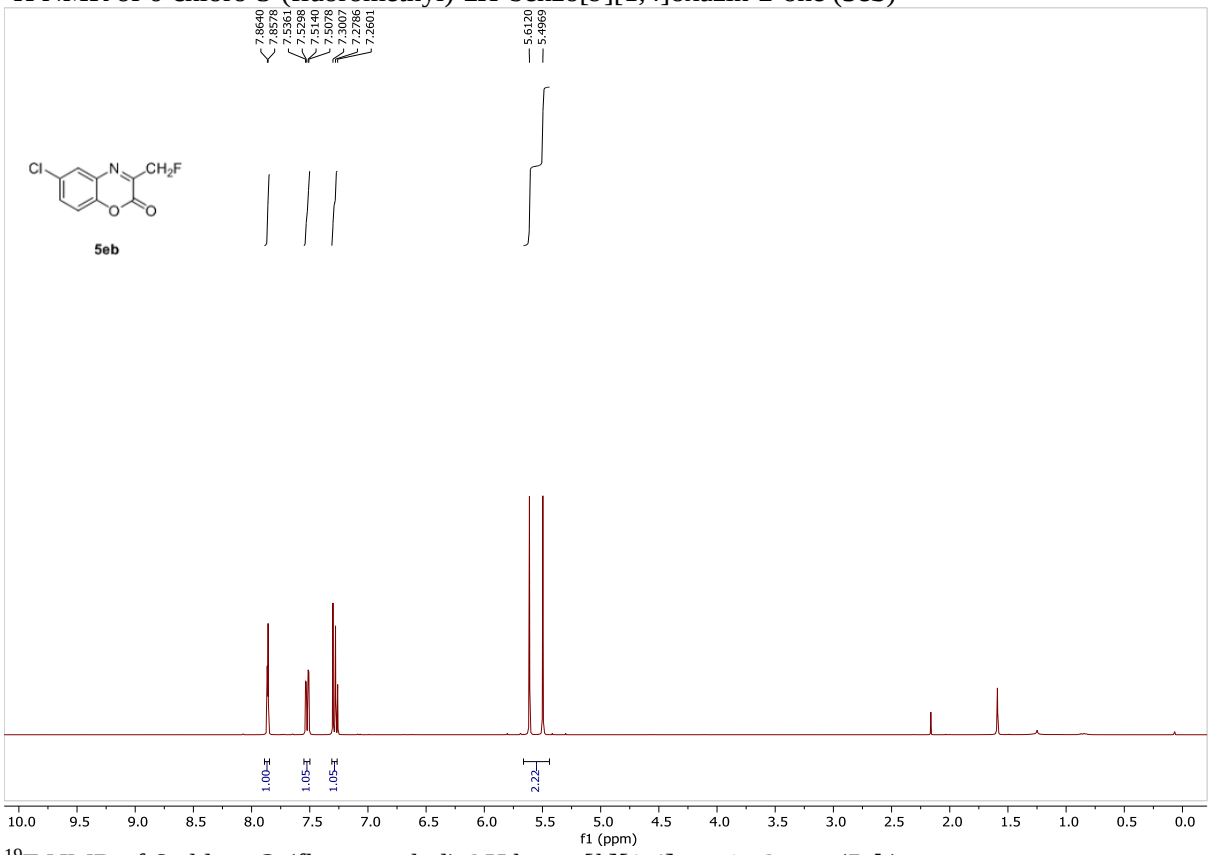
^{19}F NMR of 6-fluoro-3-(fluoromethyl)-2*H*-benzo[*b*][1,4]oxazin-2-one (**5ea**)



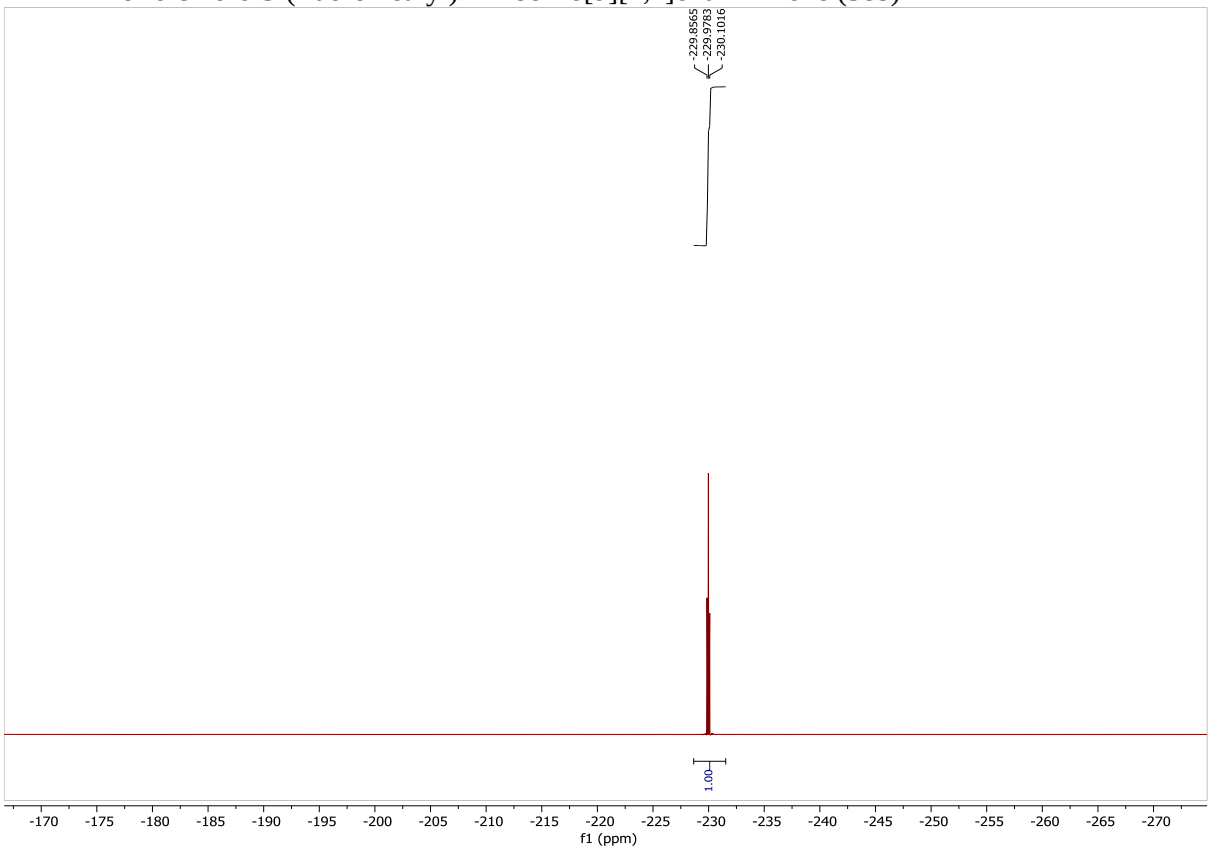
^{13}C NMR of 6-fluoro-3-(fluoromethyl)-2*H*-benzo[*b*][1,4]oxazin-2-one (**5ea**)



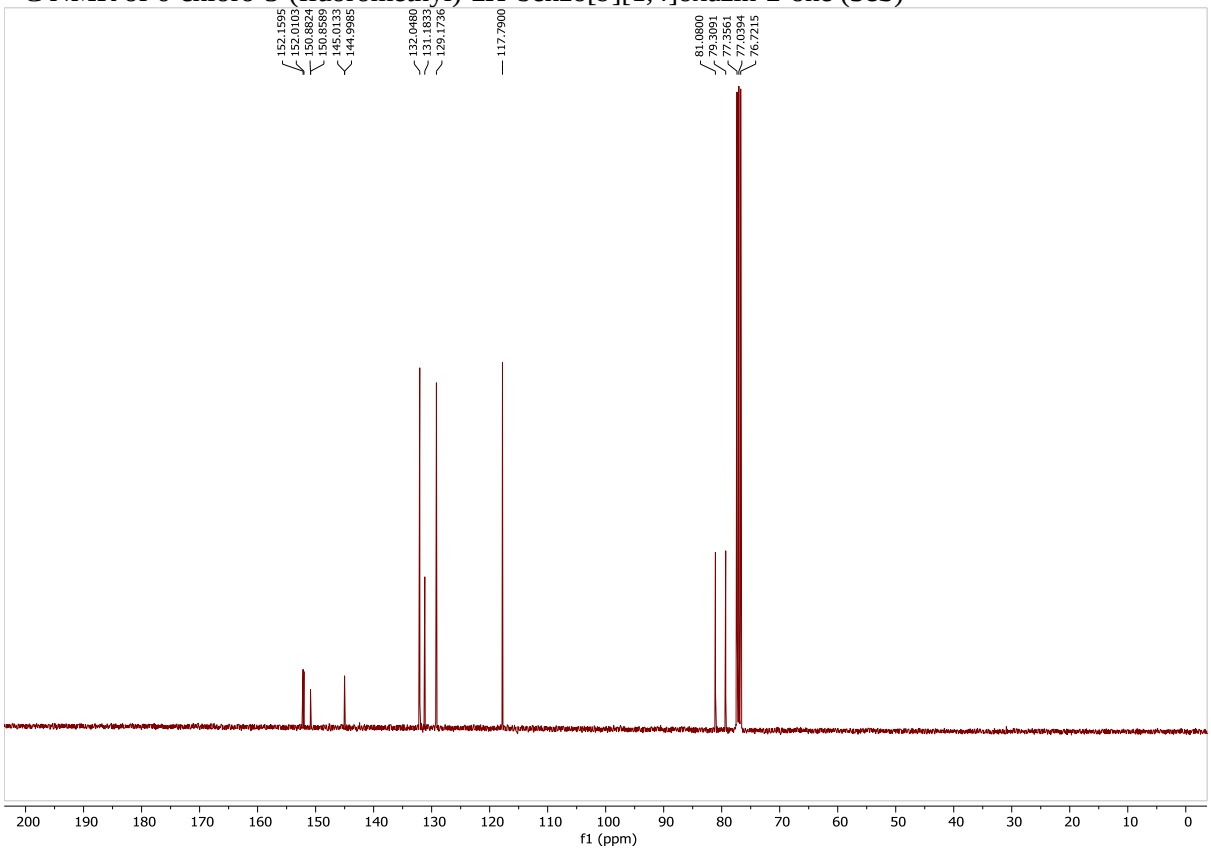
^{1}H NMR of 6-chloro-3-(fluoromethyl)-2*H*-benzo[*b*][1,4]oxazin-2-one (**5eb**)



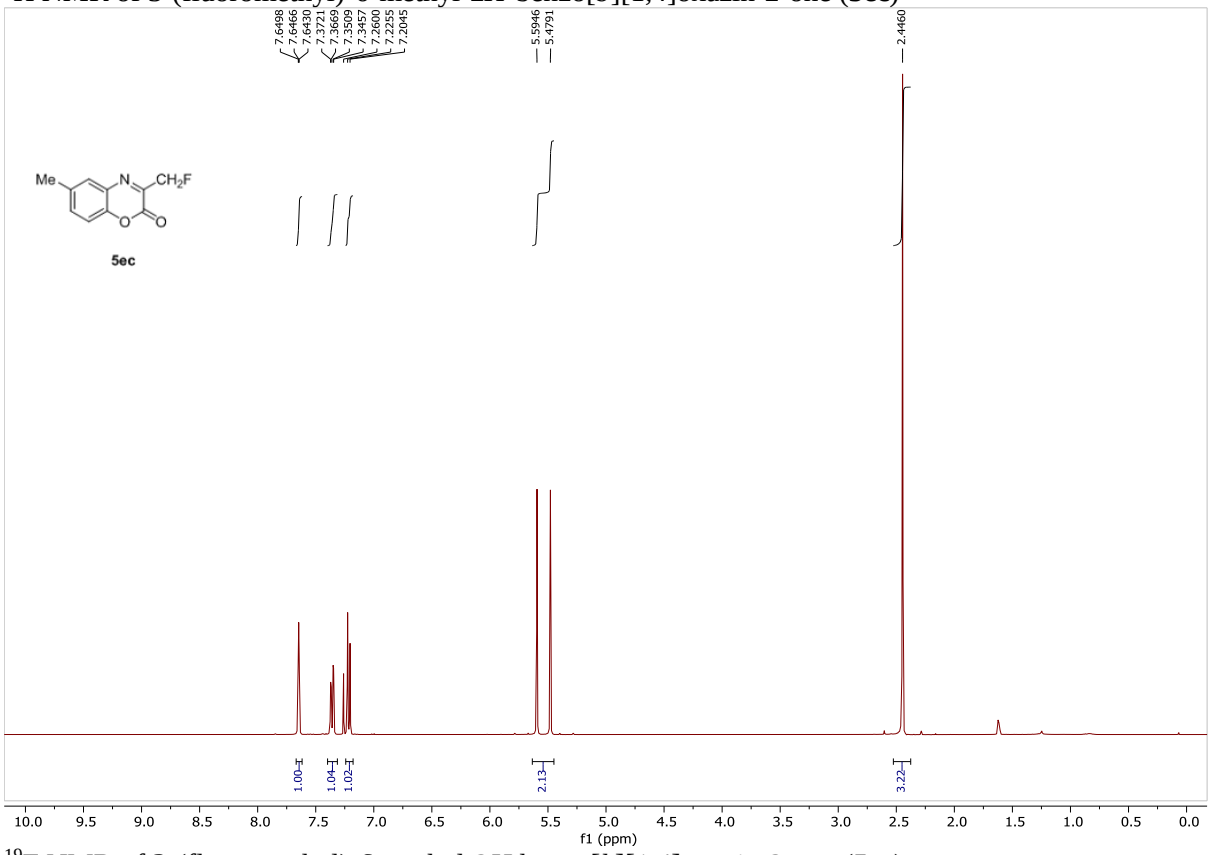
^{19}F NMR of 6-chloro-3-(fluoromethyl)-2*H*-benzo[*b*][1,4]oxazin-2-one (**5eb**)



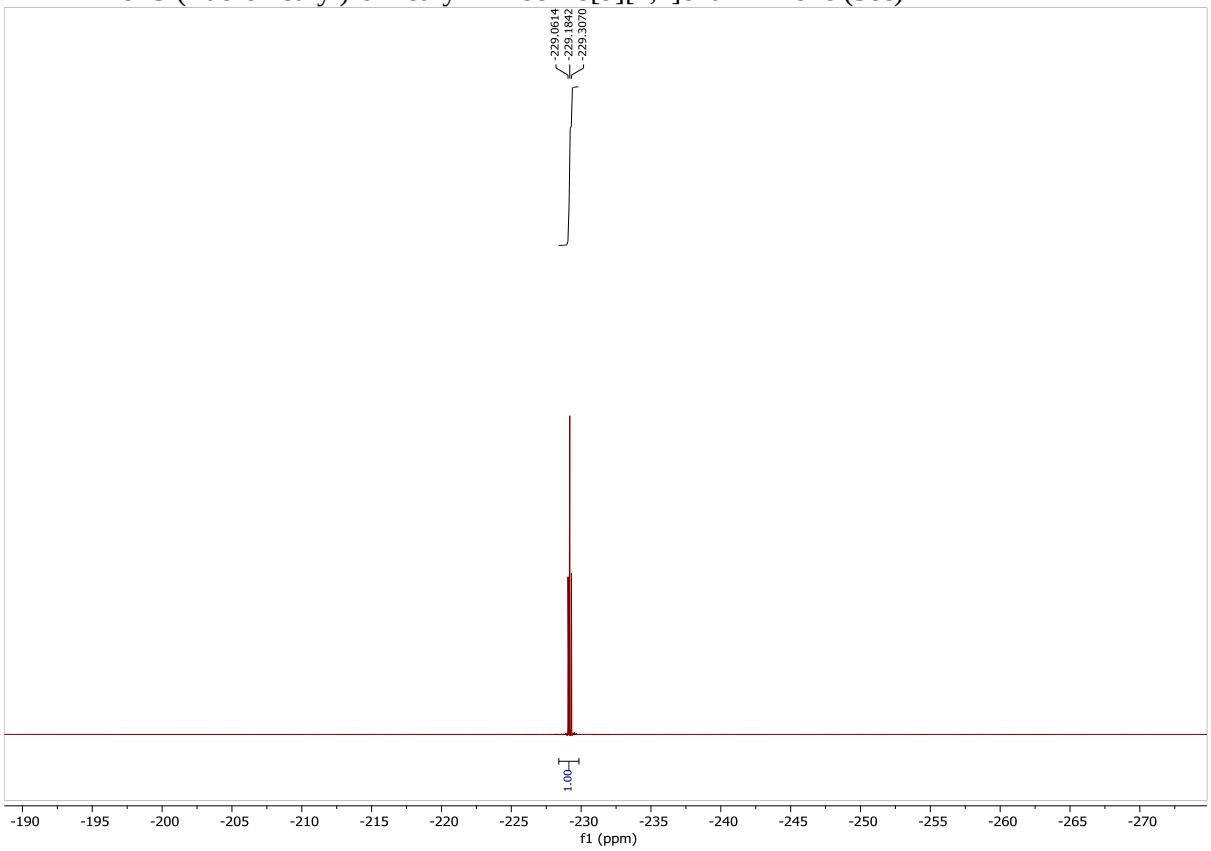
^{13}C NMR of 6-chloro-3-(fluoromethyl)-2*H*-benzo[*b*][1,4]oxazin-2-one (**5eb**)



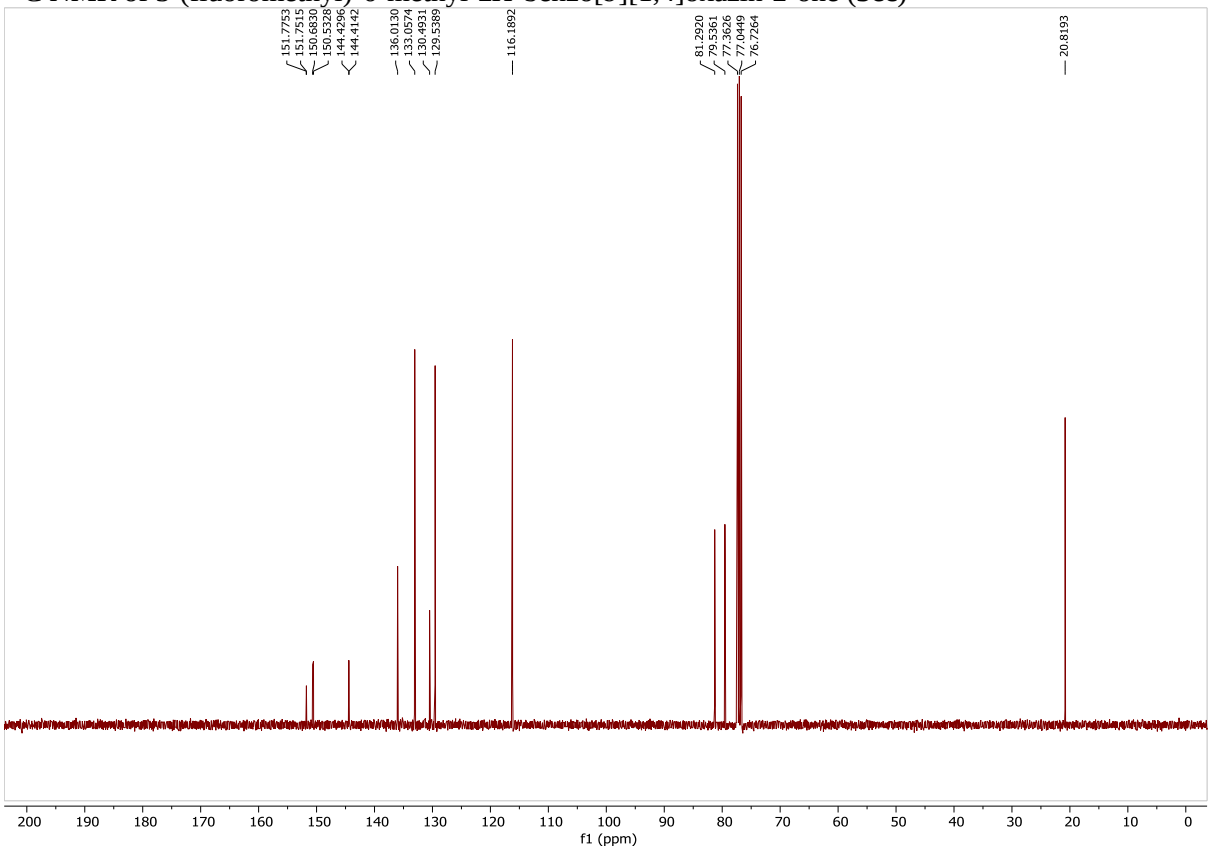
^{1}H NMR of 3-(fluoromethyl)-6-methyl-2*H*-benzo[*b*][1,4]oxazin-2-one (**5ec**)



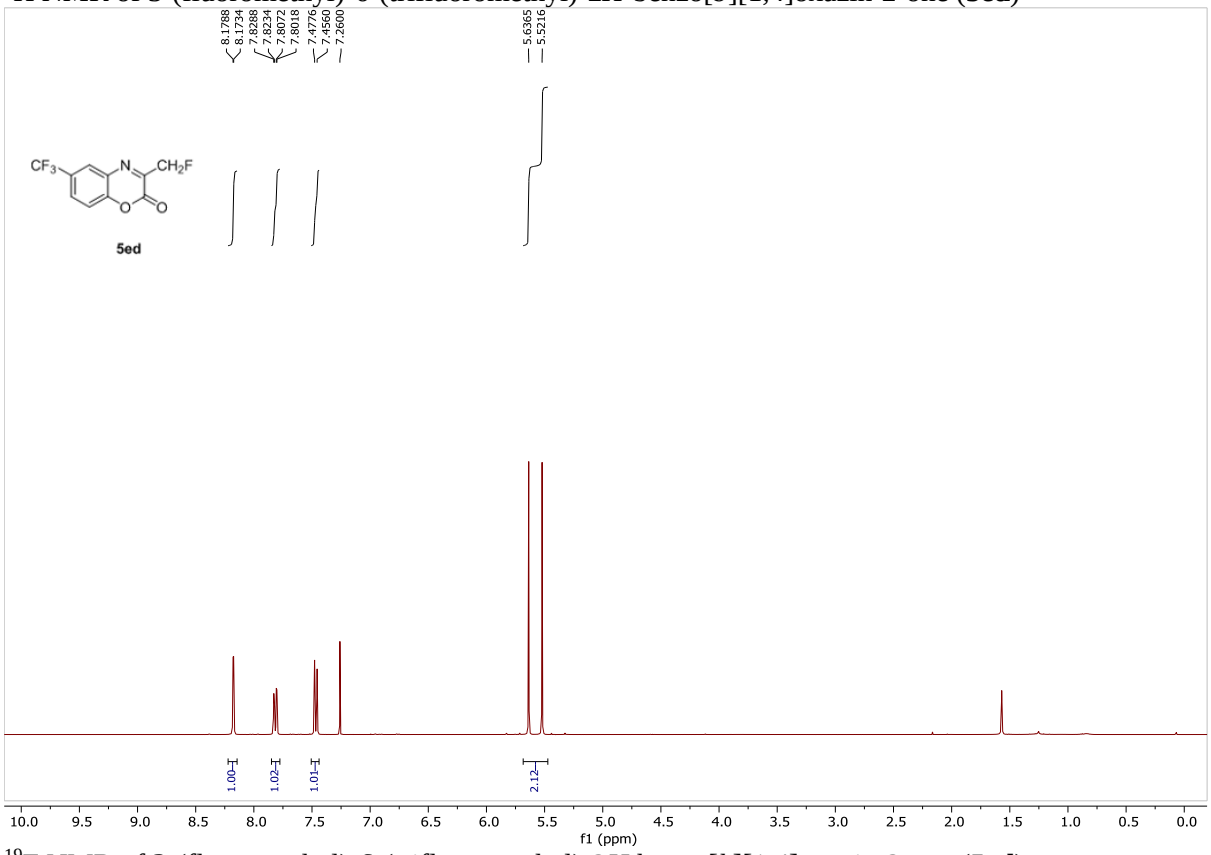
^{19}F NMR of 3-(fluoromethyl)-6-methyl-2*H*-benzo[*b*][1,4]oxazin-2-one (**5ec**)



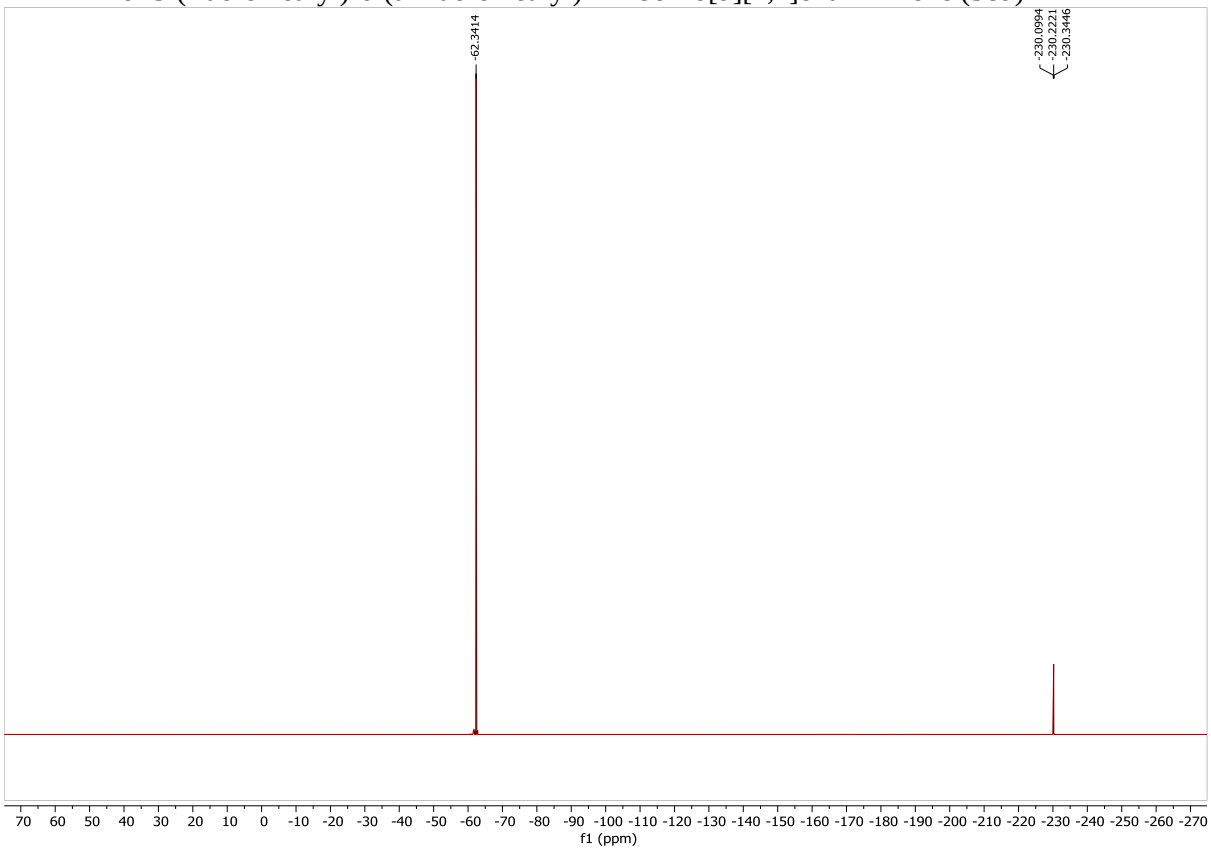
^{13}C NMR of 3-(fluoromethyl)-6-methyl-2*H*-benzo[*b*][1,4]oxazin-2-one (**5ec**)



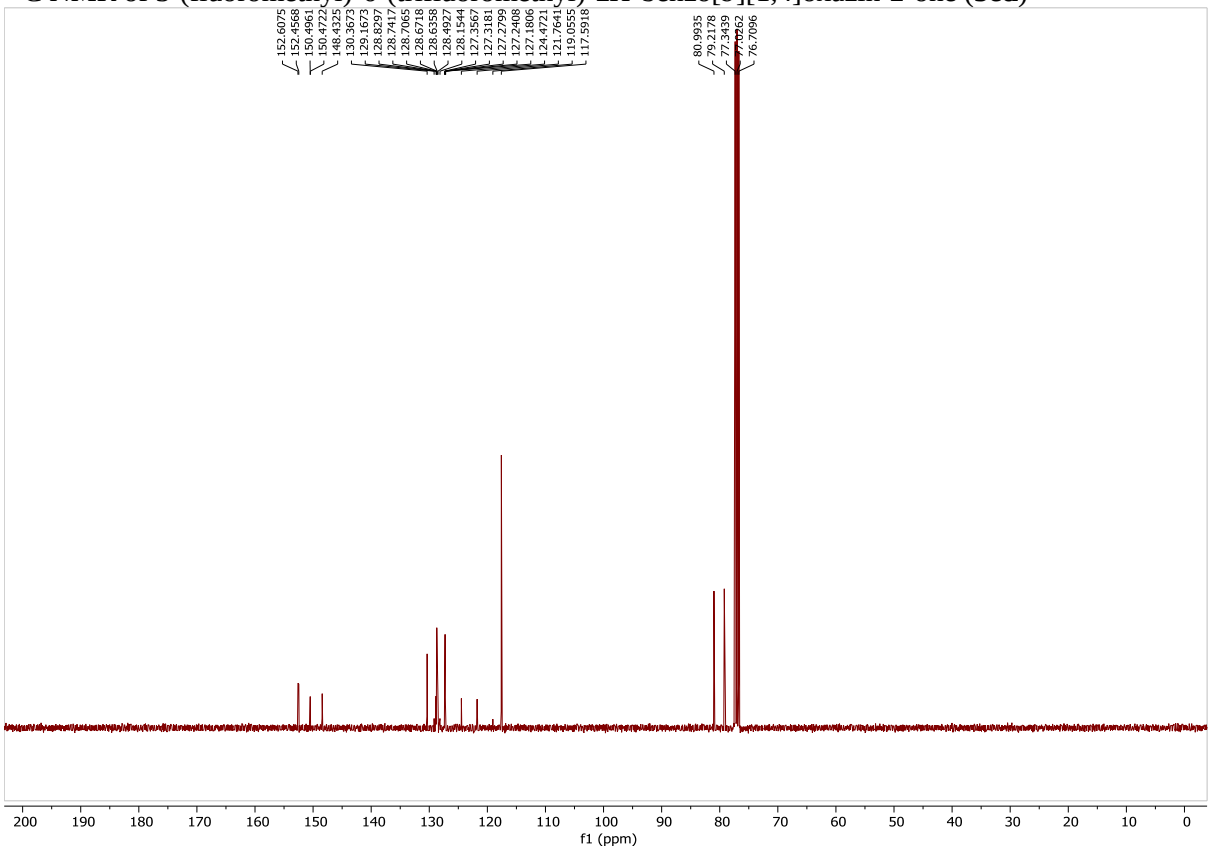
^{1}H NMR of 3-(fluoromethyl)-6-(trifluoromethyl)-2*H*-benzo[*b*][1,4]oxazin-2-one (**5ed**)



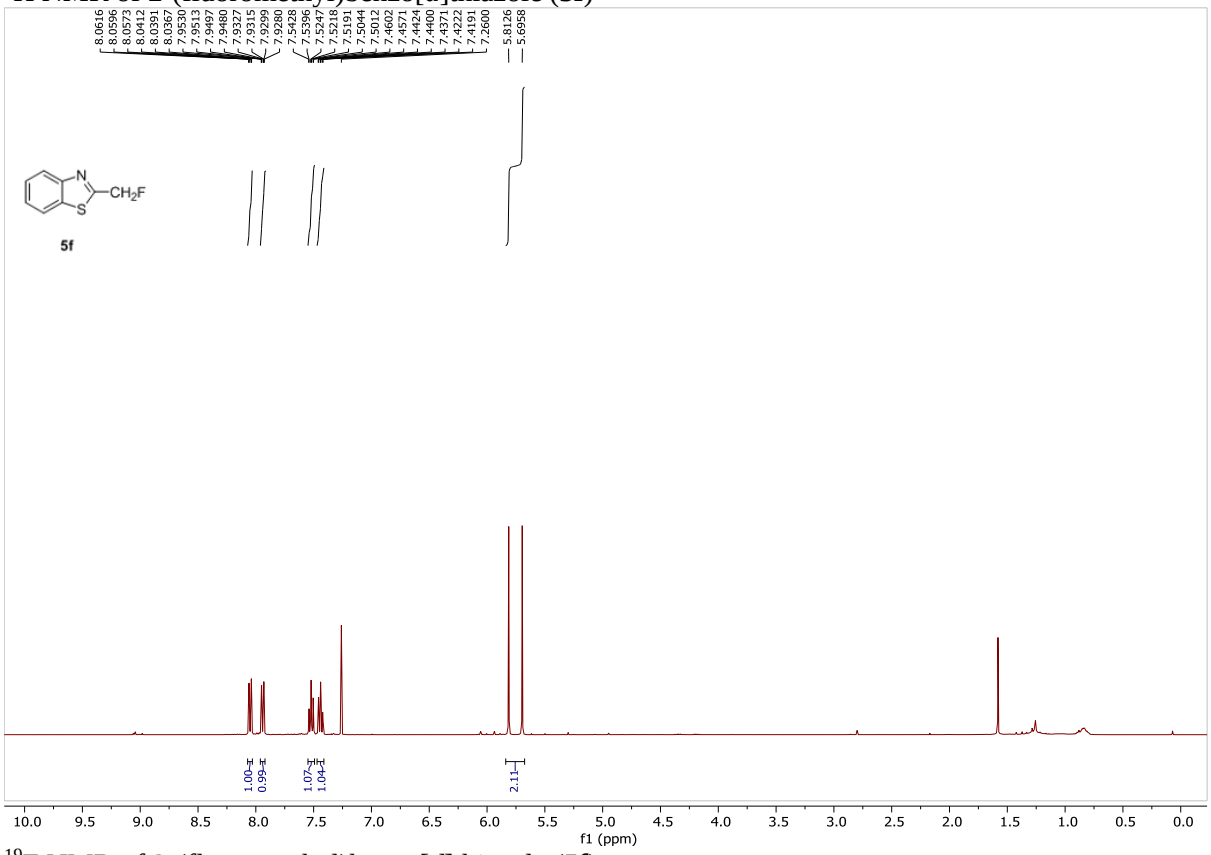
^{19}F NMR of 3-(fluoromethyl)-6-(trifluoromethyl)-2*H*-benzo[*b*][1,4]oxazin-2-one (**5ed**)



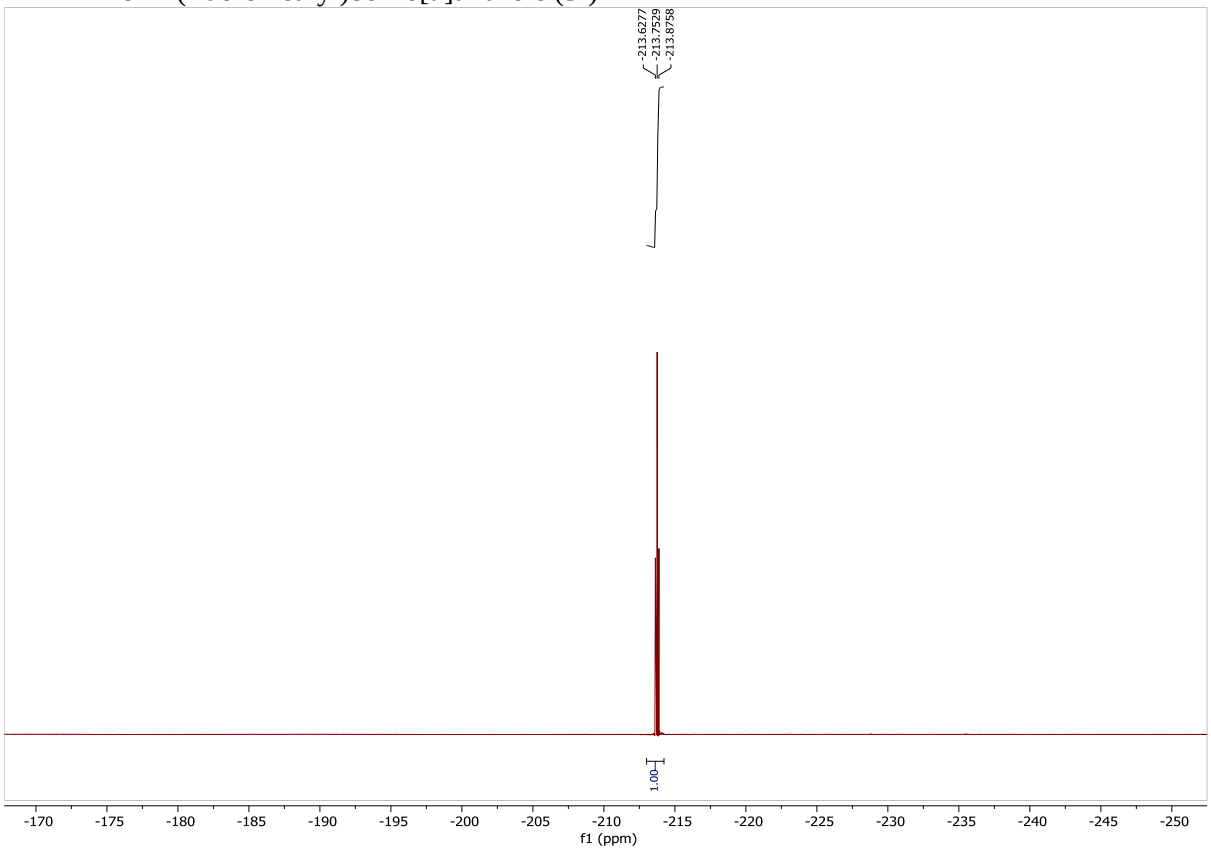
^{13}C NMR of 3-(fluoromethyl)-6-(trifluoromethyl)-2*H*-benzo[*b*][1,4]oxazin-2-one (**5ed**)



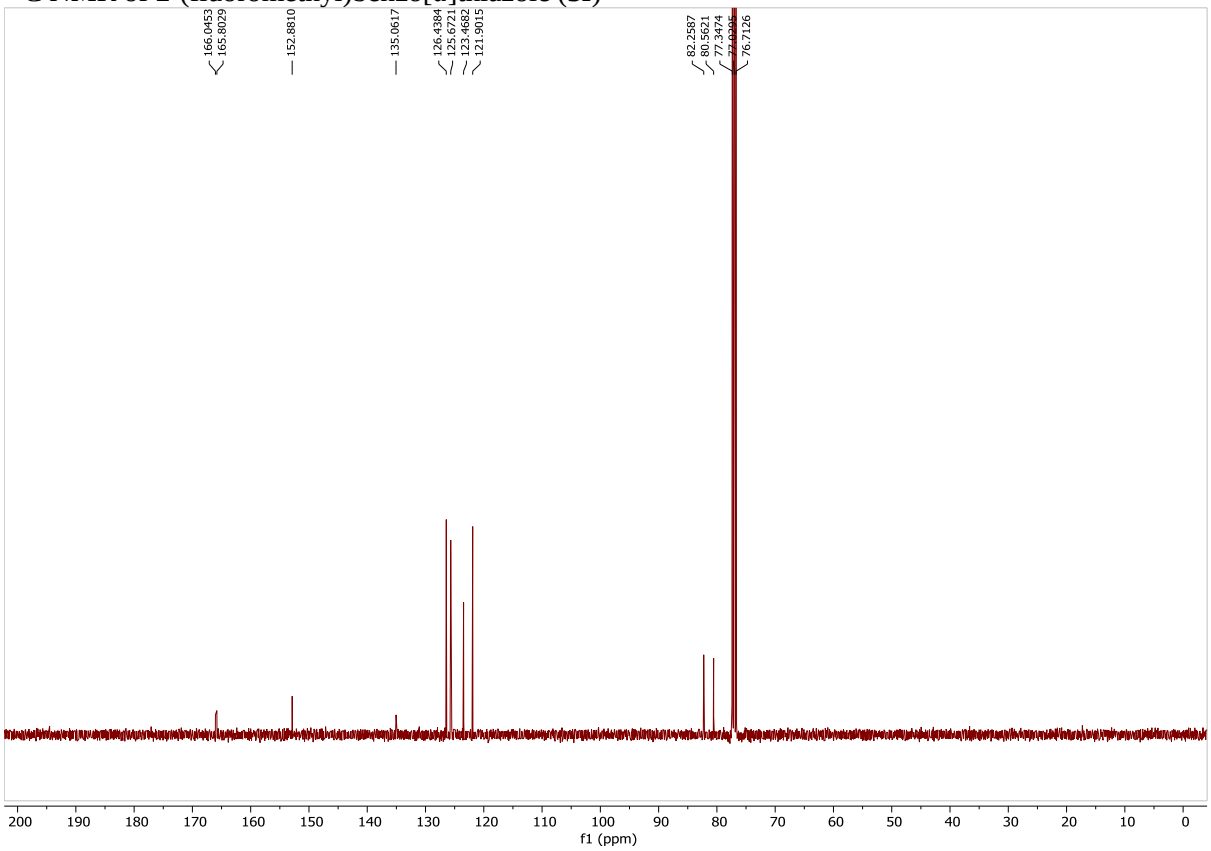
^{1}H NMR of 2-(fluoromethyl)benzo[*d*]thiazole (**5f**)



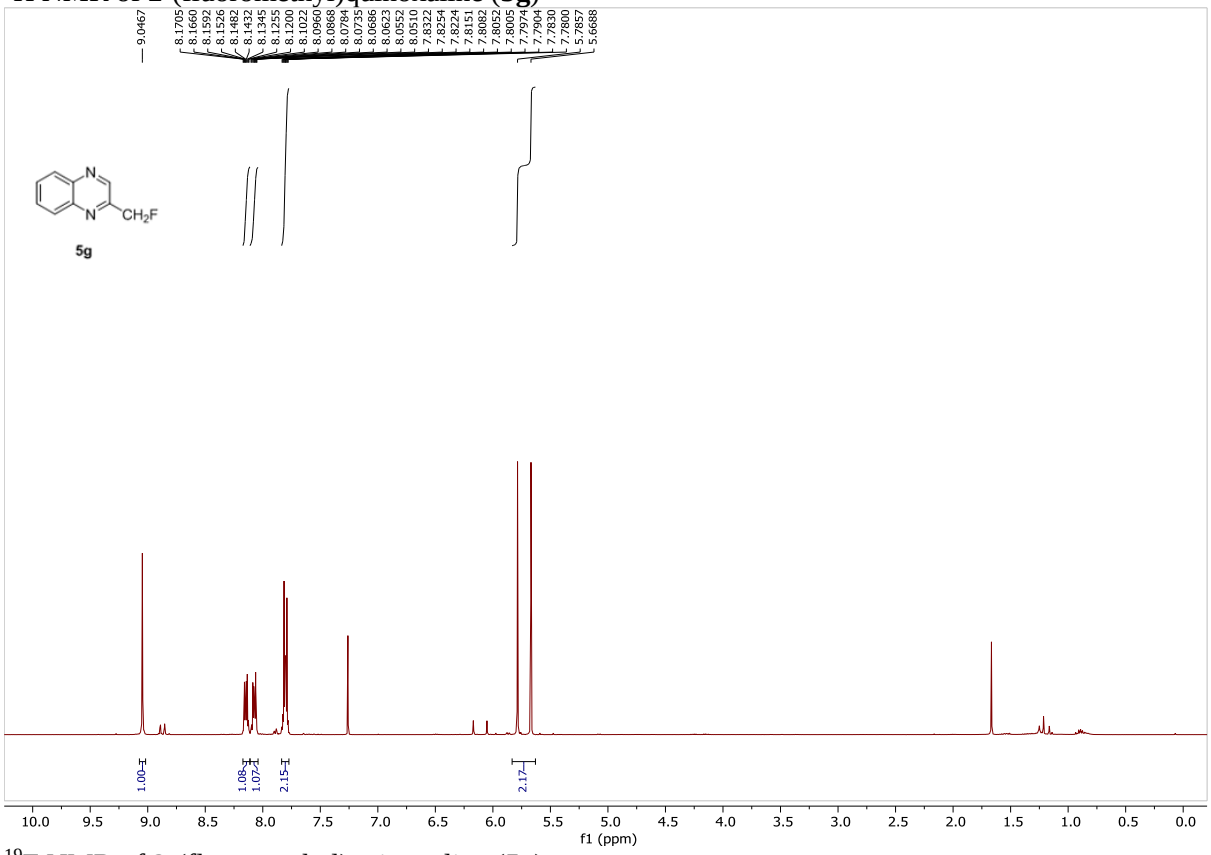
^{19}F NMR of 2-(fluoromethyl)benzo[*d*]thiazole (**5f**)



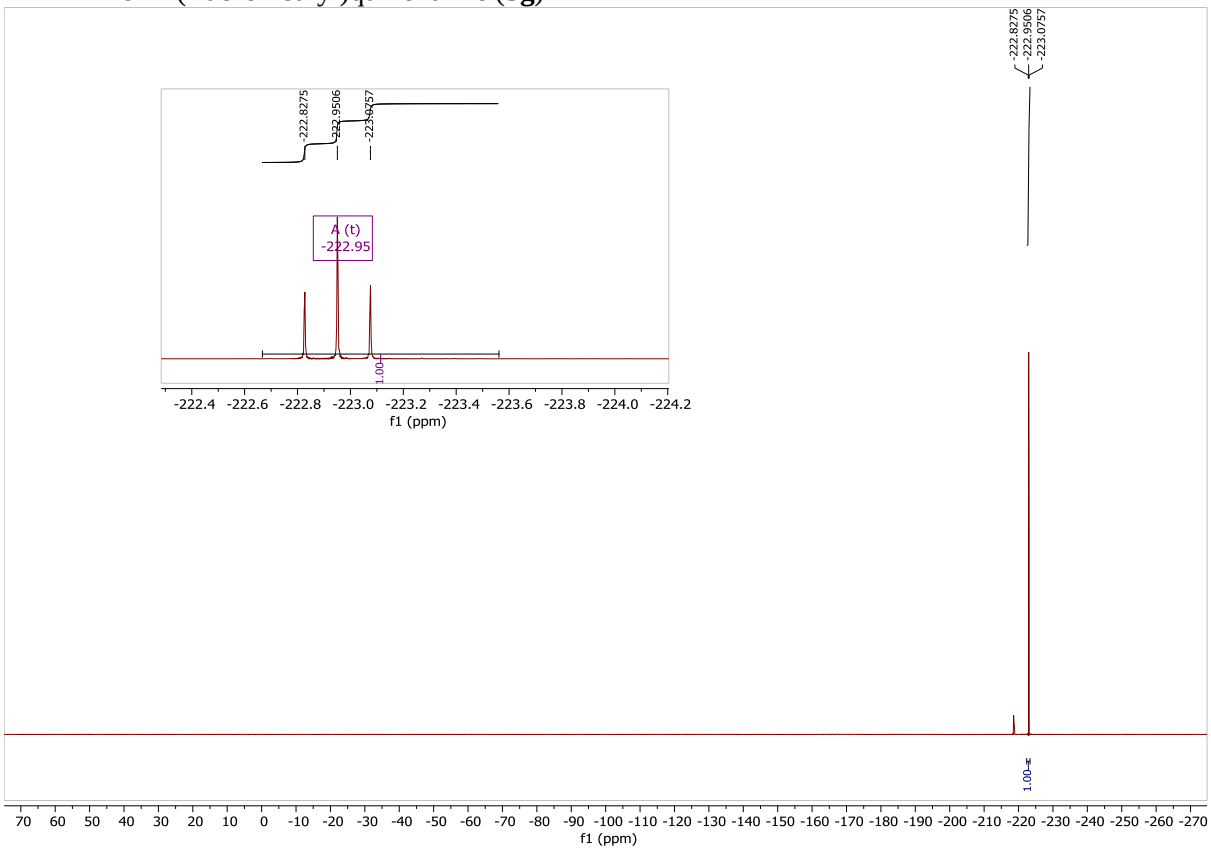
^{13}C NMR of 2-(fluoromethyl)benzo[*d*]thiazole (**5f**)



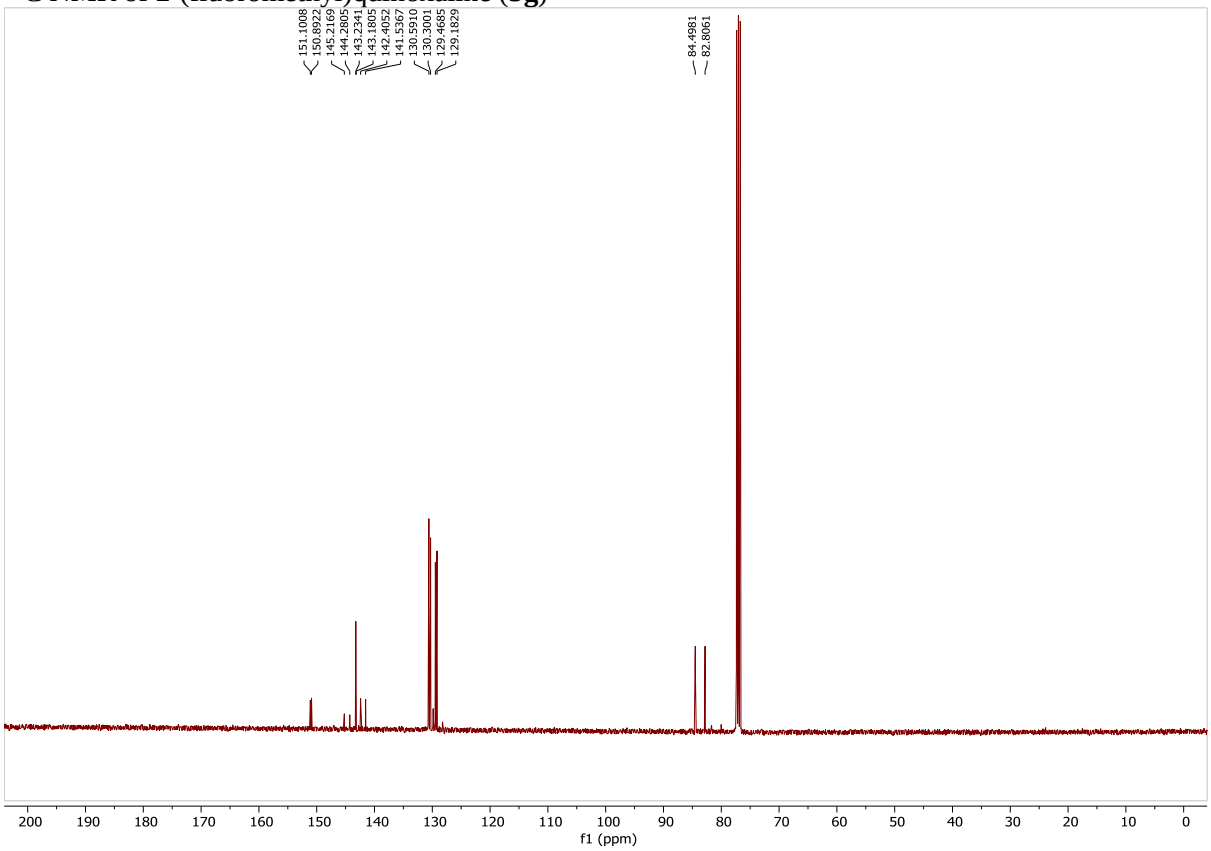
^{1}H NMR of 2-(fluoromethyl)quinoxaline (**5g**)



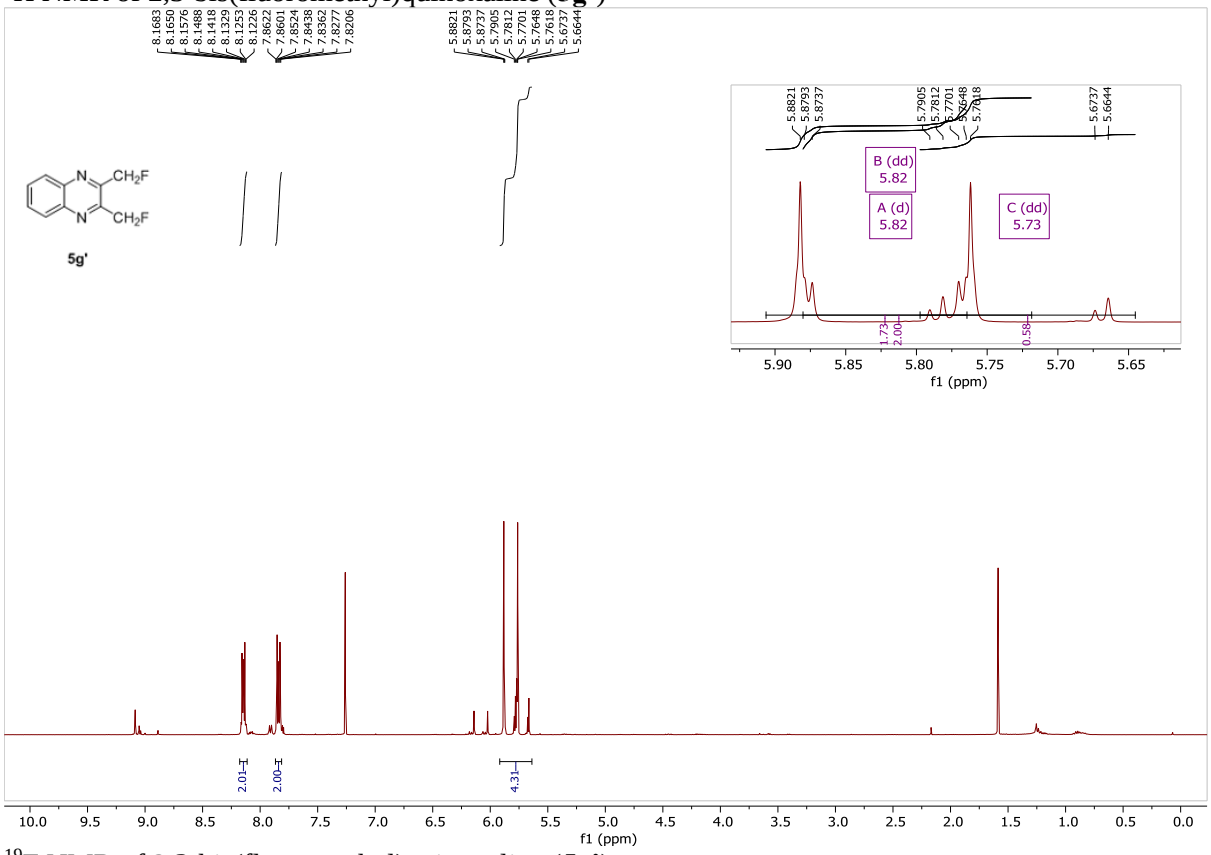
^{19}F NMR of 2-(fluoromethyl)quinoxaline (**5g**)



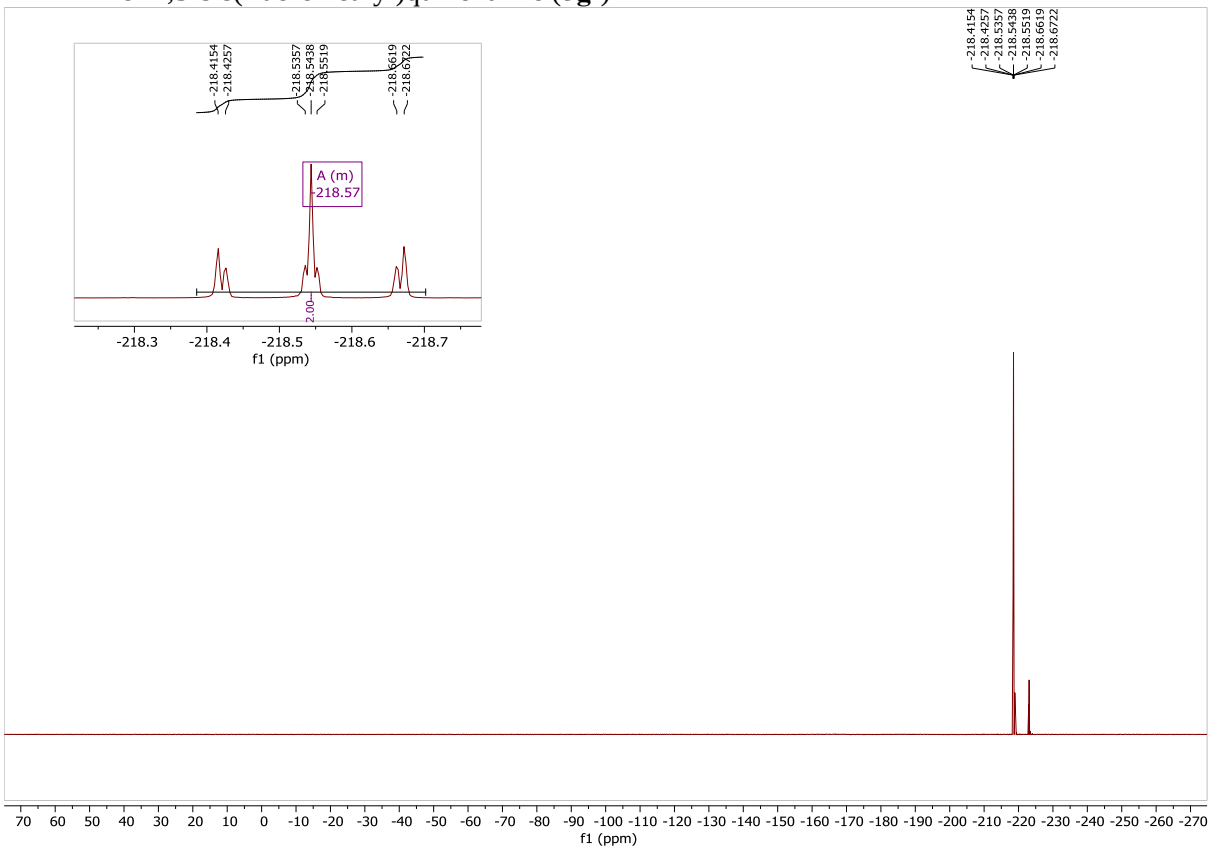
^{13}C NMR of 2-(fluoromethyl)quinoxaline (**5g**)



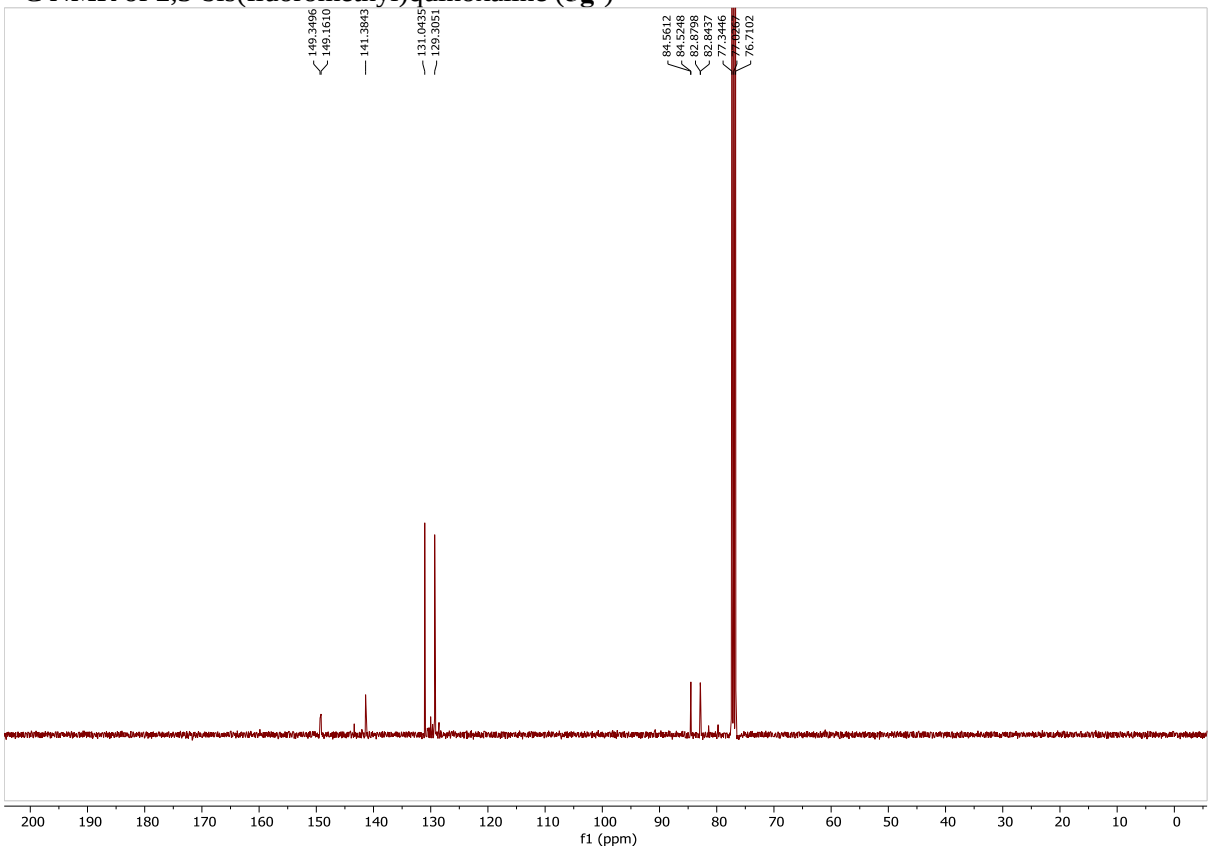
^{1}H NMR of 2,3-bis(fluoromethyl)quinoxaline (**5g'**)



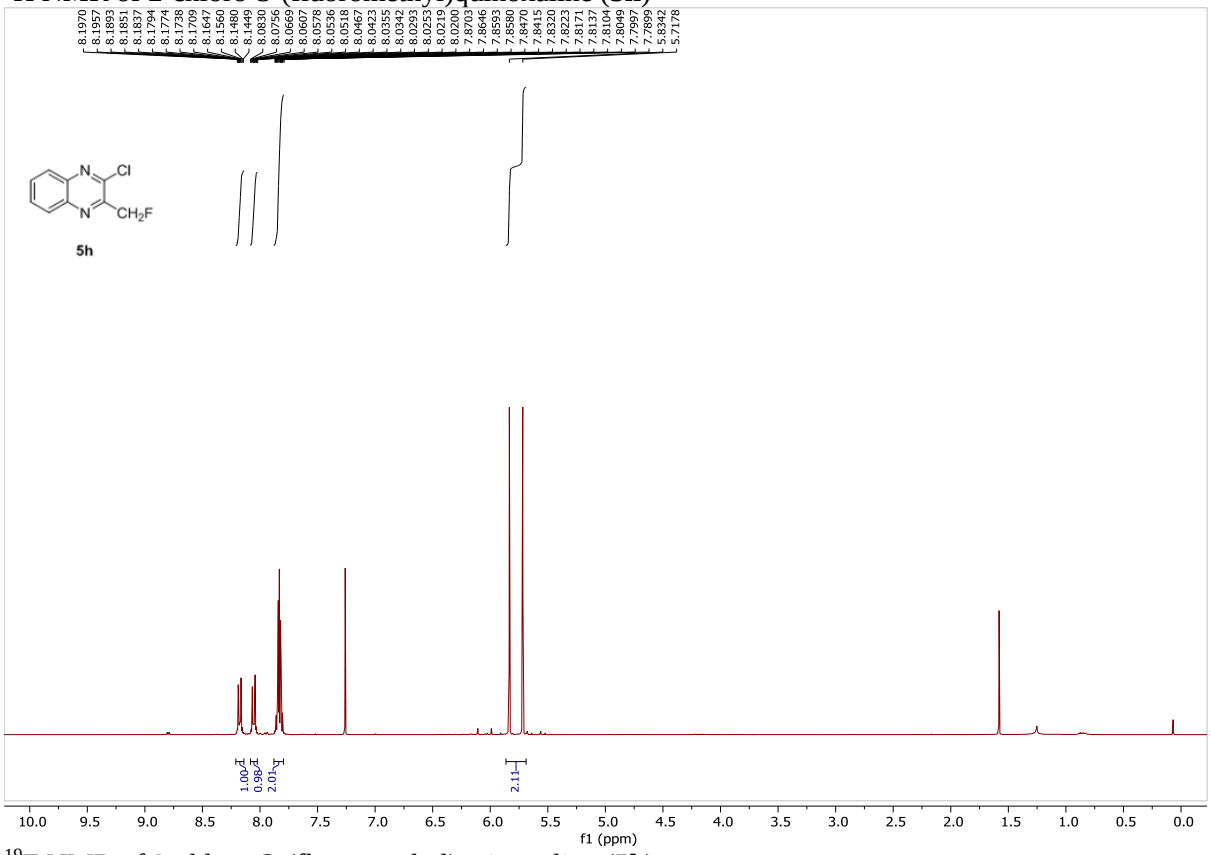
^{19}F NMR of 2,3-bis(fluoromethyl)quinoxaline (**5g'**)



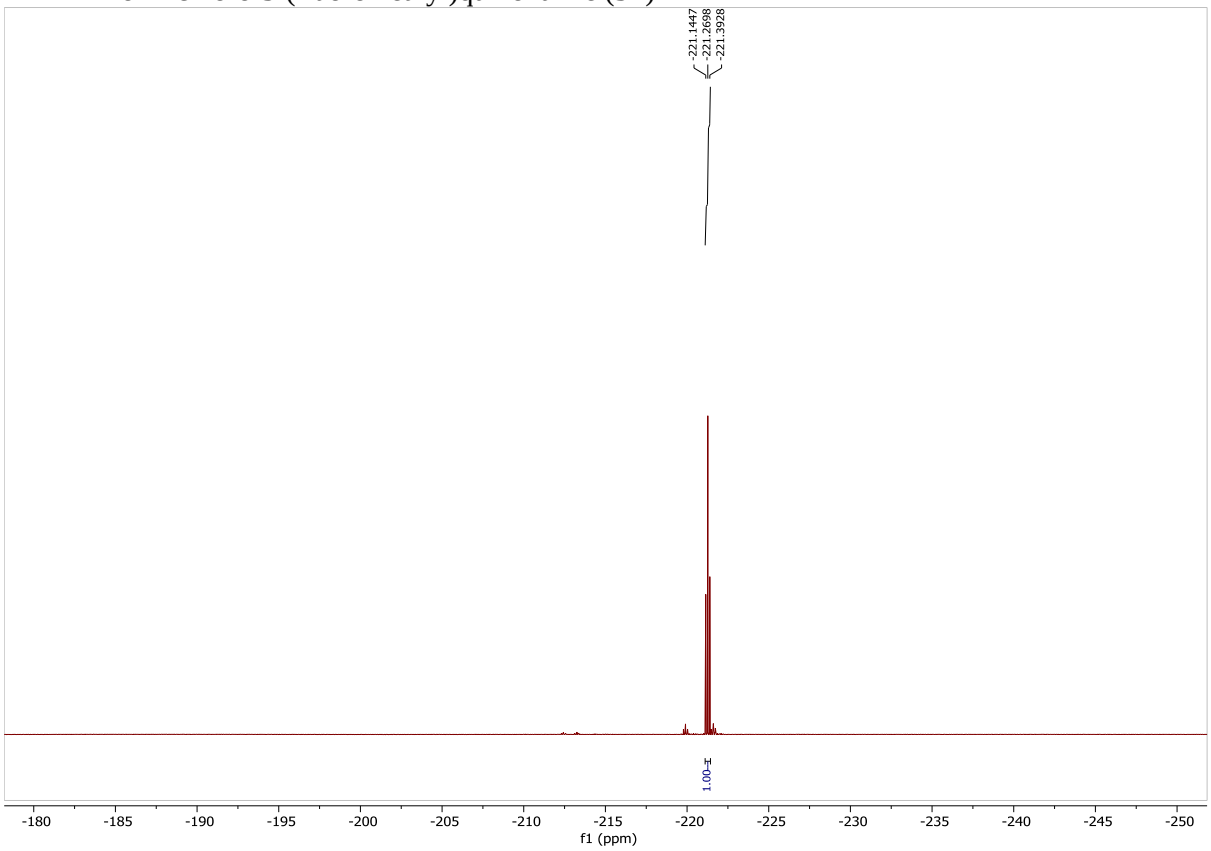
^{13}C NMR of 2,3-bis(fluoromethyl)quinoxaline (**5g'**)



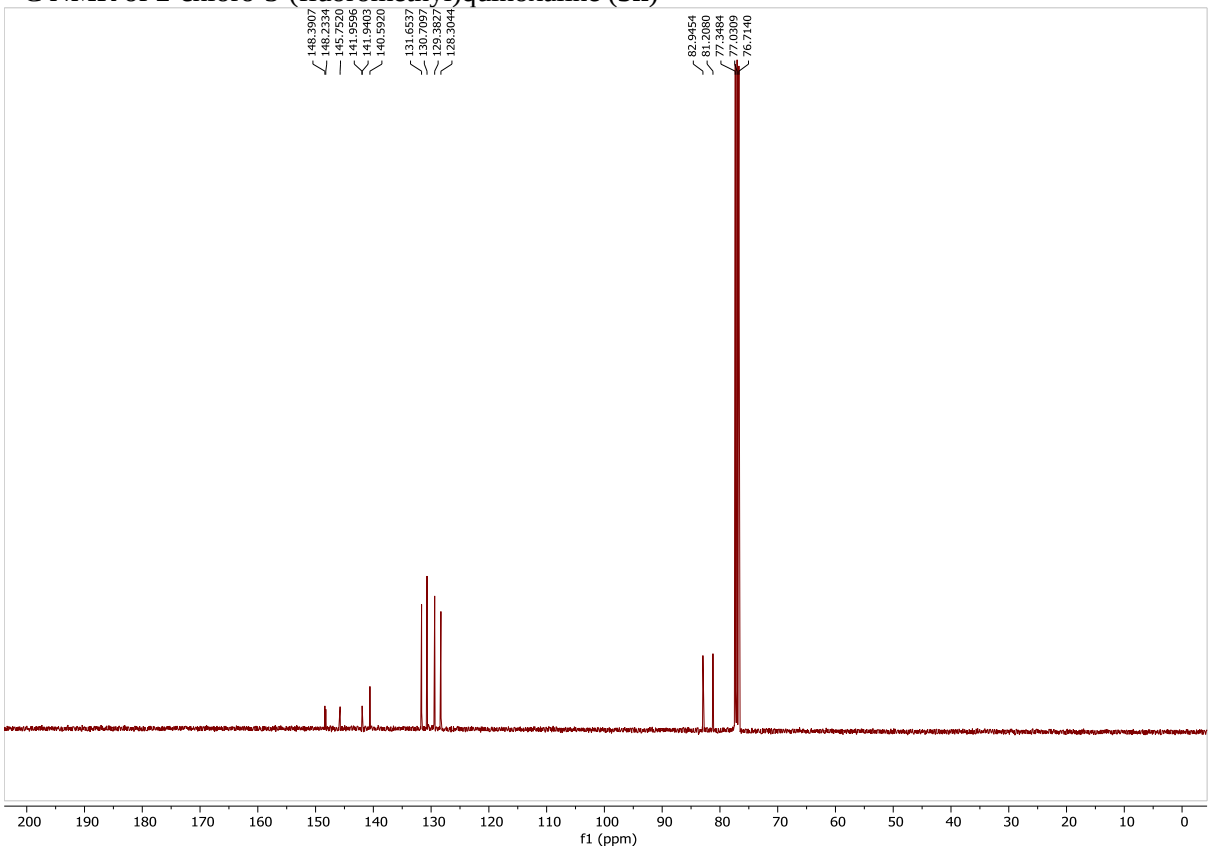
^{1}H NMR of 2-chloro-3-(fluoromethyl)quinoxaline (**5h**)



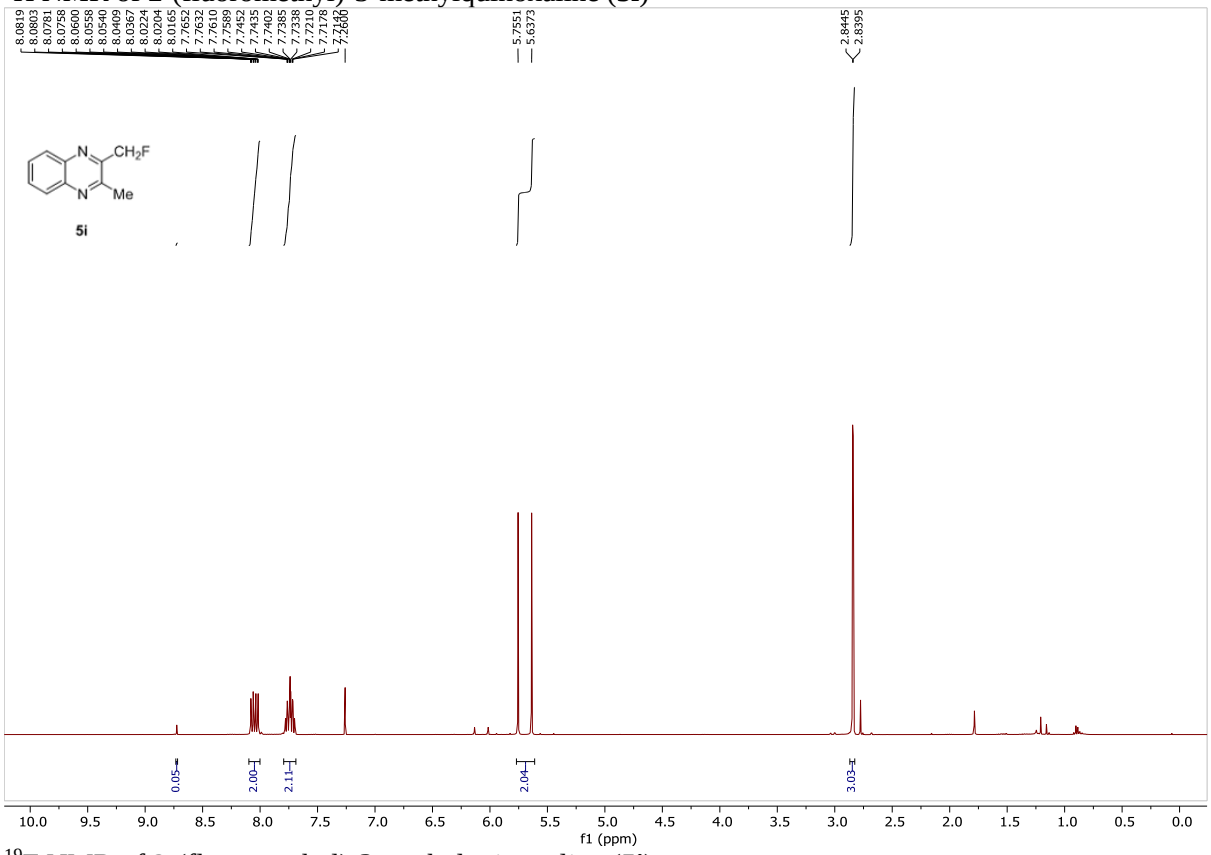
^{19}F NMR of 2-chloro-3-(fluoromethyl)quinoxaline (**5h**)



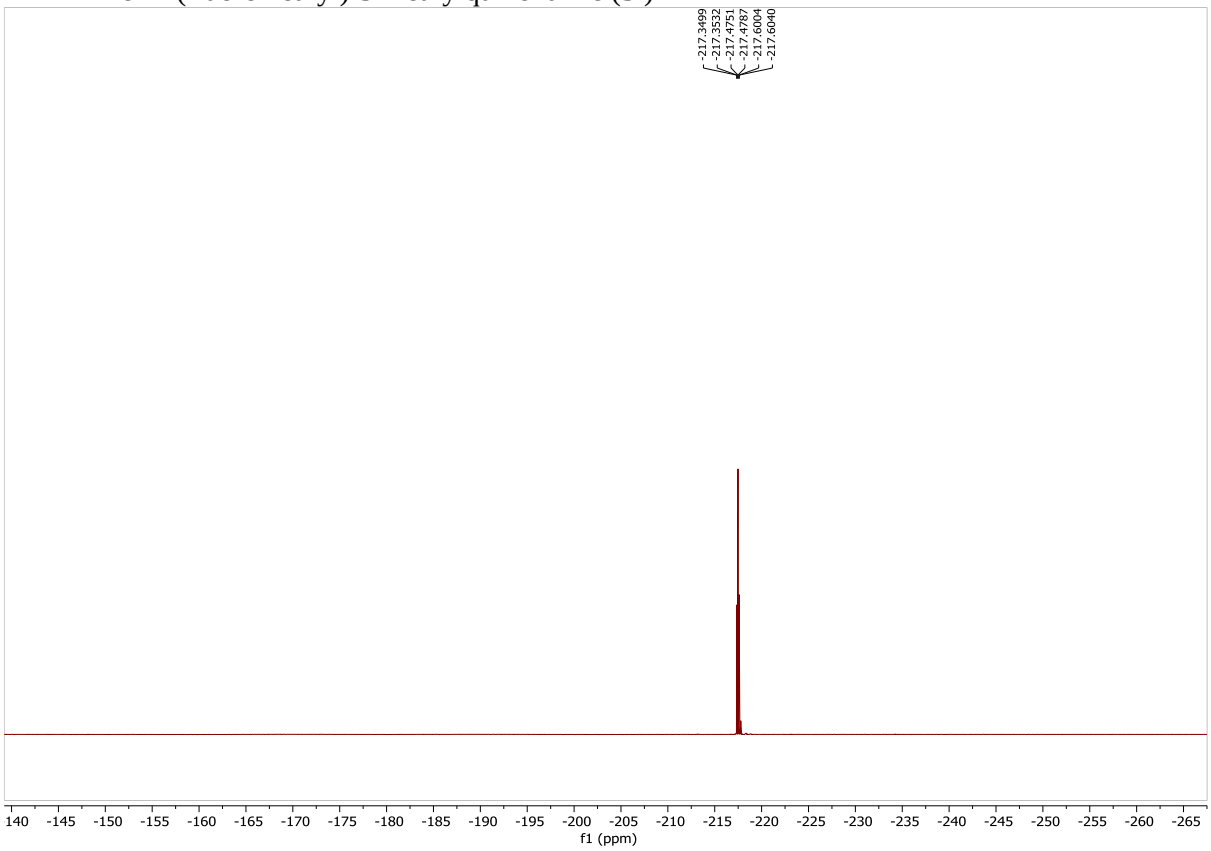
^{13}C NMR of 2-chloro-3-(fluoromethyl)quinoxaline (**5h**)



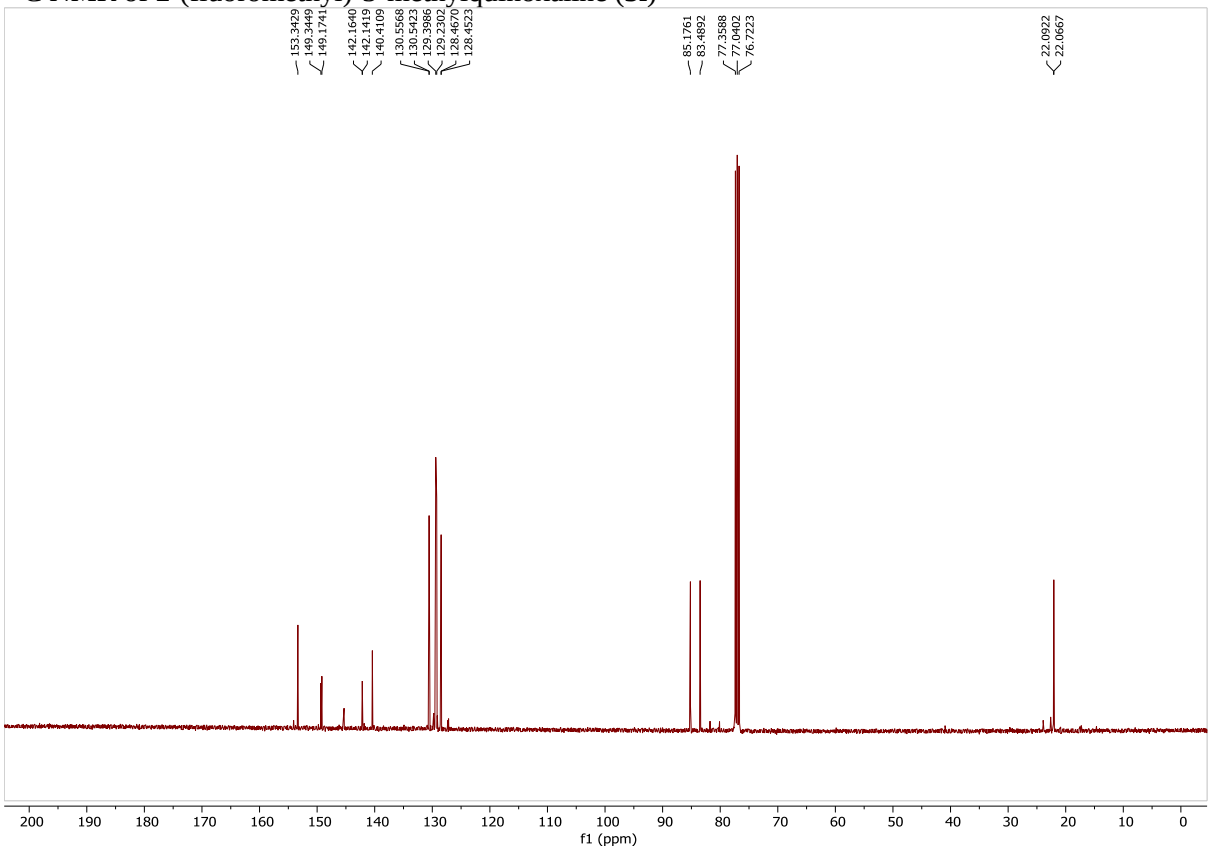
^{1}H NMR of 2-(fluoromethyl)-3-methylquinoxaline (**5i**)



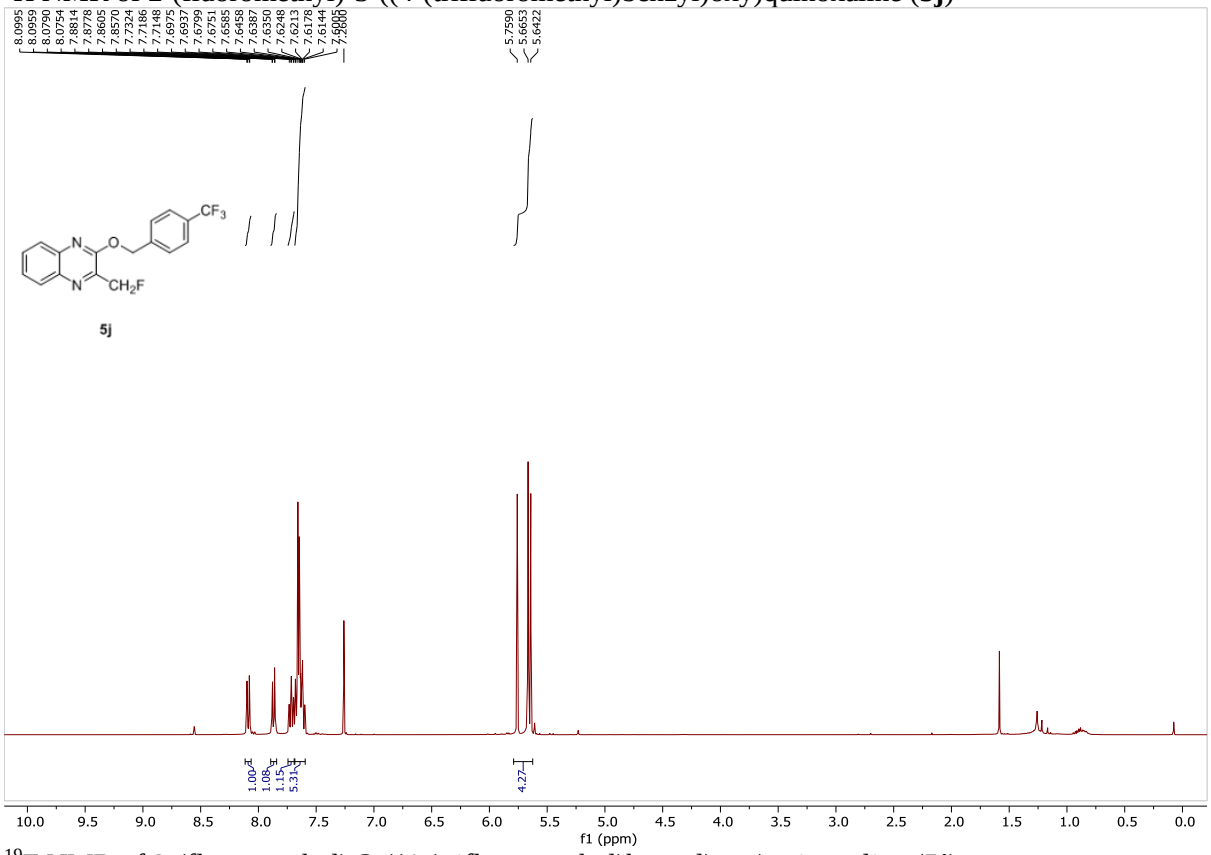
^{19}F NMR of 2-(fluoromethyl)-3-methylquinoxaline (**5i**)



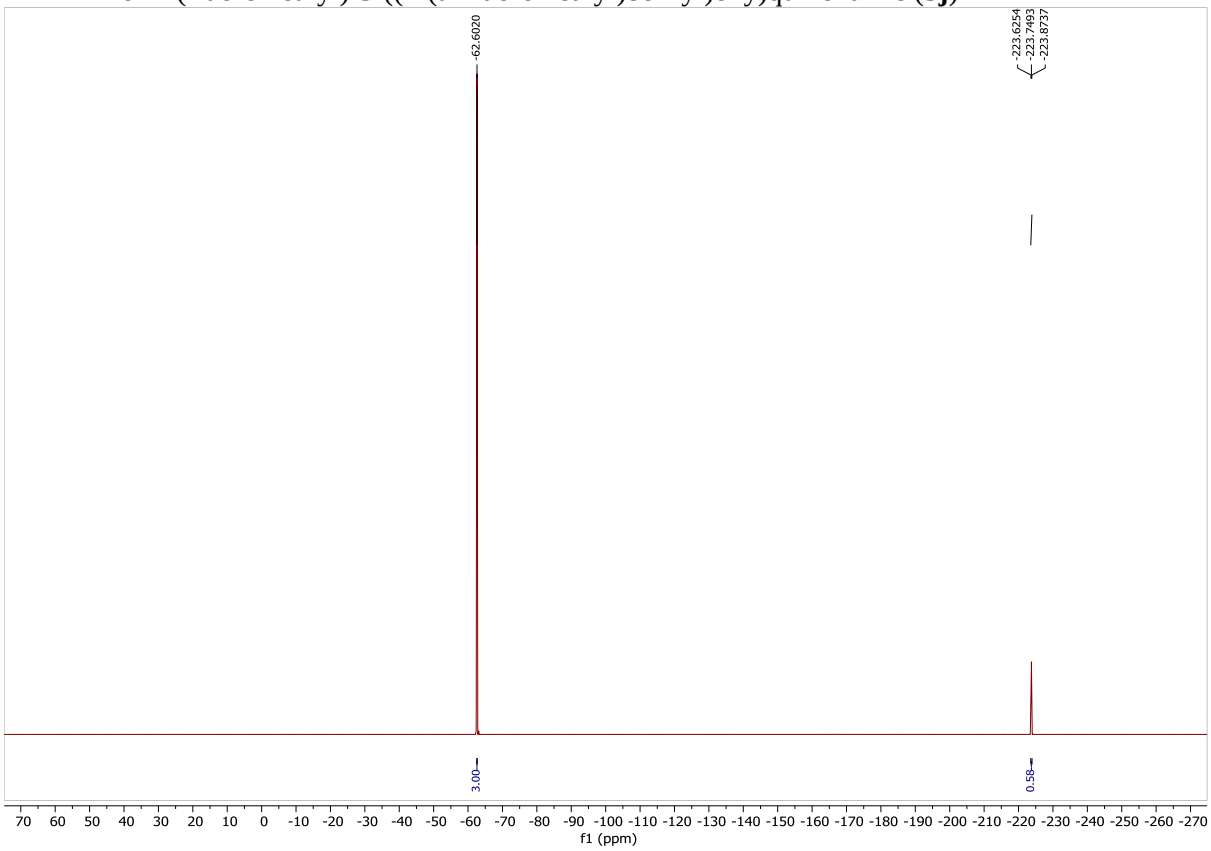
^{13}C NMR of 2-(fluoromethyl)-3-methylquinoxaline (**5i**)



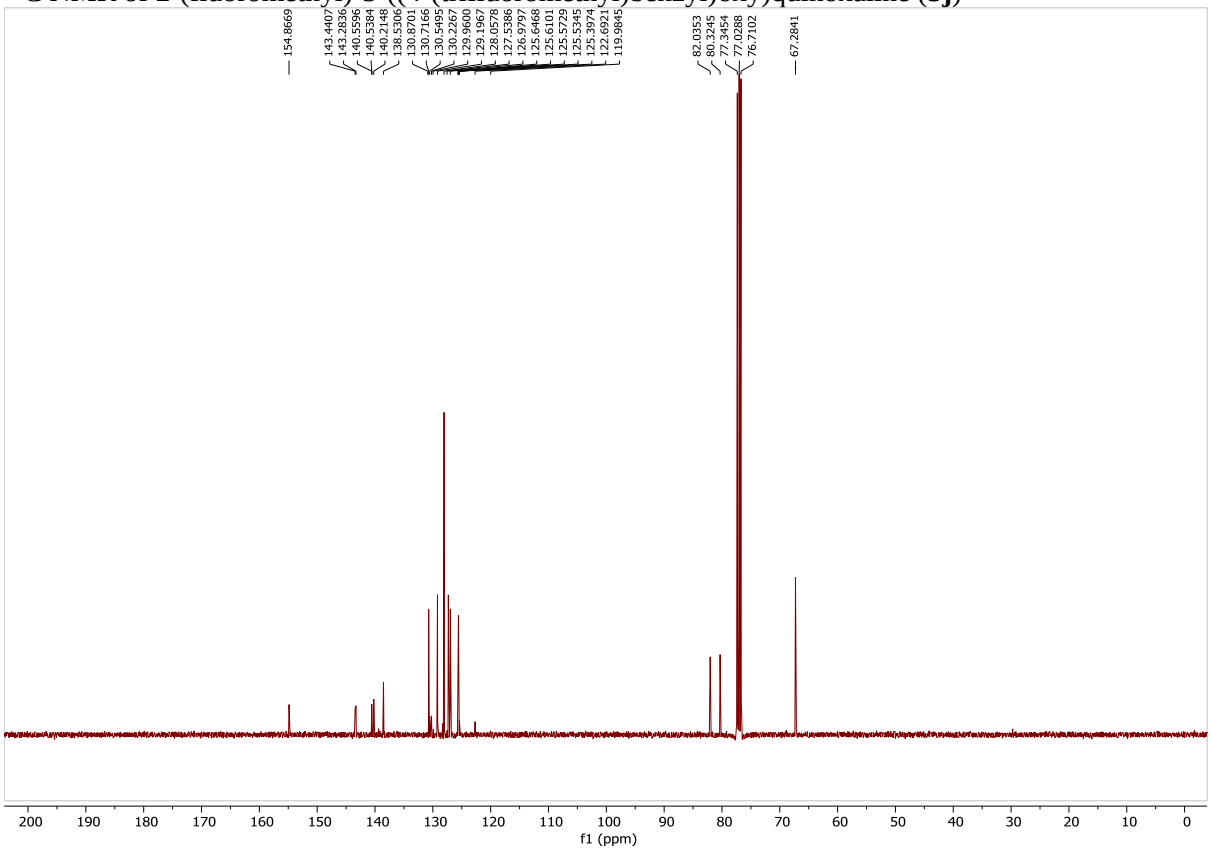
^{1}H NMR of 2-(fluoromethyl)-3-((4-(trifluoromethyl)benzyl)oxy)quinoxaline (**5j**)



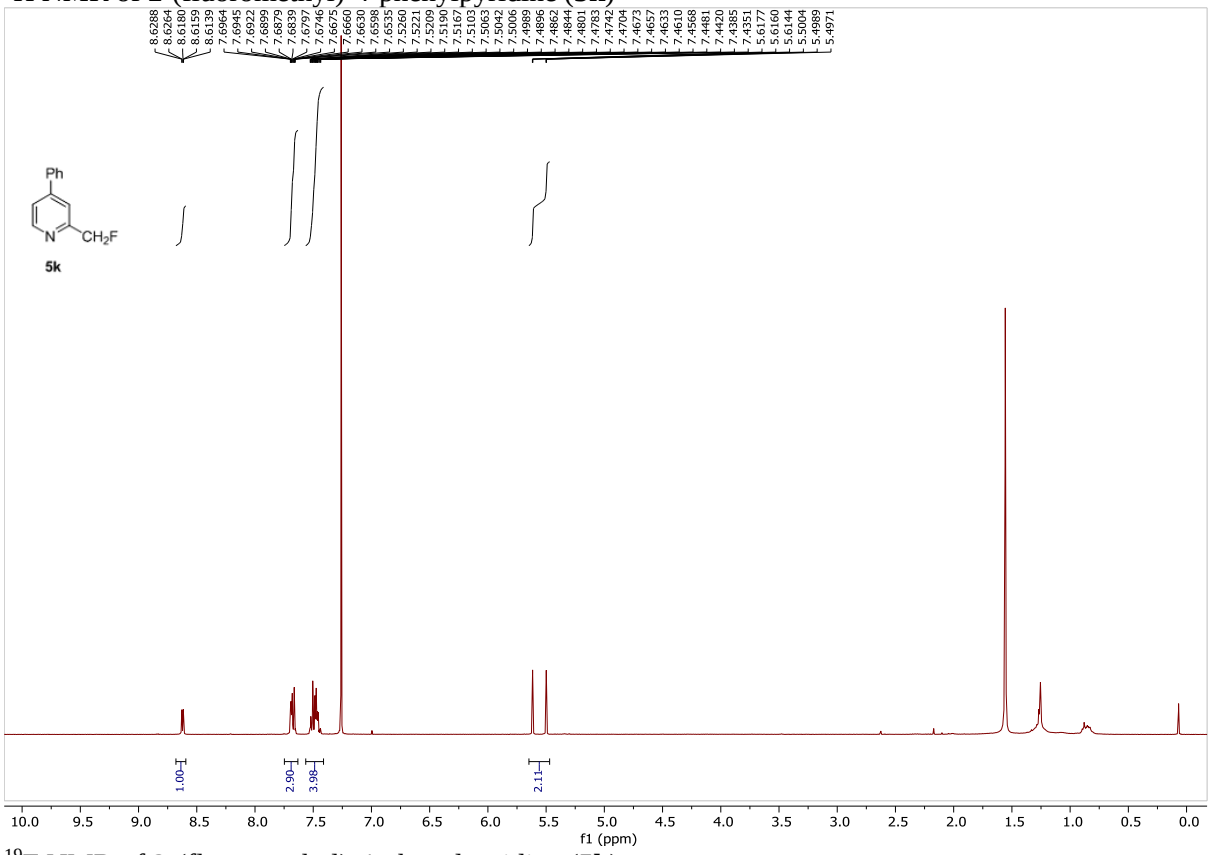
^{19}F NMR of 2-(fluoromethyl)-3-((4-(trifluoromethyl)benzyl)oxy)quinoxaline (**5j**)



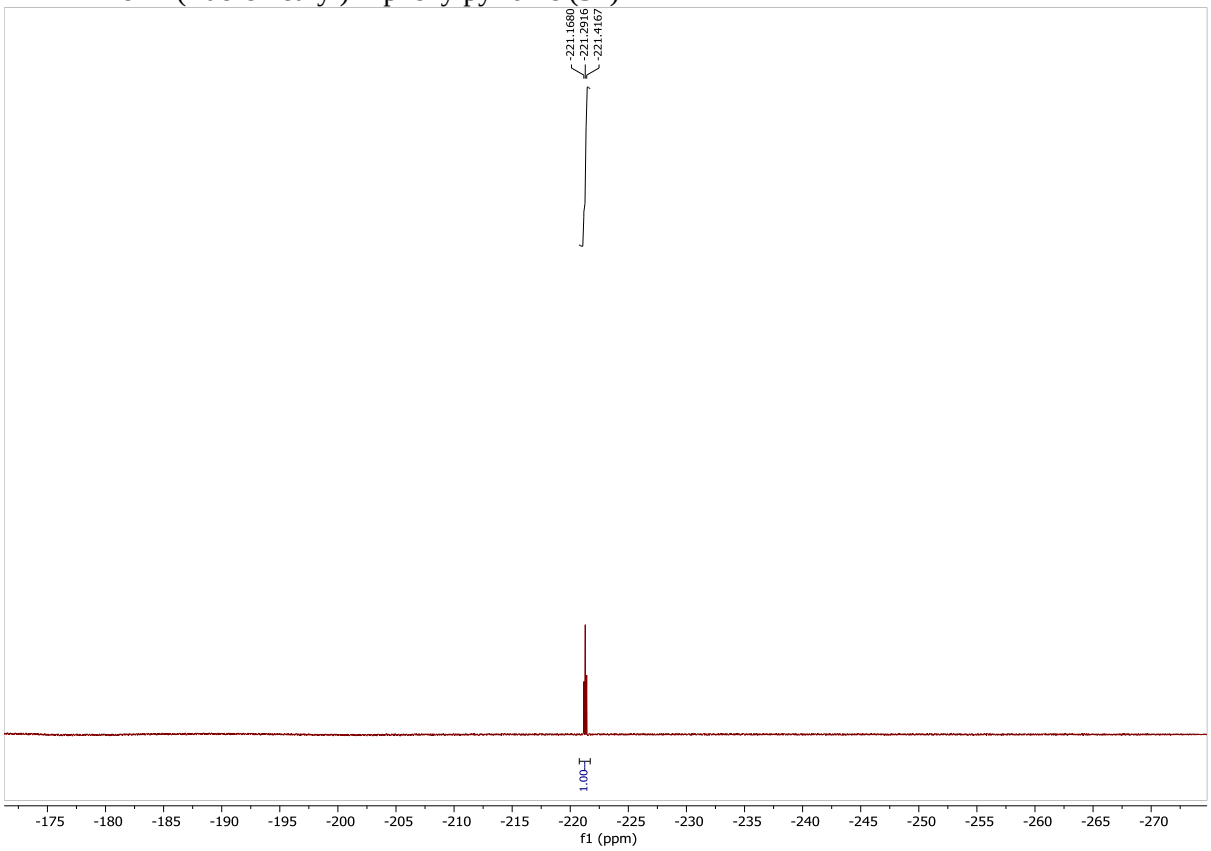
^{13}C NMR of 2-(fluoromethyl)-3-((4-(trifluoromethyl)benzyl)oxy)quinoxaline (**5j**)



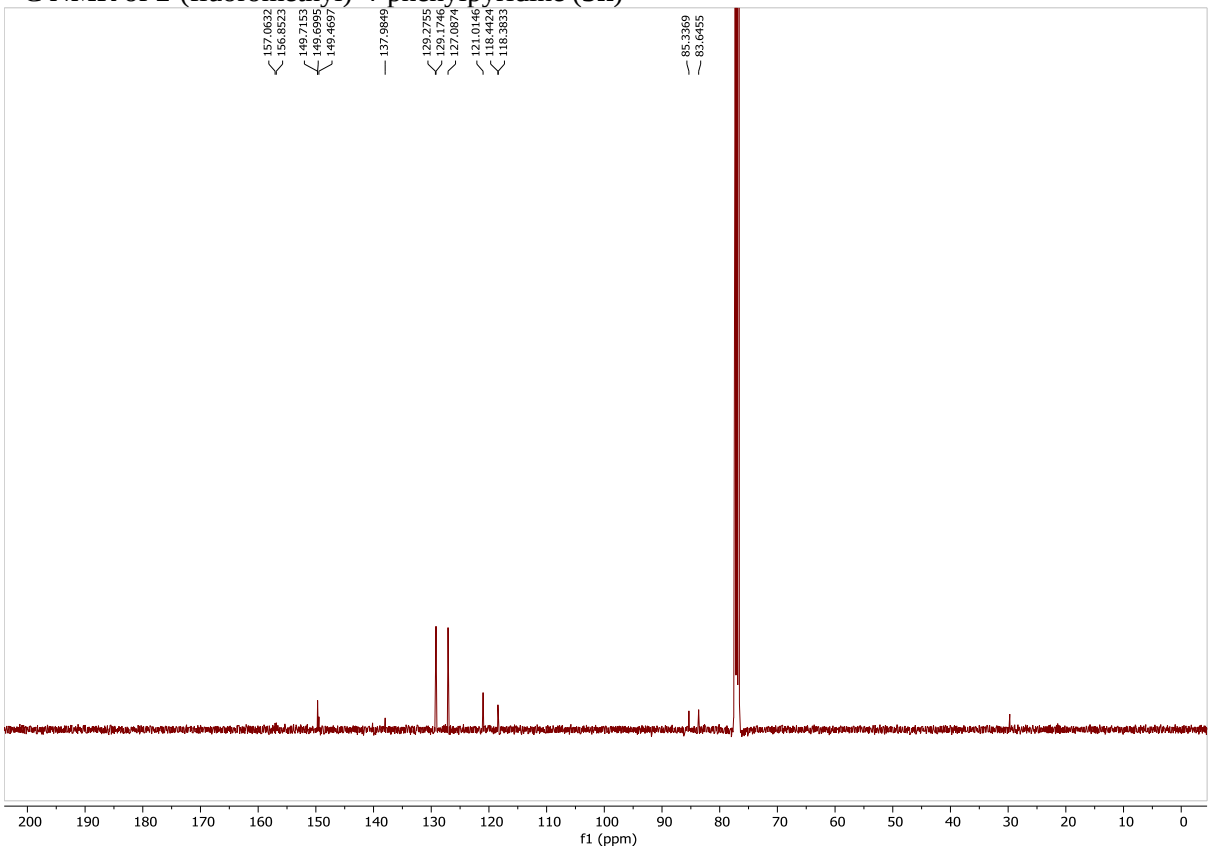
^{1}H NMR of 2-(fluoromethyl)-4-phenylpyridine (**5k**)



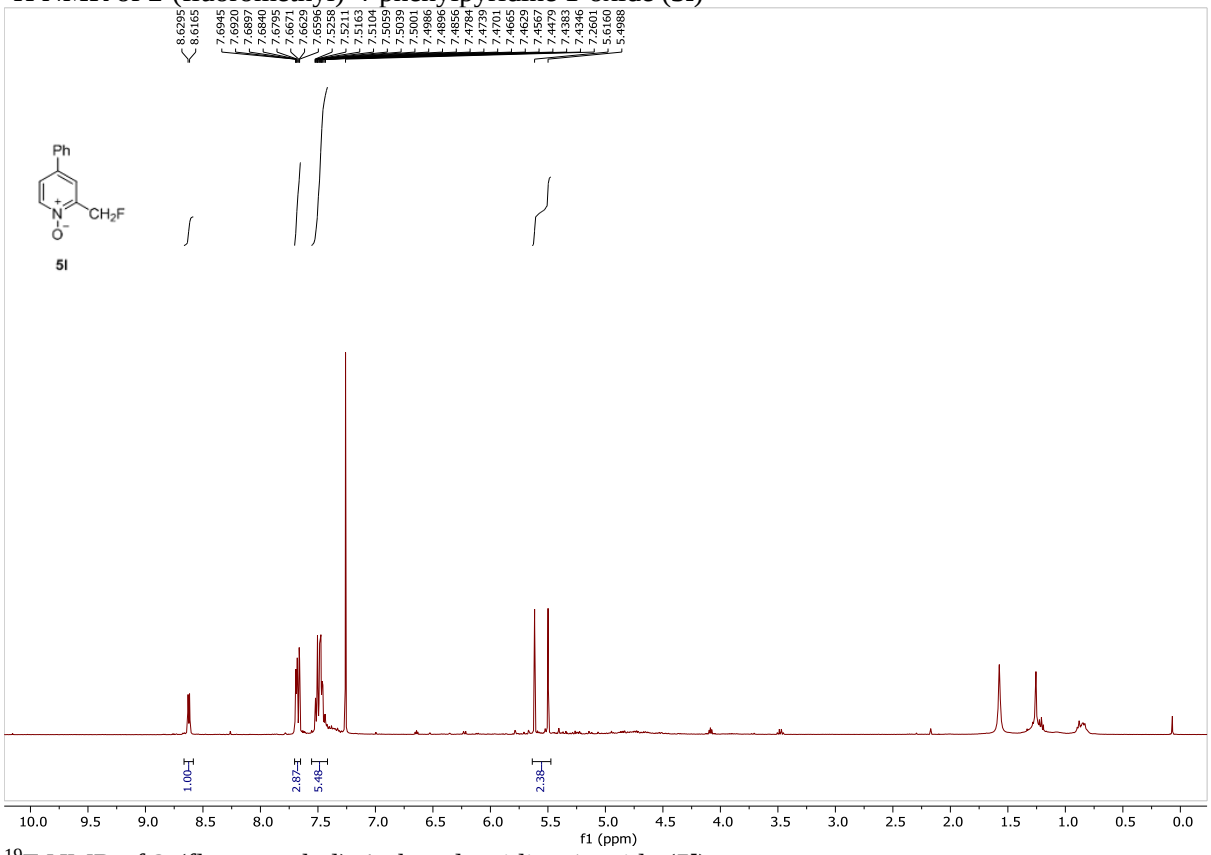
^{19}F NMR of 2-(fluoromethyl)-4-phenylpyridine (**5k**)



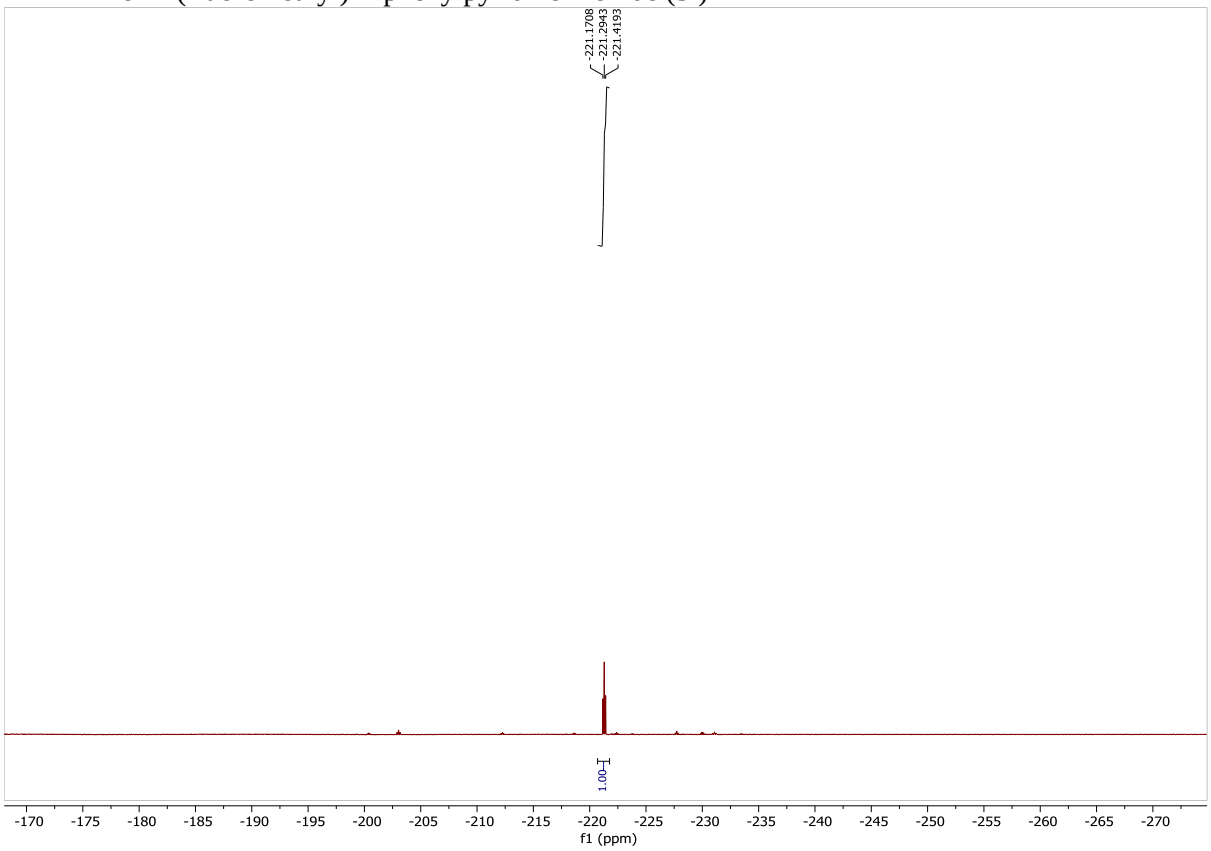
^{13}C NMR of 2-(fluoromethyl)-4-phenylpyridine (**5k**)



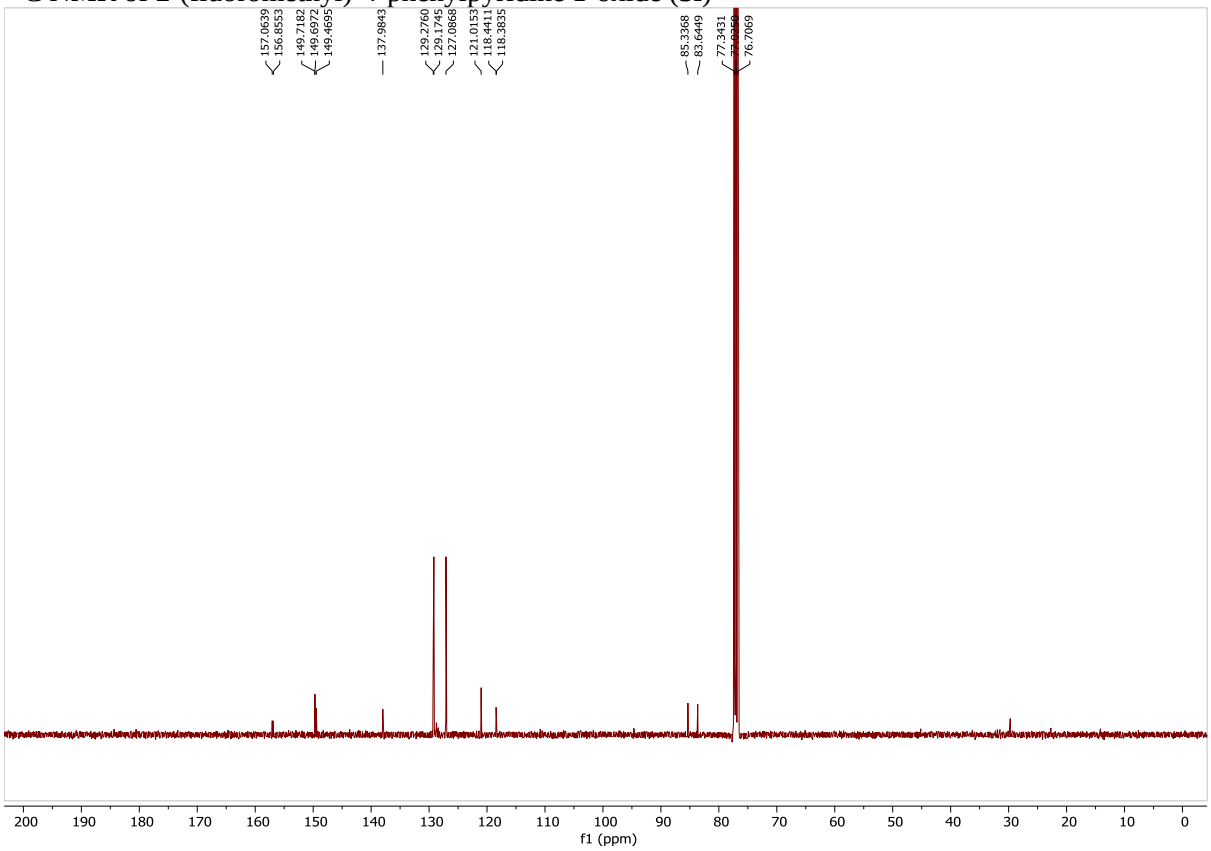
^{1}H NMR of 2-(fluoromethyl)-4-phenylpyridine 1-oxide (**5l**)



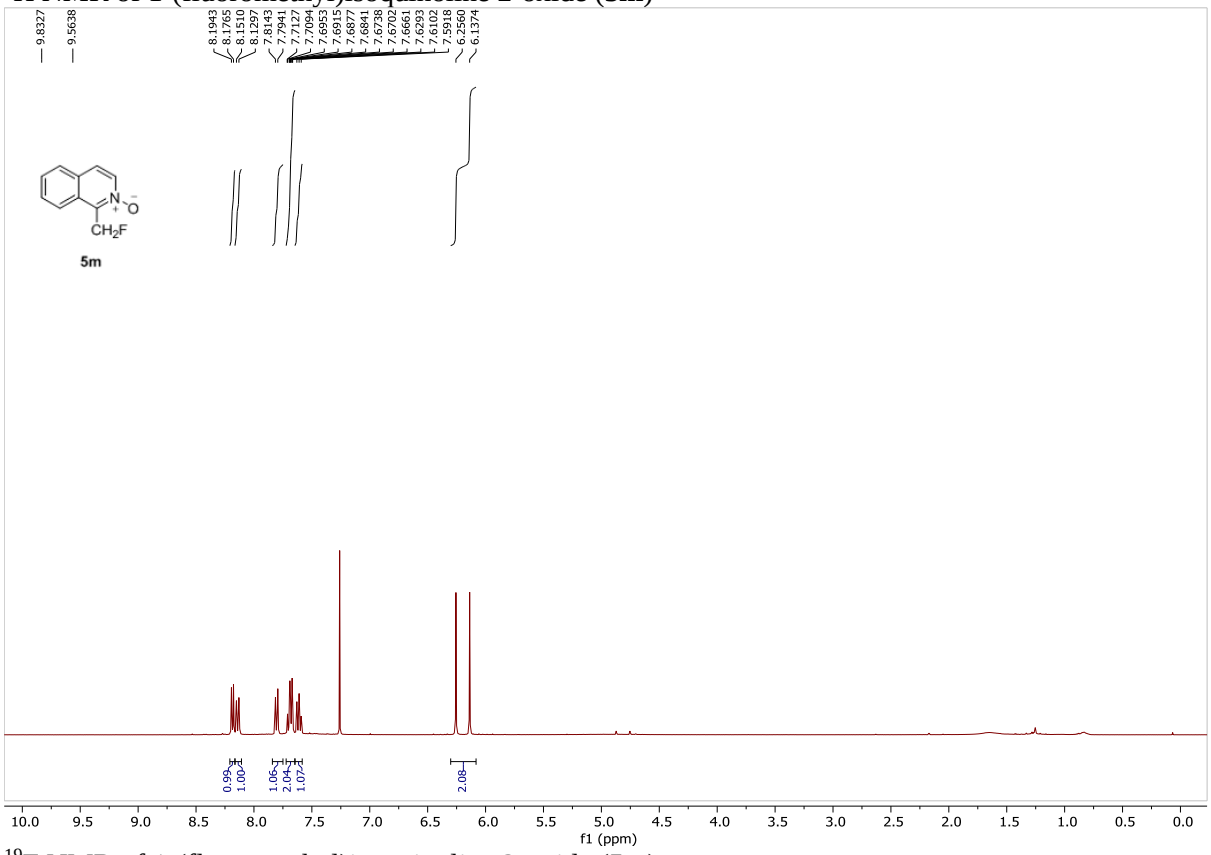
^{19}F NMR of 2-(fluoromethyl)-4-phenylpyridine 1-oxide (**5l**)



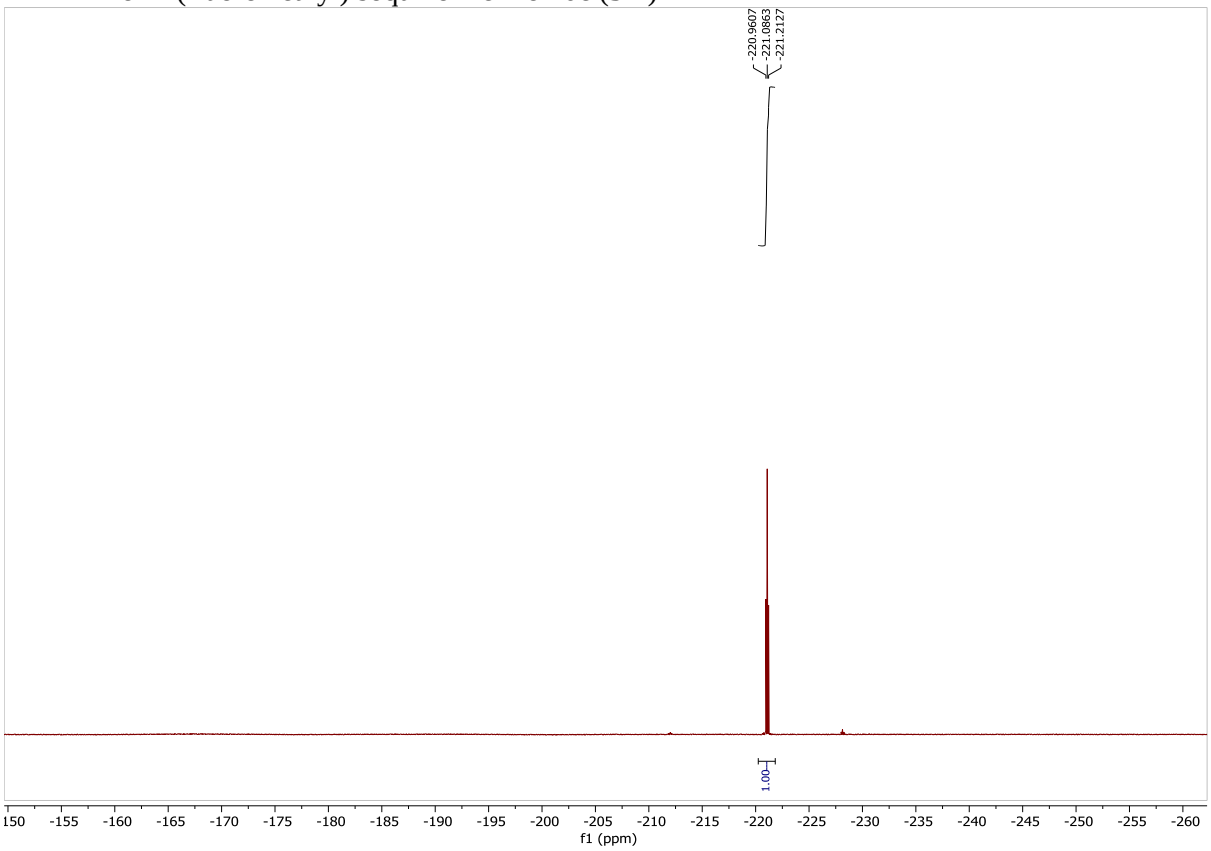
^{13}C NMR of 2-(fluoromethyl)-4-phenylpyridine 1-oxide (**5l**)



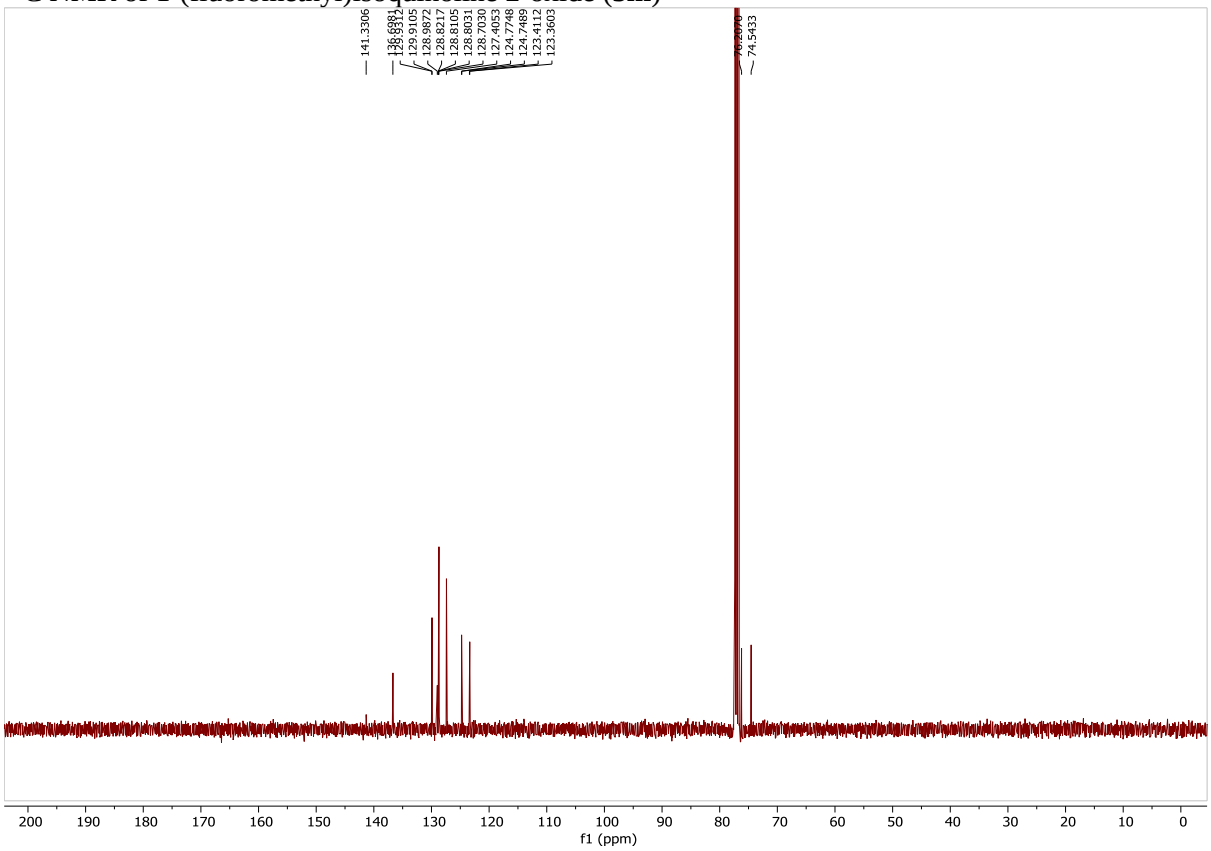
^{1}H NMR of 1-(fluoromethyl)isoquinoline 2-oxide (**5m**)



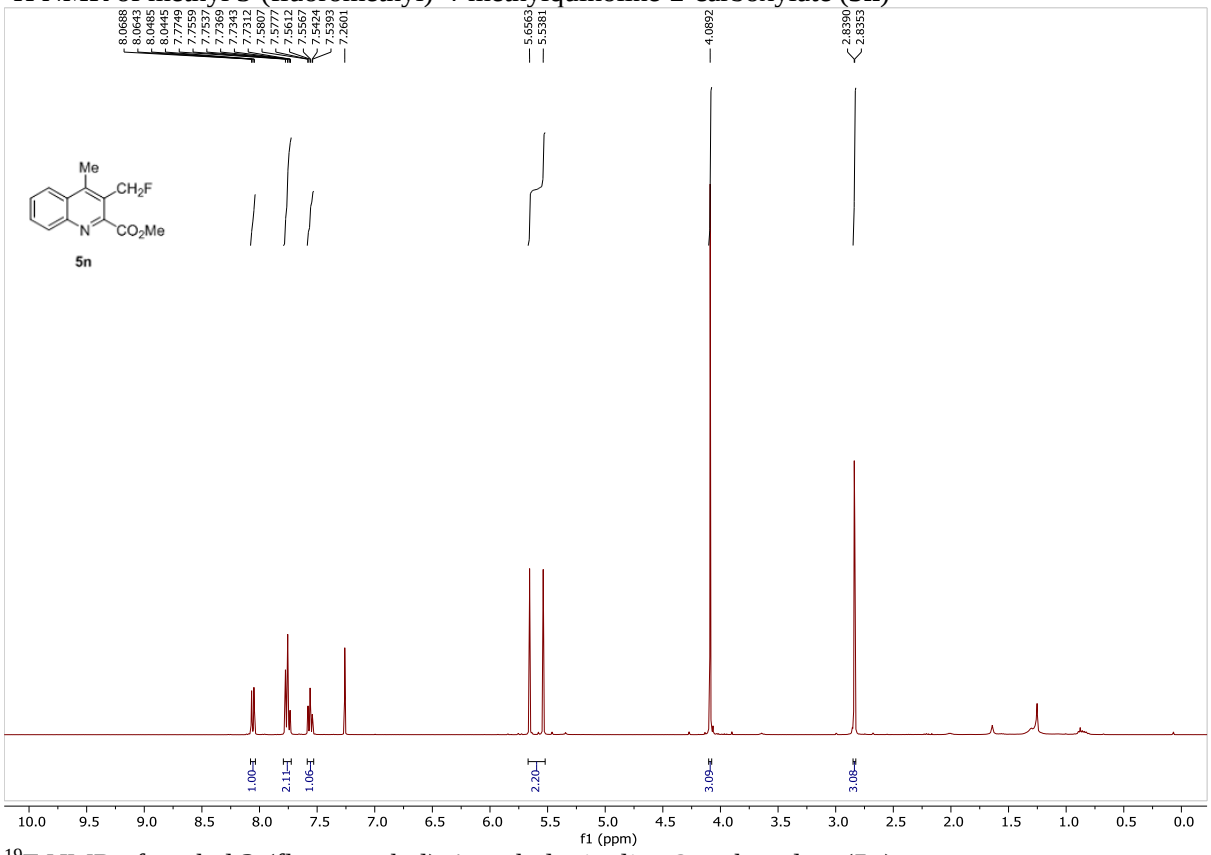
^{19}F NMR of 1-(fluoromethyl)isoquinoline 2-oxide (**5m**)



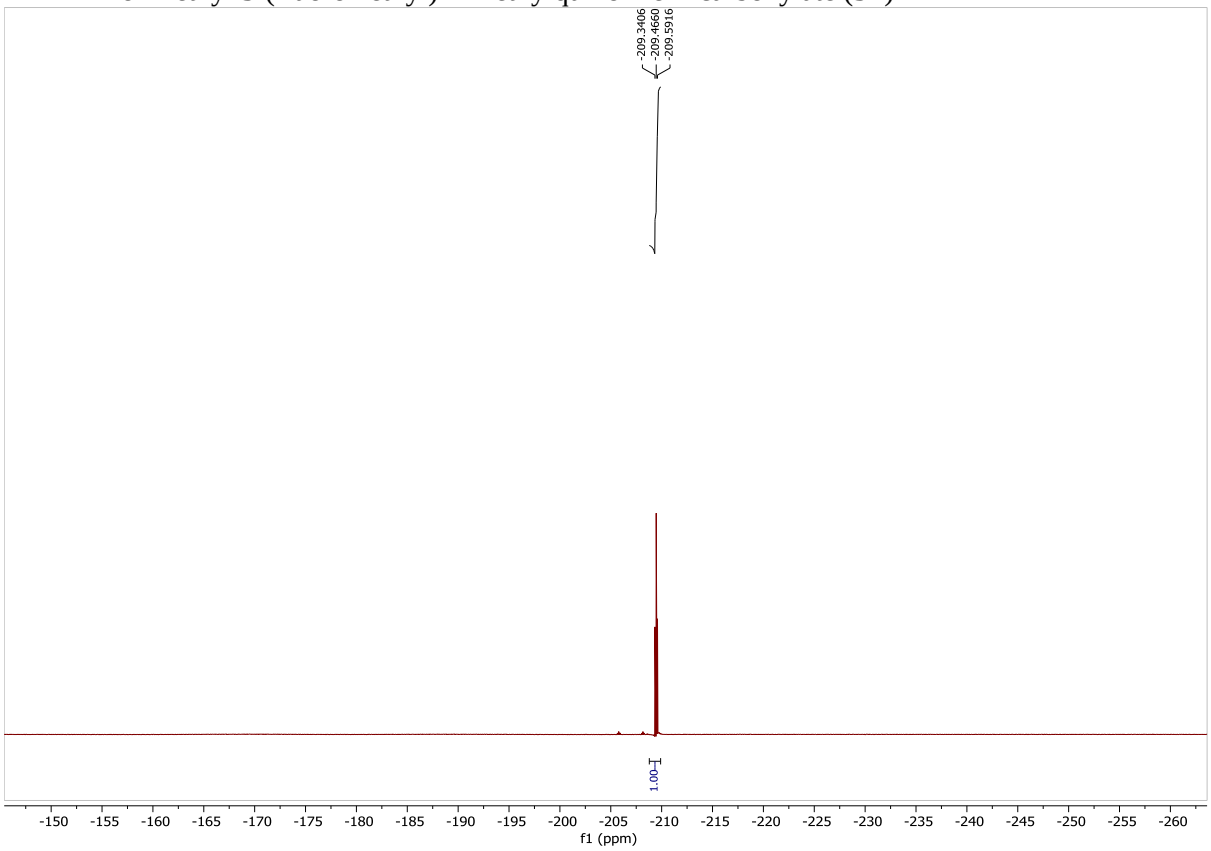
^{13}C NMR of 1-(fluoromethyl)isoquinoline 2-oxide (**5m**)



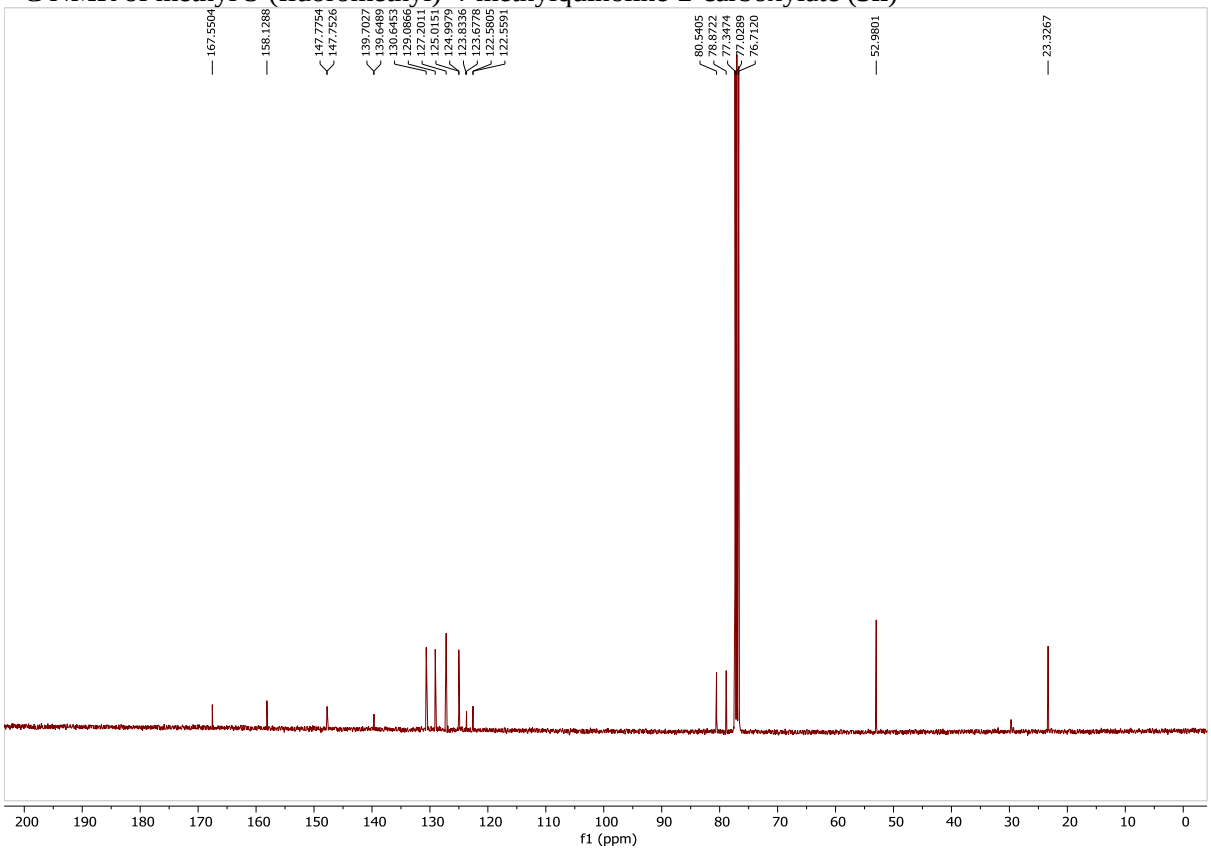
^{1}H NMR of methyl 3-(fluoromethyl)-4-methylquinoline-2-carboxylate (**5n**)



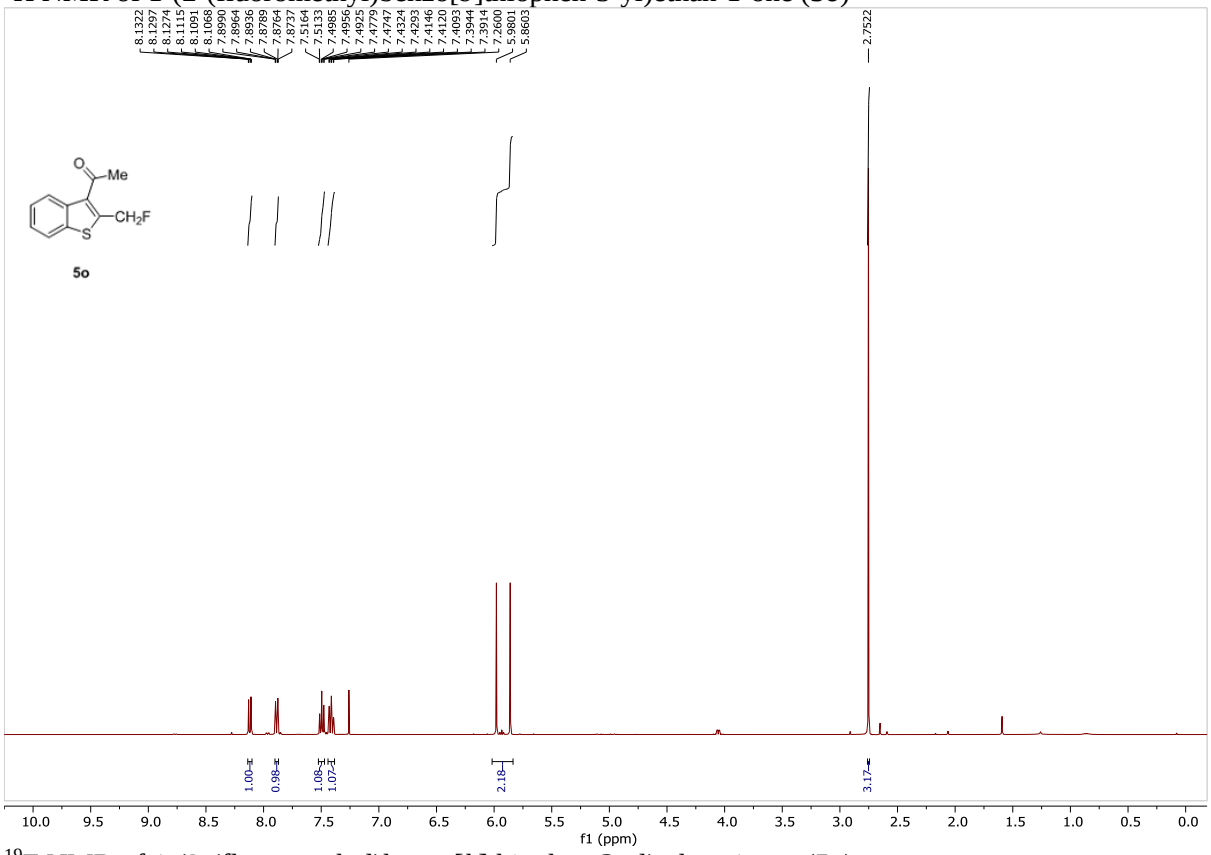
^{19}F NMR of methyl 3-(fluoromethyl)-4-methylquinoline-2-carboxylate (**5n**)



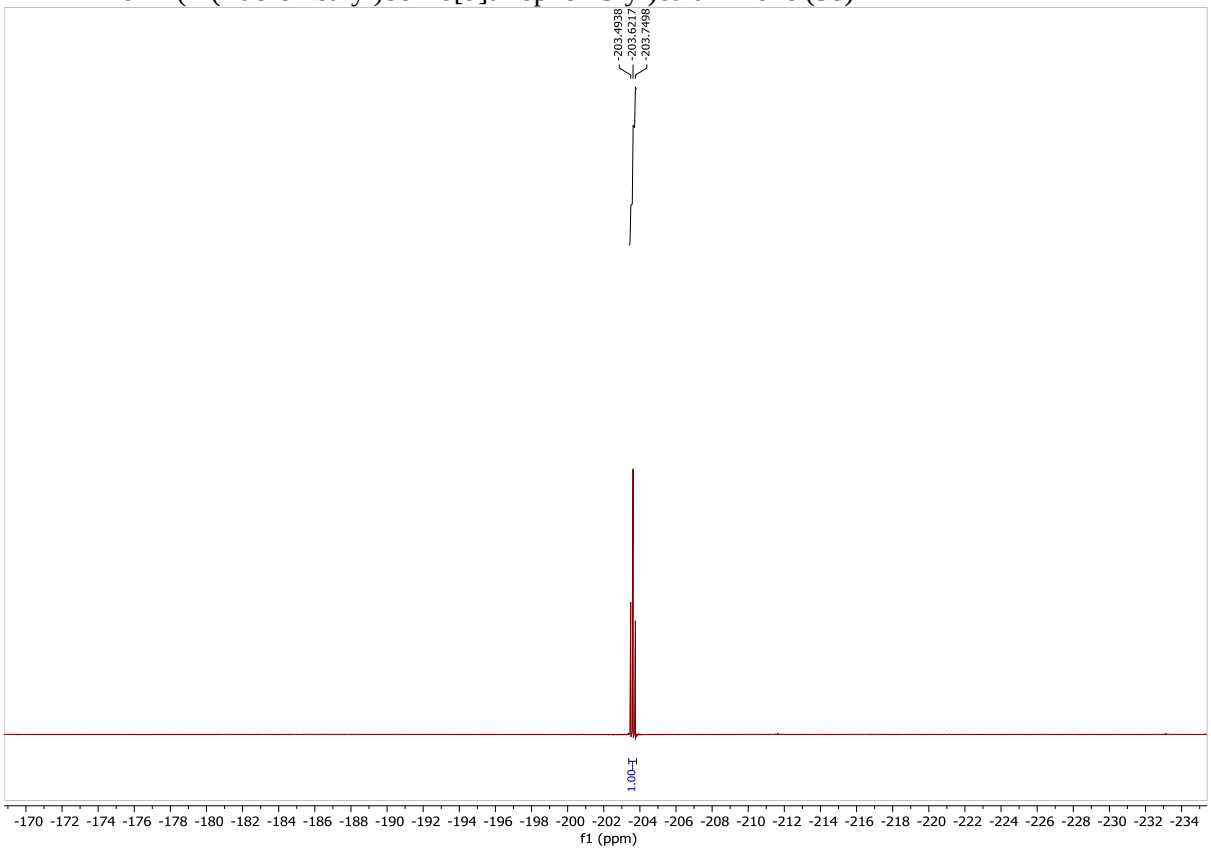
^{13}C NMR of methyl 3-(fluoromethyl)-4-methylquinoline-2-carboxylate (**5n**)



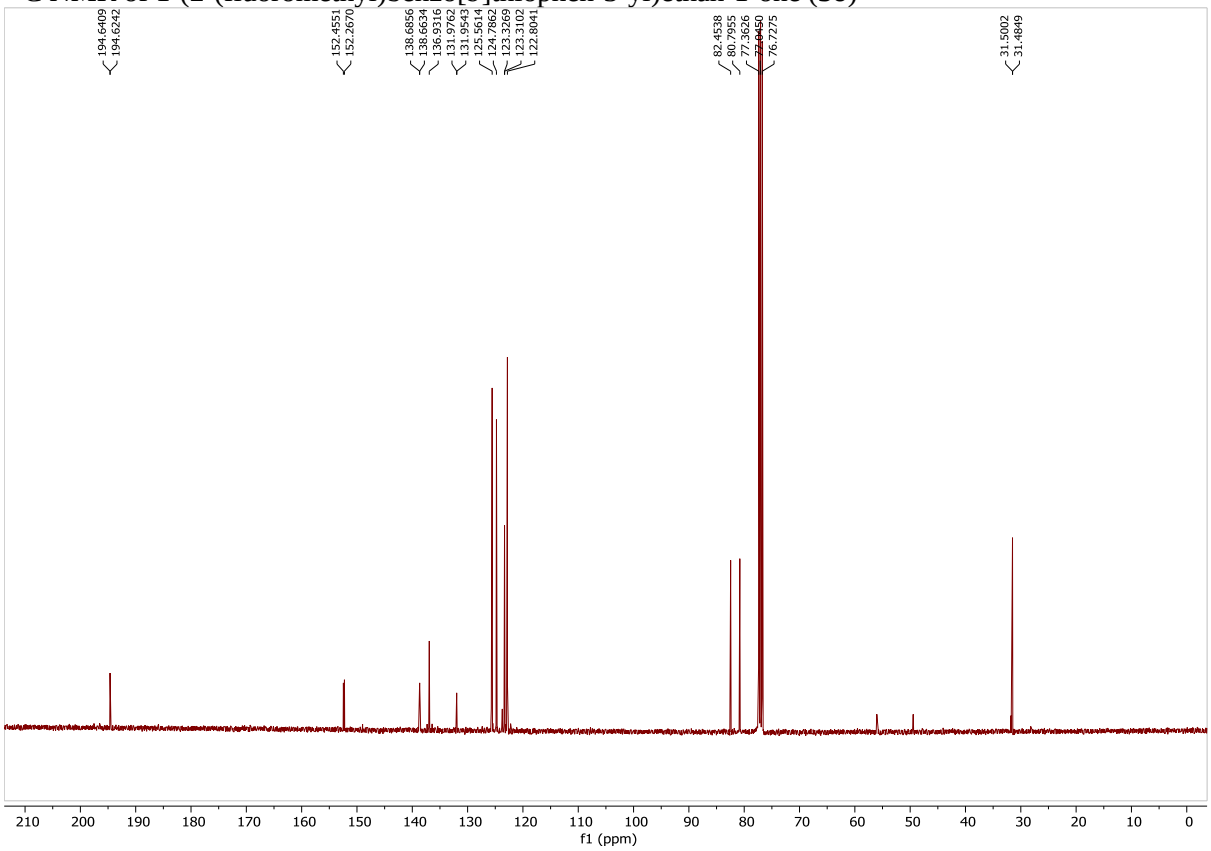
^{1}H NMR of 1-(2-(fluoromethyl)benzo[*b*]thiophen-3-yl)ethan-1-one (**5o**)



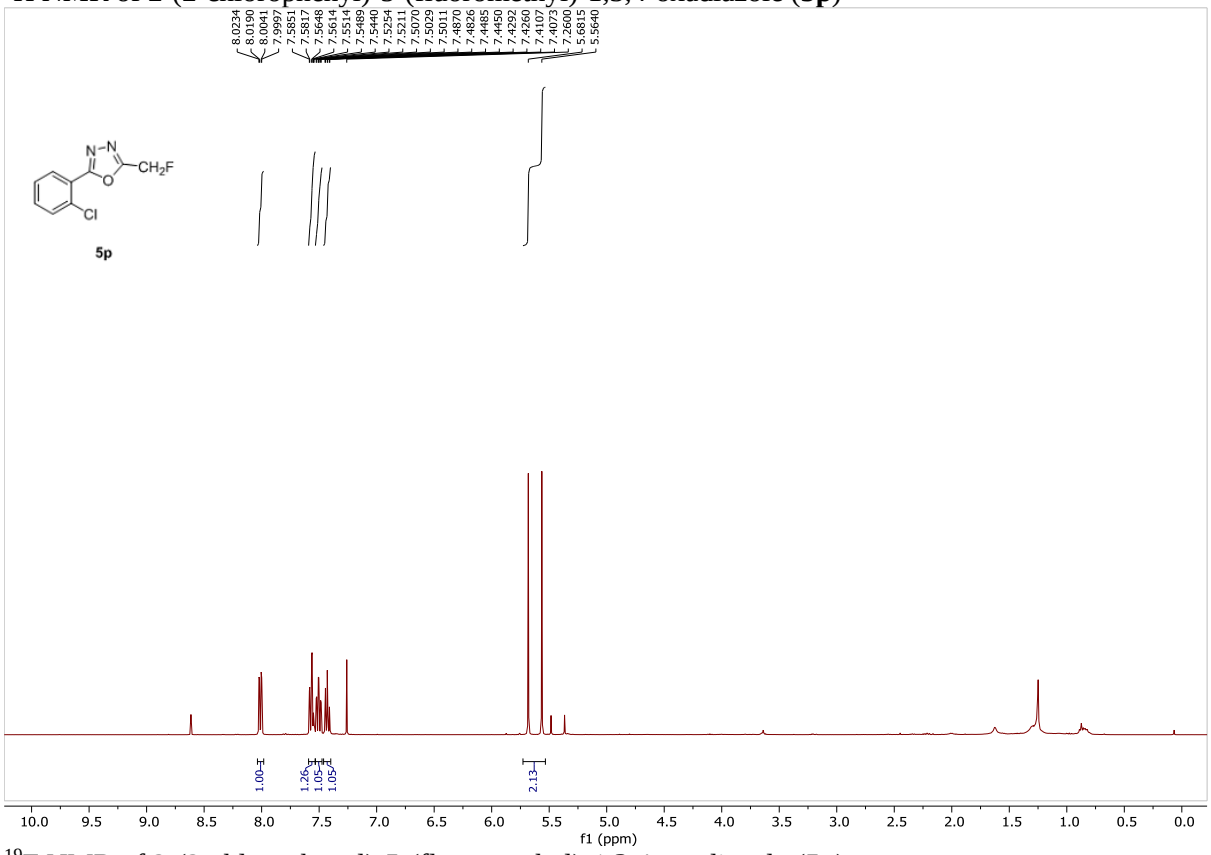
^{19}F NMR of 1-(2-(fluoromethyl)benzo[*b*]thiophen-3-yl)ethan-1-one (**5o**)



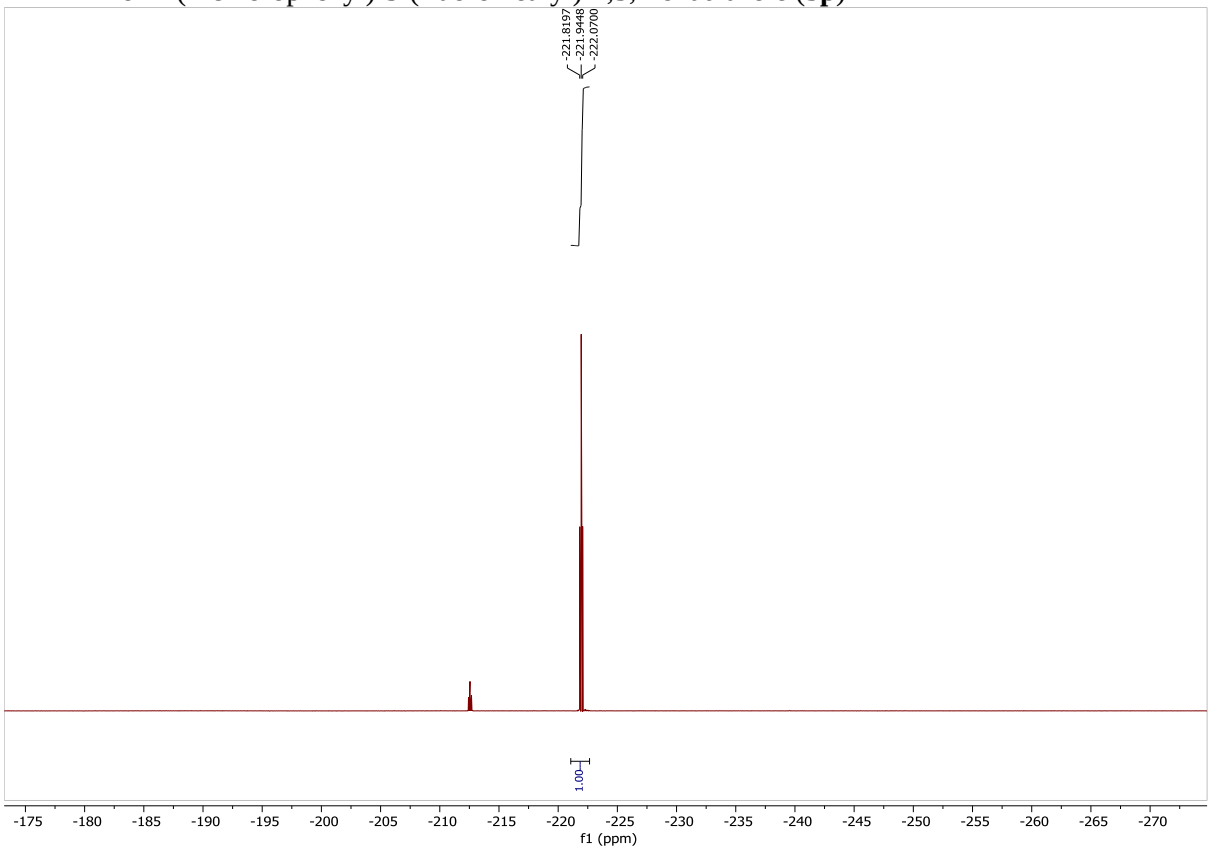
^{13}C NMR of 1-(2-(fluoromethyl)benzo[*b*]thiophen-3-yl)ethan-1-one (**5o**)



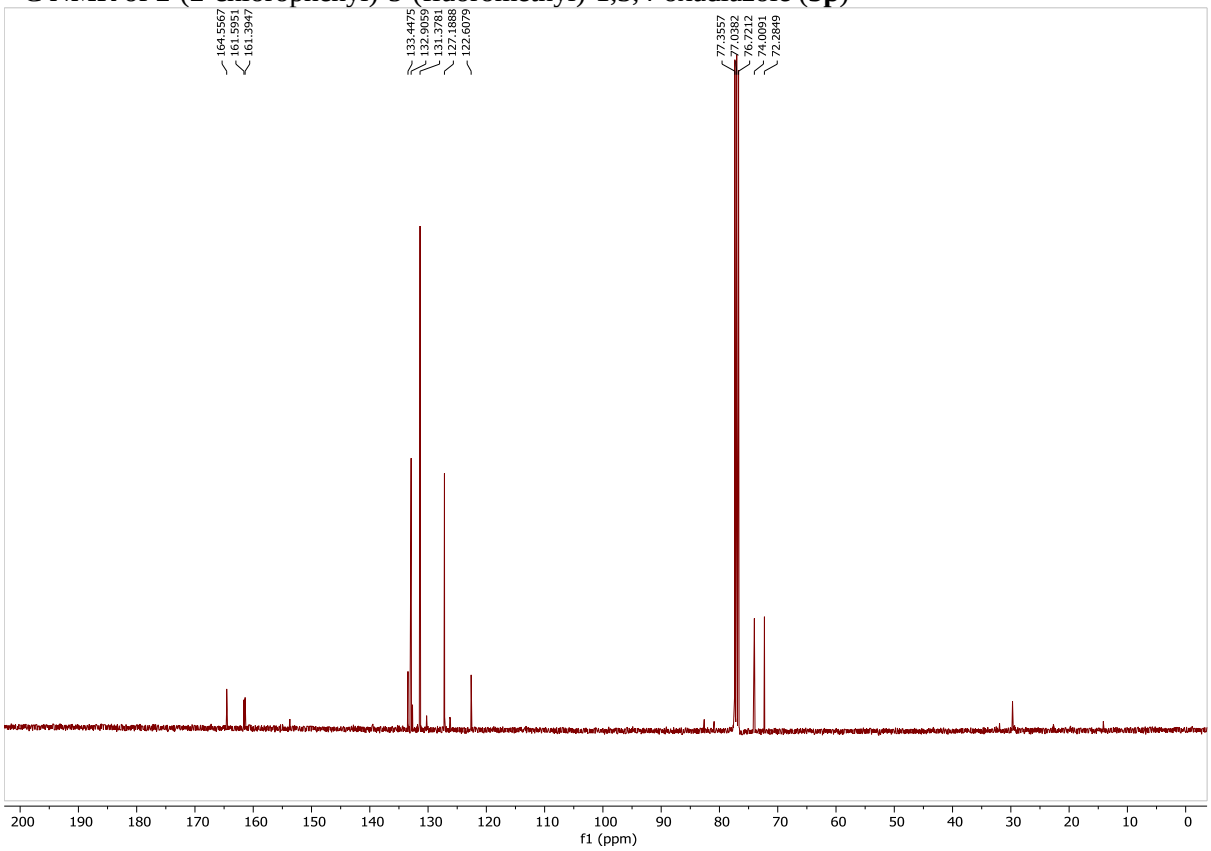
^{1}H NMR of 2-(2-chlorophenyl)-5-(fluoromethyl)-1,3,4-oxadiazole (**5p**)



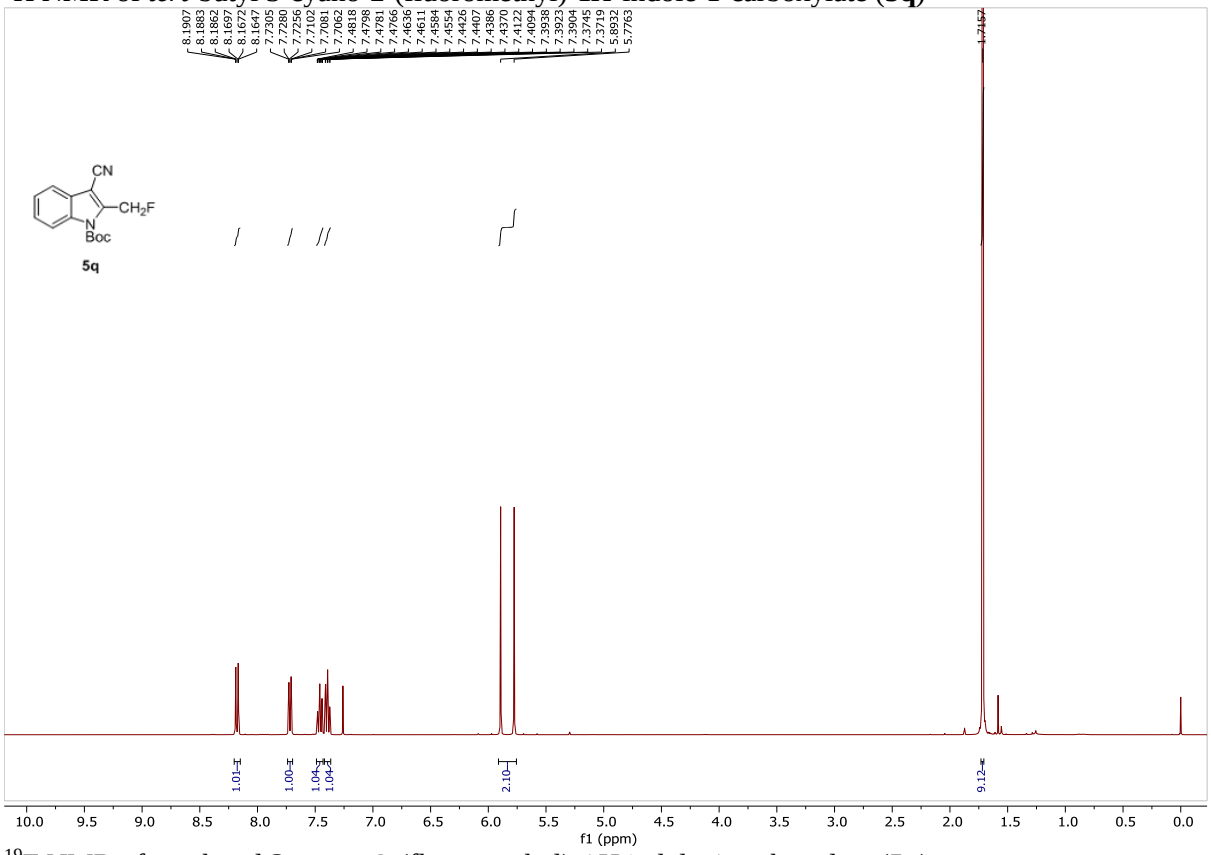
^{19}F NMR of 2-(2-chlorophenyl)-5-(fluoromethyl)-1,3,4-oxadiazole (**5p**)



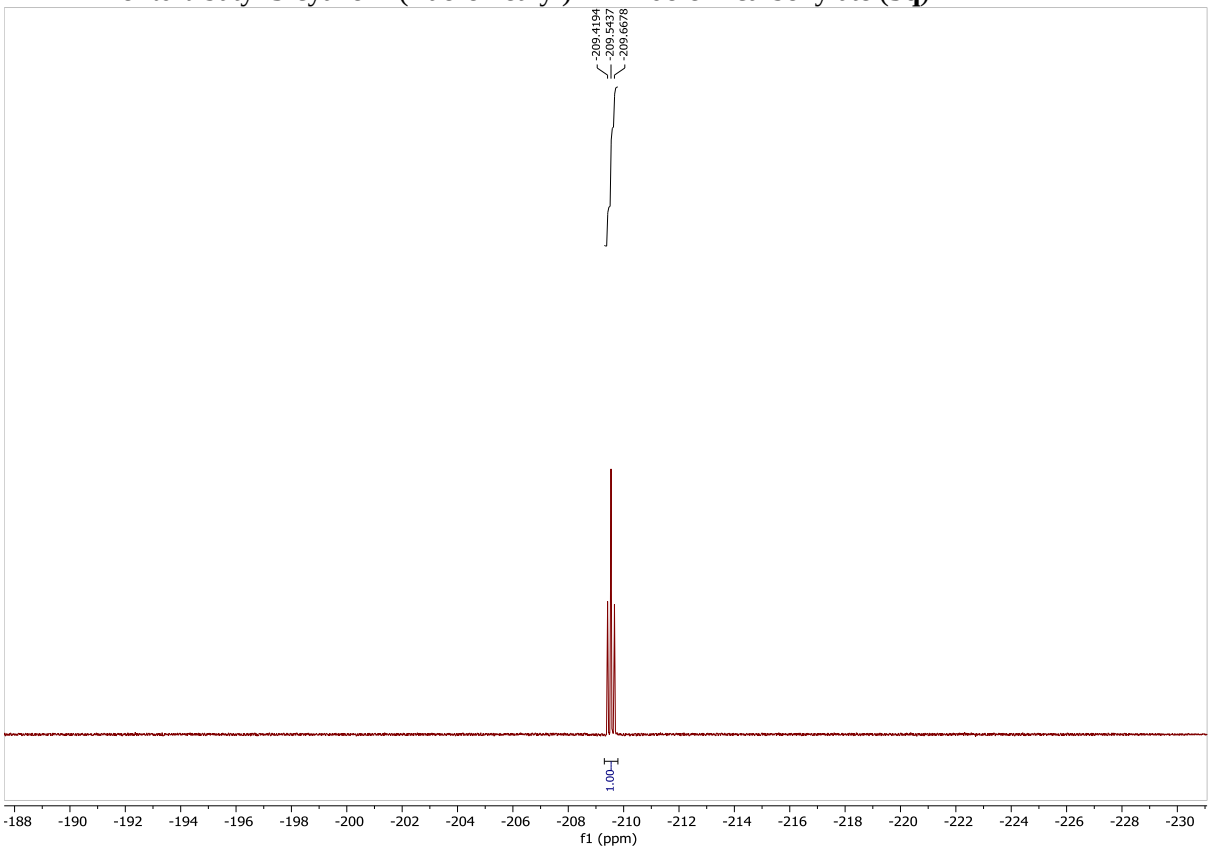
^{13}C NMR of 2-(2-chlorophenyl)-5-(fluoromethyl)-1,3,4-oxadiazole (**5p**)



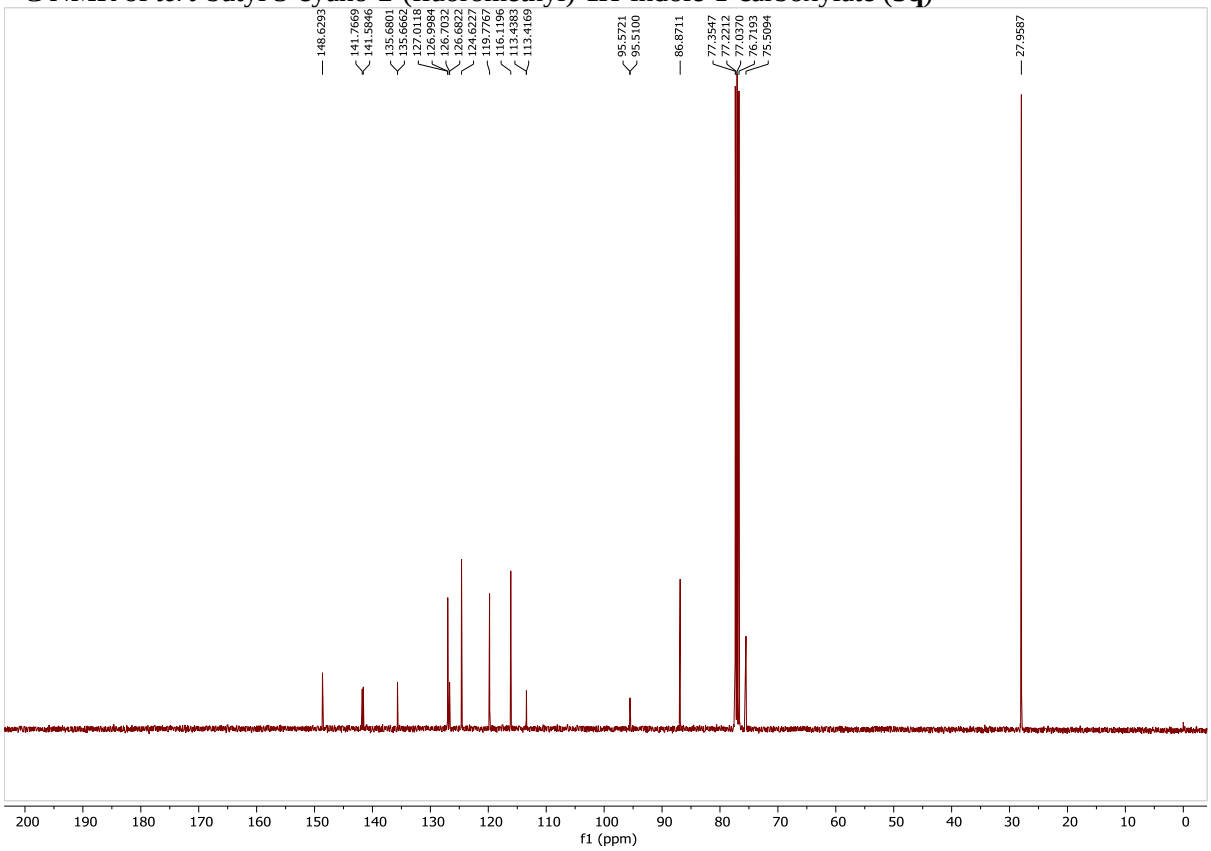
^{1}H NMR of *tert*-butyl 3-cyano-2-(fluoromethyl)-1*H*-indole-1-carboxylate (**5q**)



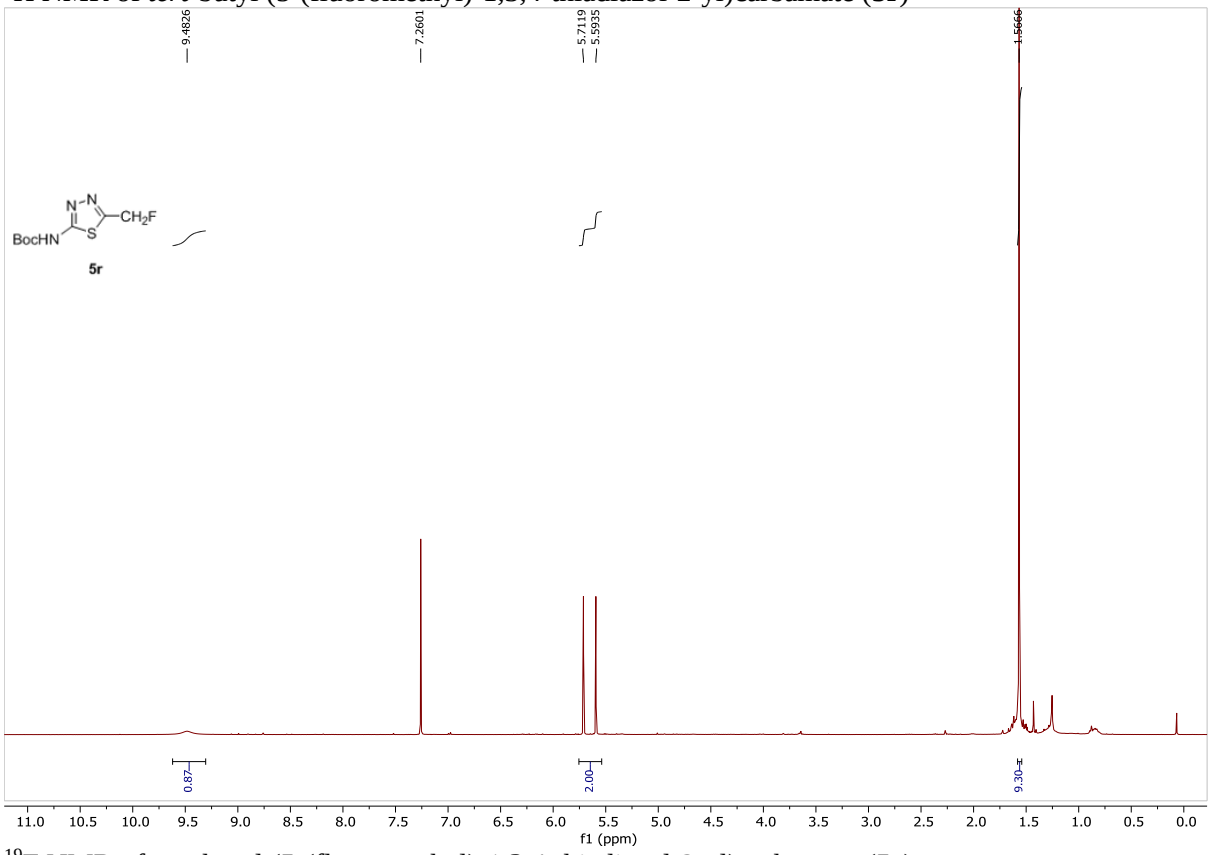
^{19}F NMR of *tert*-butyl 3-cyano-2-(fluoromethyl)-1*H*-indole-1-carboxylate (**5q**)



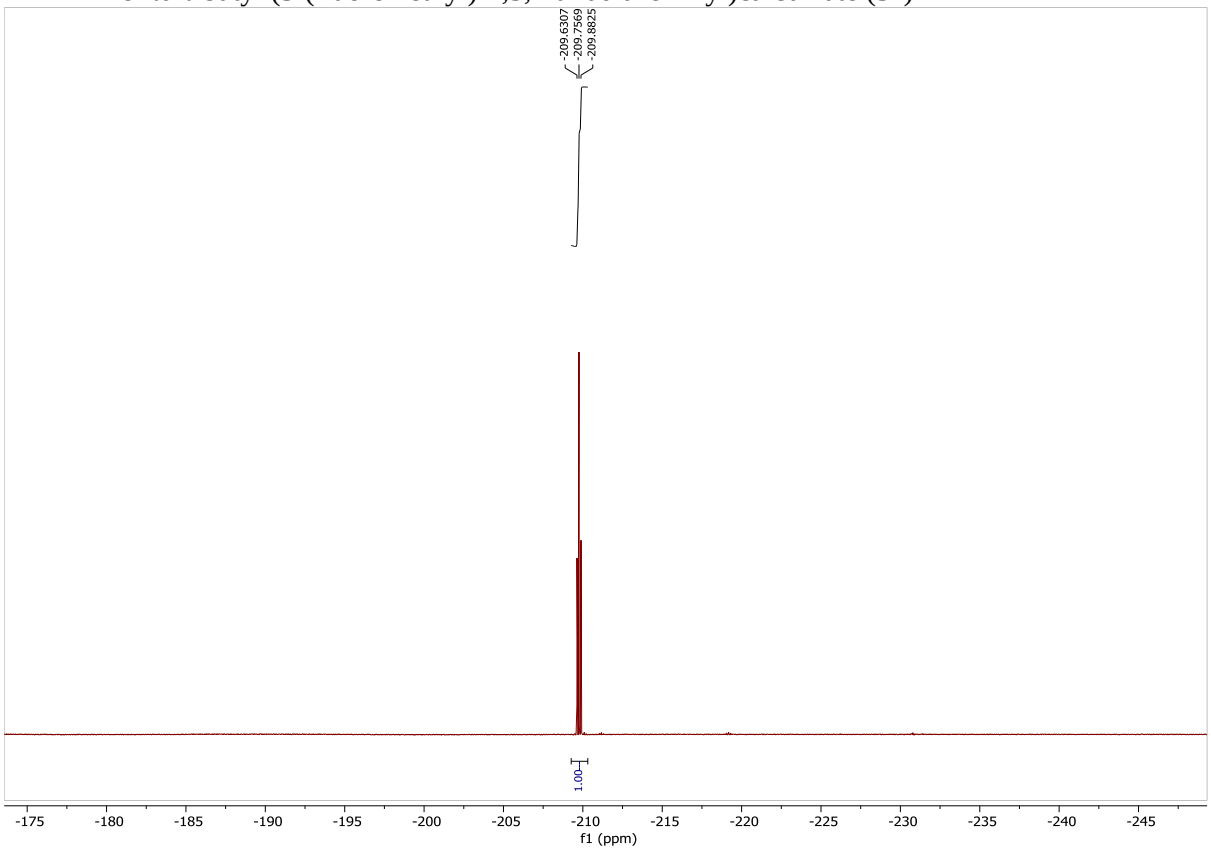
^{13}C NMR of *tert*-butyl 3-cyano-2-(fluoromethyl)-1*H*-indole-1-carboxylate (**5q**)



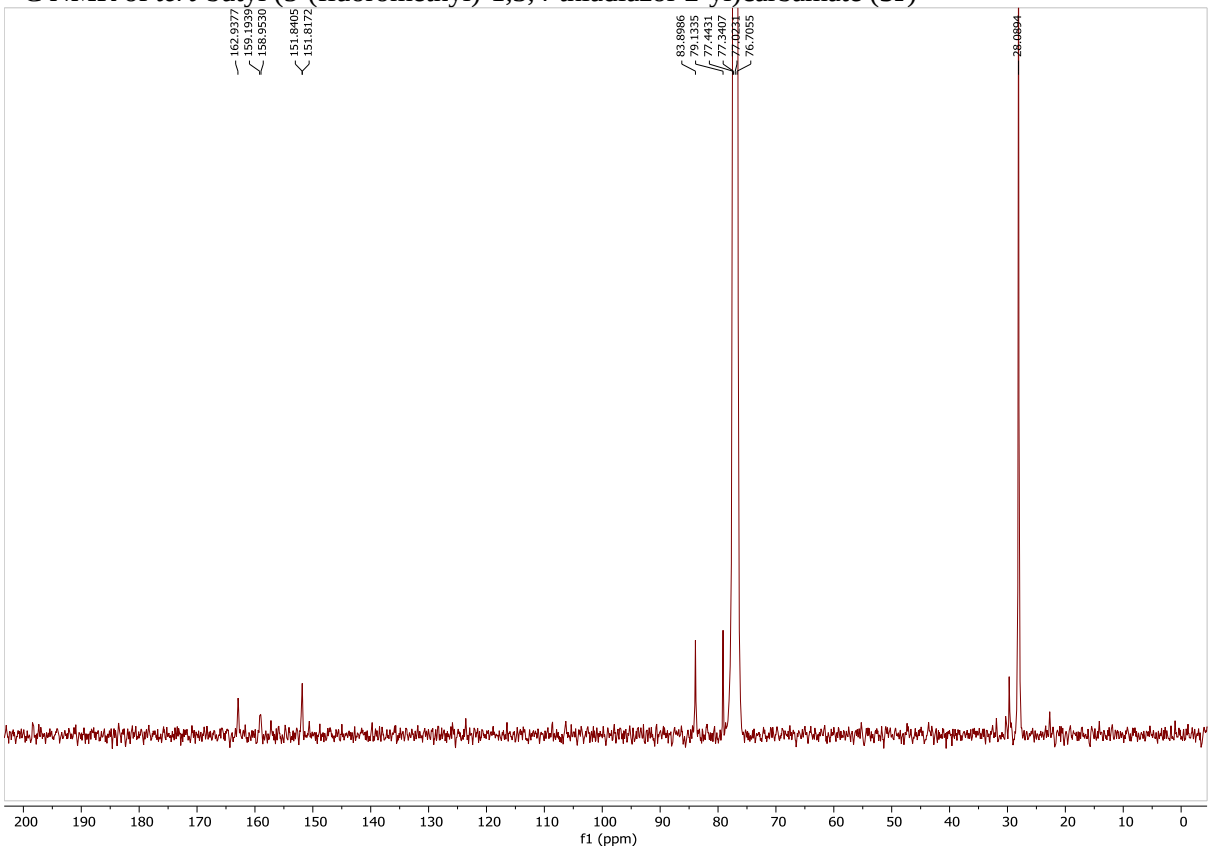
^{1}H NMR of *tert*-butyl (5-(fluoromethyl)-1,3,4-thiadiazol-2-yl)carbamate (**5r**)



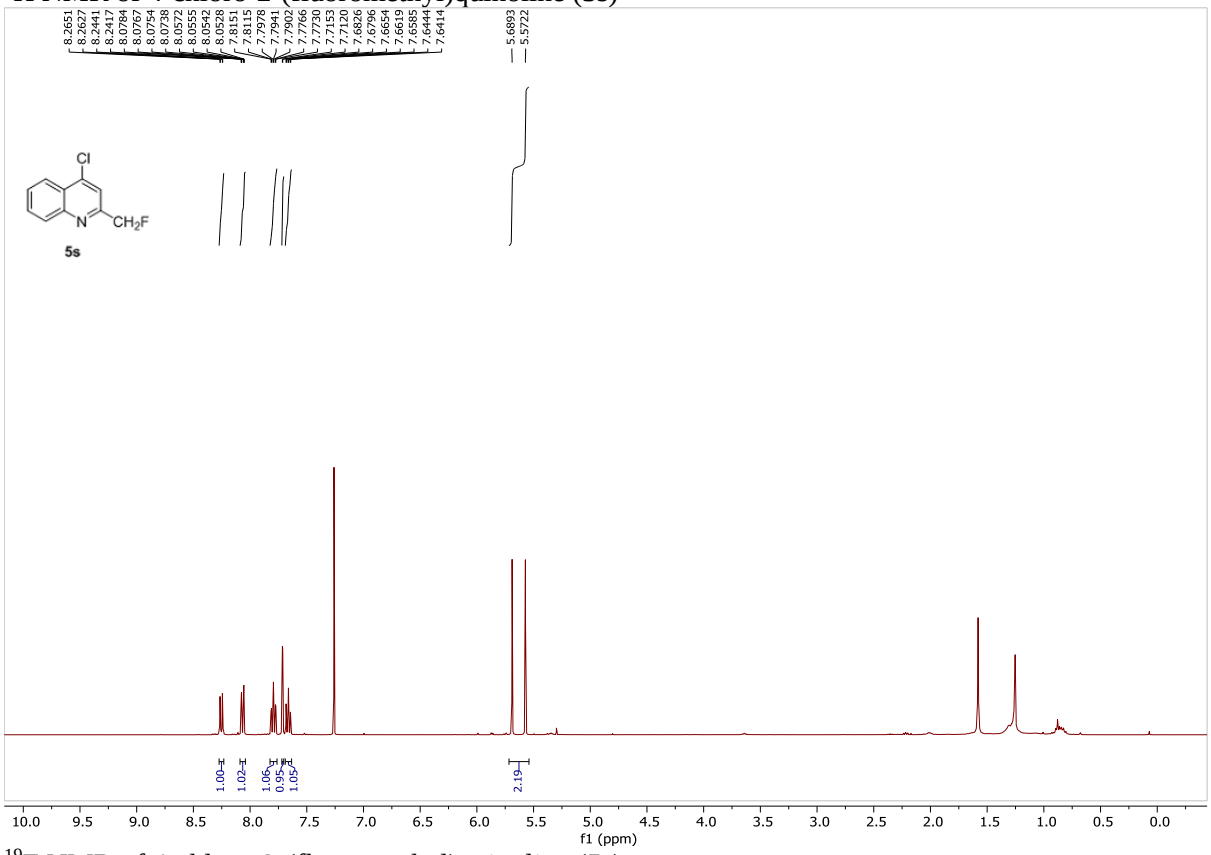
^{19}F NMR of *tert*-butyl (5-(fluoromethyl)-1,3,4-thiadiazol-2-yl)carbamate (**5r**)



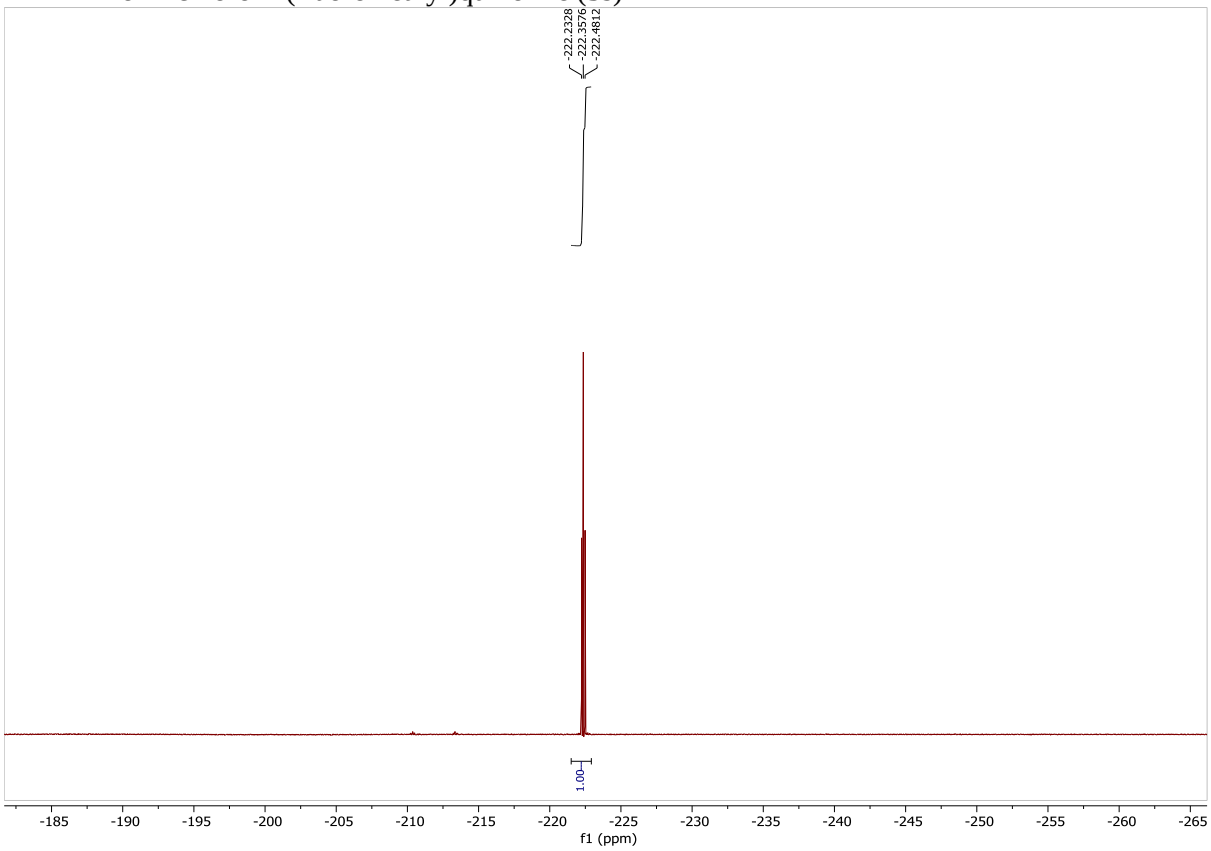
^{13}C NMR of *tert*-butyl (5-(fluoromethyl)-1,3,4-thiadiazol-2-yl)carbamate (**5r**)



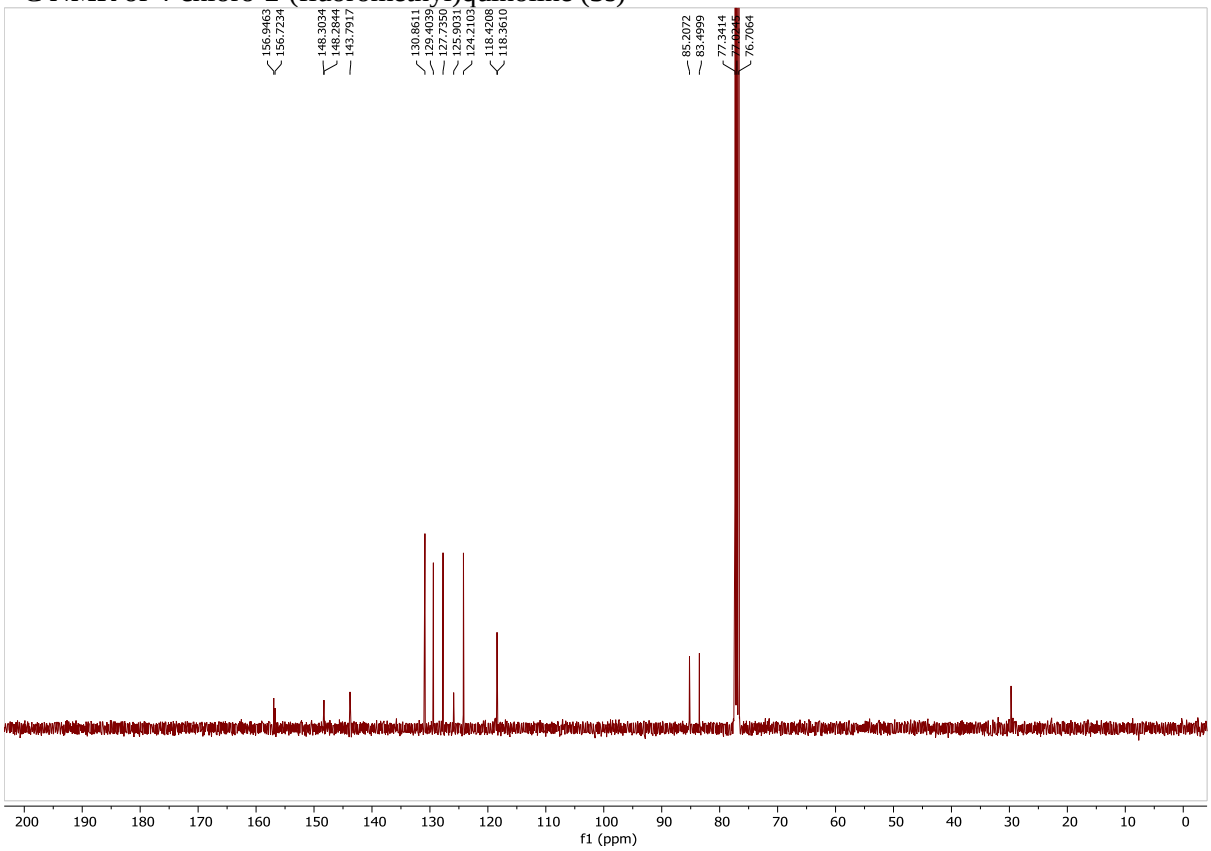
^{1}H NMR of 4-chloro-2-(fluoromethyl)quinoline (**5s**)



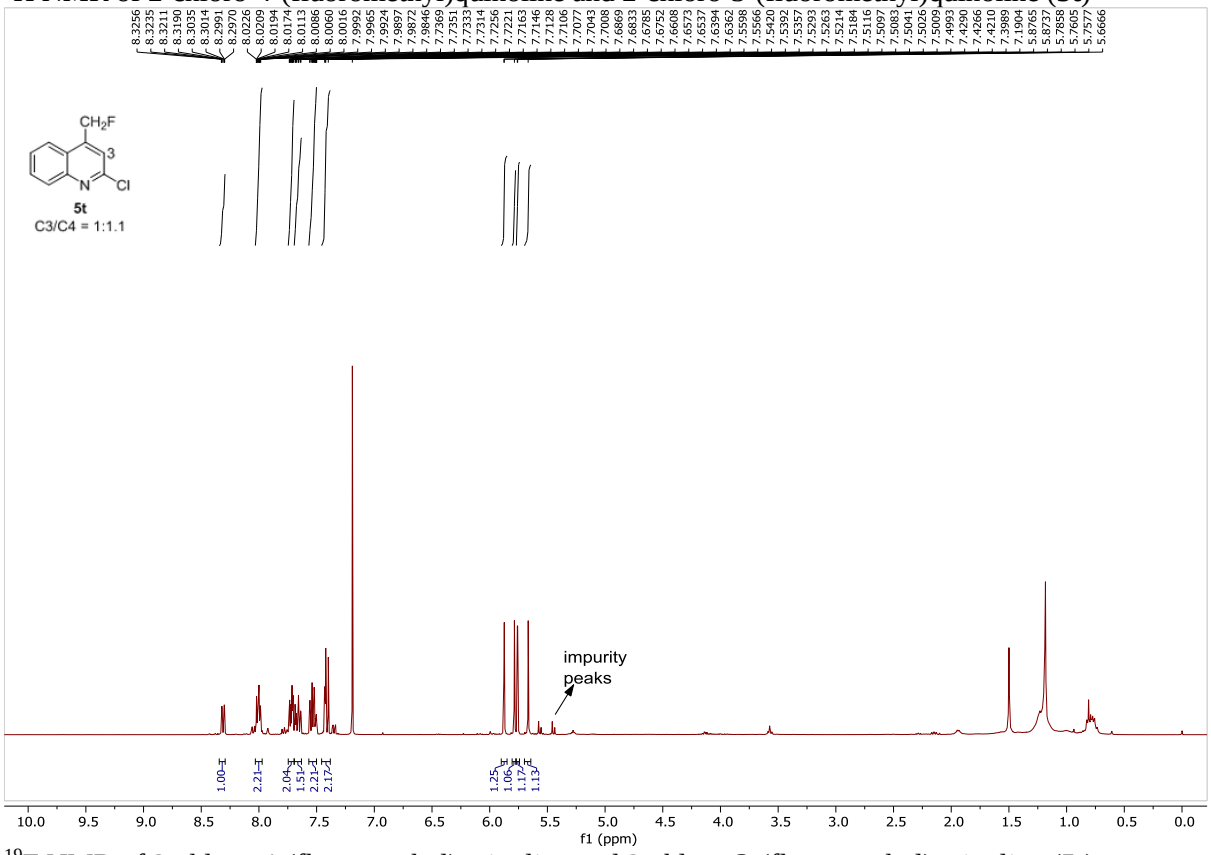
^{19}F NMR of 4-chloro-2-(fluoromethyl)quinoline (**5s**)



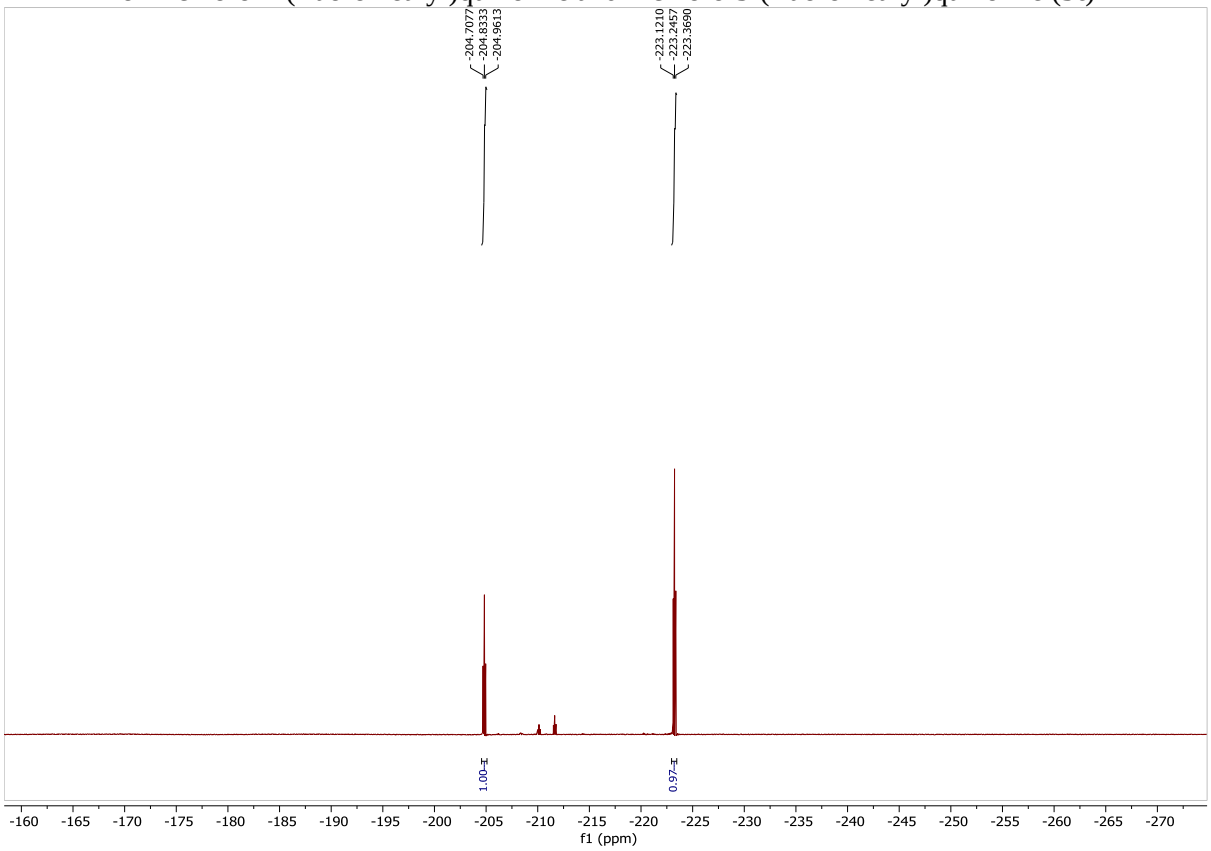
^{13}C NMR of 4-chloro-2-(fluoromethyl)quinoline (**5s**)



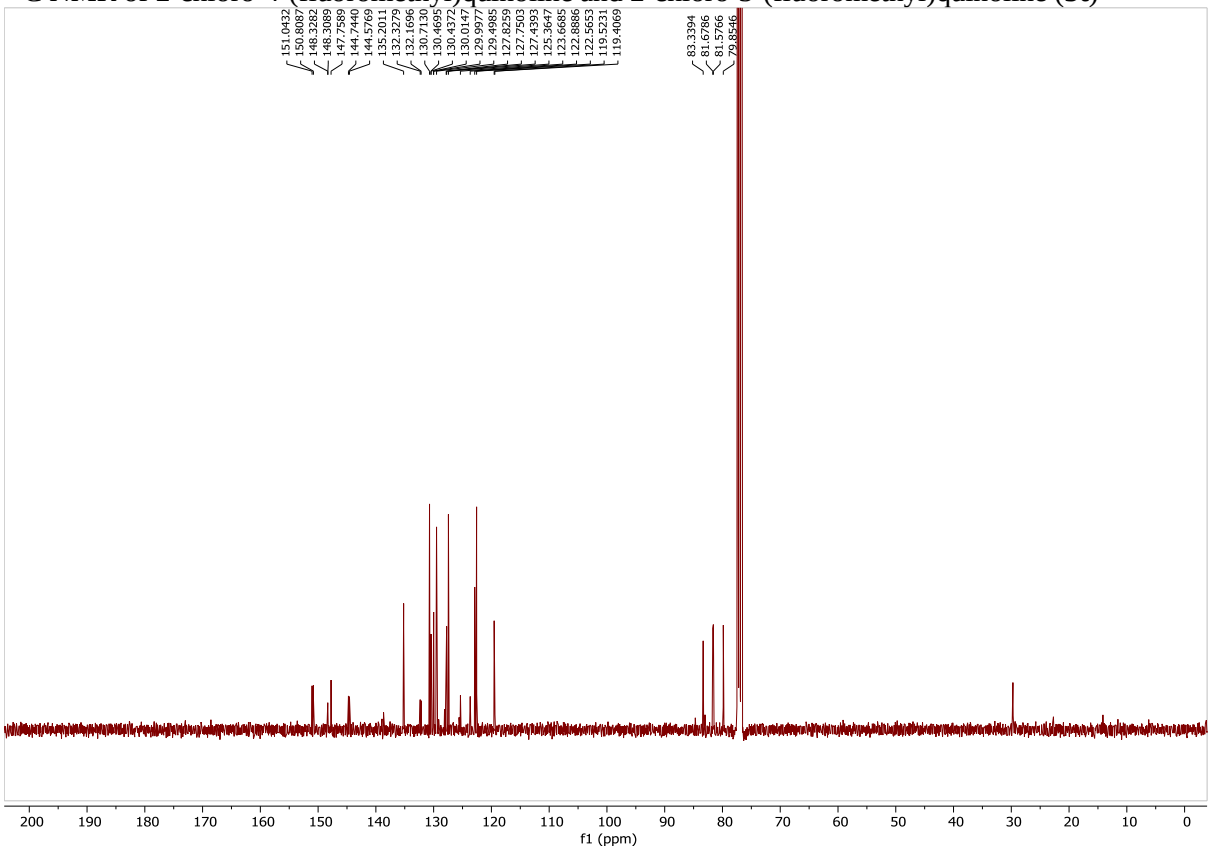
^{1}H NMR of 2-chloro-4-(fluoromethyl)quinoline and 2-chloro-3-(fluoromethyl)quinoline (**5t**)



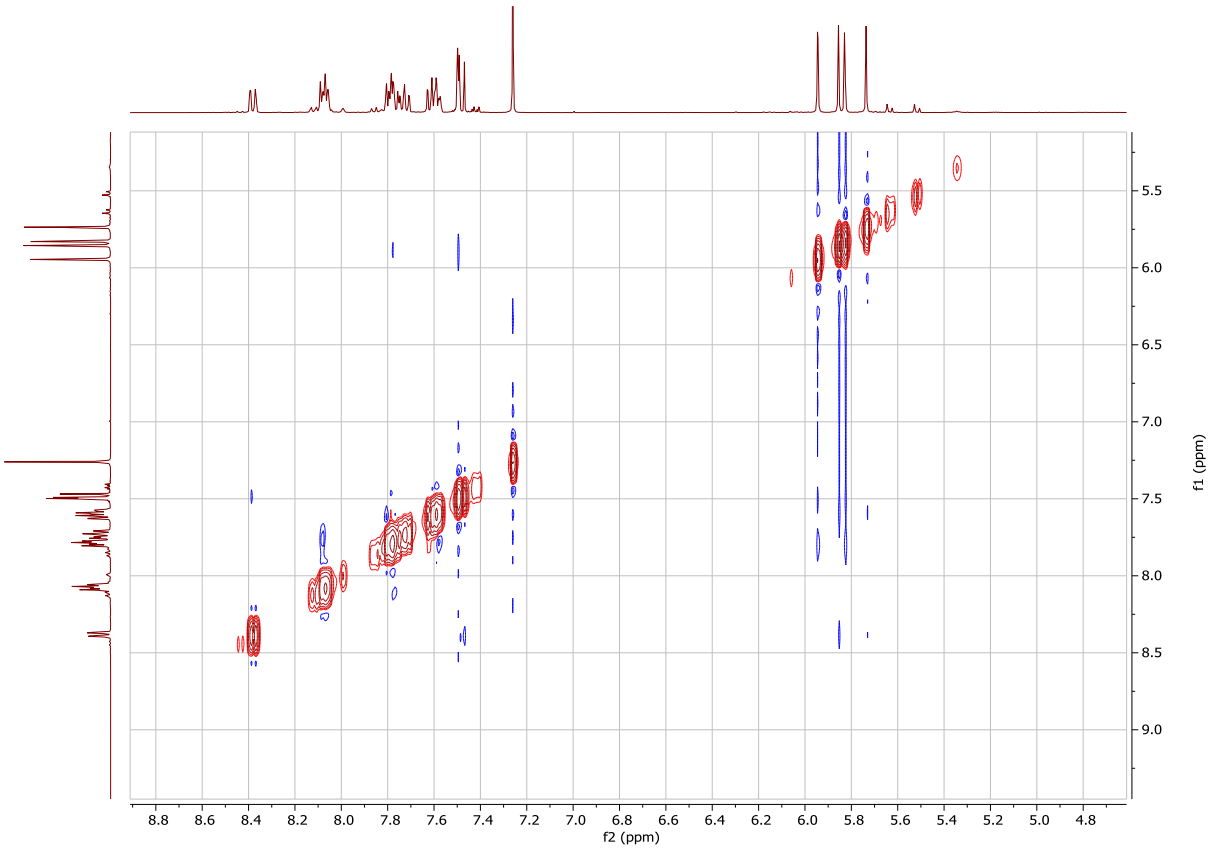
^{19}F NMR of 2-chloro-4-(fluoromethyl)quinoline and 2-chloro-3-(fluoromethyl)quinoline (**5t**)



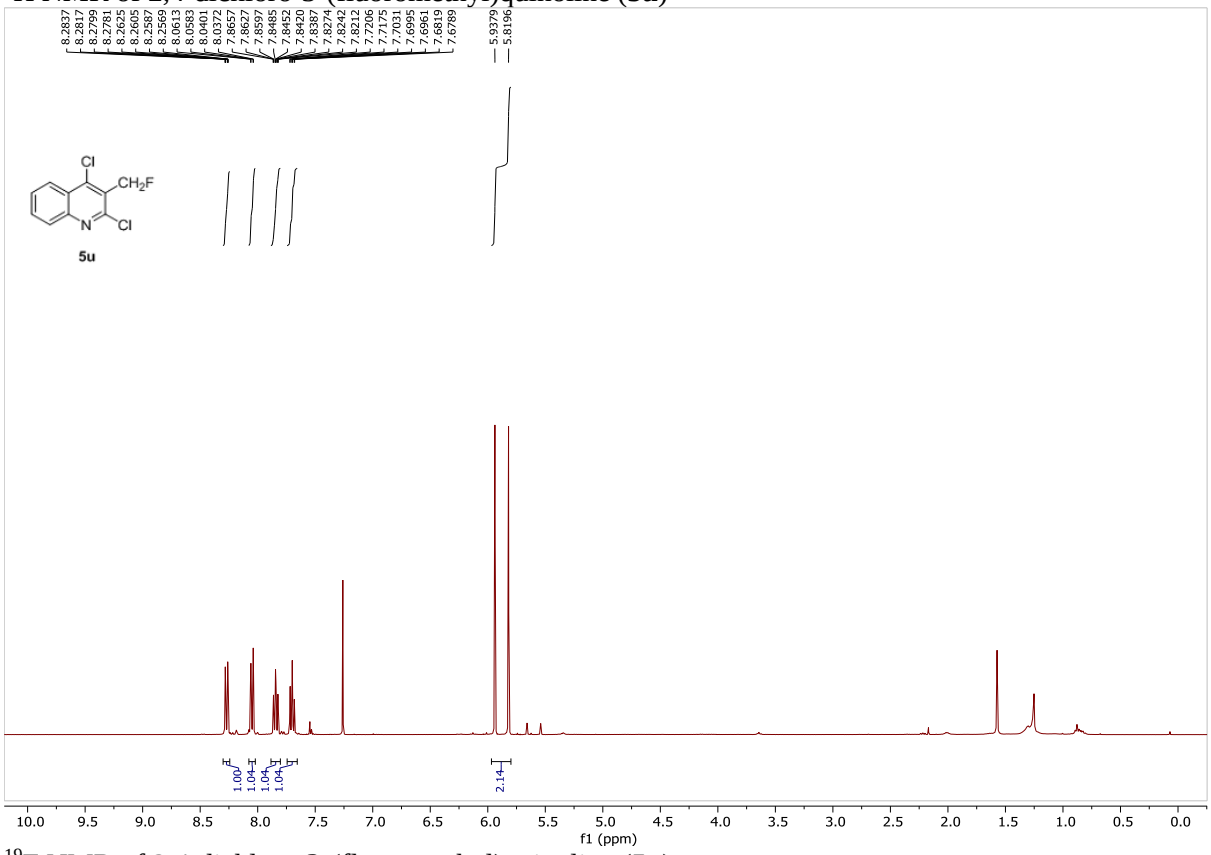
^{13}C NMR of 2-chloro-4-(fluoromethyl)quinoline and 2-chloro-3-(fluoromethyl)quinoline (**5t**)



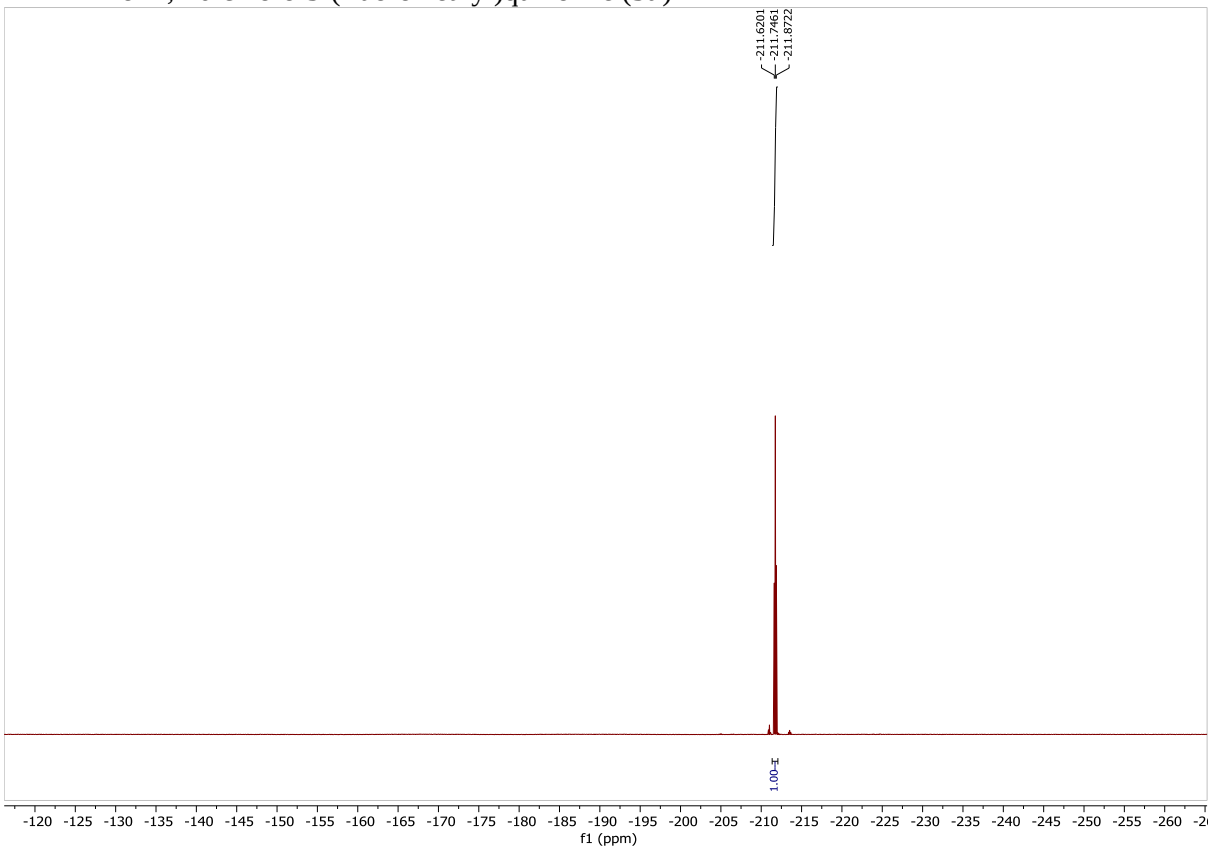
NOESY of 2-chloro-4-(fluoromethyl)quinoline and 2-chloro-3-(fluoromethyl)quinoline (**5t**)



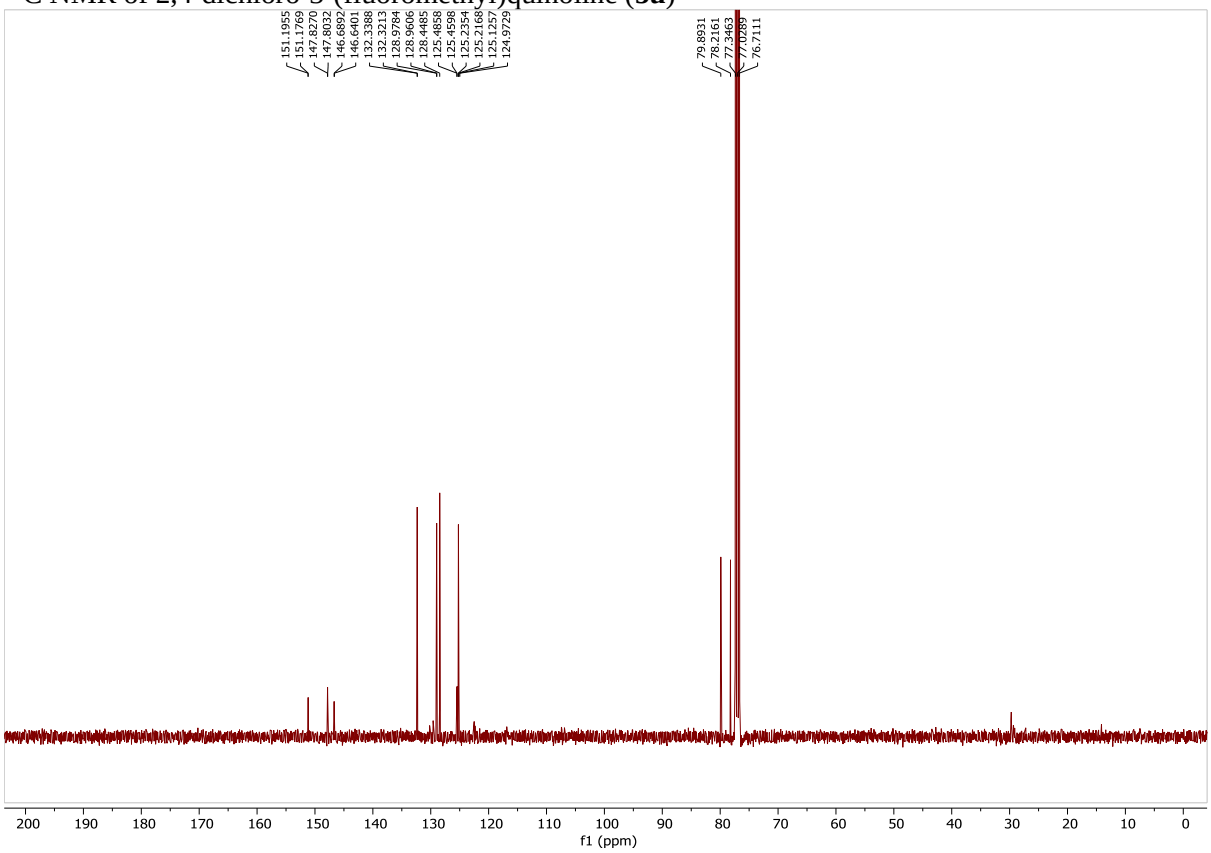
^{1}H NMR of 2,4-dichloro-3-(fluoromethyl)quinoline (**5u**)



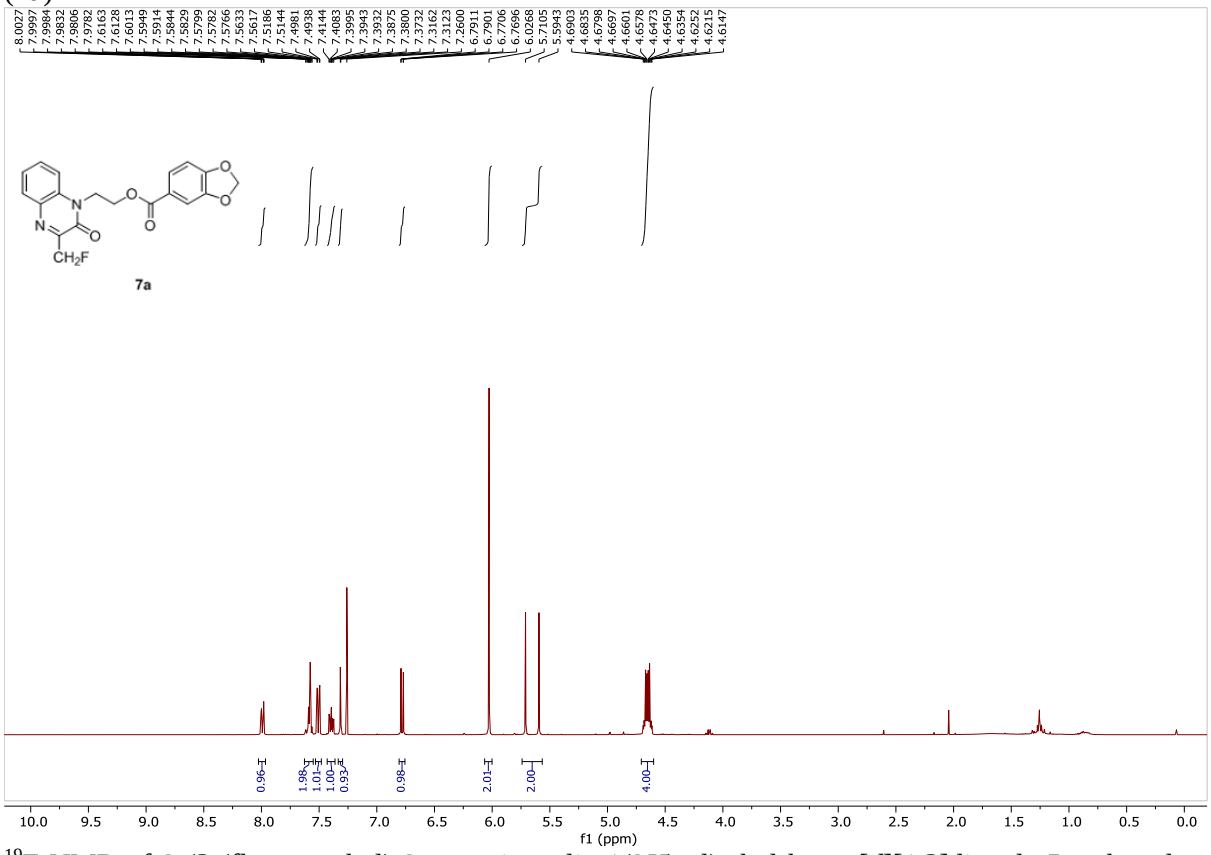
^{19}F NMR of 2,4-dichloro-3-(fluoromethyl)quinoline (**5u**)



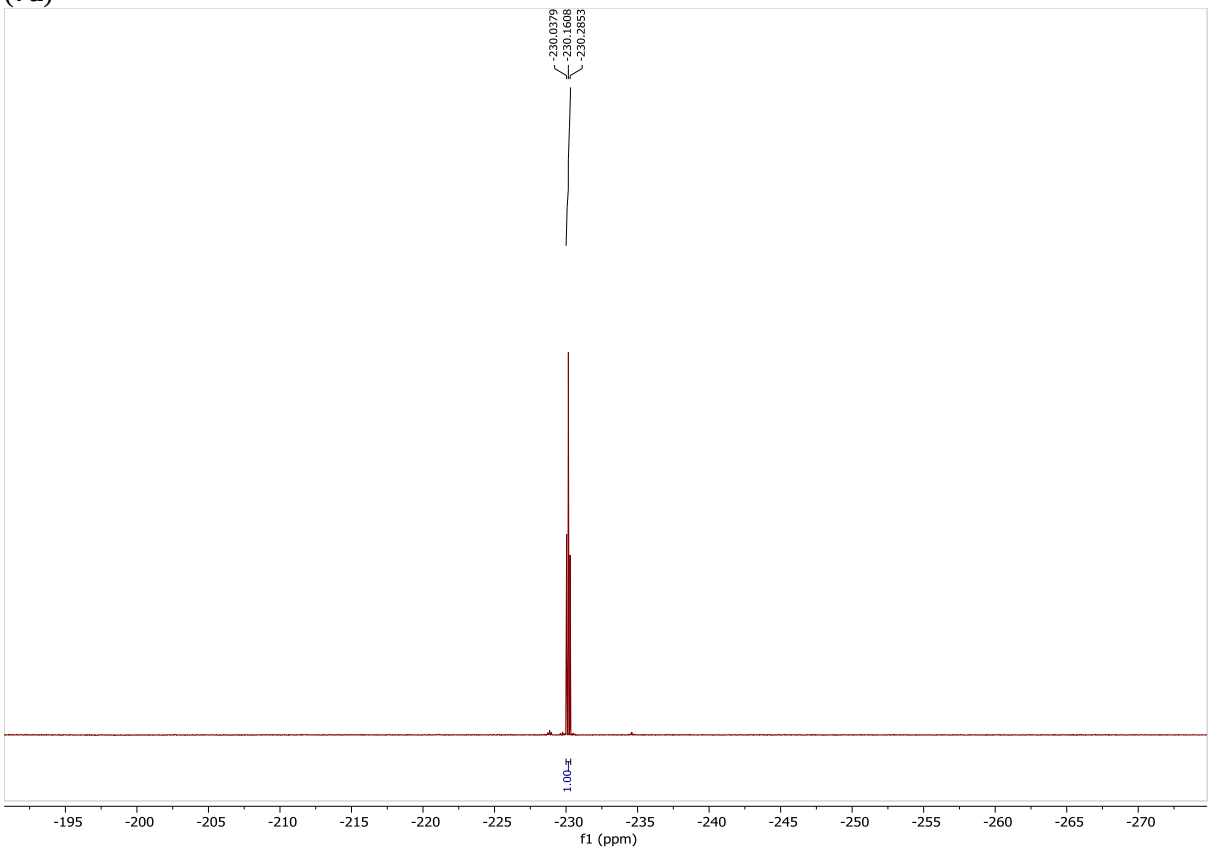
^{13}C NMR of 2,4-dichloro-3-(fluoromethyl)quinoline (**5u**)



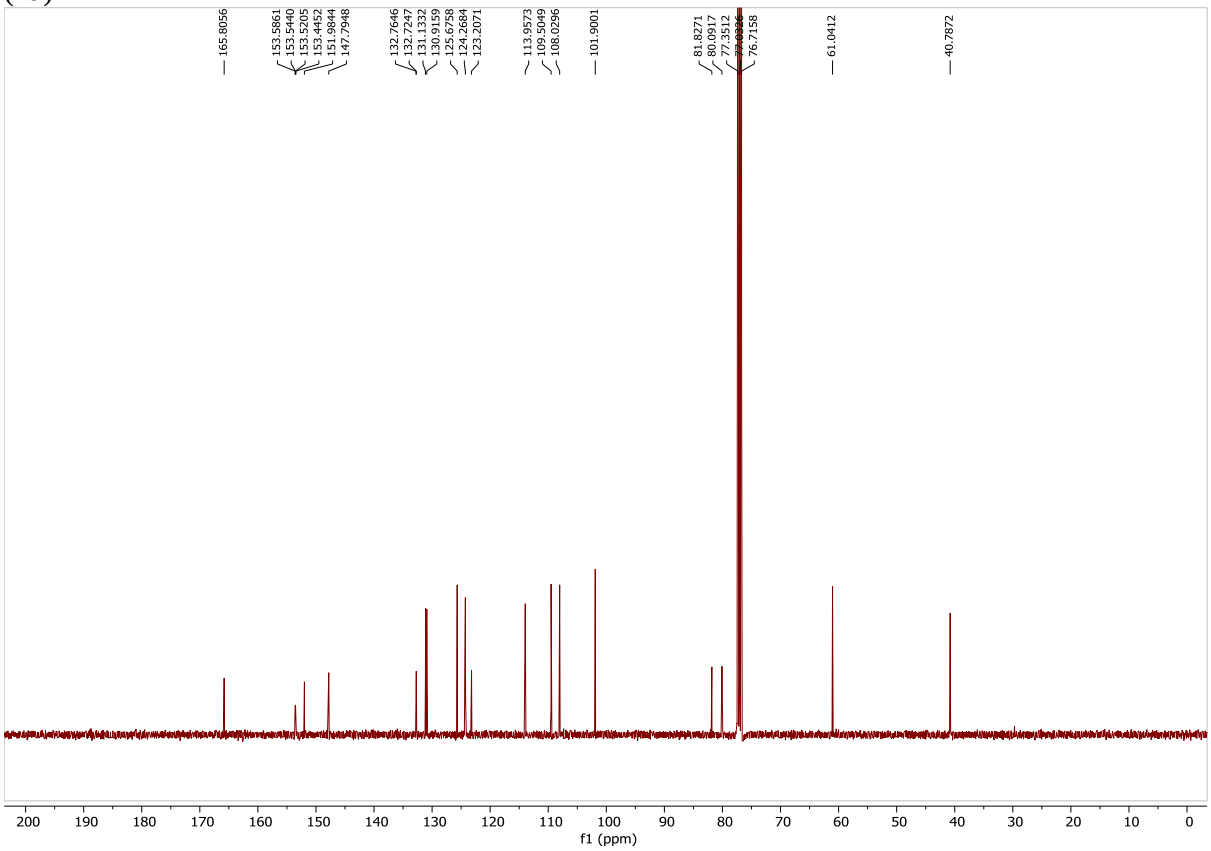
^{1}H NMR of 2-(3-(fluoromethyl)-2-oxoquinoxalin-1(2*H*)-yl)ethyl benzo[*d*][1,3]dioxole-5-carboxylate (**7a**)



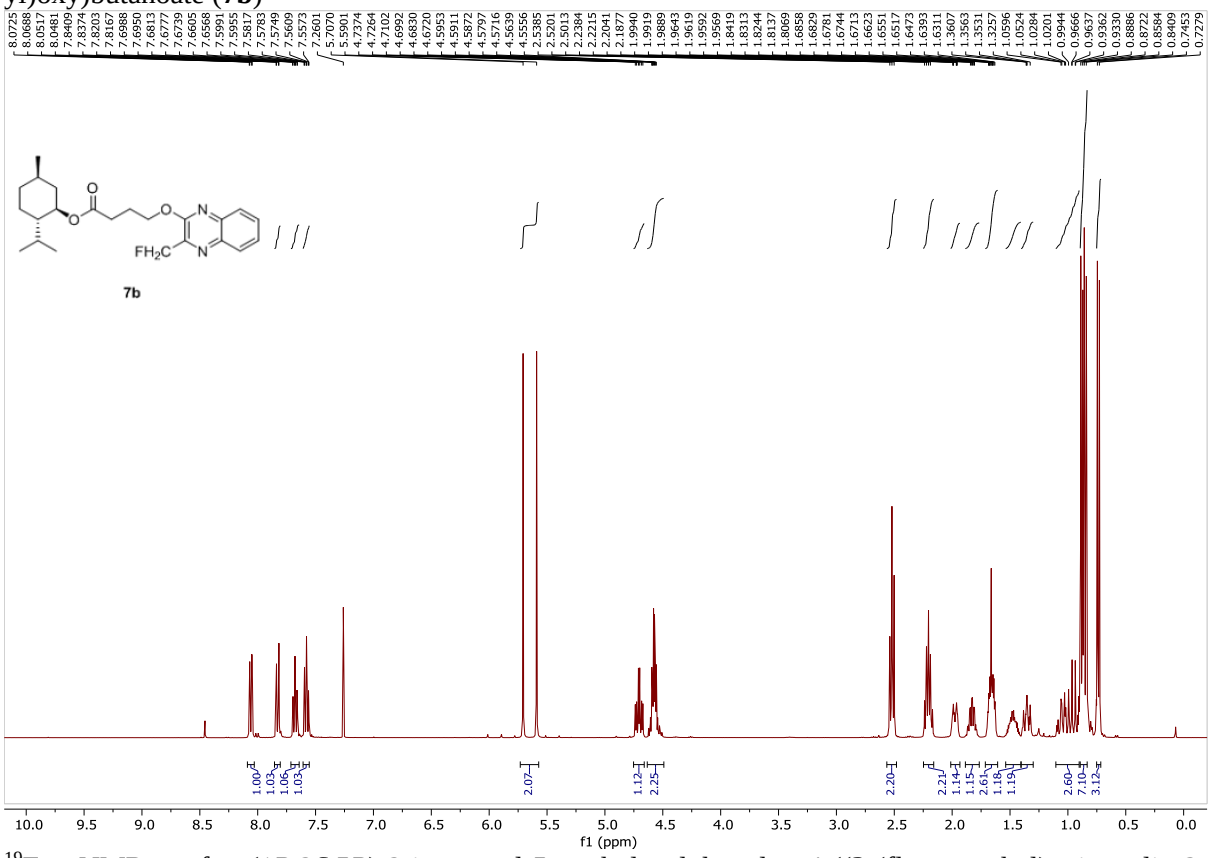
^{19}F NMR of 2-(3-(fluoromethyl)-2-oxoquinoxalin-1(2*H*)-yl)ethyl benzo[*d*][1,3]dioxole-5-carboxylate (**7a**)



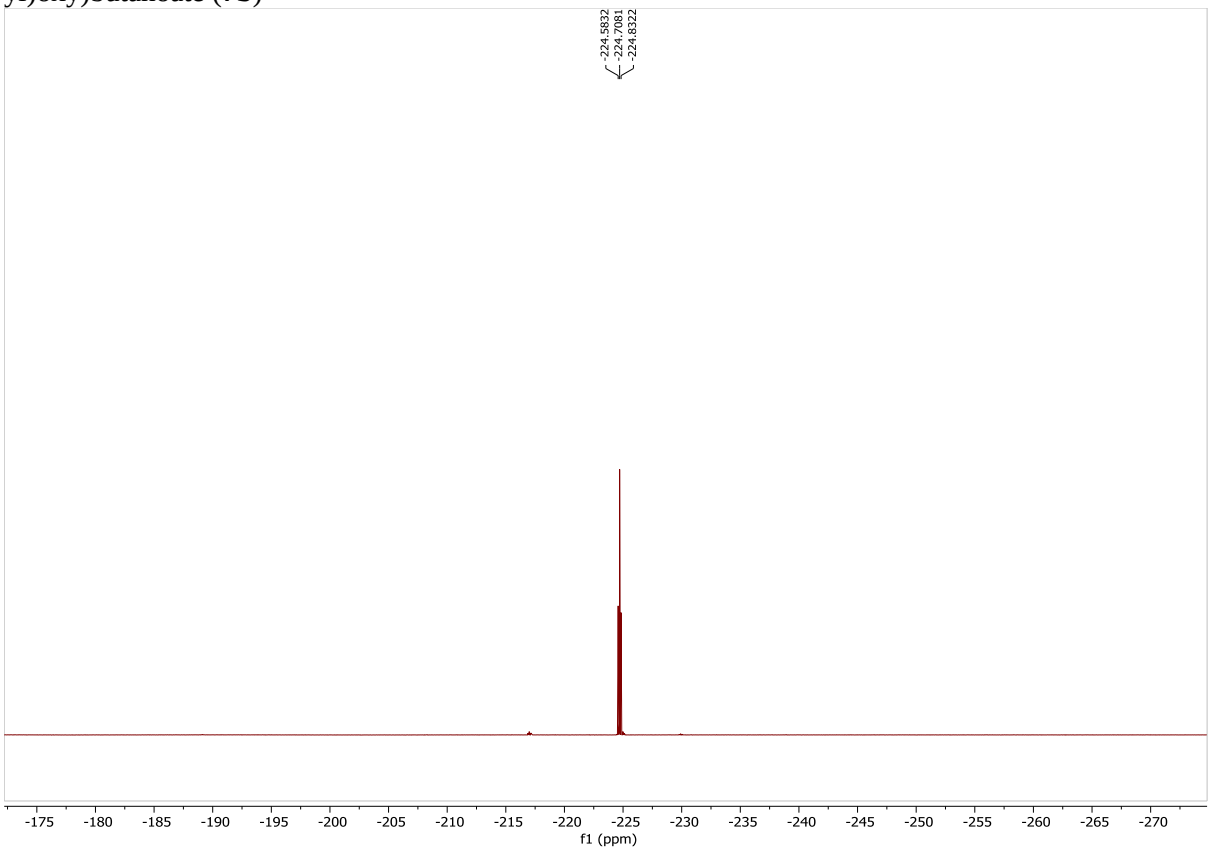
^{13}C NMR of 2-(3-(fluoromethyl)-2-oxoquinoxalin-1(2*H*)-yl)ethyl benzo[*d*][1,3]dioxole-5-carboxylate (**7a**)



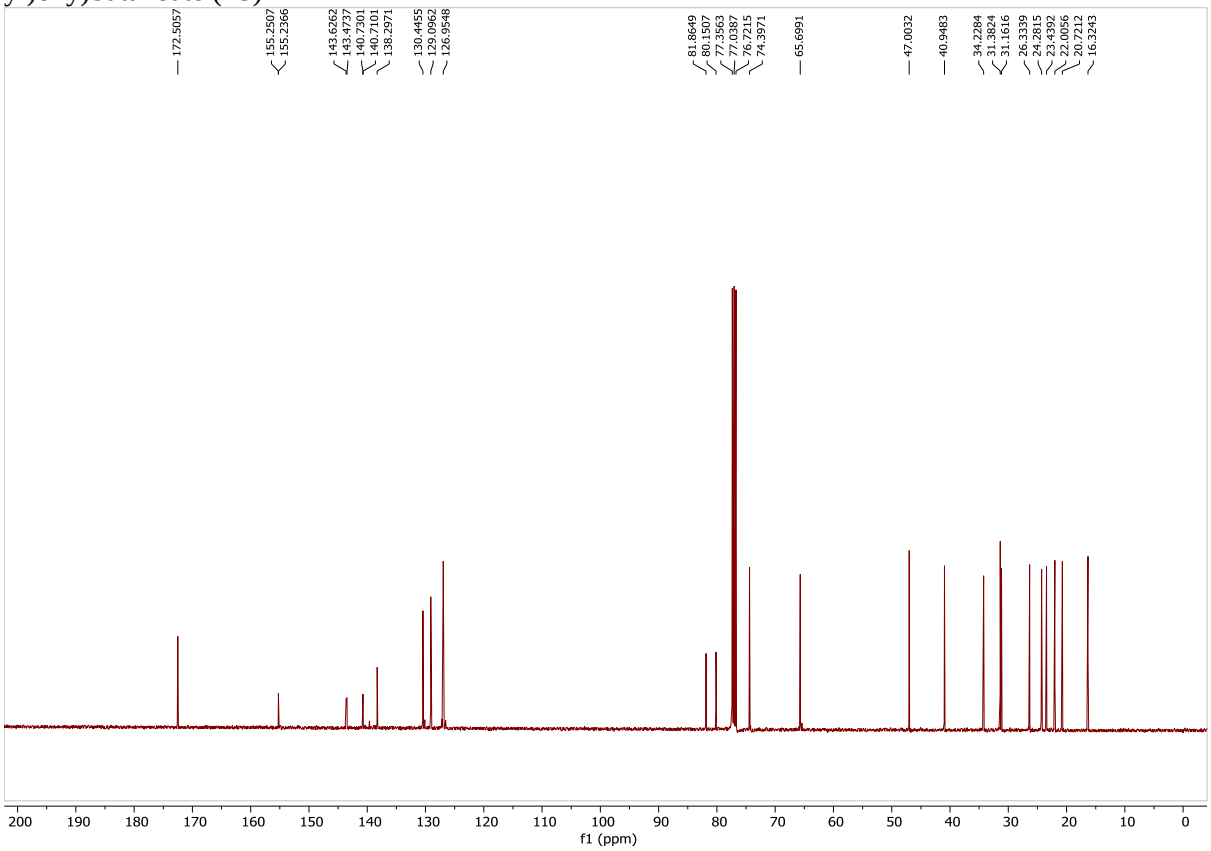
^{1}H NMR of (1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl 4-((3-(fluoromethyl)quinoxalin-2-yl)oxy)butanoate (**7b**)



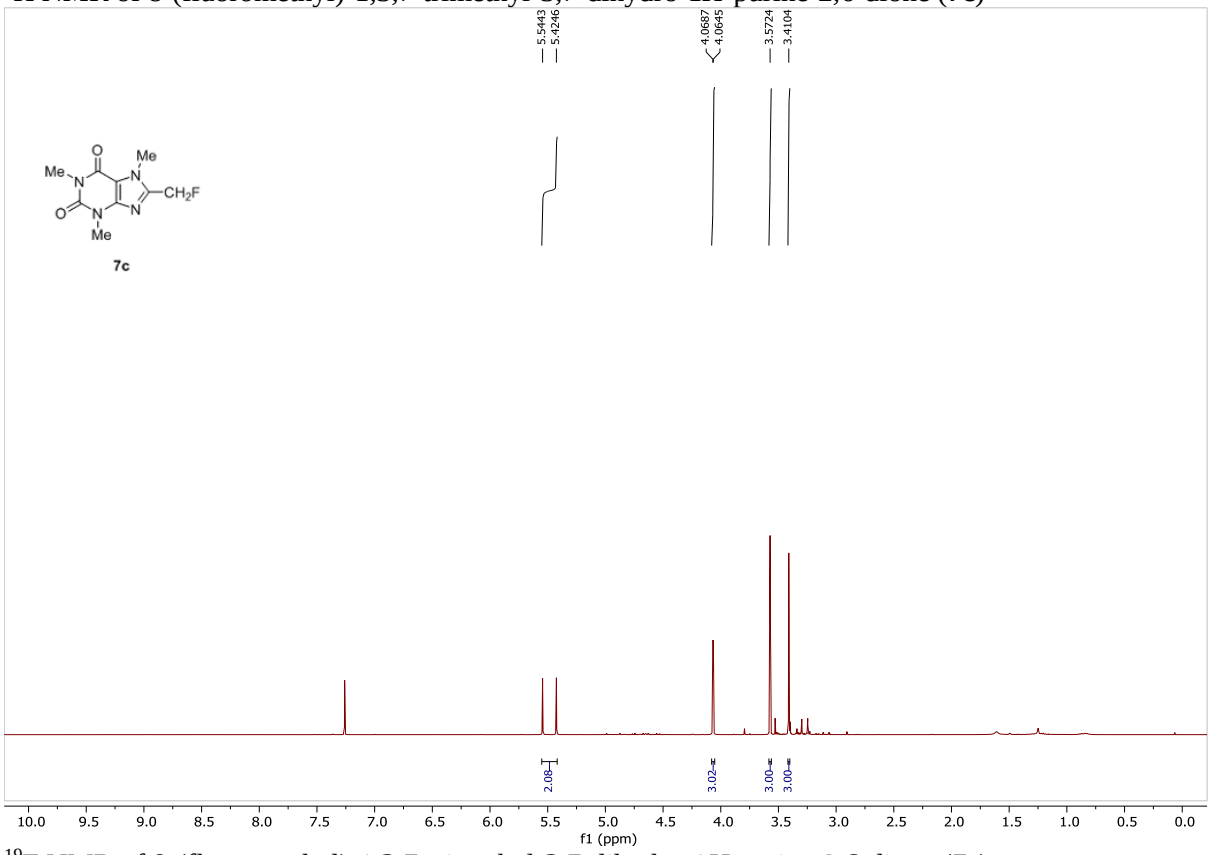
^{19}F NMR of (1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl 4-((3-(fluoromethyl)quinoxalin-2-yl)oxy)butanoate (**7b**)



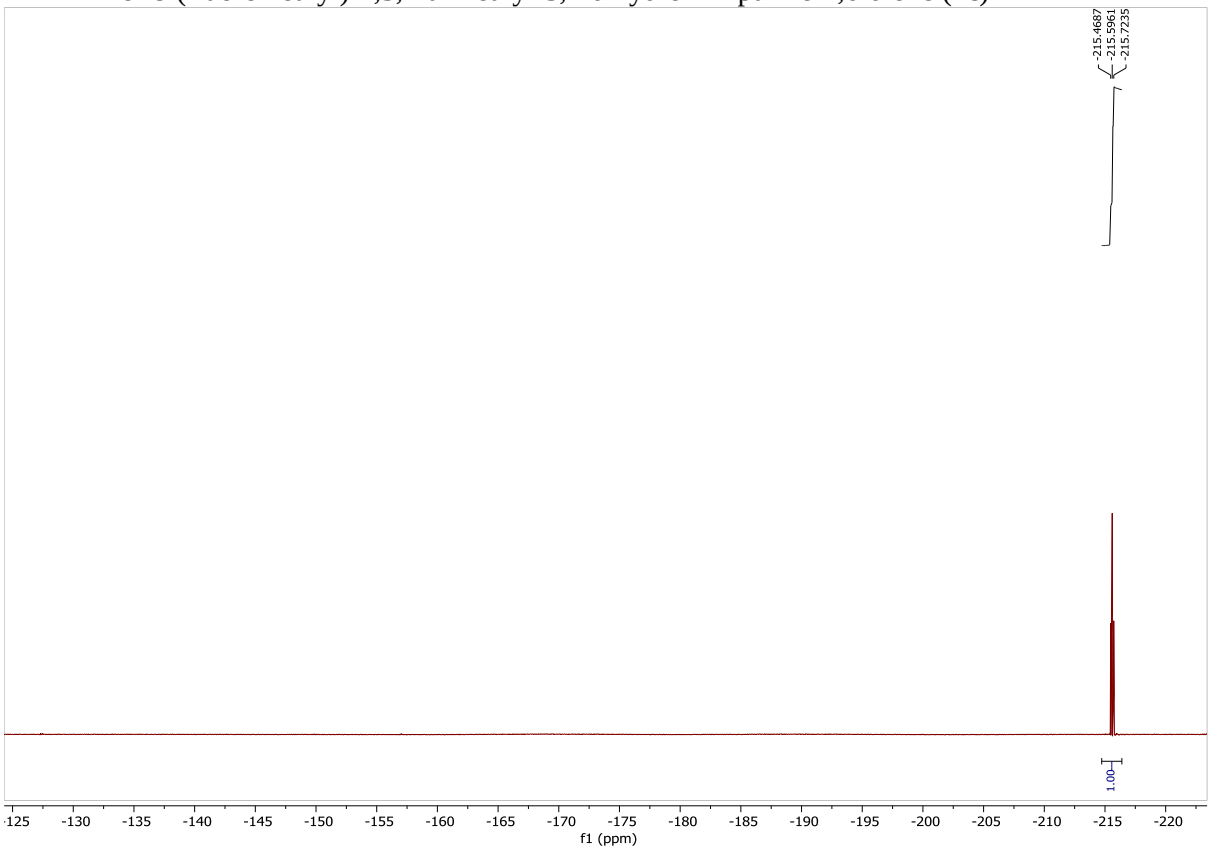
^{13}C NMR of (1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl 4-((3-(fluoromethyl)quinoxalin-2-yl)oxy)butanoate (**7b**)



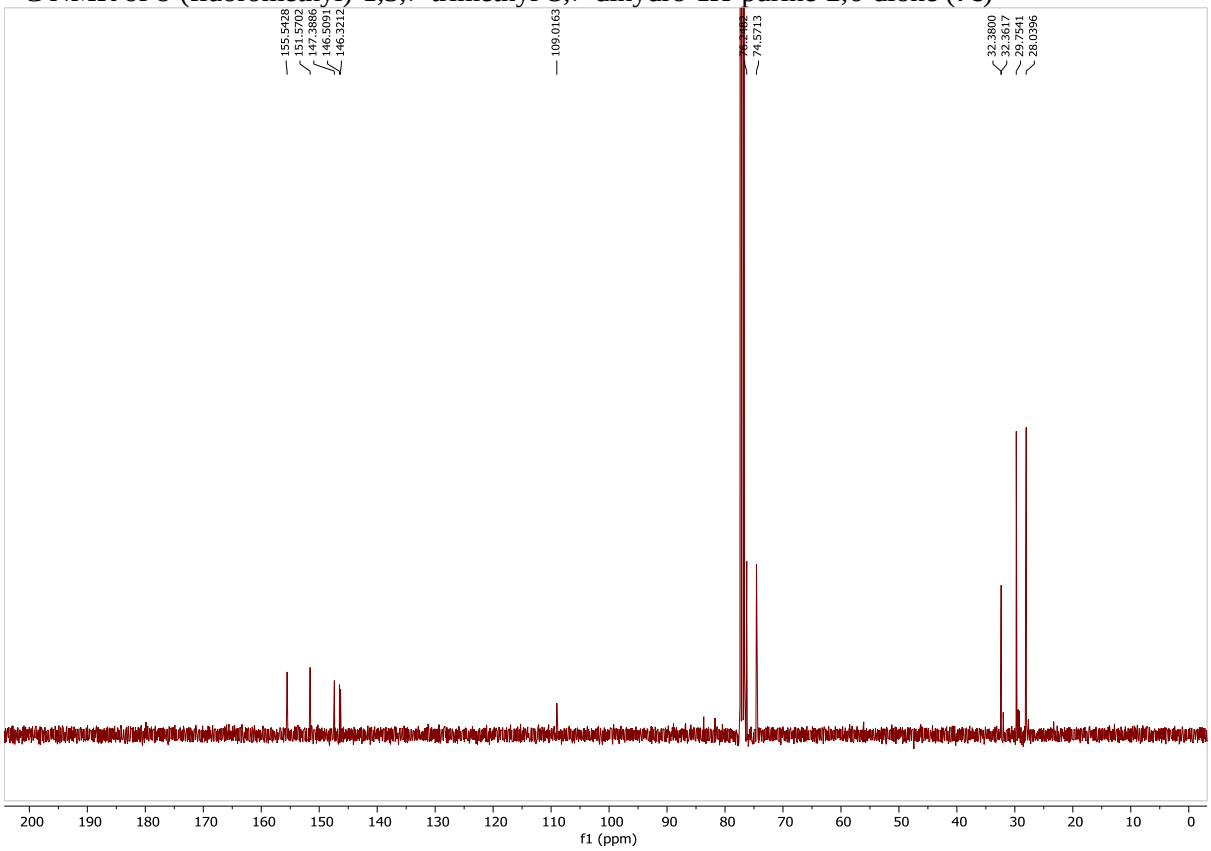
^{1}H NMR of 8-(fluoromethyl)-1,3,7-trimethyl-3,7-dihydro-1*H*-purine-2,6-dione (**7c**)



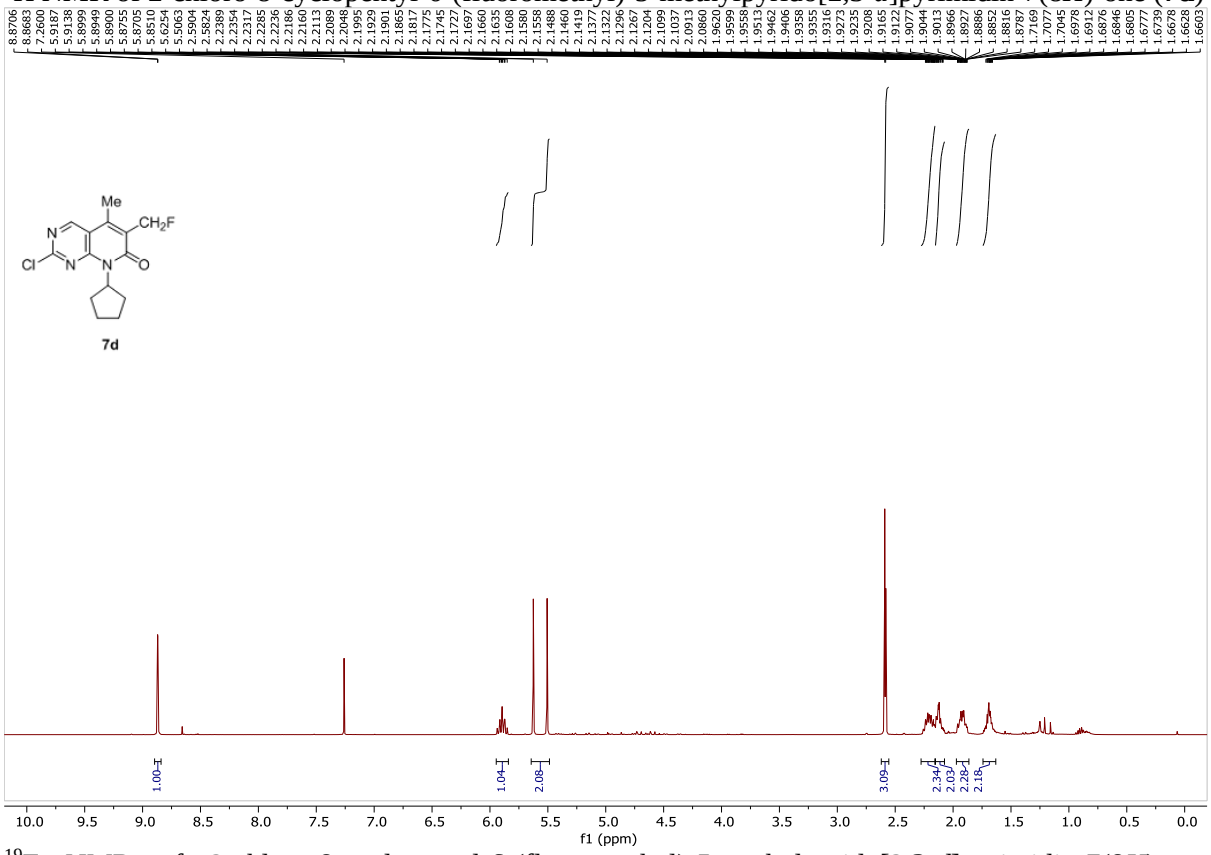
^{19}F NMR of 8-(fluoromethyl)-1,3,7-trimethyl-3,7-dihydro-1*H*-purine-2,6-dione (**7c**)



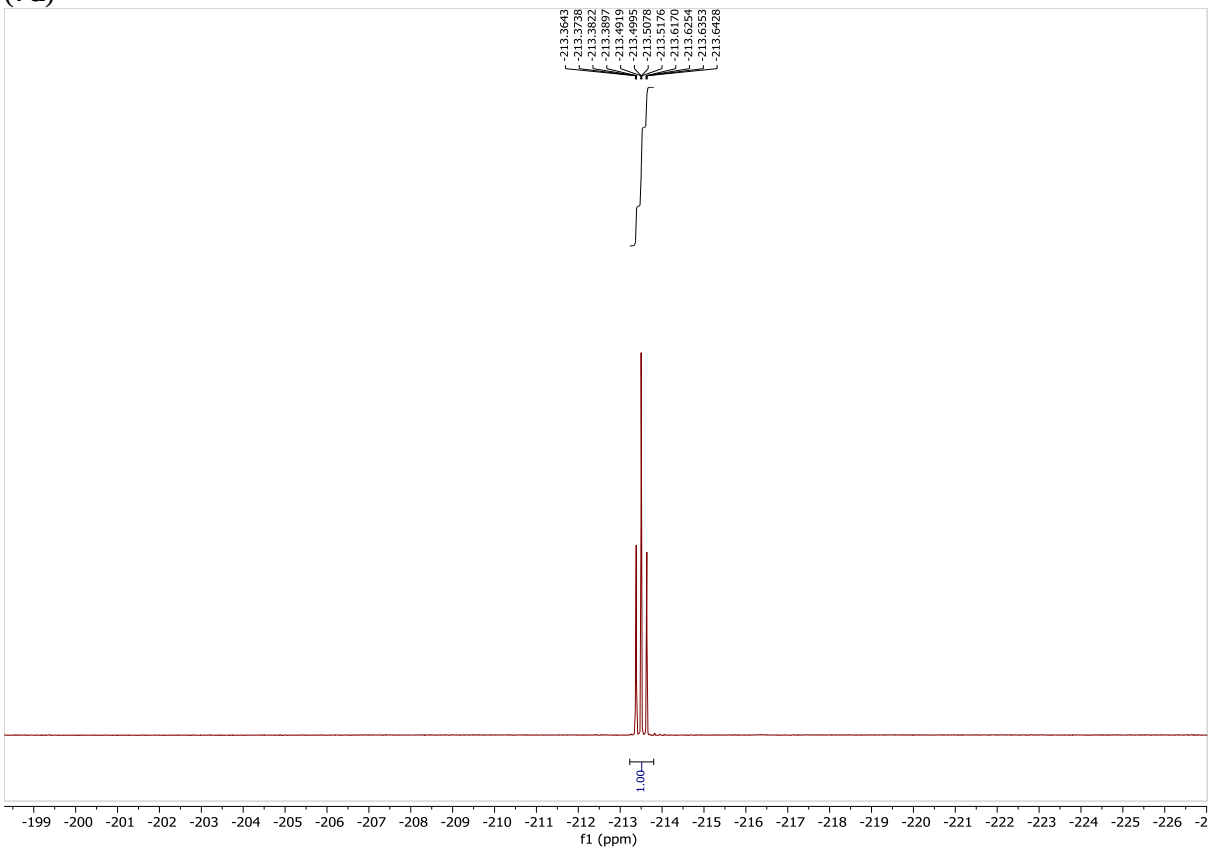
^{13}C NMR of 8-(fluoromethyl)-1,3,7-trimethyl-3,7-dihydro-1*H*-purine-2,6-dione (**7c**)



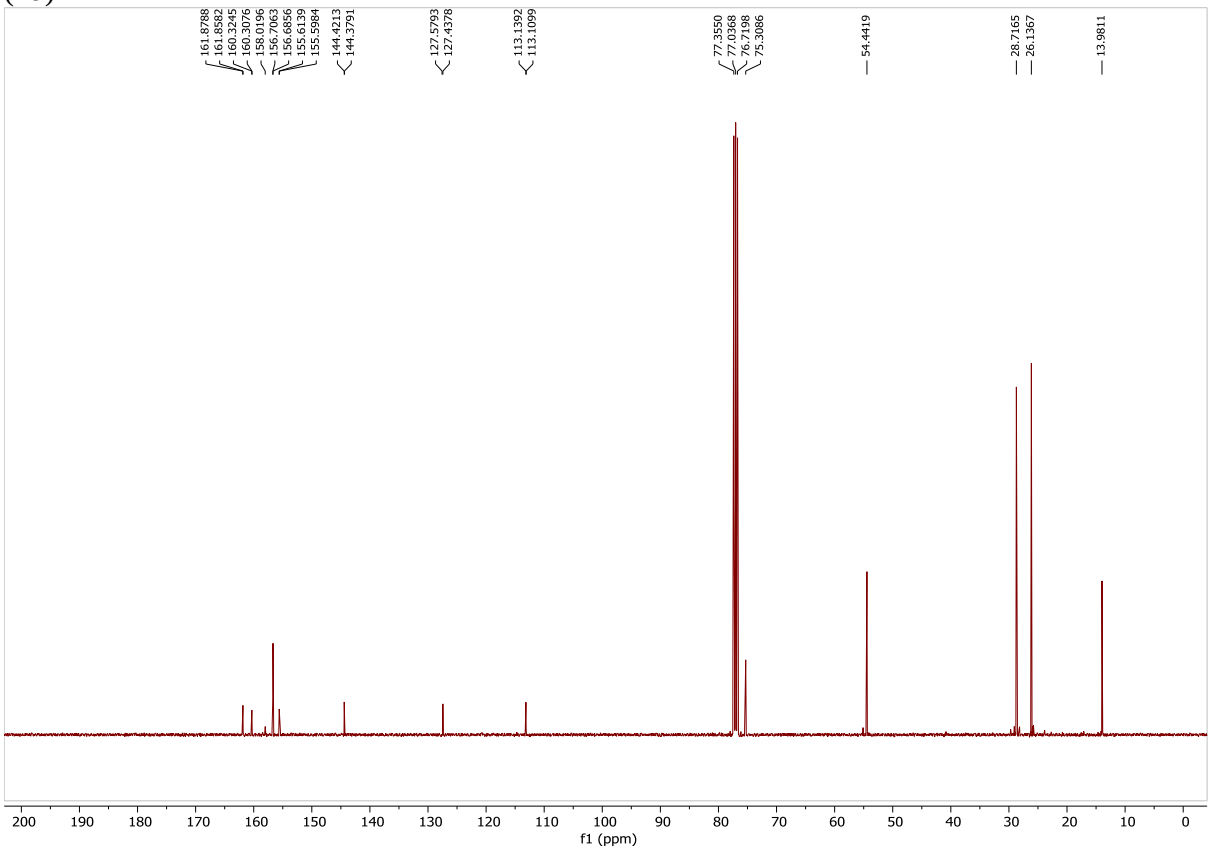
^{1}H NMR of 2-chloro-8-cyclopentyl-6-(fluoromethyl)-5-methylpyrido[2,3-*d*]pyrimidin-7(8*H*)-one (**7d**)



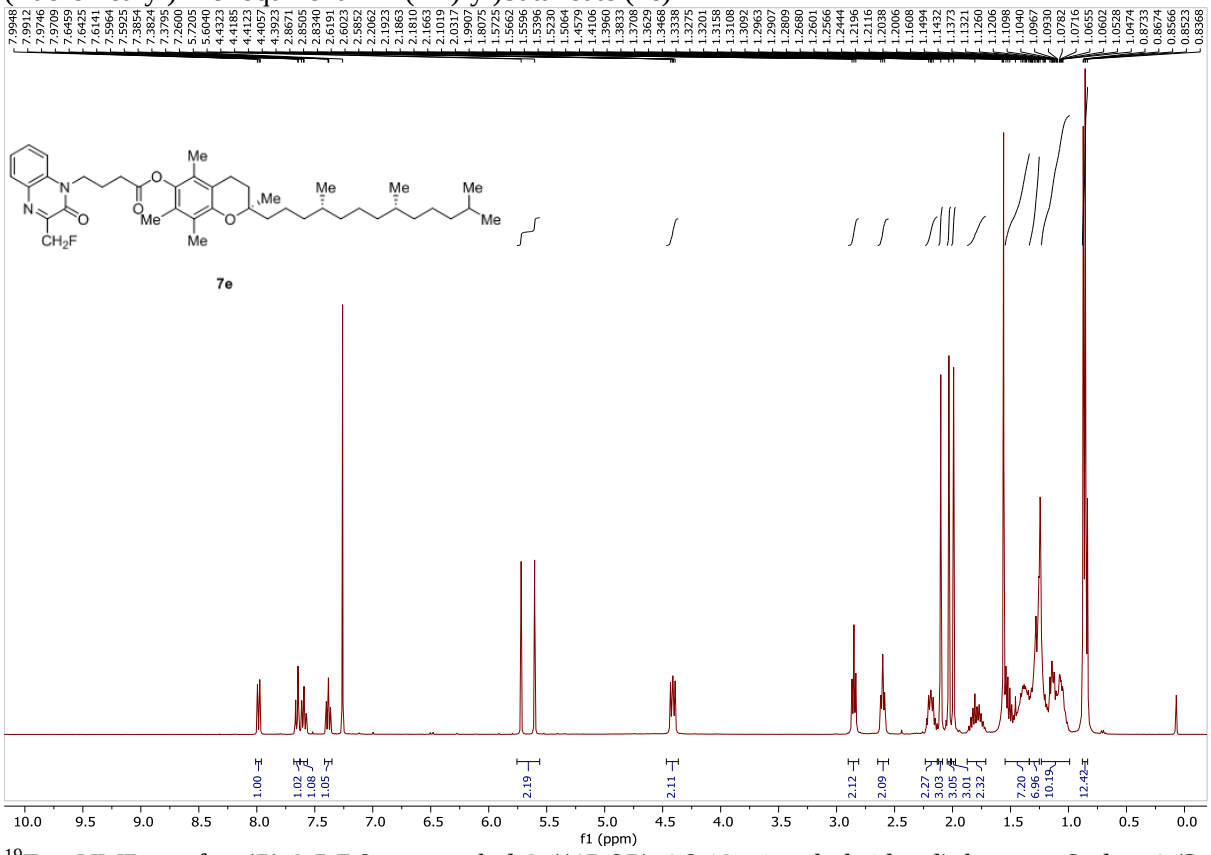
^{19}F NMR of 2-chloro-8-cyclopentyl-6-(fluoromethyl)-5-methylpyrido[2,3-*d*]pyrimidin-7(8*H*)-one (**7d**)



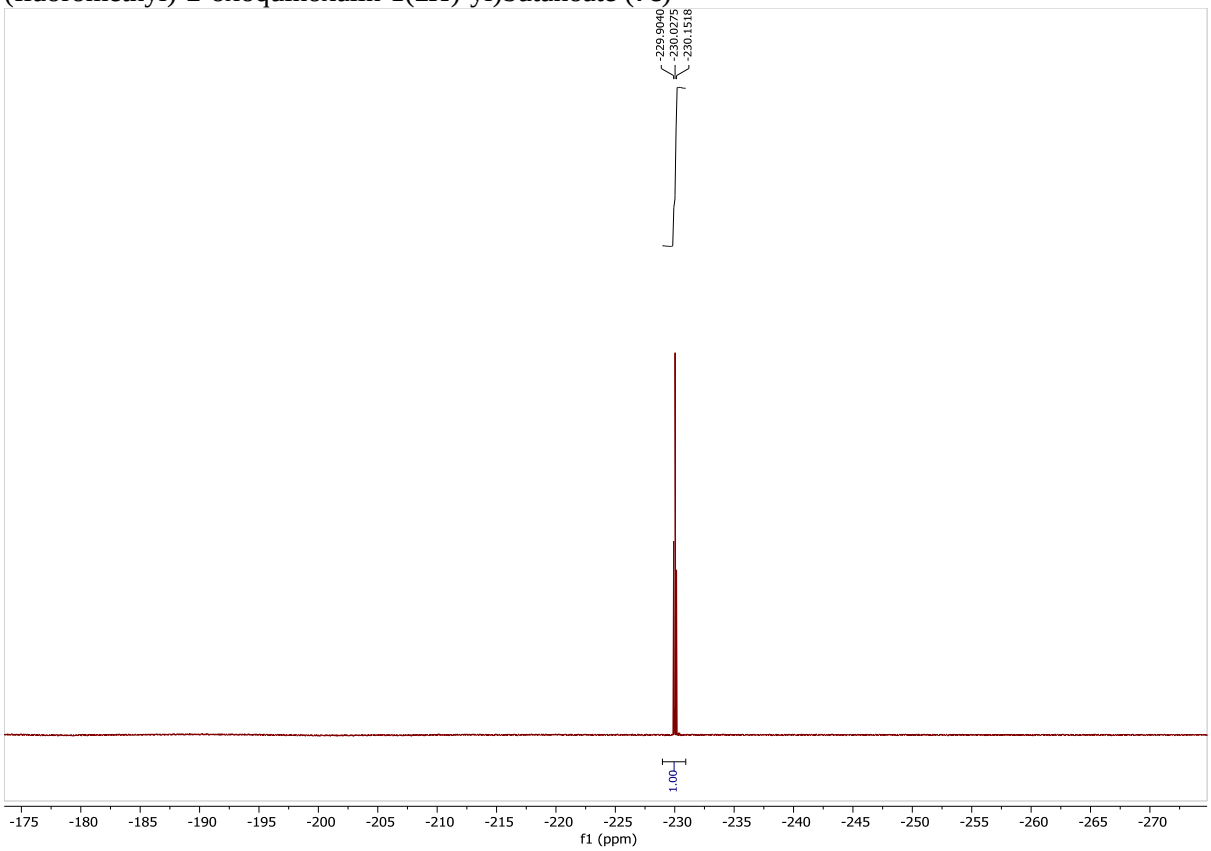
^{13}C NMR of 2-chloro-8-cyclopentyl-6-(fluoromethyl)-5-methylpyrido[2,3-*d*]pyrimidin-7(8*H*)-one (**7d**)



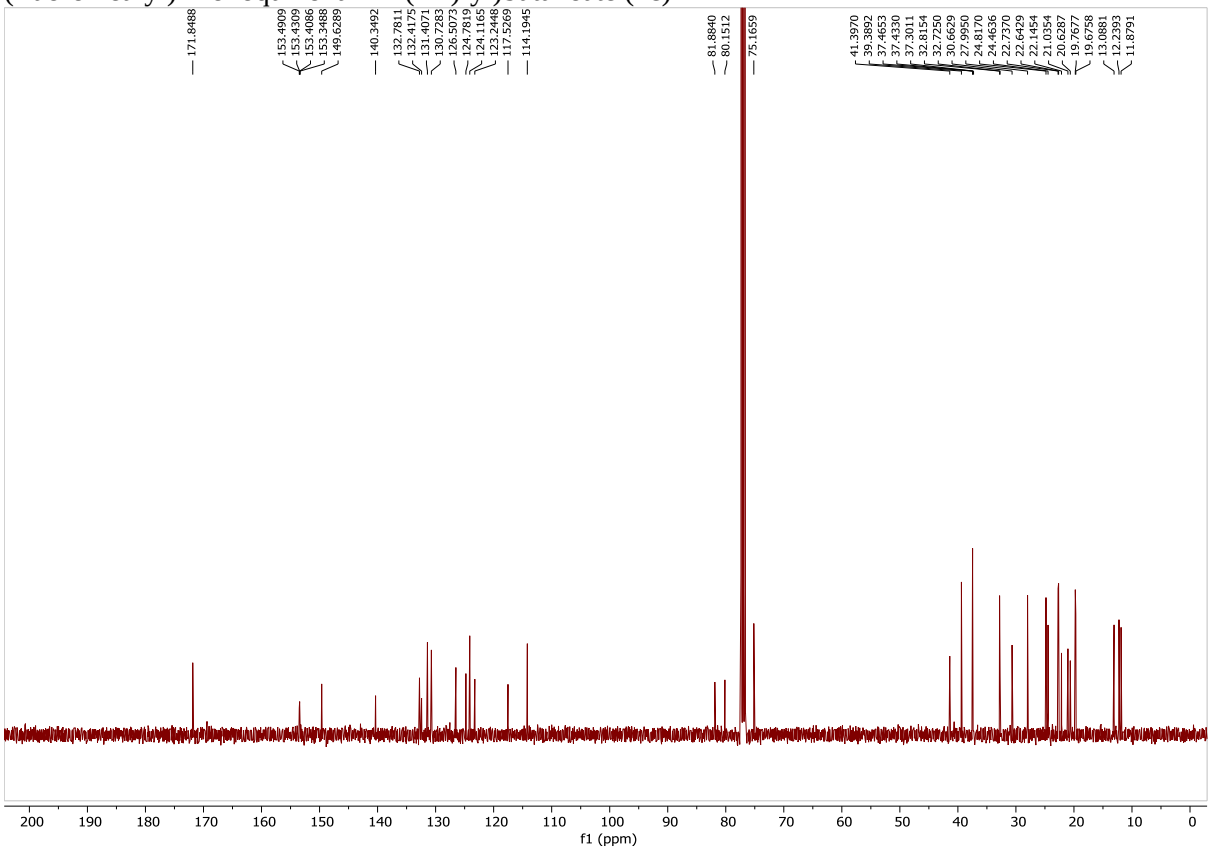
^{1}H NMR of (*R*)-2,5,7,8-tetramethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)chroman-6-yl 4-(3-(fluoromethyl)-2-oxoquinoxalin-1(2*H*)-yl)butanoate (**7e**)



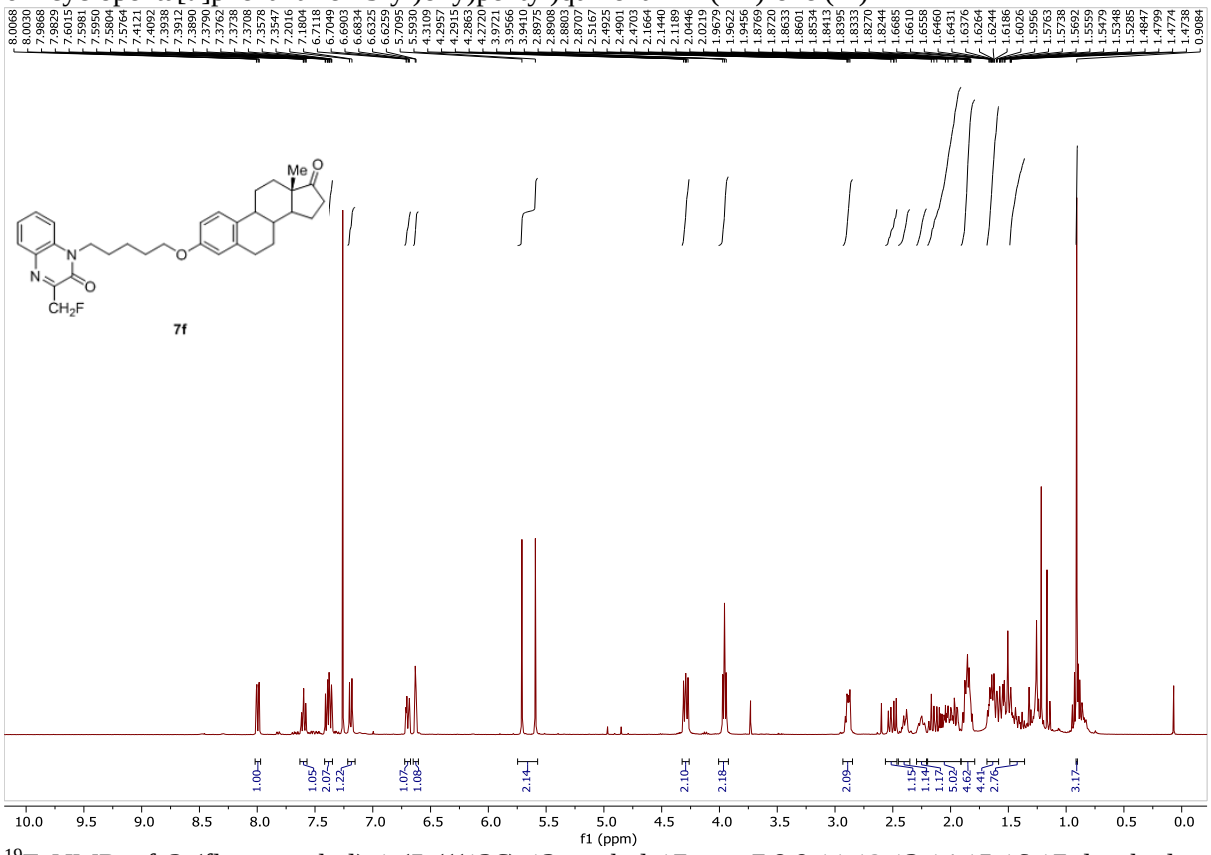
^{19}F NMR of (*R*)-2,5,7,8-tetramethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)chroman-6-yl 4-(3-(fluoromethyl)-2-oxoquinoxalin-1(2*H*)-yl)butanoate (**7e**)



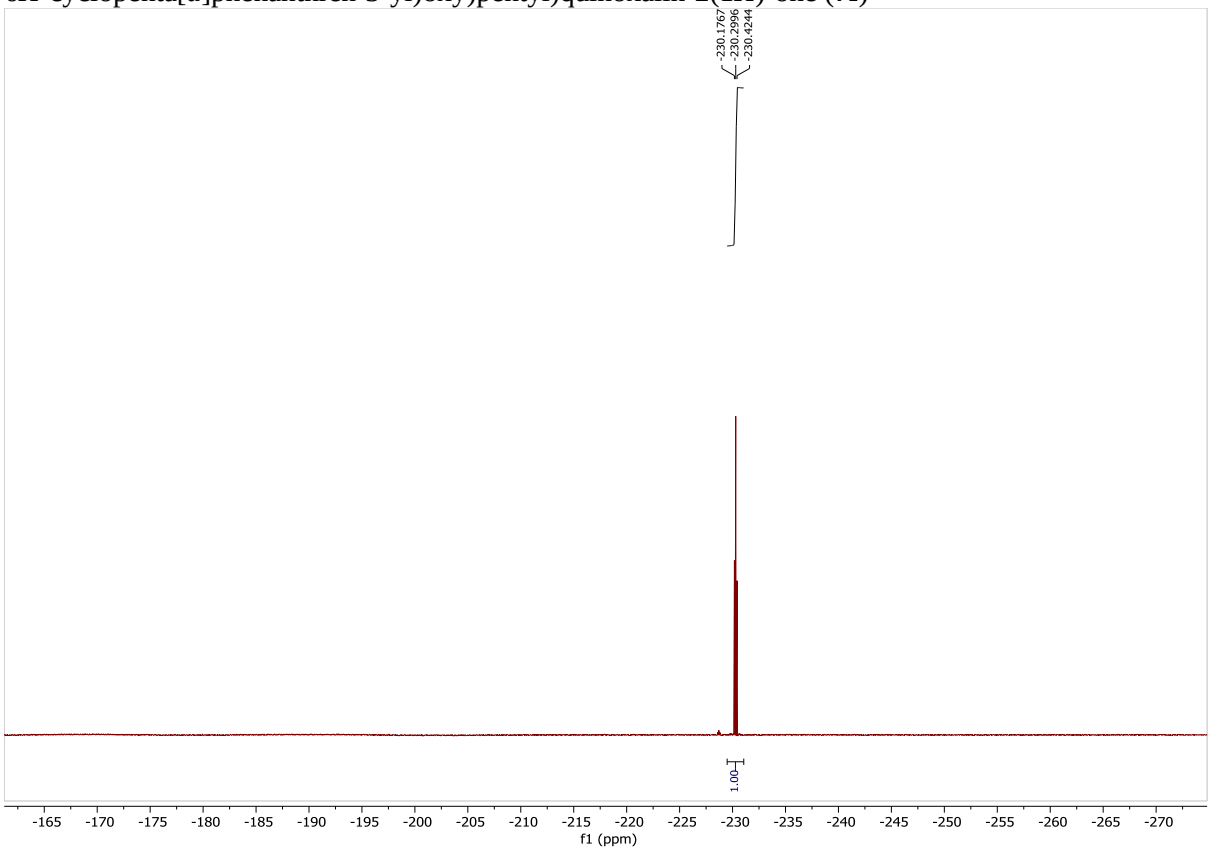
^{13}C NMR of (*R*)-2,5,7,8-tetramethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)chroman-6-yl 4-(3-(fluoromethyl)-2-oxoquinoxalin-1(2*H*)-yl)butanoate (**7e**)



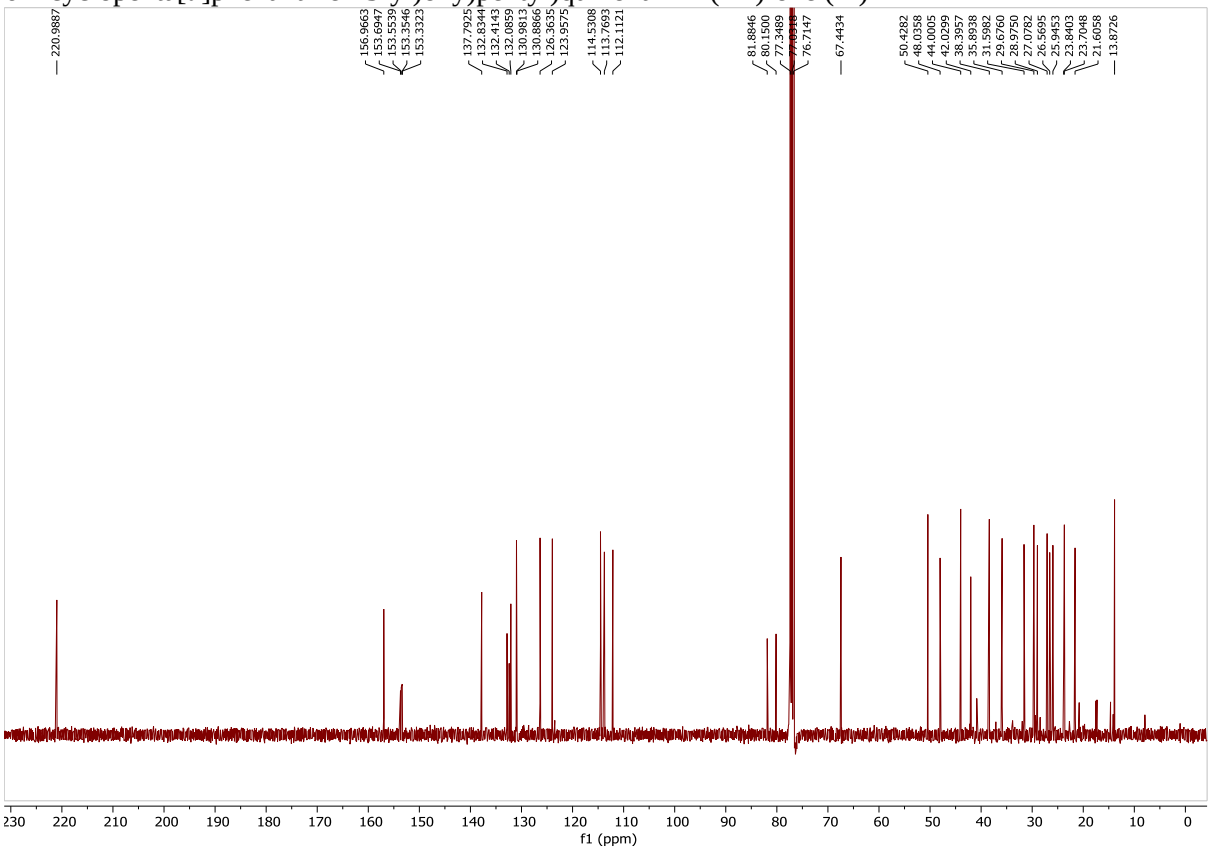
^{1}H NMR of 3-(fluoromethyl)-1-(5-(((13*S*)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl)oxy)pentyl)quinoxalin-2(1*H*)-one (**7f**)



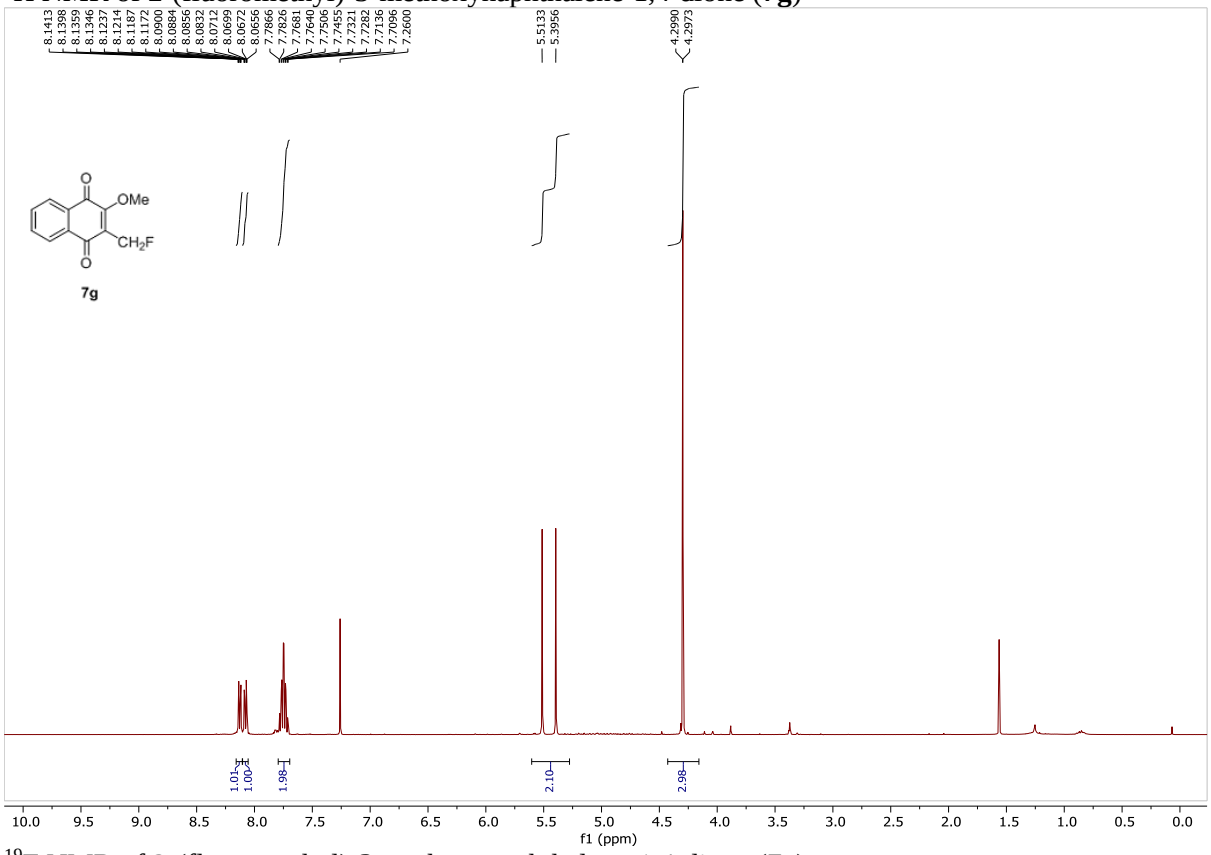
^{19}F NMR of 3-(fluoromethyl)-1-(5-(((13*S*)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl)oxy)pentyl)quinoxalin-2(1*H*)-one (**7f**)



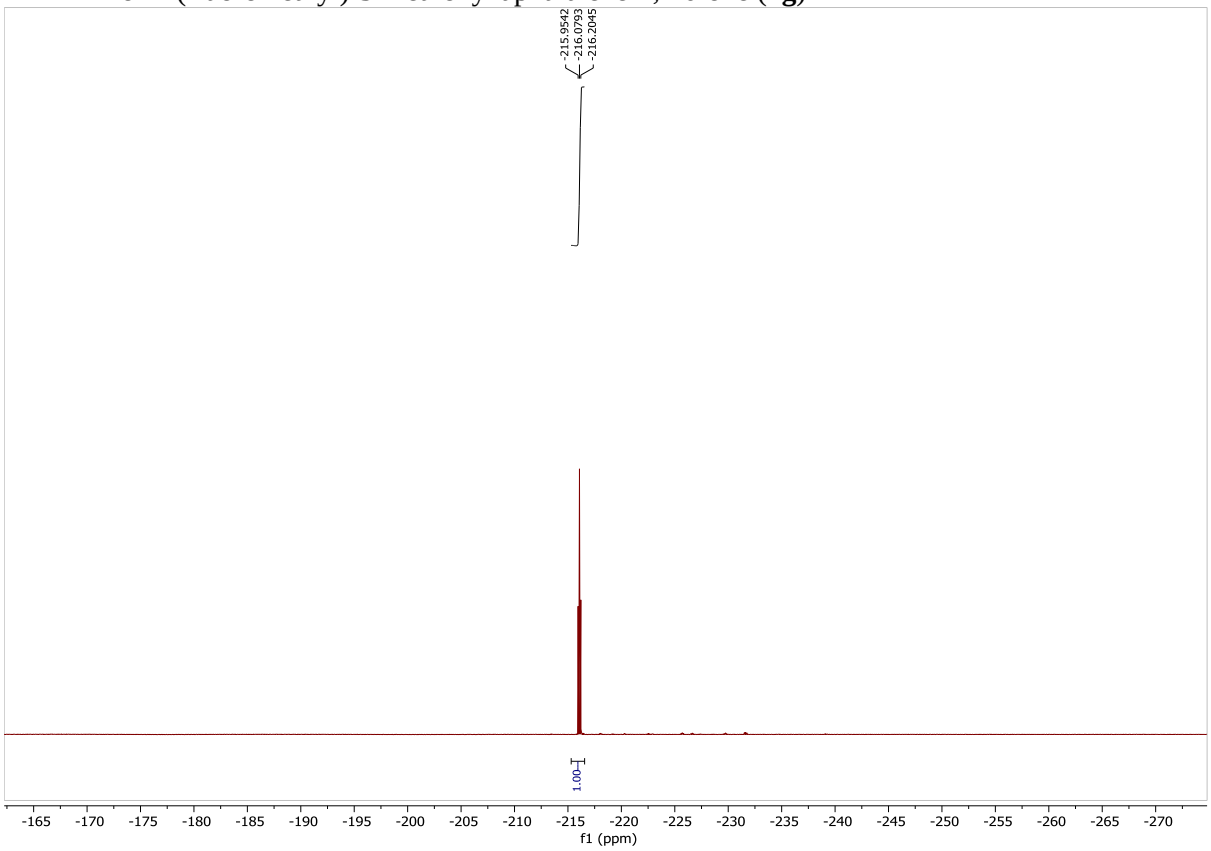
^{13}C NMR of 3-(fluoromethyl)-1-(5-(((13*S*)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl)oxy)pentyl)quinoxalin-2(1*H*)-one (**7f**)



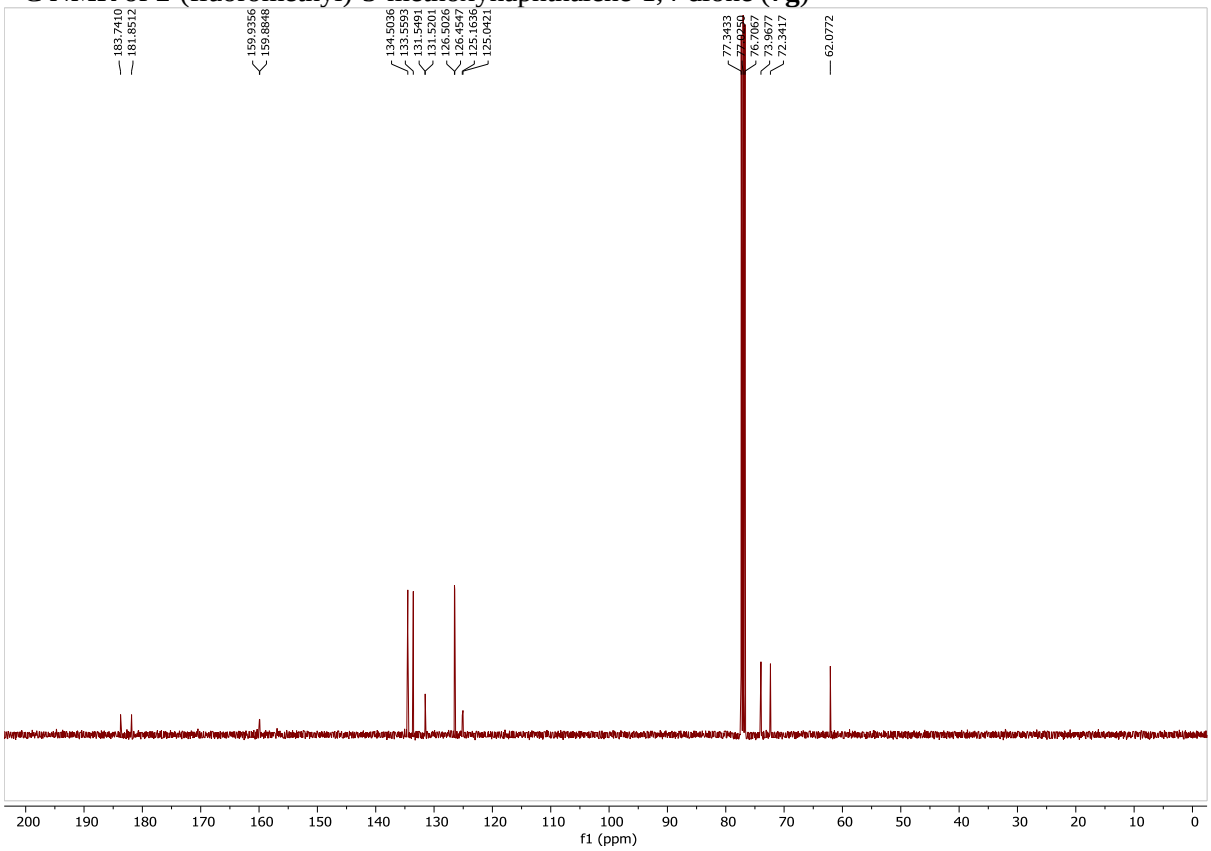
^{1}H NMR of 2-(fluoromethyl)-3-methoxynaphthalene-1,4-dione (**7g**)



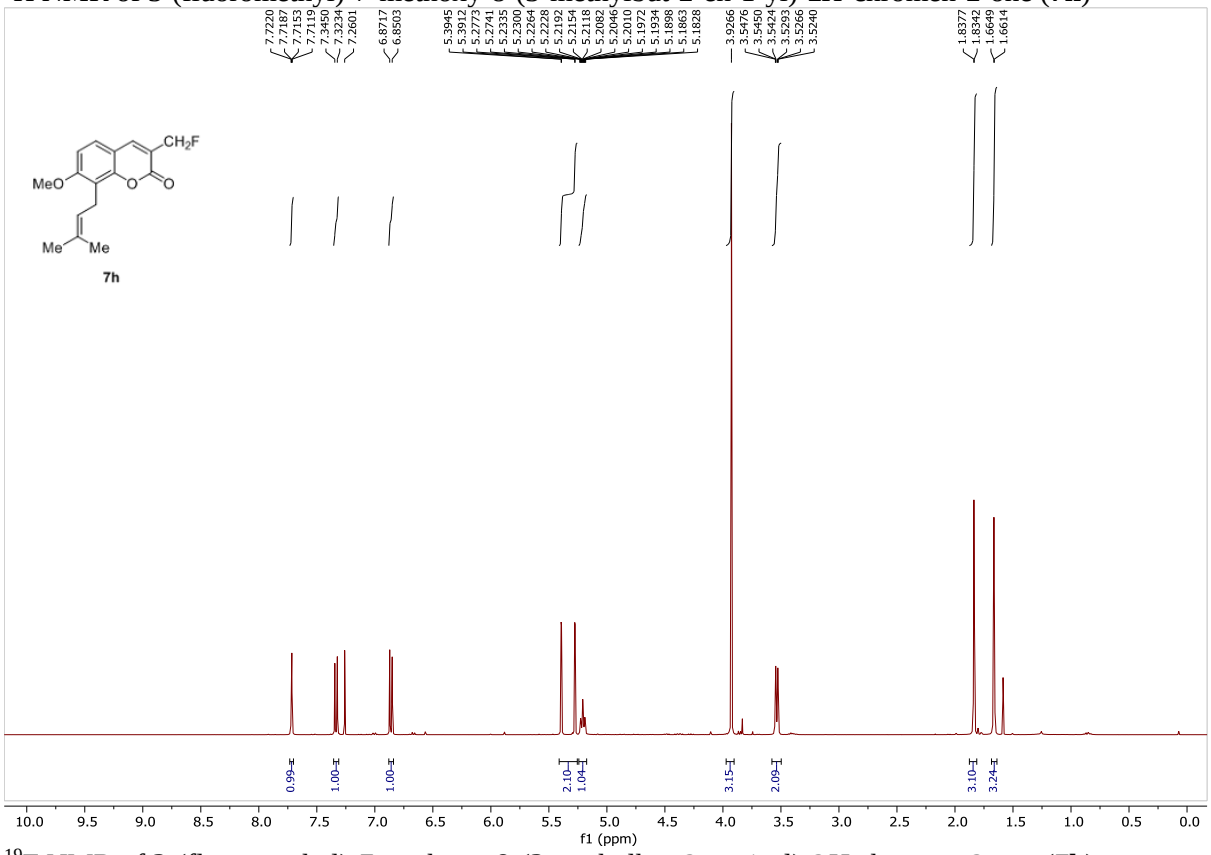
^{19}F NMR of 2-(fluoromethyl)-3-methoxynaphthalene-1,4-dione (**7g**)



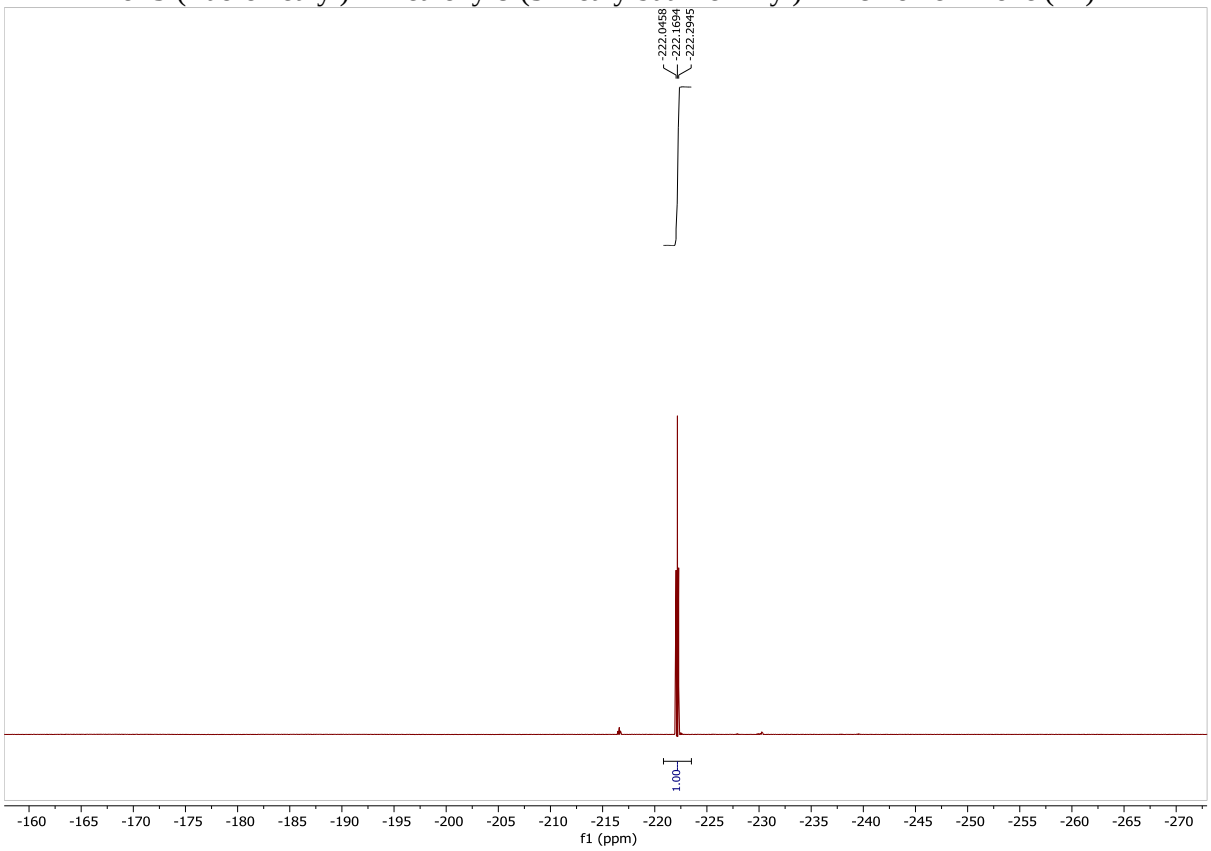
^{13}C NMR of 2-(fluoromethyl)-3-methoxynaphthalene-1,4-dione (**7g**)



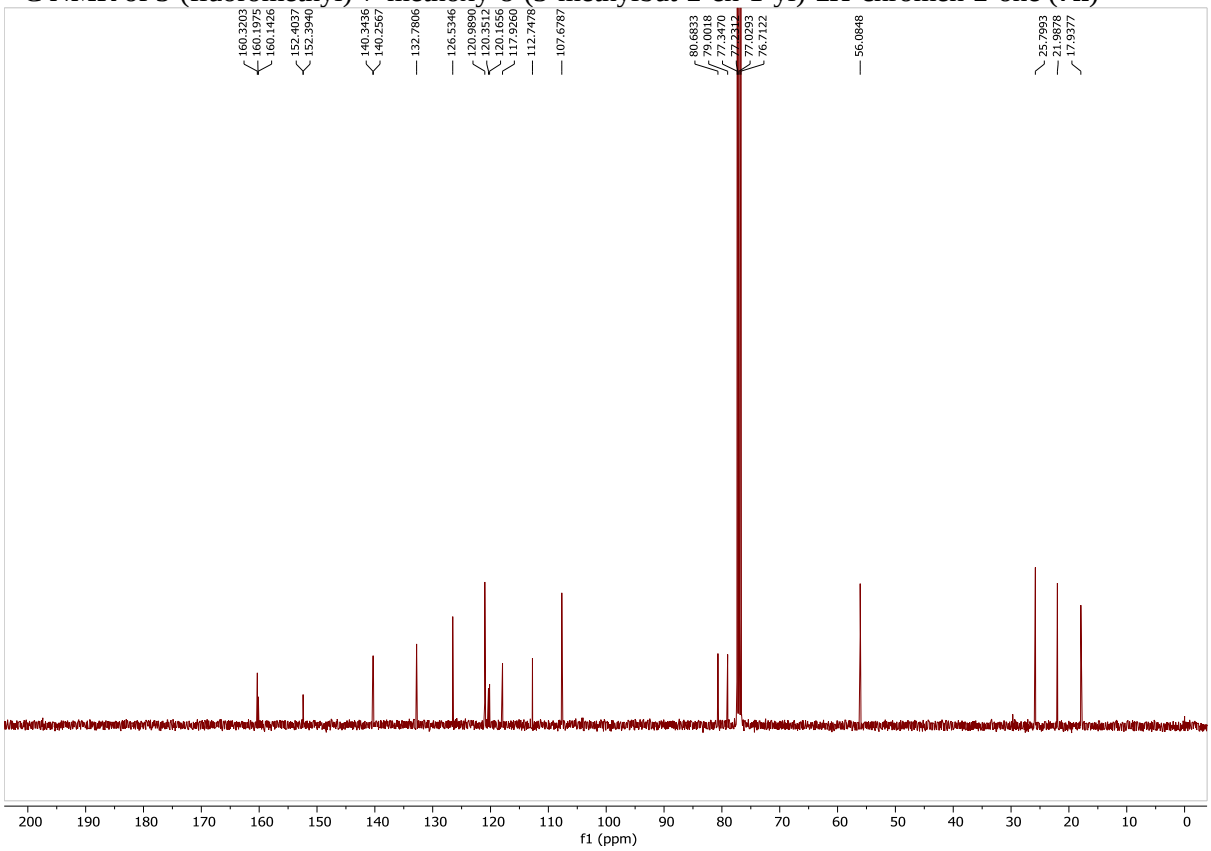
^{1}H NMR of 3-(fluoromethyl)-7-methoxy-8-(3-methylbut-2-en-1-yl)-2*H*-chromen-2-one (**7h**)



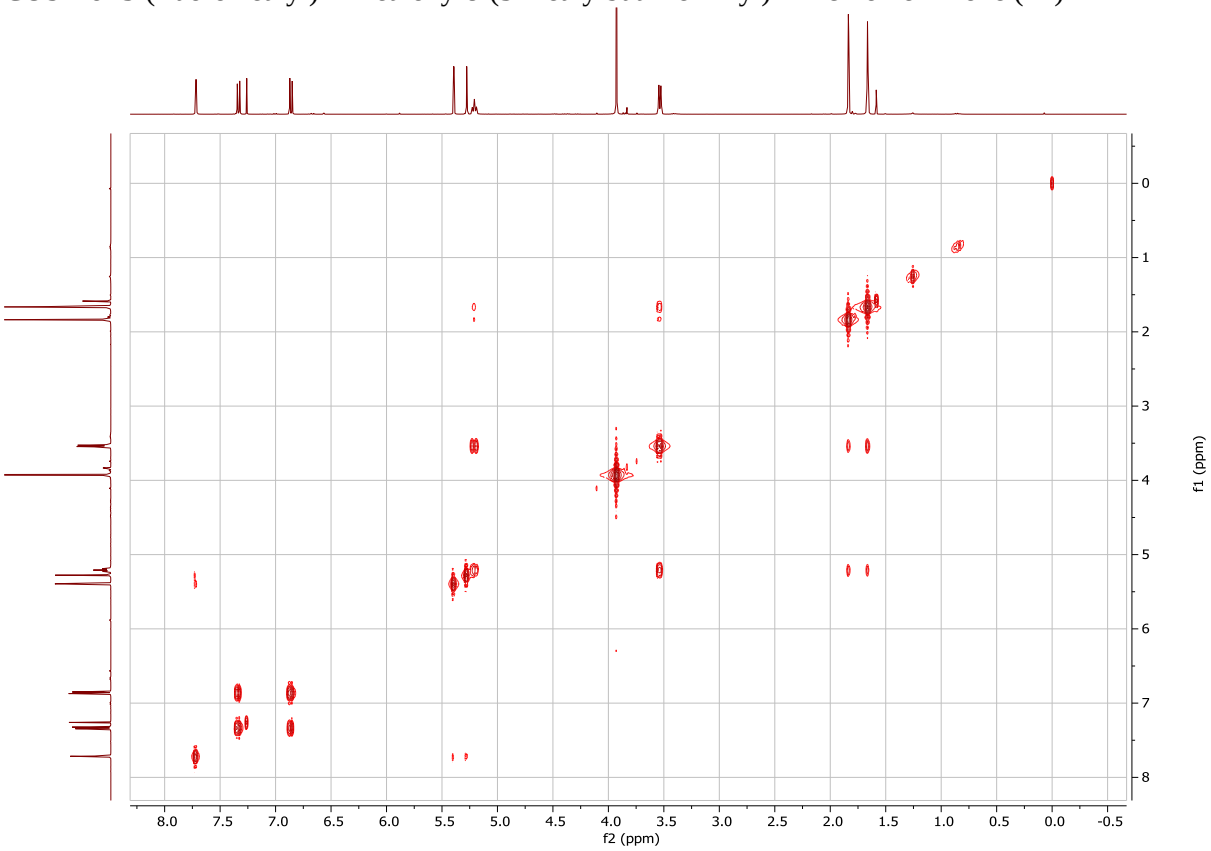
^{19}F NMR of 3-(fluoromethyl)-7-methoxy-8-(3-methylbut-2-en-1-yl)-2*H*-chromen-2-one (**7h**)



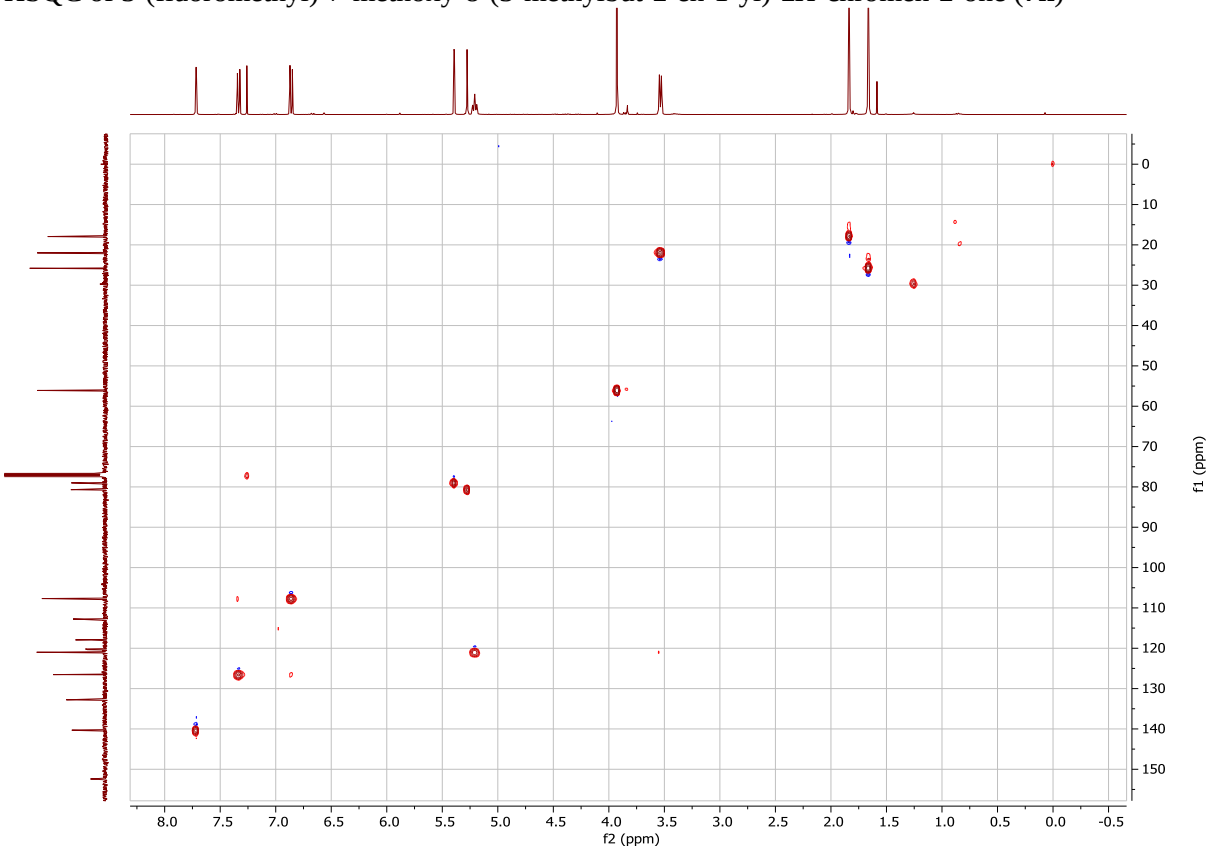
^{13}C NMR of 3-(fluoromethyl)-7-methoxy-8-(3-methylbut-2-en-1-yl)-2*H*-chromen-2-one (**7h**)



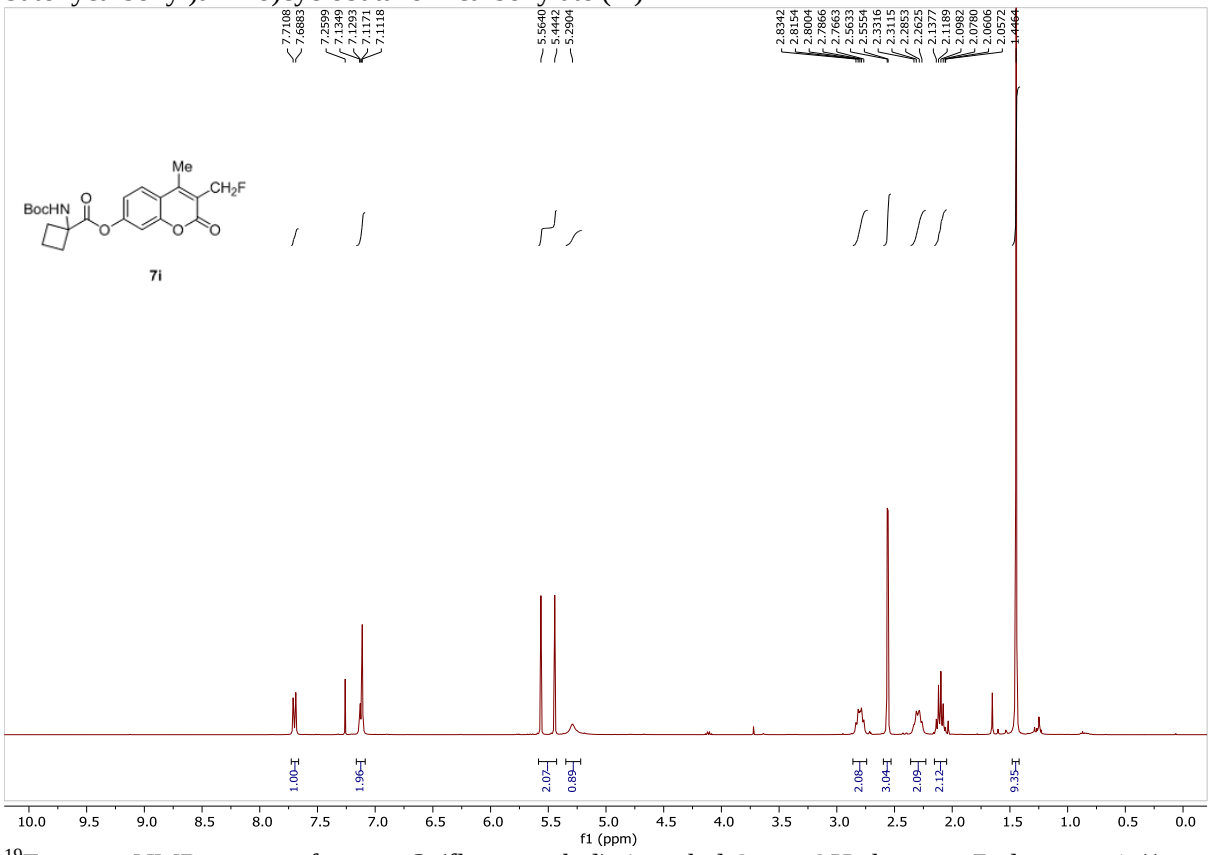
COSY of 3-(fluoromethyl)-7-methoxy-8-(3-methylbut-2-en-1-yl)-2*H*-chromen-2-one (**7h**)



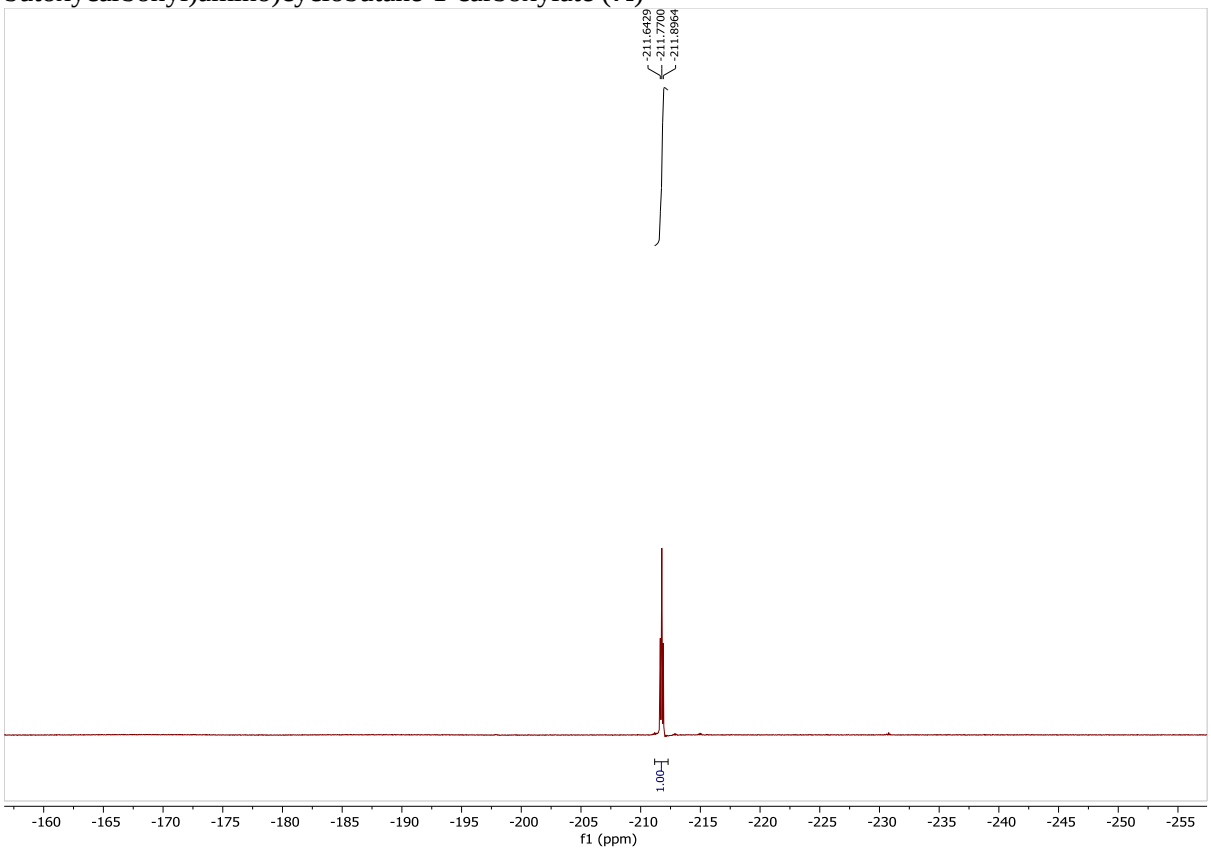
HSQC of 3-(fluoromethyl)-7-methoxy-8-(3-methylbut-2-en-1-yl)-2*H*-chromen-2-one (**7h**)



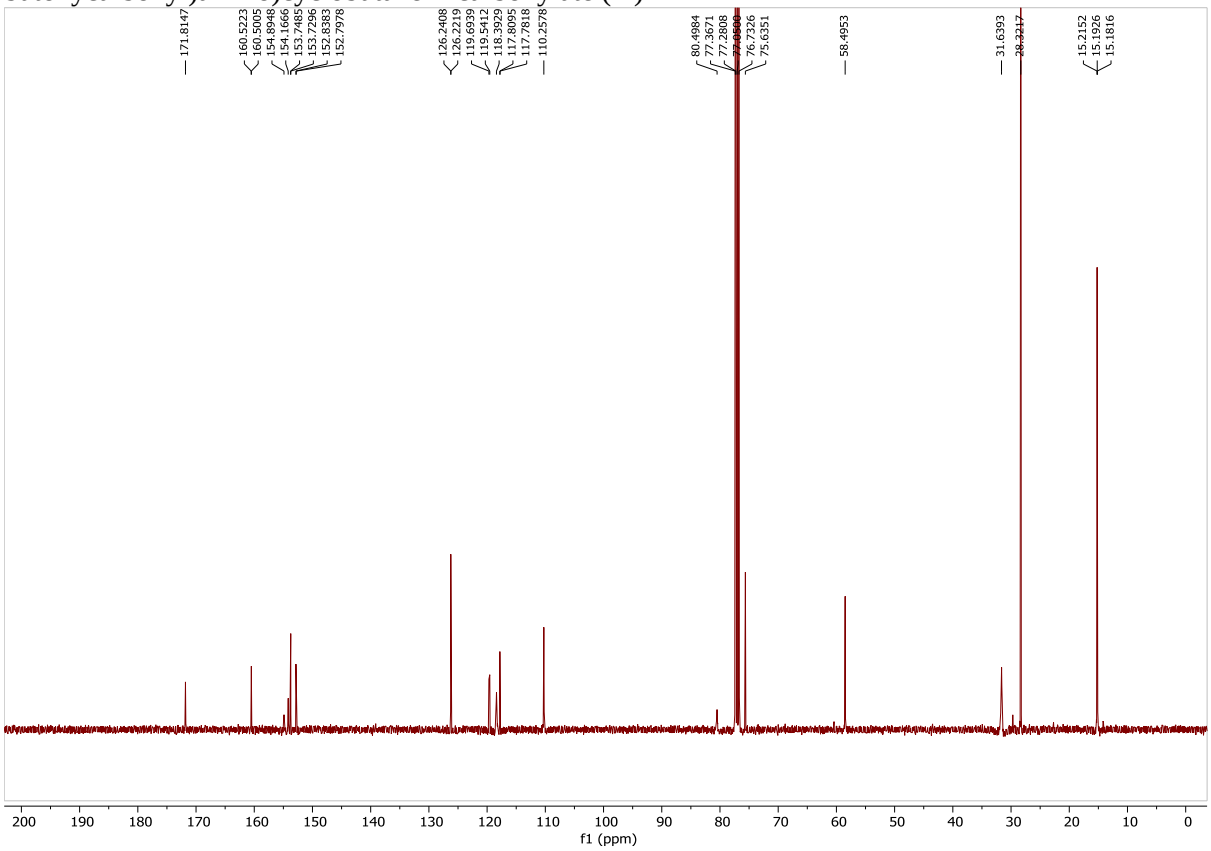
^{1}H NMR of 3-(fluoromethyl)-4-methyl-2-oxo-2*H*-chromen-7-yl 1-((*tert*-butoxycarbonyl)amino)cyclobutane-1-carboxylate (**7i**)



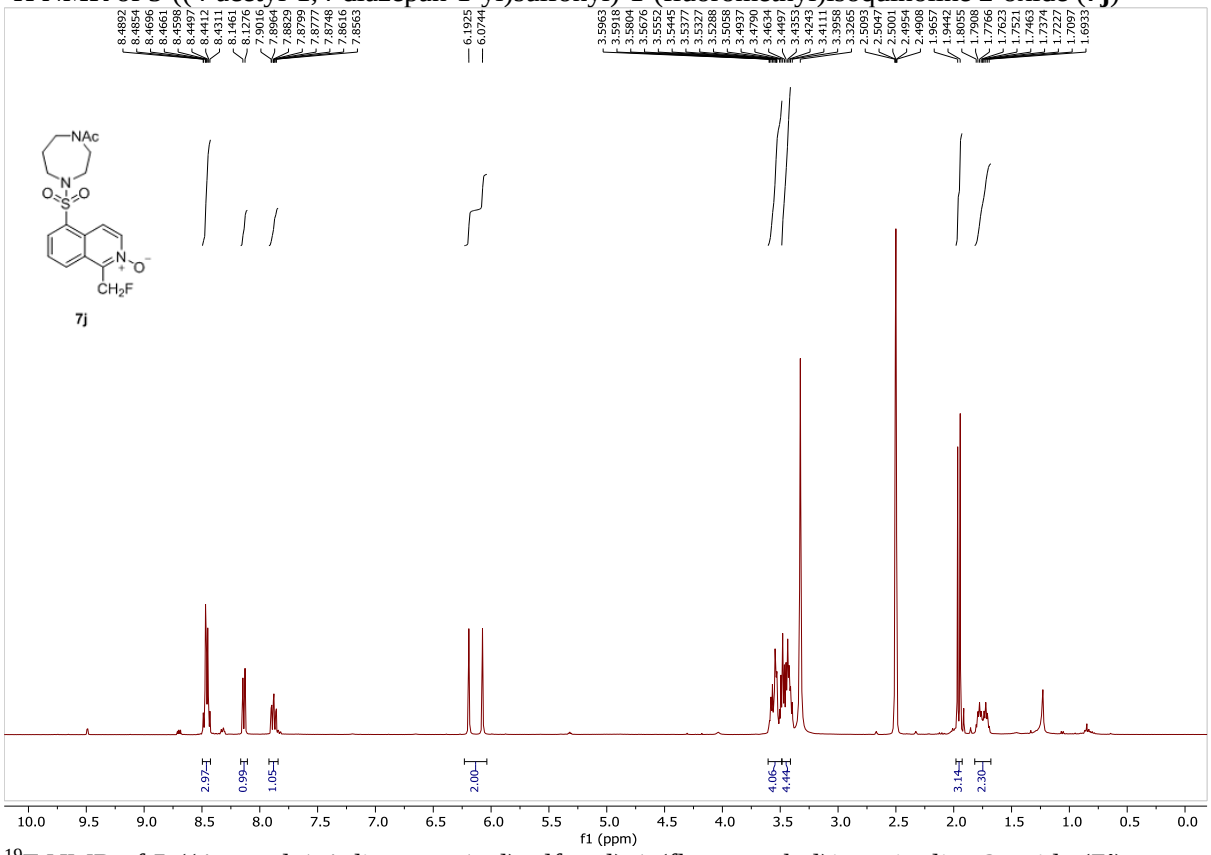
^{19}F NMR of 3-(fluoromethyl)-4-methyl-2-oxo-2*H*-chromen-7-yl 1-((*tert*-butoxycarbonyl)amino)cyclobutane-1-carboxylate (**7i**)



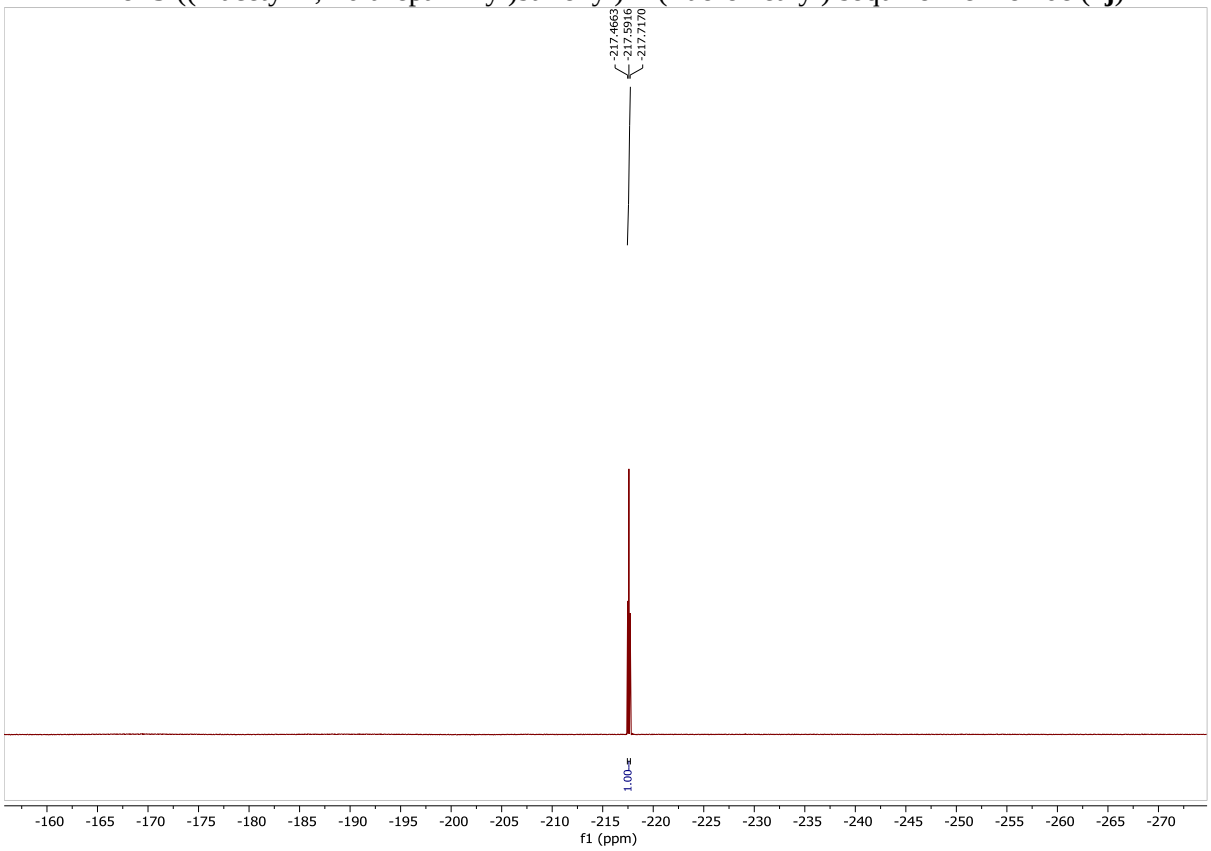
^{13}C NMR of 3-(fluoromethyl)-4-methyl-2-oxo-2*H*-chromen-7-yl 1-((*tert*-butoxycarbonyl)amino)cyclobutane-1-carboxylate (**7i**)



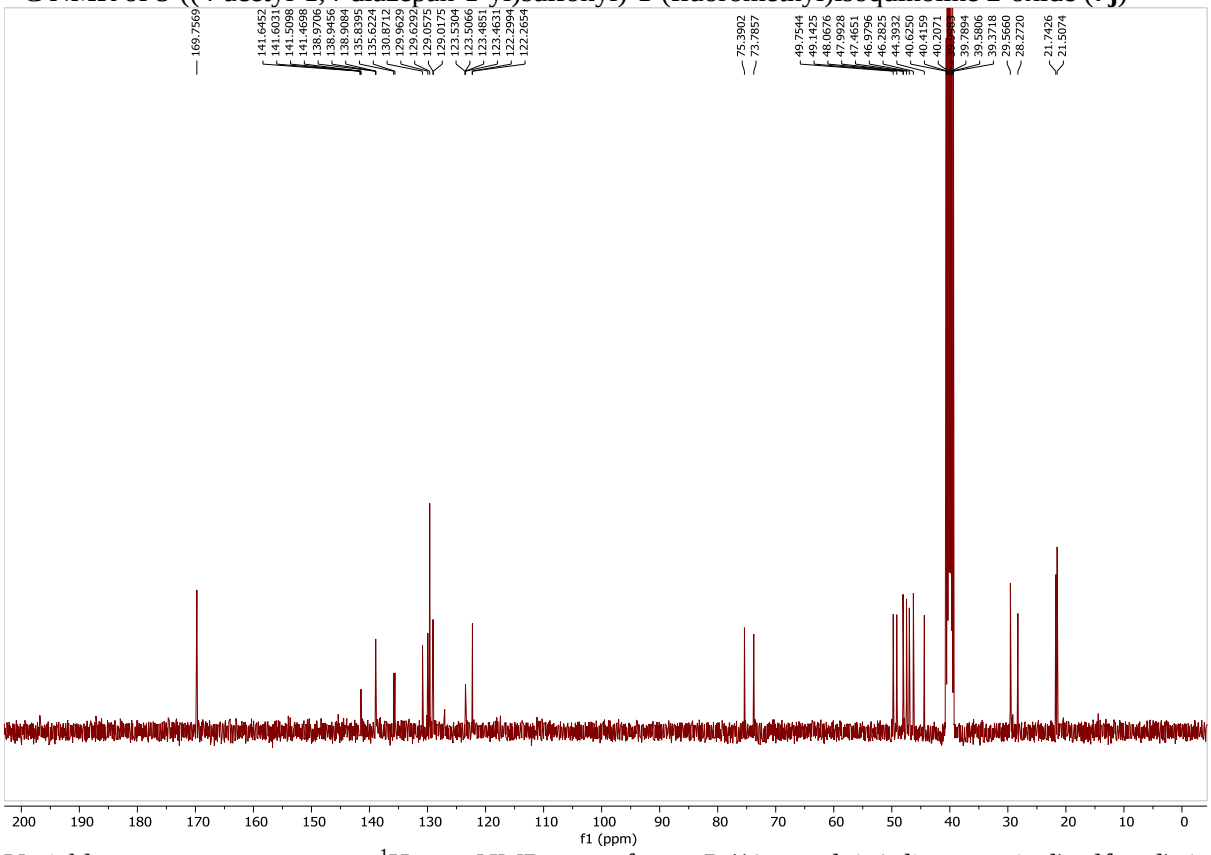
^{1}H NMR of 5-((4-acetyl-1,4-diazepan-1-yl)sulfonyl)-1-(fluoromethyl)isoquinoline 2-oxide (**7j**)



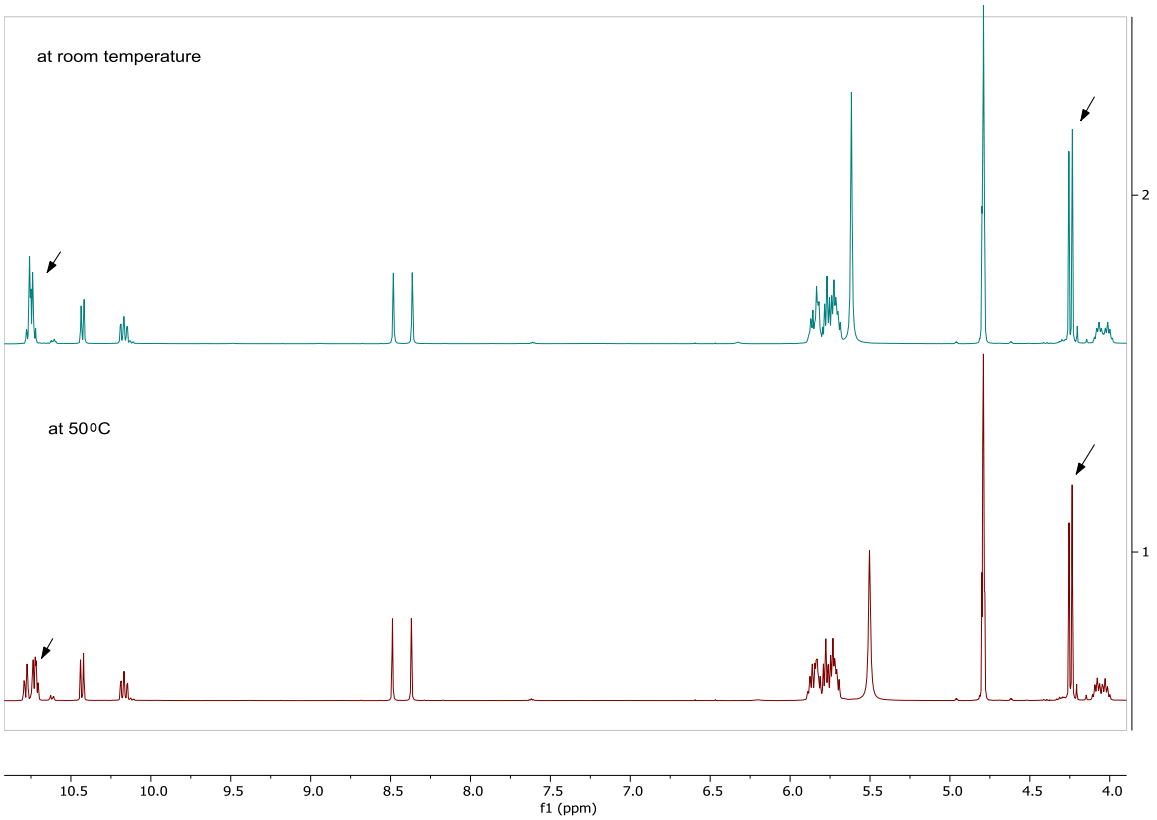
^{19}F NMR of 5-((4-acetyl-1,4-diazepan-1-yl)sulfonyl)-1-(fluoromethyl)isoquinoline 2-oxide (**7j**)



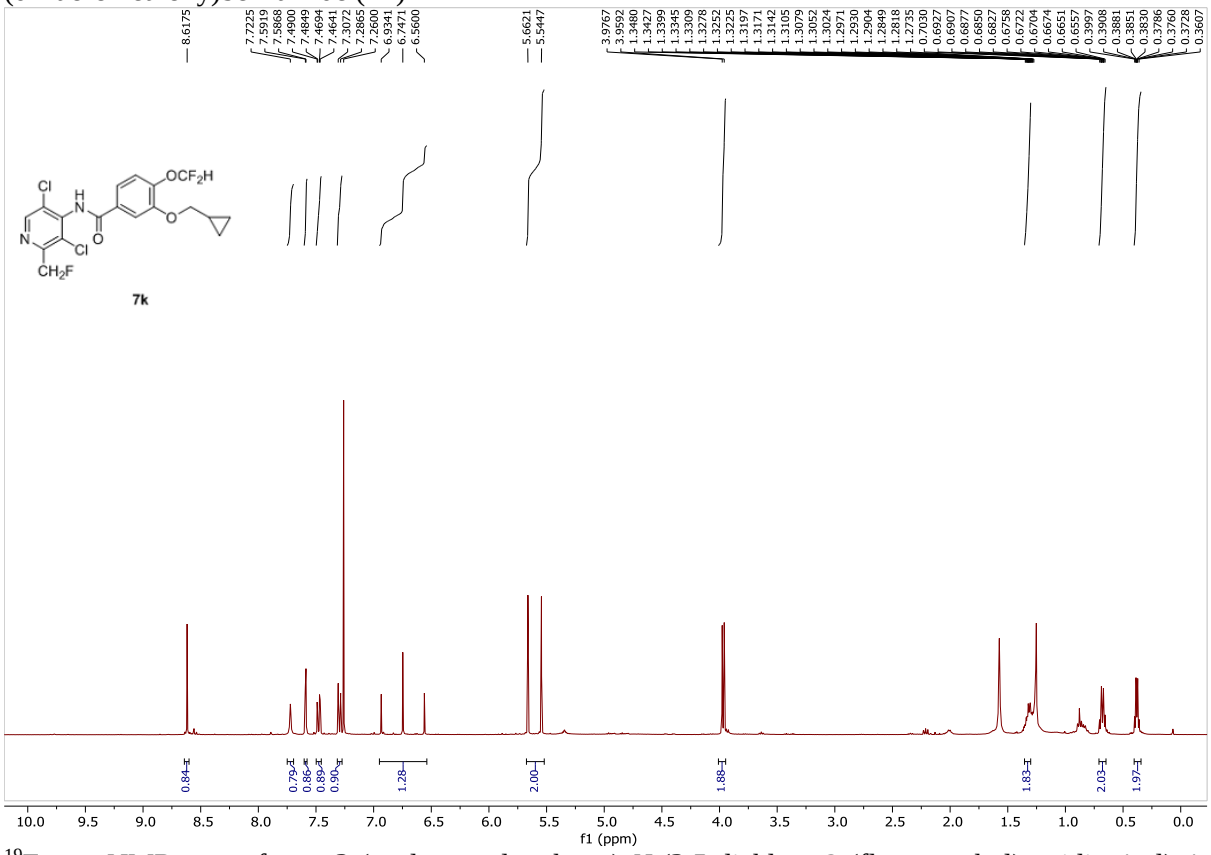
^{13}C NMR of 5-((4-acetyl-1,4-diazepan-1-yl)sulfonyl)-1-(fluoromethyl)isoquinoline 2-oxide (**7j**)



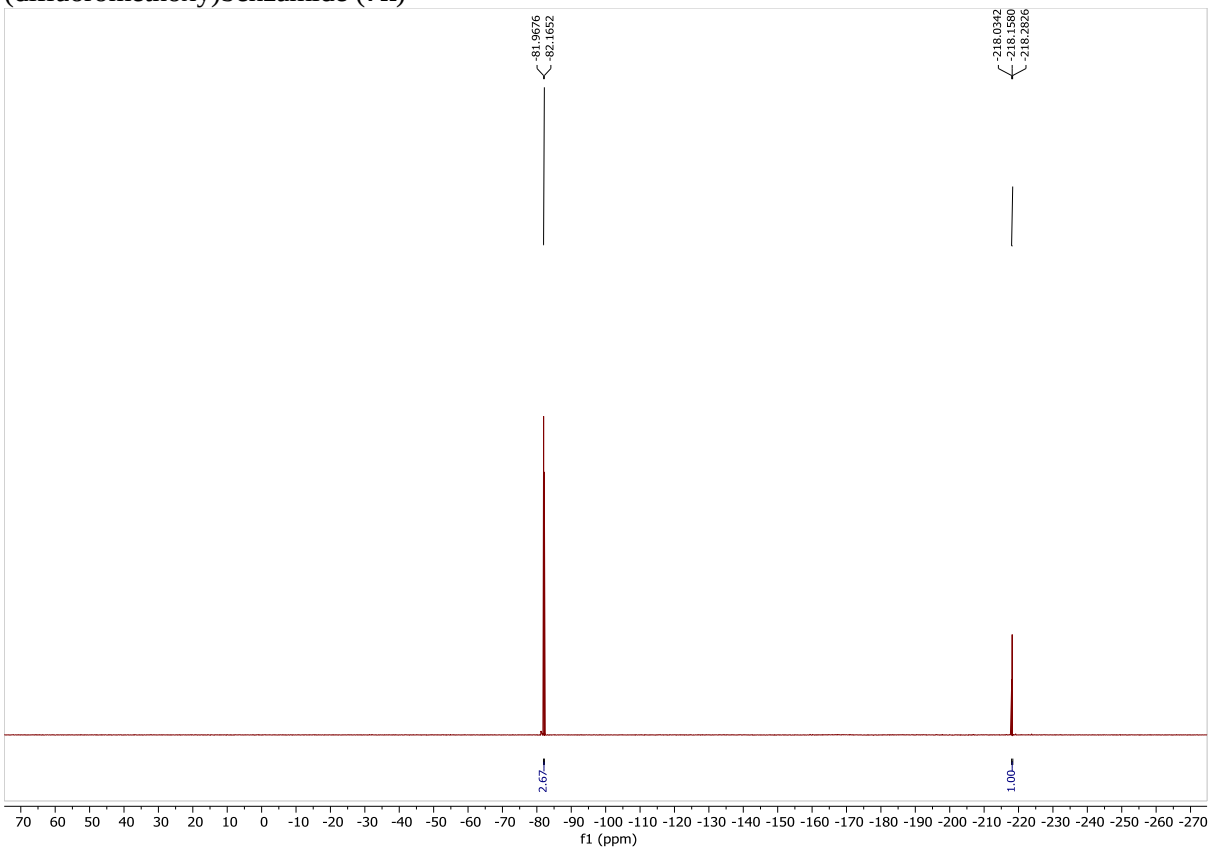
Variable temperature ^{1}H NMR of 5-((4-acetyl-1,4-diazepan-1-yl)sulfonyl)-1-(fluoromethyl)isoquinoline 2-oxide (**7j**)



^{1}H NMR of 3-(cyclopropylmethoxy)-*N*-(3,5-dichloro-2-(fluoromethyl)pyridin-4-yl)-4-(difluoromethoxy)benzamide (**7k**)



^{19}F NMR of 3-(cyclopropylmethoxy)-*N*-(3,5-dichloro-2-(fluoromethyl)pyridin-4-yl)-4-(difluoromethoxy)benzamide (**7k**)



^{13}C NMR of 3-(cyclopropylmethoxy)-*N*-(3,5-dichloro-2-(fluoromethyl)pyridin-4-yl)-4-(difluoromethoxy)benzamide (**7k**)