Supporting Information

Electrochemically Driven Direct C-H Difluoroethylation of (Hetero)arenes under Metal/Catalyst-Free Conditions

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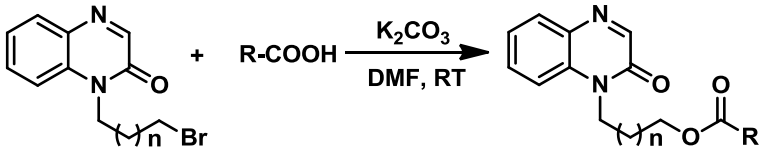
1. General Information

^{1}H, ^{19}F and ^{13}C NMR spectra were recorded on a Bruker advance III 500 or 400 spectrometer in $CDCl_3$ with TMS as internal standard. High-resolution mass spectral analysis (HRMS(TOF)) data were measured on a Bruker Apex II. All products were identified by ^{1}H, ^{19}F, ^{13}C NMR and HRMS. The starting materials were purchased from Energy, J&K Chemicals or Aldrich and used without further purification. Conversion was monitored by thin-layer chromatography (TLC). Flash column chromatography was performed over silica gel (200-300 mesh).

2. General procedures for the synthesis of starting materials

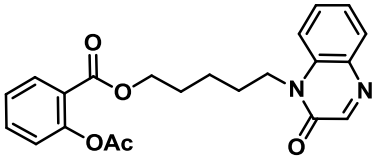
The substrates **1a-1r**[1]**, 1u-1x**[2], and the substrates **4m**[3] the were synthesized according to previously reported procedures.

General Procedure for the Synthesis of the Substrates (4a-4i)



To a 50 mL round-bottom flask was charged with carboxylic acids (1 mmol) in dry DMF (10 mL), was added K_2CO_3 (207 mg, 1.5 mmol). After stirring at room temperature for 30 min, quinoxalinones (1 mmol) was added and the resulting solution was further stirred at room temperature for overnight. The reaction mixture was then poured into 30 mL water and extracted with EtOAc (3 × 20 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 to afford the desired product.

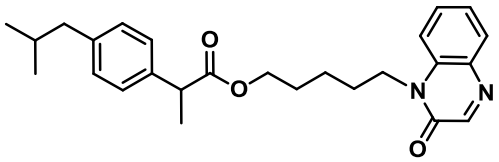
5-(2-oxoquinoxalin-1(2*H*)-yl)pentyl 2-acetoxybenzoate (4a)



The compound **4a** was obtained from 1-(5-bromopentyl)quinoxalin-2(1*H*)-one and Acetylsalicylic acid. Yield: 318 mg, 81%. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.29 (s, 1H), 7.99 (d, J = 7.6 Hz, 1H), 7.89 (d, J = 8.0 Hz, 1H), +q, J = 7.2 Hz, 2H), 7.37 – 7.29 (m, 3H), 7.10 (d,

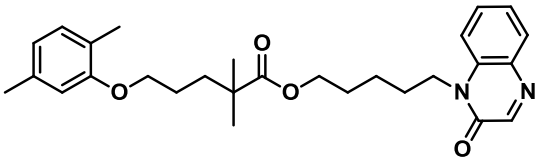
J = 8.0 Hz, 1H), 4.31 – 4.24 (m, 4H), 2.34 (s, 3H), 1.87 – 1.79 (m, 4H), 1.62 – 1.55 (m, 2H).

5-(2-oxoquinoxalin-1(2*H*)-yl)pentyl 2-(4-isobutylphenyl)propanoate (4b)



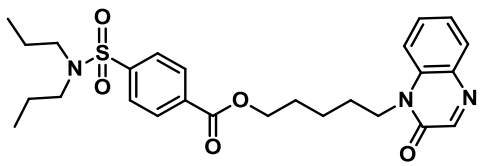
The compound **4b** was obtained from 1-(5-bromopentyl)quinoxalin-2(1*H*)-one and Ibuprofen. Yield: 357 mg, 85%. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.29 (s, 1H), 7.89 (d, J = 7.6 Hz, 1H), 7.58 (t, J = 7.6 Hz, 1H), 7.35 (t, J = 7.2 Hz, 1H), 7.27 (d, J = 11.6 Hz, 1H), 7.19 (d, J = 7.6 Hz, 2H), 7.08 (d, J = 7.2 Hz, 2H), 4.16 (t, J = 7.2 Hz, 2H), 4.07 (t, J = 6.0 Hz, 2H), 3.67 (q, J = 6.8 Hz, 1H), 2.42 (d, J = 6.8 Hz, 2H), 1.85 – 1.78 (m, 1H), 1.73 – 1.66 (m, 4H), 1.47 (d, J = 6.8 Hz, 3H), 1.44 – 1.37 (m, 2H), 0.87 (d, J = 6.0 Hz, 6H).

5-(2-oxoquinoxalin-1(2*H*)-yl)pentyl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate (4c)



The compound **4c** was obtained from 1-(5-bromopentyl)quinoxalin-2(1*H*)-one and Gemfibrozil. Yield: 385 mg, 83%. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.30 (s, 1H), 7.89 (d, J = 8.0 Hz, 1H), 7.57 (t, J = 7.6 Hz, 1H), 7.37 – 7.31 (m, 2H), 6.98 (d, J = 7.2 Hz, 1H), 6.64 (d, J = 7.6 Hz, 1H), 6.60 (s, 1H), 4.25 – 4.22 (m, 2H), 4.08 (t, J = 6.4 Hz, 2H), 3.90 (d, J = 4.8 Hz, 2H), 2.29 (s, 3H), 2.16 (s, 3H), 1.81 – 1.68 (m, 8H), 1.56 – 1.48 (m, 2H), 1.20 (s, 6H).

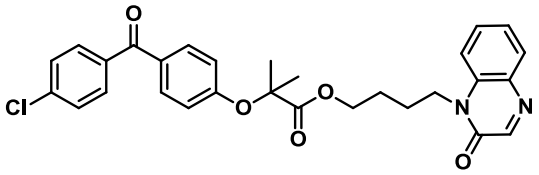
5-(2-oxoquinoxalin-1(2*H*)-yl)pentyl 4-(*N*,*N*-dipropylsulfamoyl)benzoate (4d)



The compound **4d** was obtained from 1-(5-bromopentyl)quinoxalin-2(1*H*)-one and Probenecid. Yield: 389 mg, 78%. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.29 (s, 1H), 8.13 (d, J = 8.4 Hz, 2H), 7.90 – 7.85 (m, 3H), 7.59 (t, J = 8.4 Hz, 1H), 7.36 (t, J = 8.4 Hz, 2H), 4.36 (t, J = 6.4 Hz, 2H), 4.30 – 4.26 (m, 2H), 3.11 – 3.07 (m, 4H), 1.91 – 1.81 (m, 4H), 1.65 – 1.49 (m,

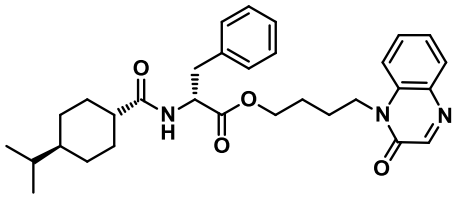
6H), 0.86 (t, J = 7.6 Hz, 6H).

4-(2-oxoquinoxalin-1(2*H*)-yl)butyl 2-(4-(4-chlorobenzoyl)phenoxy)-2-methylpropanoate (4e)



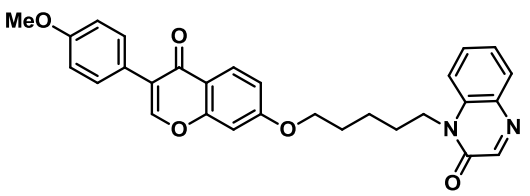
The compound **4e** was obtained from 1-(4-bromobutyl)quinoxalin-2(1*H*)-one and Fenofibric acid. Yield: 451 mg, 87%. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.25 (s, 1H), 7.86 (d, J = 7.6 Hz, 1H), 7.68 – 7.65 (m, 4H), 7.55 (t, J = 8.0 Hz, 1H), 7.43 (d, J = 8.4 Hz, 2H), 7.34 (t, J = 7.6 Hz, 1H), 7.22 (d, J = 8.4 Hz, 1H), 6.81 (d, J = 8.4 Hz, 2H), 4.24 – 4.16 (m, 4H), 1.77 – 1.72 (m, 2H), 1.68 – 1.66 (m, 8H).

(*R*)-4-(2-oxoquinoxalin-1(2*H*)-yl)butyl 2-((1*r*,4*R*)-4-isopropylcyclohexanecarboxamido)-3-phenylpropanoate (4f)



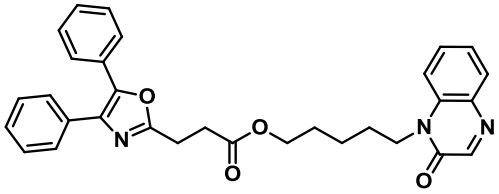
The compound **4f** was obtained from 1-(4-bromobutyl)quinoxalin-2(1*H*)-one and Nateglinide. Yield: 382 mg, 74%. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.30 (s, 1H), 7.90 (d, J = 8.0 Hz, 1H), 7.60 (t, J = 8.0 Hz, 1H), 7.37 (t, J = 7.6 Hz, 1H), 7.31 (d, J = 8.4 Hz, 1H), 7.21 (t, J = 7.2 Hz, 2H), 7.14 (t, J = 7.2 Hz, 1H), 7.06 (d, J = 7.2 Hz, 2H), 5.94 (d, J = 7.6 Hz, 1H), 4.84 (dd, J = 13.6, 6.4 Hz, 1H), 4.24 – 4.09 (m, 4H), 3.08 – 3.06 (m, 2H), 2.04 – 1.96 (m, 1H), 1.87 – 1.73 (m, 8H), 1.41 – 1.32 (m, 3H), 1.02 – 0.92 (m, 3H), 0.83 (d, J = 6.8 Hz, 6H).

1-(5-((3-(4-methoxyphenyl)-4-oxo-4H-chromen-7-yl)oxy)pentyl)quinoxalin-2(1*H*)-one (4g)



The compound **4g** was obtained from 1-(5-bromopentyl)quinoxalin-2(1*H*)-one and Formononetin. Yield: 434 mg, 90%. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.32 (s, 1H), 8.20 (d, J = 8.8 Hz, 1H), 7.91 – 7.89 (m, 2H), 7.60 (t, J = 7.2 Hz, 1H), 7.50 (d, J = 8.4 Hz, 1H), 7.39 – 7.35 (m, 2H), 6.98 – 6.95 (m, 3H), 6.82 (d, J = 2.0 Hz, 1H), 4.30 (t, J = 7.6 Hz, 2H), 4.07 (t, J = 6.4 Hz, 2H), 3.84 (s, 3H), 1.97 – 1.84 (m, 4H), 1.71 – 1.64 (m, 2H).

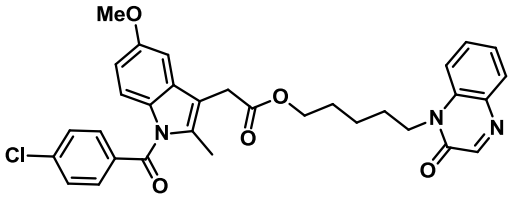
5-(2-oxoquinoxalin-1(2*H*)-yl)pentyl 3-(4,5-diphenyloxazol-2-yl)propanoate (4h)



The compound **4h** was obtained from 1-(5-bromopentyl)quinoxalin-2(1*H*)-one and from Oxaprozin. Yield: 446 mg, 88%. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.30 (s, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.63 – 7.56 (m, 5H), 7.36 – 7.28 (m, 8H), 4.20 – 4.13 (m, 4H), 3.19 (t, J = 7.6 Hz, 2H), 2.92 (t, J = 7.6 Hz, 2H), 1.79 – 1.69 (m, 4H), 1.54 – 1.46 (m, 2H).

5-(2-oxoquinoxalin-1(2*H*)-yl)pentyl

2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1*H*-indol-3-yl)acetate (4i)

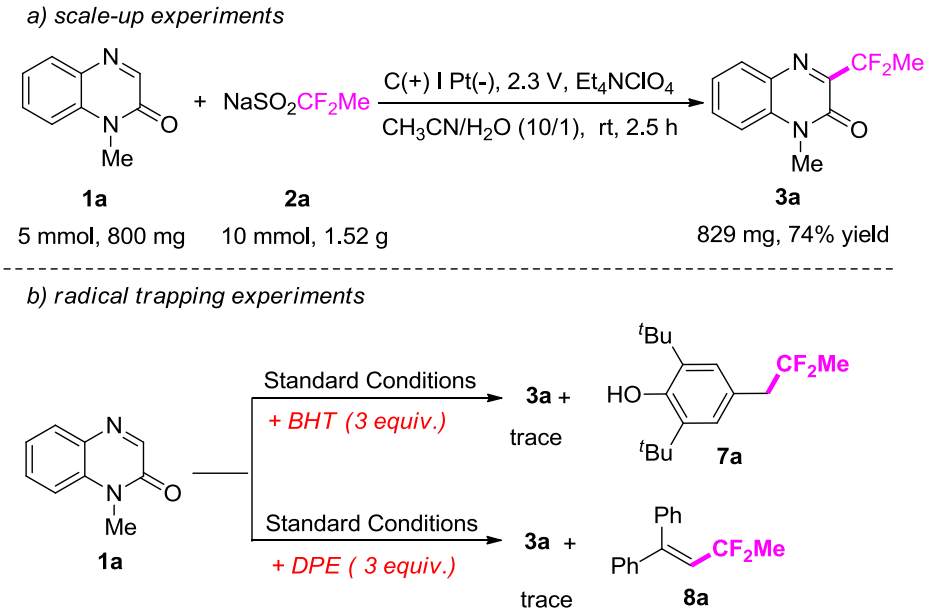


The compound **4i** was obtained from 1-(5-bromopentyl)quinoxalin-2(1*H*)-one and Indomethacin. Yield: 491 mg, 86%. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.29 (s, 1H), 7.88 (d, J = 7.6 Hz, 1H), 7.65 (d, J = 8.4 Hz, 2H), 7.58 (t, J = 7.6 Hz, 1H), 7.46 (d, J = 8.4 Hz, 2H), 7.35 (t, J = 7.6 Hz, 1H), 7.27 (d, J = 8.8 Hz, 1H), 6.97 (d, J = 2.4 Hz, 1H), 6.86 (d, J = 9.2 Hz, 1H), 6.66 (dd, J = 9.2, 2.4 Hz, 1H), 4.18 – 4.10 (m, 4H), 3.82 (s, 3H), 3.66 (s, 2H), 2.38 (s, 3H), 1.77 – 1.66 (m, 4H), 1.48 – 1.41 (m, 2H).

3. Typical procedure for the electrochemical difluoroethylation of (hetero)arenes

To a 15 mL undivided test tube was added (hetero)arenes (1 equiv., 0.2 mmol), fluorinated sulfinates (3 equiv., 0.6 mmol), Et_4ClO_4 (0.3 M), and the mixture of CH_3CN/H_2O (10/1, 6 mL). The tube was installed an carbon plate (10 mm * 10 mm * 0.33 mm) as the anode and platinum plate (10 mm × 10 mm × 0.2 mm) as the cathode. The reaction mixture was electrolyzed at RT under a constant voltage of 2.3 V for 2.5 h. After completion of the reaction, the mixture was extracted with EtOAc (10 mL × 3). The combined organic phases were dried over Na_2SO_4 and condensed under vacuum. The residue was purified by silica gel column chromatography to yield the desired product.

4. Scale-up and radical trapping experiments



Scheme S1. Scale-up experiments and radical trapping experiments

Procedure for the gram-scale reaction: To a 150 mL undivided test tube was added quinoxalin-2(1*H*)-ones **1a** (1 equiv., 0.2 mmol), sodium difluoroethylsulfinate (DFES-Na) (3 equiv., 0.6 mmol), Et_4ClO_4 (0.3 M), and the mixture of CH_3CN/H_2O (10/1, 60 mL). The tube was installed an carbon plate (20 mm * 20 mm * 0.33 mm) as the anode and platinum plate (20 mm × 20 mm × 0.2 mm) as the cathode. The reaction mixture was electrolyzed at RT under a constant voltage of 2.3 V for 24 h. After completion of the reaction, the mixture was extracted with EtOAc (30 mL × 3). The combined organic phases were dried over Na_2SO_4 and condensed under vacuum. The residue was purified by silica gel column chromatography to yield the desired product **3a**.

Procedure for the radical trapping reaction: To a 15 mL undivided test tube was added quinoxalin-2(1*H*)-ones **1a** (1 equiv., 0.2 mmol), DFES-Na (3 equiv., 0.6 mmol), additive BHT (132 mg, 0.6 mmol) or 1,1-diphenylethylene (DPE) (108 mg, 0.6 mmol), Et_4ClO_4 (0.3 M), and the mixture of CH_3CN/H_2O (10/1, 6 mL). The tube was installed an carbon plate (10 mm * 10 mm * 0.33 mm) as the anode and platinum plate (10 mm × 10 mm × 0.2 mm) as the cathode. The reaction mixture was electrolyzed at RT under a constant voltage of 2.3 V for 2.5 h. After completion of the reaction, the mixture was extracted with EtOAc (10 mL × 3). The combined organic phases were dried over Na_2SO_4 and condensed under vacuum. The difluoroethylation of quinoxalin-2(1*H*)-ones was almost prohibited and the adduct products (**7a,8a)** were detected by HRMS analysis (Figure S1-S2)

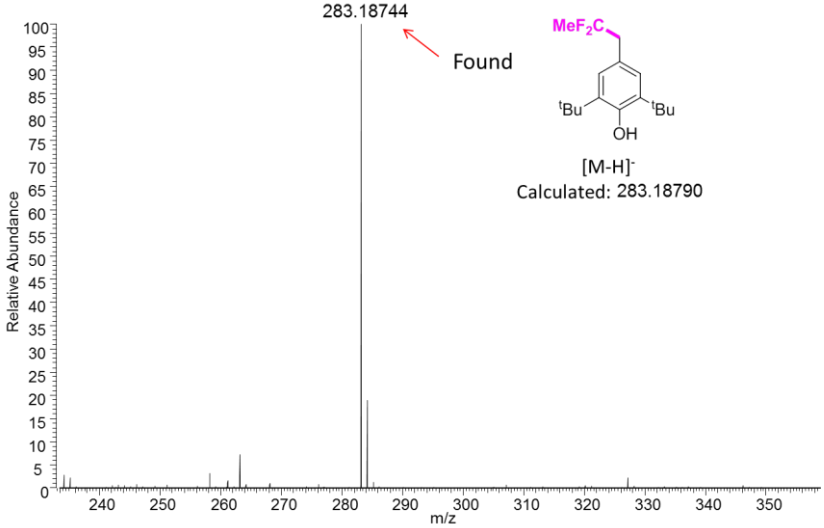


Figure S1. HRMS analysis of adduct product BHT-CF_2Me

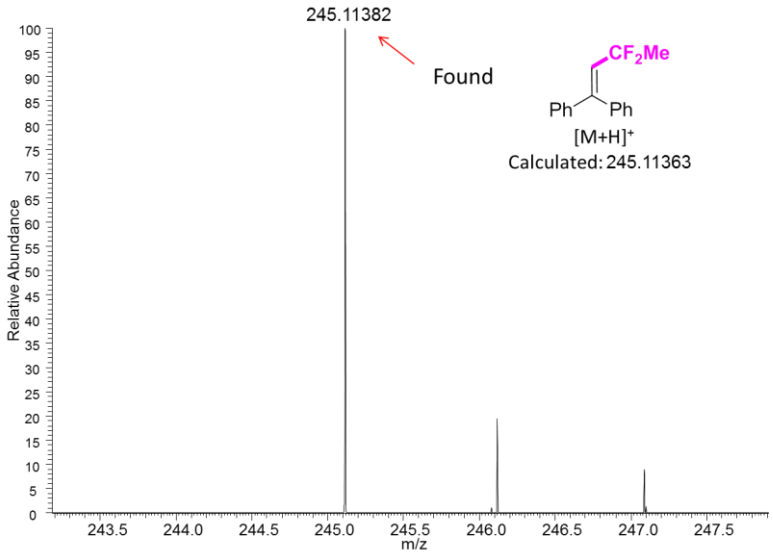


Figure S2. HRMS analysis of adduct product DPE-CF_2Me

5. Cyclic voltammetry experiments

The cyclic voltammograms experiments were performed in a three electrode system with an electrochemical workstation (CHI660E, Shanghai, China) under air at room temperature. A glassy carbon electrode working electrode, a platinum wire counter electrode and an $Ag/AgNO_3$ reference electrode were used. The scan rate was 50 mV/s, from 0 V to 2.5 V. 5 mM analyte and 0.1 M Et_4ClO_4 was dissolved in the mixture of CH_3CN and H_2O.

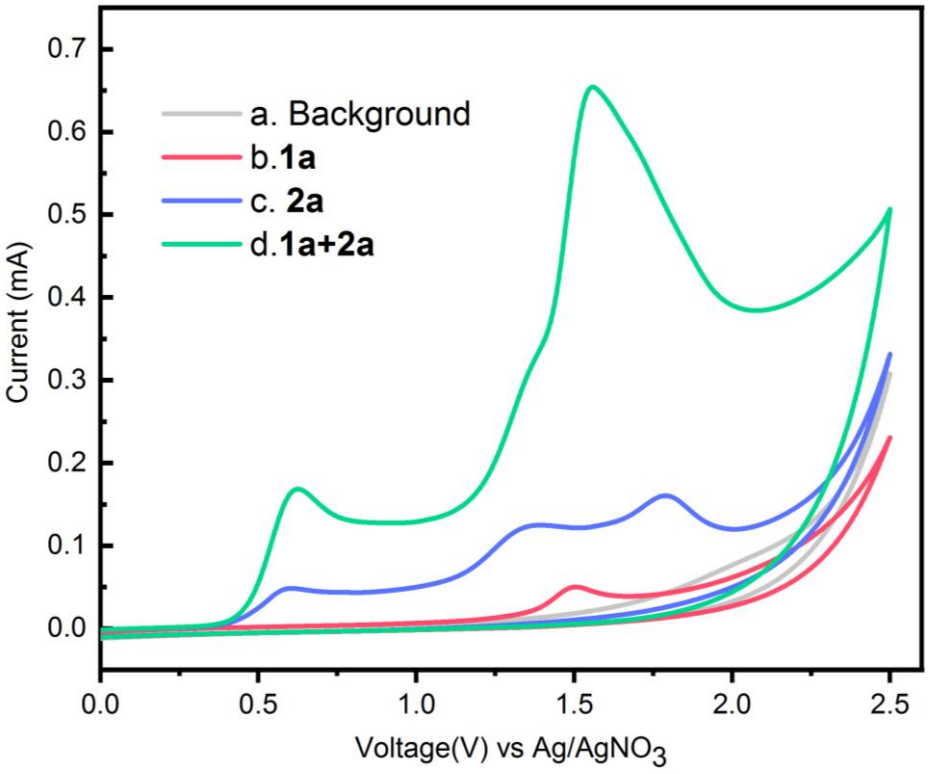


Figure S3. Cyclic voltammograms of substrates: (a) Background (0.1 M Et_4ClO_4 in CH_3CN/H_2O (10/1, V/V)), (b) **1a** (5 mM), (c) **2a** (5 mM), (d) **1a** (5 mM)+**2a** (5 mM).

6. Physical data and references for the following products

6.1 References:

[1] W. Zhang, X.-X. Xiang, J. Chen, C. Yang, Y.-L. Pan, J.-P. Cheng, Q. Meng, X. Li, *Nat. Commun.*, **2020**, *11*, 638.

[2] P. Dai, X. Yu, P. Teng, W.-H. Zhang and C. Deng, *Org. Lett.*, **2018**, *20*, 6901.

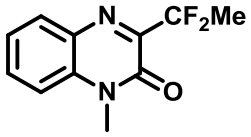
[3] R. A. Garza-Sanchez, A. Tlahuext-Aca, G. Tavakoli and F. Glorius, *ACS Catal.*, **2017**, *7*, 4057.

[4] (a) N. Ramkumar, K. Plantus, M. Ozola, A. Mishnev, V. Nikolajeva, M. Senkovs, M. Ošeka and J. Veliks, *New J. Chem.*, **2023**, *47*, 20642–20652; (b) Z. Liu, Q.-C. Qian, L.-M. Chen, X. Li, *Org. Lett.*, **2024**, *26*, 3247.

6.2 Physical data for the following products:

3a. 3-(1,1-difluoroethyl)-1-methylquinoxalin-2(1*H*)-one

A white solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 5/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, J = 8.0 Hz, 1H), 7.65 (t, J = 7.6 Hz, 1H), 7.41 – 7.34 (m, 2H), 3.72 (s, 3H), 2.13 (t, J = 18.8 Hz, 3H).

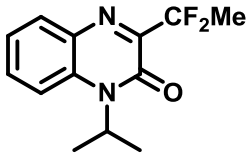
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 152.4, 150.3 (t, J = 27.0 Hz), 134.1, 132.2, 131.21, 131.17, 124.0, 119.5 (t, J = 241.7 Hz), 113.8, 29.0, 22.4 (t, J = 26.1 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ -95.00 (q, J = 18.9 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{11}H_{10}F_2N_2O$ $(M+H)^+$ 225.0834, found 225.0837.

3b. 3-(1,1-difluoroethyl)-1-isopropylquinoxalin-2(1*H*)-one

A yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 5/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, J = 8.4 Hz, 1H), 7.82 (d, J = 8.0 Hz, 1H), 7.71 (t, J = 7.2 Hz, 1H), 7.59 – 7.56 (m, 1H), 5.64 – 5.57 (m, 1H), 2.13 (t, J = 18.8 Hz, 3H), 1.46 (d, J = 6.0 Hz, 6H).

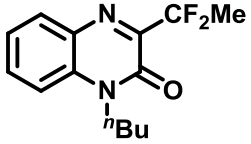
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 154.3, 141.8 (t, J = 29.2 Hz), 141.2, 136.7, 131.1, 129.4, 126.8, 126.7, 120.0 (t, J = 240.7 Hz), 69.9, 22.8 (t, J = 26.7 Hz), 21.7.

^{19}F NMR (471 MHz, $CDCl_3$): δ -92.99 (q, J = 18.7 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{13}H_{14}F_2N_2O$ $(M+H)^+$ 253.1147, found 253.1150

3c. 1-butyl-3-(1,1-difluoroethyl)quinoxalin-2(1*H*)-one

A yellowish solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 5/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, J = 7.6 Hz, 1H), 7.84 (d, J = 7.6 Hz, 1H), 7.74 – 7.70 (m, 1H), 7.61 – 7.57 (m, 1H), 4.55 (t, J = 6.4 Hz, 2H), 2.15 (t, J = 18.8 Hz, 3H), 1.90 – 1.83 (m, 2H), 1.59 – 1.50 (m, 2H), 1.00 (t, J = 7.6 Hz, 3H).

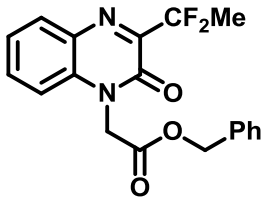
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 154.9, 141.5 (t, J = 29.8 Hz), 141.2, 136.8, 131.2, 129.4, 126.9, 126.7, 120.2 (t, J = 240.3 Hz). 66.7, 30.7, 22.7 (t, J = 26.5 Hz), 19.2, 13.8.

^{19}F NMR (471 MHz, $CDCl_3$): δ -92.89 (q, J = 18.7 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{14}H_{16}F_2N_2O$ $(M+H)^+$ 267.1303 found 267.1305.

3d. benzyl 2-(3-(1,1-difluoroethyl)-2-oxoquinoxalin-1(2*H*)-yl)acetate

A light yellow solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 5/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (dd, J = 8.0, 1.2 Hz, 1H), 7.60 – 7.56 (m, 1H), 7.41 (t, J = 7.2 Hz, 1H), 7.37 – 7.35 (m, 3H), 7.32 – 7.29 (m, 2H), 7.06 (d, J = 8.4 Hz, 1H), 5.22 (s, 2H), 5.10 (s, 2H), 2.13 (t, J = 19.2 Hz, 3H).

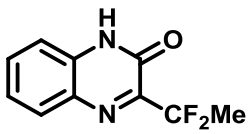
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 166.6, 151.9, 150.2 (t, J = 28.3 Hz), 134.6, 133.2, 132.4, 131.6, 131.2, 128.7, 128.7, 128.4, 124.4, 119.4 (t, J = 241.9 Hz), 113.3, 67.8, 43.3, 22.4 (t, J = 26.0 Hz)..

^{19}F NMR (471 MHz, $CDCl_3$): δ -94.91 (q, J = 18.9 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{19}H_{16}F_2N_2O_3$ $(M+H)^+$ 359.1202, found 359.1206.

3e. 3-(1,1-difluoroethyl)quinoxalin-2(1*H*)-one

A white solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 3/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 12.98 (s, 1H), 7.94 (d, J = 8.0 Hz, 1H), 7.64 (t, J = 7.6 Hz, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.42 (t, J = 7.6 Hz, 1H), 2.18 (t, J = 19.2 Hz, 3H).

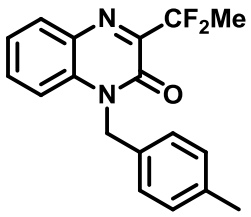
$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 154.6, 150.5 (t, J = 28.3 Hz), 132.5, 132.1, 131.3, 130.1, 124.9, 119.7 (t, J = 241.2 Hz), 116.1, 22.4 (t, J = 26.0 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ -94.36 – -94.50 (m, 2F).

HRMS (ESI, m/z): Calculated for $C_{10}H_8F_2N_2O$ $(M+H)^+$ 211.0677, found 211.0680.

3f. 3-(1,1-difluoroethyl)-1-(4-methylbenzyl)quinoxalin-2(1*H*)-one

A white solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 5/1)



^1H NMR (400 MHz, $CDCl_3$): δ 8.07 (d, J = 8.4 Hz, 1H), 7.88 (d, J = 8.4 Hz, 1H), 7.74 (t, J = 7.6 Hz, 1H), 7.61 (t, J = 7.6 Hz, 1H), 7.44 (d, J = 8.0 Hz, 2H), 7.21 (d, J = 8.0 Hz, 2H), 5.61 (s, 2H), 2.36 (s, 3H), 2.15 (t, J = 18.8 Hz, 3H)..

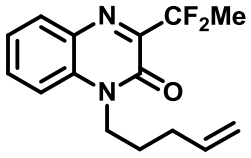
$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 154.4, 141.5 (t, J = 30.1 Hz), 141.0, 137.7, 137.0, 133.2, 131.3, 129.4, 129.2, 127.9, 127.2, 126.8, 120.2 (t, J = 240.2 Hz), 68.2, 22.8 (t, J = 26.5 Hz), 21.2.

^{19}F NMR (471 MHz, $CDCl_3$): δ -92.63 (q, J = 18.8 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{18}H_{16}F_2N_2O$ $(M+H)^+$ 315.1303, found 315.1308.

3g. 3-(1,1-difluoroethyl)-1-(pent-4-en-1-yl)quinoxalin-2(1*H*)-one

A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 5/1)



^1H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, J = 8.4 Hz, 1H), 7.84 (d, J = 8.4 Hz, 1H), 7.72 (t, J = 7.2 Hz, 1H), 7.59 (t, J = 7.2 Hz, 1H), 5.94 – 5.84 (m, 1H), 5.11 – 5.01 (m, 2H), 4.58 (t, J = 6.4 Hz, 2H), 2.30 (dd, J = 14.4, 7.2 Hz, 2H), 2.15 (t, J = 18.8 Hz, 3H), 2.02 – 1.96 (m, 2H).

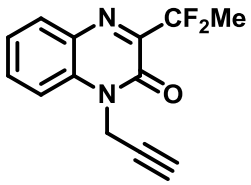
$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 154.8, 141.6 (d, J = 30.0 Hz), 141.1, 137.6, 136.8, 131.2, 129.4, 127.0, 126.7, 120.2 (t, J = 240.2 Hz), 115.3, 66.1, 30.1, 27.8, 22.7 (t, J = 26.5 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ -92.79 (q, J = 18.8 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{15}H_{16}F_2N_2O$ $(M+H)^+$ 279.1303, found 279.1309.

3h. 3-(1,1-difluoroethyl)-1-(prop-2-yn-1-yl)quinoxalin-2(1*H*)-one

A white solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 5/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (d, J = 8.0 Hz, 1H), 7.70 (t, J = 7.6 Hz, 1H), 7.52 (d, J = 8.4 Hz, 1H), 7.43 (t, J = 7.6 Hz, 1H), 5.08 (d, J = 2.0 Hz, 2H), 2.32 (t, J = 2.4 Hz, 1H), 2.13 (t, J = 19.2 Hz, 3H).

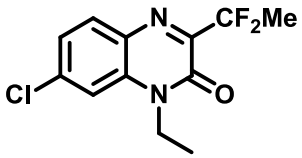
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 151.3, 150.2 (t, J = 27.5 Hz), 132.6, 132.4, 131.4, 131.3, 124.4, 119.5 (t, J = 242.0 Hz), 114.3, 76.3, 73.6, 31.3, 22.4 (t, J = 26.0 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ -94.84 (q, J = 18.9 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{13}H_{10}F_2N_2O$ $(M+H)^+$ 249.0834, found 249.0838.

3i. 7-chloro-3-(1,1-difluoroethyl)-1-ethylquinoxalin-2(1*H*)-one

A yellow solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 5/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (s, 1H), 7.61 (d, J = 8.8 Hz, 1H), 7.31 (d, J = 8.8 Hz, 1H), 4.32 (q, J = 7.2 Hz, 2H), 2.12 (t, J = 19.2 Hz, 3H), 1.39 (t, J = 7.2 Hz, 3H).

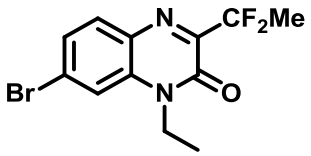
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 151.6 (t, J = 27.7 Hz), 151.5, 132.2, 132.0, 131.9, 130.7, 129.2, 119.4 (t, J = 242.1 Hz), 114.8, 37.7, 22.3 (t, J = 26.0 Hz), 12.3.

^{19}F NMR (471 MHz, $CDCl_3$): δ -95.02 (q, J = 18.9 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{12}H_{11}ClF_2N_2O$ $(M+H)^+$ 273.0601, found 273.0604

3j. 7-bromo-3-(1,1-difluoroethyl)-1-ethylquinoxalin-2(1*H*)-one

A white solid after purification by flash column chromatography (petroleum ether/ethyl acetate =5/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, J = 8.4 Hz, 1H), 7.51 (s, 1H), 7.49 (d, J = 8.8 Hz, 1H), 4.28 (q, J = 7.2 Hz, 2H), 2.11 (t, J = 19.2 Hz, 3H), 1.39 (t, J = 7.2 Hz, 3H).

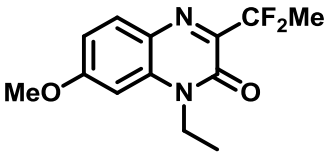
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 151.5, 150.6 (t, J = 27.4 Hz), 134.2, 132.6, 130.3, 127.2, 126.7, 119.5 (t, J = 242.0 Hz), 116.6, 37.6, 22.3 (t, J = 26.1 Hz), 12.3.

^{19}F NMR (471 MHz, $CDCl_3$): δ -94.88 (q, J = 18.9 Hz. 2F).

HRMS (ESI, m/z): Calculated for $C_{12}H_{11}BrF_2N_2O$ $(M+H)^+$ 317.0096, found 317.0099

3k. 3-(1,1-difluoroethyl)-1-ethyl-7-methoxyquinoxalin-2(1H)-one

A gray solid after purification by flash column chromatography (petroleum ether/ethyl acetate =4/1)



^{1}H NMR (500 MHz, $CDCl_3$): δ 7.82 (d, J = 8.5 Hz, 1H), 6.93 (dd, J = 9.0, 2.0 Hz, 1H), 6.73 (d, J = 2.5 Hz, 1H), 4.27 (q, J = 7.0 Hz, 2H), 3.92 (s, 3H), 2.09 (t, J = 19.0 Hz, 3H), 1.36 (t, J = 7.0 Hz, 3H).

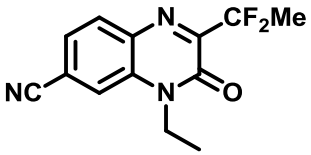
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 162.8, 152.2, 146.70 (t, J = 27.1 Hz), 134.9, 132.8, 126.4, 119.8 (t, J = 239.8 Hz), 111.2, 97.6, 55.8, 37.3, 22.4 (t, J = 26.3 Hz), 12.0.

^{19}F NMR (471 MHz, $CDCl_3$): δ -94.21 (q, J = 18.9 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{13}H_{14}F_2N_2O_2$ $(M+H)^+$ 269.1096, found 269.1099

3l. 2-(1,1-difluoroethyl)-4-ethyl-3-oxo-3,4-dihydroquinoxaline-6-carbonitrile

A yellowish solid after purification by flash column chromatography (petroleum ether/ethyl acetate =4/1)



^{1}H NMR (500 MHz, $CDCl_3$): δ 8.27 (s, 1H), 7.86 (d, J = 9.0 Hz, 1H), 7.46 (d, J = 9.0 Hz, 1H), 4.34 (q, J = 7.0 Hz, 2H), 2.12 (t, J = 19.0 Hz, 3H), 1.41 (t, J = 7.0 Hz, 3H).

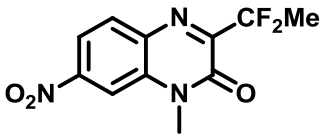
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 152.5 (t, J = 28.0 Hz), 151.4, 136.4, 135.8, 134.4, 131.0, 119.3 (t, J = 241.0 Hz), 117.4, 114.8, 107.6, 37.9, 22.3 (t, J = 25.8 Hz), 12.3.

^{19}F NMR (471 MHz, $CDCl_3$): δ -95.14 (q, J = 19.0 Hz. 2F).

HRMS (ESI, m/z): Calculated for $C_{13}H_{11}F_2N_3O$ $(M+H)^+$ 264.0943, found 264.0947

3m. 3-(1,1-difluoroethyl)-1-methyl-7-nitroquinoxalin-2(1H)-one

A yellow solid after purification by flash column chromatography (petroleum ether/ethyl acetate =4/1)



^{1}H NMR (500 MHz, $CDCl_3$): δ 8.24 (d, J = 1.5 Hz, 1H), 8.21 (dd, J = 8.5, 2.0 Hz, 1H), 8.11 (d, J = 8.5 Hz, 1H), 3.80 (s, 3H), 2.13 (t, J = 19.0 Hz, 3H).

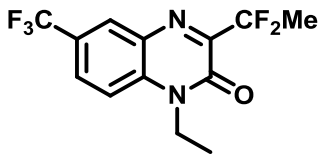
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 153.9 (t, J = 27.6 Hz), 151.7, 149.2, 134.7, 134.3, 132.5, 119.1 (t, J = 241.5 Hz), 118.3, 109.7, 29.5, 22.3 (t, J = 25.8 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ -95.40 (q, J = 18.9 Hz. 2F).

HRMS (ESI, m/z): Calculated for $C_{11}H_9F_2N_3O_3$ $(M+H)^+$ 270.0685, found 270.0688

3n. 3-(1,1-difluoroethyl)-1-ethyl-6-(trifluoromethyl)quinoxalin-2(1H)-one

A white solid after purification by flash column chromatography (petroleum ether/ethyl acetate =4/1)



^{1}H NMR (500 MHz, $CDCl_3$): δ 8.08 (d, J = 8.0 Hz, 1H), 7.61 (d, J = 8.5 Hz, 1H), 7.59 (s, 1H), 4.36 (q, J = 7.0 Hz, 2H), 2.13 (t, J = 19.0 Hz, 3H), 1.42 (t, J = 7.0 Hz, 3H).

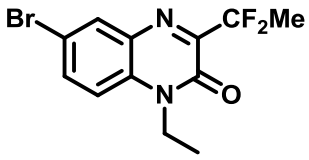
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 152.8 (t, J = 27.4 Hz), 151.5, 133.6 (q, J = 32.9 Hz), 133.3, 133.1, 132.4, 123.4 (q, J = 271.5 Hz), 120.2 (q, J = 3.4 Hz), 119.3 (t, J = 240.9 Hz), 111.0 (q, J = 4.0 Hz), 37.7, 22.3 (t, J = 25.9 Hz), 12.3.

^{19}F NMR (471 MHz, $CDCl_3$): δ -62.67 (s, 3F), -95.17 (q, J = 18.9 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{13}H_{11}F_5N_2O$ $(M+H)^+$ 307.0864, found 307.0869

3o. 6-bromo-3-(1,1-difluoroethyl)-1-ethylquinoxalin-2(1*H*)-one

A yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 5/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (s, 1H), 7.78 (d, J = 8.8 Hz, 1H), 7.70 (d, J = 8.8 Hz, 1H), 4.61 (q, J = 6.8 Hz, 2H), 2.13 (t, J = 18.8 Hz, 3H), 1.50 (t, J = 6.8 Hz, 3H).

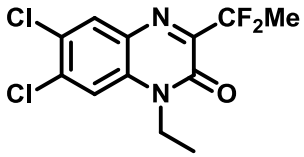
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 155.0, 142.4 (t, J = 30.3 Hz), 140.1, 137.4, 134.5, 131.7, 128.1, 120.1 (t, J = 240.6 Hz), 120.1, 63.1, 22.6 (t, J = 26.4 Hz), 14.2.

^{19}F NMR (471 MHz, $CDCl_3$): δ -93.00 (q, J = 18.8 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{12}H_{11}BrF_2N_2O$ $(M+H)^+$ 317.0096, found 317.0098.

3p. 6,7-dichloro-3-(1,1-difluoroethyl)-1-ethylquinoxalin-2(1*H*)-one

A white solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 5/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (s, 1H), 7.95 (s, 1H), 4.60 (q, J = 7.2 Hz, 2H), 2.12 (t, J = 18.8 Hz, 3H), 1.50 (t, J = 7.2 Hz, 3H).

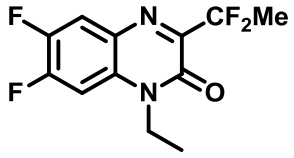
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 155.3, 142.7 (t, J = 30.6 Hz), 140.1, 135.7, 135.5, 131.1, 130.0, 127.5, 120.0 (t, J = 240.5 Hz), 63.4, 22.6 (t, J = 26.3 Hz), 14.2.

^{19}F NMR (471 MHz, $CDCl_3$): δ -93.03 (q, J = 18.8 Hz, 2F).

HRMS (ESI, m/z): Calculated for: $C_{12}H_{10}Cl_2F_2N_2O$ $(M+H)^+$ 307.0211, found 307.0215.

3q. 6,7-dichloro-3-(1,1-difluoroethyl)-1-ethylquinoxalin-2(1*H*)-one

A yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 5/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 – 7.78 (m, 1H), 7.58 (dd, J = 10.4, 8.4 Hz, 1H), 4.59 (q, J = 7.2 Hz, 2H), 2.12 (t, J = 18.8 Hz, 3H), 1.50 (t, J = 7.2 Hz, 3H).

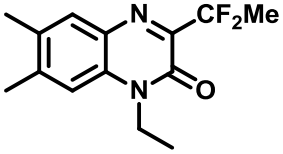
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 155.1 (d, J = 2.1 Hz), 153.1 (dd, J = 256.4, 15.7 Hz), 150.1 (dd, J = 252.0, 15.6 Hz), 141.7 (td, J = 30.5, 3.6 Hz), 138.7 (d, J = 11.9 Hz), 133.4 (d, J = 10.3 Hz), 120.1 (t, J = 240.3 Hz), 115.4 (dd, J = 17.5, 2.1 Hz), 112.8 (d, J = 17.8 Hz), 63.2, 22.6 (t, J = 26.4 Hz), 14.2.

^{19}F NMR (471 MHz, $CDCl_3$): δ -92.95 (q, J = 18.8 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{12}H_{10}F_4N_2O$ $(M+H)^+$ 275.0802, found 275.0807.

3r. 3-(1,1-difluoroethyl)-1-ethyl-6,7-dimethylquinoxalin-2(1*H*)-one

A white solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 5/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (s, 1H), 7.59 (s, 1H), 4.58 (q, J = 7.2 Hz, 2H), 2.44 (s, 3H), 2.42 (s, 3H), 2.13 (t, J = 18.8 Hz, 3H), 1.49 (t, J = 7.2 Hz, 3H).

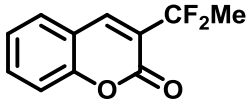
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 154.5, 141.7, 140.2 (t, J = 29.7 Hz), 139.8, 136.9, 135.6, 128.6, 126.1, 120.4 (t, J = 239.9 Hz), 62.5, 22.8 (t, J = 26.7 Hz), 20.4, 19.9, 14.3.

^{19}F NMR (471 MHz, $CDCl_3$): δ -92.48 (q, J = 18.7 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{14}H_{16}F_2N_2O$ $(M+H)^+$ 267.1303, found 267.1306.

3s. 3-(1,1-difluoroethyl)-2*H*-chromen-2-one

A yellowish solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 10/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (s, 1H), 7.62 – 7.57 (m, 2H), 7.37 – 7.31 (m, 2H), 2.07 (t, J = 19.2 Hz, 3H).

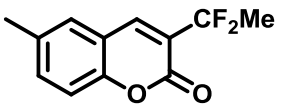
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 157.9, 154.2, 140.3 (t, J = 8.4 Hz), 133.0, 128.9, 124.8, 124.3 (t, J = 27.3 Hz), 119.2(t, J = 240.7 Hz), 117.8, 116.7, 23.4 (t, J = 27.6 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ -90.69 (q, J = 19.0 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{11}H_8F_2O_2$ $(M+H)^+$ 211.0565, found 211.0569.

3t. 3-(1,1-difluoroethyl)-6-methyl-2*H*-chromen-2-one

A yellowish solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 10/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (s, 1H), 7.40 (dd, J = 8.4, 1.6 Hz, 1H), 7.34 (s, 1H), 7.24 (d, J = 8.4 Hz, 1H), 2.42 (s, 3H), 2.06 (t, J = 19.2 Hz, 3H).

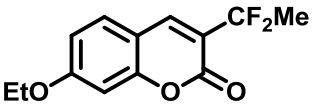
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 158.1, 152.3, 140.3 (t, J = 8.4 Hz), 134.6, 134.1, 128.7, 124.1 (t, J = 27.3 Hz), 119.3 (t, J = 240.6 Hz), 117.5, 116.3, 23.4 (t, J = 27.6 Hz), 20.7.

^{19}F NMR (471 MHz, $CDCl_3$): δ -90.62 (q, J = 18.9 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{12}H_{10}F_2O_2$ $(M+H)^+$ 225.0722, found 225.0725.

3u. 3-(1,1-difluoroethyl)-7-ethoxy-2*H*-chromen-2-one

A white solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 40/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (s, 1H), 7.45 (d, J = 8.8 Hz, 1H), 6.87 (dd, J = 8.8, 2.4 Hz, 1H), 6.81 (d, J = 2.4 Hz, 1H), 4.10 (q, J = 7.2 Hz, 2H), 2.05 (t, J = 19.2 Hz, 3H), 1.46 (t, J = 6.8 Hz, 3H).

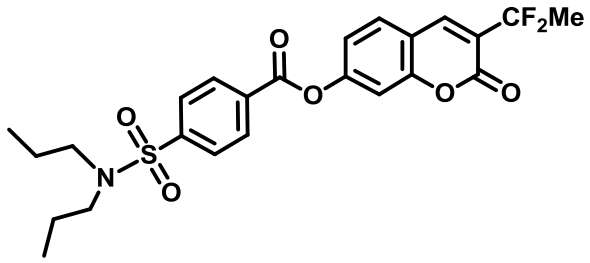
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 163.2, 158.5 (t, J = 4.5 Hz), 156.1, 140.5 (t, J = 8.3 Hz), 129.9, 121.9, 120.3 (t, J = 27.5 Hz), 119.5, 117.1, 113.6, 111.1, 100.8, 64.3, 23.4 (t, J = 27.9 Hz), 14.5.

^{19}F NMR (471 MHz, $CDCl_3$): δ -90.07 (q, J = 18.9 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{13}H_{12}F_2O_3(M+H)^+$ 255.0827, found 255.0831.

3v. 3-(1,1-difluoroethyl)-2-oxo-2*H*-chromen-7-yl 4-(*N*,*N*-dipropylsulfamoyl)benzoate

A yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 4/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 (d, J = 8.0 Hz, 2H), 8.05 (s, 1H), 7.97 (d, J = 8.4 Hz, 2H), 7.66 (d, J = 8.4 Hz, 1H), 7.30 (d, J = 1.6 Hz, 1H), 7.26 – 7.23 (m, 1H), 3.15 – 3.11 (m, 4H), 2.07 (t, J = 18.8 Hz, 3H), 1.59 – 1.54 (m, 4H), 0.88 (t, J = 7.2 Hz, 6H).

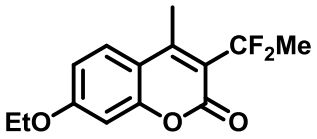
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 163.1, 157.5, 154.8, 153.9, 145.5, 139.7 (t, J = 8.2 Hz), 131.8, 130.9, 130.0, 127.3, 123.9 (t, J = 27.6 Hz), 119.1 (t, J = 241.0 Hz), 118.9, 115.9, 110.3, 49.9, 23.3 (t, J = 27.4 Hz), 21.9, 11.1.

^{19}F NMR (471 MHz, $CDCl_3$): δ -90.68 (q, J = 18.9 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{24}H_{25}F_2NO_6S$ $(M+H)^+$ 494.1443, found 494.1447.

3w. 3-(1,1-difluoroethyl)-7-ethoxy-4-methyl-2*H*-chromen-2-one

A white solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 10/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (d, J = 8.8 Hz, 1H), 6.86 (dd, J = 8.8, 2.4 Hz, 1H), 6.75 (d, J = 2.4 Hz, 1H), 4.09 (q, J = 6.8 Hz, 2H), 2.59 (t, J = 2.9 Hz, 3H), 2.09 (t, J = 19.2 Hz, 3H), 1.45 (t, J = 7.2 Hz, 3H).

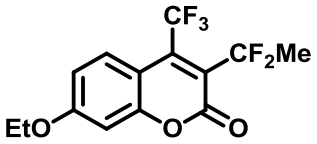
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 162.7, 158.4 (t, J = 4.8 Hz), 154.4, 152.4, 126.6, 122.1 (t, J = 240.1 Hz), 118.0 (t, J = 26.2 Hz), 113.3, 113.2, 100.5, 64.2, 25.2 (t, J = 27.5 Hz), 16.0 (t, J = 7.3 Hz), 14.5.

^{19}F NMR (471 MHz, $CDCl_3$): δ -78.88 (qd, J = 19.5, 1.8 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{14}H_{14}F_2O_3(M+H)^+$ 269.0984, found 269.0989.

3x. 3-(1,1-difluoroethyl)-7-ethoxy-4-(trifluoromethyl)-2*H*-chromen-2-one

A yellowish solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 10/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (dd, J = 9.2, 1.6 Hz, 1H), 6.89 (dd, J = 9.2, 2.4 Hz, 1H), 6.80 (d, J = 2.4 Hz, 1H), 4.11 (q, J = 6.8 Hz, 2H), 2.12 (t, J = 18.4 Hz, 3H), 1.47 (t, J = 6.8 Hz, 3H).

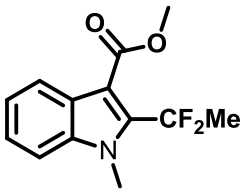
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 163.2, 156.9 (t, J = 4.0 Hz), 154.8, 139.8 (q, J = 33.8 Hz), 127.9 (q, J = 5.1 Hz), 122.8 (td, J = 29.9, 1.8 Hz), 121.6 (q, J = 278.6 Hz), 120.3 (t, J = 241.6 Hz), 113.9, 107.8, 101.1, 64.5, 23.7 (t, J = 26.7 Hz), 14.4.

^{19}F NMR (471 MHz, $CDCl_3$):δ -55.06 (t, J = 19.3 Hz, 3F), -82.26 (dt, J = 37.5, 18.8 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{14}H_{11}F_5O_3$ $(M+H)^+$ 323.0701, found 323.0707.

3y. methyl 2-(1,1-difluoroethyl)-1-methyl-1*H*-indole-3-carboxylate

A yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, J = 8.0 Hz, 1H), 7.41 – 7.33 (m, 2H), 7.29 (d, J = 7.6 Hz, 1H), 3.95 (s, 3H), 3.90 (s, 3H), 2.23 (t, J = 18.4 Hz, 3H).

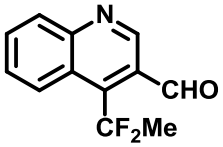
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 164.9, 137.6 (t, J = 29.7 Hz), 136.7, 125.8, 124.0, 122.2, 122.00, 119.96 (t, J = 240.6 Hz), 109.9, 107.1 (t, J = 3.4 Hz), 51.5, 32.4 (t, J = 7.1 Hz), 25.6 (t, J = 27.9 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ -80.69 (q, J = 18.5 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{13}H_{13}F_2NO_2$ $(M+H)^+$254.0988, found 254.0992.

3z. 4-(1,1-difluoroethyl)quinoline-3-carbaldehyde

A yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 10/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 10.61 (t, J = 4.6 Hz, 1H), 9.29 (s, 1H), 8.31 (d, J = 8.4 Hz, 1H), 8.22 (d, J = 8.8 Hz, 1H), 7.88 (t, J = 7.6 Hz, 1H), 7.71 (t, J = 7.6 Hz, 1H), 2.33 (t, J = 18.8 Hz, 3H).

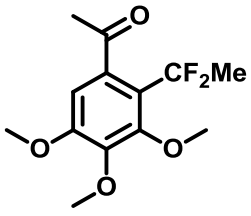
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 190.8 (t, J = 10.3 Hz), 150.4, 148.7, 143.7 (t, J = 26.2 Hz), 131.8, 130.7, 128.5, 126.0, 125.8 (t, J = 7.1 Hz), 122.8 (t, J = 243.9 Hz), 122.7 – 122.6 (m), 27.6 (t, J = 27.3 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ -74.78 (qd, J = 18.1, 4.1 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{12}H_9F_2NO$ $(M+H)^+$ 222.0725, found 222.0728.

3aa. 1-(2-(1,1-difluoroethyl)-3,4,5-trimethoxyphenyl)ethanone

A yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 10/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 6.43 (s, 1H), 3.91 (s, 3H), 3.87 (s, 6H), 2.50 (s, 3H), 2.01 (t, J = 18.8 Hz, 3H).

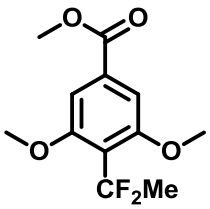
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 204.2, 154.4, 151.9 (t, J = 4.6 Hz), 143.2, 136.8, 122.2 (t, J = 240.5 Hz), 120.7, 103.8, 61.7, 60.8, 56.1, 31.4, 25.9 (t, J = 28.5 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ -78.11 (q, J = 18.7 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{13}H_{16}F_2O_4$ $(M+H)^+$ 275.1089, found 275.1092.

3ab. methyl 4-(1,1-difluoroethyl)-3,5-dimethoxybenzoate

A white solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 (s, 2H), 3.93 (s, 3H), 3.89 (s, 6H), 1.99 (t, J = 19.2 Hz, 3H).

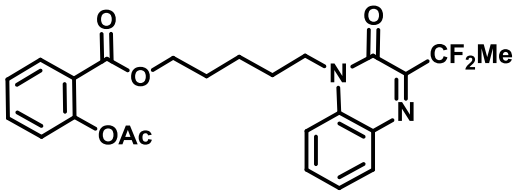
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 166.3, 158.6 (t, J = 2.4 Hz), 132.3, 122.0 (t, J = 241.3 Hz), 118.0 (t, J = 25.0 Hz), 106.1, 56.5, 52.5, 25.7 (t, J = 27.8 Hz)..

^{19}F NMR (471 MHz, $CDCl_3$): δ -81.15 (q, J = 19.0 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{12}H_{14}F_2O_4$ $(M+H)^+$ 261.0933, found 261.0936.

5a. 5-(3-(1,1-difluoroethyl)-2-oxoquinoxalin-1(2*H*)-yl)pentyl 2-acetoxybenzoate

A colourless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 4/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (dd, J = 14.4, 8.0 Hz, 2H), 7.63 (t, J = 8.0 Hz, 1H), 7.55 (t, J = 8.0 Hz, 1H), 7.39 – 7.28 (m, 3H), 7.10 (d, J = 8.0 Hz, 1H), 4.29 (dd, J = 12.8, 6.4 Hz, 4H), 2.33 (s, 3H), 2.12 (t, J = 18.8 Hz, 3H), 1.85 – 1.80 (m, 4H), 1.63 – 1.55 (m, 2H).

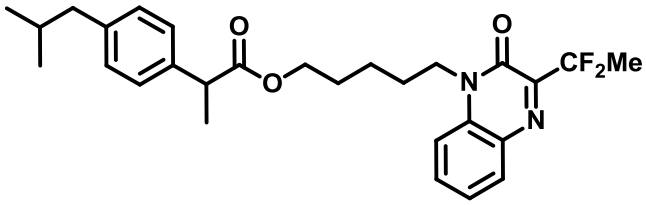
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 169.6, 164.4, 152.1, 150.6, 150.3 (t, J = 27.2 Hz), 133.8, 133.3, 132.2, 131.6, 131.5, 131.4, 126.0, 123.9, 123.8, 123.3, 119.6 (t, J = 241.8 Hz), 113.7, 64.6, 42.1, 28.3, 26.8, 23.4, 22.4 (t, J = 26.2 Hz), 21.0.

^{19}F NMR (471 MHz, $CDCl_3$): δ -94.82 (q, J = 18.9 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{24}H_{24}F_2N_2O_5$ $(M+H)^+$ 459.1726, found 459.1729.

5b. 5-(3-(1,1-difluoroethyl)-2-oxoquinoxalin-1(2*H*)-yl)pentyl 2-(4-isobutylphenyl)propanoate

A yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 4/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, J = 8.0 Hz, 1H), 7.64 (t, J = 7.6 Hz, 1H), 7.39 (t, J = 8.0 Hz, 1H), 7.29 (d, J = 8.4 Hz, 1H), 7.19 (d, J = 8.0 Hz, 2H), 7.08 (d, J = 7.6 Hz, 2H), 4.21 – 4.17 (m, 2H), 4.08 (t, J = 6.4 Hz, 2H), 3.68 (q, J = 7.2 Hz, 1H), 2.42 (d, J = 7.2 Hz, 2H), 2.13 (t, J = 18.8 Hz, 3H), 1.85 – 1.64 (m, 6H), 1.48 (d, J = 7.2 Hz, 3H), 1.45 – 1.38 (m, 2H), 0.87 (d, J = 6.8 Hz, 6H).

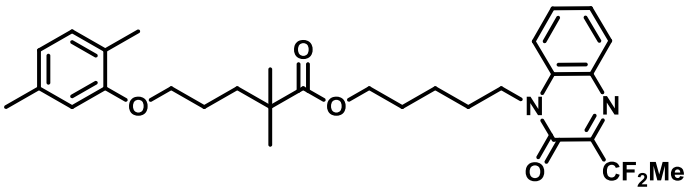
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 174.8, 152.0, 150.3 (t, J = 27.3 Hz), 140.5, 137.8, 133.3, 132.2, 131.5, 131.4, 129.2, 127.1, 123.9, 119.6 (t, J = 241.8 Hz), 113.6, 64.1, 45.1, 44.9, 42.1, 30.1, 28.1, 26.7, 23.2, 22.4 (t, J = 26.1 Hz), 22.3, 18.4.

^{19}F NMR (471 MHz, $CDCl_3$): δ -94.83 (q, J = 18.9 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{28}H_{34}F_2N_2O_3$ $(M+H)^+$ 485.2610, found 485.2615.

5c. 5-(3-(1,1-difluoroethyl)-2-oxoquinoxalin-1(2*H*)-yl)pentyl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate

A yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 4/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, J = 8.0 Hz, 1H), 7.63 (t, J = 8.0 Hz, 1H), 7.38 (t, J = 7.6 Hz, 1H), 7.32 (d, J = 8.4 Hz, 1H), 6.98 (d, J = 7.6 Hz, 1H), 6.63 (d, J = 7.6 Hz, 1H), 6.60 (s, 1H), 4.28 – 4.24 (m, 2H), 4.08 (t, J = 6.8 Hz, 2H), 3.91 (d, J = 5.2 Hz, 2H), 2.29 (s, 3H), 2.16 (s, 3H), 2.13 (t, J = 18.8 Hz, 3H), 1.85 – 1.69 (m, 8H), 1.57 – 1.49 (m, 2H), 1.20 (s, 6H).

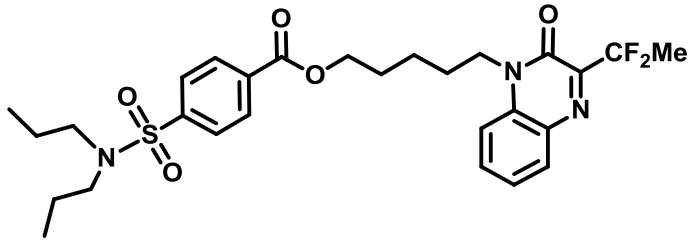
$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 177.8, 156.9, 152.1, 150.3 (t, J = 27.0 Hz), 136.4, 133.4, 132.2, 131.6, 131.5, 130.3, 123.9, 123.5, 120.7, 118.4 (t, J = 241.8 Hz), 113.6, 112.0, 67.9, 63.9, 42.12, 42.08, 37.0, 28.3, 26.8, 25.2, 25.1, 23.41, 22.4 (t, J = 26.2 Hz), 21.4, 15.7.

^{19}F NMR (471 MHz, $CDCl_3$): δ -94.85 (q, J = 18.9 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{30}H_{38}F_2N_2O_4$ $(M+H)^+$ 529.2872, found 529.2878.

5d. 5-(3-(1,1-difluoroethyl)-2-oxoquinoxalin-1(2*H*)-yl)pentyl 4-(*N*,*N*-dipropylsulfamoyl)benzoate

A yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 3/1)



^1H NMR (400 MHz, $CDCl_3$): δ 8.13 (d, J = 8.4 Hz, 2H), 7.96 (dd, J = 8.0, 1.2 Hz, 1H), 7.86 (d, J = 8.8 Hz, 2H), 7.66 – 7.62 (m, 1H), 7.41 – 7.34 (m, 2H), 4.37 (t, J = 6.4 Hz, 2H), 4.32 – 4.28 (m, 2H), 3.11 – 3.07 (m, 4H), 2.12 (t, J = 18.8 Hz, 3H), 1.91 – 1.82 (m, 4H), 1.66 – 1.49 (m, 6H), 0.86 (t, J = 7.2 Hz, 6H).

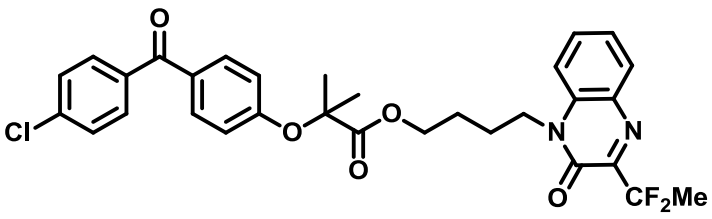
$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 165.2, 152.1, 150.2 (t, J = 27.4 Hz), 144.2, 133.5, 133.3, 132.2, 131.6, 131.5, 130.2, 127.0, 124.0, 119.6 (t, J = 241.7 Hz), 113.6, 65.2, 49.9, 42.0, 28.3, 26.9, 23.5, 22.4 (t, J = 26.1 Hz), 21.9, 11.1.

^{19}F NMR (471 MHz, $CDCl_3$): δ -94.82 (q, J = 18.9 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{28}H_{35}F_2N_3O_5S$ $(M+H)^+$ 564.2338, found 564.2341.

5e. 4-(3-(1,1-difluoroethyl)-2-oxoquinoxalin-1(2*H*)-yl)butyl 2-(4-(4-chlorobenzoyl)phenoxy)-2-methylpropanoate

A yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 3/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, J = 7.6 Hz, 1H), 7.66 (dd, J = 8.8, 2.8 Hz, 4H), 7.61 (t, J = 8.4 Hz, 1H), 7.43 (d, J = 8.4 Hz, 2H), 7.37 (t, J = 7.6 Hz, 1H), 7.22 (d, J = 8.4 Hz, 1H), 6.82 (d, J = 8.8 Hz, 2H), 4.25 – 4.19 (m, 4H), 2.11 (t, J = 18.8 Hz, 3H), 1.78 – 1.67 (m, 4H), 1.67 (s, 6H).

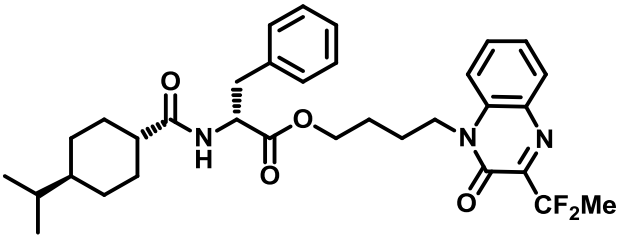
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 194.0, 173.6, 159.5, 152.0, 150.2 (t, J = 27.4 Hz), 138.4, 136.1, 133.1, 132.2, 131.9, 131.5, 131.4, 131.1, 130.2, 128.5, 124.0, 119.6 (t, J = 241.7 Hz), 117.0, 113.5, 79.3, 64.9, 41.6, 25.8, 25.4, 23.7, 22.3 (t, J = 26.1 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ -94.83 (q, J = 19.0 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{31}H_{29}ClF_2N_2O_5$ $(M+H)^+$ 583.1806, found 583.1809.

5f. (*R*)-4-(3-(1,1-difluoroethyl)-2-oxoquinoxalin-1(2*H*)-yl)butyl 2-((*1r,4R*)-4-isopropylcyclohexanecarboxamido)-3-phenylpropanoate

A light yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 2/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (dd, J = 8.0, 0.8 Hz, 1H), 7.66 (t, J = 7.2 Hz, 1H), 7.40 (t, J = 7.6 Hz, 1H), 7.32 (d, J = 8.4 Hz, 1H), 7.21 (t, J = 7.2 Hz, 2H), 7.14 (d, J = 7.2 Hz, 1H), 7.07 (d, J = 7.2 Hz, 2H), 6.00 (d, J = 8.0 Hz, 1H), 4.84 (dd, J = 14.0, 6.4 Hz, 1H), 4.29 – 4.18 (m, 3H), 4.13 – 4.09 (m, 1H), 3.08 – 3.06 (m, 2H), 2.13 (t, J = 19.2 Hz, 3H), 2.00 (tt, J = 12.0, 3.2 Hz, 1H), 1.86 – 1.81 (m, 2H), 1.75 – 1.36 (m, 6H), 1.41 – 1.31 (m, 3H), 1.03 – 0.91 (m, 3H), 0.83 (d, J = 6.8 Hz, 6H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 175.8, 171.7, 152.0, 150.2 (t, J = 27.4 Hz), 135.8, 133.2, 132.3, 131.5, 131.4, 129.2, 128.4, 126.9, 124.0, 119.6 (t, J = 241.7 Hz), 113.6, 64.5, 52.8, 45.3, 43.1, 41.7, 38.0, 32.7, 29.6, 29.4, 28.8, 28.8, 25.7, 23.7, 22.4 (t, J = 26.1 Hz), 19.6.

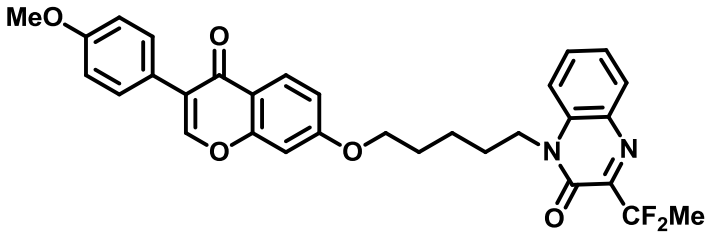
^{19}F NMR (471 MHz, $CDCl_3$): δ -94.78 (q, J = 19.0 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{33}H_{41}F_2N_3O_4$ $(M+H)^+$ 582.3138, found 582.3144.

5g.

3-(1,1-difluoroethyl)-1-(5-((3-(4-methoxyphenyl)-4-oxo-4*H*-chromen-7-yl)oxy)pentyl)quinoxalin-2(1H)-one

A yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 40/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19 (d, J = 8.8 Hz, 1H), 7.97 (dd, J = 8.0, 1.2 Hz, 1H), 7.92 (s, 1H), 7.67 – 7.63 (m, 1H), 7.49 (d, J = 8.8 Hz, 2H), 7.42 – 7.36 (m, 2H), 6.96 (dd, J = 8.8, 2.4 Hz, 3H), 6.85 (d, J = 2.4 Hz, 1H), 4.34 – 4.30 (m, 2H), 4.11 (t, J = 6.4 Hz, 2H), 3.83 (s, 3H), 2.14 (t, J = 18.8 Hz, 3H), 1.98 – 1.85 (m, 4H), 1.72 – 1.65 (m, 2H).

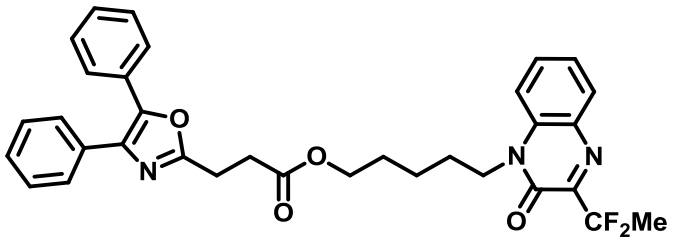
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 175.9, 163.3, 159.5, 157.9, 152.14, 154.10, 133.3, 132.2, 131.6, 131.5, 130.1, 127.7, 124.8, 124.2, 124.0, 119.6 (t, J = 241.8 Hz), 118.3, 114.8, 113.9, 113.6, 100.6, 68.2, 55.3, 42.1, 28.5, 26.9, 23.5, 22.4 (t, J = 26.1 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ -94.80 (q, J = 18.9 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{31}H_{28}F_2N_2O_5$ $(M+H)^+$ 547.2039, found 547.2044.

5h. 5-(3-(1,1-difluoroethyl)-2-oxoquinoxalin-1(2*H*)-yl)pentyl 3-(4,5-diphenyloxazol-2-yl)propanoate

A yellowish liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 3/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, J = 8.0 Hz, 1H), 7.65 – 7.61 (m, 3H), 7.57 – 7.55 (m, 2H), 7.40 – 7.28 (m, 8H), 4.22 – 4.14 (m, 4H), 3.19 (t, J = 8.0 Hz, 2H), 2.92 (t, J = 7.6 Hz, 2H), 2.13 (t, J = 19.2 Hz, 3H), 1.80 – 1.69 (m, 4H), 1.55 – 1.47 (m, 2H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 172.0, 161.7, 152.0, 150.3 (t, J = 27.2 Hz), 145.4, 135.0, 133.3, 132.4, 132.2, 131.5, 131.4, 128.9, 128.6, 128.5, 128.4, 128.0, 127.8, 126.4,

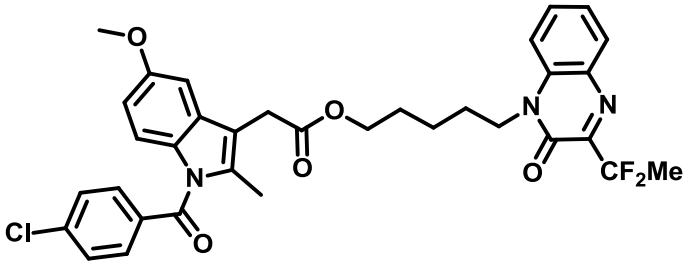
123.9, 119.6 (t, J = 241.8 Hz), 113.7, 64.3, 42.1, 31.1, 28.2, 26.7, 23.5, 23.3, 22.4 (t, J = 26.1 Hz).

^{19}F NMR (471 MHz, $CDCl_3$): δ -94.84 (q, J = 18.9 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{33}H_{31}F_2N_3O_4$ $(M+H)^+$ 572.2355, found 572.2359.

5i 5-(3-(1,1-difluoroethyl)-2-oxoquinoxalin-1(2*H*)-yl)pentyl 2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1*H*-indol-3-yl)acetate

A yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 2/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, J = 8.0 Hz, 1H), 7.67 – 7.61 (m, 3H), 7.46 (d, J = 8.4 Hz, 2H), 7.39 (t, J = 8.0 Hz, 1H), 7.27 (d, J = 10.0 Hz, 1H), 6.97 (d, J = 1.6 Hz, 1H), 6.87 (d, J = 8.8 Hz, 1H), 6.66 (dd, J = 8.8, 2.0 Hz, 1H), 4.20 – 4.16 (m, 2H), 4.12 (t, J = 6.4 Hz, 2H), 3.82 (s, 3H), 3.66 (s, 2H), 2.38 (s, 3H), 2.13 (t, J = 18.8 Hz, 3H), 1.78 – 1.67 (m, 4H), 1.49 – 1.41 (m, 2H).

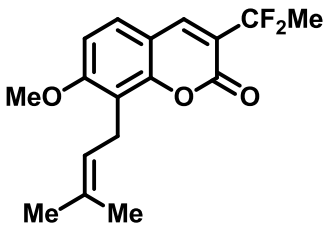
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 170.9, 168.3, 156.0, 152.1, 150.3 (t, J = 27.0 Hz), 139.3, 135.9, 133.8, 133.3, 132.2, 131.5, 131.4, 131.1, 130.8, 130.6, 129.1, 123.9, 119.6 (t, J = 241.8 Hz), 114.9, 113.6, 112.6, 111.5, 101.4, 64.6, 55.7, 42.0, 30.4, 28.2, 26.7, 23.3, 22.4 (t, J = 26.2 Hz), 13.3.

^{19}F NMR (471 MHz, $CDCl_3$): δ -94.82 (q, J = 18.9 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{34}H_{32}ClF_2N_3O_5$ $(M+H)^+$ 636.2071, found 636.2077.

5j. 3-(1,1-difluoroethyl)-7-methoxy-8-(3-methylbut-2-en-1-yl)-2*H*-chromen-2-one

A orange liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 10/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (s, 1H), 7.46 (d, J = 8.8 Hz, 1H), 6.89 (d, J = 8.4 Hz, 1H), 4.00 (s, 2H), 3.88 (s, 3H), 2.86 – 2.79 (m, 1H), 2.02 (t, J = 18.8 Hz, 3H), 1.22 (s, 3H), 1.20 (s, 3H).

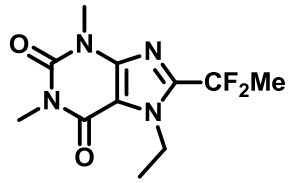
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 210.6, 204.8, 161.3, 158.0 (t, J = 4.5 Hz), 153.4, 140.7 (t, J = 8.2 Hz), 128.8, 120.6 (t, J = 27.4 Hz), 119.5 (t, J = 240.3 Hz), 111.8, 111.7, 107.7, 56.2, 40.9, 34.6, 23.4 (t, J = 27.8 Hz), 18.4.

^{19}F NMR (471 MHz, $CDCl_3$): δ -90.13 (q, J = 18.9 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{17}H_{18}F_2O_3$ $(M+H)^+$ 309.1297, found 309.1300.

5k. 8-(1,1-difluoroethyl)-7-ethyl-1,3-dimethyl-1*H*-purine-2,6(3*H*,7*H*)-dione

A yellow solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 40/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 4.56 (q, J = 7.2 Hz, 2H), 3.56 (s, 3H), 3.42 (s, 3H), 2.16 (t, J = 19.2 Hz, 3H), 1.48 (t, J = 7.1 Hz, 3H).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 155.1, 151.6, 146.7, 144.7 (t, J = 32.0 Hz), 118.4 (t, J = 234.8 Hz), 108.6, 42.4, 29.7, 28.1, 23.2 (t, J = 25.1 Hz), 16.6.

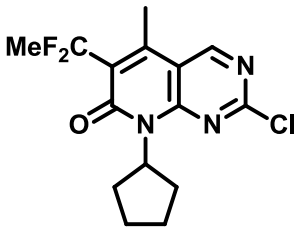
^{19}F NMR (471 MHz, $CDCl_3$): δ -86.02 (q, J = 19.2 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{11}H_{14}F_2N_4O_2$ $(M+H)^+$ 273.1158, found 273.1161.

5l.

2-chloro-8-cyclopentyl-6-(1,1-difluoroethyl)-5-methylpyrido[2,3-d]pyrimidin-7(8*H*)-one

A white solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 10/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.44 (s, 1H), 5.47 – 5.39 (m, 1H), 3.27 (dd, J = 22.8, 5.6 Hz, 1H), 2.89 (s, 1H), 2.11 – 1.98 (m, 2H), 1.87 – 1.84 (m, 2H), 1.80 (s, 3H), 1.73 (t, J = 19.6 Hz, 3H), 1.71 – 1.62 (m, 2H).

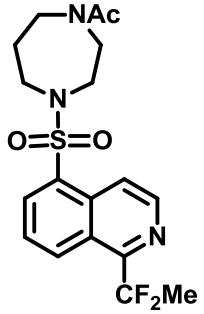
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 166.5, 166.4, 159.7, 158.9, 155.8, 153.8, 122.5 (t, J = 245.8 Hz), 121.8, 68.7, 60.5 (t, J = 23.2 Hz), 54.5, 28.4 (d, J = 46.6 Hz), 25.7 (d, J = 11.4 Hz), 24.5 (t, J = 26.4 Hz), 24.5.

^{19}F NMR (471 MHz, $CDCl_3$): δ -84.54 – -85.15 (m, 1F), -93.87 – -94.47 (m, 1F).

HRMS (ESI, m/z): Calculated for $C_{15}H_{16}ClF_2N_3O$ $(M+H)^+$ 328.1023, found 328.1027.

5m. 1-(4-((1-(1,1-difluoroethyl)isoquinolin-5-yl)sulfonyl)-1,4-diazepan-1-yl)ethanone

A yellowish liquid after purification by flash column chromatography (dichloromethane/MeOH = 10/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.84 (d, J = 8.4 Hz, 1H), 8.62 (d, J = 5.6 Hz, 1H), 8.52 (d, J = 5.6 Hz, 1H), 8.34 – 8.31 (m, 1H), 7.73 (t, J = 8.0 Hz, 1H), 3.75 – 3.59 (m, 4H), 3.50 – 3.37 (m, 4H), 2.26 (t, J = 19.6 Hz, 3H), 2.06 (s, 3H), 2.02 – 1.95 (m, 2H).

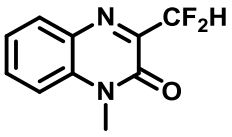
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 170.3, 170.1, 153.92 (t, J = 28.9 Hz), 153.88 (t, J = 31.1 Hz), 142.3, 134.7, 132.9, 132.7, 132.6, 132.2 (d, J = 5.9 Hz), 132.0 (d, J = 6.3 Hz), 126.2, 125.9 (d, J = 1.8 Hz), 122.7 (d, J = 238.5 Hz), 119.63, 119.58, 50.7, 50.0, 49.2, 48.4, 47.9, 47.6, 46.9, 44.4, 29.7, 28.9, 27.6, 23.0 (td, J = 25.9, 2.6 Hz), 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.

^{19}F NMR (471 MHz, $CDCl_3$): δ -81.14 – -81.30 (m, 2F).

HRMS (ESI, m/z): Calculated for $C_{18}H_{21}F_2N_3O_3S$ $(M+H)^+$ 398.1344, found 398.1347.

6ab. 3-(difluoromethyl)-1-methylquinoxalin-2(1*H*)-one

A yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 40/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, J = 8.0 Hz, 1H), 7.69 (t, J = 7.6 Hz, 1H), 7.45 – 7.38 (m, 2H), 6.96 (t, J = 53.6 Hz, 1H), 3.74 (s, 3H).

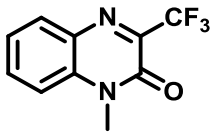
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 153.2, 148.6 (t, J = 22.5 Hz), 134.0, 132.7, 131.9, 131.4, 124.4, 113.9, 110.1 (t, J = 241.6 Hz), 29.0.

^{19}F NMR (471 MHz, $CDCl_3$): δ -124.37 (d, J = 53.7 Hz, 2F).

HRMS (ESI, m/z): Calculated for $C_{10}H_8F_2N_2O$ $(M+H)^+$ 211.0677, found 211.0680.

6ac. 1-methyl-3-(trifluoromethyl)quinoxalin-2(1*H*)-one

A colourless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 40/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (d, J = 8.0 Hz, 1H), 7.74 (t, J = 8.0 Hz, 1H), 7.47 – 7.39 (m, 2H), 3.76 (s, 3H).

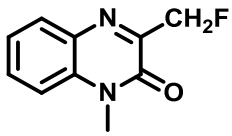
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 151.6, 143.9 (q, J = 33.8 Hz), 134.6, 133.5, 131.8, 130.9, 124.5, 119.9 (q, J = 276.4 Hz), 114.0, 29.2.

^{19}F NMR (471 MHz, $CDCl_3$): δ -70.13 (s, 3F).

HRMS (ESI, m/z): Calculated for $C_{10}H_7F_3NO$ $(M+H)^+$ 229.0583, found 229.0586.

6ad. 3-(fluoromethyl)-1-methylquinoxalin-2(1*H*)-one

A yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 40/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, J = 8.0 Hz, 1H), 7.61 (t, J = 8.0 Hz, 1H), 7.41 – 7.34 (m, 2H), 5.64 (d, J = 46.4 Hz, 2H), 3.71 (s, 3H).

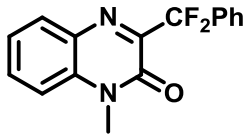
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 153.7, 153.5, 133.2, 132.5, 131.0, 130.6, 124.1, 113.7, 81.0 (d, J = 174.4 Hz), 28.8.

^{19}F NMR (471 MHz, $CDCl_3$): δ -230.30 (t, J = 46.6 Hz, 1F).

HRMS (ESI, m/z): Calculated for $C_{10}H_9FN_2O$ $(M+H)^+$ 193.0772, found 193.0776.

6ae. 3-(difluoro(phenyl)methyl)-1-methylquinoxalin-2(1*H*)-one

A colourless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 40/1)



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (d, J = 8.0 Hz, 1H), 7.75 – 7.73 (m, 2H), 7.64 (t, J = 8.0 Hz, 1H), 7.43 – 7.39 (m, 4H), 7.32 (d, J = 8.4 Hz, 1H), 3.63 (s, 3H).

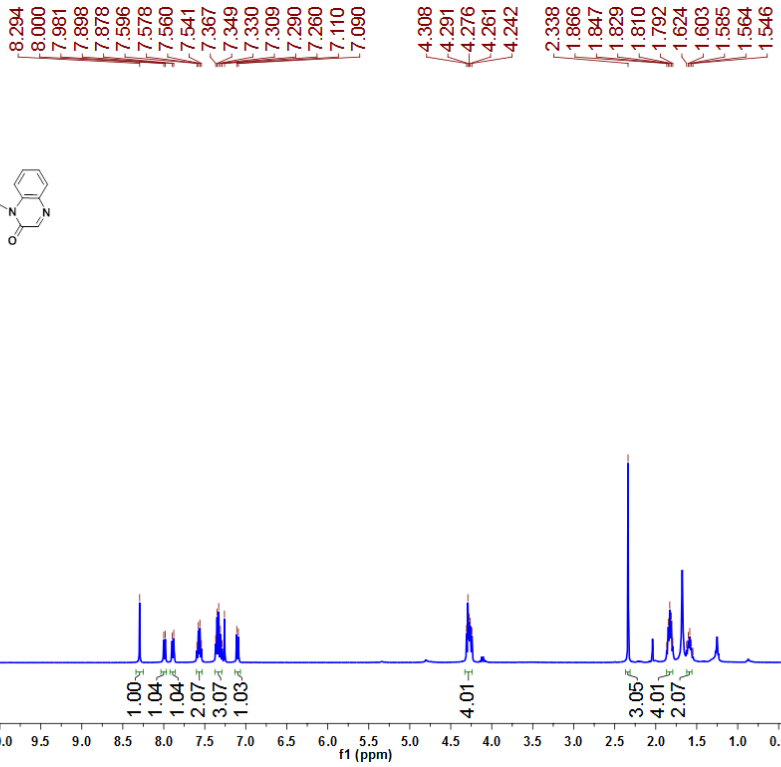
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 152.0, 150.4 (t, J = 28.2 Hz), 134.8 (t, J = 26.4 Hz), 134.1, 132.2, 131.34, 131.30, 130.2, 128.2, 125.9 (t, J = 5.8 Hz), 124.1, 117.3 (t, J = 247.0 Hz), 113.7, 28.9.

^{19}F NMR (471 MHz, $CDCl_3$): δ -99.64 (s, 2F).

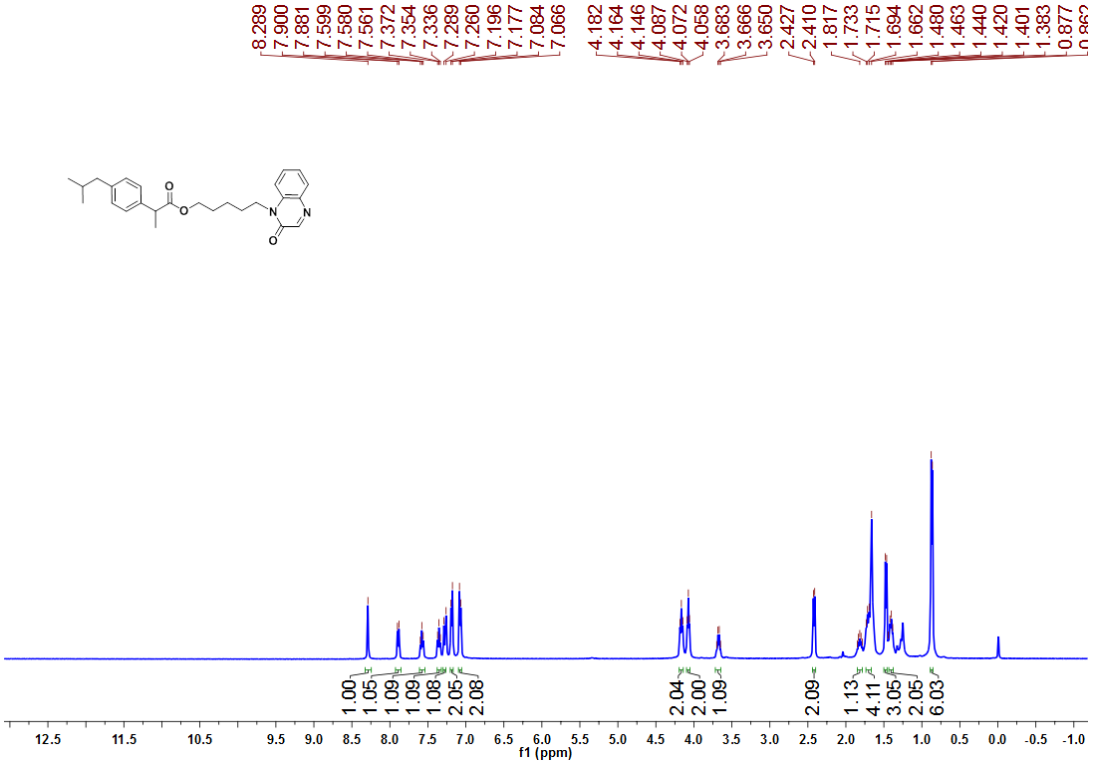
HRMS (ESI, m/z): Calculated for $C_{16}H_{12}F_2N_2O$ $(M+H)^+$ 287.0990, found 287.0994.

7. Copies of the ^{1}H NMR, ^{13}C NMR and ^{19}F NMR

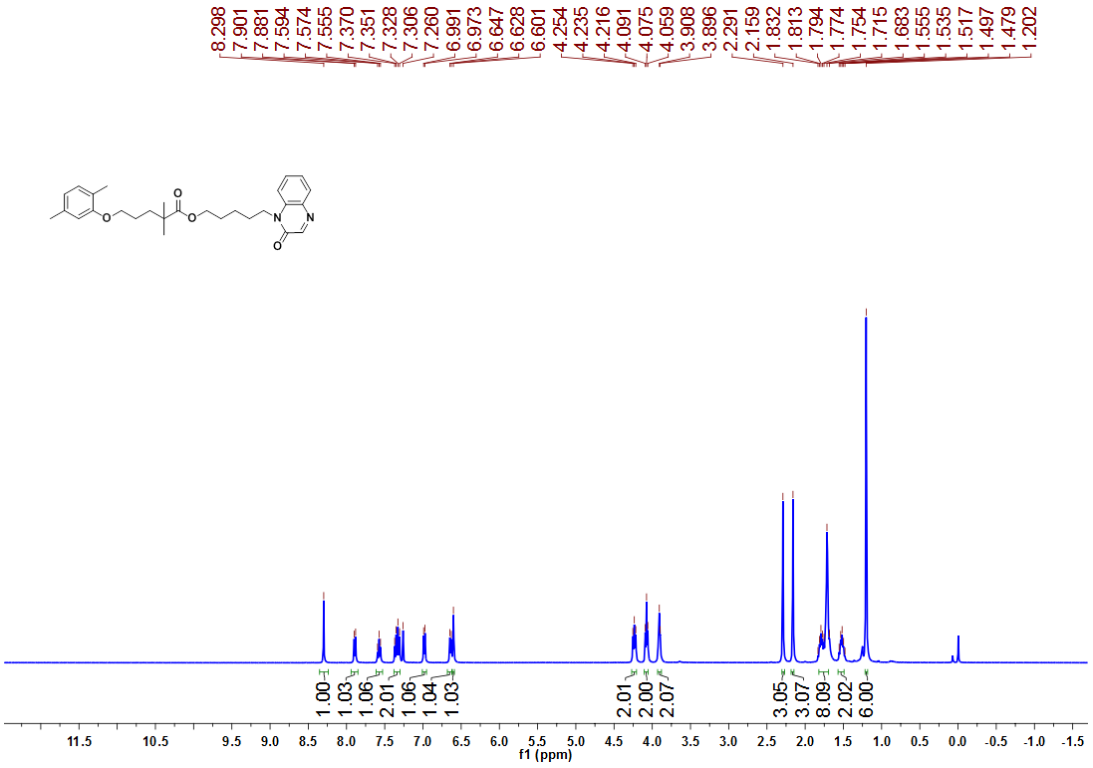
4a-^{1}H NMR (400 MHz, $CDCl_3$)



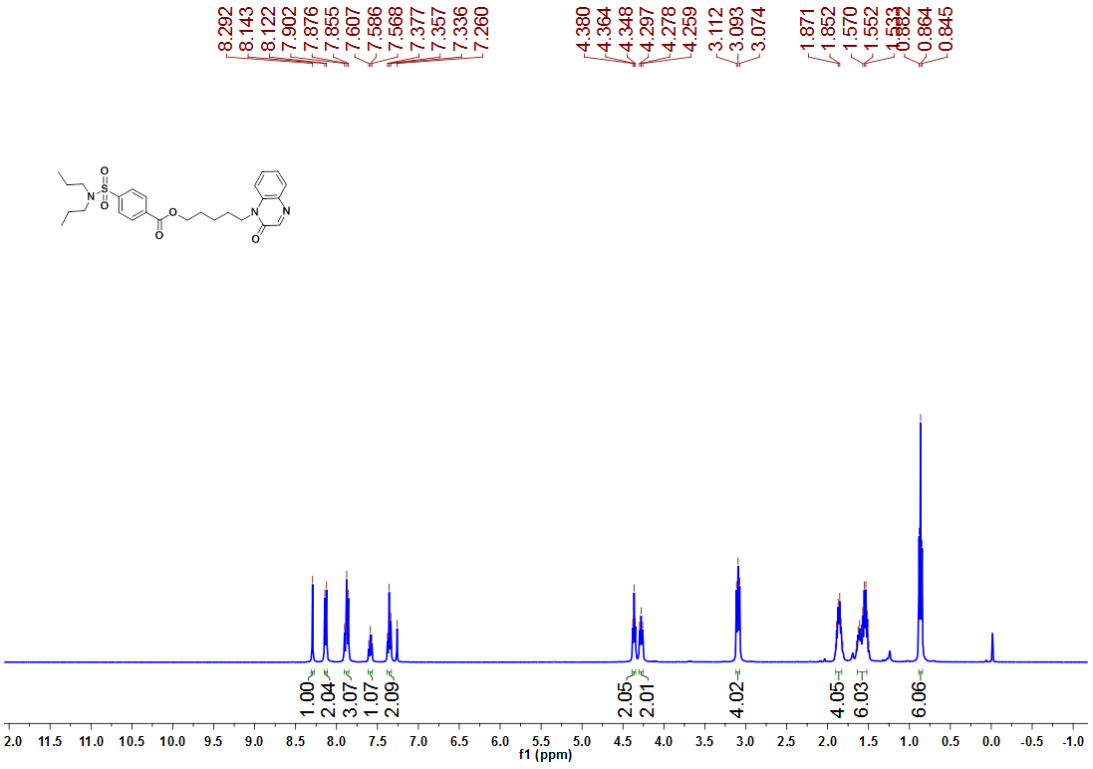
4b-^{1}H NMR (400 MHz, $CDCl_3$)



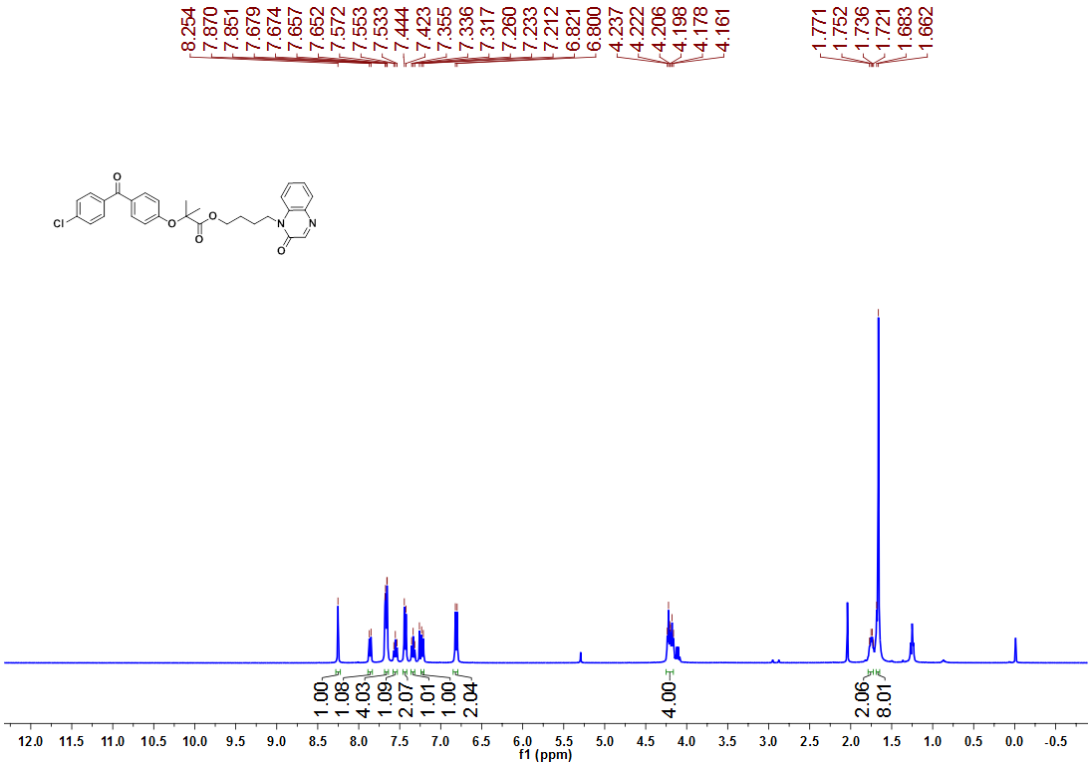
4c-^{1}H NMR (400 MHz, $CDCl_3$)



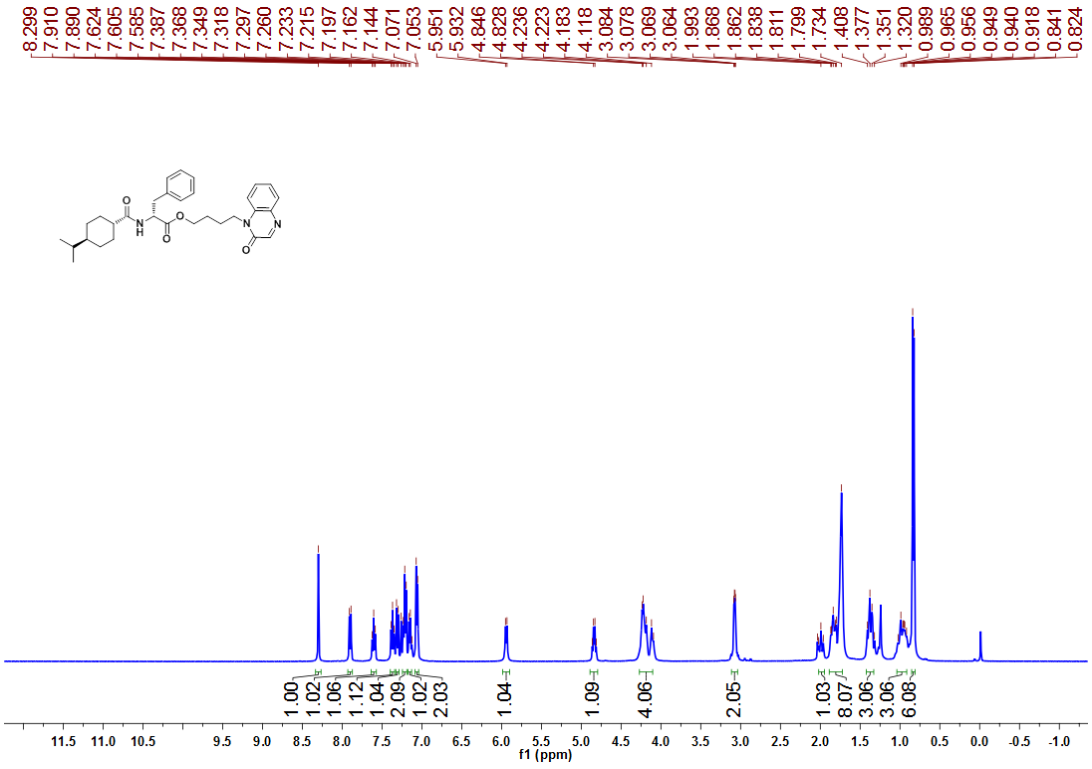
4d-^{1}H NMR (400 MHz, $CDCl_3$)



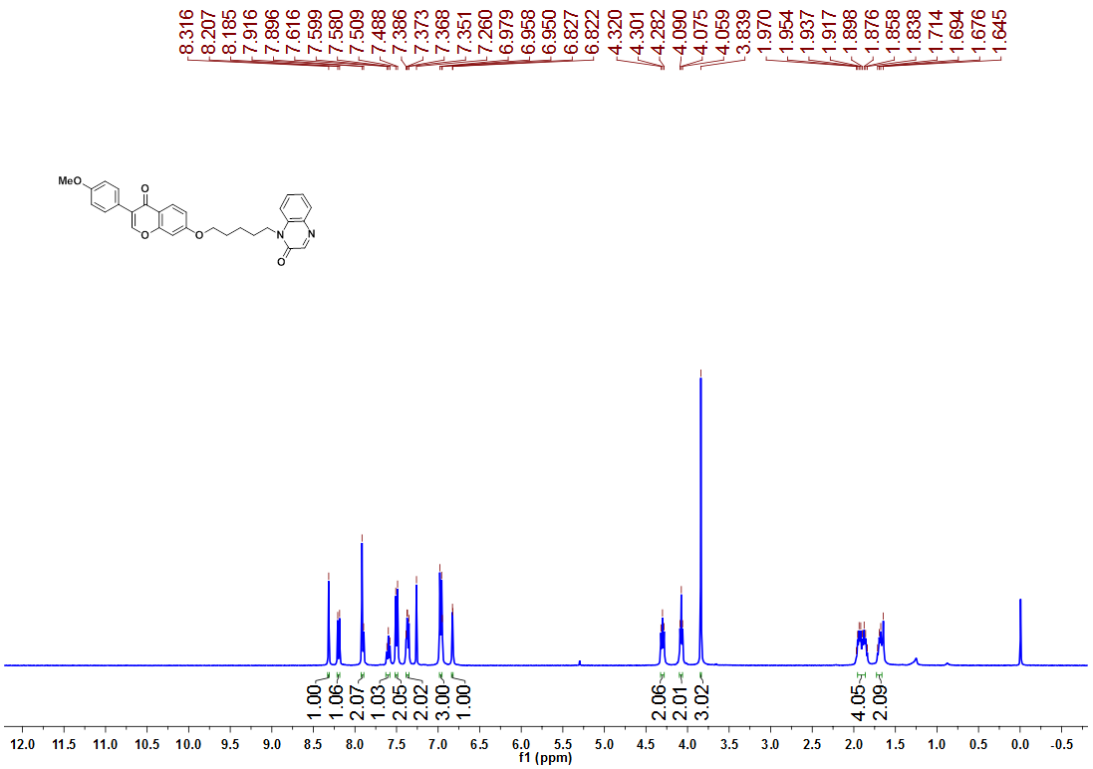
4e-^{1}H NMR (400 MHz, $CDCl_3$)



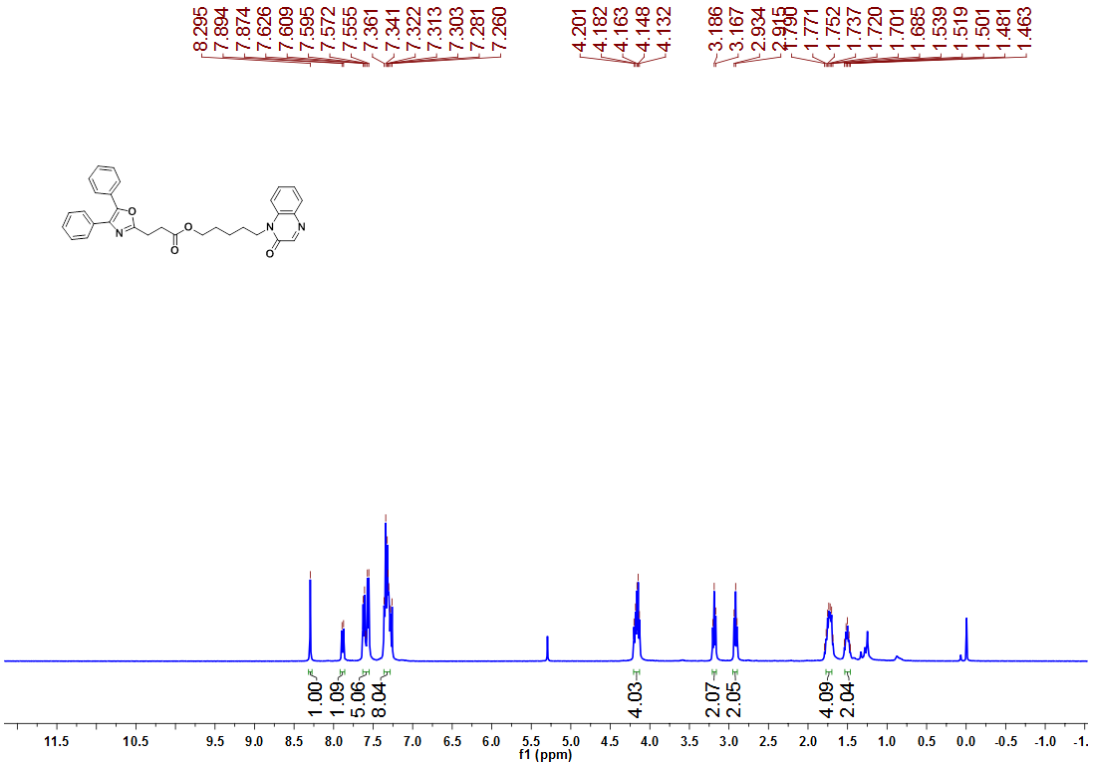
4f-^{1}H NMR (400 MHz, $CDCl_3$)



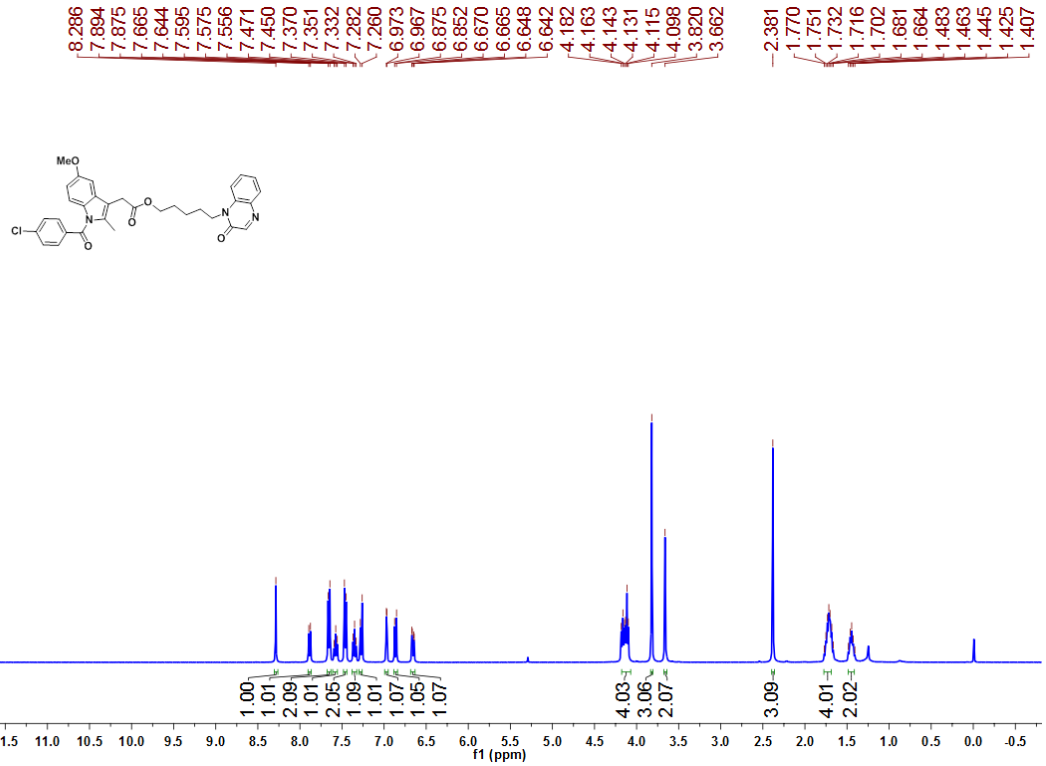
4g-^{1}H NMR (400 MHz, $CDCl_3$)



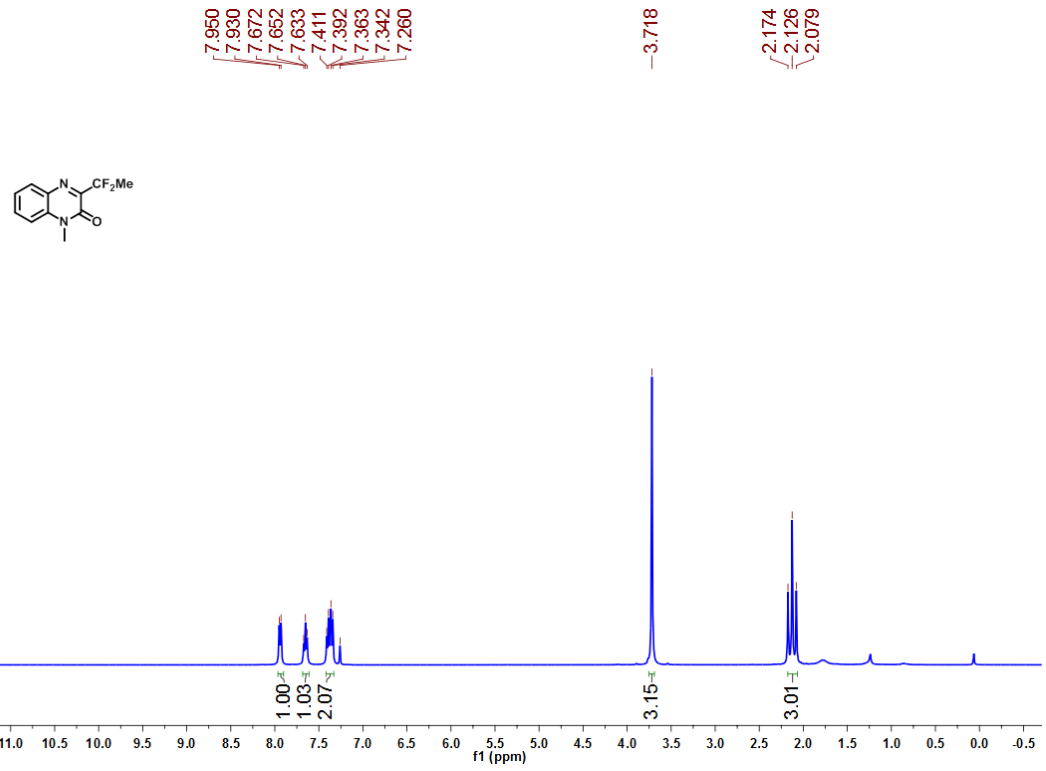
4h-^{1}H NMR (400 MHz, $CDCl_3$)



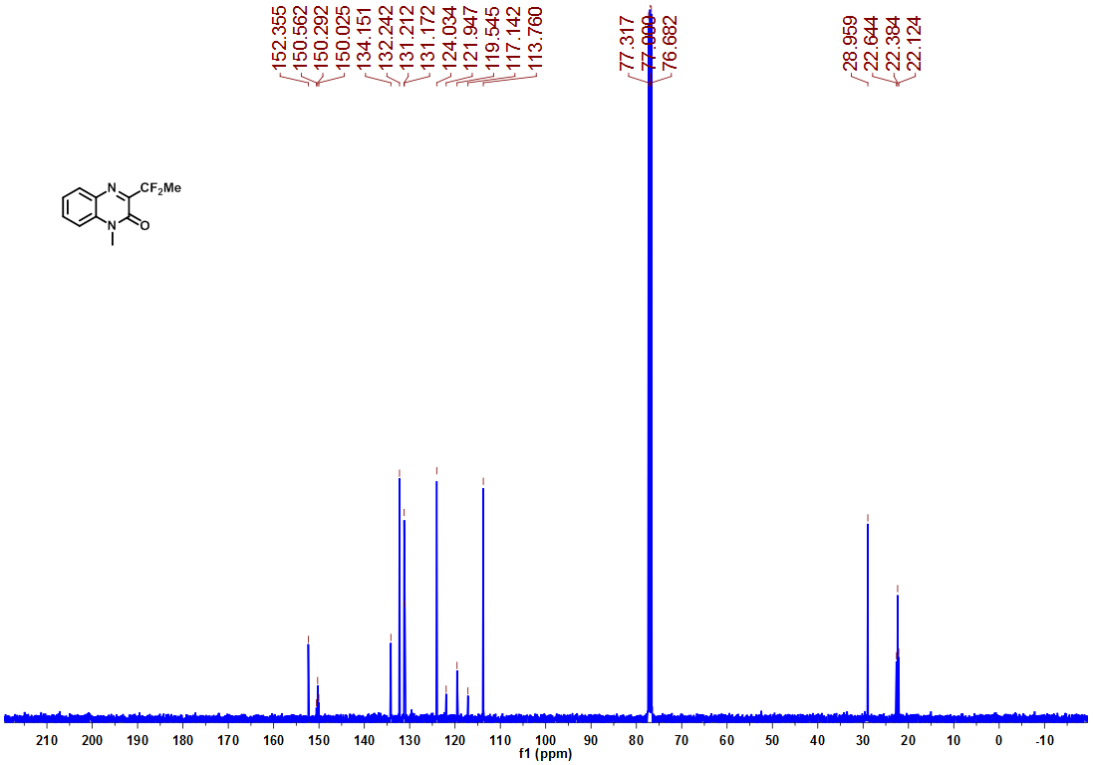
4i-^{1}H NMR (400 MHz, $CDCl_3$)



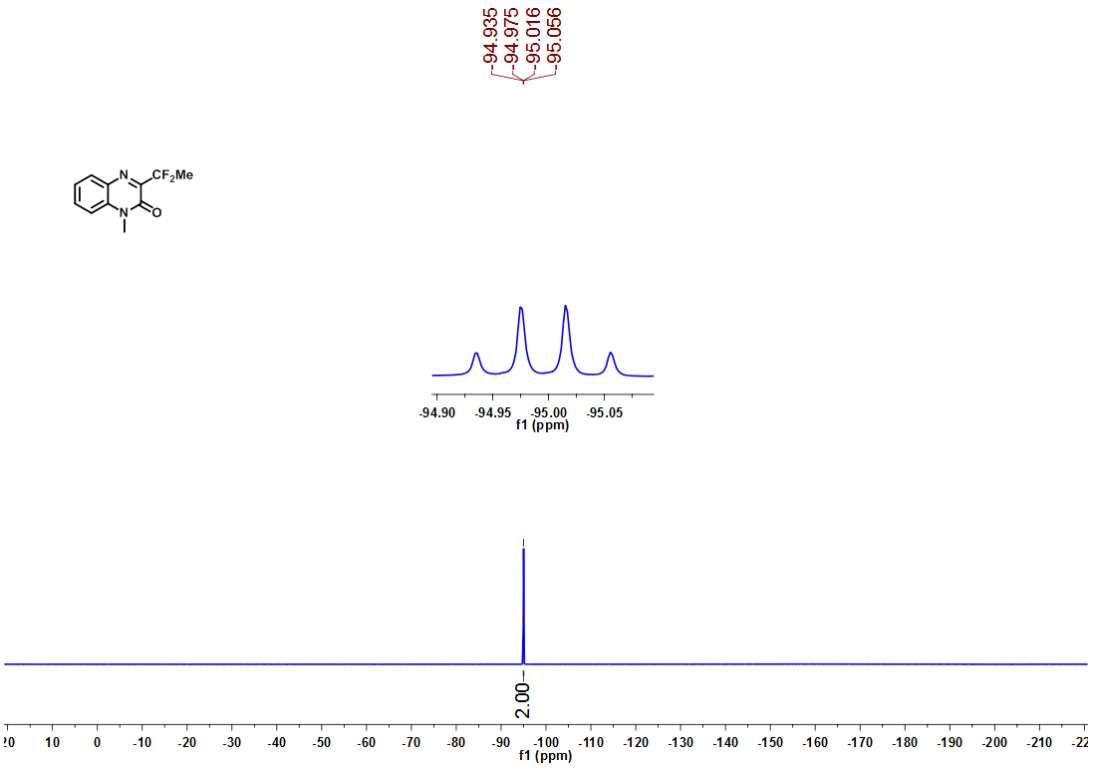
3a-^{1}H NMR (400 MHz, $CDCl_3$)



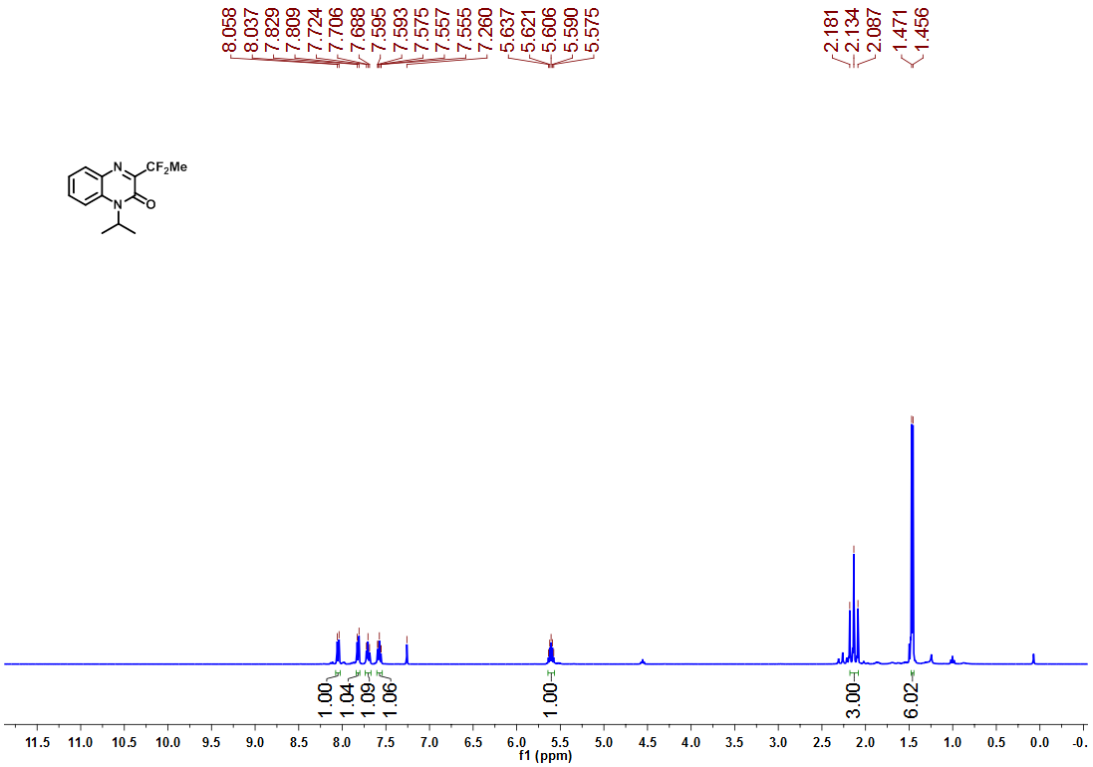
3a-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



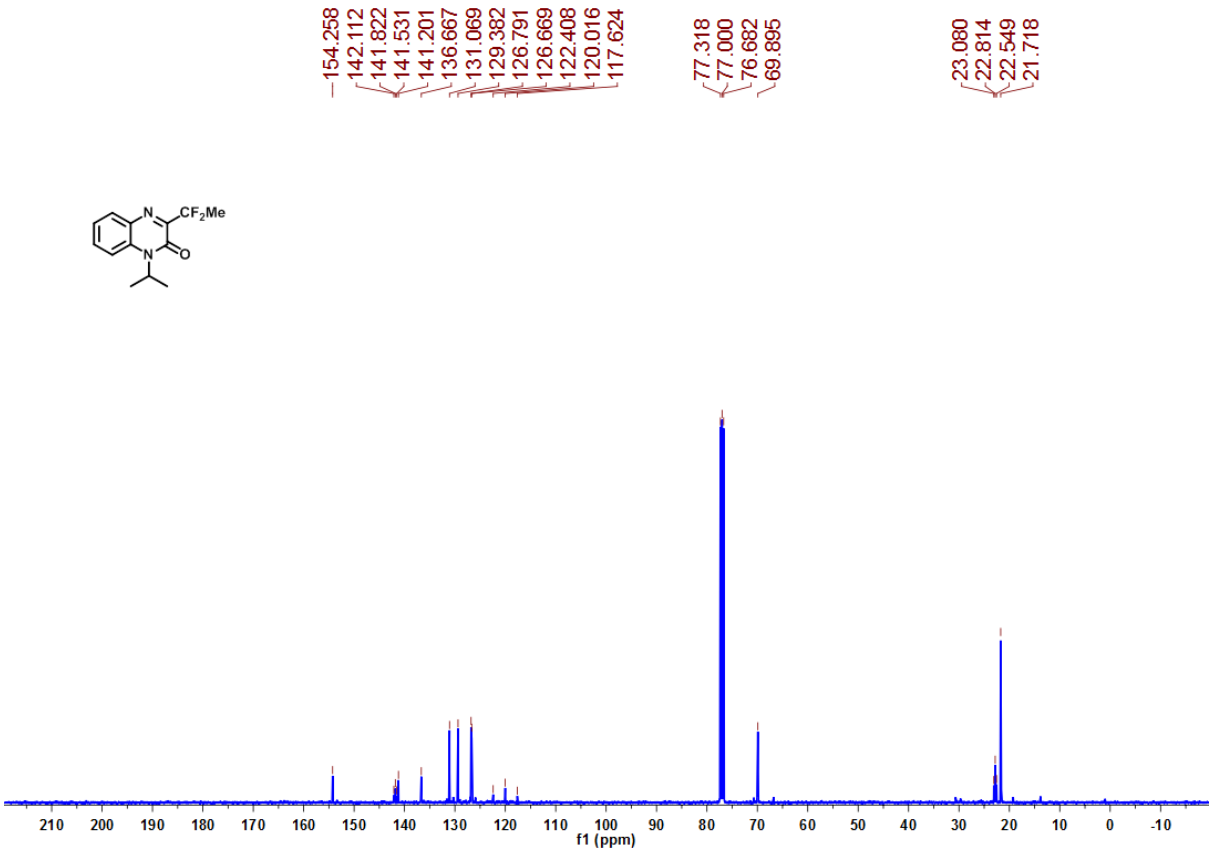
3a-^{19}F NMR (471 MHz, $CDCl_3$)



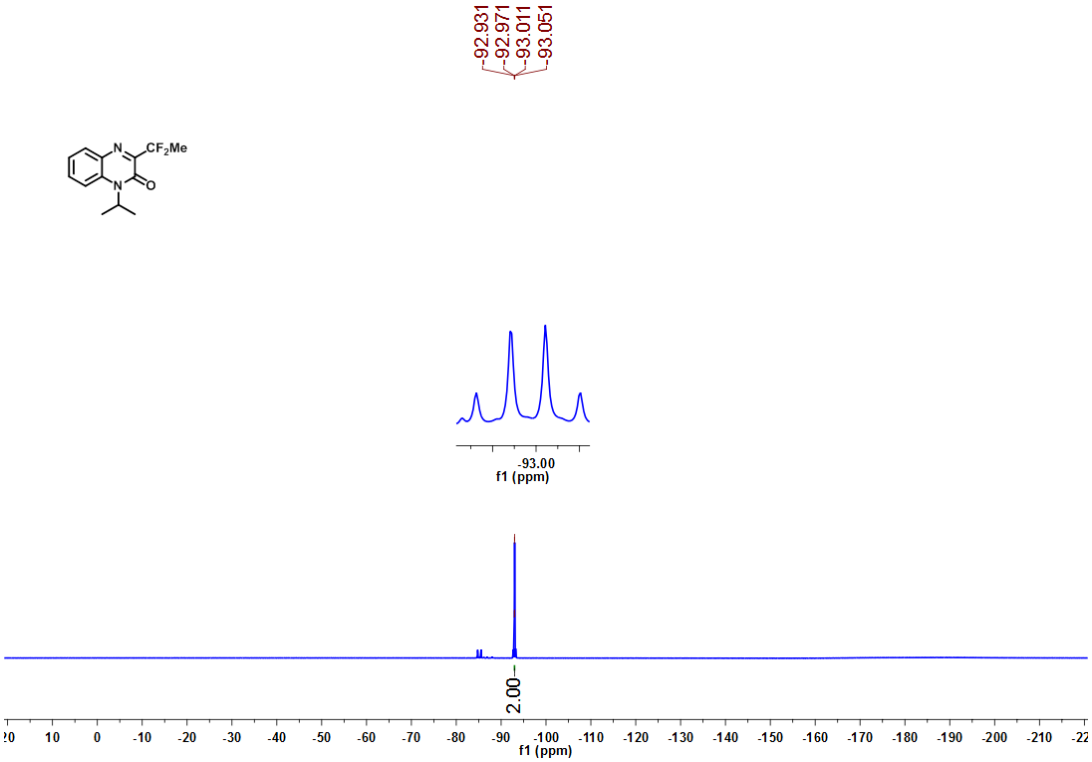
3b-^{1}H NMR (400 MHz, $CDCl_3$)



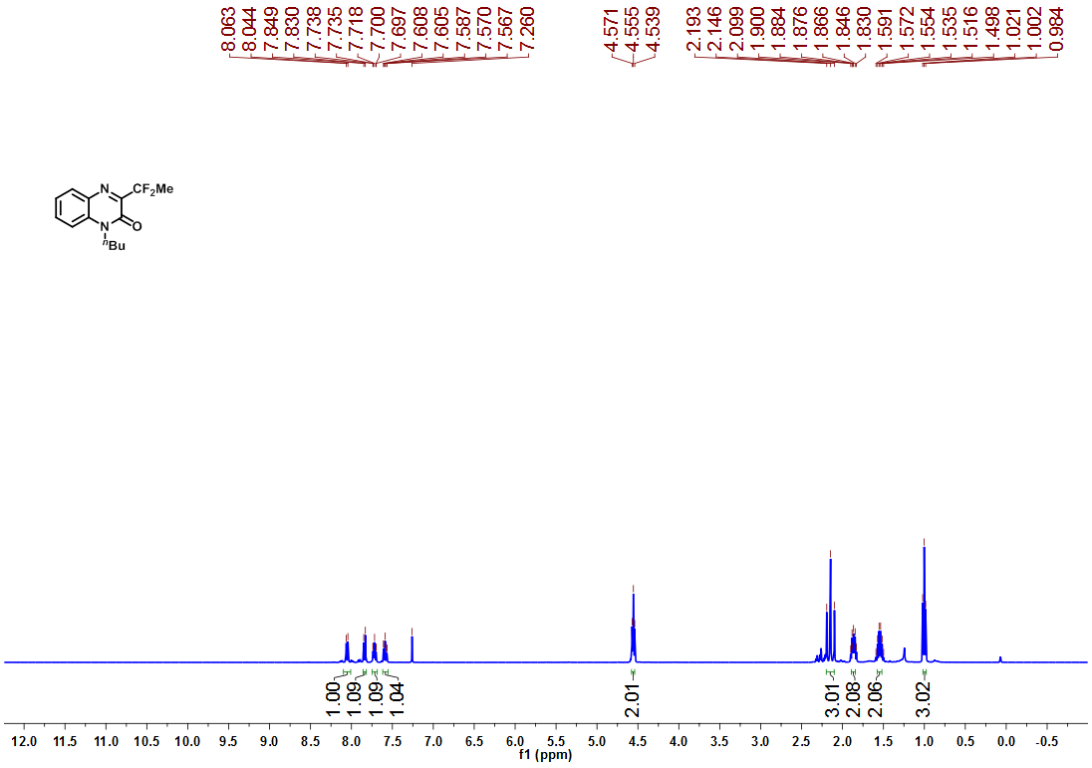
3b-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



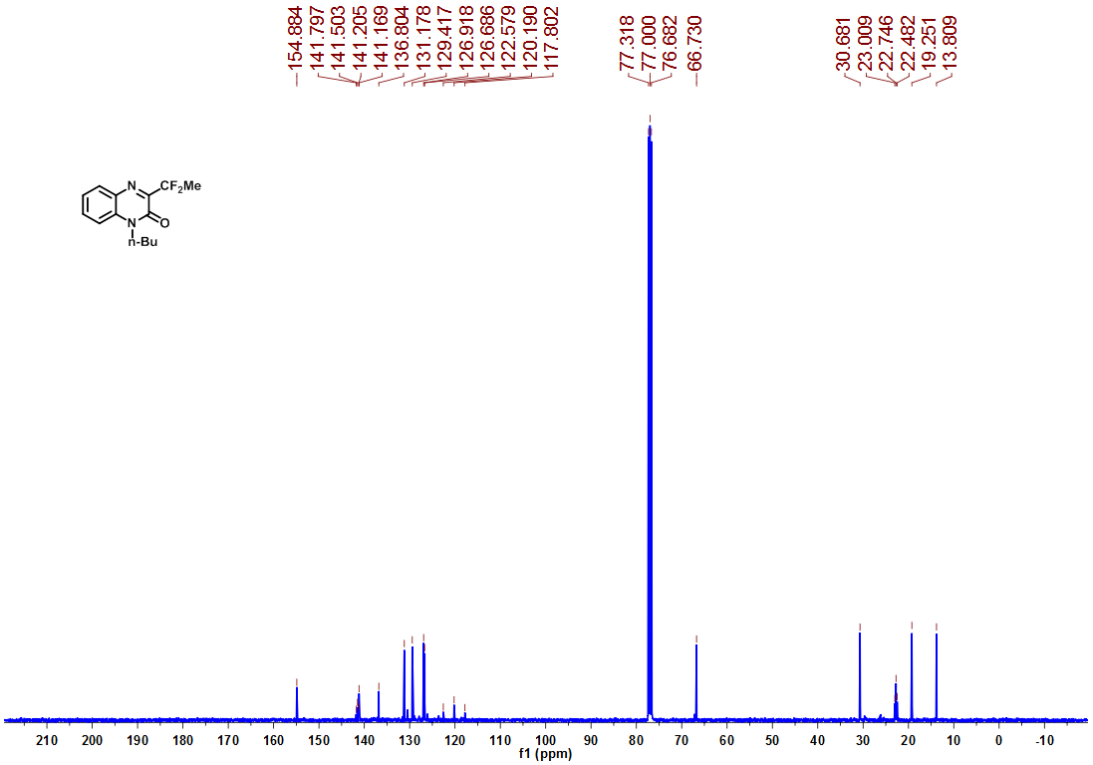
3b-^{19}F NMR (471 MHz, $CDCl_3$)



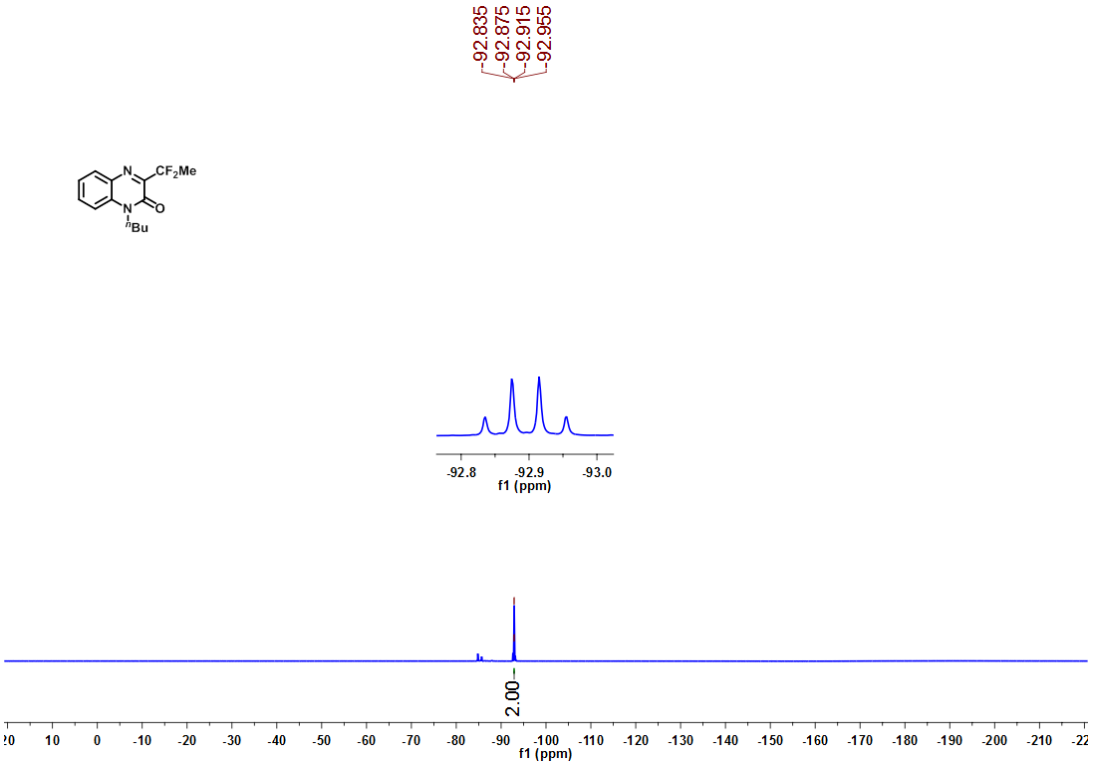
3c-^{1}H NMR (400 MHz, $CDCl_3$)



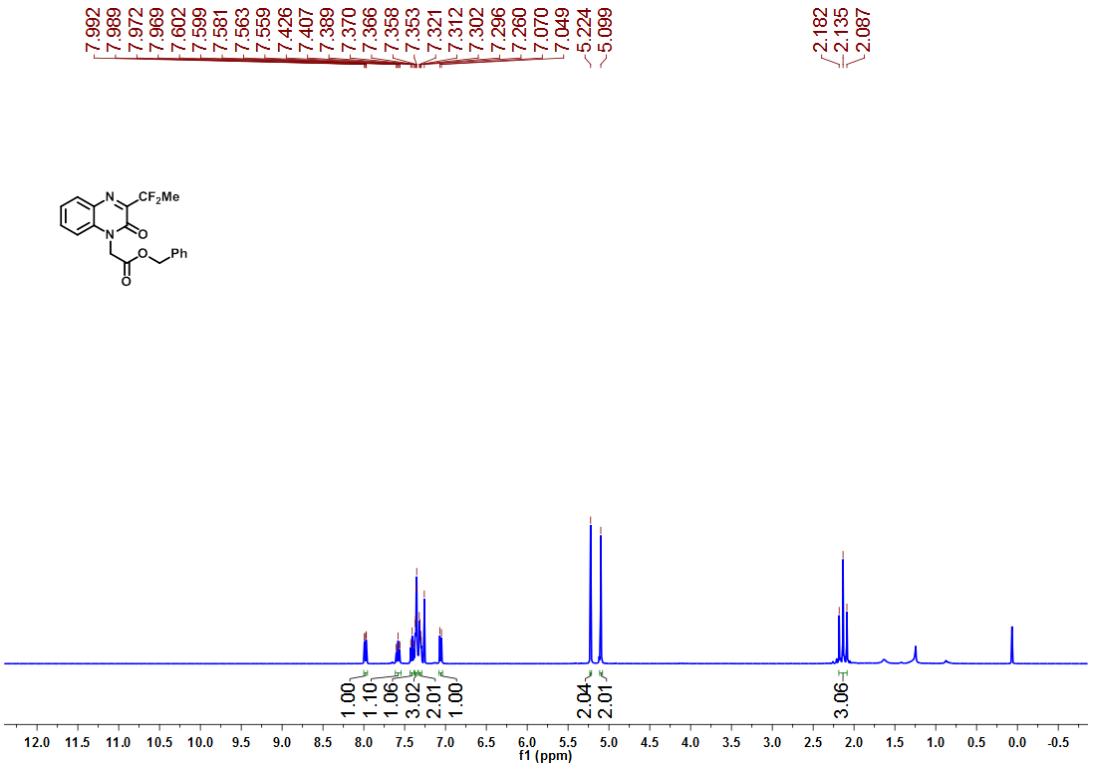
3c-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



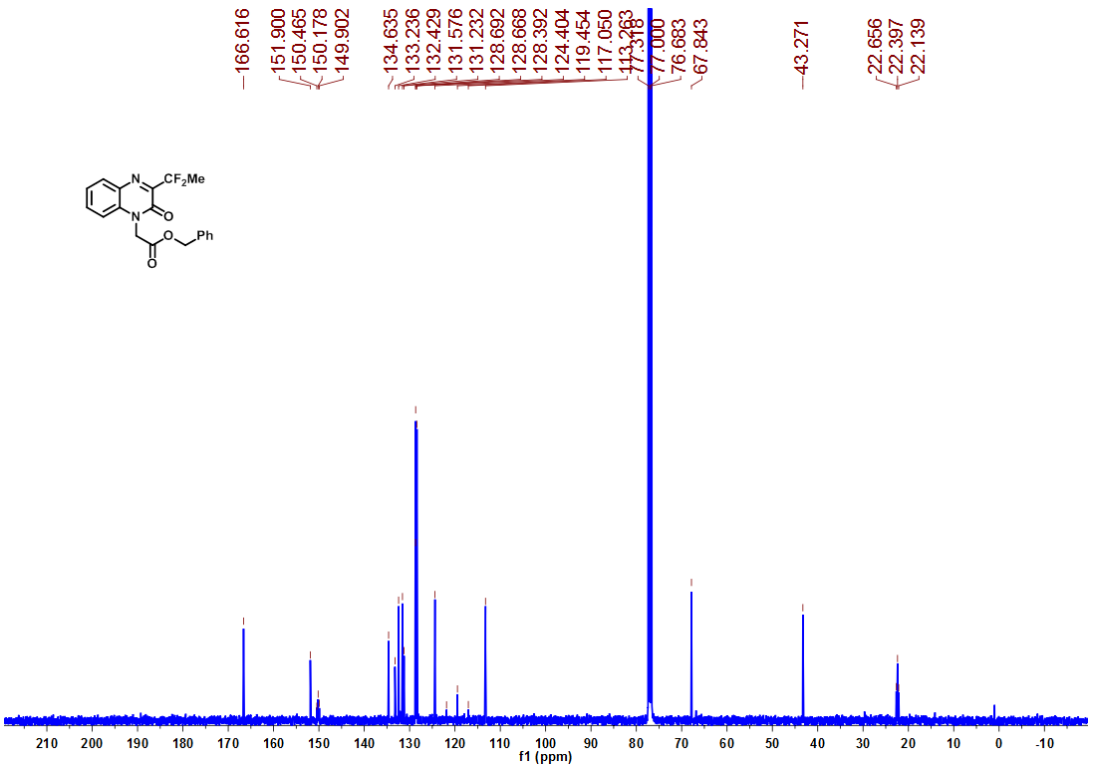
3c-^{19}F NMR (471 MHz, $CDCl_3$)



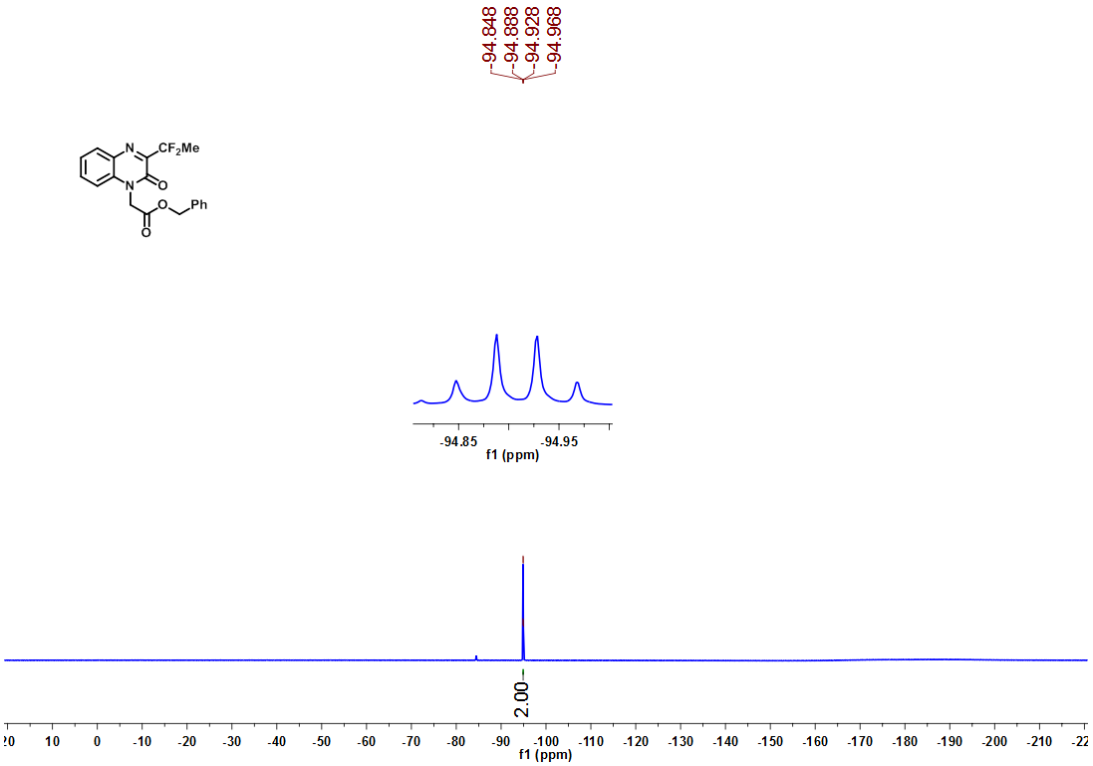
3d-^{1}H NMR (400 MHz, $CDCl_3$)



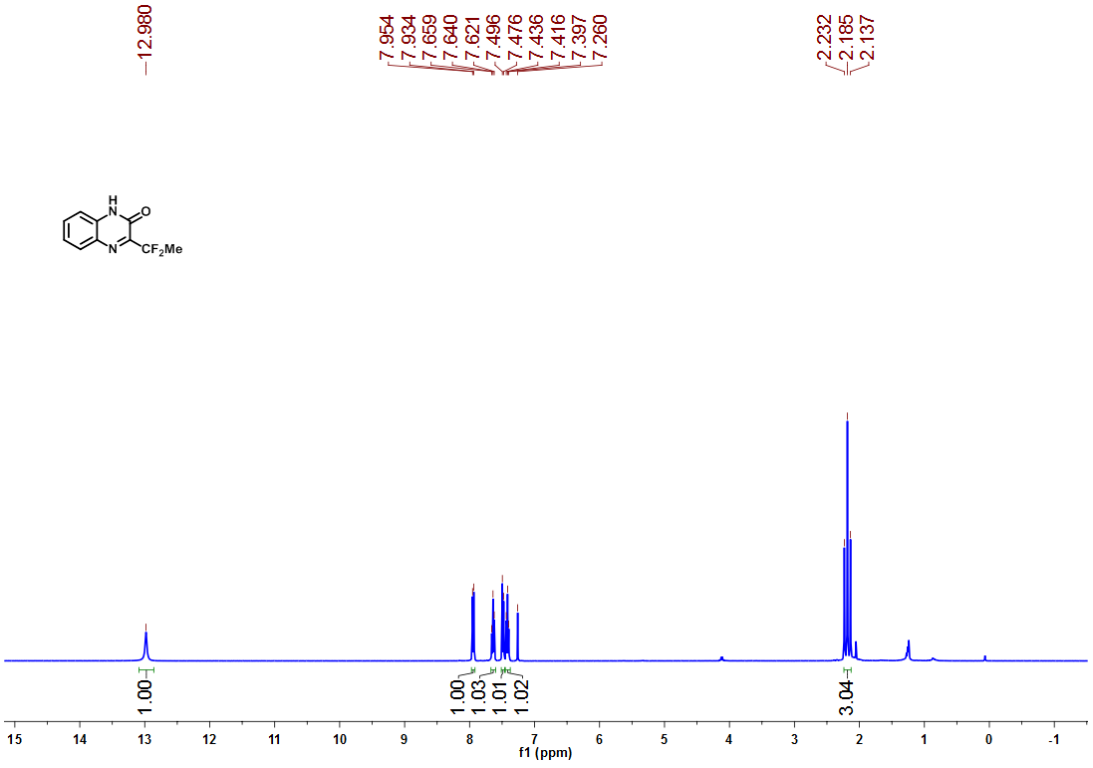
3d-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



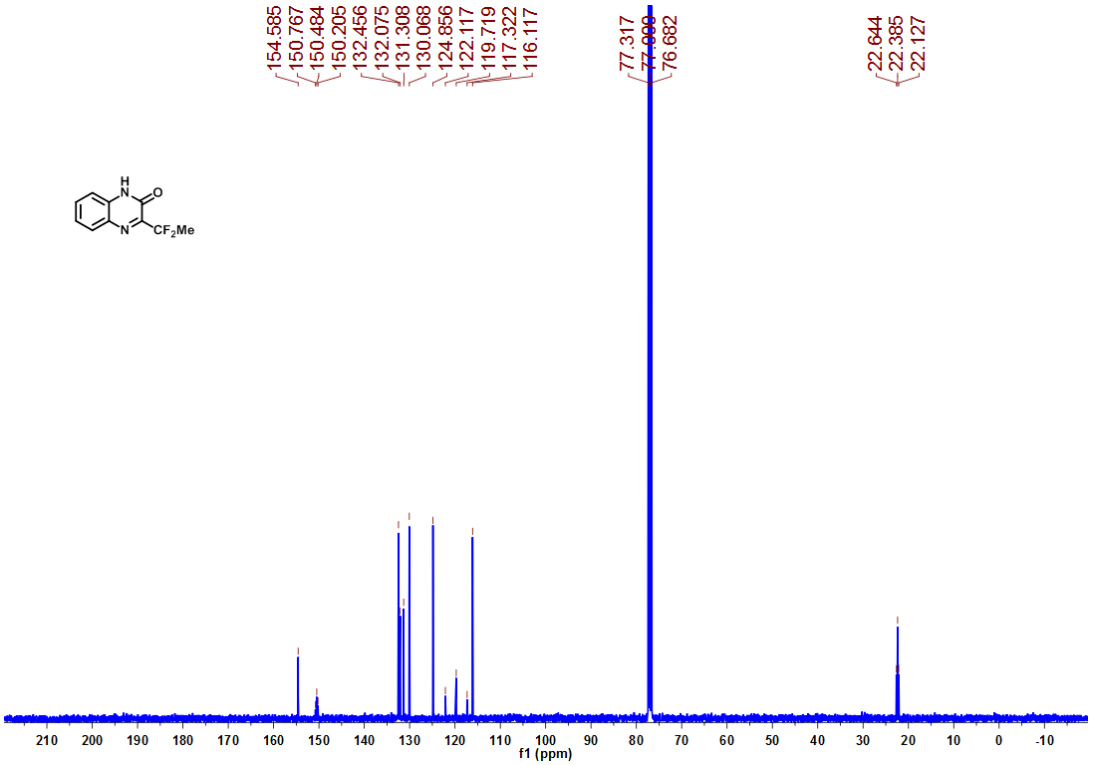
3d-^{19}F NMR (471 MHz, $CDCl_3$)



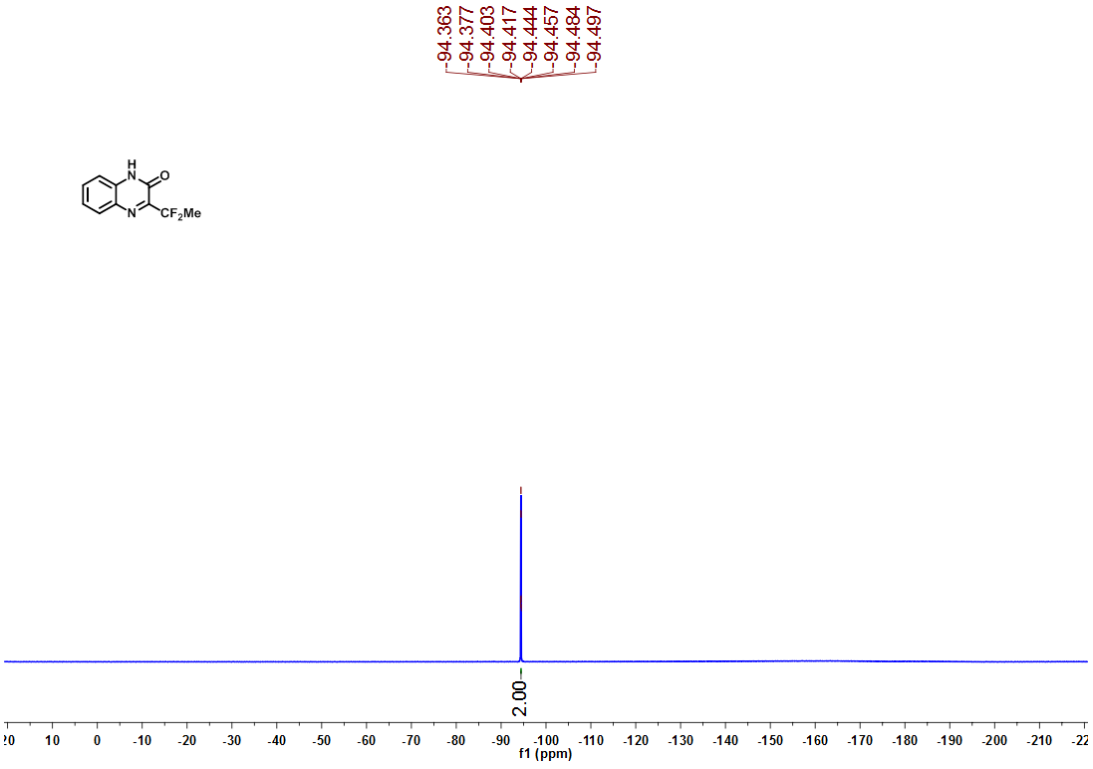
3e-^{1}H NMR (400 MHz, $CDCl_3$)



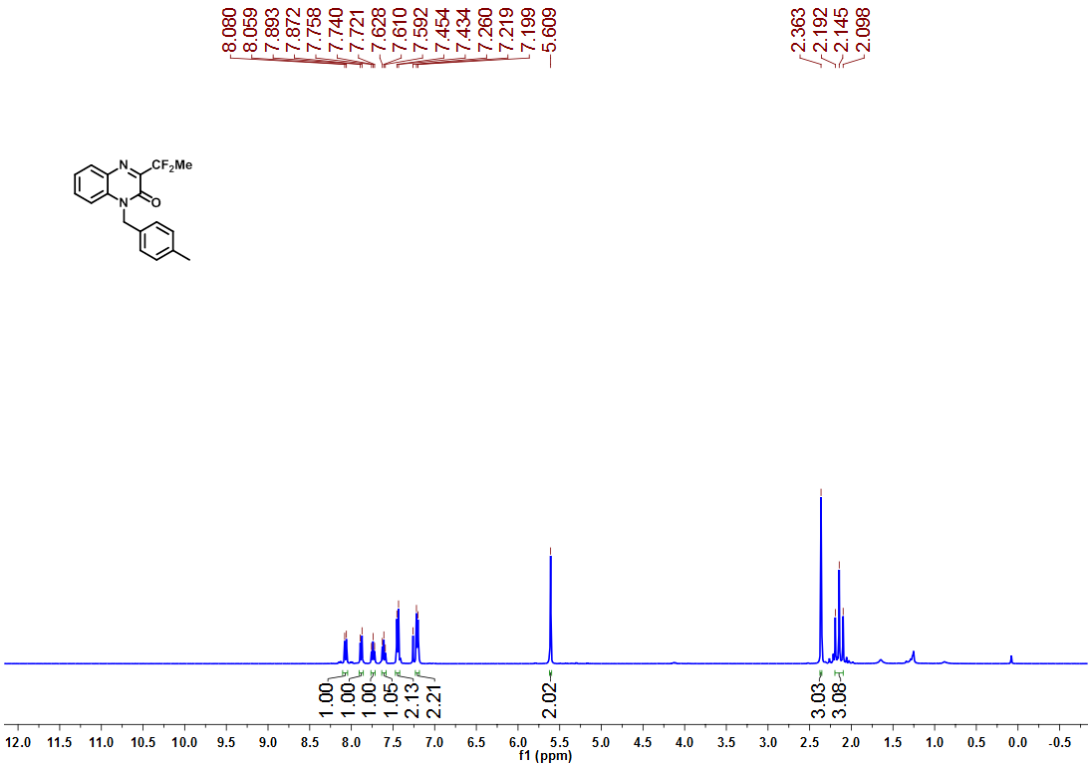
3e-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



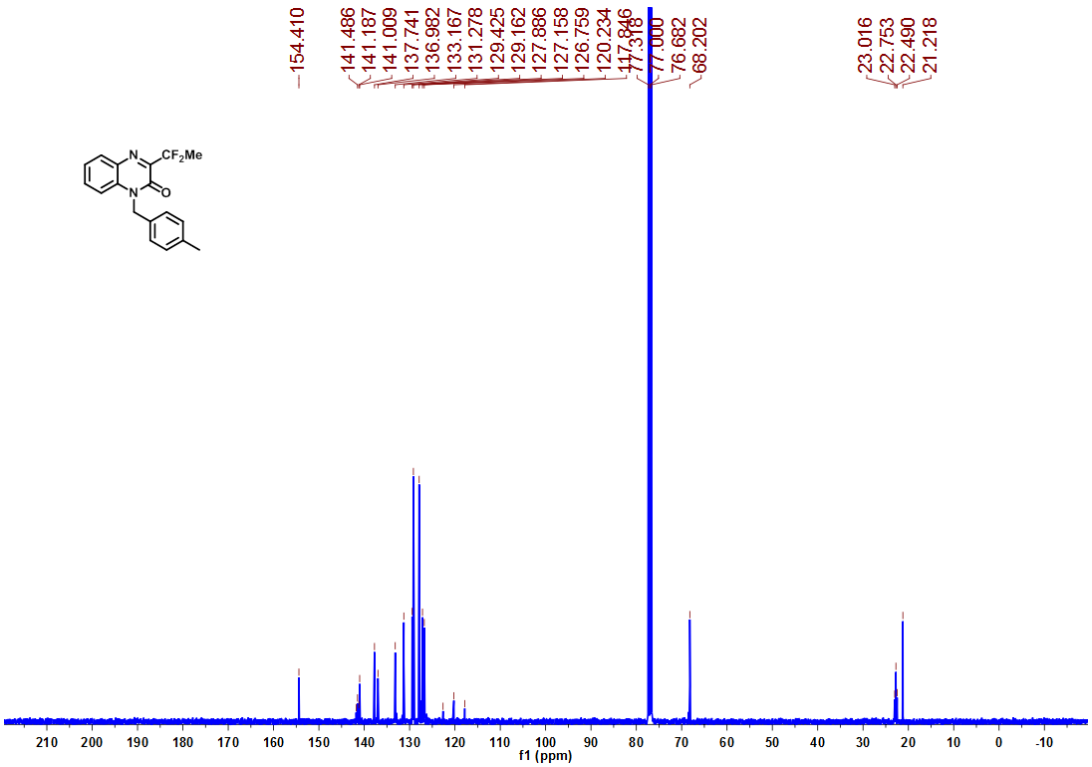
3e-^{19}F NMR (471 MHz, $CDCl_3$)



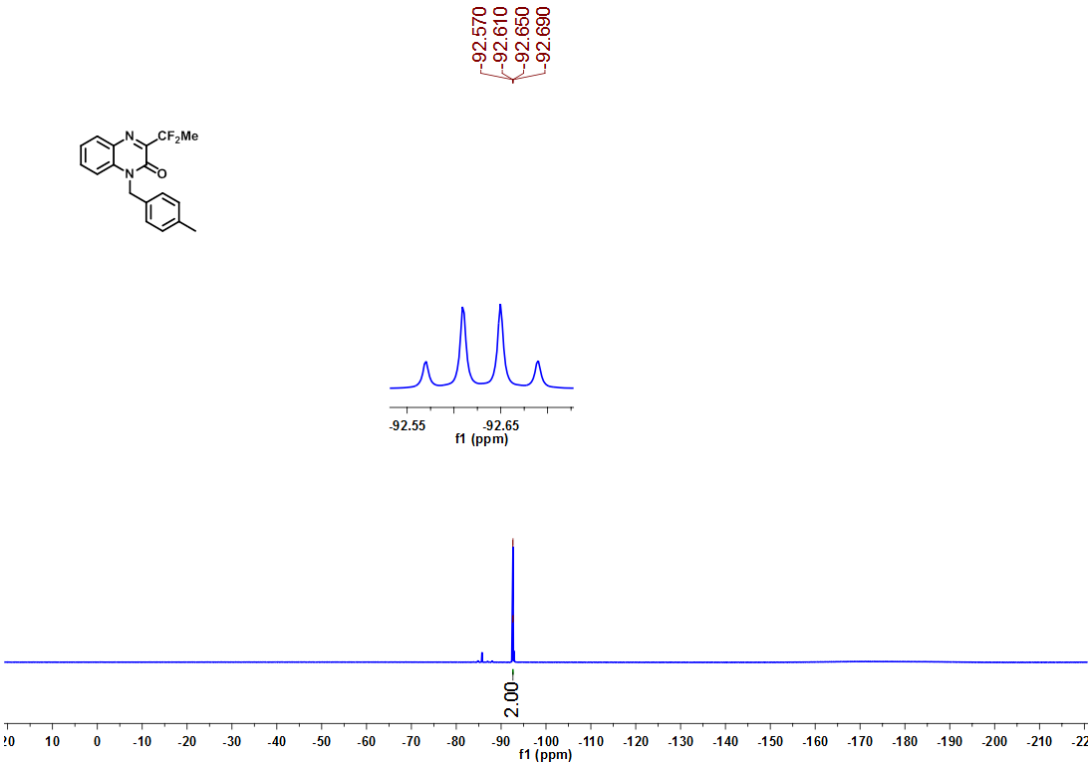
3f-^{1}H NMR (400 MHz, $CDCl_3$)



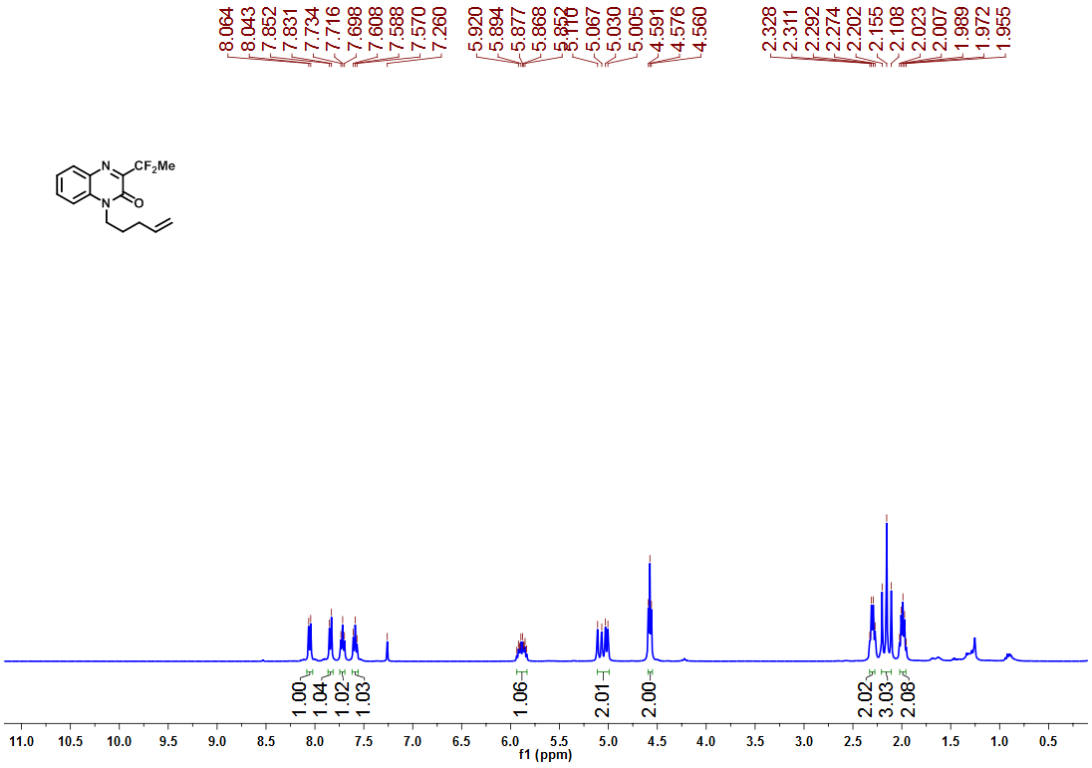
3f-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



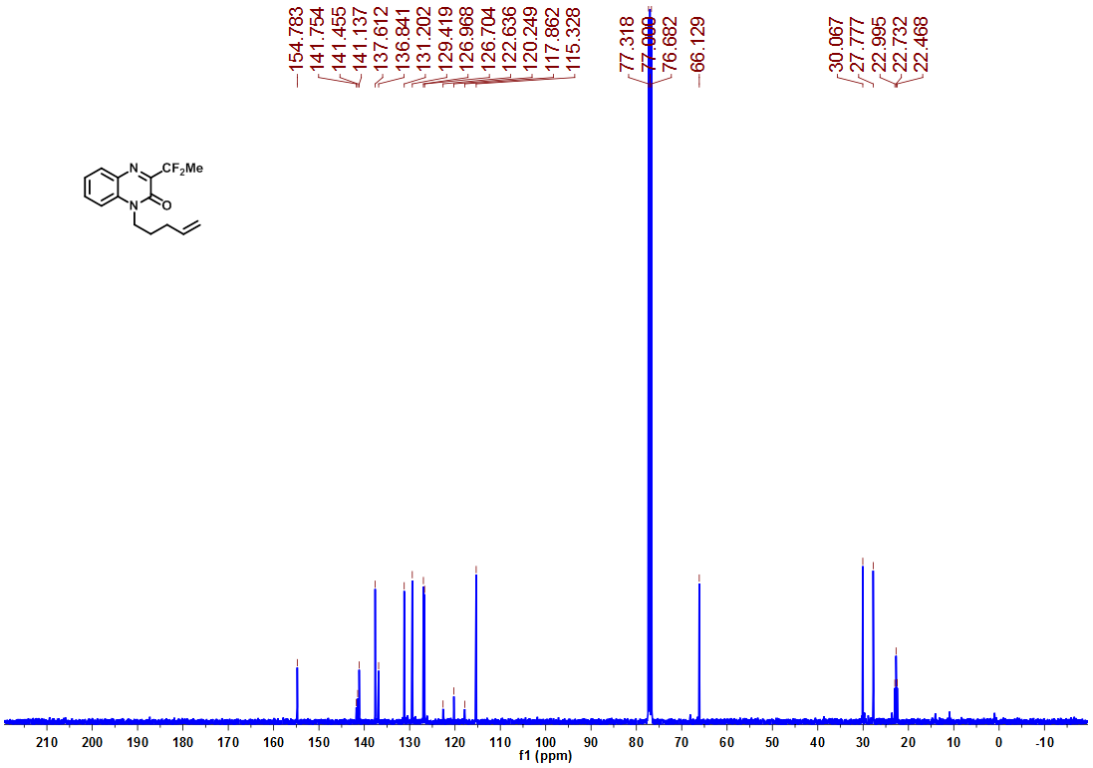
3f-^{19}F NMR (471 MHz, $CDCl_3$)



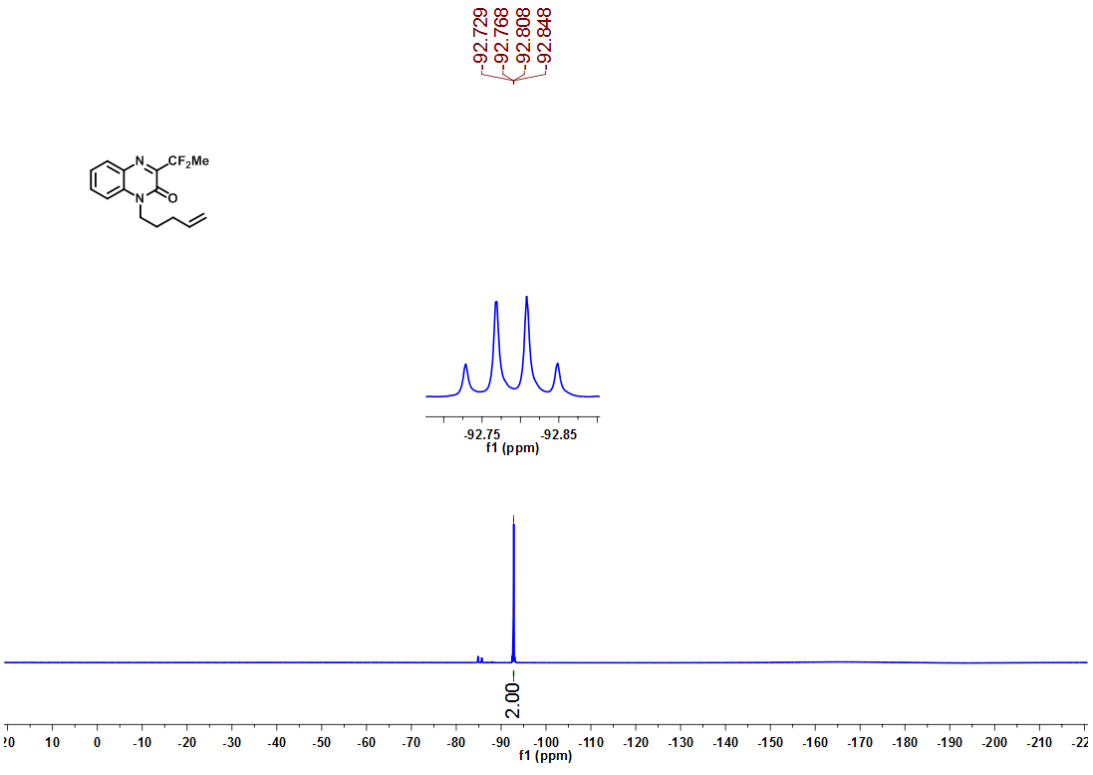
3g-^{1}H NMR (400 MHz, $CDCl_3$)



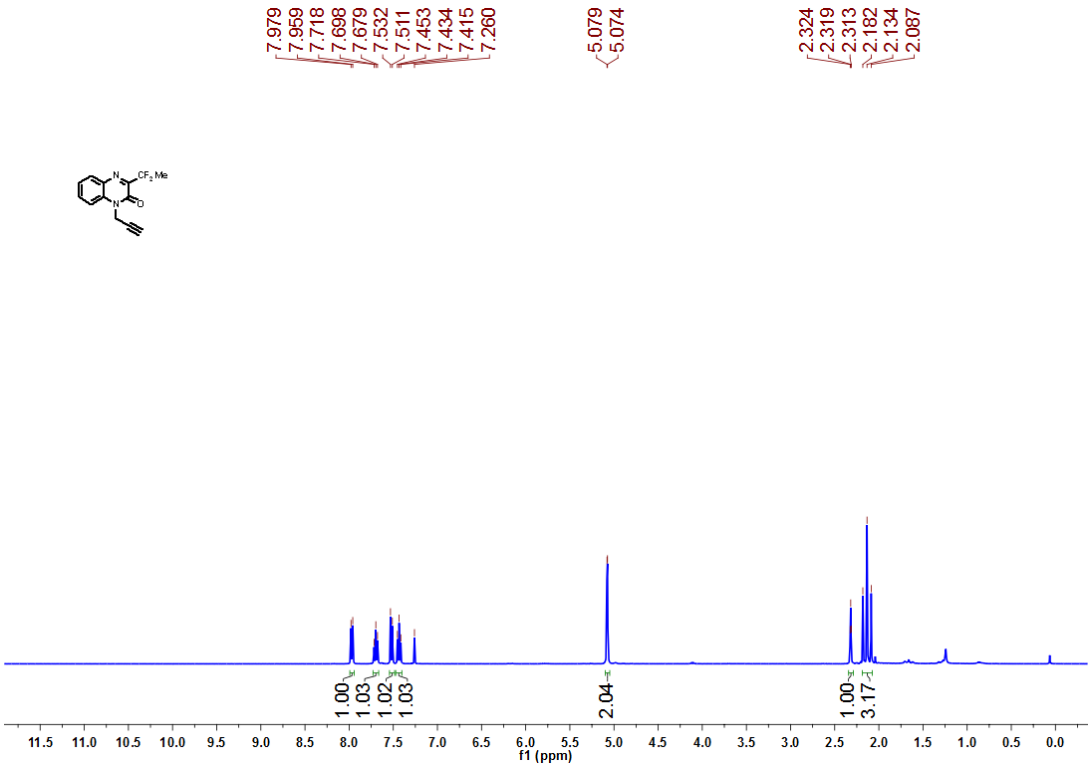
3g-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



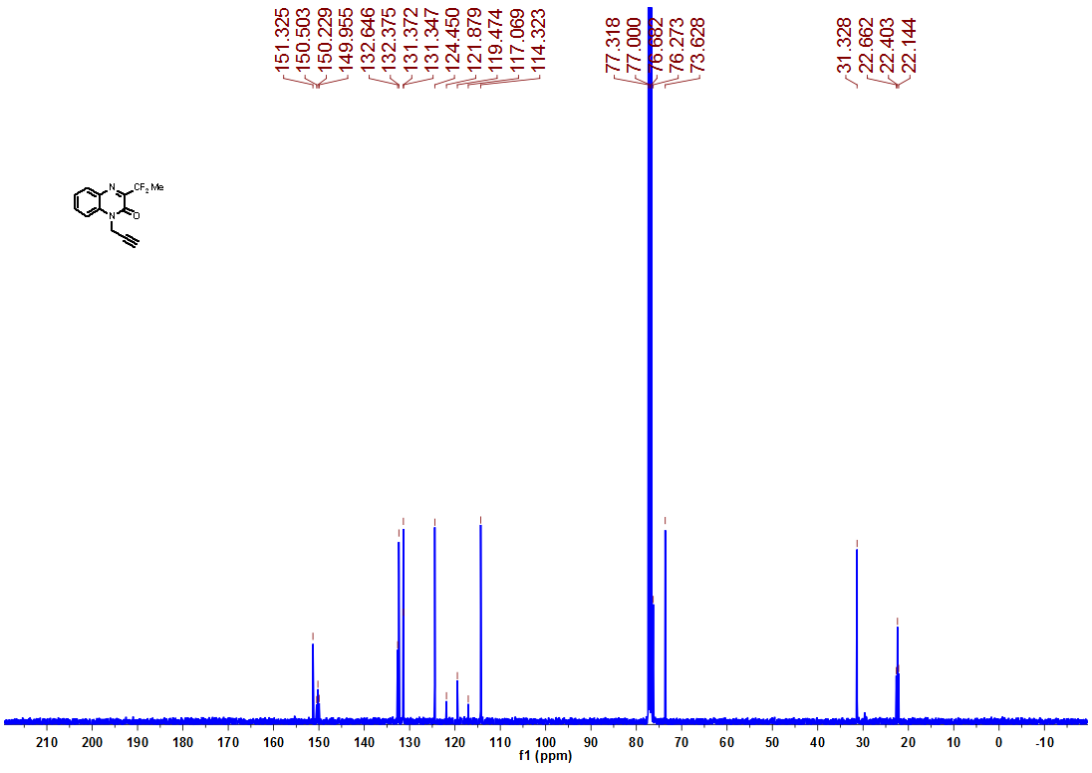
3g-^{19}F NMR (471 MHz, $CDCl_3$)



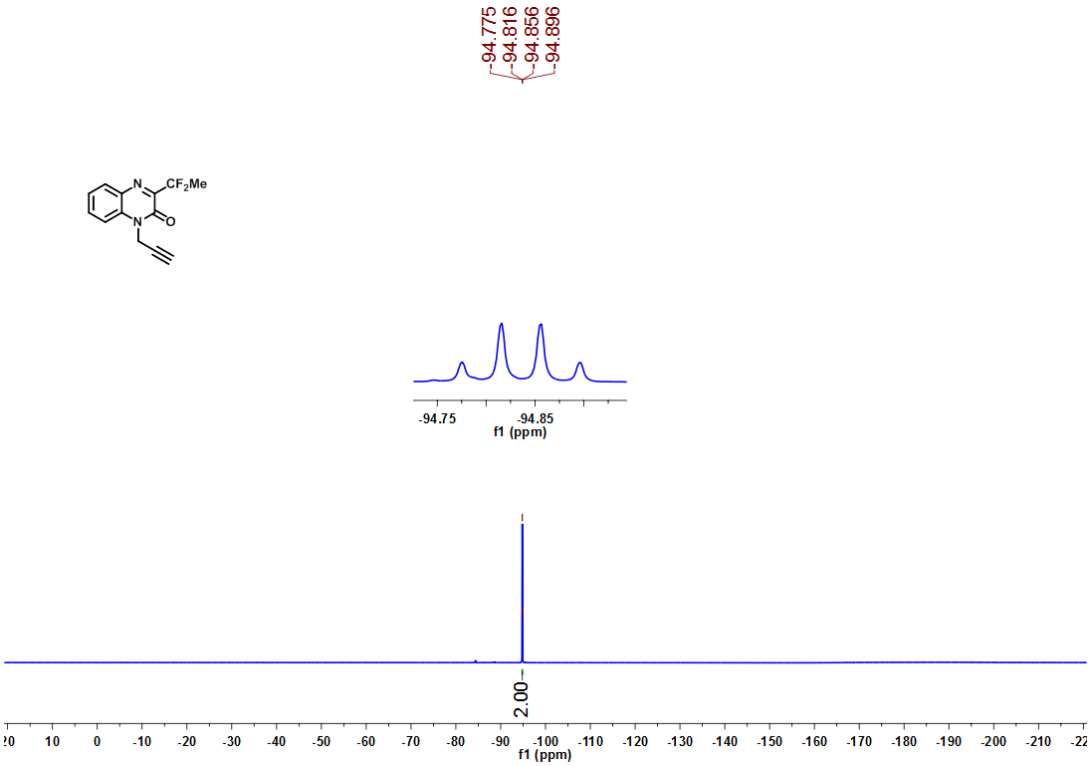
3h-^{1}H NMR (400 MHz, $CDCl_3$)



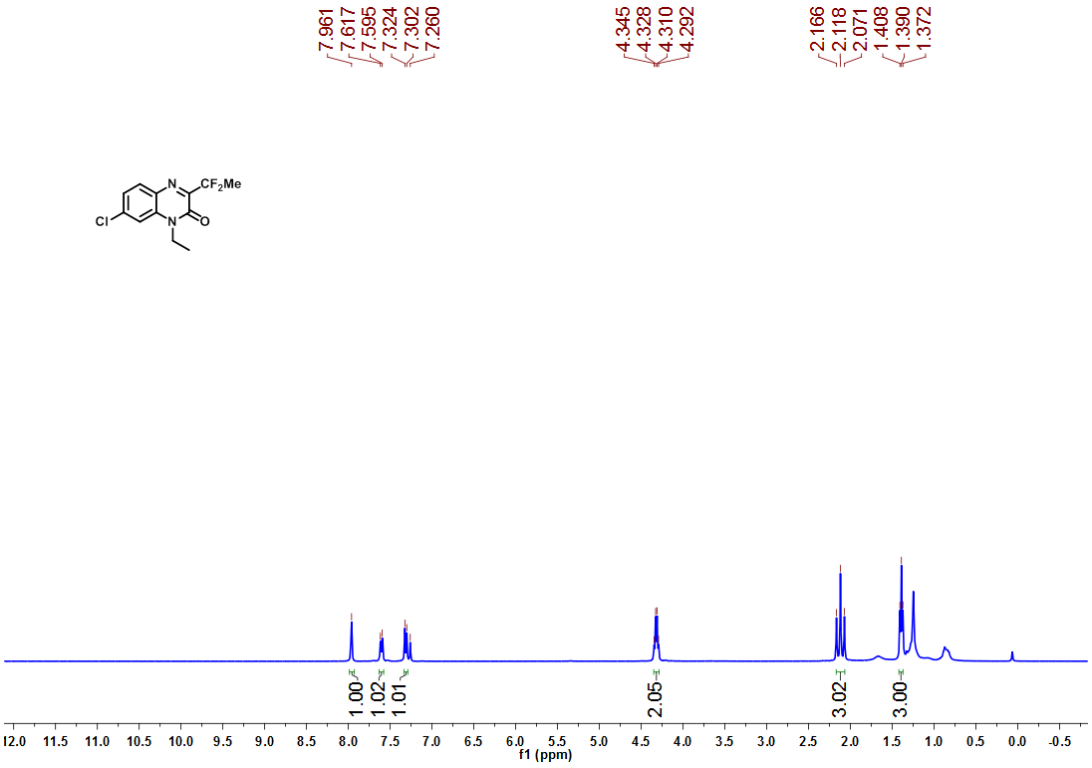
3h-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



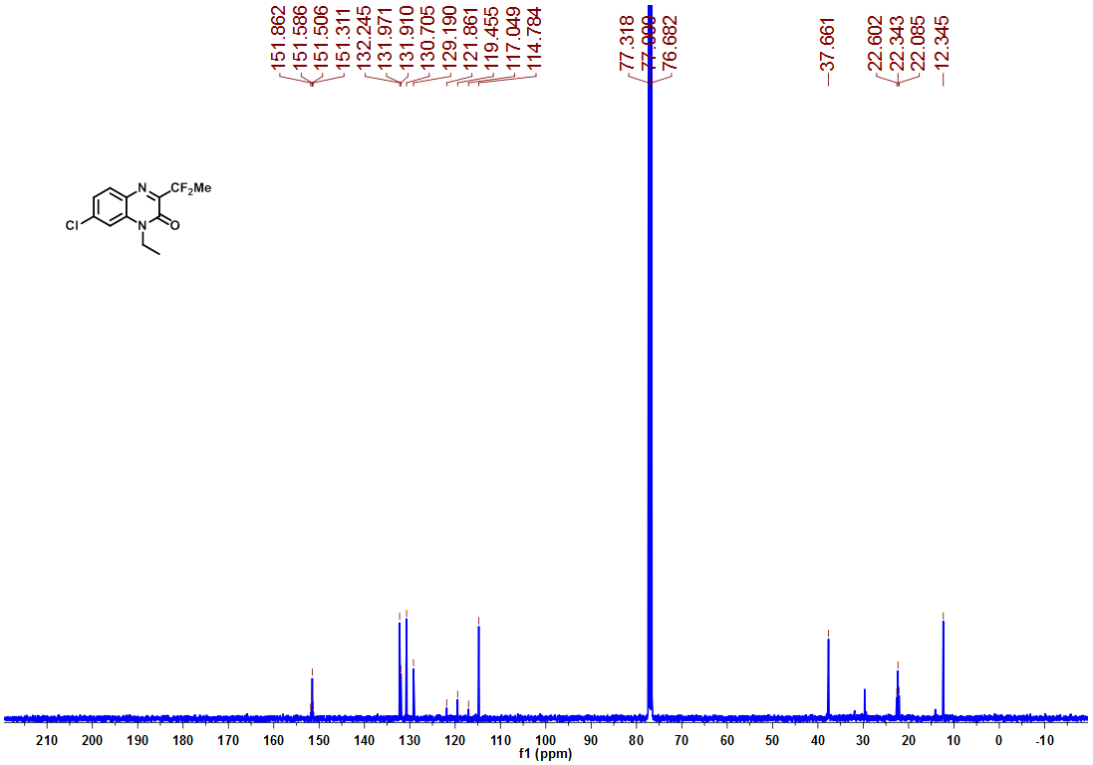
3h-^{19}F NMR (471 MHz, $CDCl_3$)



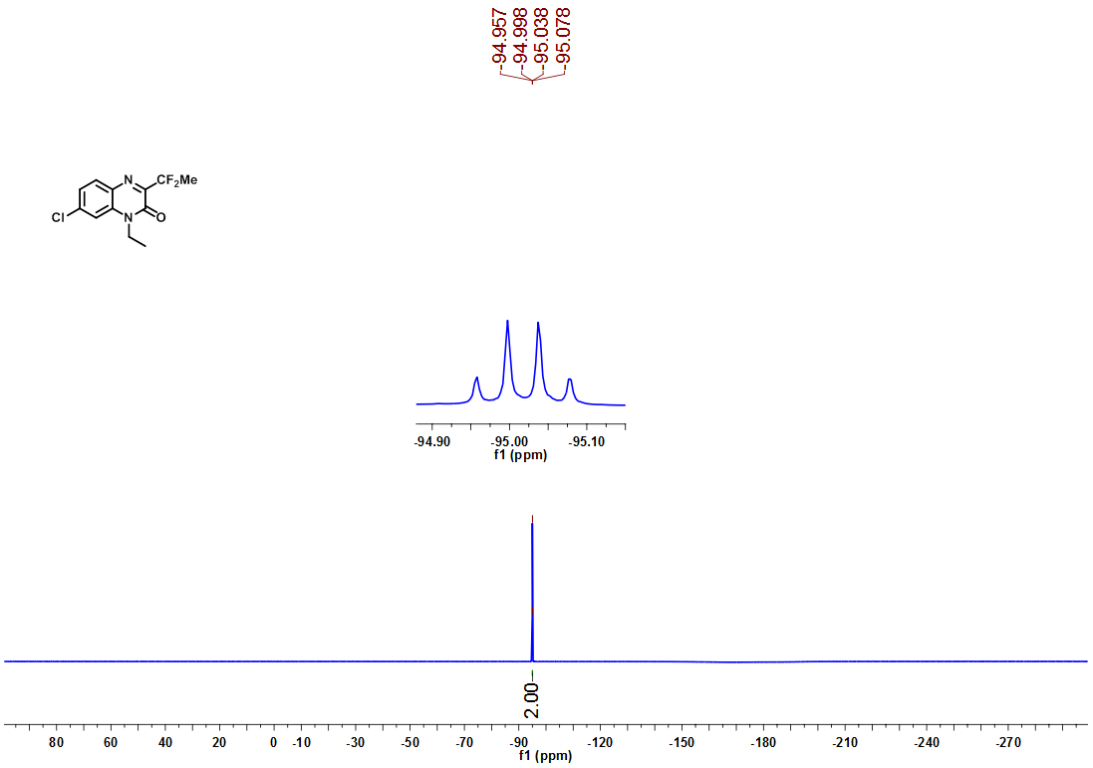
3i-^{1}H NMR (400 MHz, $CDCl_3$)



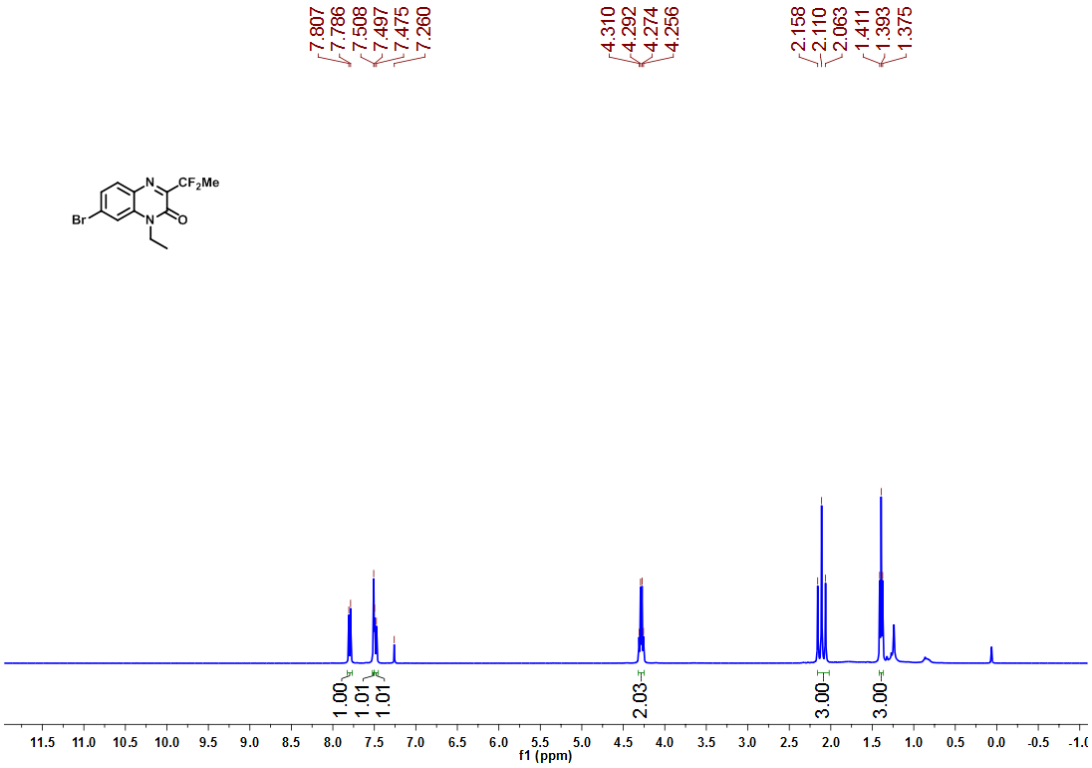
3i-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



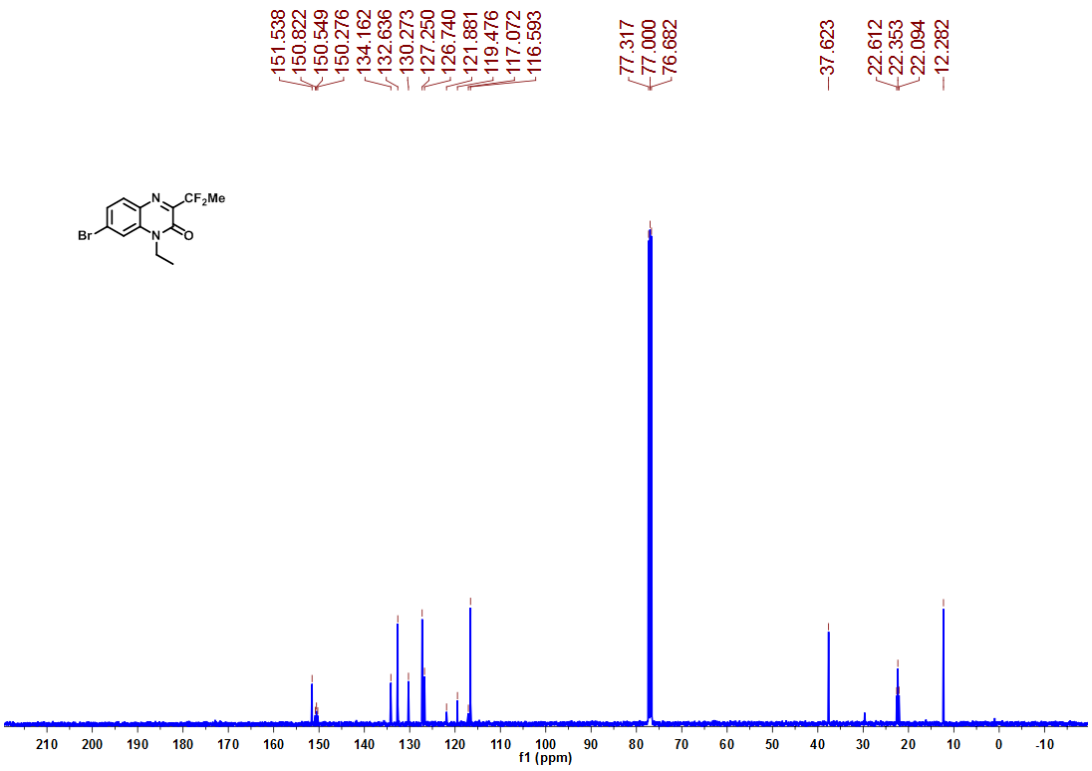
3i-^{19}F NMR (471 MHz, $CDCl_3$)



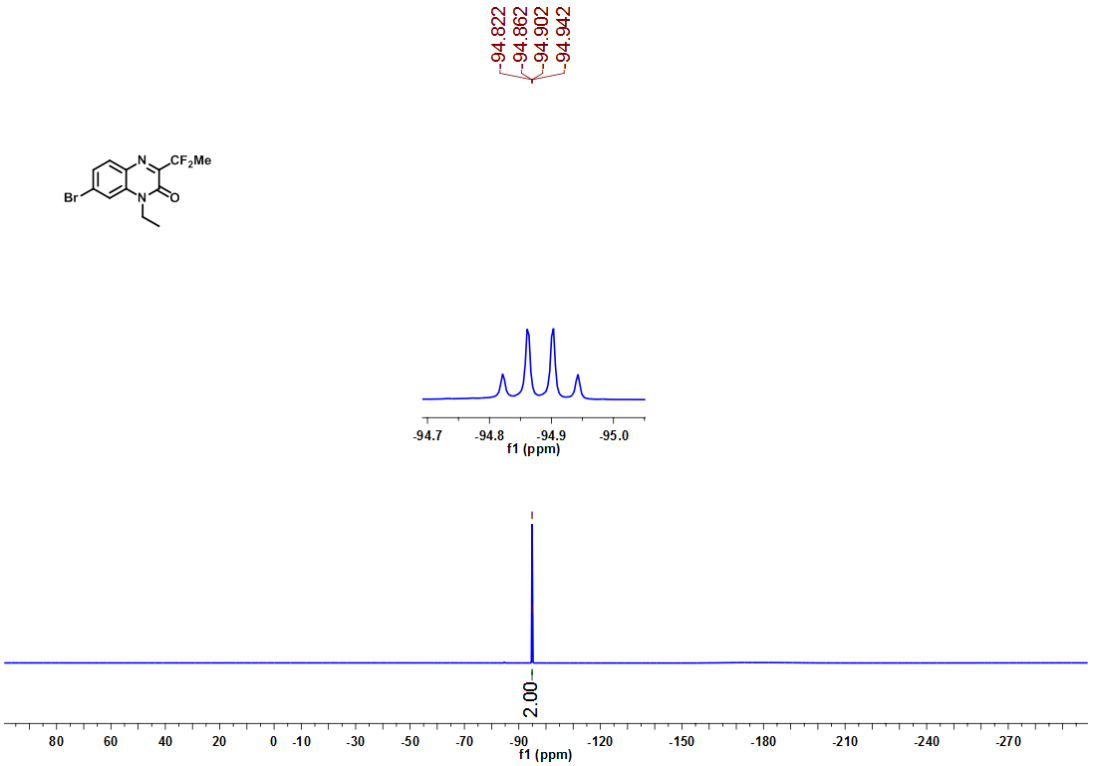
3j-^{1}H NMR (400 MHz, $CDCl_3$)



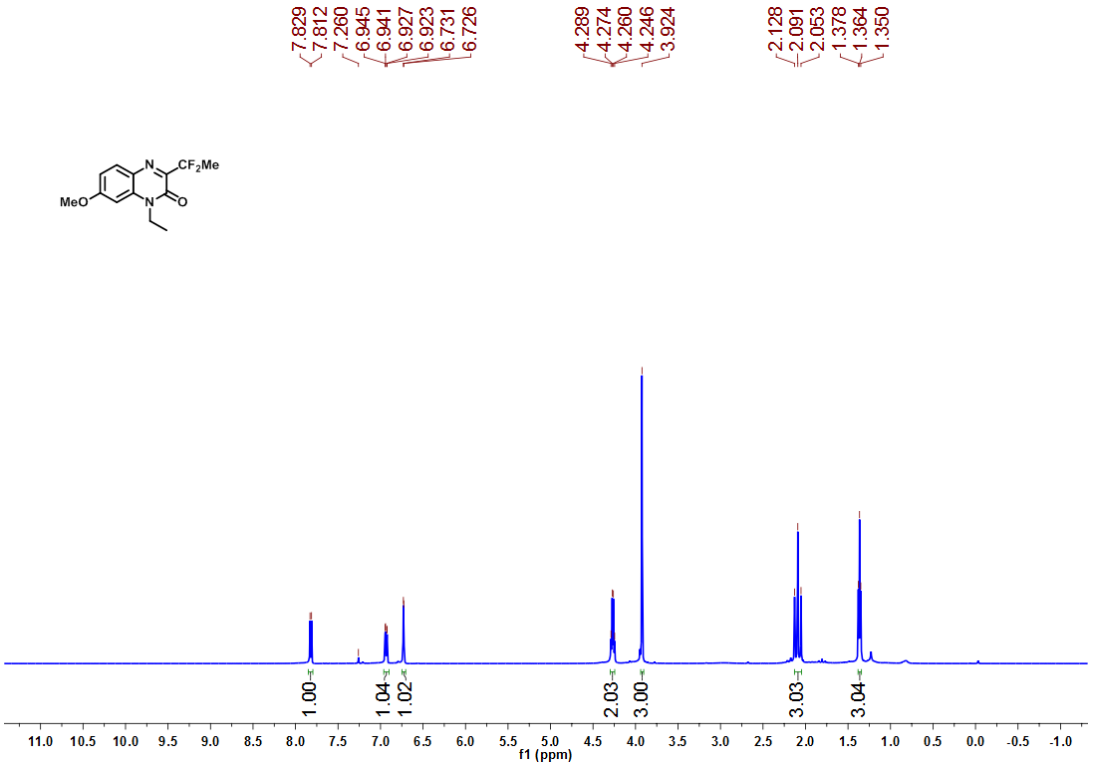
3j-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



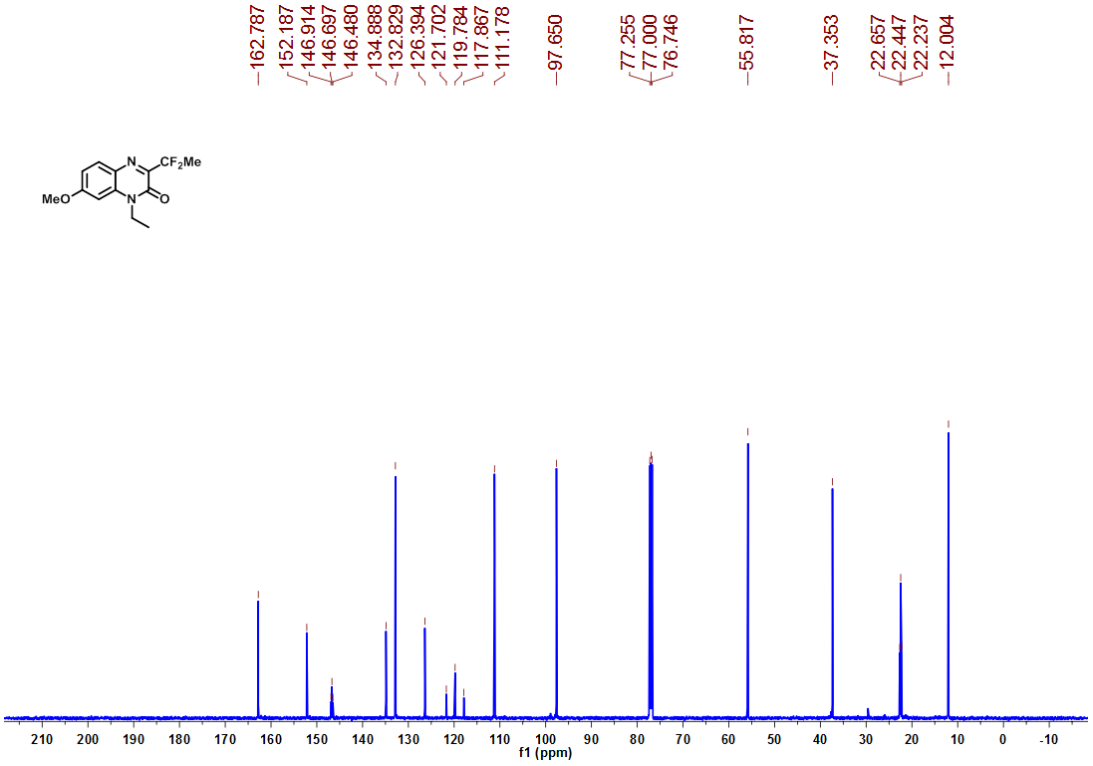
3j-^{19}F NMR (471 MHz, $CDCl_3$)



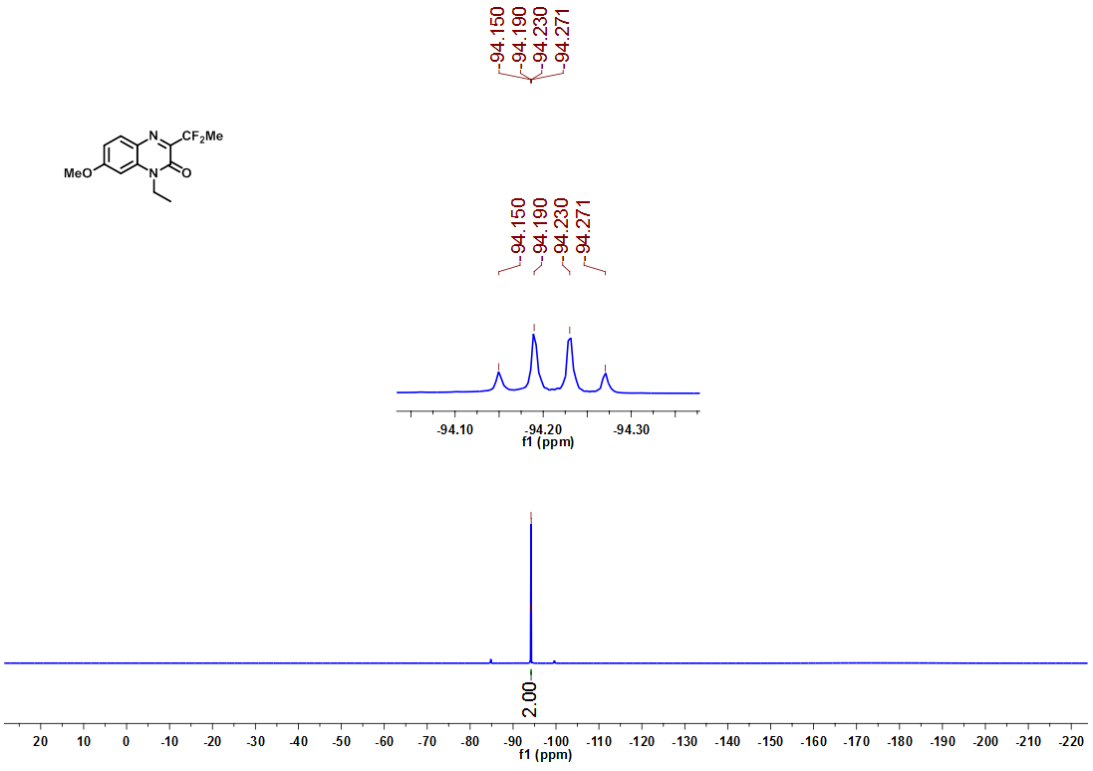
3k-^{1}H NMR (500 MHz, $CDCl_3$)



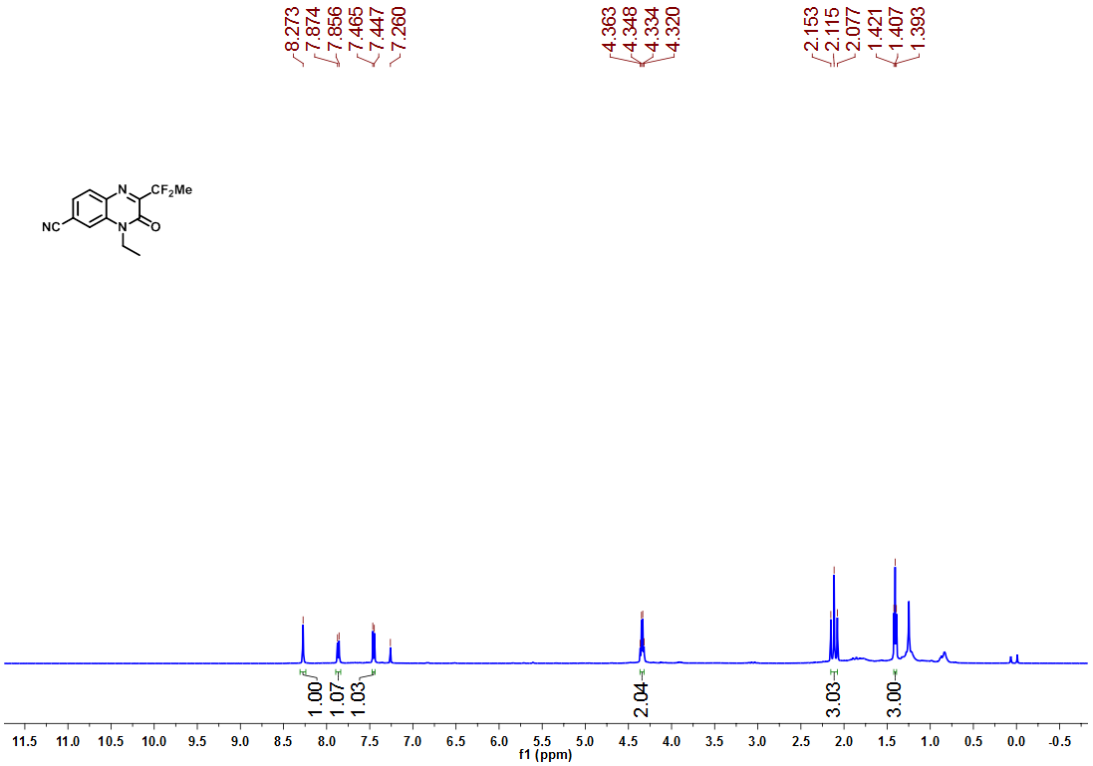
3k-$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)



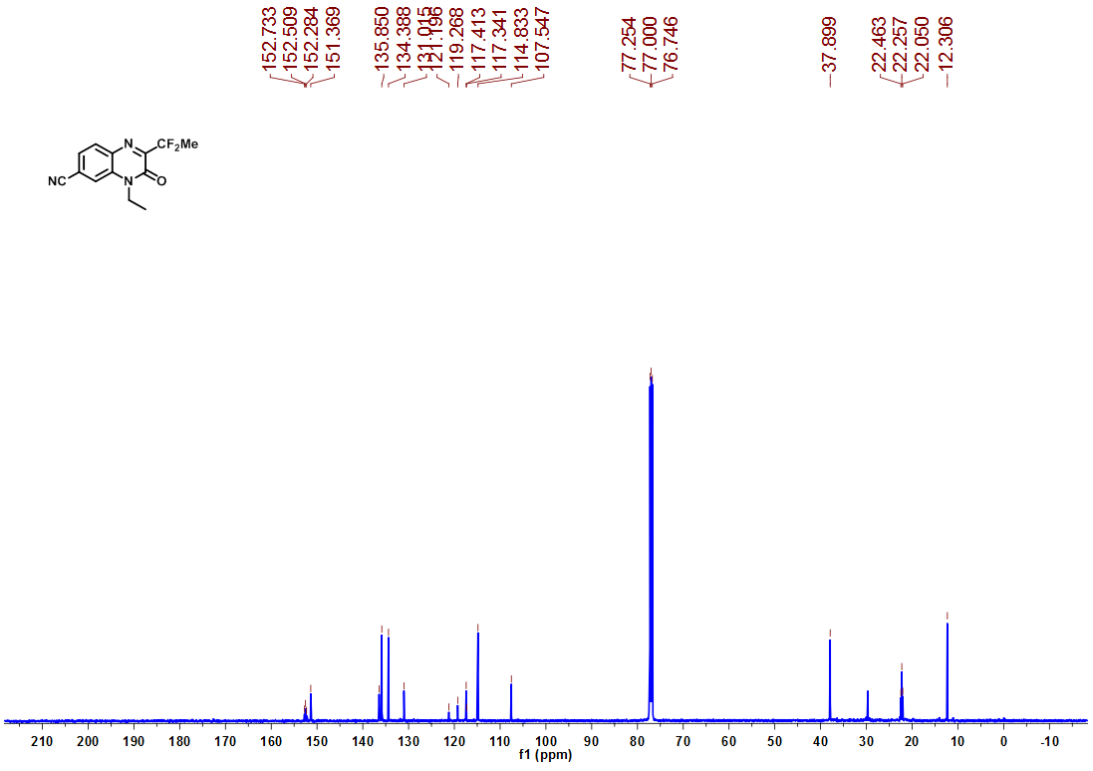
3k-^{19}F NMR (471 MHz, $CDCl_3$)



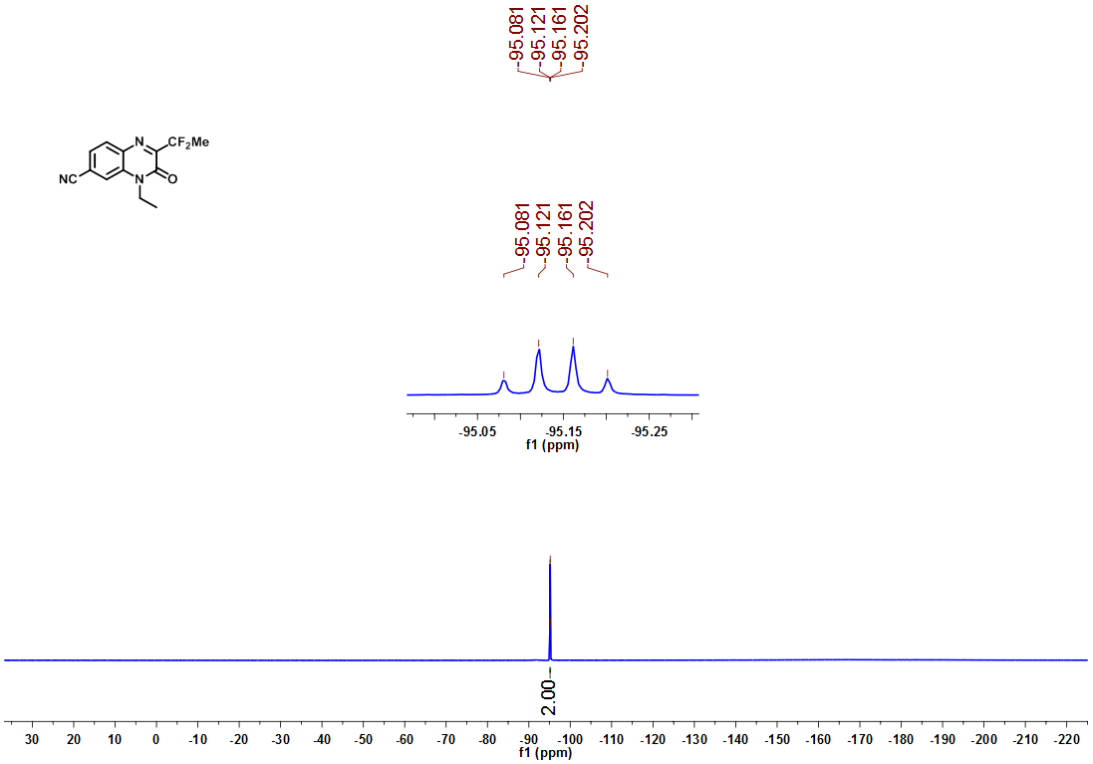
3l-^{1}H NMR (500 MHz, $CDCl_3$)



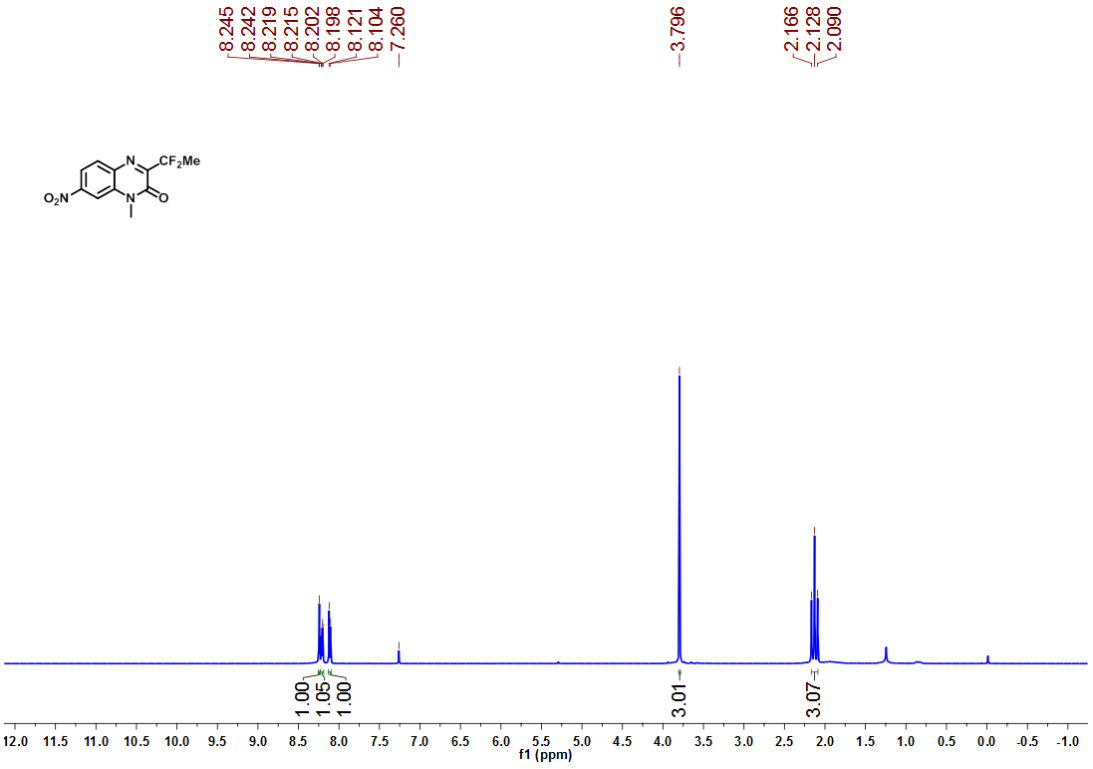
3l-^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)



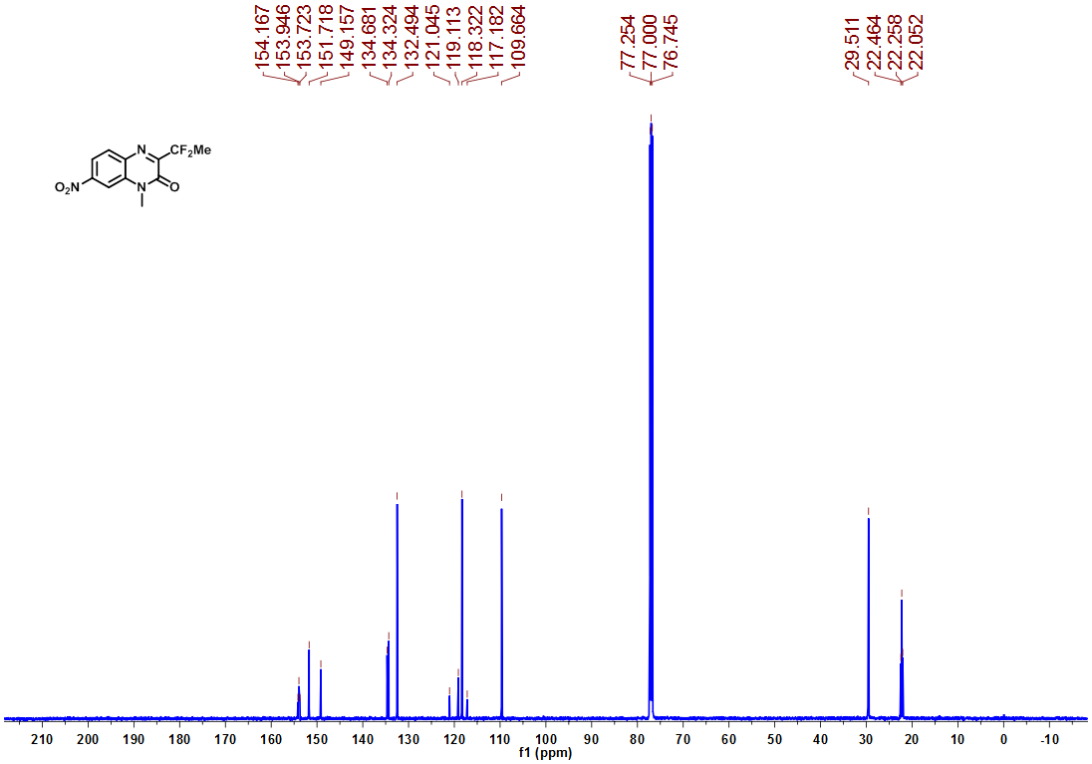
3l-^{19}F NMR (471 MHz, $CDCl_3$)



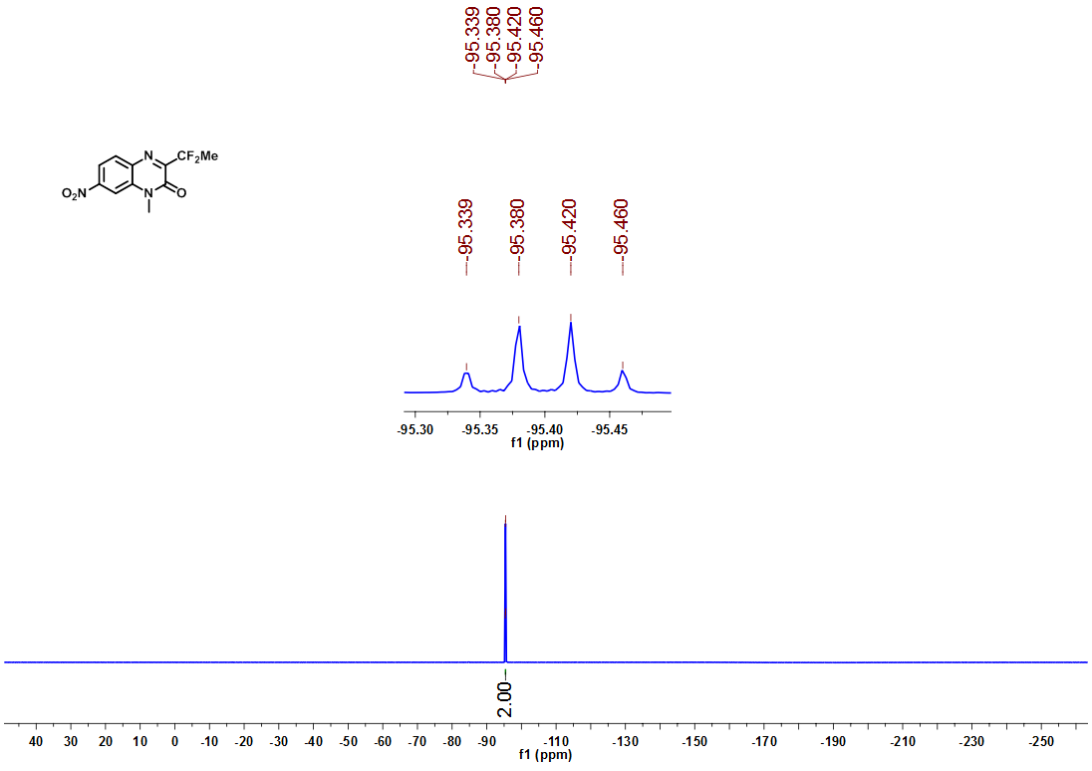
3m-^{1}H NMR (500 MHz, $CDCl_3$)



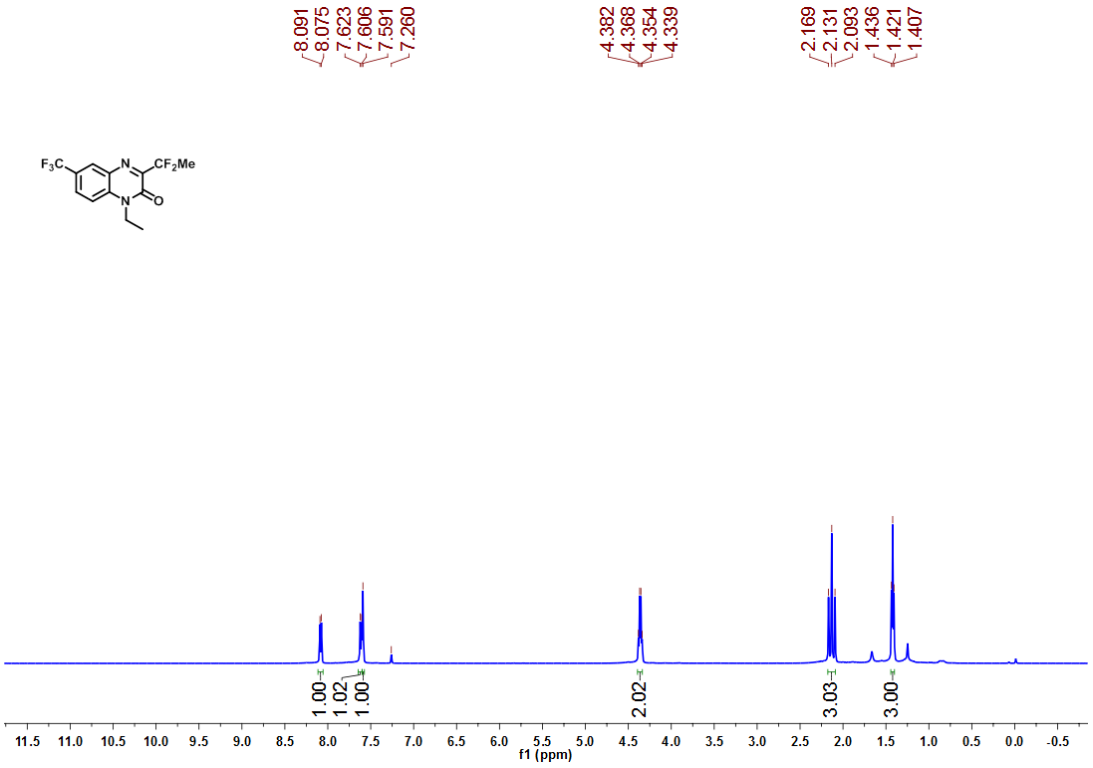
3m-$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$)



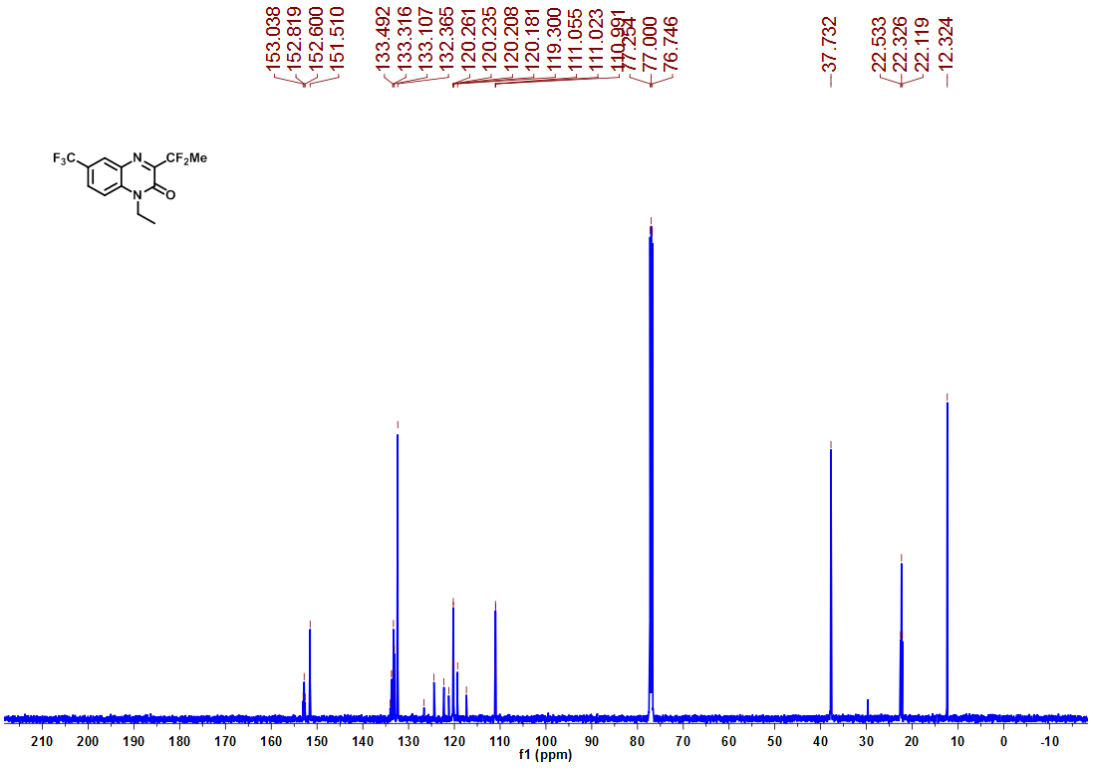
3m-^{19}F NMR (471 MHz, $CDCl_3$)



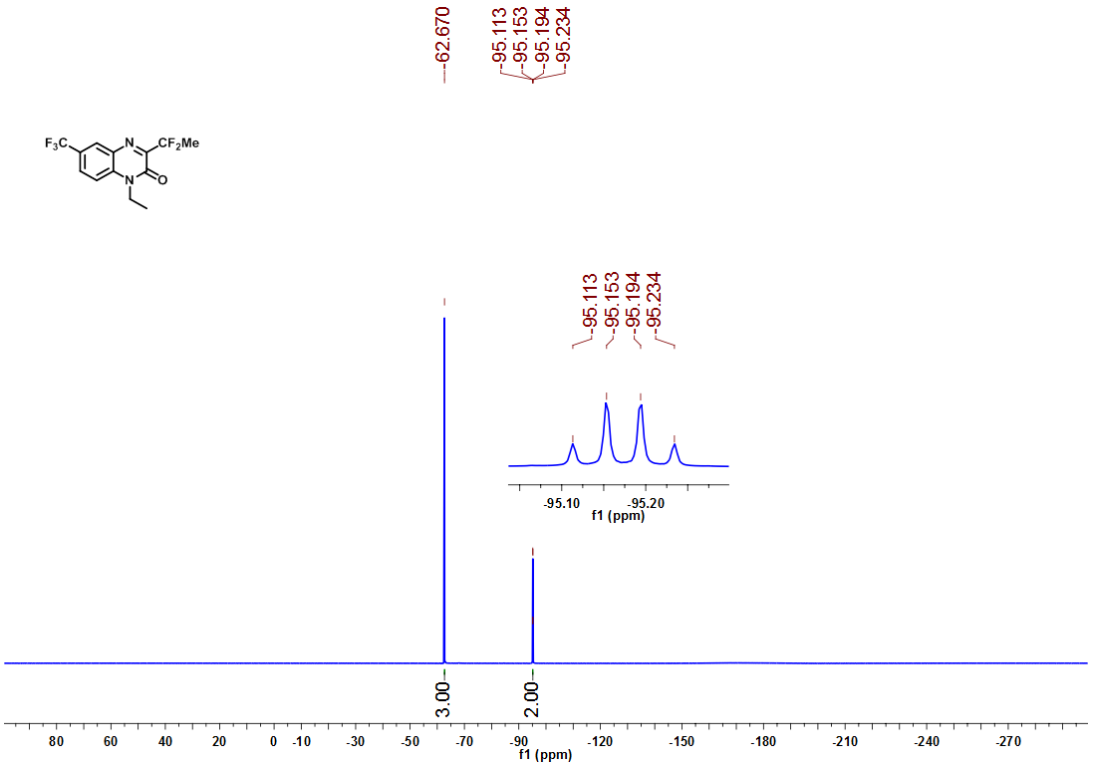
3n-^{1}H NMR (500 MHz, $CDCl_3$)



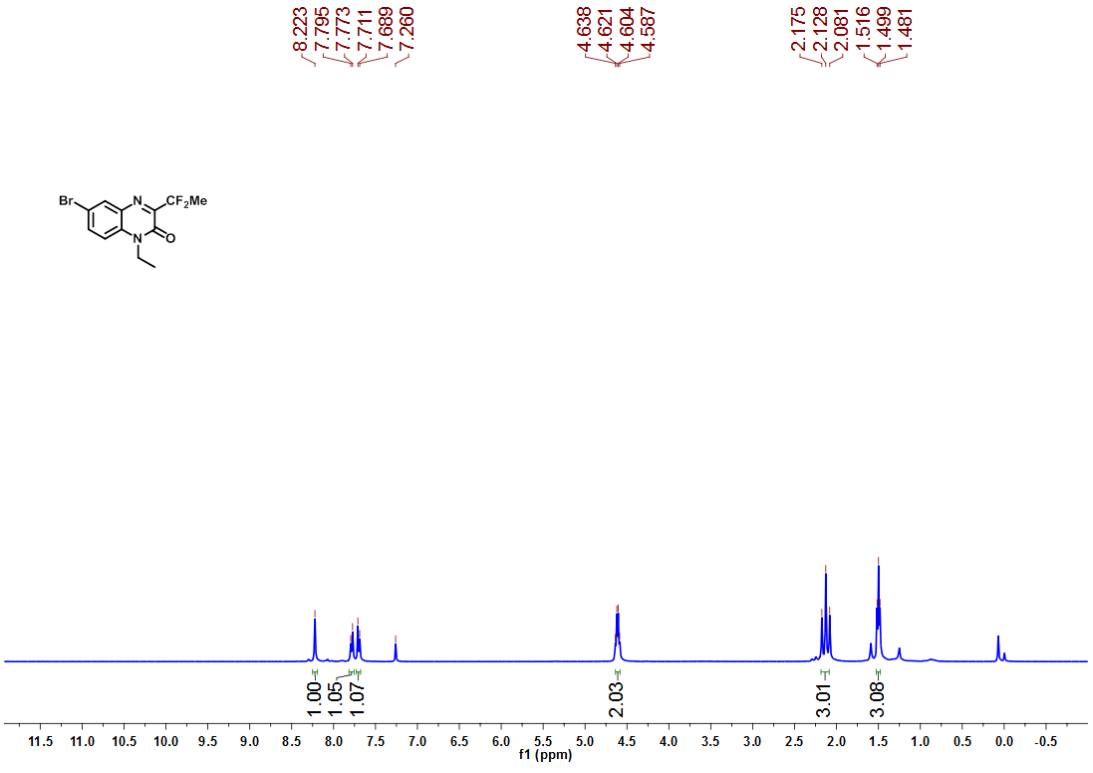
3n-^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$)



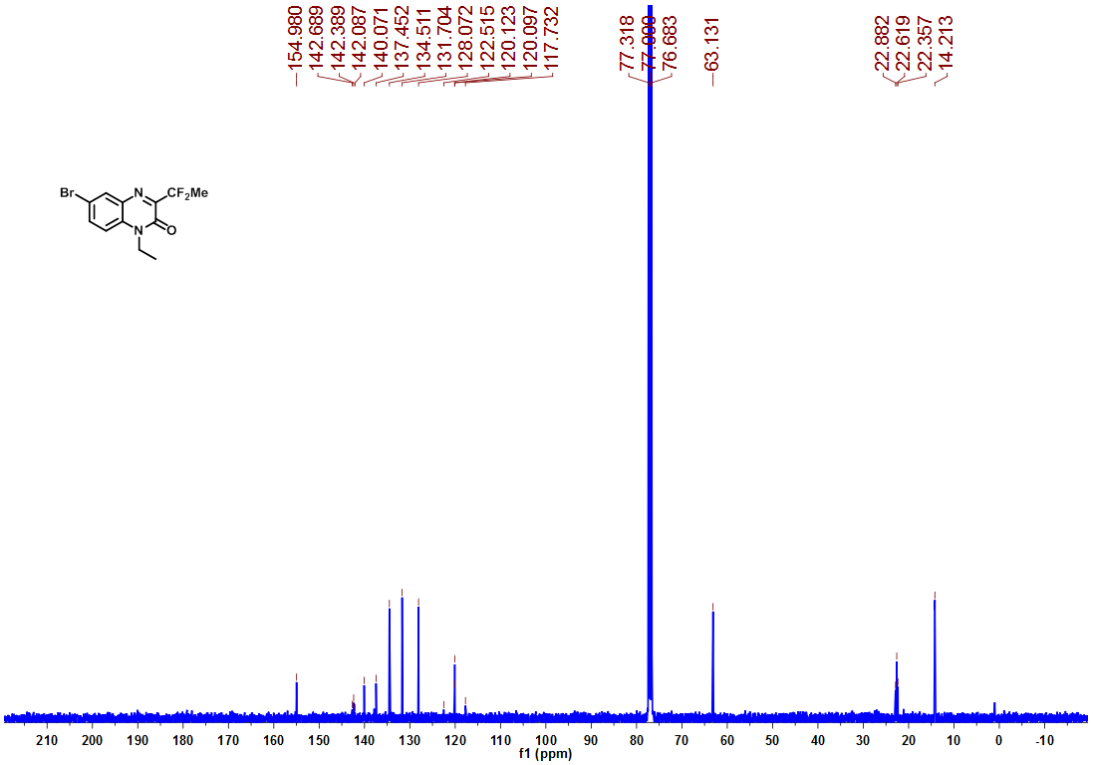
3n-^{19}F NMR (471 MHz, $CDCl_3$)



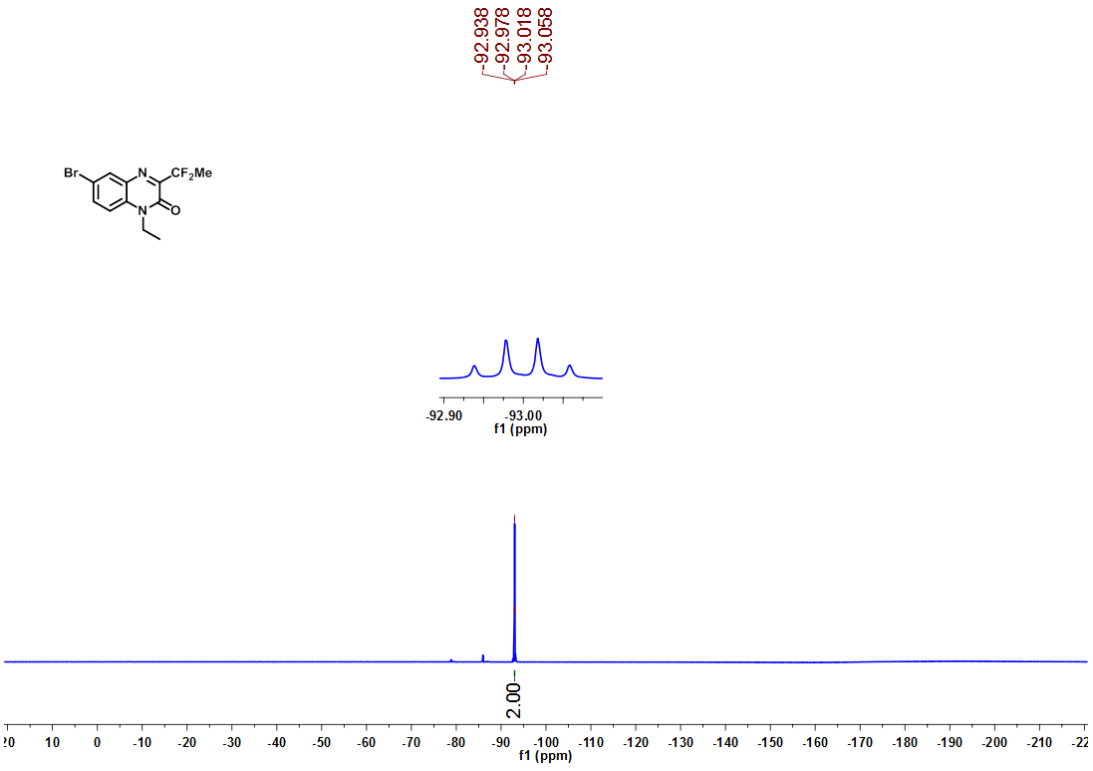
3o-^{1}H NMR (400 MHz, $CDCl_3$)



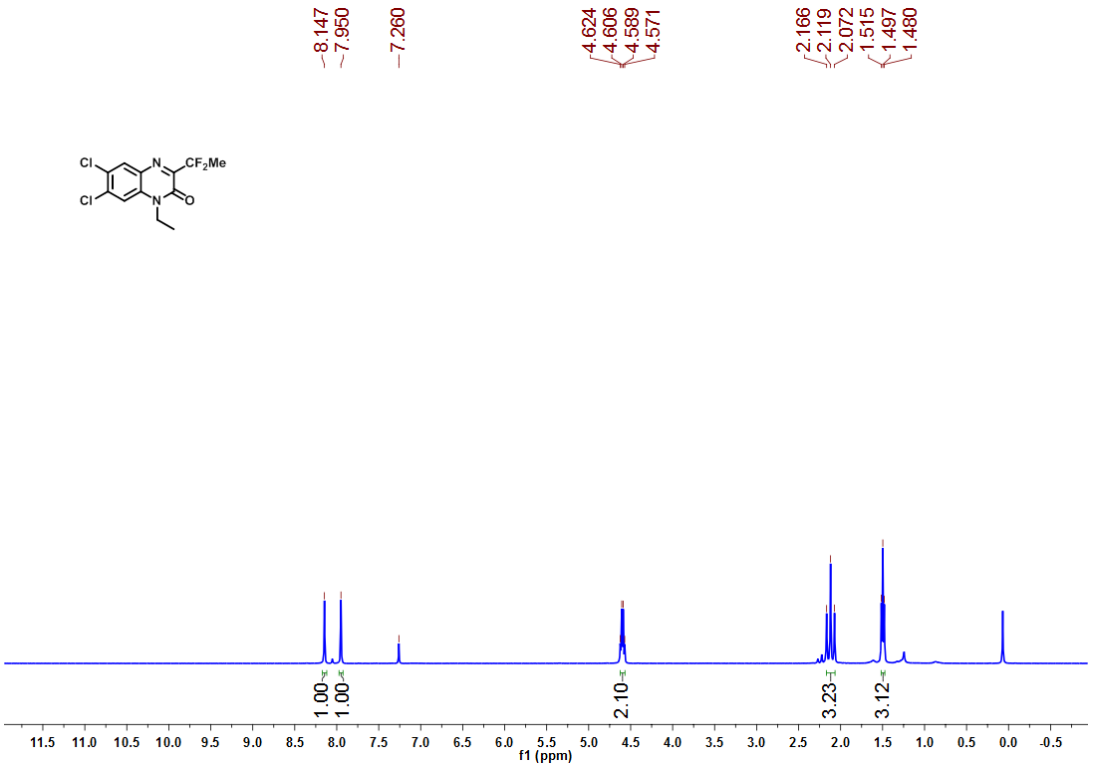
3o-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



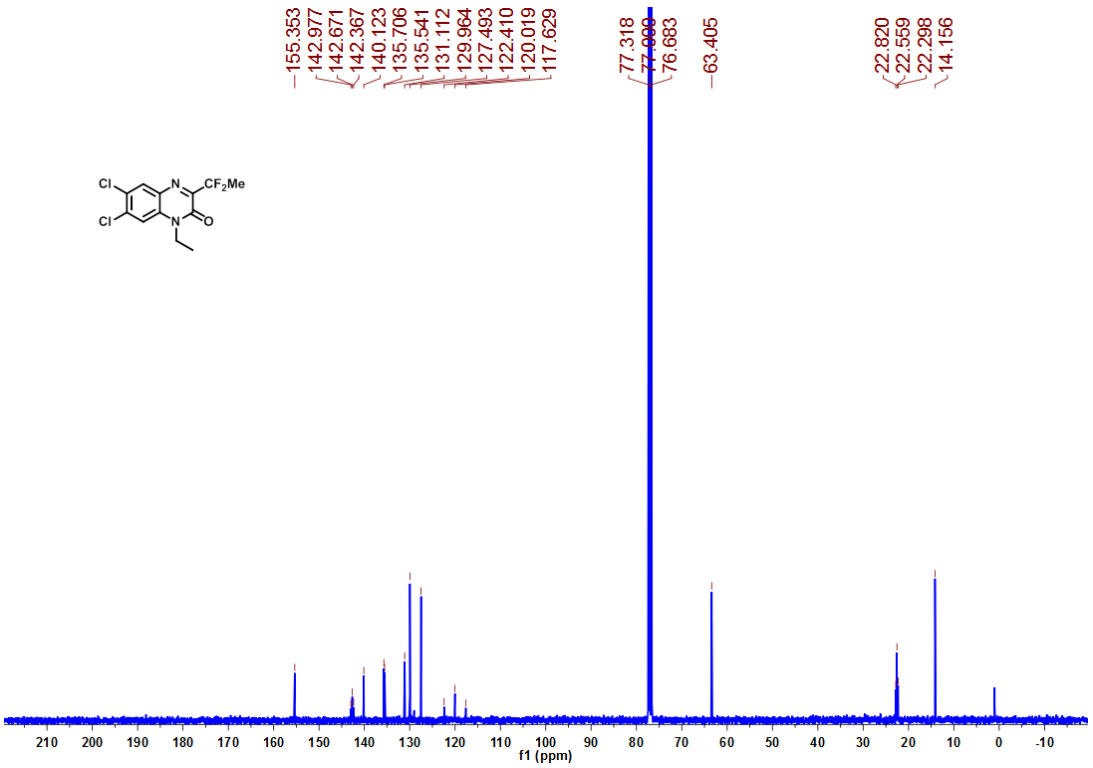
3o-^{19}F NMR (471 MHz, $CDCl_3$)



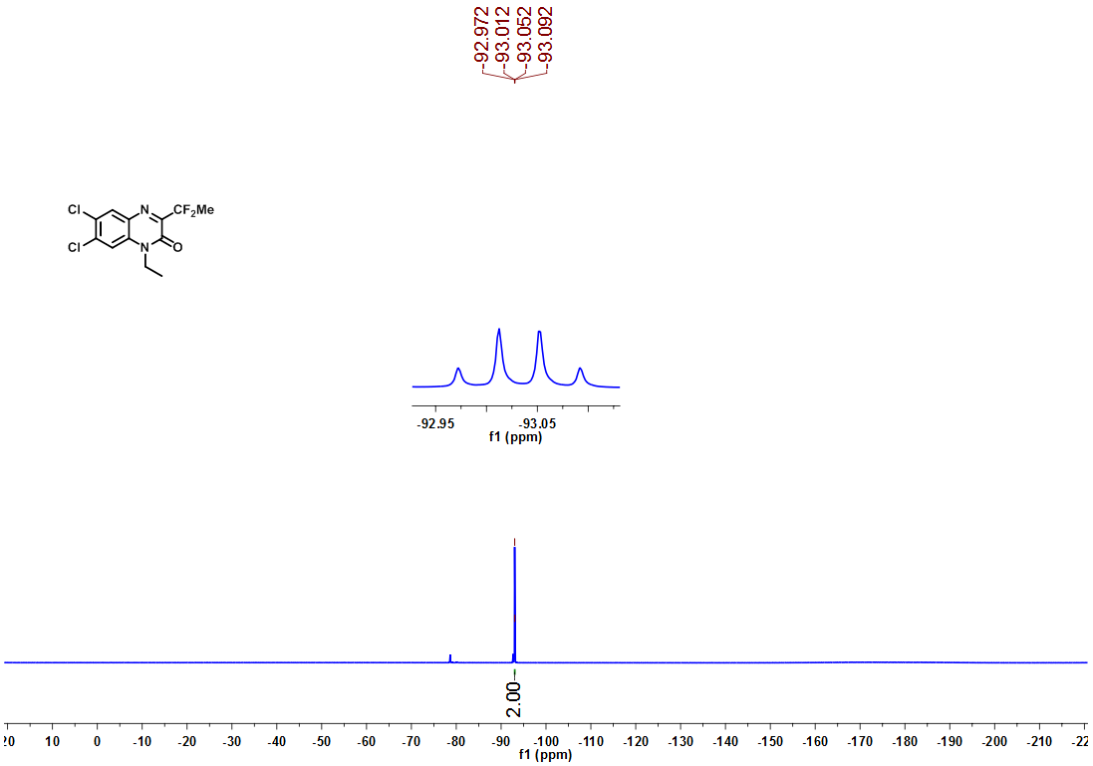
3p-^{1}H NMR (400 MHz, $CDCl_3$)



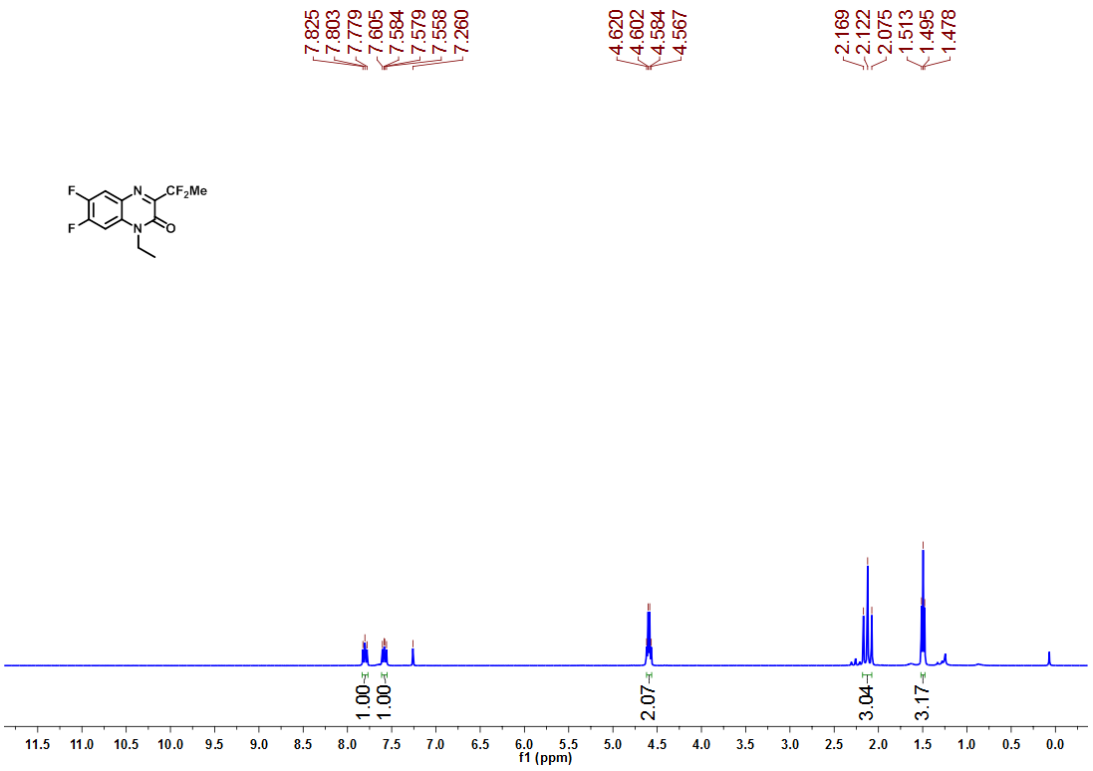
3p-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



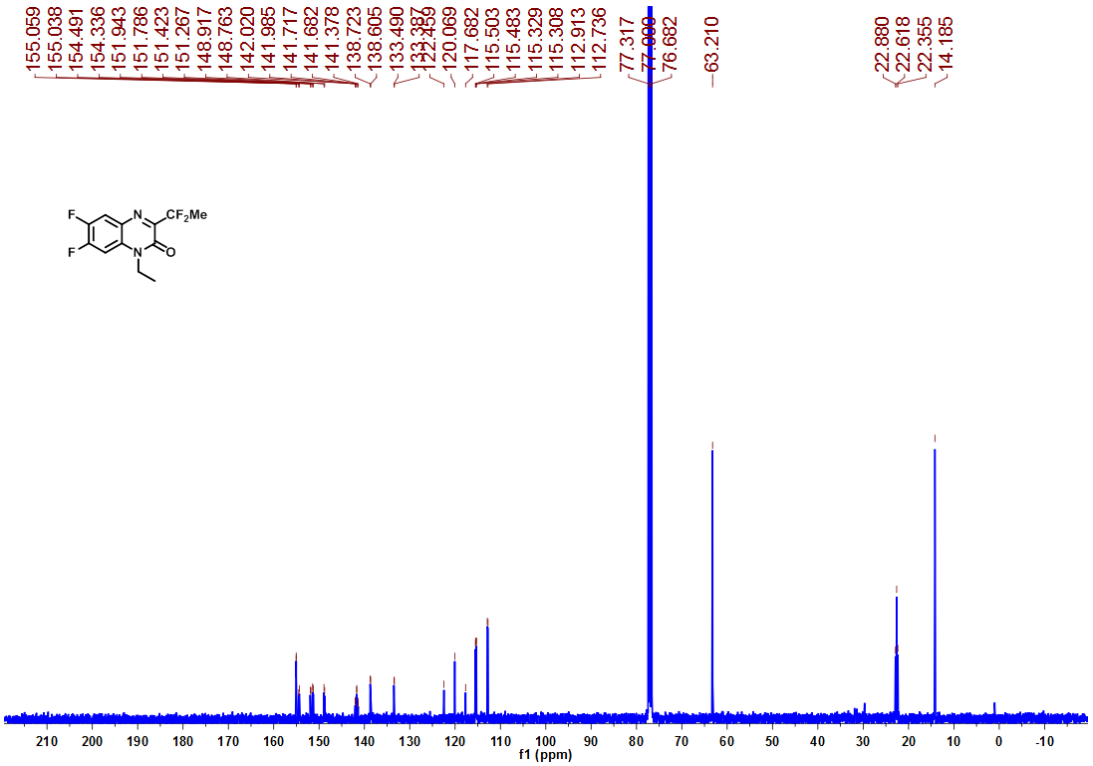
3p-^{19}F NMR (471 MHz, $CDCl_3$)



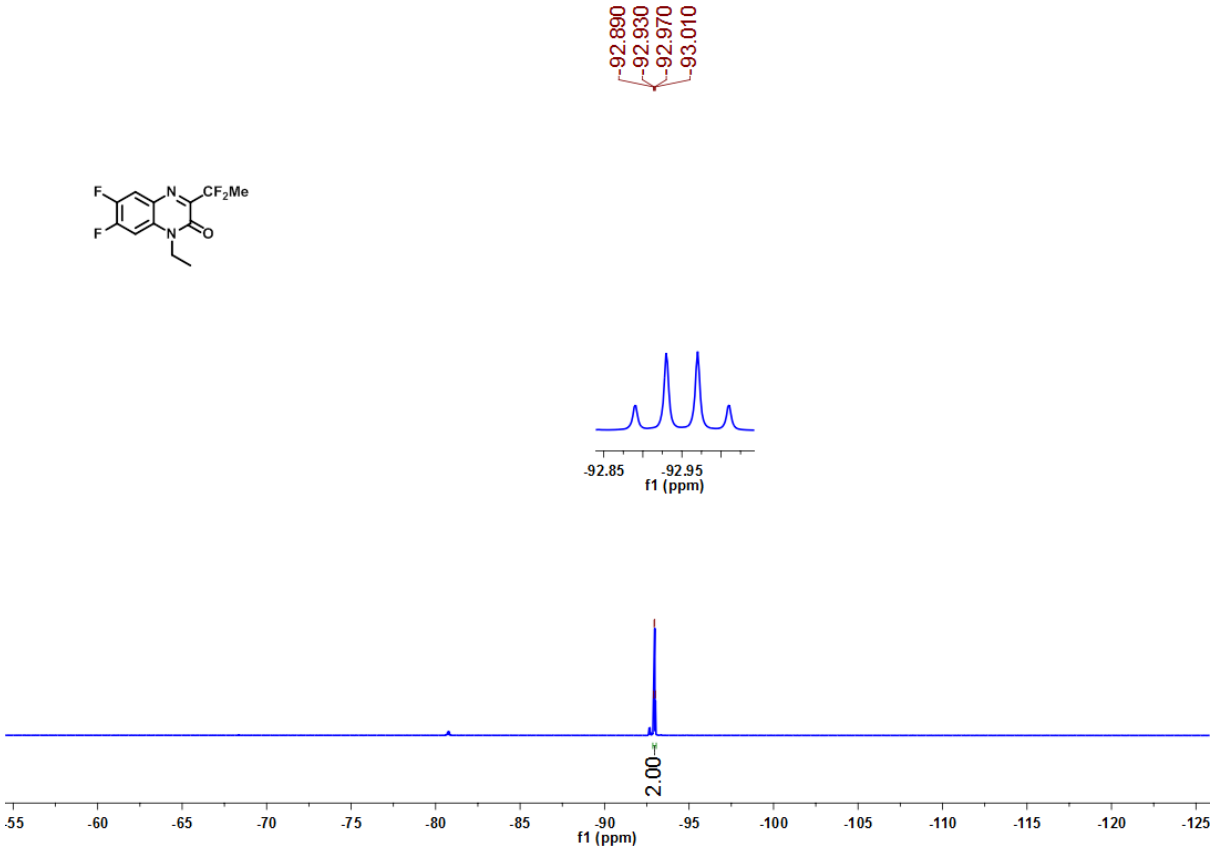
3q-^{1}H NMR (400 MHz, $CDCl_3$)



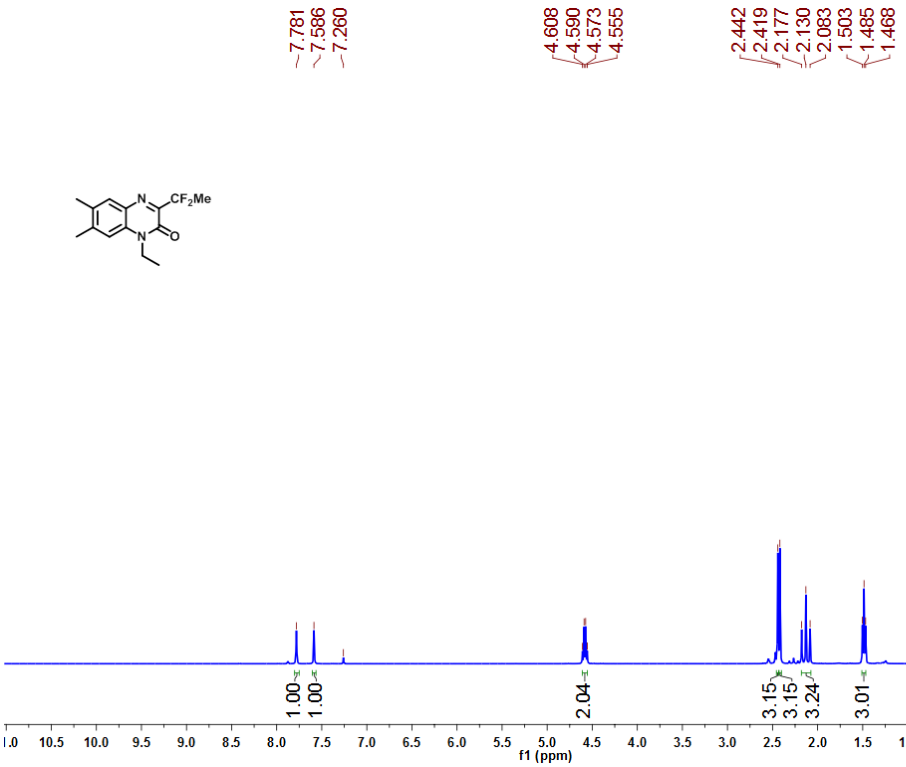
3q-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



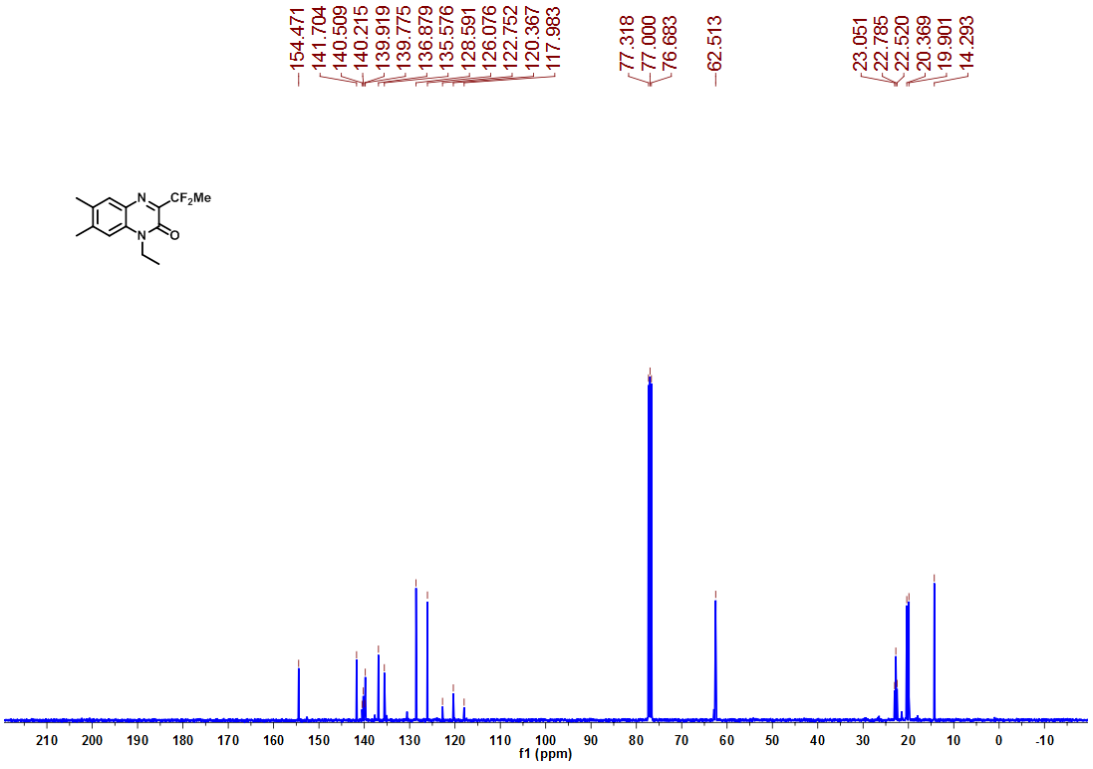
3q-^{19}F NMR (471 MHz, $CDCl_3$)



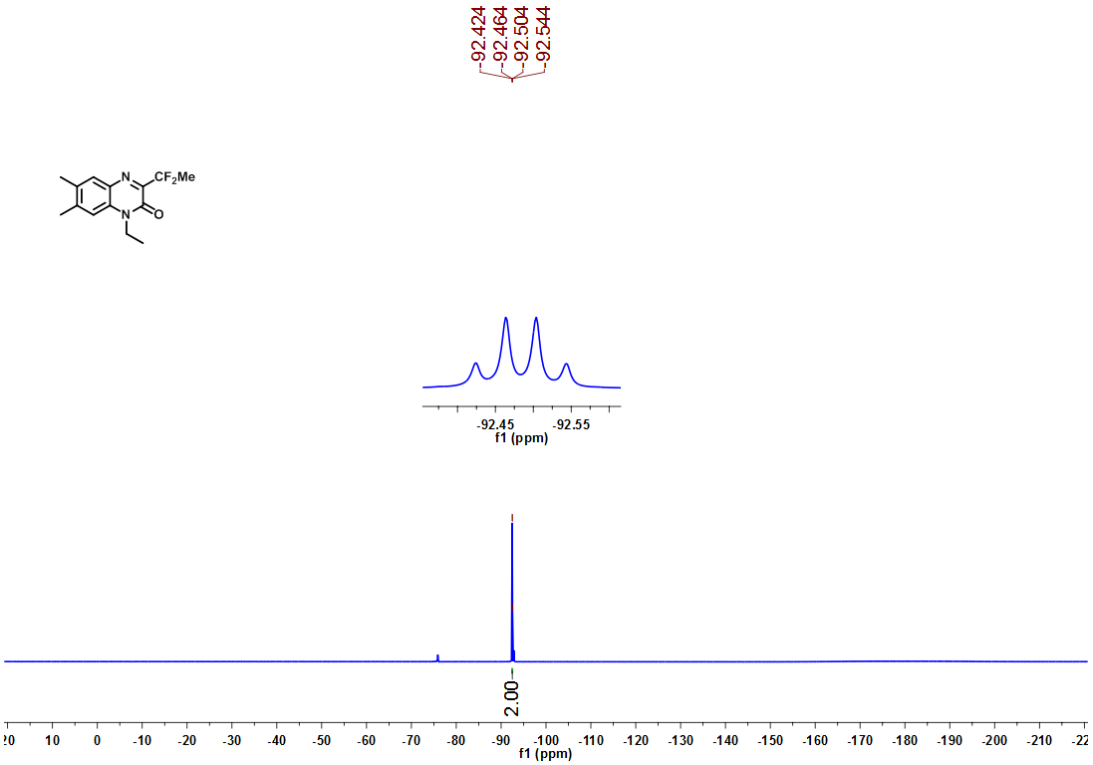
3r-^{1}H NMR (400 MHz, $CDCl_3$)



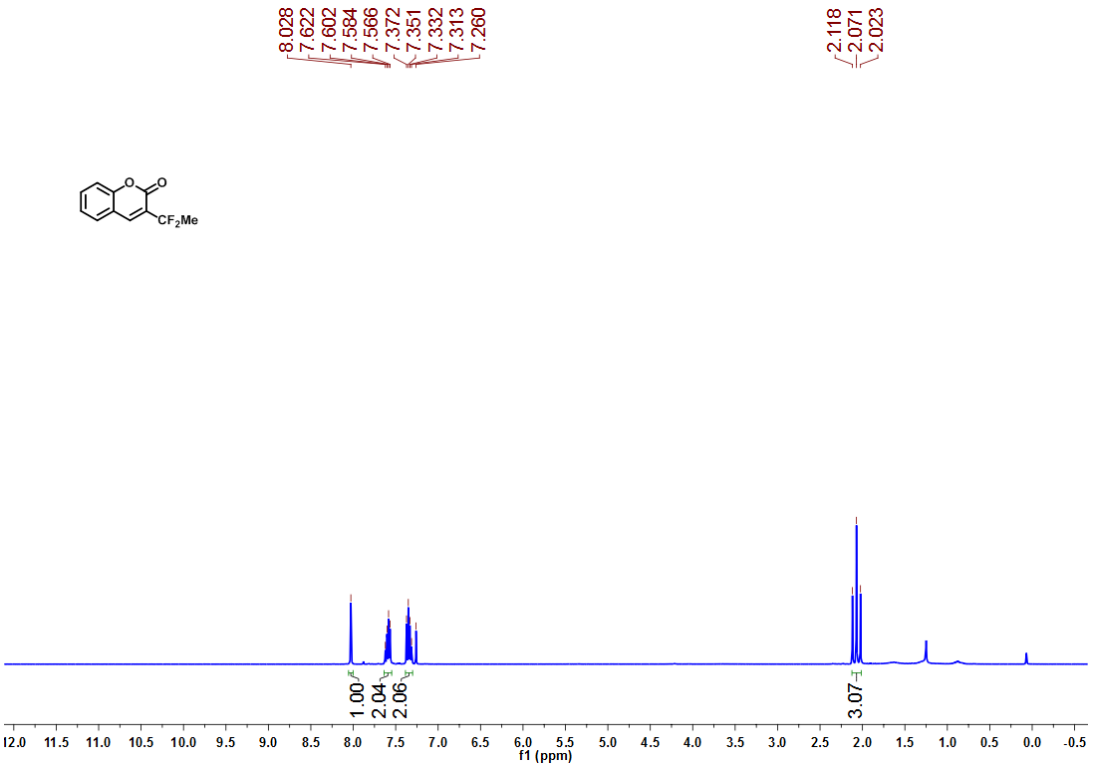
3r-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



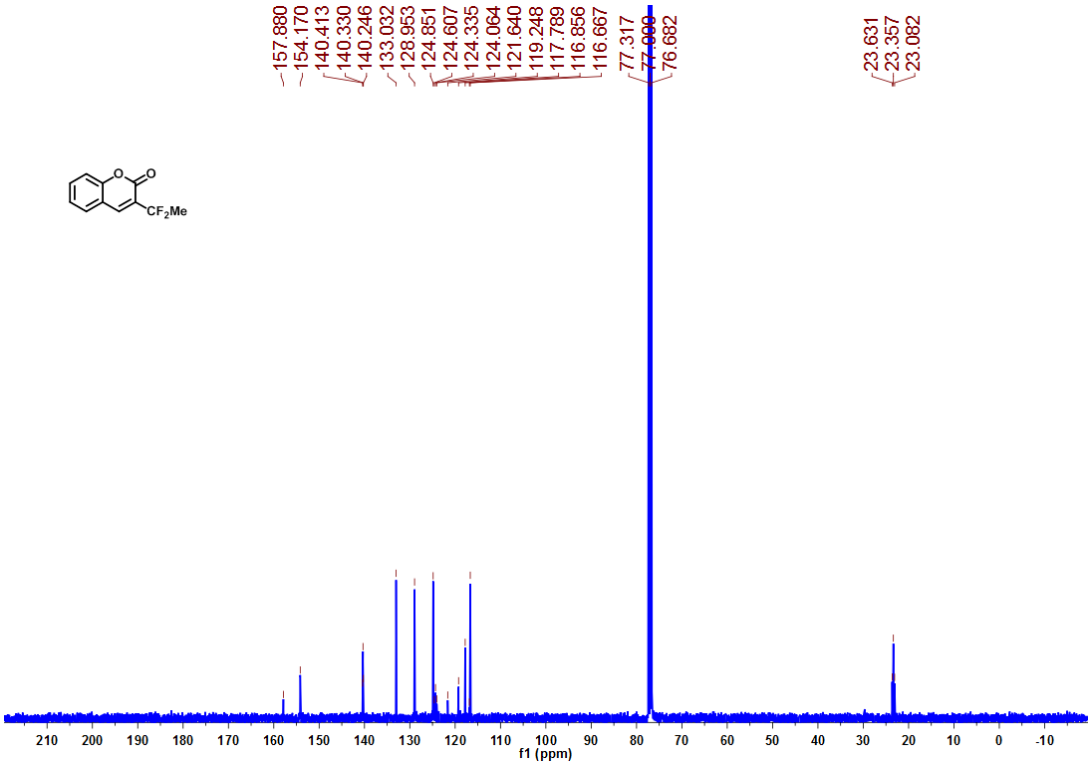
3r-^{19}F NMR (471 MHz, $CDCl_3$)



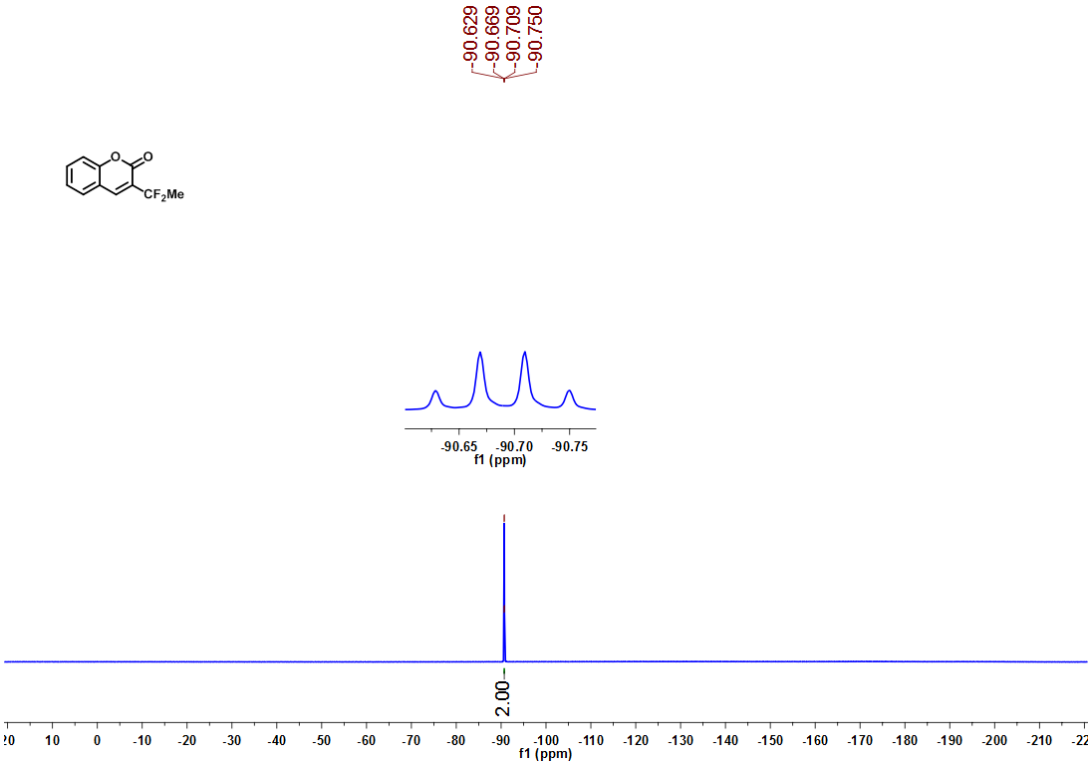
3s-^{1}H NMR (400 MHz, $CDCl_3$)



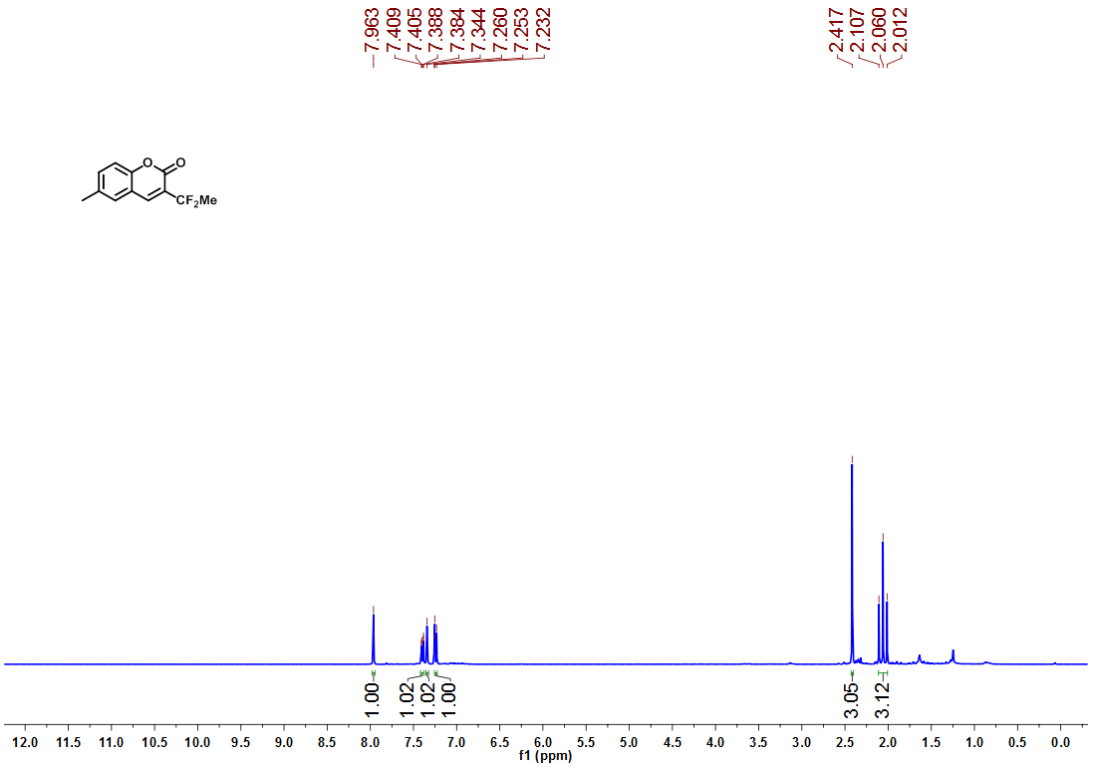
3s-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



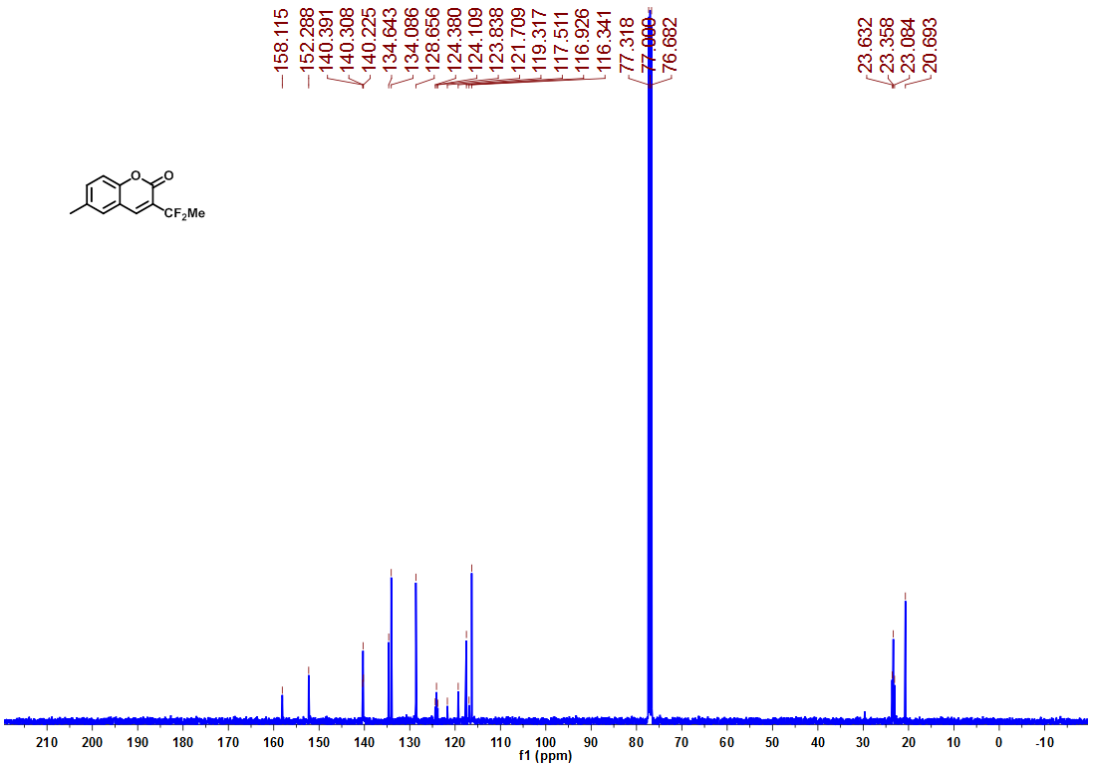
3s-^{19}F NMR (471 MHz, $CDCl_3$)



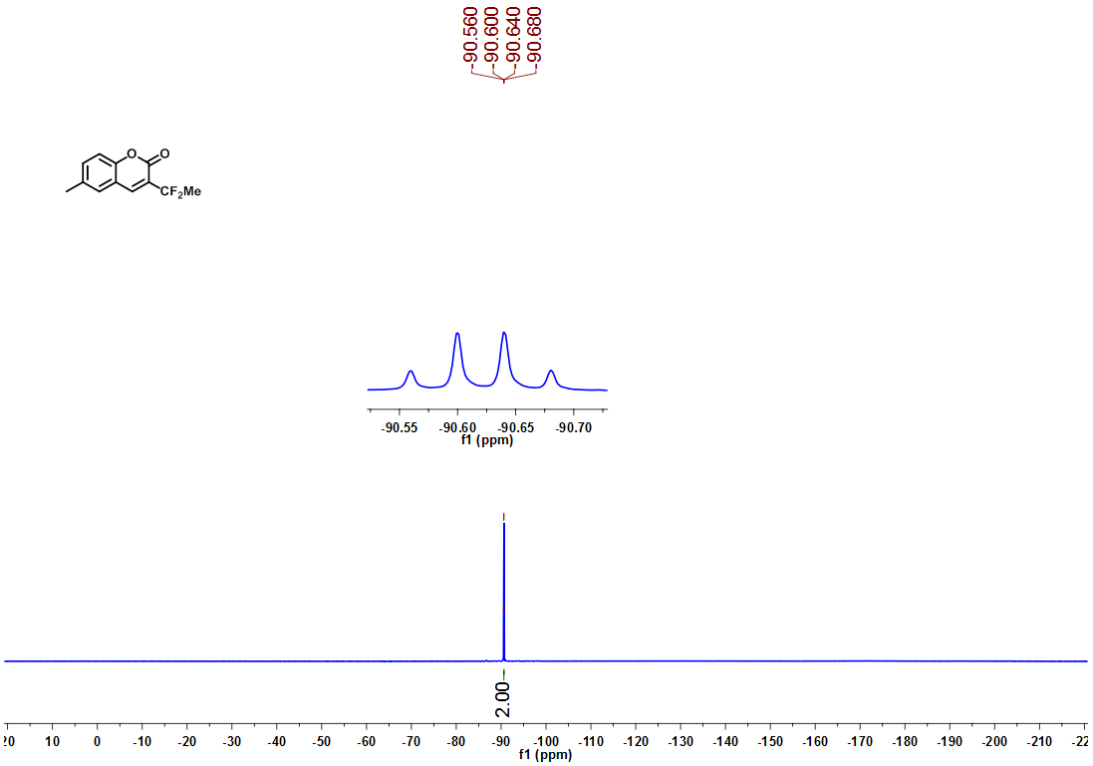
3t-^{1}H NMR (400 MHz, $CDCl_3$)



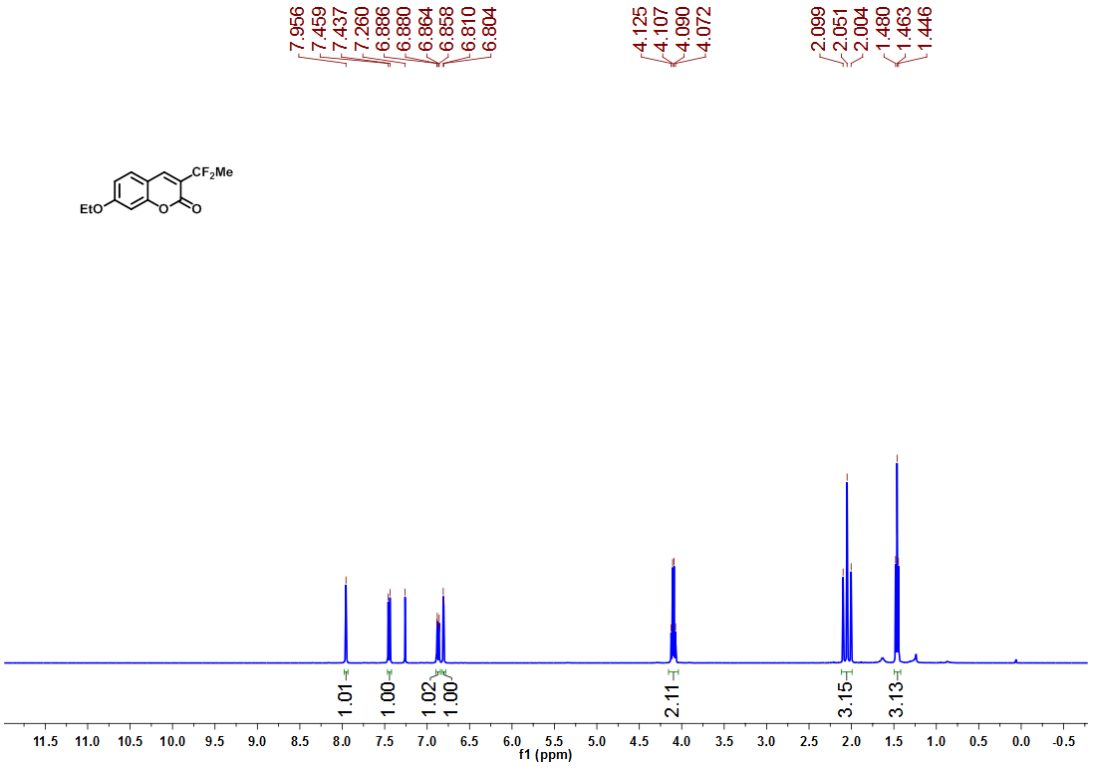
3t-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



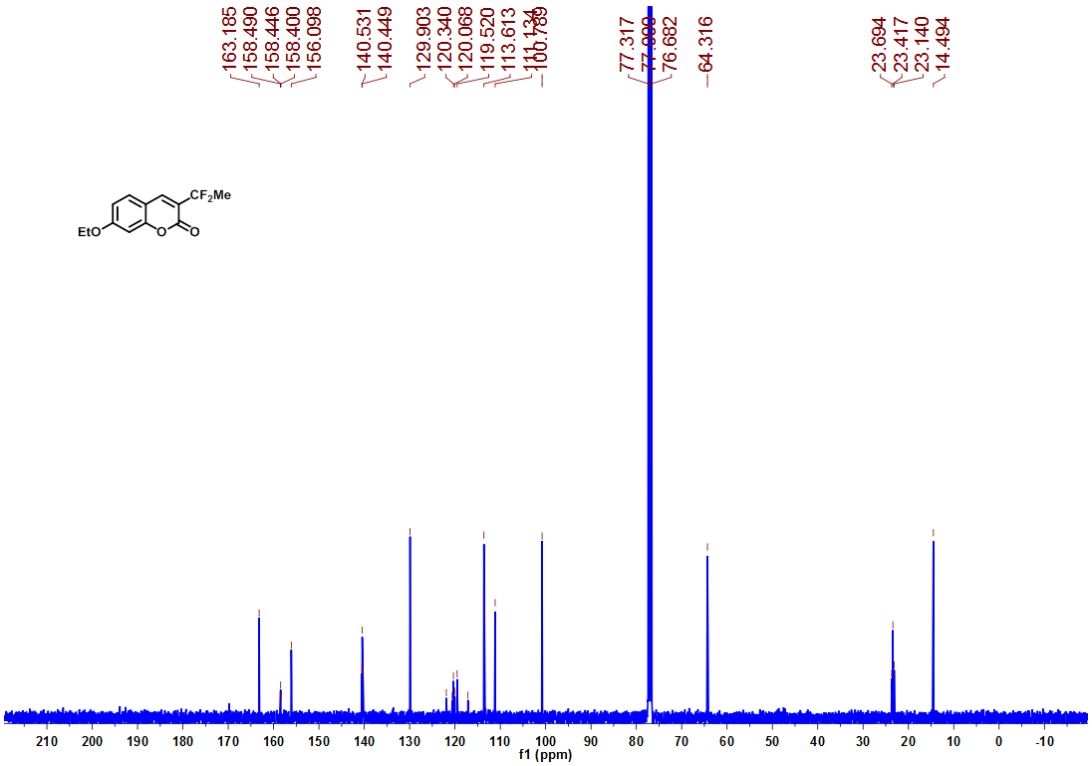
3t-^{19}F NMR (471 MHz, $CDCl_3$)



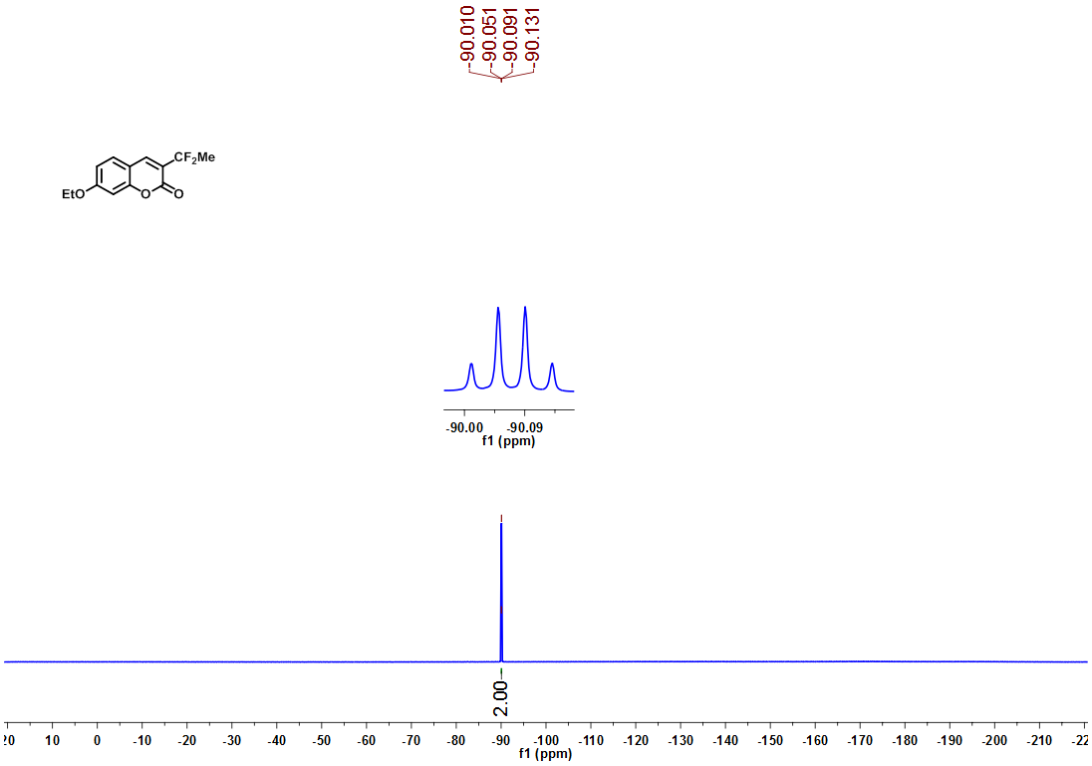
3u-^{1}H NMR (400 MHz, $CDCl_3$)



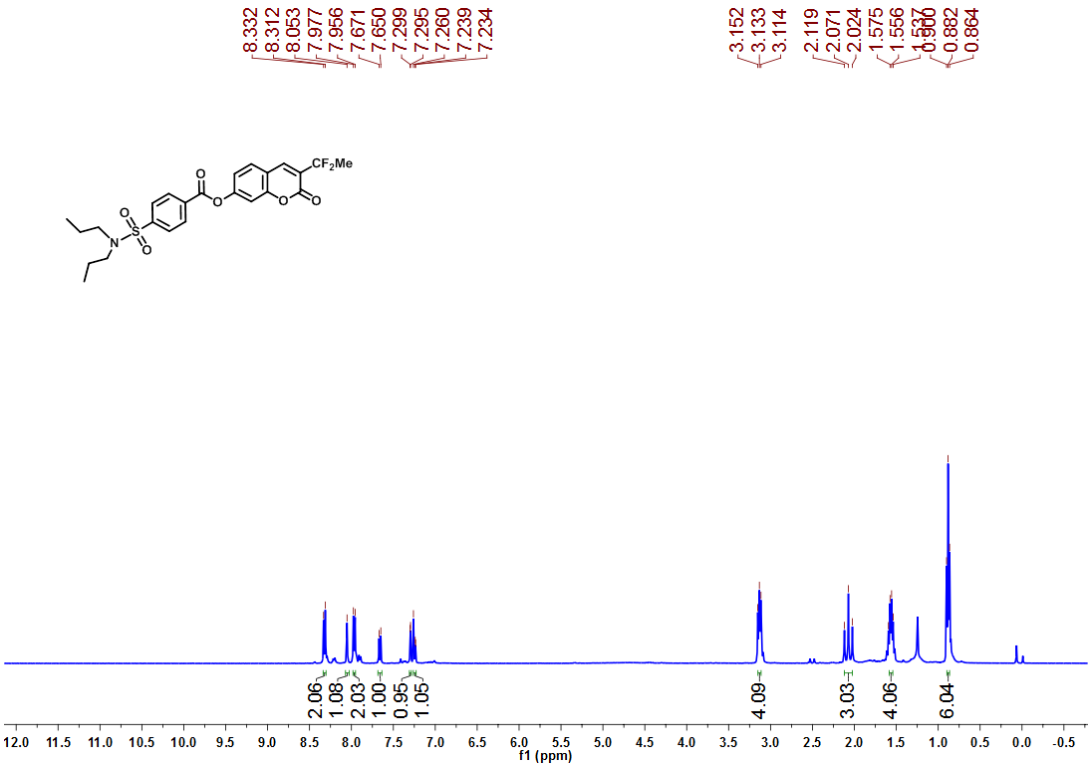
3u-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



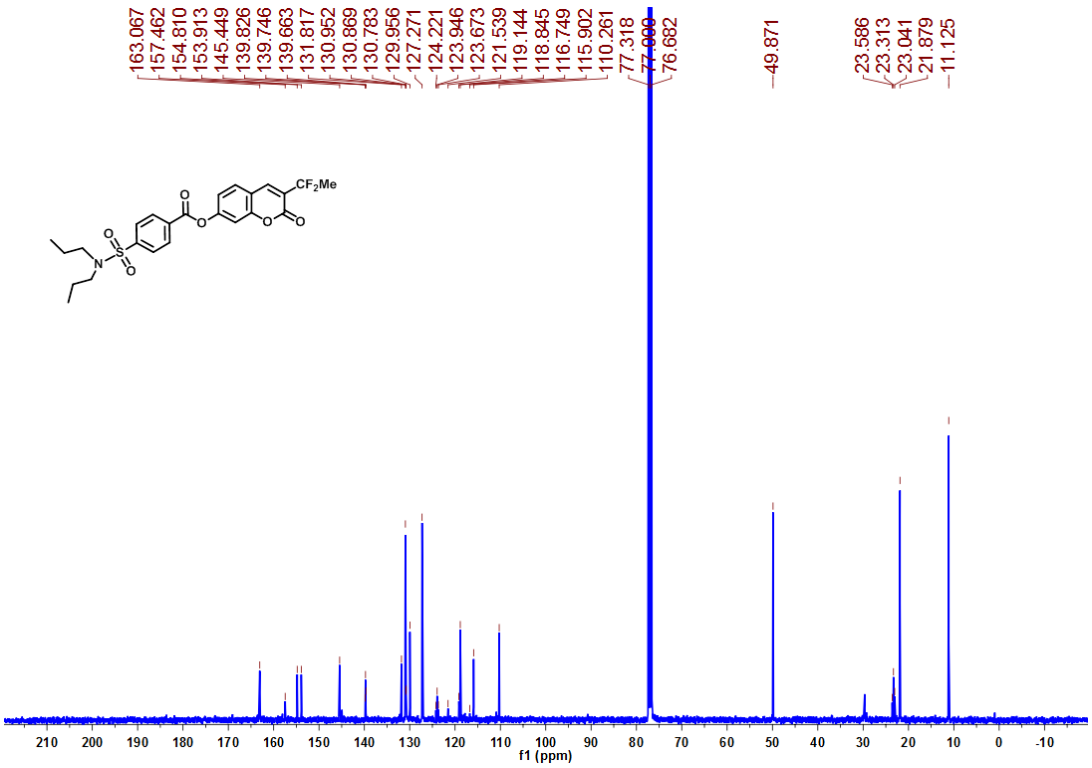
3u-^{19}F NMR (471 MHz, $CDCl_3$)



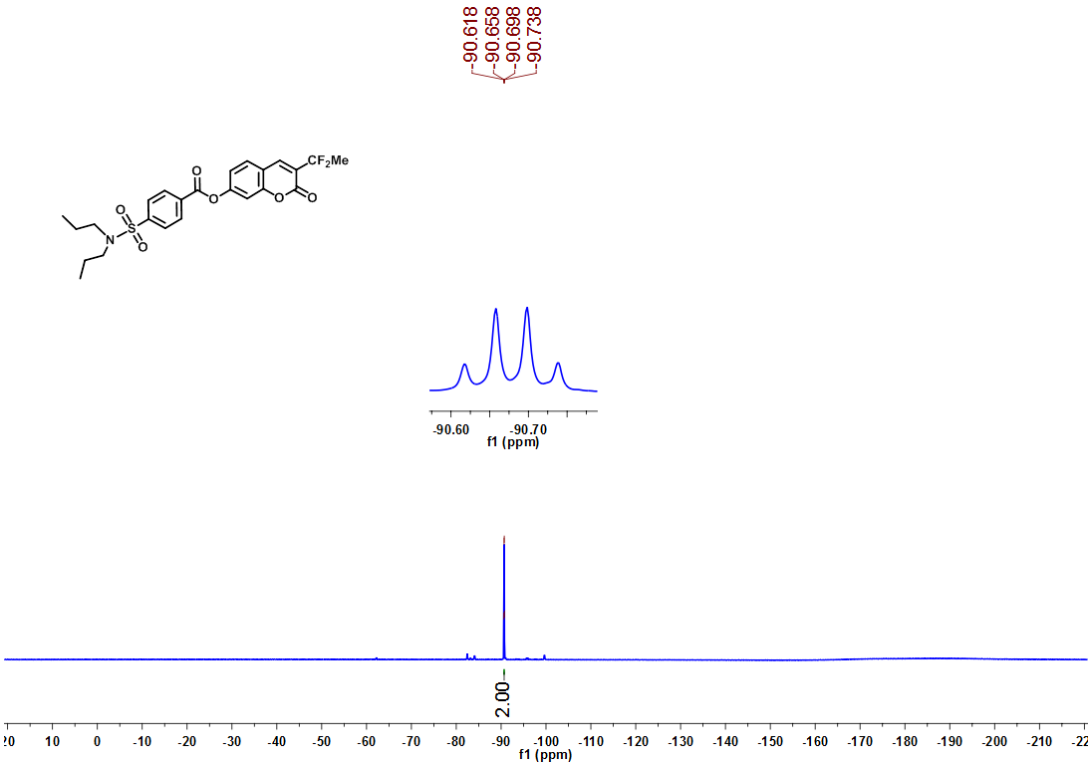
3v-^{1}H NMR (400 MHz, $CDCl_3$)



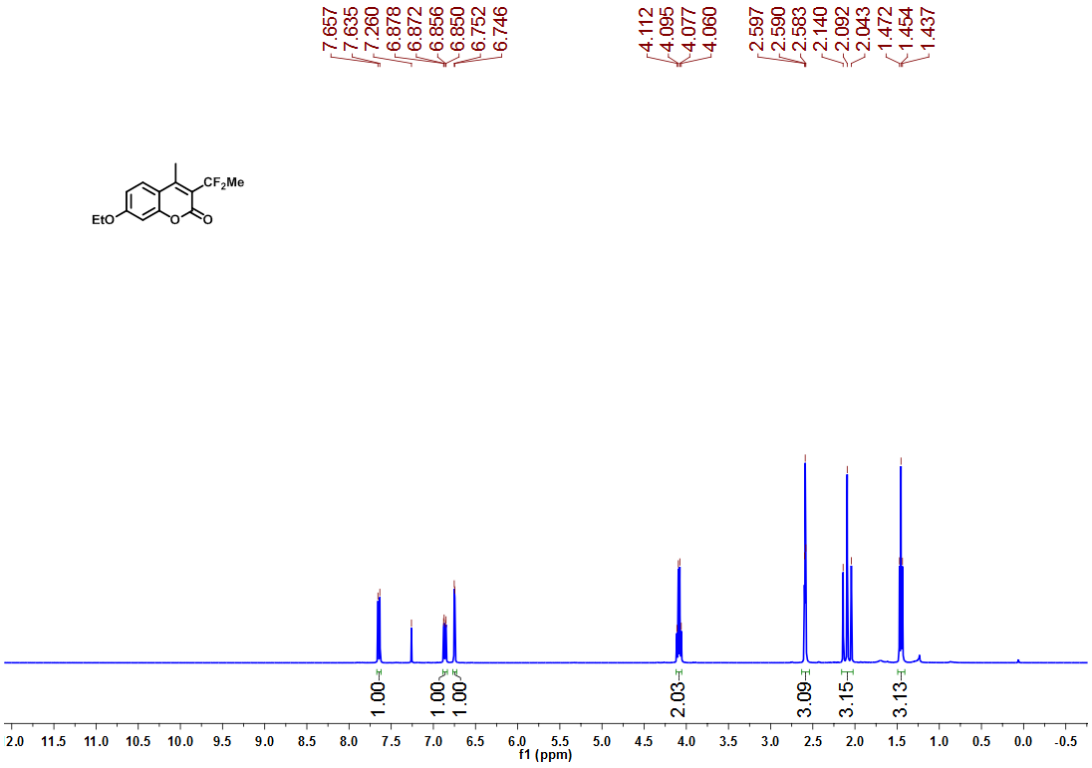
3v-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



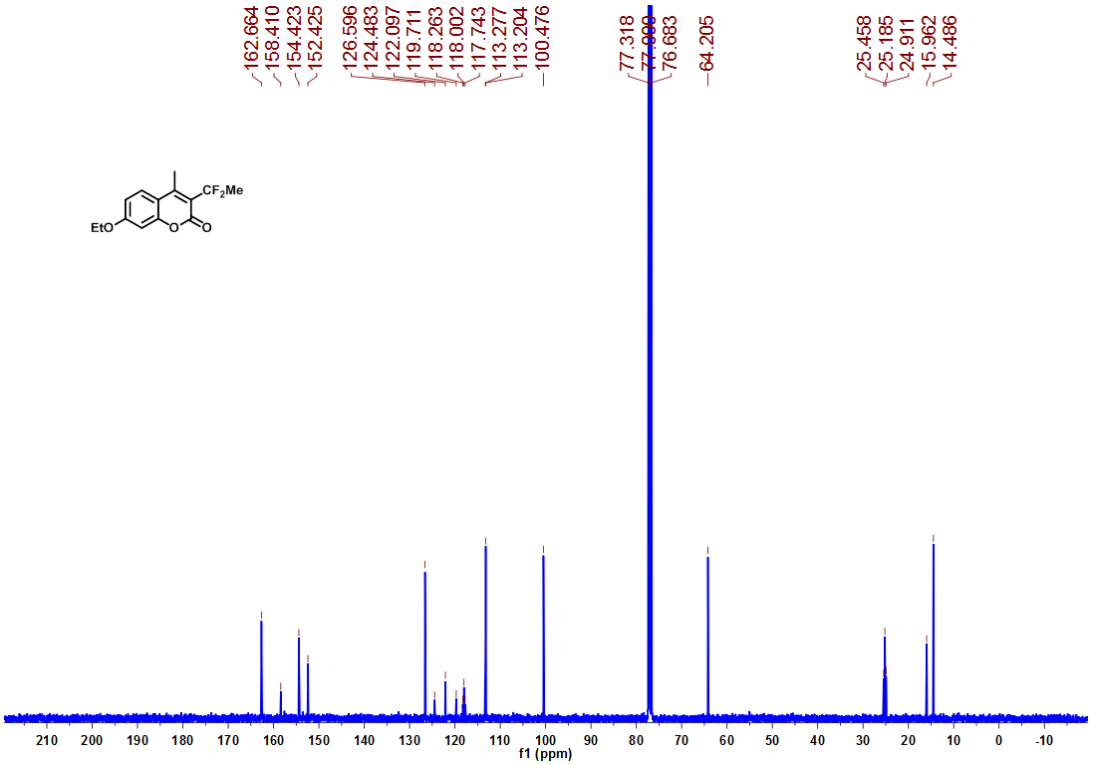
3v-^{19}F NMR (471 MHz, $CDCl_3$)



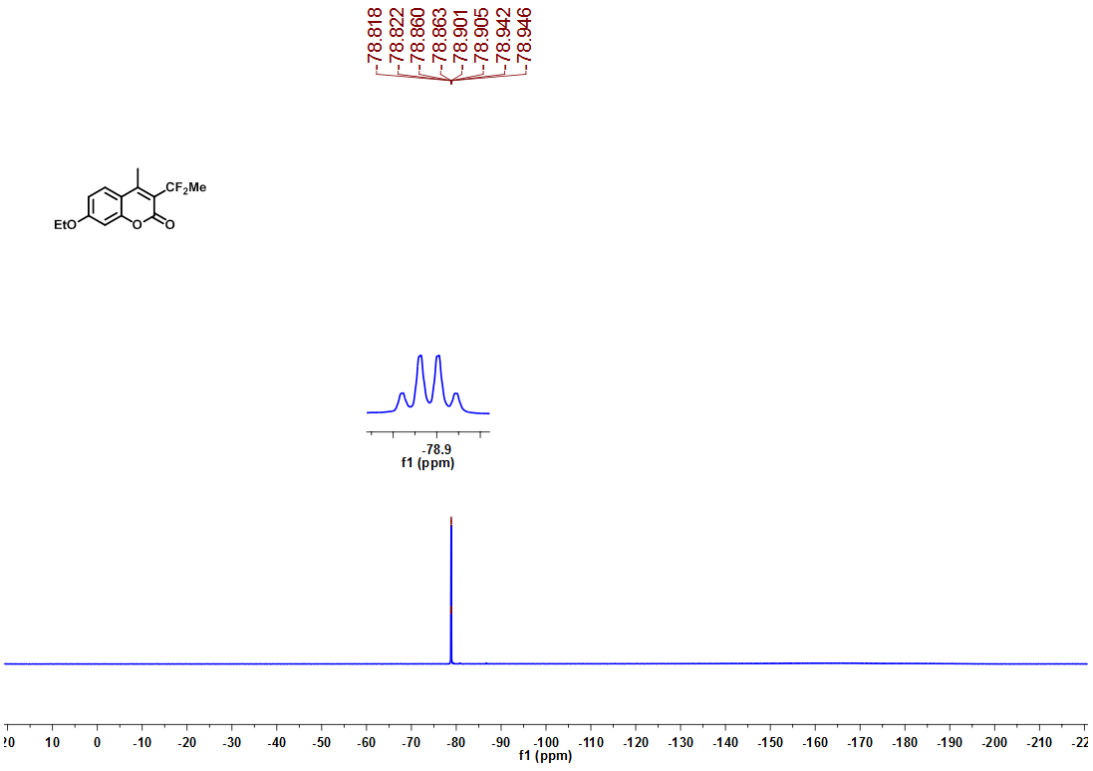
3w-^{1}H NMR (400 MHz, $CDCl_3$)



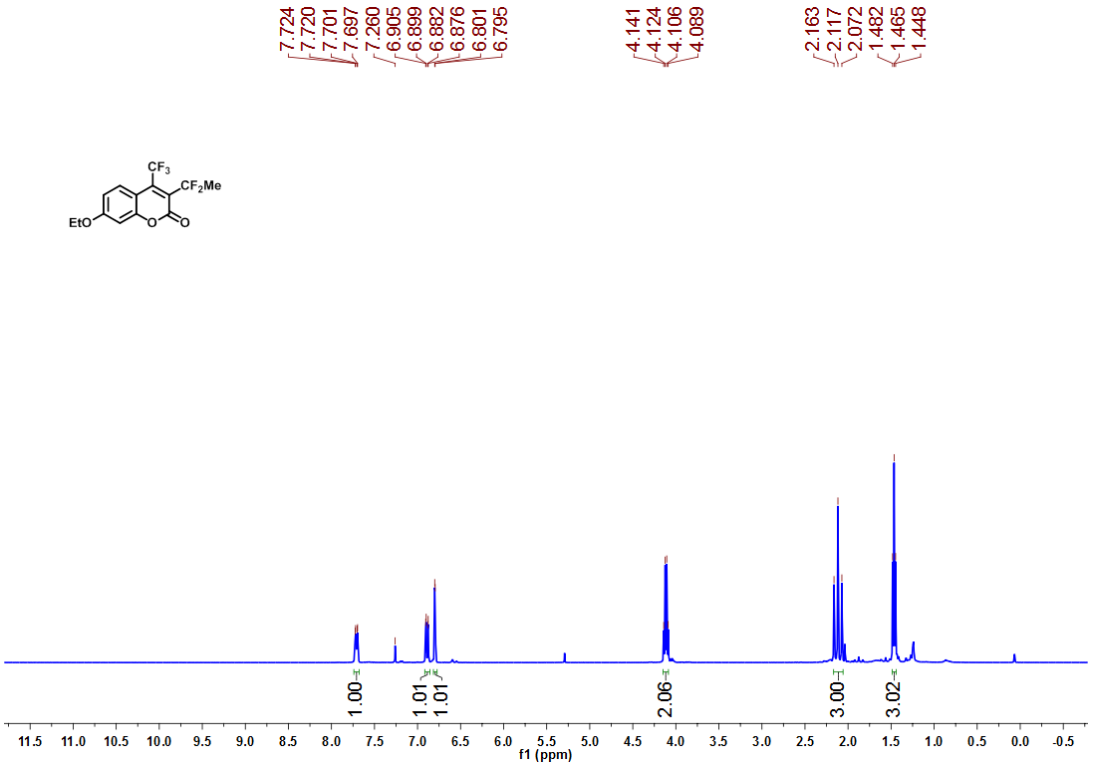
3w-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



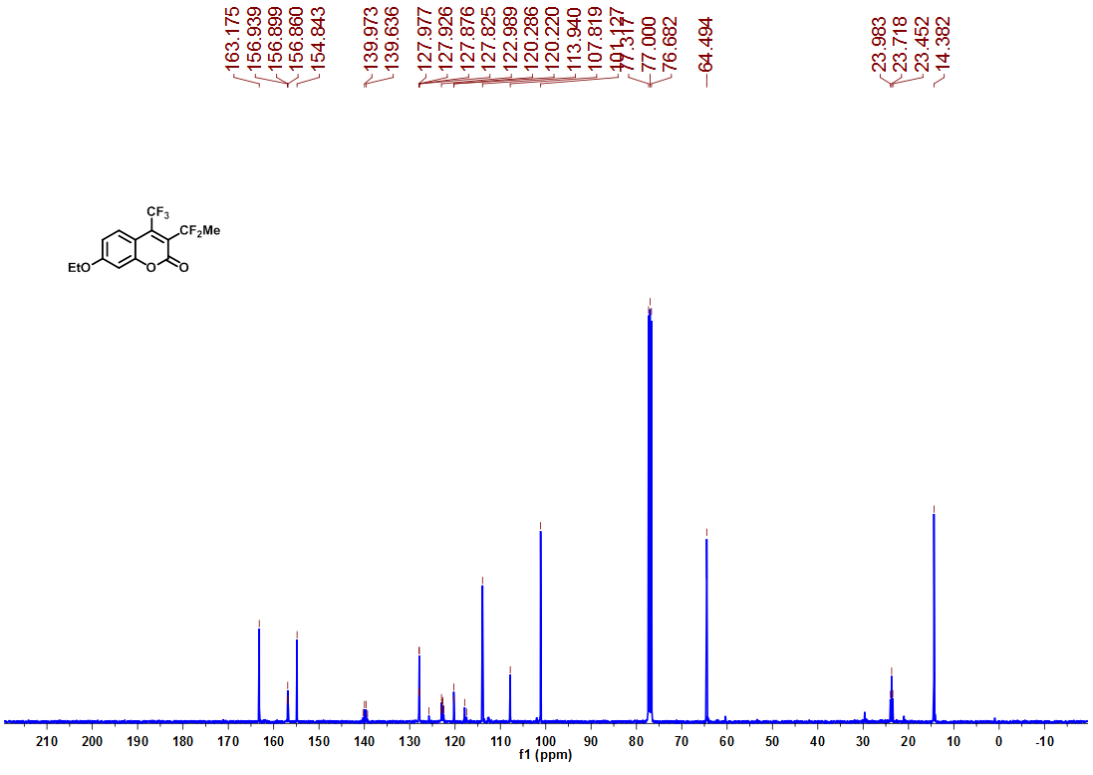
3w-^{19}F NMR (471 MHz, $CDCl_3$)



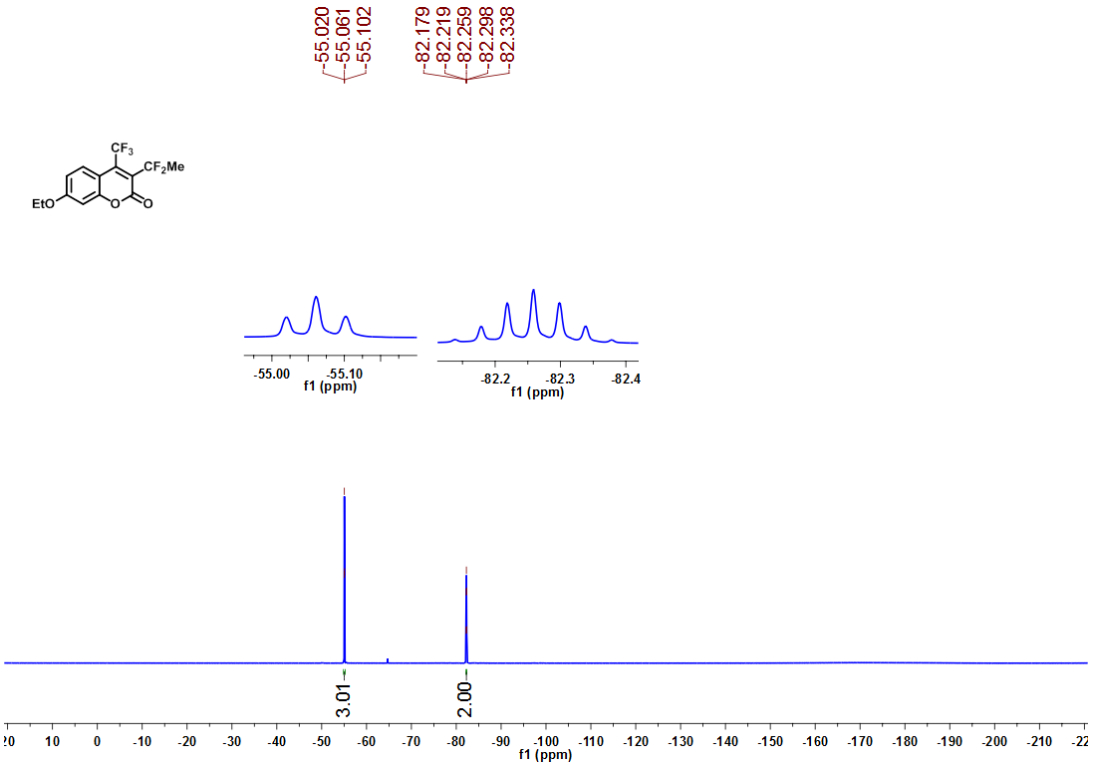
3x-^{1}H NMR (400 MHz, $CDCl_3$)



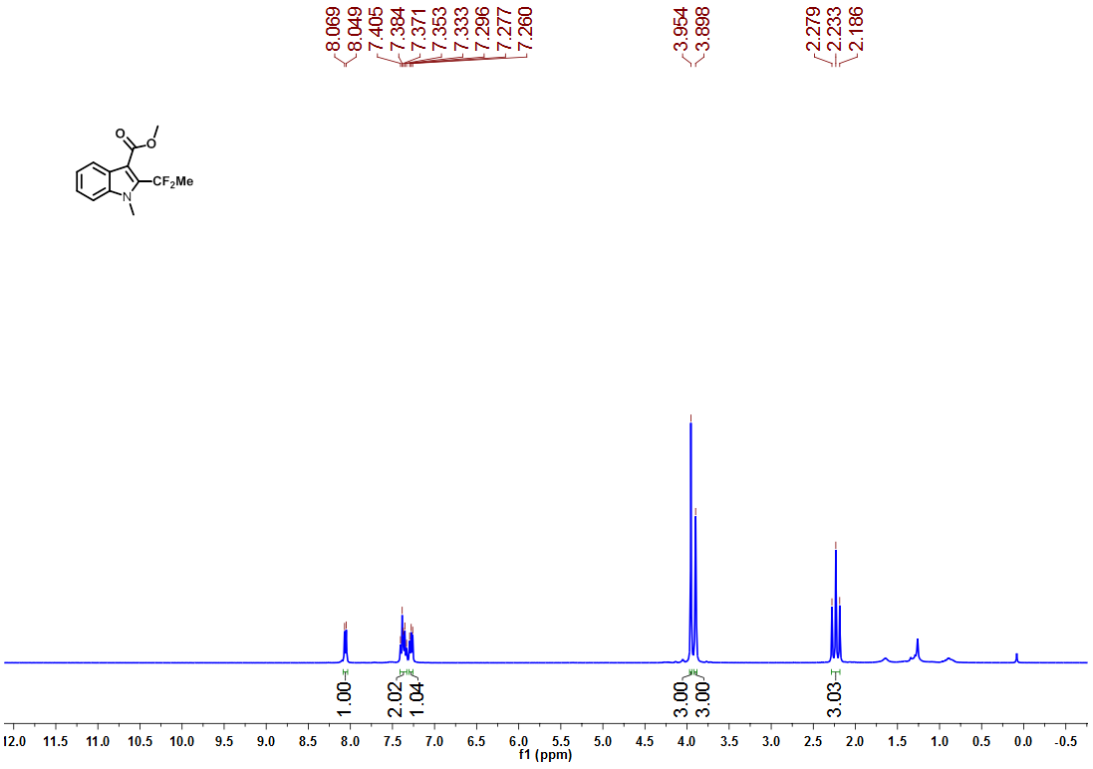
3x-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



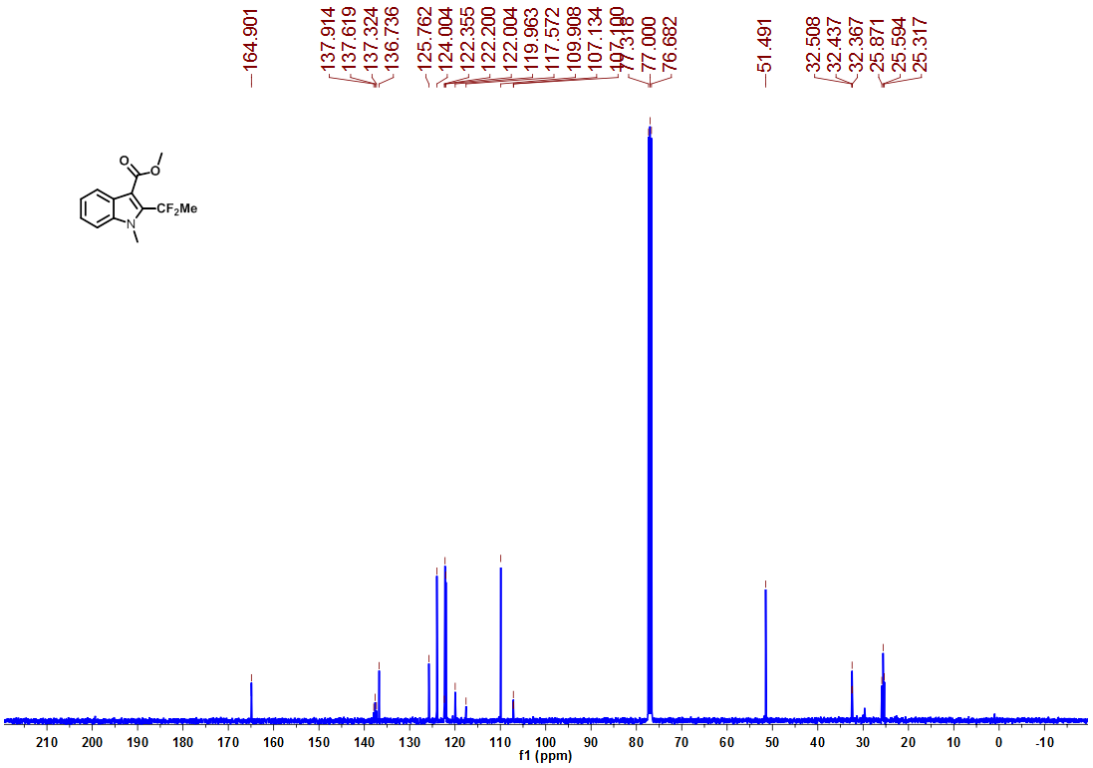
3x-^{19}F NMR (471 MHz, $CDCl_3$)



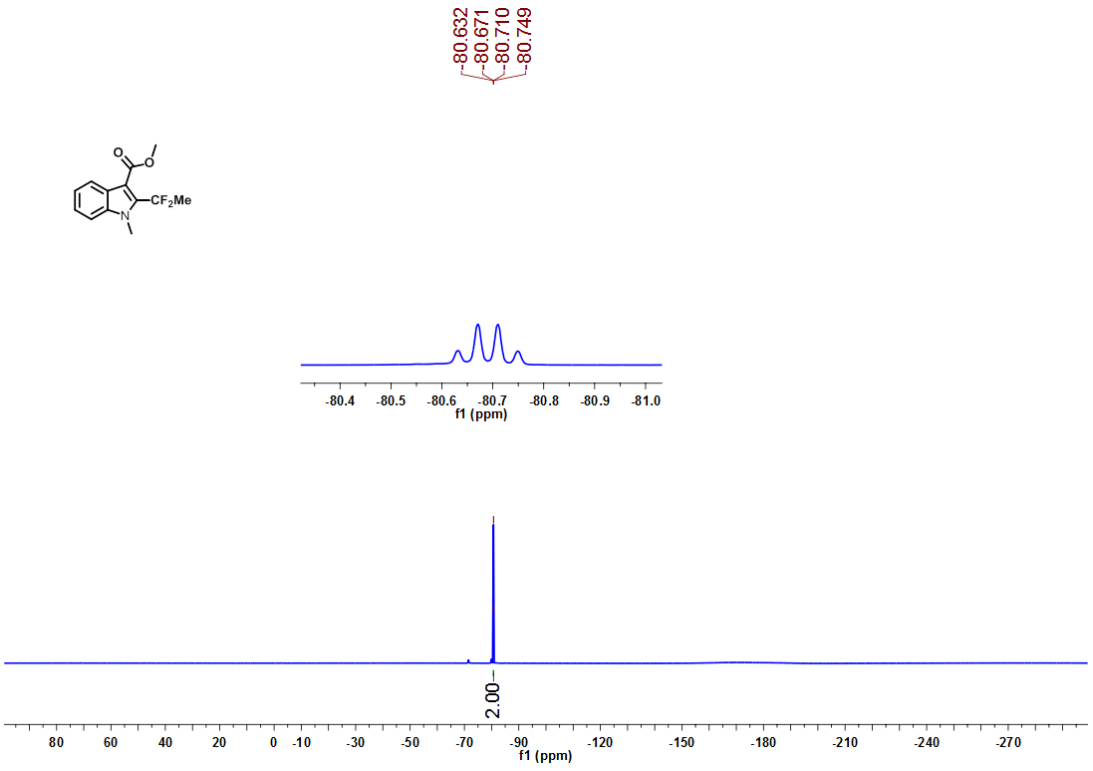
3y-^{1}H NMR (400 MHz, $CDCl_3$)



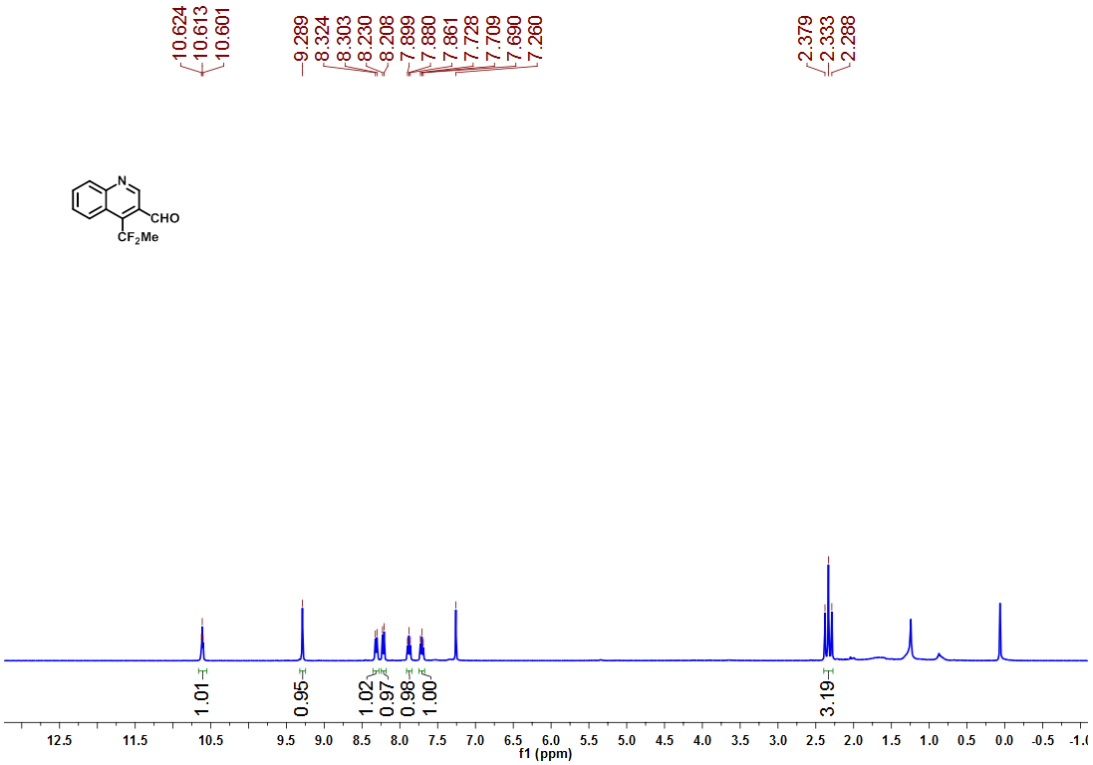
3y-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



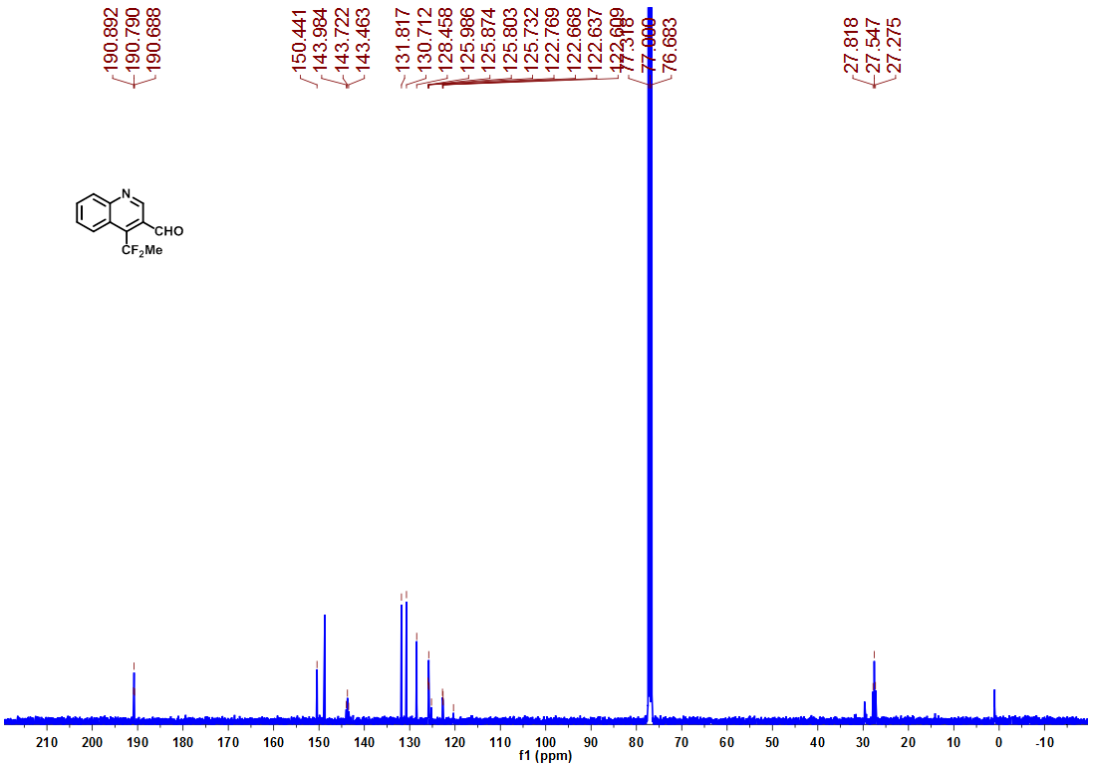
3y-^{19}F NMR (471 MHz, $CDCl_3$)



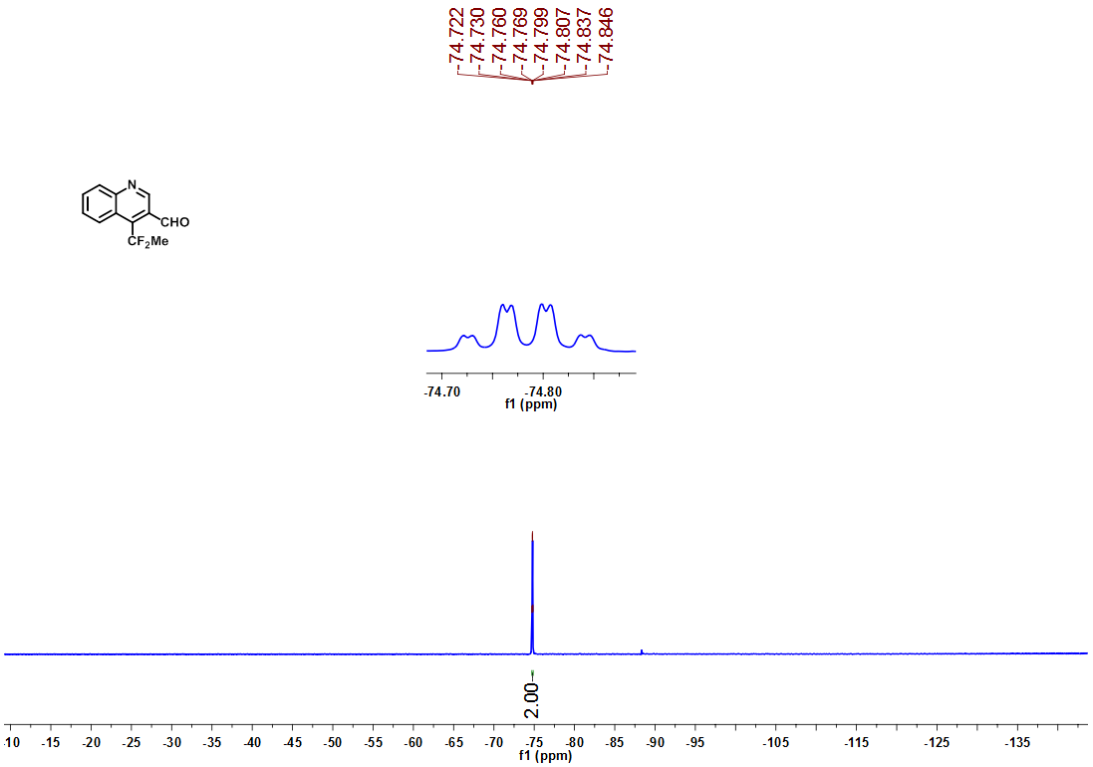
3z-^{1}H NMR (400 MHz, $CDCl_3$)



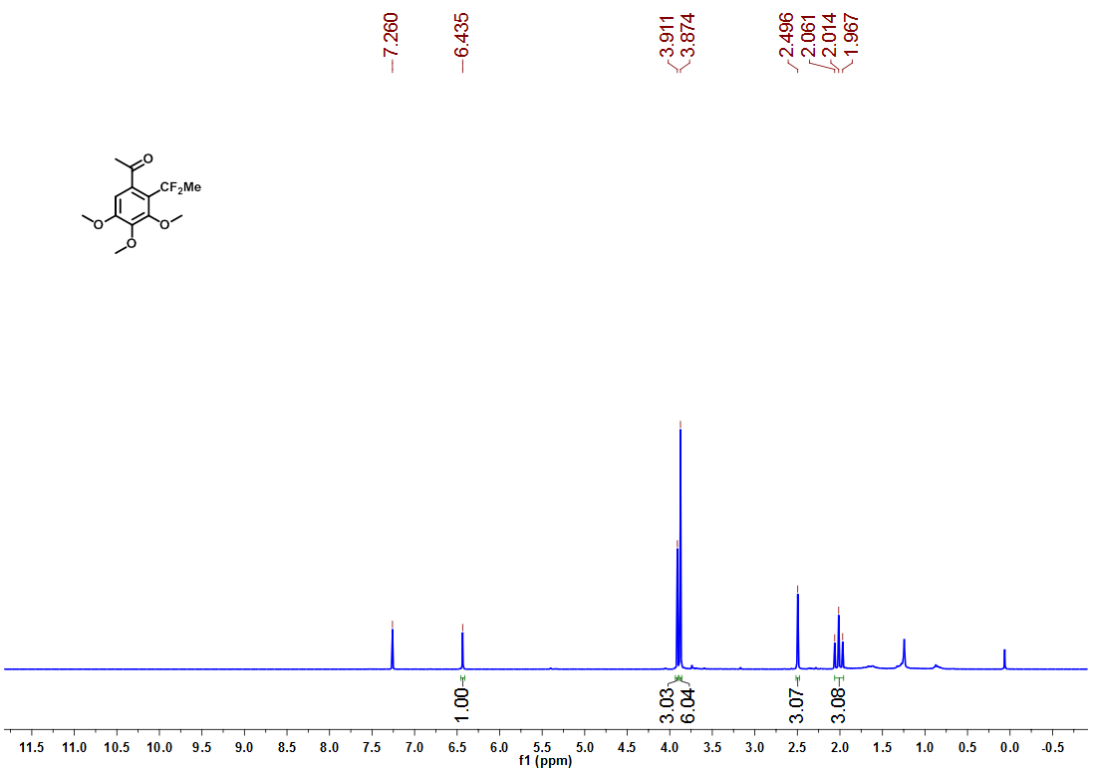
3z-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



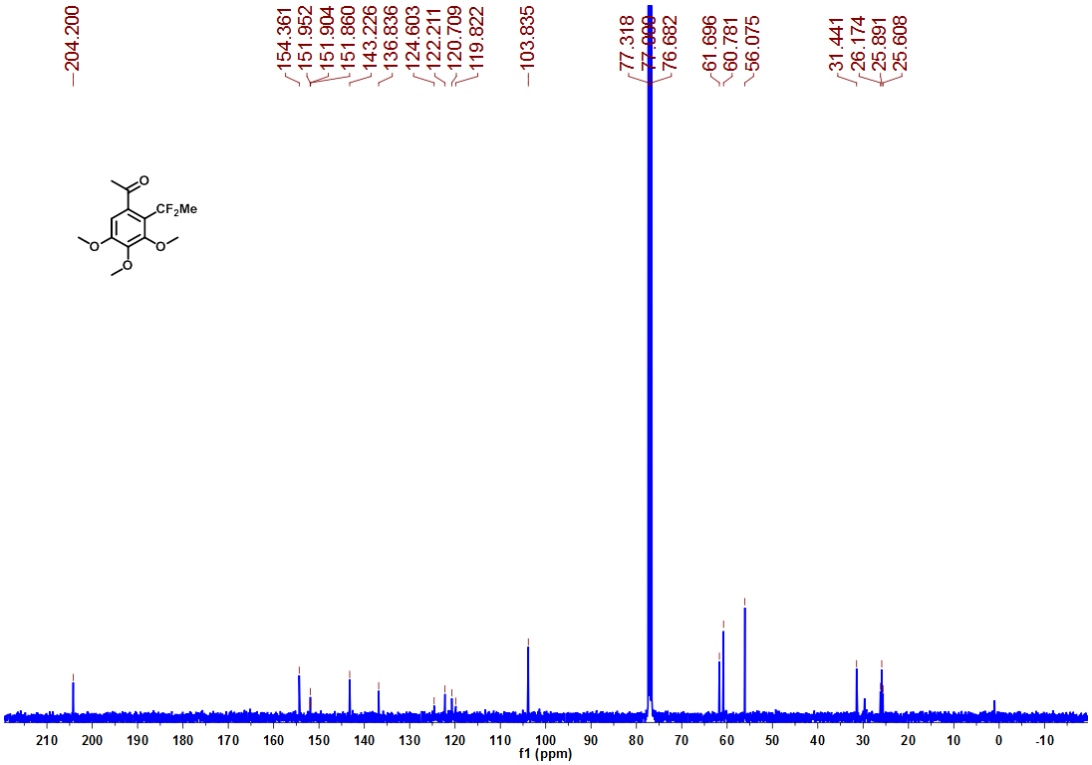
3z-^{19}F NMR (471 MHz, $CDCl_3$)



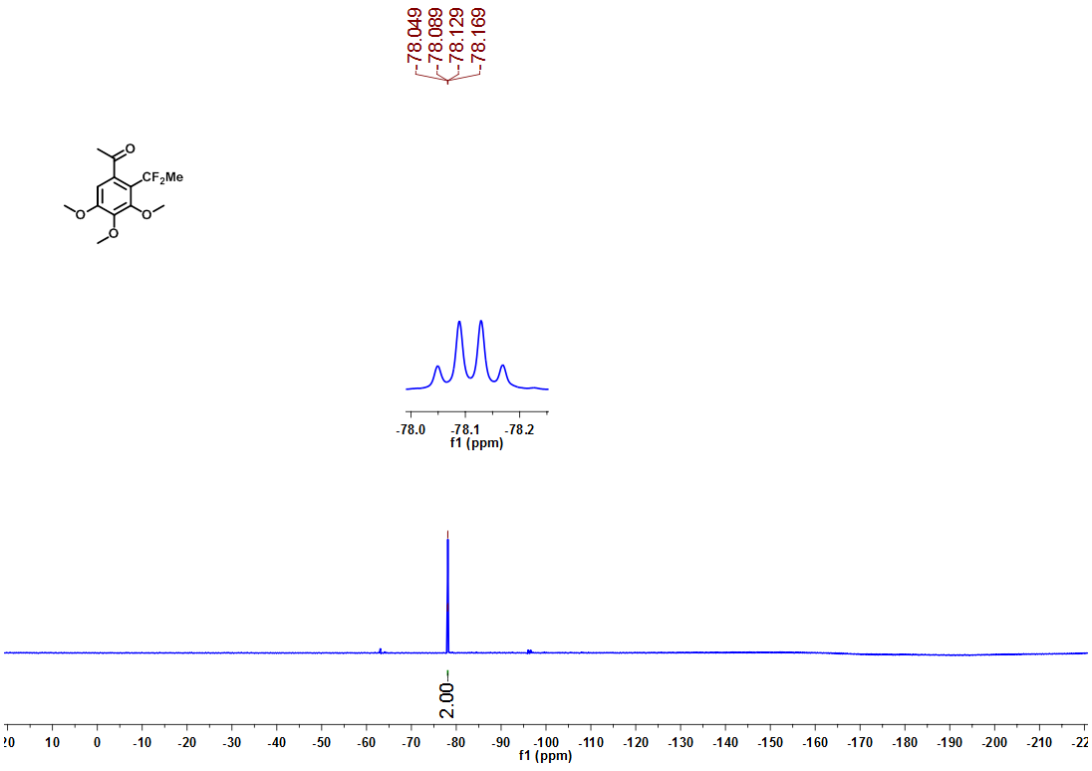
3aa-^{1}H NMR (400 MHz, $CDCl_3$)



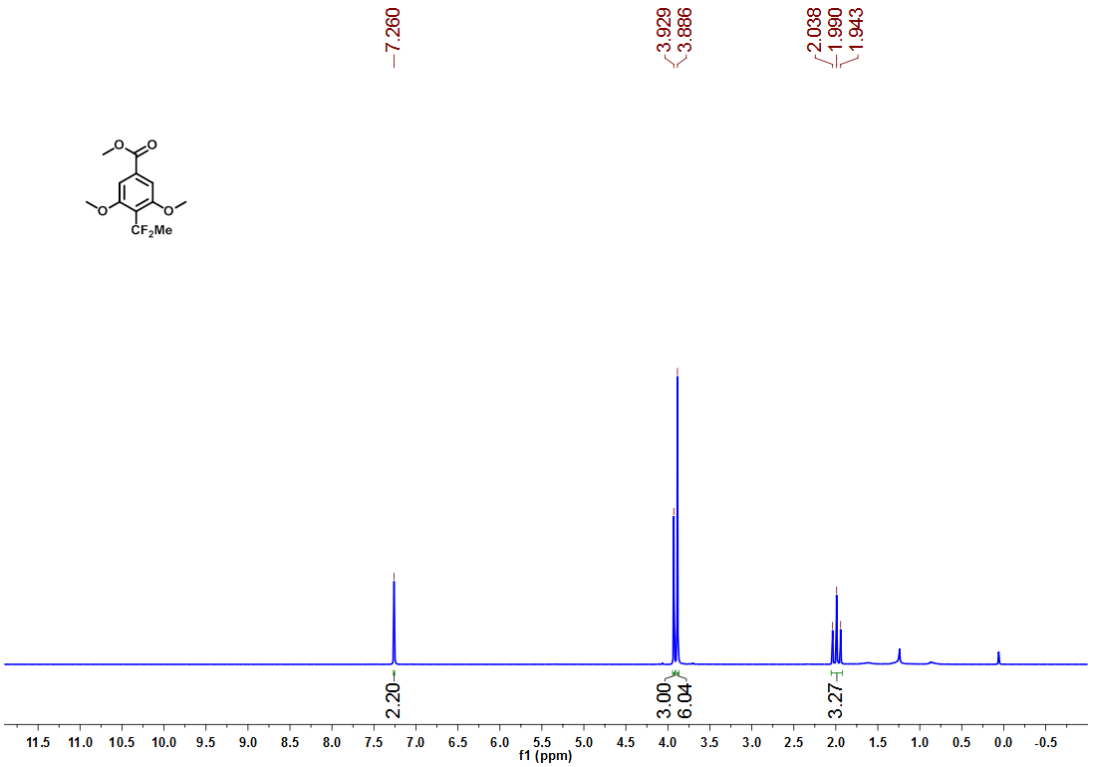
3aa-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



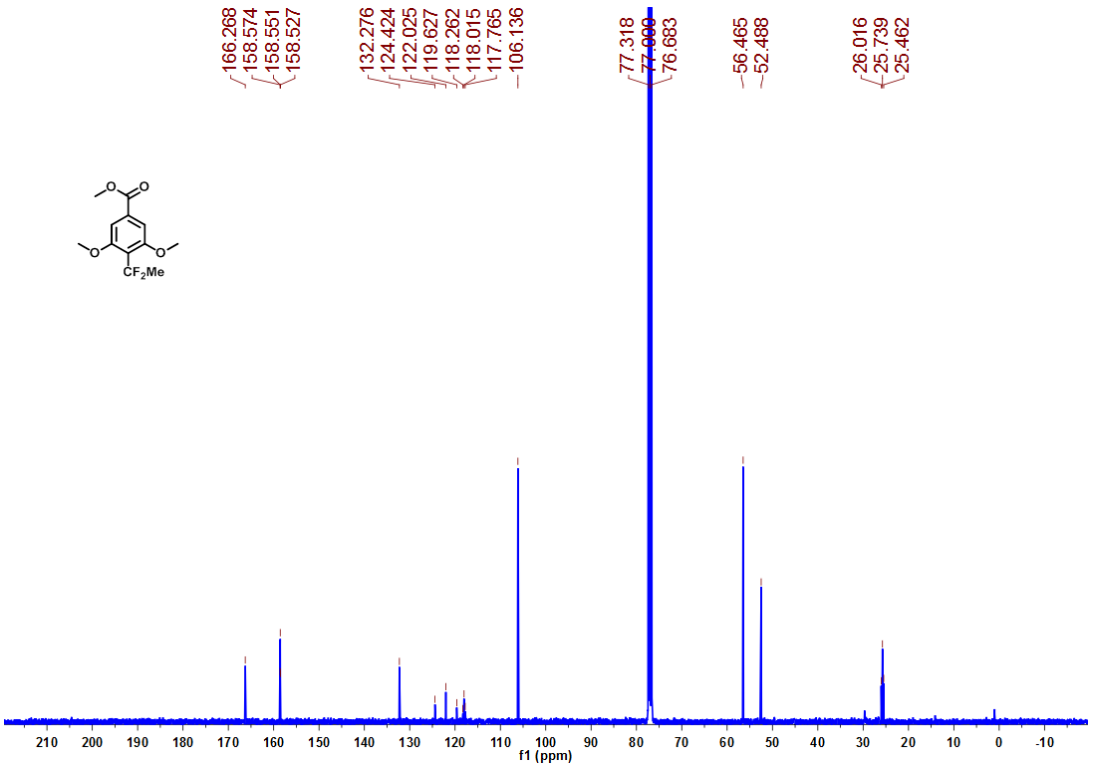
3aa-^{19}F NMR (471 MHz, $CDCl_3$)



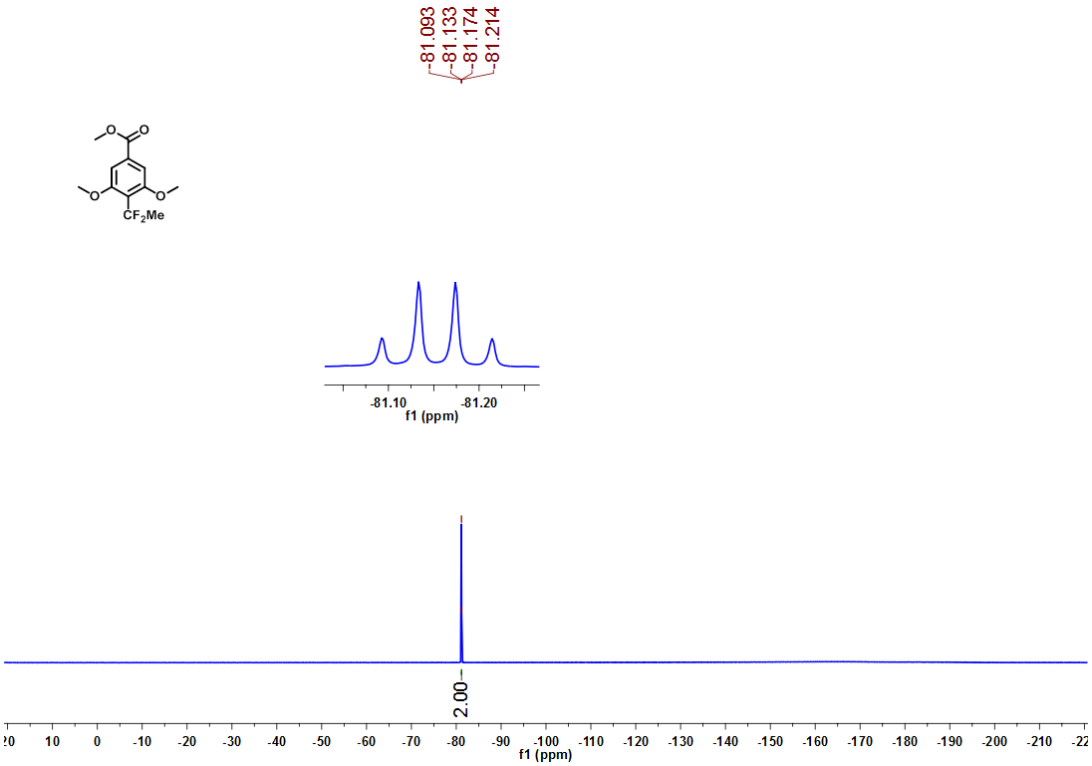
3ab-^{1}H NMR (400 MHz, $CDCl_3$)



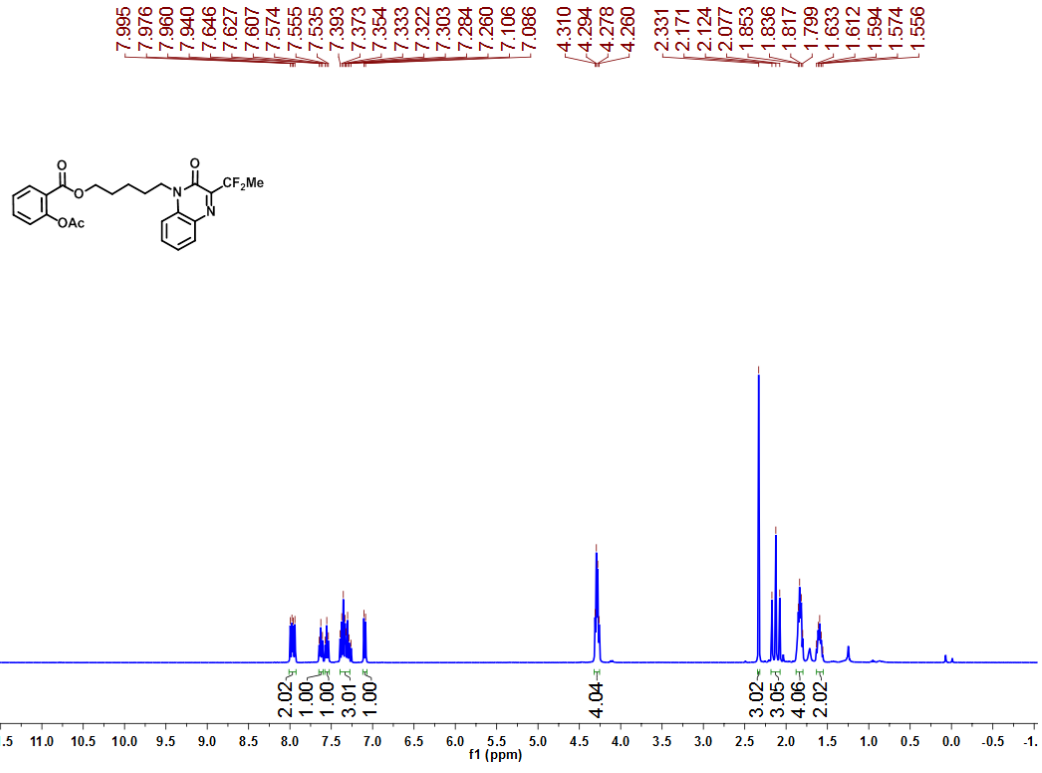
3ab-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



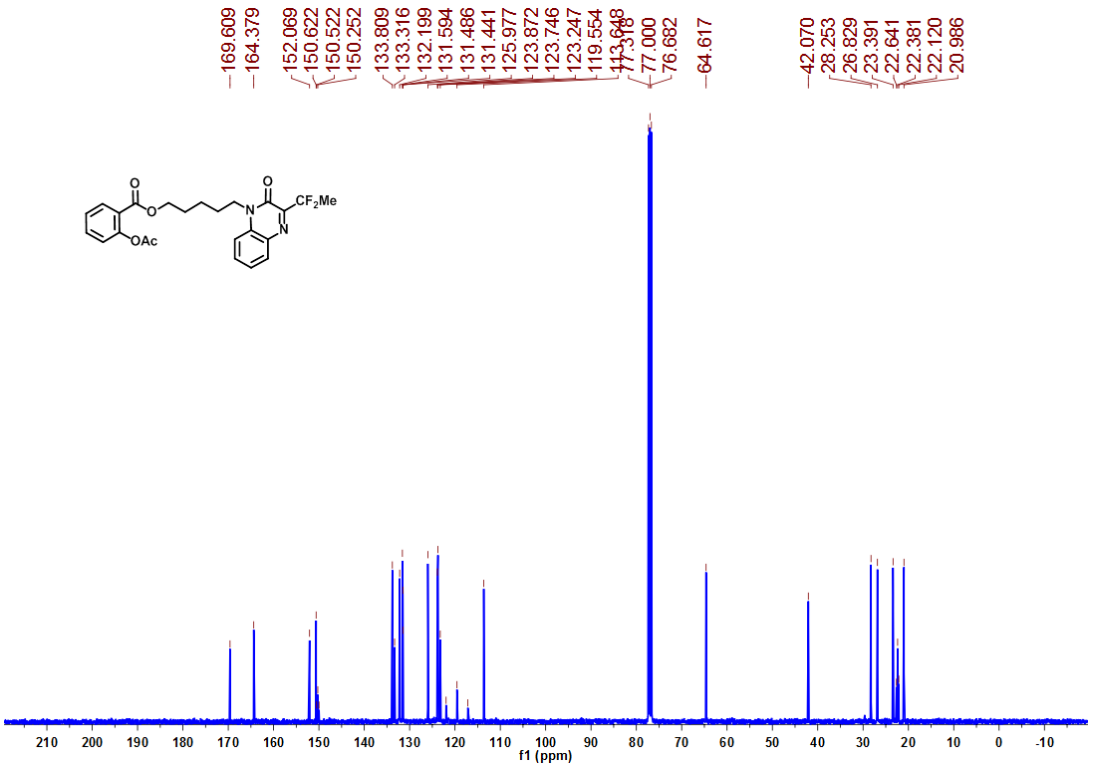
3ab-^{19}F NMR (471 MHz, $CDCl_3$)



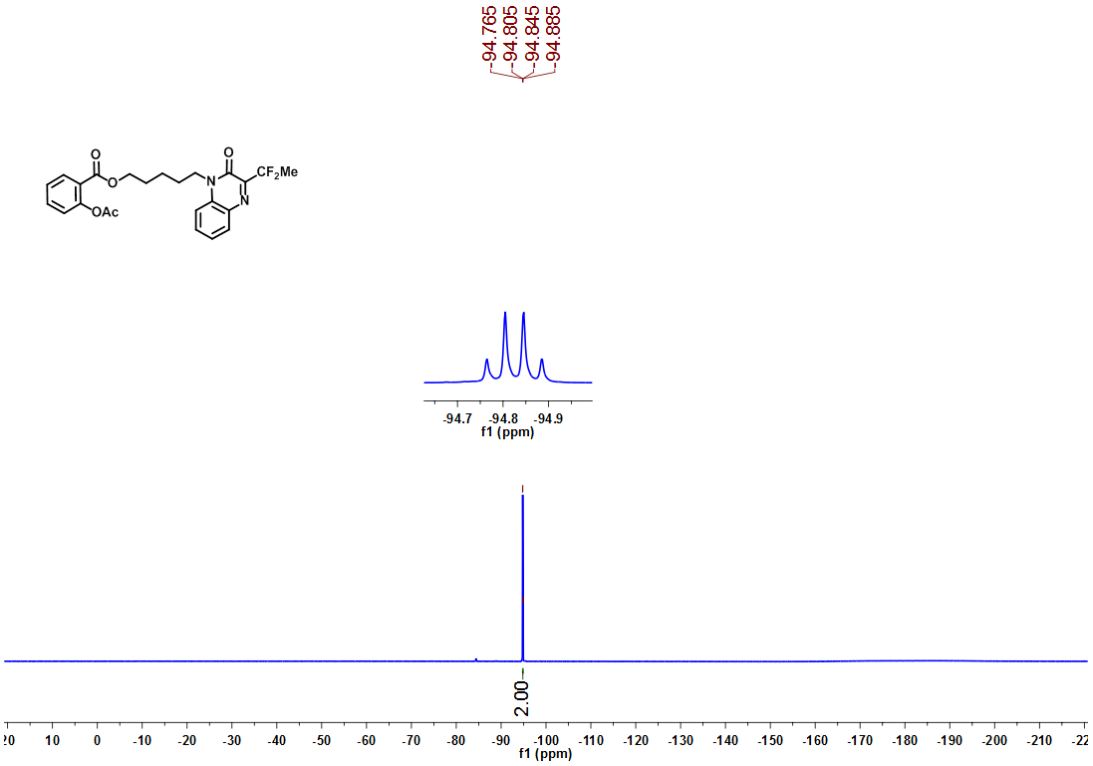
5a-^{1}H NMR (400 MHz, $CDCl_3$)



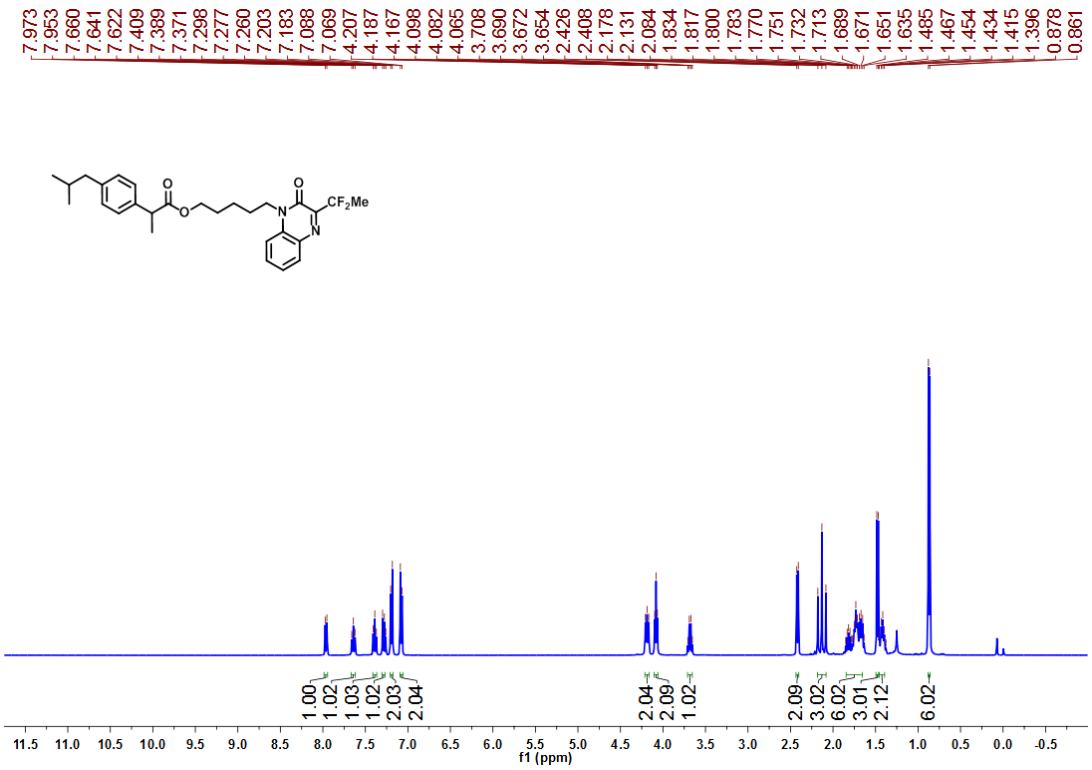
5a-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



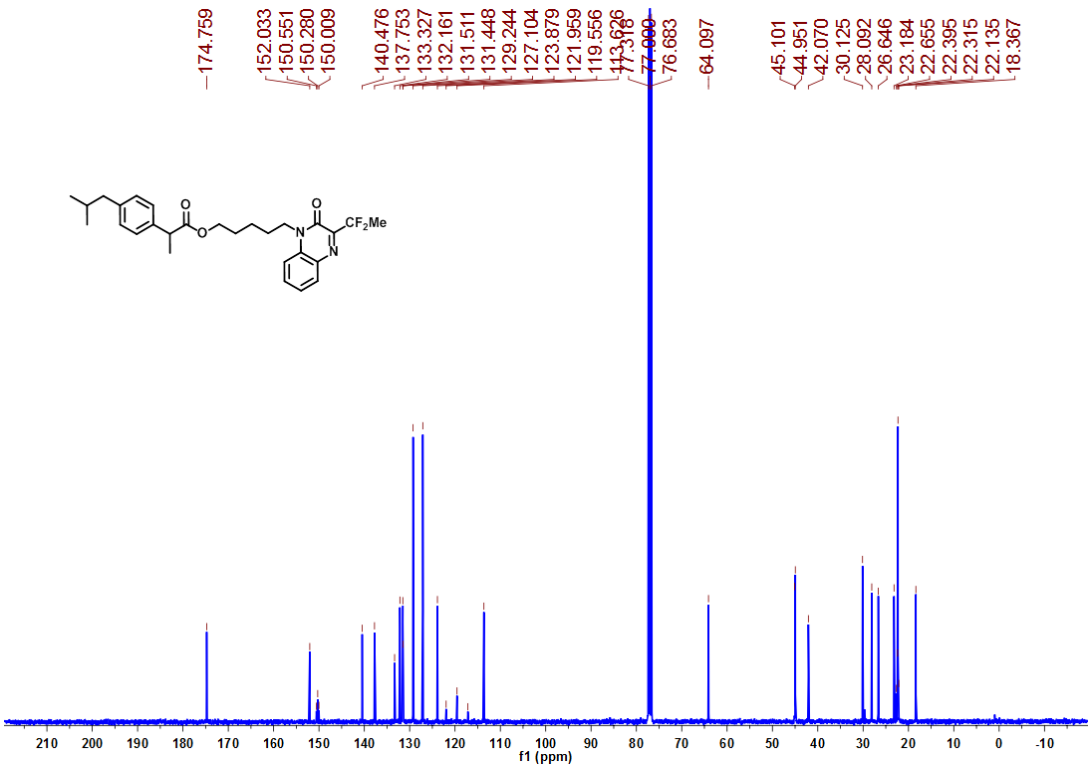
5a-^{19}F NMR (471 MHz, $CDCl_3$)



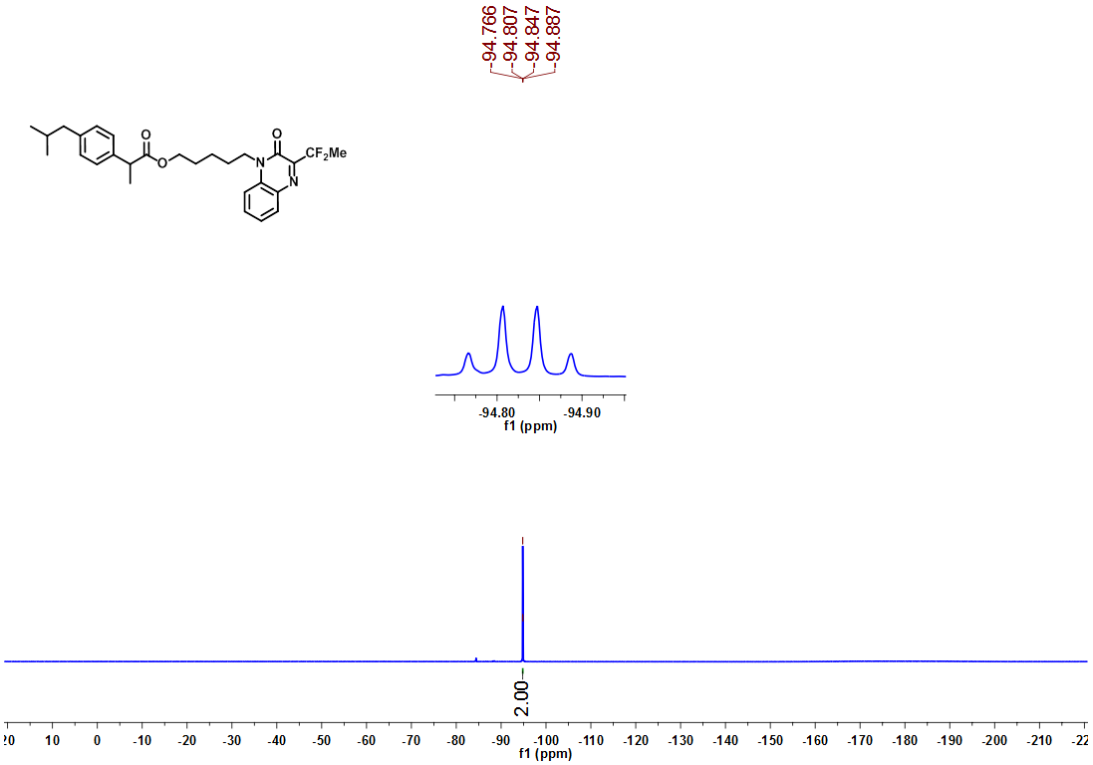
5b-^{1}H NMR (400 MHz, $CDCl_3$)



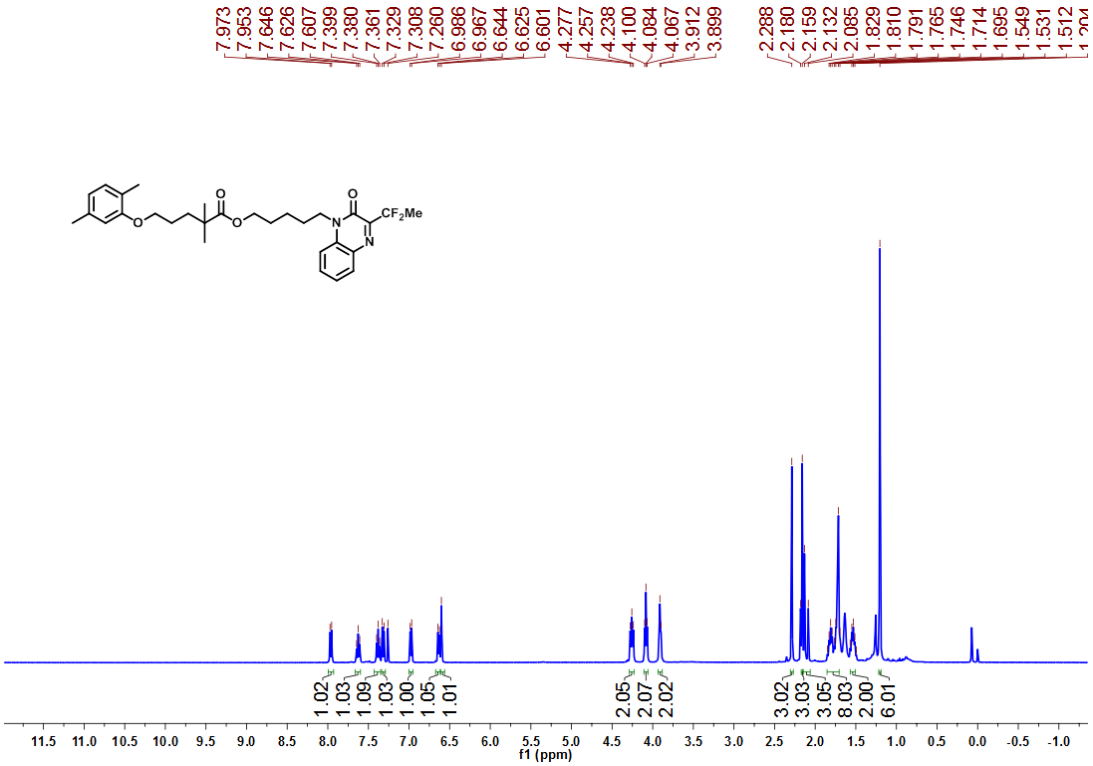
5b-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



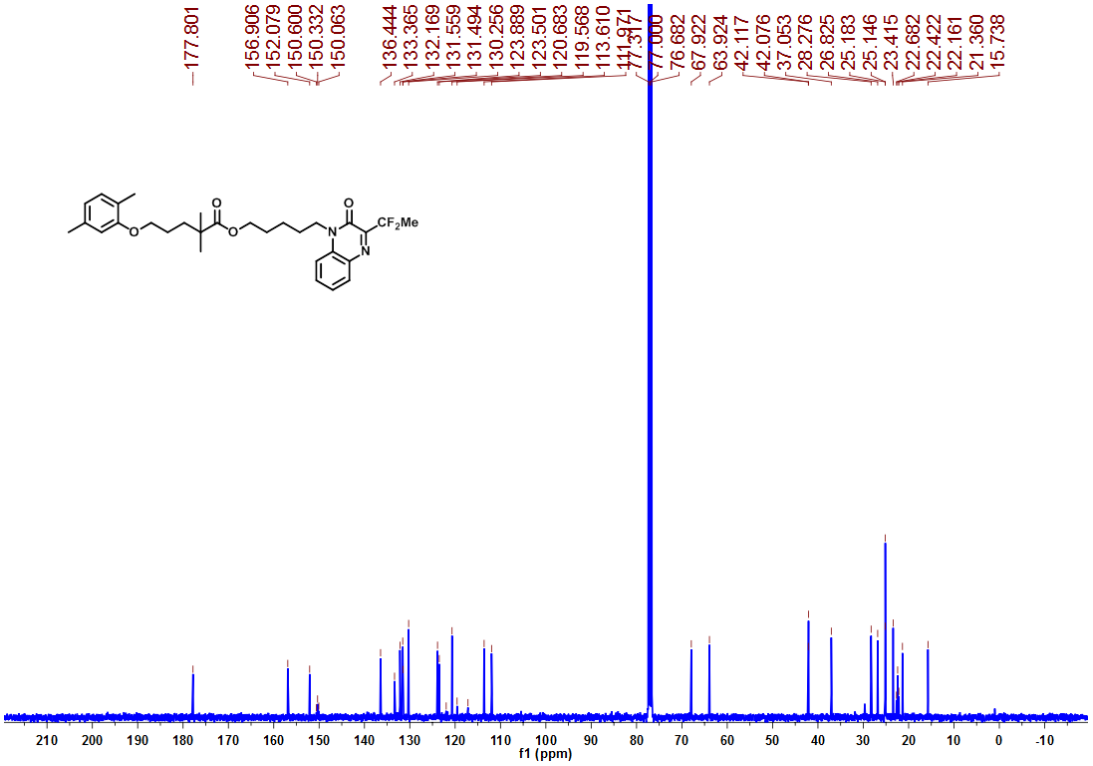
5b-^{19}F NMR (471 MHz, $CDCl_3$)



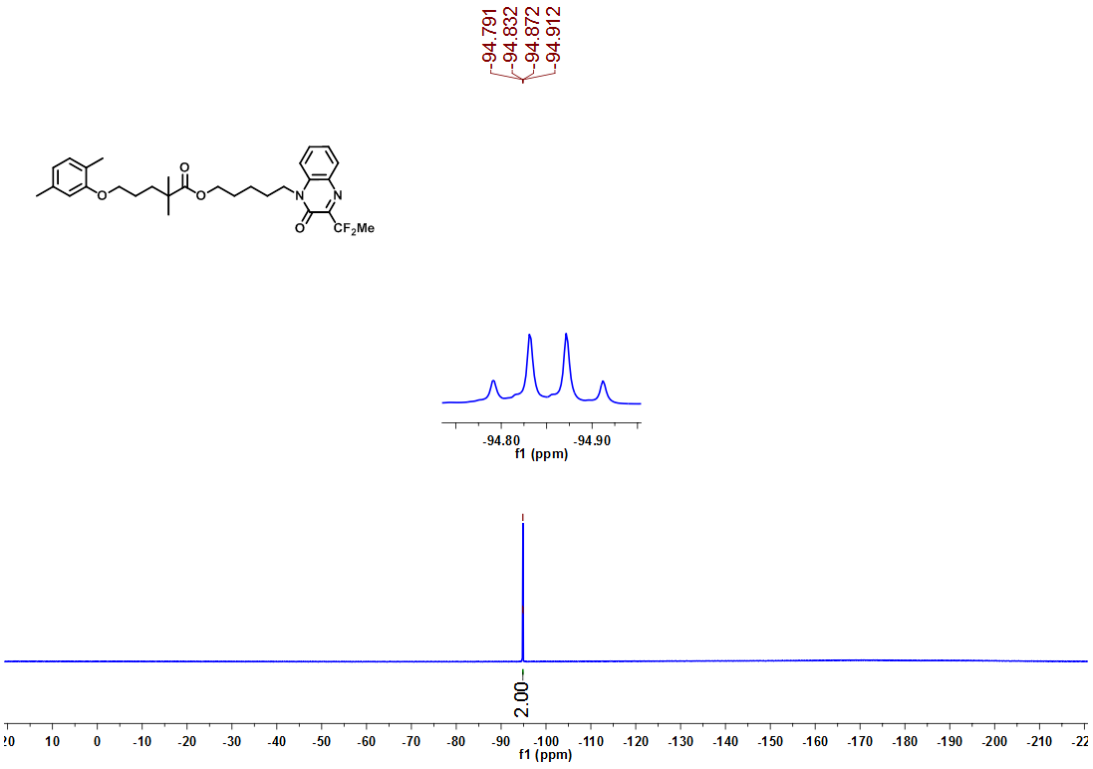
5c-^{1}H NMR (400 MHz, $CDCl_3$)



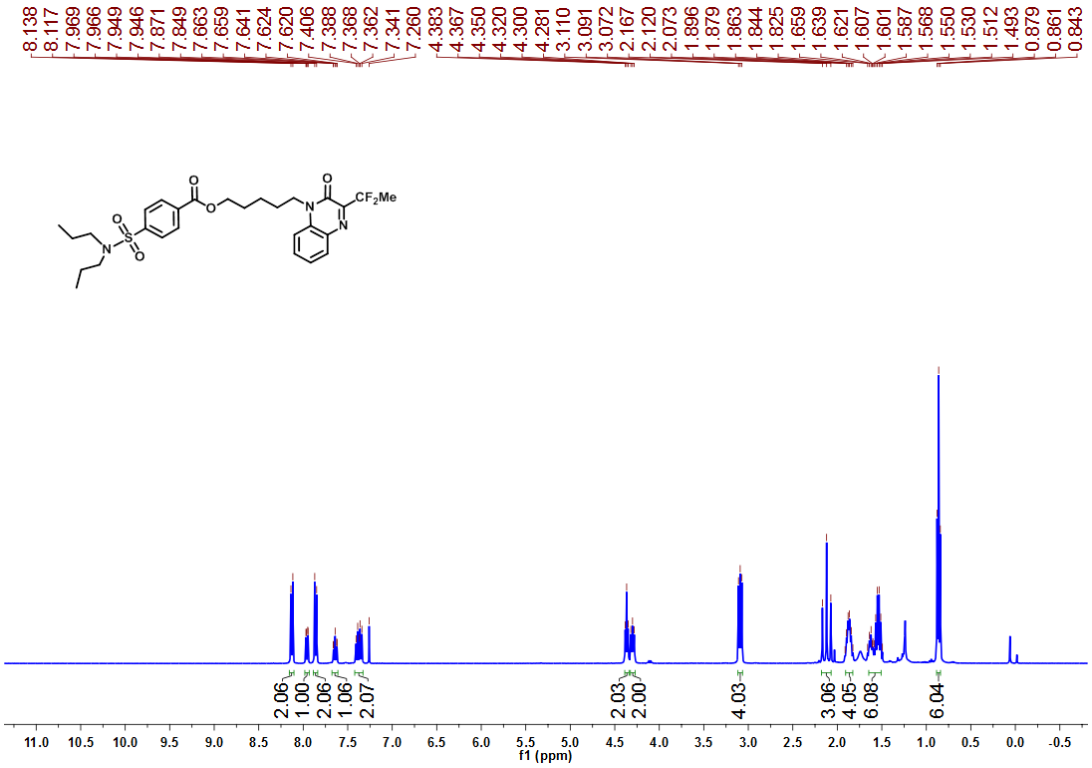
5c-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



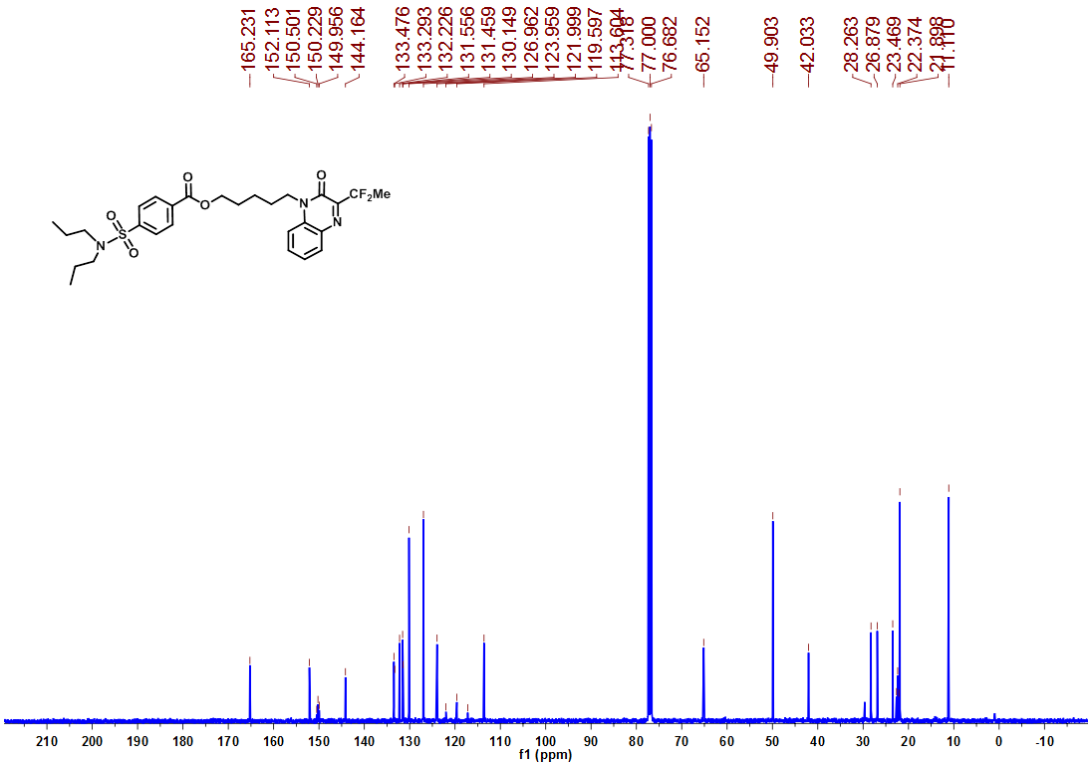
5c-^{19}F NMR (471 MHz, $CDCl_3$)



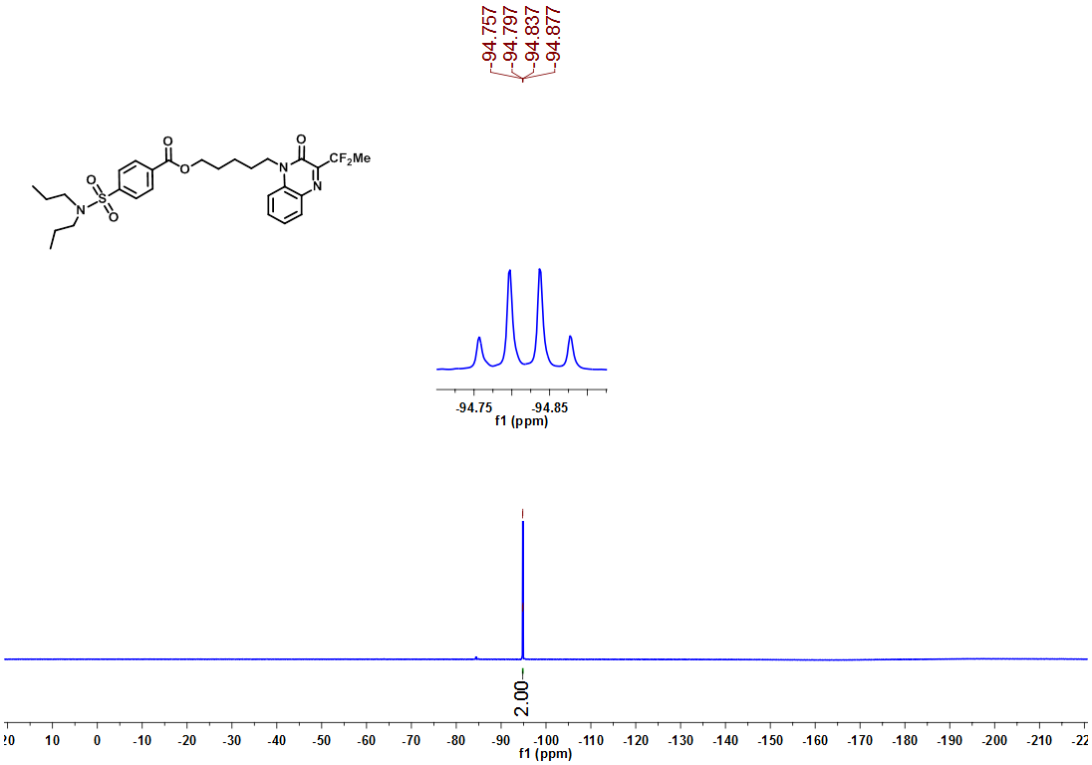
5d-^{1}H NMR (400 MHz, $CDCl_3$)



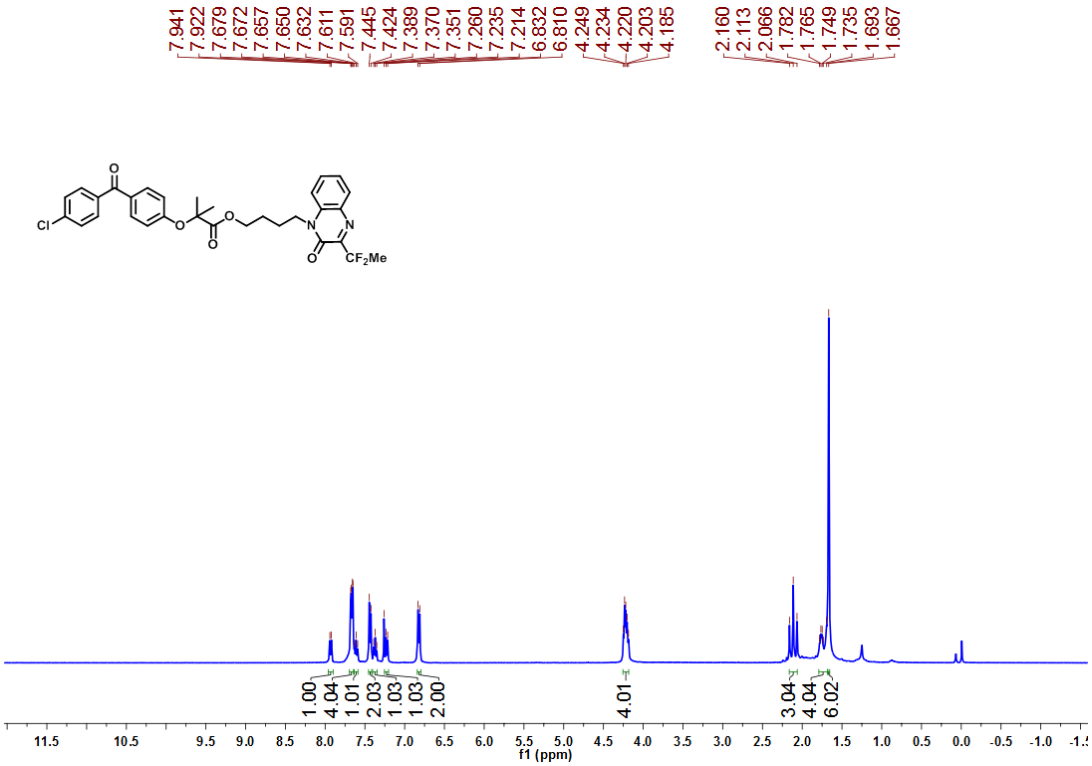
5d-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



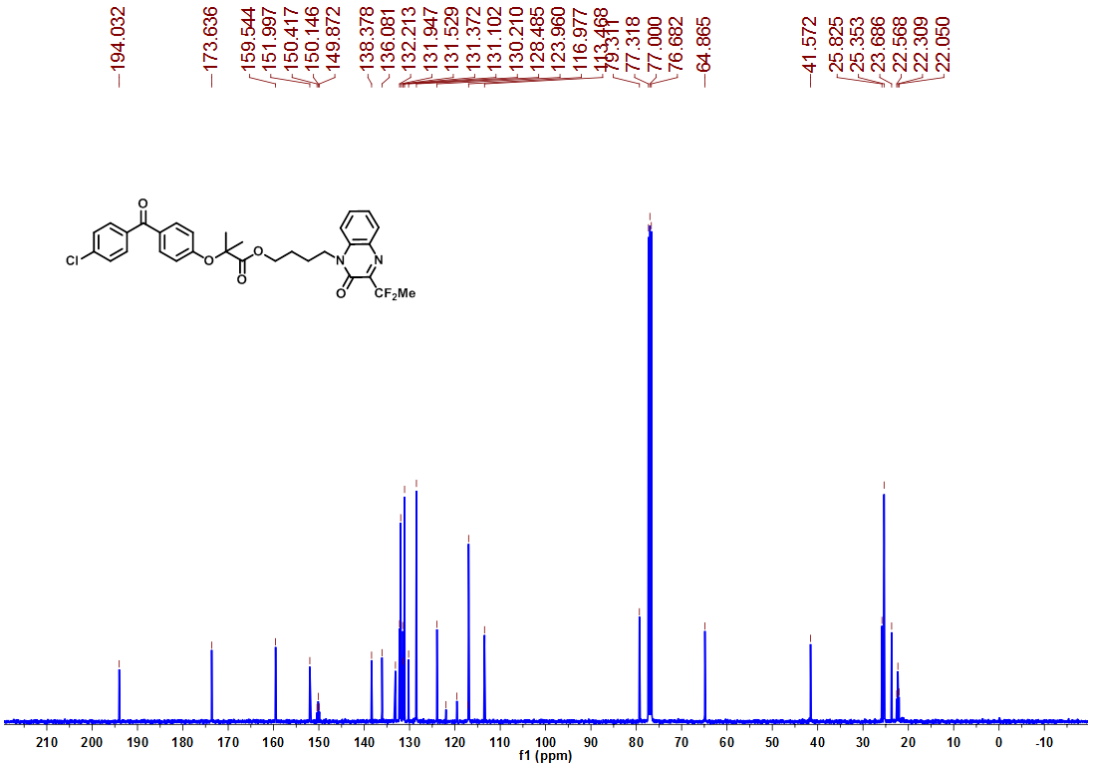
5d-^{19}F NMR (471 MHz, $CDCl_3$)



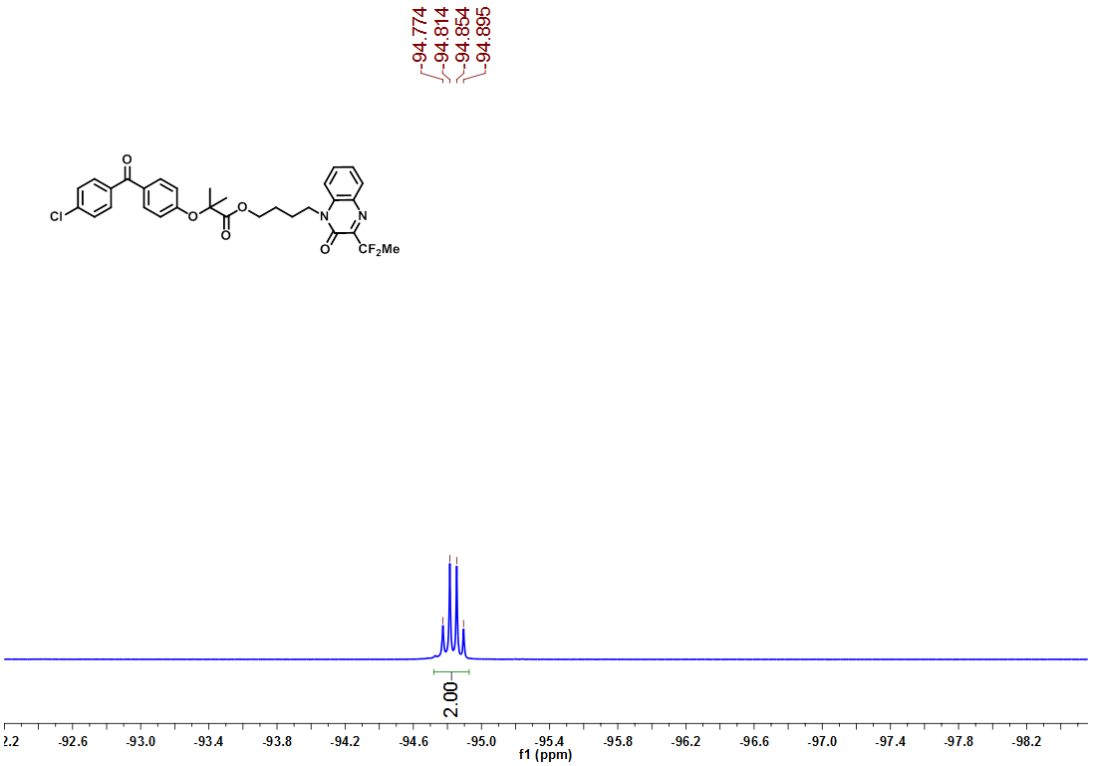
5e-^{1}H NMR (400 MHz, $CDCl_3$)



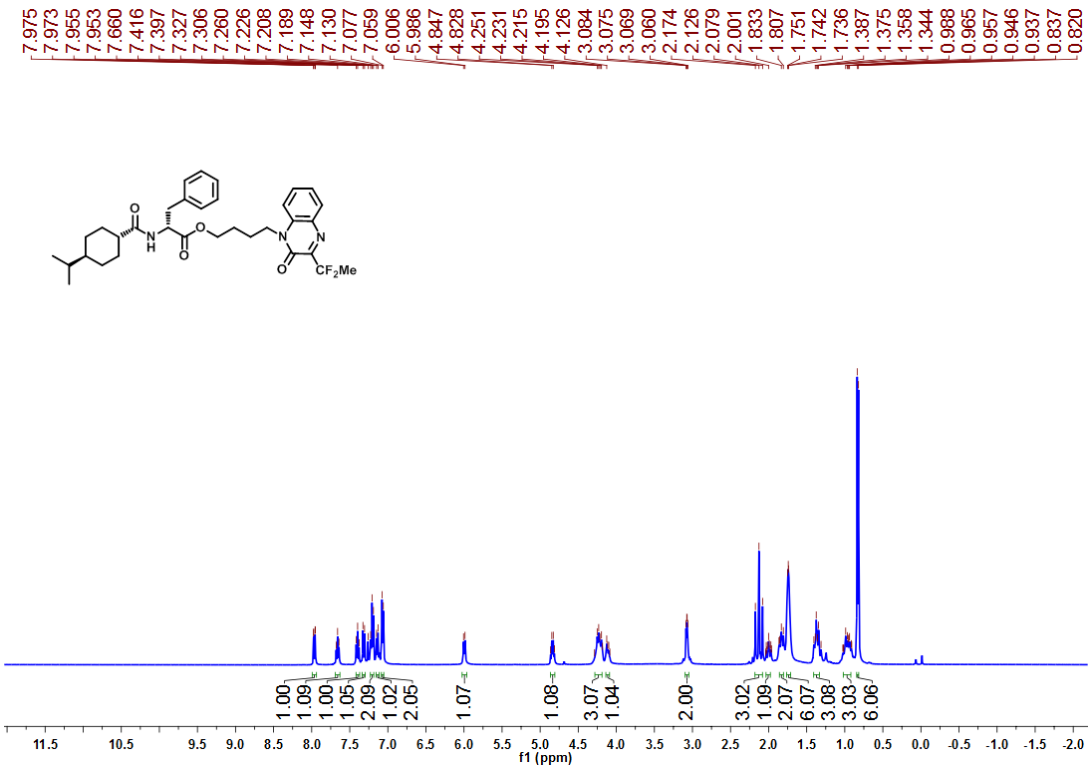
5e-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



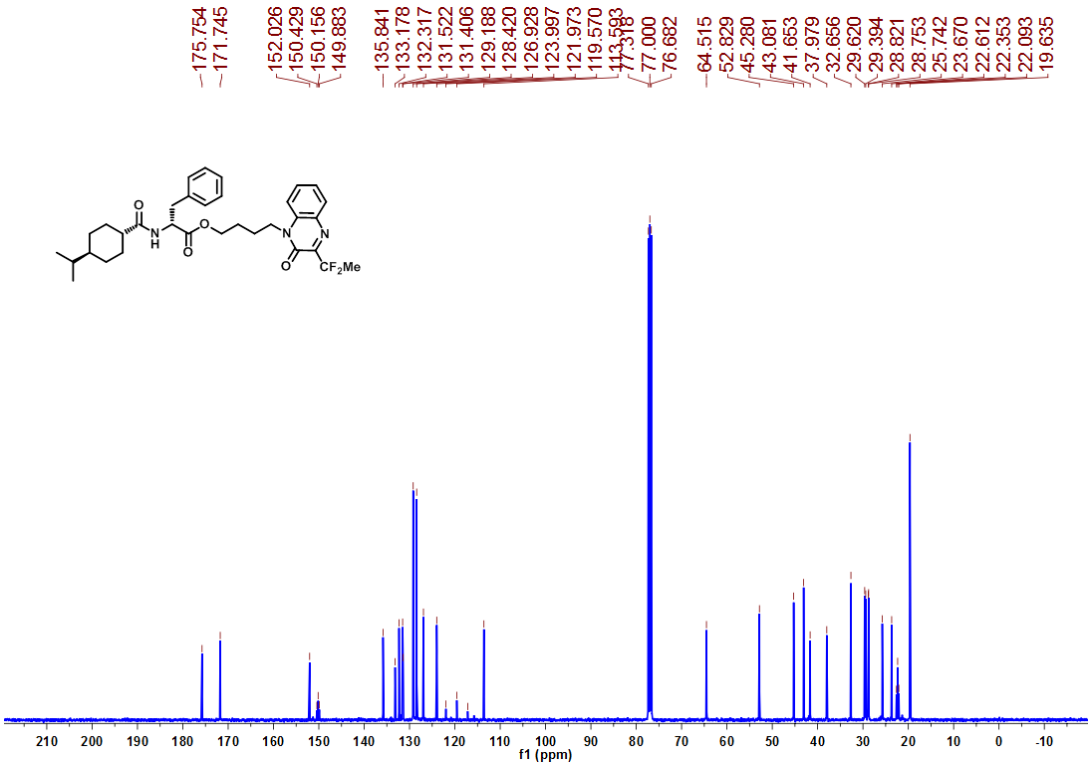
5e-^{19}F NMR (471 MHz, $CDCl_3$)



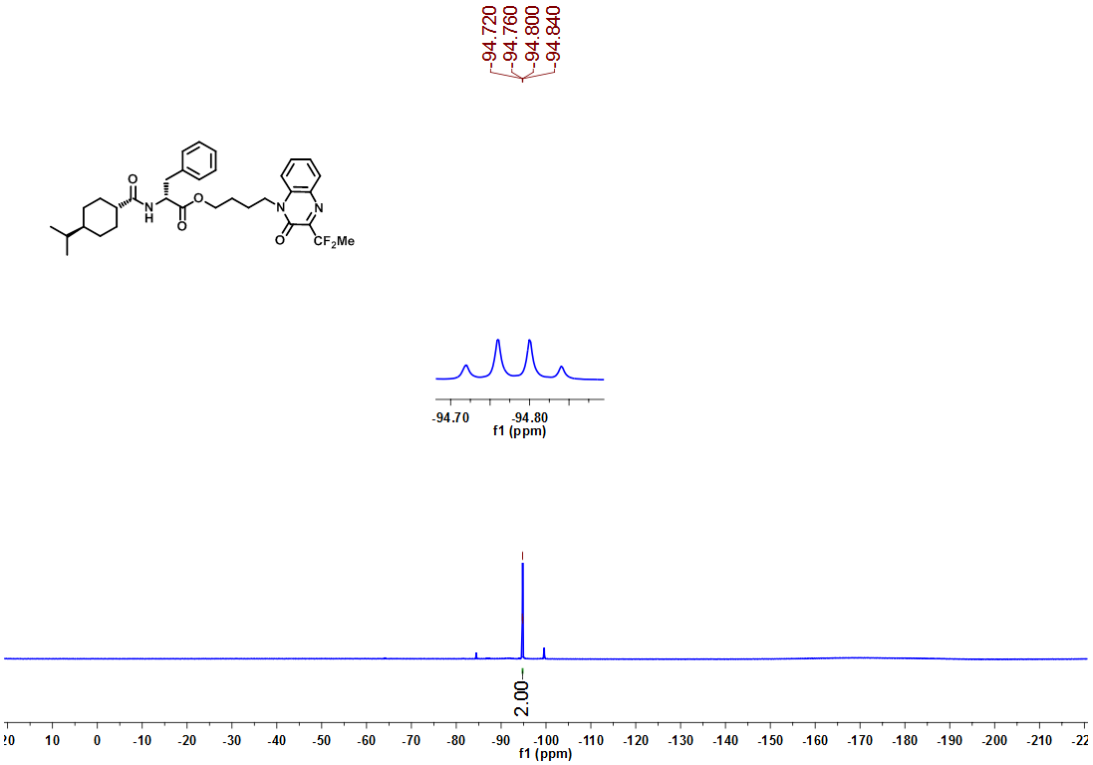
5f-^{1}H NMR (400 MHz, $CDCl_3$)



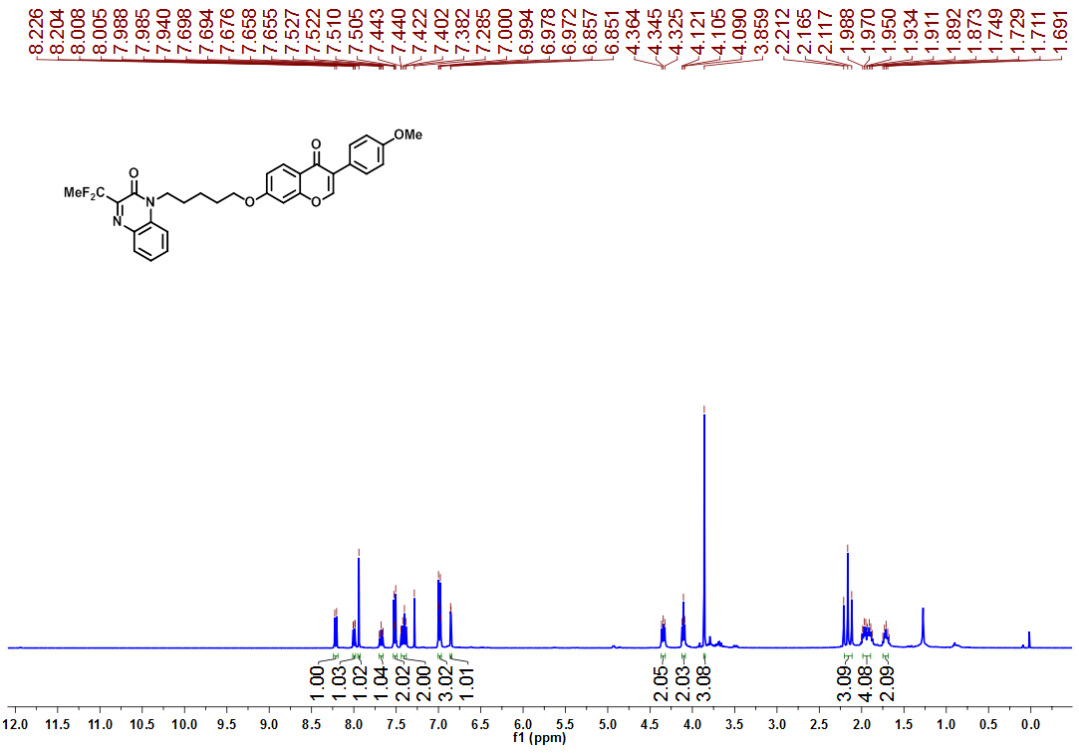
5f-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



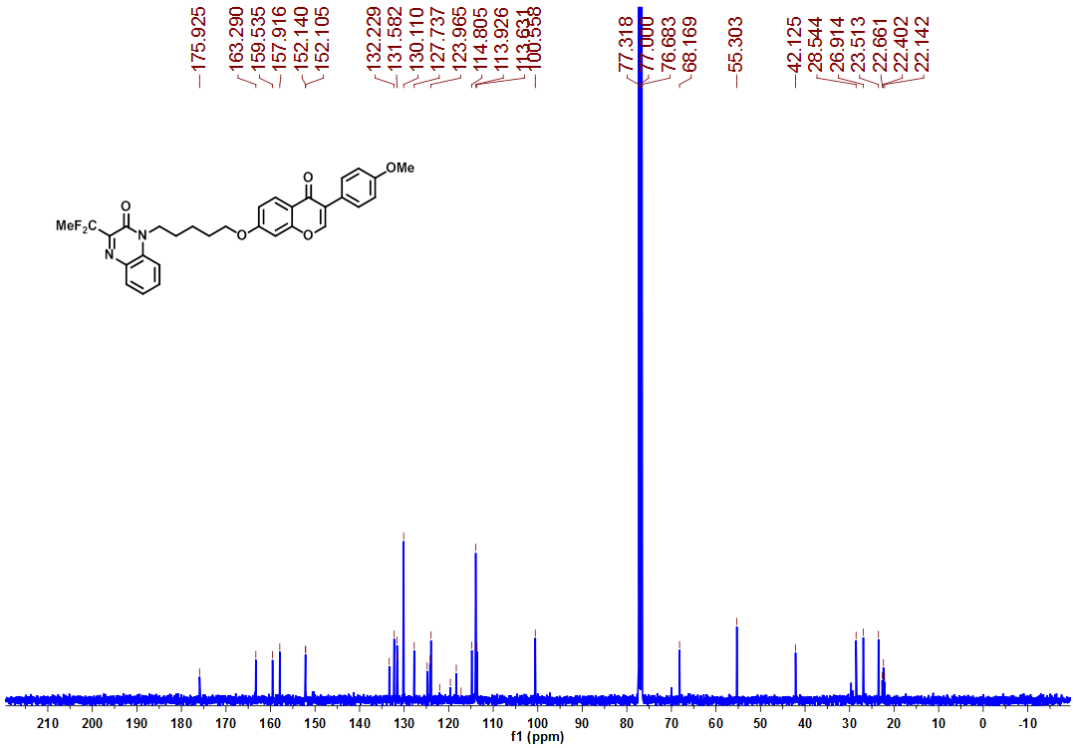
5f-^{19}F NMR (471 MHz, $CDCl_3$)



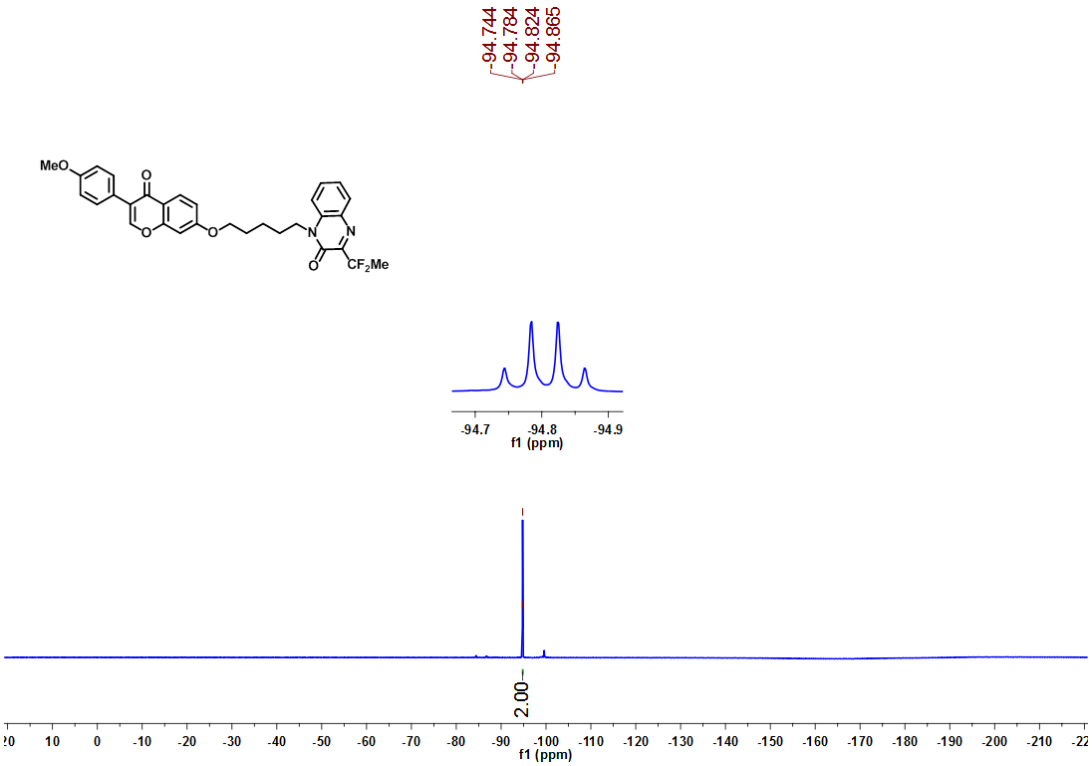
5g-^{1}H NMR (400 MHz, $CDCl_3$)



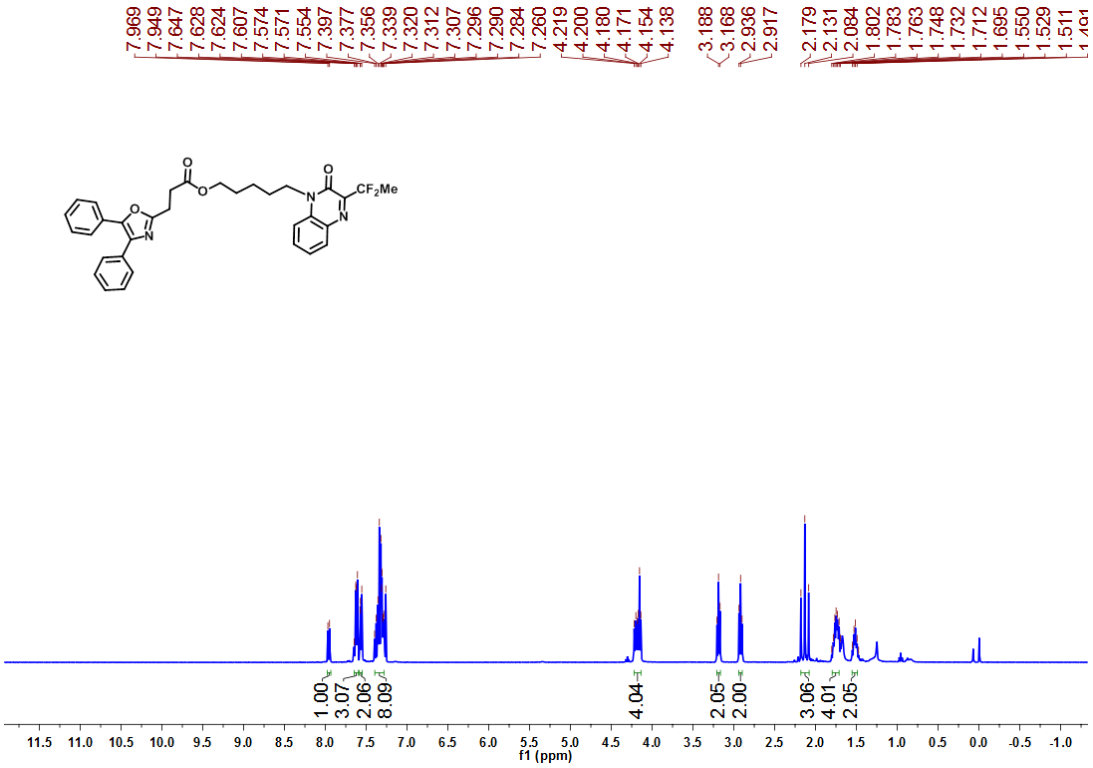
5g-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



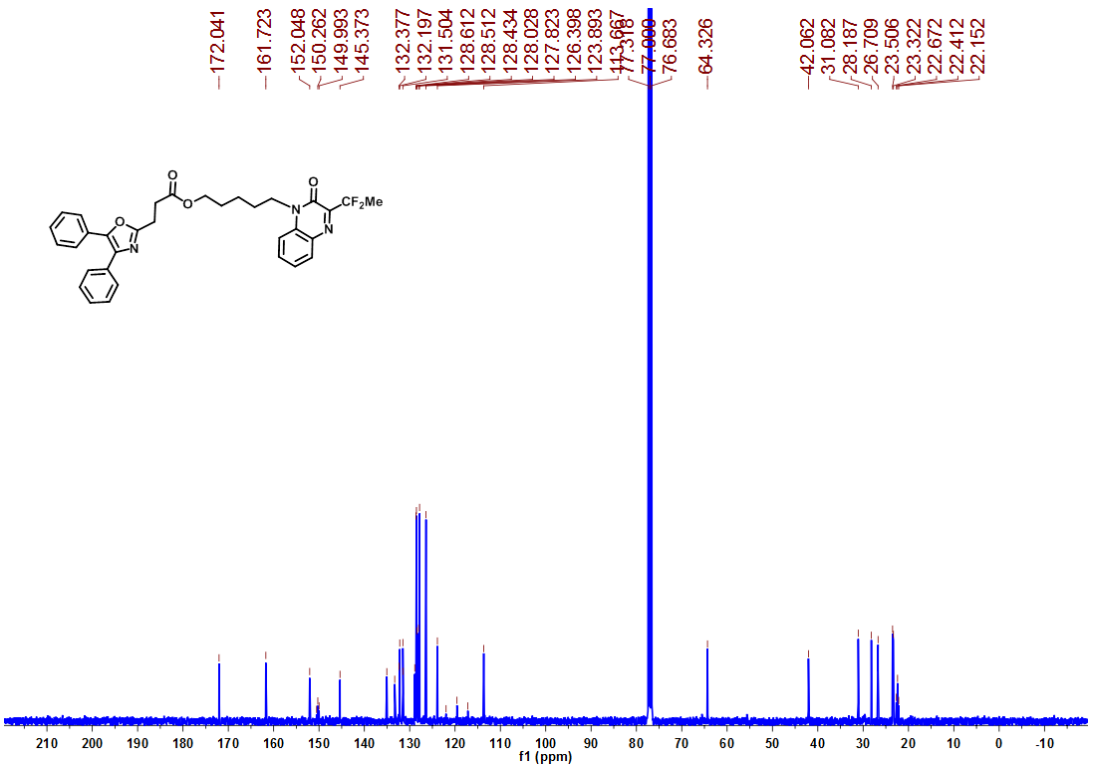
5g-^{19}F NMR (471 MHz, $CDCl_3$)



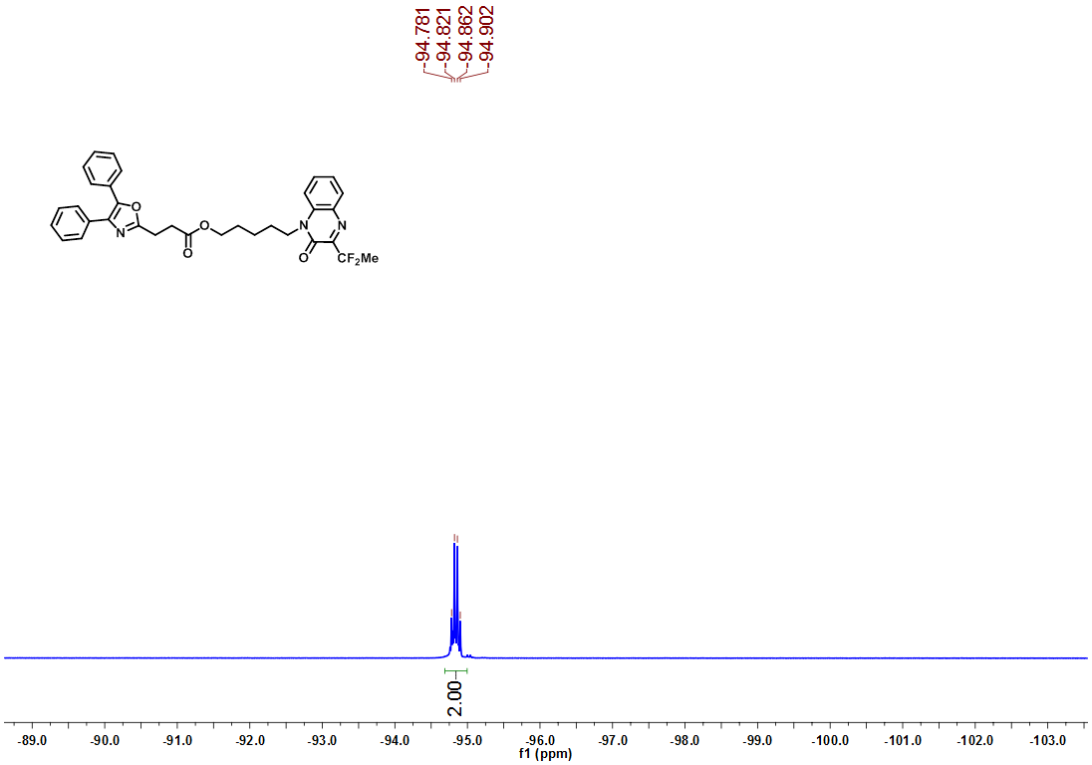
5h-^{1}H NMR (400 MHz, $CDCl_3$)



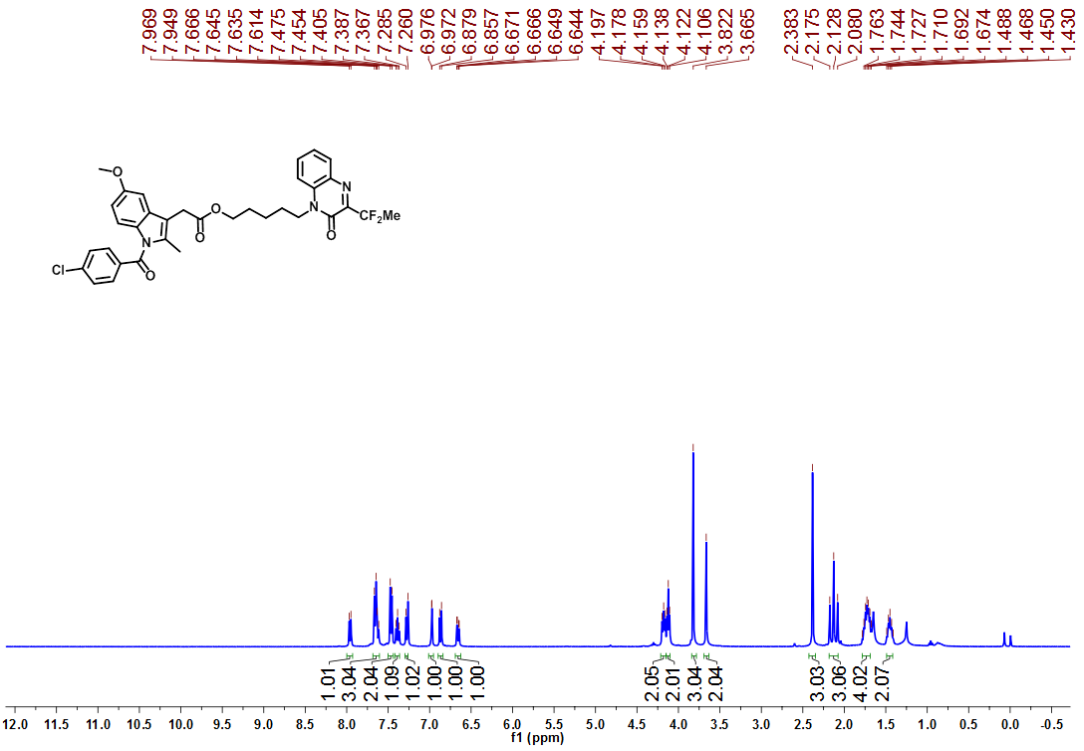
5h-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



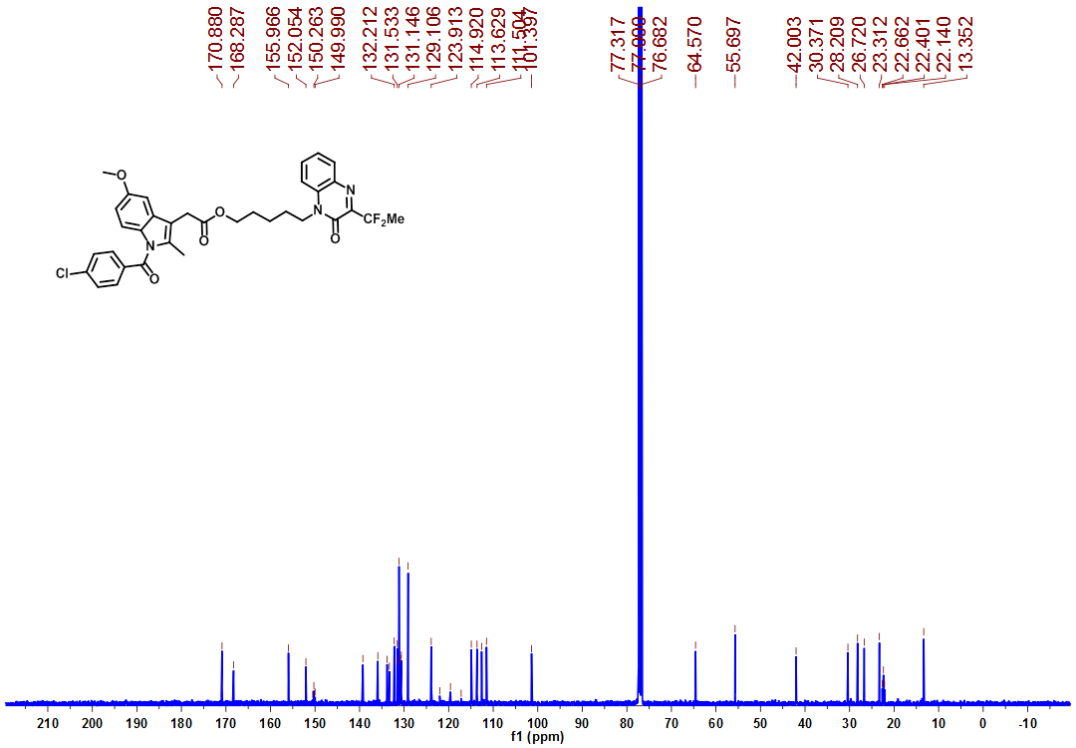
5h-^{19}F NMR (471 MHz, $CDCl_3$)



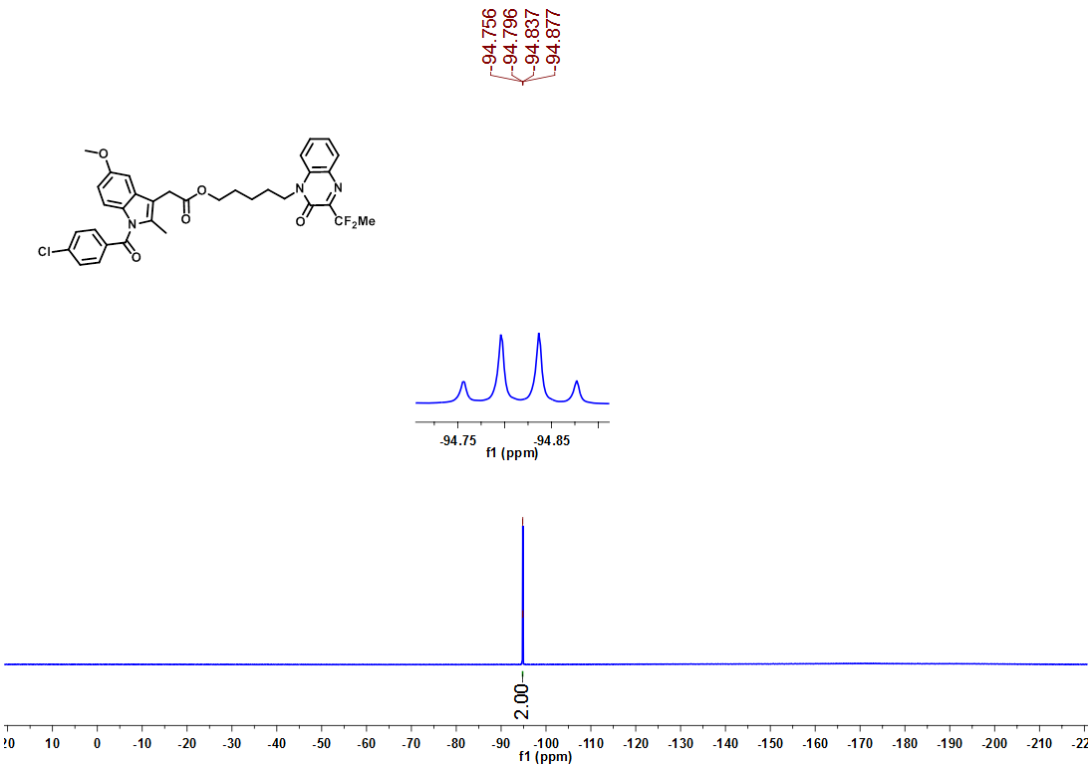
5i-^{1}H NMR (400 MHz, $CDCl_3$)



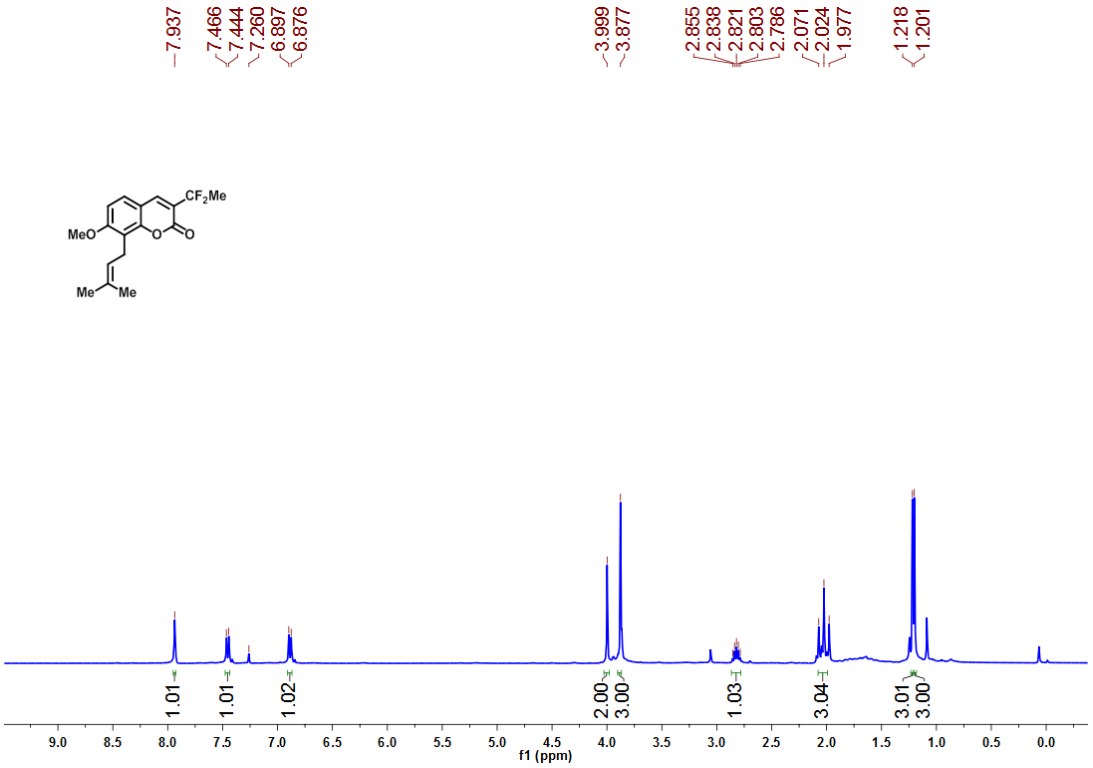
5i-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



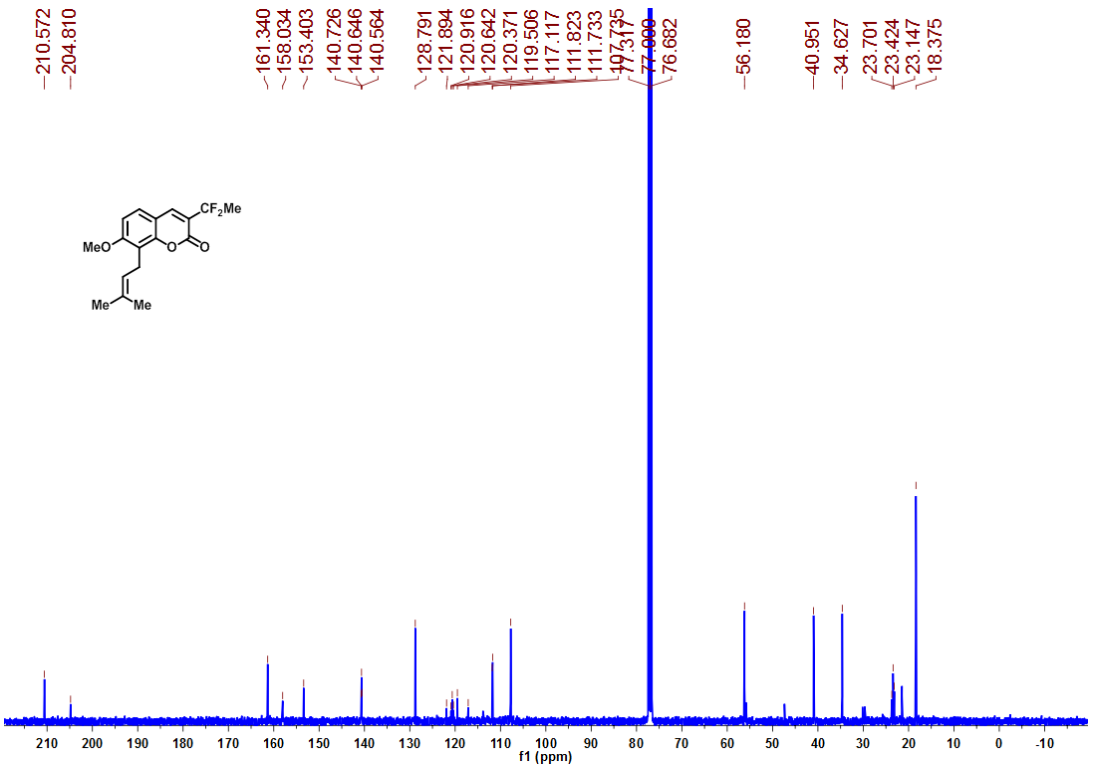
5i-^{19}F NMR (471 MHz, $CDCl_3$)



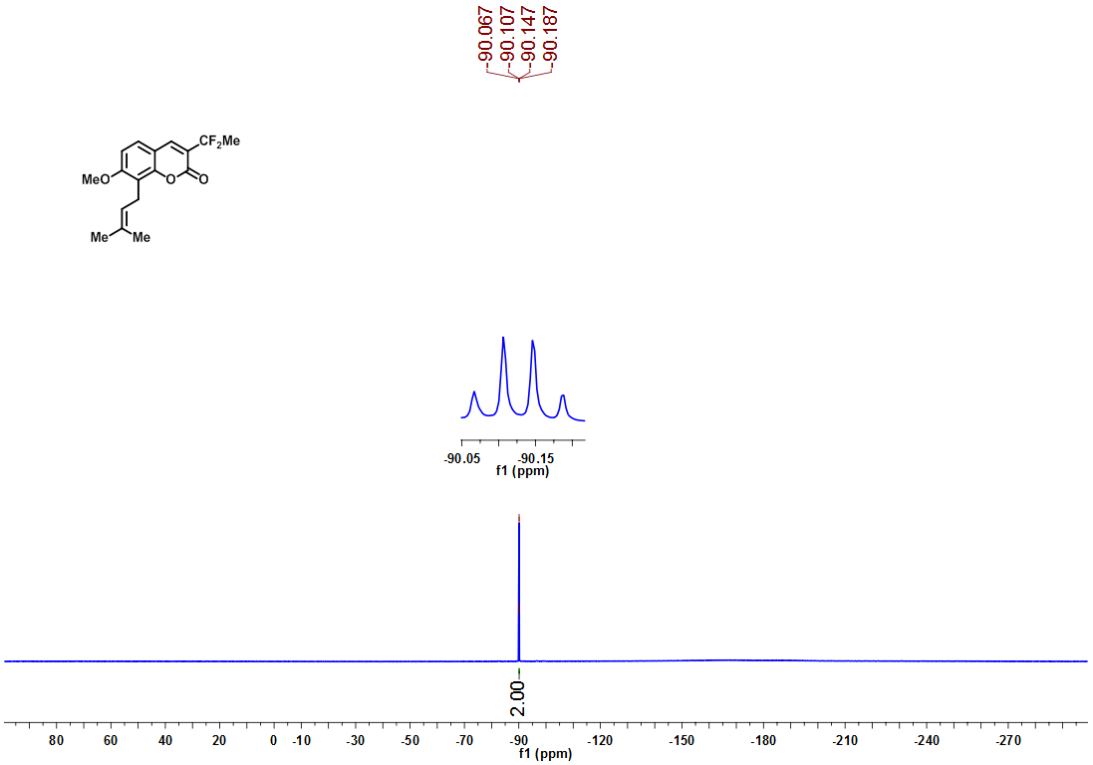
5j-^{1}H NMR (400 MHz, $CDCl_3$)



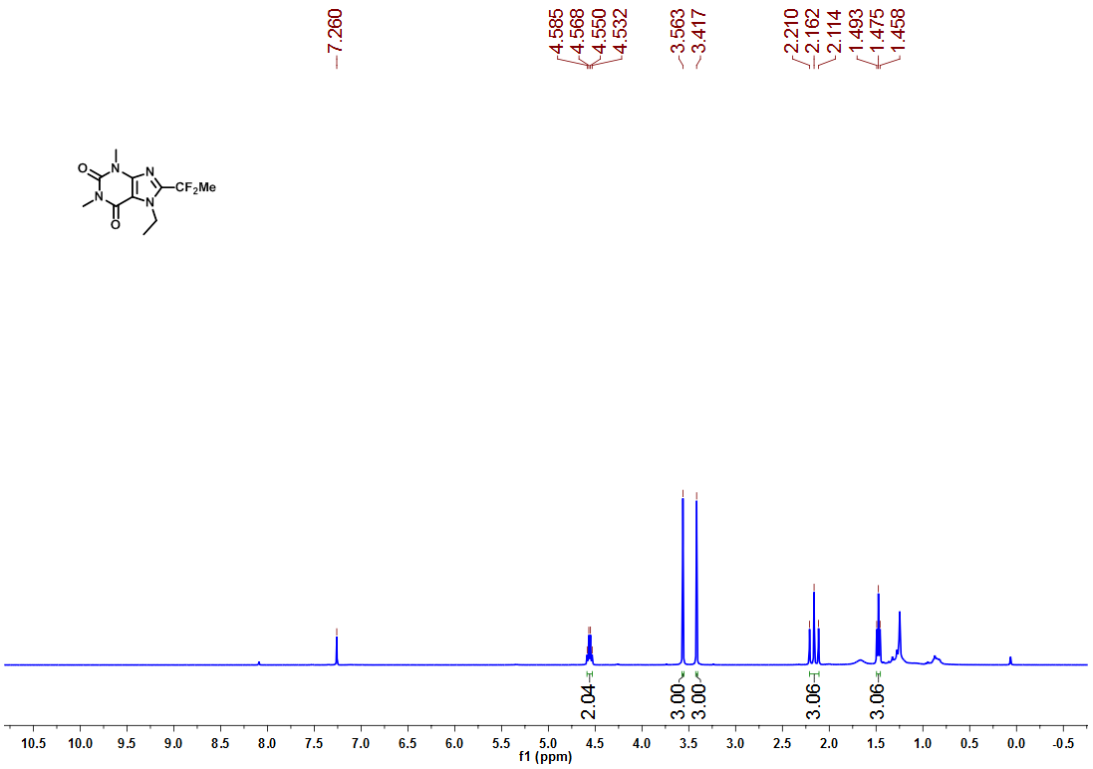
5j-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



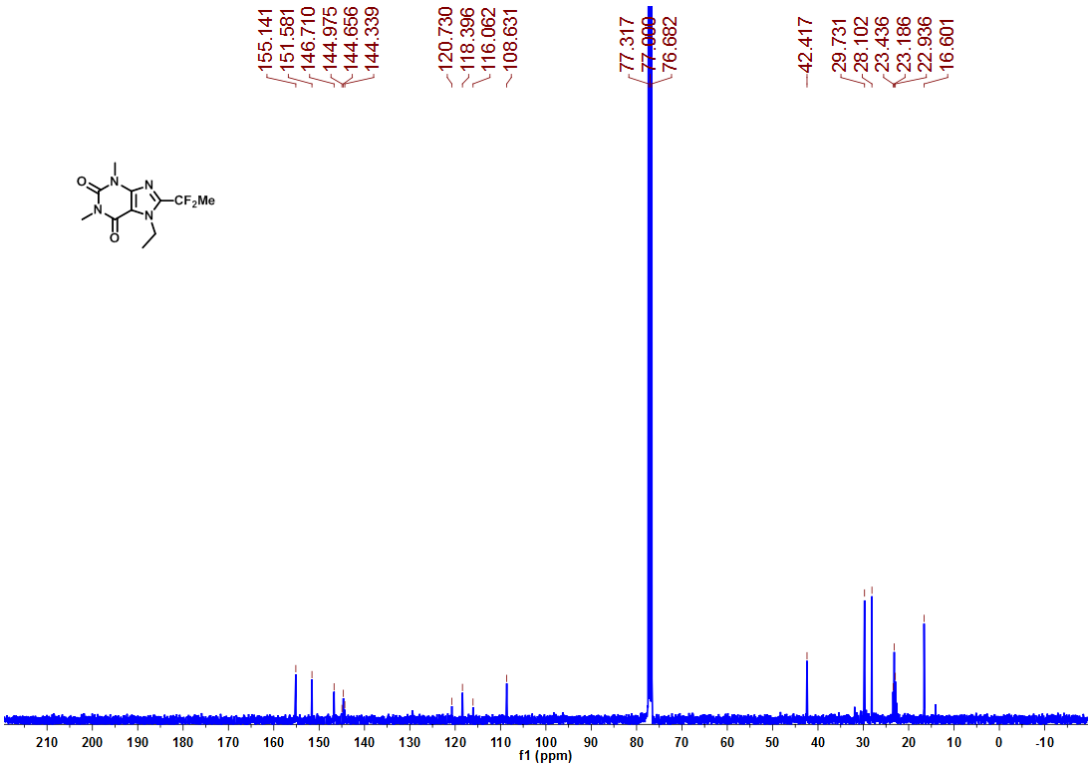
5j-^{19}F NMR (471 MHz, $CDCl_3$)



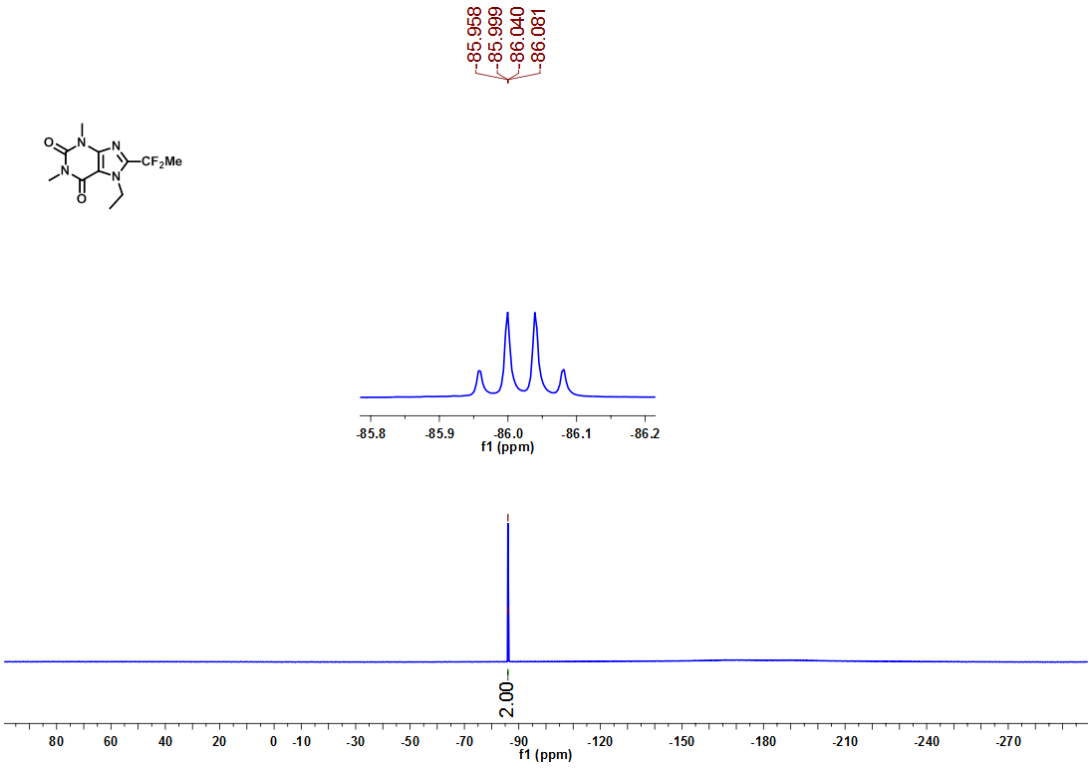
5k-^{1}H NMR (400 MHz, $CDCl_3$)



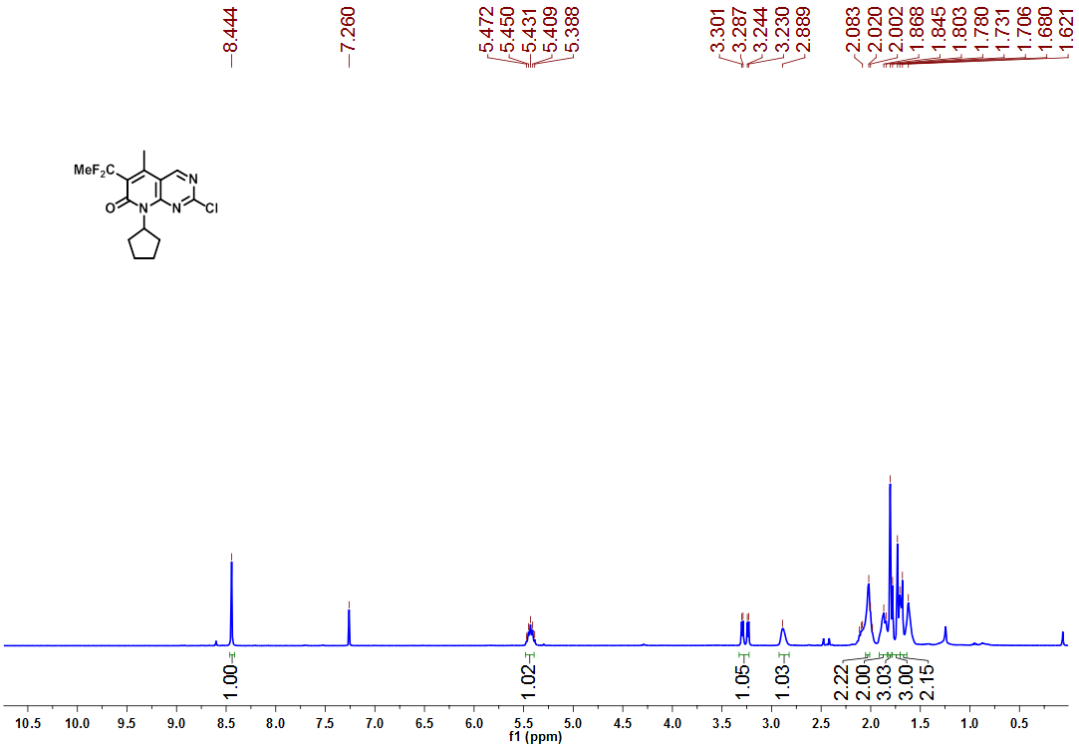
5k-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



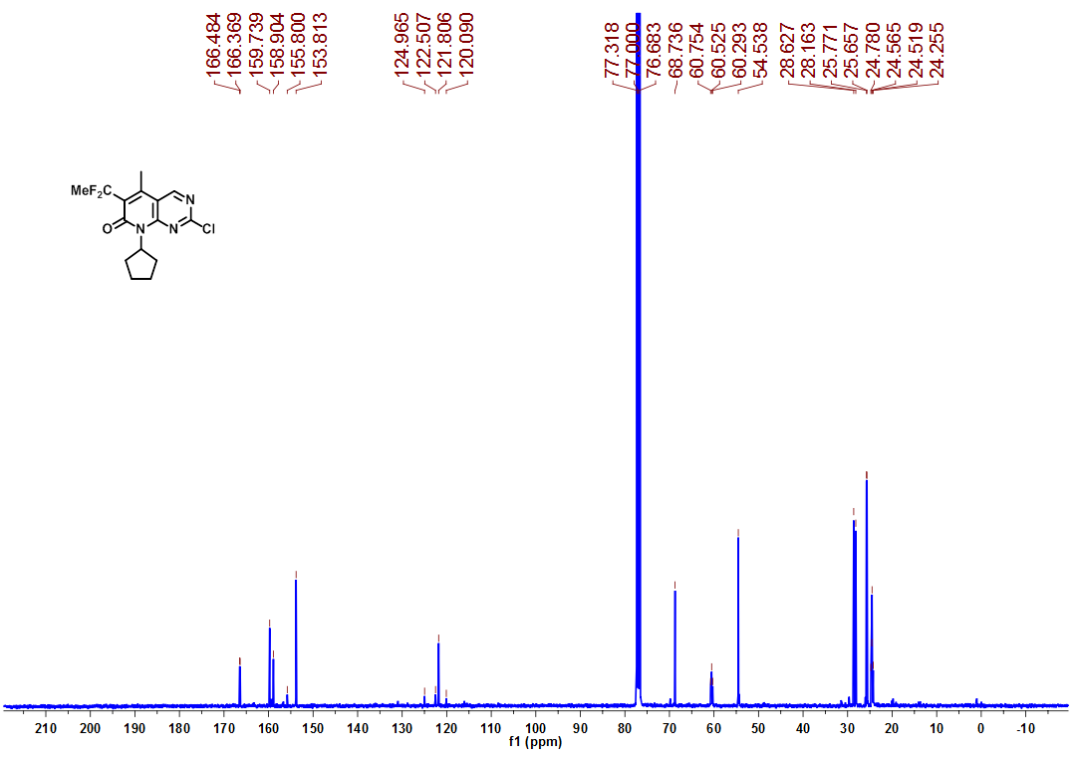
5k-^{19}F NMR (471 MHz, $CDCl_3$)



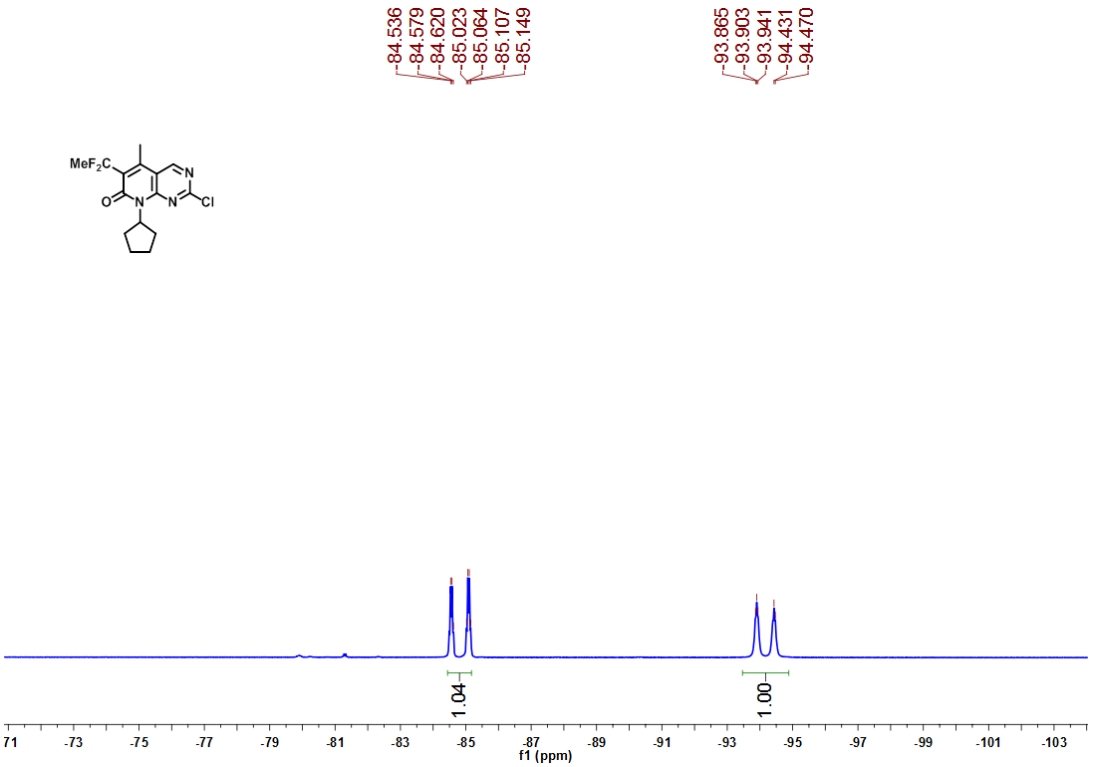
5l-^{1}H NMR (400 MHz, $CDCl_3$)



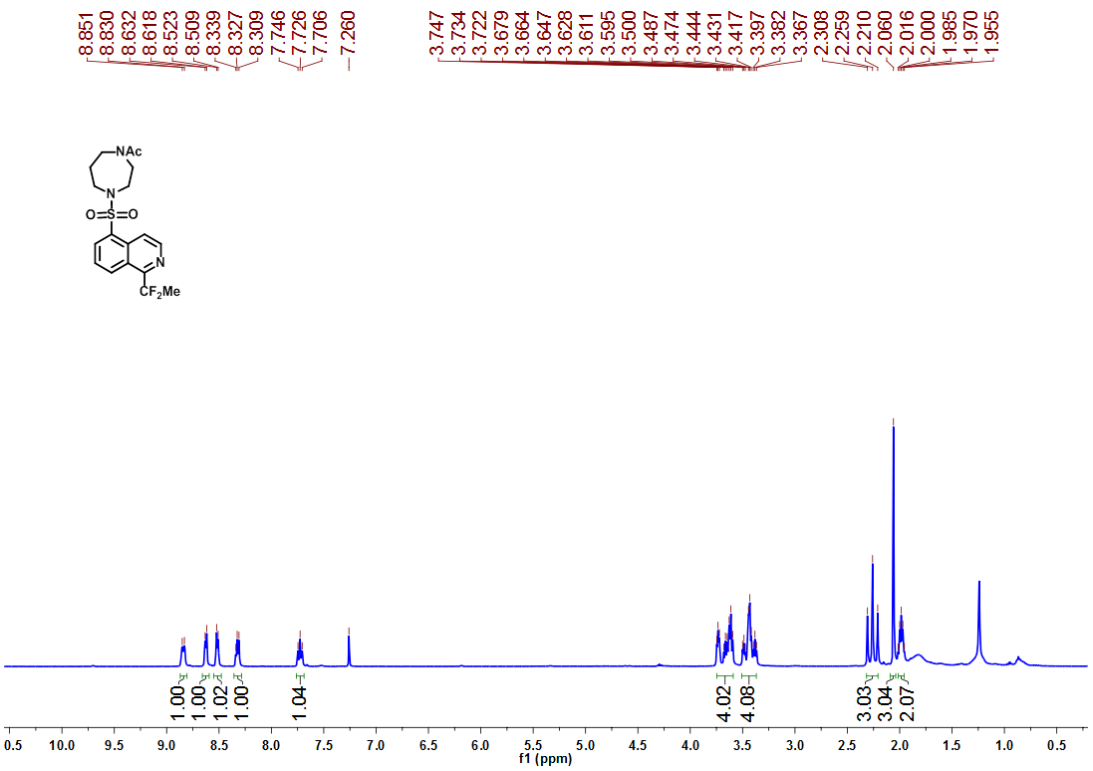
5l-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



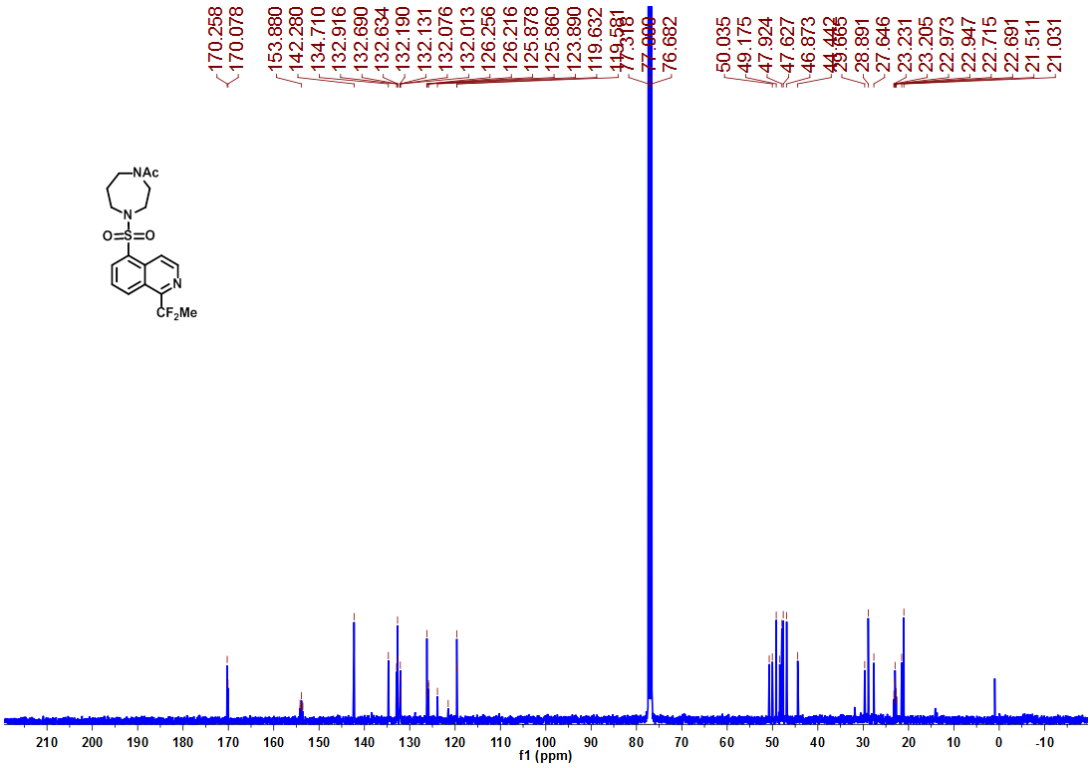
5l-^{19}F NMR (471 MHz, $CDCl_3$)



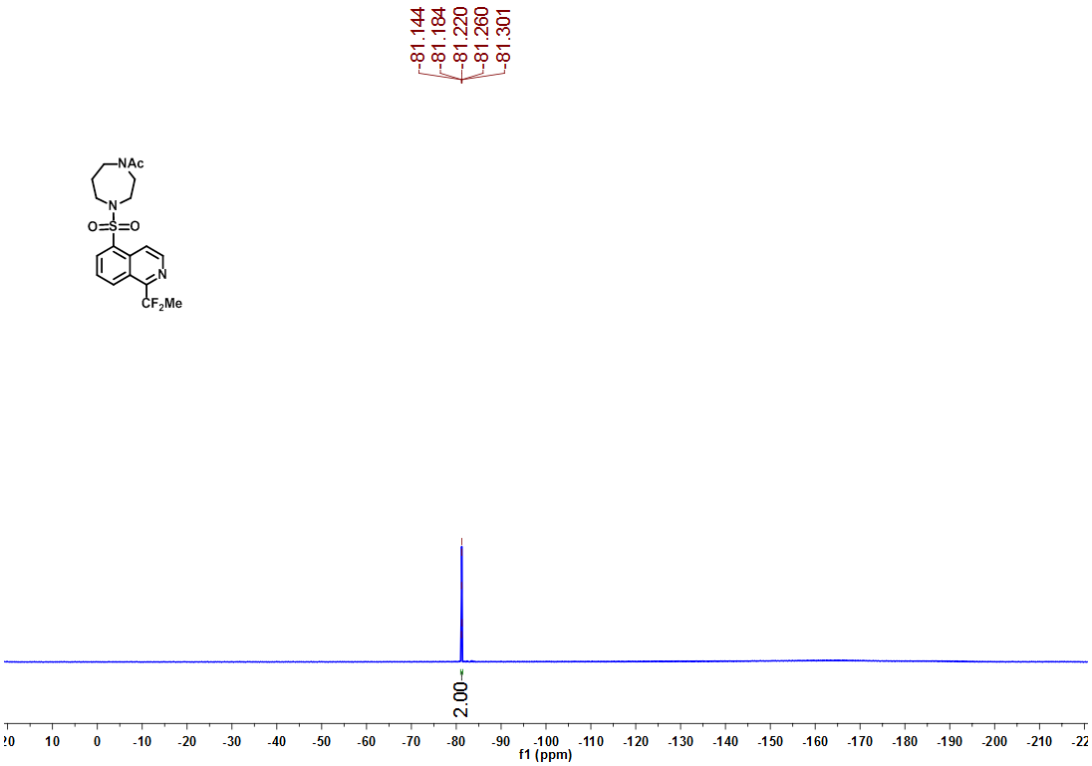
5m-^{1}H NMR (400 MHz, $CDCl_3$)



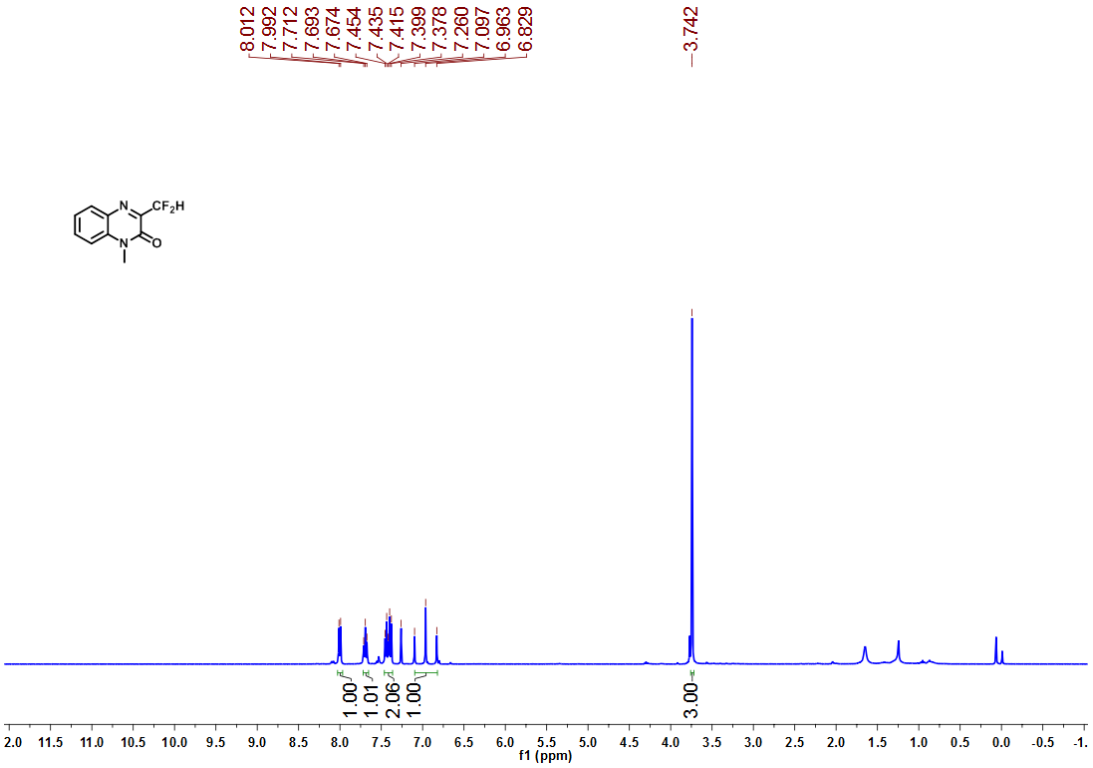
5m-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



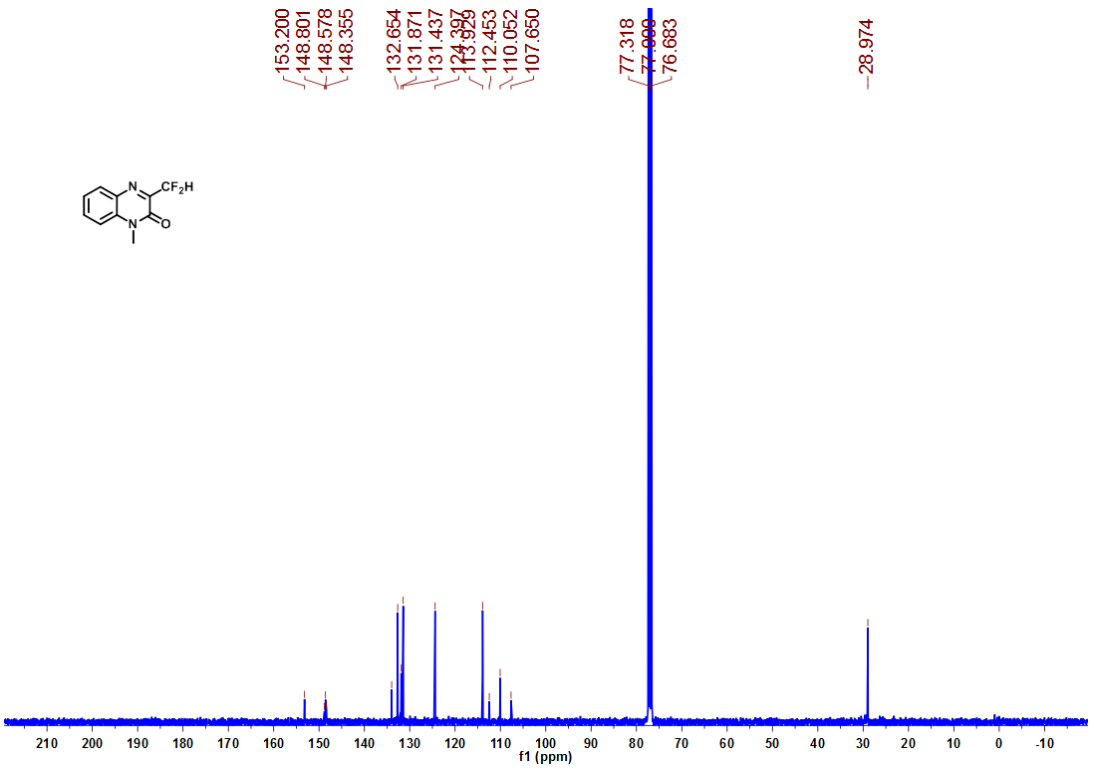
5m-^{19}F NMR (471 MHz, $CDCl_3$)



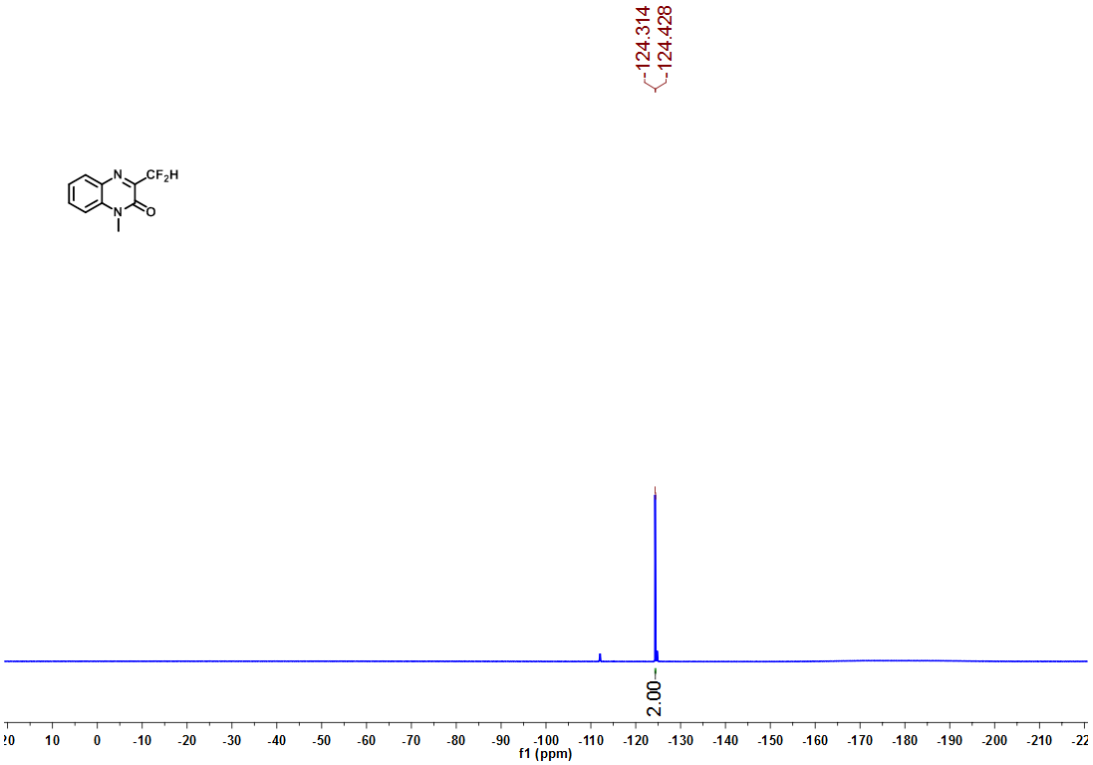
6ab-^{1}H NMR (400 MHz, $CDCl_3$)



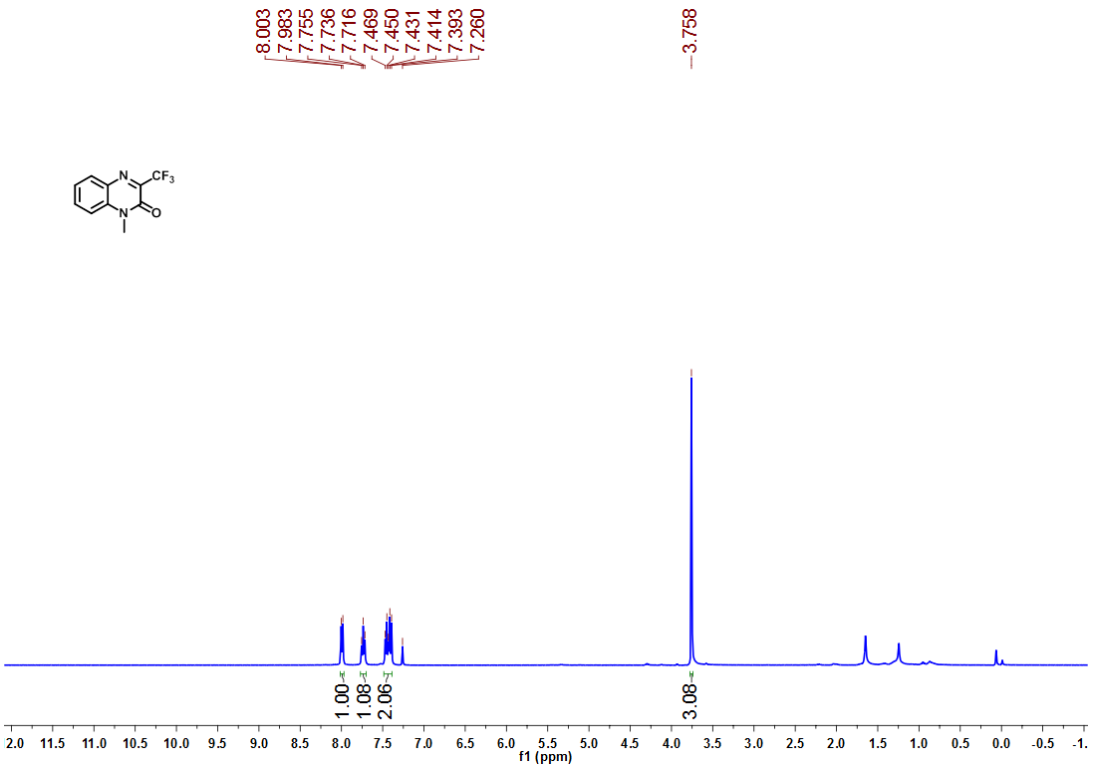
6ab-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



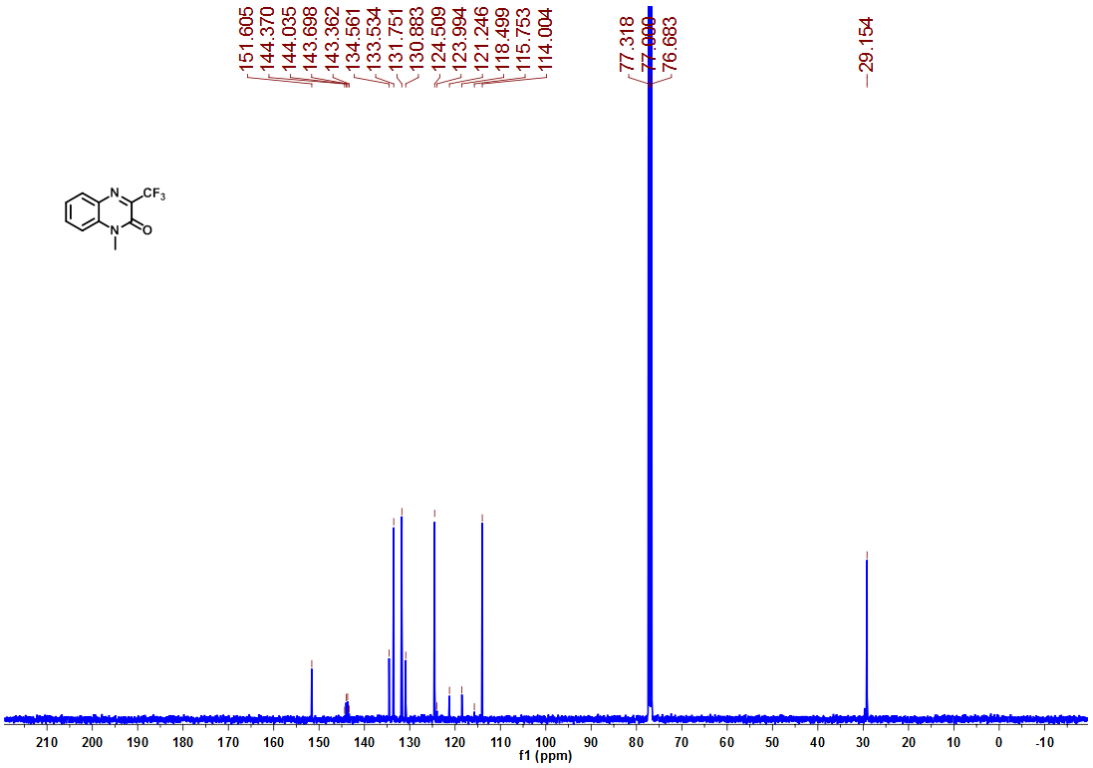
6ab-^{19}F NMR (471 MHz, $CDCl_3$)



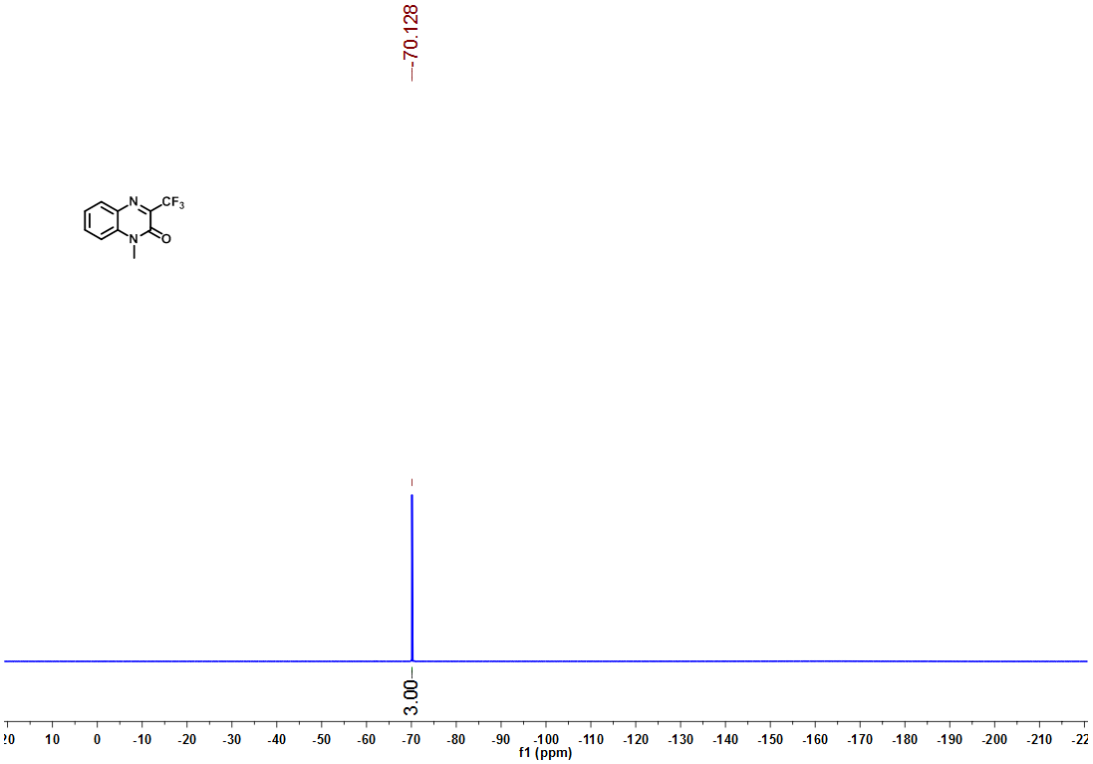
6ac-^{1}H NMR (400 MHz, $CDCl_3$)



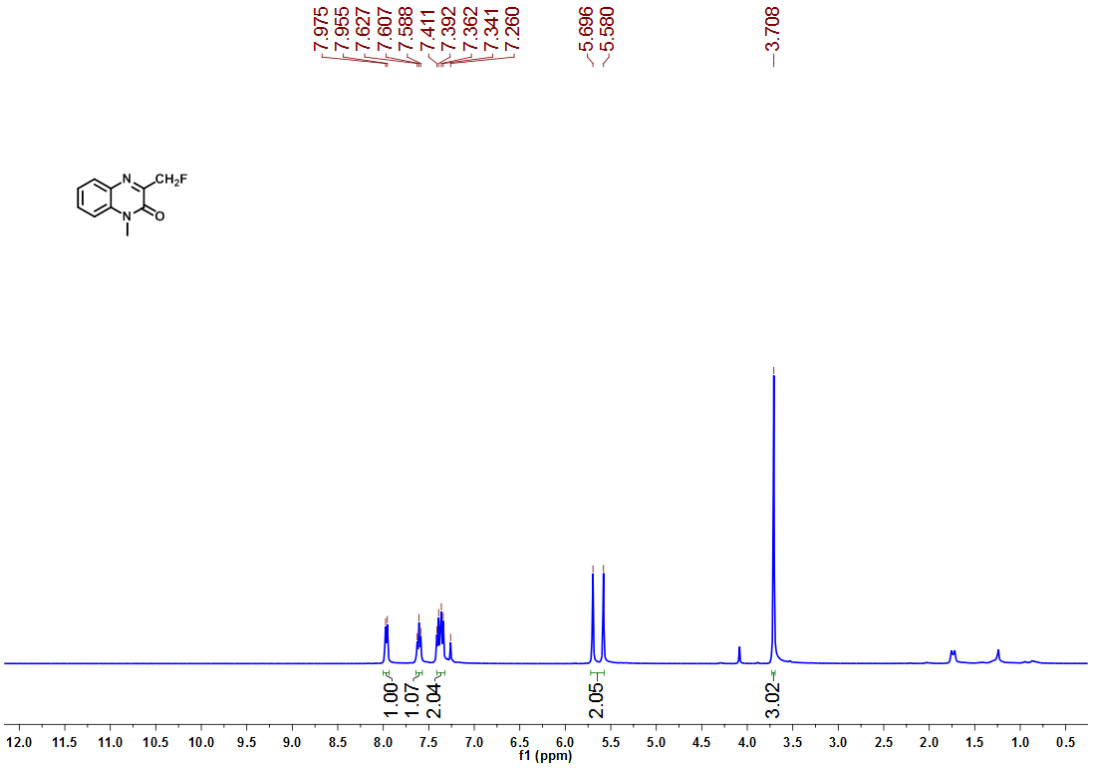
6ac-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



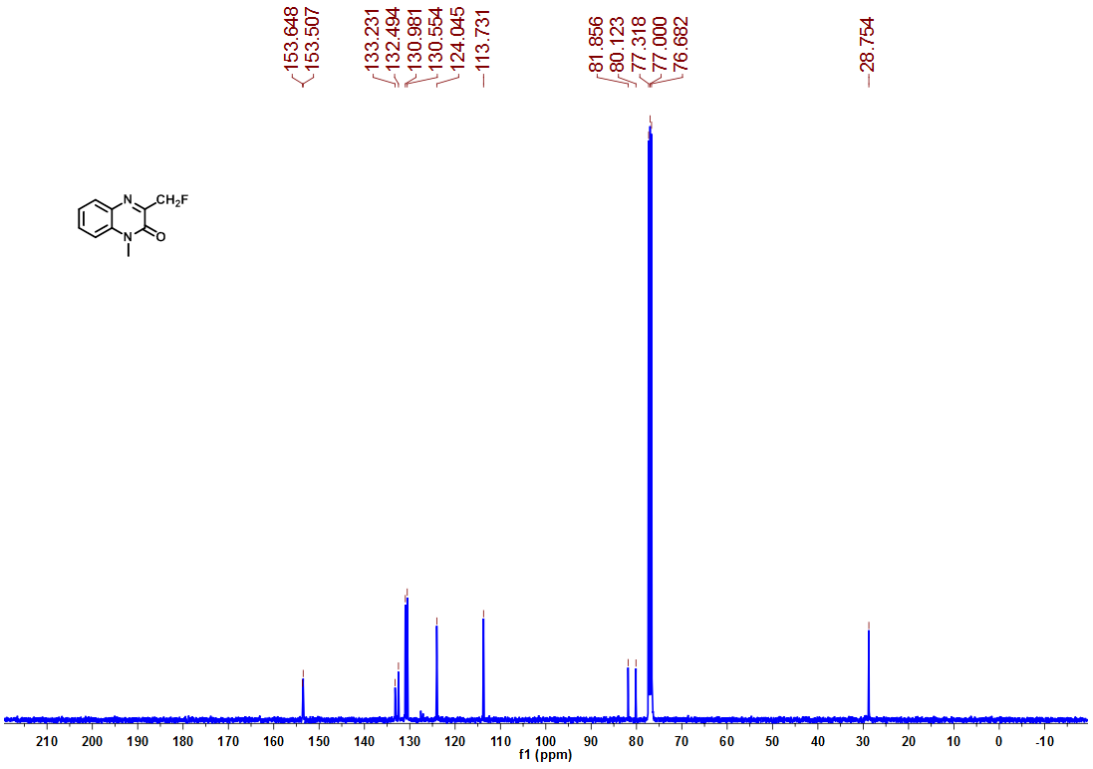
6ac-^{19}F NMR (471 MHz, $CDCl_3$)



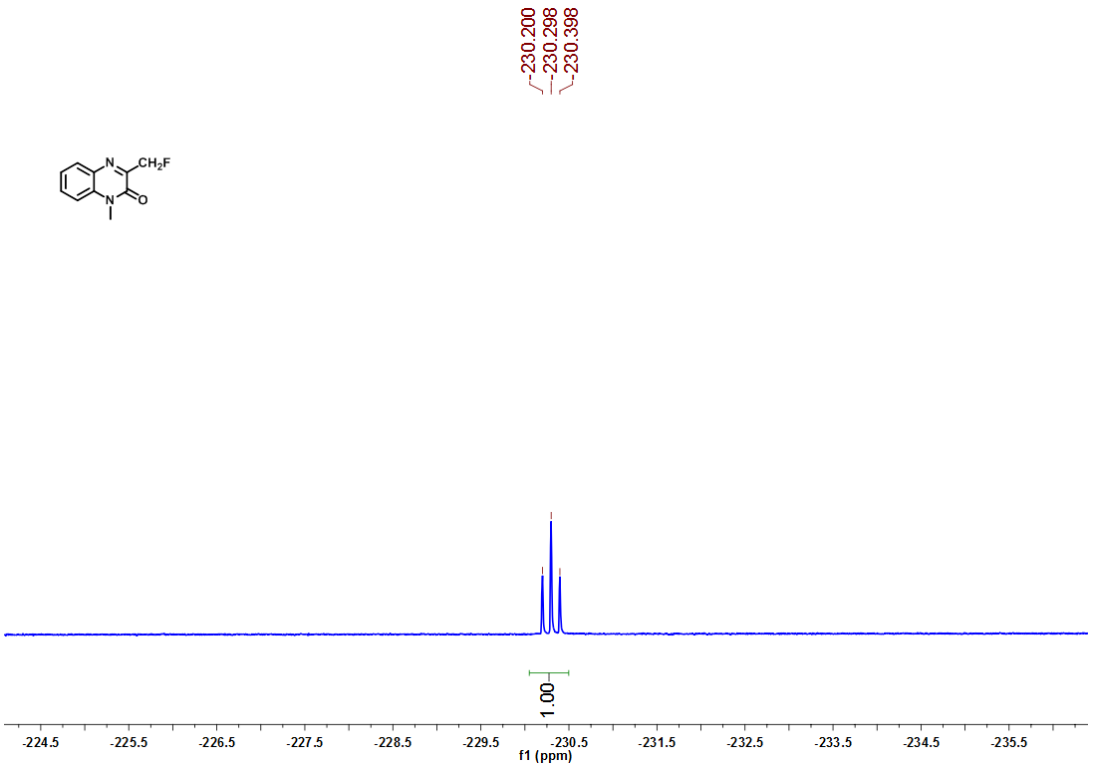
6ad-^{1}H NMR (400 MHz, $CDCl_3$)



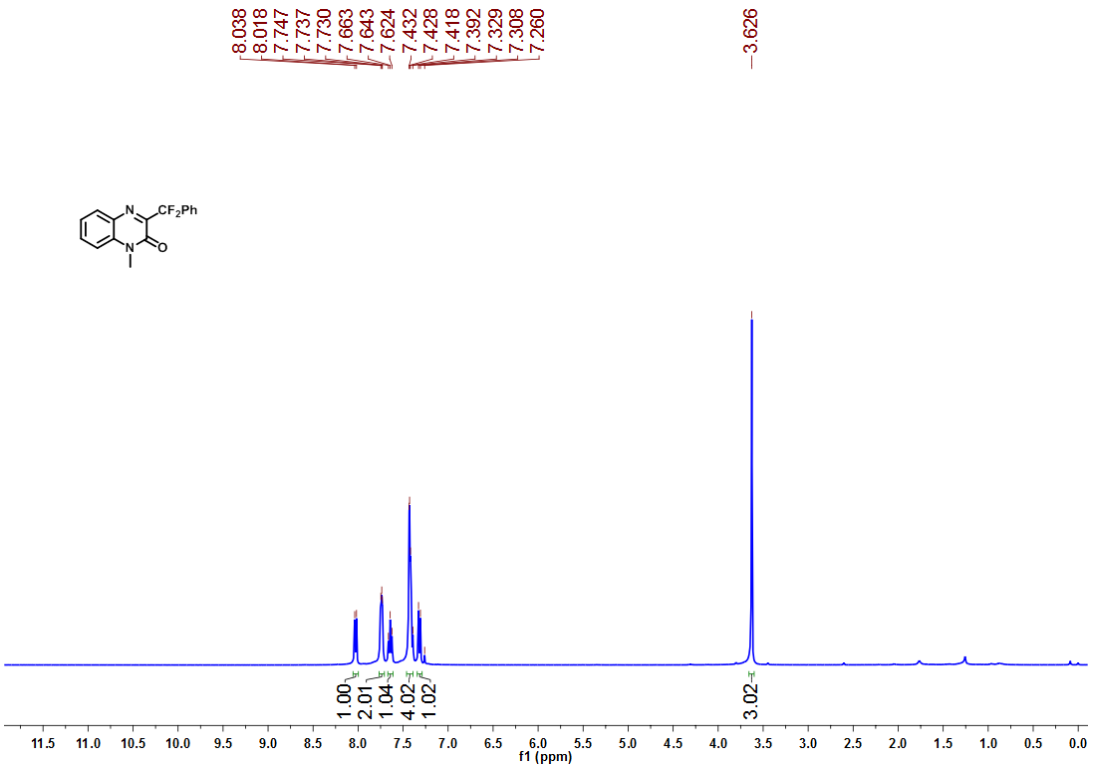
6ad-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



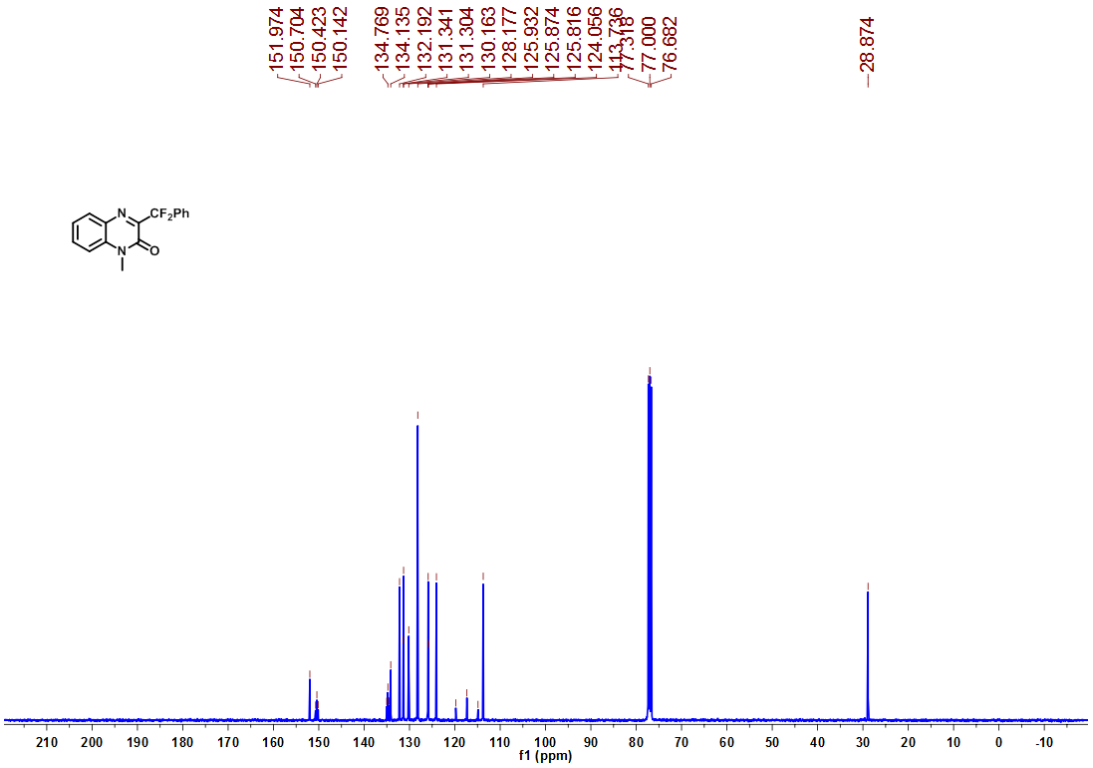
6ad-^{19}F NMR (471 MHz, $CDCl_3$)



6ae-^{1}H NMR (400 MHz, $CDCl_3$)



6ae-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



6ae-^{19}F NMR (471 MHz, $CDCl_3$)