Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

Zinc-Mediated Radiosynthesis of Unprotected Fluorine-18 Labelled α-Tertiary Amides

J. S. Wright, R. Ma, E. W. Webb, W. P. Winton, J. Stauff, K. Cheng, A. F. Brooks, M. S. Sanford, P. J. H. Scott**

Supporting Information

Table of Contents

1. General 3

1.1 Instrument Information 3

1.2 Materials and Methods 3

2. Synthesis of Precursors and Reference Standards 3

2.1 Synthesis of Precursors 3

2.1.1 General Procedure A for the Synthesis of α-Haloamide Precursors 3

2.2 Synthesis of α-Fluoroamide Reference Standards 11

2.2.1 General Procedure B for the Synthesis of Fluorine-19 Reference Standards 11

2.2.2 General Procedure C for the Synthesis of Fluorine-19 Reference Standards 11

3. Radiolabelling Procedures 18

3.1 Materials and Methods 18

3.2 General Procedure for the Preparation of [^{18}F]Fluoride Salts 19

3.3 HPLC Conditions 19

3.4 General Procedure for the Radiofluorination of Amides 20

3.5 Analytical Data for the Radiolabelling of α-Haloamides 21

3.6 General Procedure for Automated Synthesis 52

3.6.1 2-(fluoro-^{18}F)-2-methyl-N-phenylpropanamide (1-^{18}F) 52

3.6.2 N-((3-(3-fluoro-4-morpholinophenyl)-2-oxooxazolidin-5-yl)methyl)-2-(fluoro-^{18}F)-2-methylpropanamide (27-^{18}F) 54

4. Stability Studies 57

4.1 1-^{18}F and 27-^{18}F Buffer and Radiolytic Stability Analysis 57

4.2 Plasma Stability Analysis 57

4.2.1 General Considerations 57

4.2.2 Rodent Plasma Metabolite Study 57

5. Reaction Development 57

5.1 Radiochemical Corrections 57

5.2 Screening Data 58

5.3 Reaction Scope with [^{18}F]CsF 75

5.4 ^{19}F-Fluorination of α-Haloamides 76

5.5 Amination of 1-Br 76

5.6 Attempted Cycloaddition Reaction of 1-Br 78

6. NMR Spectra 78

7. References 158

8. Acknowledgements 158

9. Author Contributions 158

1. General

1.1 Instrument Information

NMR spectra were obtained at 25 °C on a Varian VNMRS 700 (699.76 MHz for ^{1}H; 175.95 MHz for ^{13}C), Varian VNMRS 500 (500.09 MHz for ^{1}H; 470.56 MHz for ^{19}F; 125.75 MHz for ^{13}C), Varian MR400 (401 MHz for ^{1}H; 376 MHz for ^{19}F; 123 MHz for ^{13}C), spectrometers. ^{1}H and ^{13}C NMR chemical shifts are reported in parts per million (ppm), with the residual solvent peak used as an internal reference. ^{1}H and ^{19}F NMR multiplicities are reported as follows: singlet (s), doublet (d), triplet (t), quartet (q), quintet (quin), and multiplet (m). Compounds were characterised via NMR spectroscopy, high-resolution mass spectrometry, and/or analytical high-performance liquid chromatography. Mass spectral data were obtained on a Micromass Magnetic Sector Mass Spectrometer in electrospray (ESI), ionization mode or Micromass AutoSpec Ultima Magnetic Sector Mass Spectrometer in electron ionization m/z (EI), mode. Radio-thin-layer chromatography (rTLC) analysis was performed using a Bioscan AR 2000 Radio-TLC scanner with EMD Millipore TLC silica gel 60 plates (ca. 3.0 cm wide x 6.5 cm long). Automated flash chromatography was conducted on a Biotage Isolera Prime or One system equipped with a KP-Sil or KP-Sfär cartridge (10-50 g). Analytical HPLC analysis was performed using a Shimadzu LC-20AD/T LPGEKIT system fitted with a CBM-20A controller, SIL 20AHT injector, SPD 20A UV detector, DGU 20A SR degasser, and CTO-20A column oven with an in-series B-FC-3300 radiation detector for observing gamma emissions.

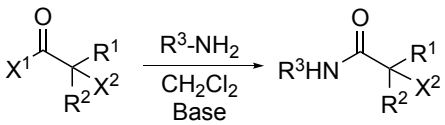
1.2 Materials and Methods

Unless otherwise stated, all non-radioactive chemicals were synthesised or obtained commercially. Chemical vendors used include Millipore Sigma, Fisher, Oakwood Chemicals, Astatech, Ambeed, TCI, Acros, VWR, and Combi-Blocks. **1-Br** was purchased from Enamine and purified with SiO_2 gel chromatography (hexanes/EtOAc,) followed by recrystallization from hexanes to obtain long, off-white shards. **1-^{19}F** was purchased or synthesised according to a procedure from Mizuta.[1] **5-Br** was purchased from Astatech and used as received. **7-Br** and **8-Br** were purchased from Oakwood and used as received. **12-Br** was purchased from Combi-Blocks and used as received. Solvents, including deuterated solvents for NMR analysis, were purchased from Fisher and Cambridge Isotope Laboratories. 1,5,7-Triazabicyclo[4.4.0]dec-5-ene (TBD), and $Zn(OTf)_2$ were obtained from Millipore Sigma and used as received. Anhydrous bottles of dimethylsulfoxide (DMSO, ≥99.9%), and acetonitrile (99.8%), fitted with a Sure/Seal™ septum, were obtained from Millipore Sigma and used as received. CsOTf was synthesised according to a procedure from Jarosz and Dabrowa.[2] Me_4NOTf was synthesised by the slow addition of Me_4NOH pentahydrate (10 g, 55.2 mmol, 1 equiv.) in 20 mL H_2O to a 0 °C solution of Tf_2O (4.6 mL, 27.6 mmol, 0.5 equiv.), in H_2O (20 mL), over 20 min. The reaction was allowed to warm to room temperature over 1 h before azeotropic removal of the volatiles with MeCN (3x75 mL) and recrystallization from anhydrous iPrOH to obtain a solid residue that was dried under high vacuum (0.1 Pa) at 150 °C for 3 d. Me_4NOTf was obtained as a free-flowing white powder (11.1 g, 49.7 mmol, 90%), with characterization data matching previous reports.[3–5] **31-Br** and **31-^{18}F** were prepared according to procedures described by Mizuta, and the spectral data obtained matched this report.[1]

2. Synthesis of Precursors and Reference Standards

2.1 Synthesis of Precursors

2.1.1 General Procedure A for the Synthesis of α-Haloamide Precursors

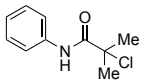


X^1 and X^2 = halide

SUPPORTING INFORMATION

Under Ar in a brine/ice cooling bath, a solution of an amine substrate (1.0 equiv.) and Et_3N or Hünig's Base (2.0 equiv.) in CH_2Cl_2 (1.5M) was treated with an α-halo acid halide (1.1 equiv.), The reaction was warmed to room temperature and stirred overnight before removing the volatiles and purification with SiO_2 gel chromatography.

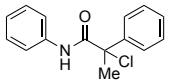
2-Chloro-2-methyl-*N*-phenylpropanamide (**1-Cl**)



1-Cl

Synthesised according to General Procedure A using aniline (0.5 mmol, 46 µL), Hünig's Base (1.0 mmol, 180 µL), and 2-chloro-2-methylpropanoyl chloride (0.55 mmol, 63 µL). SiO_2 gel chromatography (0→100% EtOAc in hexanes) afforded **1-Cl** as a white solid (78 mg, 0.39 mmol, 79% yield).
HRMS m/z (ESI+) calculated for $[C_{10}H_{13}ClON]^+$: 198.0680, found $[M+H]^+$ 198.0680.
δ^{1}H (700 MHz, $CDCl_3$) 8.58 (br, s), 7.57 (d, 2H, *J* = 7.6 Hz), 7.35 (t, 2H, *J* = 7.6 Hz), 7.15 (t, 1H, *J* = 7.6 Hz), 1.88 (s, 6H).
δ^{13}C (176 MHz, $CDCl_3$) 170.2, 137.3, 129.1, 125.0, 120.1, 70.0, 31.1.

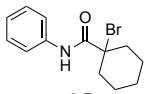
2-Chloro-*N*,2-diphenylpropanamide (**2-Cl**)



2-Cl

Synthesised according to General Procedure A (with modifications) using aniline (1.30 mmol, 120 µL), Hünig's Base (2.60 mmol, 450 µL), and 2-chloro-2-phenylpropanoyl chloride[6] (1.43 mmol, 289 mg). SiO_2 gel chromatography (5→15% EtOAc in hexanes) afforded **2-Cl** as an orange solid (40 mg, 0.15 mmol, 12% yield).
HRMS m/z (ESI+) calculated for $[C_{15}H_{15}ClON]^+$: 260.0837, found $[M+H]^+$ 260.0833.
δ^{1}H (499 MHz, $CDCl_3$) 8.38 (br s, 1H), 7.62 (d, 2H, *J* = 7.6 Hz), 7.56 (d, 2H, *J* = 7.6 Hz), 7.41-7.34 (multiple peaks, 5H), 7.16 (t, 1H, 7.6 Hz), 2.23 (s, 3H).
δ^{13}C (126 MHz, $CDCl_3$) 168.7, 141.5, 137.4, 129.2, 128.8, 128.7, 126.1, 125.1, 120.0, 73.4, 30.5.

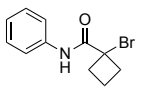
1-Bromo-*N*-phenylcyclohexane-1-carboxamide (**3-Br**)



3-Br

Synthesised according to General Procedure A (with modifications) using aniline (0.50 mmol, 46 µL), Et_3N (1 mmol, 140 µL), and 1-bromocyclohexane-1-carbonyl chloride (0.55 mmol, 78 µL) instead of 2-bromo-2-methylpropanoyl bromide. SiO_2 gel chromatography (0→100% EtOAc in pentanes) afforded **3-Br** as a white solid (7 mg, 0.025 mmol, 5% yield).
HRMS m/z (ESI+) calculated for $[C_{13}H_{17}BrON]^+$: 282.0488, found $[M+H]^+$ 282.0484.
δ^{1}H (400 MHz, $CDCl_3$) 8.37 (br s, 1H), 7.55 (d, 2H, *J* = 7.7 Hz), 7.36 (t, 2H, *J* = 7.7 Hz), 7.15 (t, 1H, *J* = 7.7 Hz), 2.26-2.12 (m, 4H), 1.86-1.68 (m, 5H), 1.42-1.25 (m, 1H).
δ^{13}C (101 MHz, $CDCl_3$) 169.9, 137.6, 129.2, 124.9, 120.1, 77.4, 38.3, 24.9, 22.9.

1-Bromo-*N*-phenylcyclobutane-1-carboxamide (**4-Br**)



4-Br

Synthesised according to General Procedure A (with modifications) using aniline (0.5 mmol, 46 µL), Et_3N (1 mmol, 140 µL), and 1-bromocyclobutane-1-carbonyl chloride (0.55 mol, 109 mg) instead of 2-bromo-2-methylpropanoyl bromide. SiO_2 gel chromatography (0→50% EtOAc in hexanes) afforded **4-Br** as a white solid (80 mg, 0.31 mmol, 63% yield).
HRMS m/z (ESI+) calculated for $[C_{11}H_{13}BrON]^+$: 254.0175, found $[M+H]^+$ 254.0184.
δ^{1}H (400 MHz, $CDCl_3$) 8.05 (br s, 1H), 7.57-7.54 (m, 2H), 7.34 (t, 2H, *J* = 7.8 Hz), 7.16-7.12 (m, 1H), 3.15-3.07 (m, 2H), 2.69-2.62 (m, 2H), 2.36-2.28 (m, 1H), 2.07-1.97 (m, 1H).
δ^{13}C (101 MHz, $CDCl_3$) 169.1, 137.6, 129.1, 124.8, 120.0, 60.6, 37.9, 17.1.

2-Bromo-*N*-cyclohexyl-2-phenylacetamide (**6-Br**)[7]



6-Br

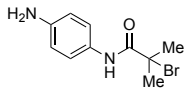
To a solution of 2-bromo-2-phenylacetic acid (2.0 mmol, 1.0 equiv., 530 mg), cyclohexylamine (2.0 mmol, 1.0 equiv., 0.23 mL), and *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (2.4 mmol, 1.2 equiv., 460 mg) in CH_2Cl_2 (20 mL) was added DMAP (0.4 mmol, 20 mol%, 50 mg) at room temperature. The reaction was stirred overnight, filtered over Celite®, and purified via SiO_2 gel chromatography (0→50% EtOAc in hexanes) to afford the corresponding amide as a white solid (420 mg, 1.42 mmol, 71%). Obtained and characterised as a ca. 5.7:1 mixture of rotational isomers.

HRMS m/z (ESI+) calculated for $[C_{14}H_{19}BrON]^+$: 296.0645, found $[M+H]^+$ 296.0645.

δ^{1}H (499 MHz, $CDCl_3$) 7.44-7.38 (m, 2H), 7.38-7.30 (m, 3H), 6.65-6.58 (br m, 1H) 5.41 (s, 0.15H), 5.34 (s, 0.85H), 3.84-3.76 (m, 1H), 1.98-1.90 (m, 2H) 1.76-1.69 (m, 2H), 1.65-1.59 (m, 1H), 1.43-1.33 (m, 2H), 1.28-1.16 (m, 3H).

δ^{13}C (125 MHz, $CDCl_3$) 166.4, 166.0, 137.9, 137.5, 129.1, 129.0, 129.0, 128.4, 127.9, 61.9, 51.9, 49.3, 49.0, 33.0, 32.9, 32.8, 32.7, 25.5, 24.8, 24.8.

N-(4-Aminophenyl)-2-bromo-2-methylpropanamide (**9-Br**)



9-Br

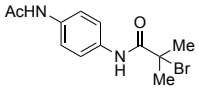
Synthesised according to General Procedure A (with modifications) using *tert*-butyl (4-aminophenyl)carbamate (0.5 mmol, 104 mg), Et_3N (1 mmol, 140 µL), and 2-bromo-2-methylpropanoyl bromide (0.55 mmol, 68 µL) in CH_2Cl_2 (40 mL). After 16 h, HCl (8 mL, 2.0M in diethyl ether) was added at rt, and the reaction was stirred overnight. The reaction was filtered and rinsed with cold Et_2O (2 x 5 mL). The yellow precipitate was dissolved in H_2O (5 mL) and $NaHCO_3$ (5 mL). The aqueous layer was extracted with CH_2Cl_2 (5x5 mL), and the combined organic fractions were dried with $MgSO_4$, filtered, and evaporated before purification with SiO_2 gel chromatography (0→100% EtOAc in hexanes) to afford **9-Br** as a white solid (45 mg, 0.18 mmol, 35% yield).

HRMS m/z (ESI+) calculated for $[C_{10}H_{14}BrON_2]^+$: 257.0284, found $[M+H]^+$ 257.0281.

δ^{1}H (400 MHz, $CDCl_3$) 8.30 (br s, 1H), 7.29 (d, 2H, *J* = 8.7 Hz), 6.67 (d, 2H, *J* = 8.7 Hz), 3.58 (br s, 2H), 2.03 (s, 6H).

δ^{13}C (101 MHz, $CDCl_3$) 169.8, 143.9, 128.6, 121.1, 115.5, 63.7, 32.8.

N-(4-Acetamidophenyl)-2-bromo-2-methylpropanamide (**10-Br**)



10-Br

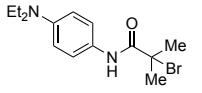
Synthesised according to General Procedure A using *N*-(4-aminophenyl)acetamide (2.0 mmol, 300 mg), Et_3N (4.0 mmol, 560 µL), and 2-bromo-2-methylpropanoyl bromide (2.2 mmol, 272 µL). SiO_2 gel chromatography (0→50% EtOAc in CH_2Cl_2) afforded **10-Br** as a white solid (517 mg, 1.73 mmol, 87% yield).

HRMS m/z (EI+) calculated for $[C_{12}H_{15}BrO_2N_2]^+$: 298.0317, found $[M^+]$ 298.0315.

δ^{1}H (499 MHz, DMSO) 9.89 (br s, 1H), 9.72 (br s, 1H), 7.56-7.51 (m, 4H), 2.02 (s, 3H), 1.99 (s, 6H).

δ^{13}C (126 MHz, DMSO) 169.1, 168.0, 135.5, 133.6, 121.0, 119.0, 60.8, 30.8, 23.9.

2-Bromo-*N*-(4-(diethylamino)phenyl)-2-methylpropanamide (**11-Br**)



11-Br

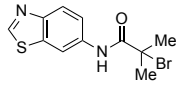
Synthesised according to General Procedure A using N^1,N^1-diethylbenzene-1,4-diamine (2.0 mmol, 329 mg), Et_3N (4.0 mmol, 560 µL), and 2-bromo-2-methylpropanoyl bromide (2.2 mmol, 272 µL). SiO_2 gel chromatography (0→30% Et_2O in hexanes) afforded **11-Br** as a black/grey solid (401 mg, 1.28 mmol, 64% yield).

HRMS m/z (EI+) calculated for $[C_{14}H_{21}BrO_2N]^+$: 312.0837, found $[M]^+$: 312.0828.

δ^{1}H (400 MHz, $CDCl_3$) 8.27 (br s, 1H), 7.34 (d, 2H, *J* = 9.3 Hz), 6.65 (d, 2H, *J* = 9.3 Hz), 3.34 (q, 4H, *J* = 7.0 Hz), 2.04 (s, 6H), 1.14 (t, 6H, *J* = 7.0 Hz).

δ^{13}C (101 MHz, $CDCl_3$) 169.7, 145.7, 126.1, 122.3, 112.4, 63.8, 44.7, 32.8, 12.6.

N-(Benzo[*d*]thiazol-6-yl)-2-bromo-2-methylpropanamide (**13-Br**)



13-Br

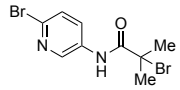
Synthesised according to General Procedure A using benzo[*d*]thiazol-6-amine (2.0 mmol, 300 mg), Et_3N (4.0 mmol, 560 µL), and 2-bromo-2-methylpropanoyl bromide (2.2 mmol, 272 µL). SiO_2 gel chromatography (0→100% Et_2O in hexanes) afforded **13-Br** as an orange solid (313 mg, 1.04 mmol, 52% yield).

HRMS m/z (EI+) calculated for $[C_{11}H_{11}BrOSN_2]^+$: 297.9775, found $[M]^+$ 297.9776.

δ^{1}H (500 MHz, $CDCl_3$) 8.92 (s, 1H), 8.69 (br s, 1H), 8.50 (d, 1H, *J* = 2.1 Hz), 8.04 (d, 1H, *J* = 8.7 Hz), 7.40 (dd, 1H, *J* = 8.9, 2.1 Hz), 2.05 (s, 6H),

δ^{13}C (126 MHz, $CDCl_3$) 170.3, 153.8, 150.4, 135.2, 134.8, 123.7, 119.4, 112.8, 62.9, 32.6.

2-Bromo-*N*-(6-bromopyridin-3-yl)-2-methylpropanamide (**14-Br**)



14-Br

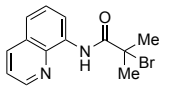
Synthesised according to General Procedure A using 6-bromopyridin-3-amine (2.0 mmol, 346 mg), Et_3N (4.0 mmol, 560 µL), and 2-bromo-2-methylpropanoyl bromide (2.2 mmol, 272 µL). SiO_2 gel chromatography (0→50% Et_2O in hexanes) afforded **14-Br** as a white solid (209 mg, 0.66 mmol, 33% yield).

HRMS m/z (EI+) calculated for $[C_9H_{10}Br_2ON_2]^+$: 319.9160, found $[M]^+$: 319.9170.

δ^{1}H (500 MHz, $CDCl_3$) 8.48 (br s, 1H), 8.44 (d, 1H, *J* = 2.8 Hz), 8.00 (dd, 1H, *J* = 8.6, 2.8 Hz), 7.47 (d, 1H, *J* = 8.6 Hz), 2.05 (s, 6H)

δ^{13}C (126 MHz, $CDCl_3$) 170.7, 141.6, 136.8, 134.0, 130.0, 128.2, 62.4, 32.6.

2-Bromo-2-methyl-*N*-(quinolin-8-yl)propanamide (**15-Br**)



15-Br

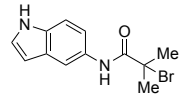
Synthesised according to General Procedure A using 8-aminoquinoline (2.0 mmol, 288 mg), Et_3N (4.0 mmol, 560 µL), and 2-bromo-2-methylpropanoyl bromide (2.2 mmol, 272 µL). SiO_2 gel chromatography (0→20% Et_2O in hexanes) afforded **15-Br** as a black/grey solid (483 mg, 1.64 mmol, 82% yield).

HRMS m/z (EI+) calculated for $[C_{13}H_{13}BrON_2]^+$: 292.0211, found $[M]^+$: 292.0215.

δ^{1}H (500 MHz, $CDCl_3$) 11.03 (br s, 1H), 8.86 (dd, 1H, *J* = 4.3, 1.3 Hz), 8.74 (dd, 1H, *J* = 6.5, 2.4 Hz), 8.16 (dd, 1H, *J* = 8.2, 1.3 Hz), 7.57-7.52 (m, 2H), 7.47 (dd, 1H, *J* = 8.2, 4.3 Hz), 2.14 (s, 6H)

δ^{13}C (126 MHz, $CDCl_3$) 170.4, 148.7, 139.0, 136.4, 134.4, 128.1, 127.3, 122.2, 121.8, 116.4, 61.8, 32.5.

2-Bromo-*N*-(1*H*-indol-5-yl)-2-methylpropanamide (**16-Br**)



16-Br

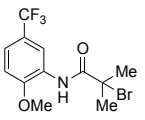
Synthesised according to General Procedure A using 1*H*-indol-5-amine (2.0 mmol, 292 mg), Et_3N (4.0 mmol, 560 µL), and 2-bromo-2-methylpropanoyl bromide (2.2 mmol, 272 µL). SiO_2 gel chromatography (0→10% EtOAc in CH_2Cl_2) afforded **16-Br** as an orange solid (351 mg, 1.24 mmol, 62% yield).

HRMS m/z (EI+) calculated for $[C_{12}H_{13}BrON_2]^+$: 280.0211, found $[M]^+$: 280.0213.

δ^{1}H (500 MHz, $CDCl_3$) 8.52 (br s, 1H), 8.39 (br s, 1H), 7.86 (d, 1H, *J* = 1.4 Hz), 7.30-7.15 (m, 2H), 7.16 (t, 1H, *J* = 2.9 Hz), 6.50 (s, 1H), 2.09 (s, 6H).

δ^{13}C (126 MHz, $CDCl_3$) 170.2, 133.7, 129.9, 128.1, 125.5, 116.4, 113.0, 111.4, 102.8, 63.7, 32.8.

2-Bromo-*N*-(2-methoxy-5-(trifluoromethyl)phenyl)-2-methylpropanamide (**17-Br**)



17-Br

Synthesised according to General Procedure A using 2-methoxy-5-(trifluoromethyl)aniline (2.0 mmol, 382 mg), Et_3N (4.0 mmol, 560 µL), and 2-bromo-2-methylpropanoyl bromide (2.2 mmol, 272 µL). SiO_2 gel chromatography (0→40% Et_2O in Hexanes) afforded **17-Br** as a white solid (477 mg, 1.40 mmol, 70% yield).

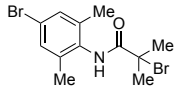
HRMS m/z (EI+) calculated for $[C_{12}H_{13}BrO_2F_3N]^+$: 339.0082, found $[M^+]$: 339.0077.

δ^{1}H (500 MHz, $CDCl_3$) 9.17 (br s, 1H), 8.69 (d, 1H, *J* = 2.0 Hz), 7.36 (dd, 1H, *J* = 8.5, 1.5 Hz), 6.96 (d, 1H, *J* = 8.5), 3.98 (s, 3H), 2.06 (s, 6H).

δ^{19}F (470 MHz, $CDCl_3$) -61.73 (s).

δ^{13}C (126 MHz, $CDCl_3$) 170.3, 150.7, 127.8, 124.3 (q, *J* = 272 Hz), 123.5 (q, *J* = 32 Hz), 121.6 (q, *J* = 4 Hz), 116.5 (q, *J* = 4 Hz), 109.8, 62.6, 56.4, 32.6.

2-Bromo-*N*-(4-bromo-2,6-dimethylphenyl)-2-methylpropanamide (**18-Br**)



18-Br

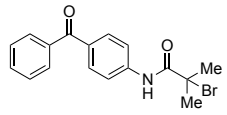
Synthesised according to General Procedure A using 4-bromo-2,6-dimethylaniline (2.0 mmol, 400 mg), Et_3N (4.0 mmol, 560 µL), and 2-bromo-2-methylpropanoyl bromide (2.2 mmol, 272 µL). SiO_2 gel chromatography (0→40% Et_2O in Hexanes) afforded **18-Br** as a white solid (437 mg, 1.25 mmol, 63% yield).

HRMS m/z (EI+) calculated for $[C_{12}H_{15}Br_2ON]^+$: 346.9520, found $[M]^+$: 346.9521.

δ^{1}H (500 MHz, $CDCl_3$) 7.92 (br s, 1H), 7.23 (s, 2H), 2.20 (s, 6H), 2.07 (s, 6H).

δ^{13}C (126 MHz, $CDCl_3$) 170.5, 137.7, 132.8, 131.2, 121.1, 62.9, 32.7, 18.2.

N-(4-Benzoylphenyl)-2-bromo-2-methylpropanamide (**19-Br**)



19-Br

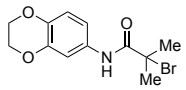
Synthesised according to General Procedure A using (4-aminophenyl)(phenyl)methanone (2.0 mmol, 394 mg), Et_3N (4.0 mmol, 560 µL), and 2-bromo-2-methylpropanoyl bromide (2.2 mmol, 272 µL). SiO_2 gel chromatography (0→100% Et_2O in Hexanes) afforded **19-Br** as a white solid (477 mg, 1.38 mmol, 69% yield).

HRMS m/z (EI+) calculated for $[C_{17}H_{16}BrO_2N]^+$: 345.0364, found $[M]^+$: 345.0359.

δ^{1}H (500 MHz, $CDCl_3$) 8.64 (br s, 1H), 7.85 (d, 2H, *J* = 8.7 Hz), 7.77 (d, 2H, *J* = 7.9 Hz), 7.69 (d, 2H, *J* = 8.7 Hz), 7.58 (t, 1H, *J* = 7.3 Hz), 7.48 (t, 2H, *J* = 7.9 Hz), 2.07 (s, 6H).

δ^{13}C (126 MHz, $CDCl_3$) 195.6, 170.4, 141.3, 137.9, 133.8, 132.4, 131.7, 130.0, 128.4, 119.1, 62.8, 32.6.

2-Bromo-*N*-(2,3-dihydrobenzo[*b*][1,4]dioxin-6-yl)-2-methylpropanamide (**20-Br**)



20-Br

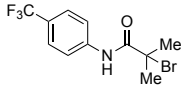
Synthesised according to General Procedure A using 2,3-dihydrobenzo[*b*][1,4]dioxin-6-amine (2.0 mmol, 302 mg), Et_3N (4.0 mmol, 560 µL), and 2-bromo-2-methylpropanoyl bromide (2.2 mmol, 272 µL). SiO_2 gel chromatography (0→60% Et_2O in Hexanes) afforded **20-Br** as a yellow solid (444 mg, 1.48 mmol, 74% yield).

HRMS m/z (EI+) calculated for $[C_{12}H_{14}BrON_3]^+$: 299.0157, found $[M]^+$: 299.0165.

δ^{1}H (500 MHz, $CDCl_3$) 8.30 (br s, 1H), 7.15 (d, 1H, *J* = 2.5 Hz), 6.90 (dd, 1H, *J* = 8.8, 2.5 Hz), 6.81 (d, 1H, *J* = 8.8 Hz), 4.22 (s, 4H), 2.02 (s, 6H).

δ^{13}C (126 MHz, $CDCl_3$) 169.8, 143.6, 140.9, 131.1, 117.3, 113.7, 110.0, 64.5, 64.4, 63.3, 32.7.

2-Bromo-2-methyl-*N*-(4-(trifluoromethyl)phenyl)propanamide (**21-Br**)



21-Br

Synthesised according to General Procedure A using 4-(trifluoromethyl)aniline (2.0 mmol, 0.25 mL), Et_3N (4.0 mmol, 560 µL), and 2-bromo-2-methylpropanoyl bromide (2.2 mmol, 272 µL). SiO_2 gel chromatography (0→20% Et_2O in Hexanes) afforded **21-Br** as a white solid (515 mg, 1.66 mmol, 83% yield).

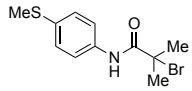
HRMS m/z (EI+) calculated for $[C_{11}H_{11}BrF_3NO]^+$: 308.9976, found $[M]^+$: 308.9982.

δ^{1}H (499 MHz, $CDCl_3$) 8.57 (br s, 1H), 7.68 (d, 2H, *J* = 8.4 Hz), 7.61 (d, 2H, *J* = 8.4 Hz), 2.06 (s, 6H).

δ^{19}F (470 MHz, $CDCl_3$) -62.21 (s).

δ^{13}C (126 MHz, $CDCl_3$) 170.4, 140.6, 126.9 (q, *J* = 34 Hz), 126.5 (q, *J* = 4 Hz), 124.1 (q, *J* = 272 Hz), 119.7, 62.9, 32.6.

2-Bromo-2-methyl-*N*-(4-(methylthio)phenyl)propanamide (**22-Br**)



22-Br

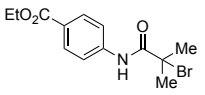
Synthesised according to General Procedure A using 4-(methylthio)aniline (2.0 mmol, 0.25 mL), Et_3N (4.0 mmol, 560 µL), and 2-bromo-2-methylpropanoyl bromide (2.2 mmol, 272 µL). SiO_2 gel chromatography (0→50% Et_2O in Hexanes) afforded **22-Br** as a pink solid (434 mg, 1.50 mmol, 75% yield).

HRMS m/z (ESI+) calculated for $[C_{11}H_{15}BrONS]^+$: 288.0057, found $[M+H]^+$ 288.0022 m/z.

δ^{1}H (499 MHz, $CDCl_3$) 8.41 (br s, 1H), 7.48 (d, 2H, *J* = 8.6 Hz), 7.26 (d, 2H, *J* = 8.6 Hz), 2.47 (s, 3H), 2.04 (s, 6H).

δ^{13}C (126 MHz, $CDCl_3$) 170.0, 135.1, 134.6, 128.0, 120.7, 63.3, 32.7, 16.7.

Ethyl 4-(2-bromo-2-methylpropanamido)benzoate (**23-Br**)



23-Br

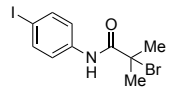
Synthesised according to General Procedure A using ethyl 4-aminobenzoate (2.0 mmol, 330 mg), Et_3N (4.0 mmol, 560 µL), and 2-bromo-2-methylpropanoyl bromide (2.2 mmol, 272 µL). SiO_2 gel chromatography (0→40% Et_2O in Hexanes) afforded **23-Br** as a white solid (541 mg, 1.72 mmol, 86% yield).

HRMS m/z (EI+) calculated for $C_{13}H_{16}BrO_3N^+$: 313.0314, found $[M]^+$: 313.0349.

δ^{1}H (499 MHz, $CDCl_3$) 8.59 (br s, 1H), 8.04 (d, 2H, *J* = 8.7 Hz), 7.63 (d, 2H, *J* = 8.7 Hz), 4.37 (q, 2H, *J* = 7.2 Hz), 2.05 (s, 6H), 1.39 (t, 3H, *J* = 7.2 Hz).

δ^{13}C (126 MHz, $CDCl_3$) 170.3, 166.1, 141.5, 130.9, 126.6, 119.1, 62.9, 61.1, 32.6, 14.5.

2-Bromo-*N*-(4-iodophenyl)-2-methylpropanamide (**24-Br**)



24-Br

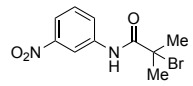
Synthesised according to General Procedure A using 4-iodoaniline (2.0 mmol, 438 mg), Et_3N (4.0 mmol, 560 µL), and 2-bromo-2-methylpropanoyl bromide (2.2 mmol, 272 µL). SiO_2 gel chromatography (0→30% Et_2O in Hexanes) afforded **24-Br** as a white solid (642 mg, 1.74 mmol, 87% yield).

HRMS m/z (EI+) calculated for $[C_{10}H_{11}BrION]^+$: 366.9069, found $[M]^+$: 366.9084.

δ^{1}H (500 MHz, $CDCl_3$) 8.42 (br s, 1H), 7.65 (d, 2H, *J* = 8.8 Hz), 7.33 (d, 2H, *J* = 8.8 Hz), 2.04 (s, 6H).

δ^{13}C (126 MHz, $CDCl_3$) 170.1, 138.1, 137.3, 121.9, 88.4, 63.1, 32.6.

2-Bromo-2-methyl-*N*-(3-nitrophenyl)propanamide (**25-Br**)



25-Br

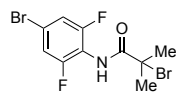
Synthesised according to General Procedure A using 3-nitroaniline (2.0 mmol, 276 mg), Et_3N (4.0 mmol, 560 µL), and 2-bromo-2-methylpropanoyl bromide (2.2 mmol, 272 µL). SiO_2 gel chromatography (0→40% Et_2O in Hexanes) afforded **25-Br** as a white solid (480 mg, 1.67 mmol, 84% yield).

HRMS m/z (EI+) calculated for $[C_{10}H_{11}BrO_3N_2]^+$: 285.9953, found $[M]^+$: 285.9954.

δ^{1}H (500 MHz, $CDCl_3$) 8.64 (br s, 1H), 8.46 (t, 1H, *J* = 2.2 Hz), 8.00 (dd, 1H, *J* = 8.2, 1.4 Hz), 7.90 (dd, 1H, *J* = 8.2, 1.4 Hz), 7.53 (t, 1H, *J* = 8.2 Hz), 2.06 (s, 6H).

δ^{13}C (126 MHz, $CDCl_3$) 170.6, 148.8, 138.7, 130.0, 125.7, 119.6, 115.0, 62.6, 32.5.

2-Bromo-*N*-(4-bromo-2,6-difluorophenyl)-2-methylpropanamide (**26-Br**)



26-Br

Synthesised according to General Procedure A using 4-bromo-2,6-difluoroaniline (2.0 mmol, 416 mg), Et_3N (4.0 mmol, 560 µL), and 2-bromo-2-methylpropanoyl bromide (2.2 mmol, 272 µL). SiO_2 gel chromatography (0→50% Et_2O in Hexanes) afforded **26-Br** as a white solid (437 mg, 1.22 mmol, 61% yield).

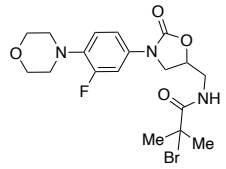
HRMS m/z (EI+) calculated for $[C_{10}H_9Br_2F_2ON]^+$: 354.9019, found $[M]^+$: 354.9024.

δ^{1}H (499 MHz, $CDCl_3$) 7.93 (br s, 1H), 7.17 (d, 2H, *J* = 6.8 Hz), 2.06 (s, 6H).

δ^{19}F (470 MHz, $CDCl_3$) -115.93 (d, *J* = 6.8 Hz).

δ^{13}C (126 MHz, $CDCl_3$) 170.8, 157.8 (dd, *J* = 255, 6 Hz), 120.1 (t, *J* = 12 Hz), 116.1-115.9 (m), 113.5 (t, *J* = 16 Hz), 61.7, 32.6.

2-Bromo-*N*-((3-(3-fluoro-4-morpholinophenyl)-2-oxooxazolidin-5-yl)methyl)-2-methylpropanamide (**27-Br**)



27-Br

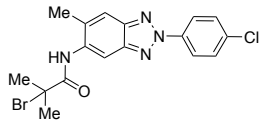
Synthesised according to General Procedure A using 5-(aminomethyl)-3-(3-fluoro-4-morpholinophenyl)oxazolidin-2-one (0.5 mmol, 148 mg), Et_3N (1.0 mmol, 140 µL), and 2-bromo-2-methylpropanoyl bromide (0.55 mmol, 68 µL). SiO_2 gel chromatography (0→100% EtOAc in pentanes) afforded **27-Br** as a white solid (116 mg, 0.26 mmol, 52% yield).

HRMS m/z (ESI+) calculated for $[C_{18}H_{24}BrFO_4N_3]^+$: 444.0929, found $[M+H]^+$: 444.0929.

δ^{1}H (499 MHz, $CDCl_3$) 7.42 (dd, 1H, *J* = 14.3, 2.5 Hz), 7.12-7.07 (m, 2H), 6.91 (m, 1H), 4.79 (sext, 1H, *J* = 4.7 Hz), 4.03 (m 1H), 3.86-3.85 (m, 4H), 3.77- 3.74 (m, 1H), 3.68 (t, 2H, *J* = 5.6 Hz), 3.05-3.03 (m, 4H), 1.93 (s, 3H), 1.86 (s, 3H).

δ^{13}C (126 MHz, $CDCl_3$) 173.4, 155.6 (d, *J* = 247 Hz),154.3, 136.7 (d, *J* = 10 Hz), 133.0 (d, *J* = 10 Hz), 119.0 (d, *J* = 4.0 Hz), 114.1 (d, *J* = 4.0 Hz), 107.7 (d, *J* = 26 Hz), 71.6, 67.1, 61.3, 51.1, 47.8, 43.1, 32.4, 32.3.

2-Bromo-*N*-(2-(4-chlorophenyl)-6-methyl-2*H*-benzo[*d*][1,2,3]triazol-5-yl)-2-methylpropanamide (**28-Br**)



28-Br

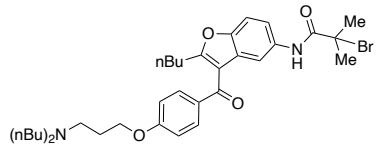
Synthesised according to General Procedure A using 2-(4-chlorophenyl)-6-methyl-2H-benzo[*d*]1,2,3triazol-5-amine (0.5 mmol, 129 mg), Et_3N (1.0 mmol, 140 µL), and 2-bromo-2-methylpropanoyl bromide (0.55 mmol, 68 µL). SiO_2 gel chromatography (0→100% EtOAc in pentanes) afforded **28-Br** as a white solid (175 mg, 0.43 mmol, 86% yield).

HRMS m/z (ESI+) calculated for $[C_{17}H_{17}BrClON_4]^+$: 407.0269, found $[M+H]^+$: 407.0269.

δ^{1}H (400 MHz, $CDCl_3$) 8.74 (br s, 1H), 8.62 (s, 1H), 8.27 (d, 2H, *J* = 8.9 Hz), 7.72 (m, 1H), 7.50 (d, 2H, *J* = 8.9 Hz), 2.51 (s, 3H), 2.12 (s, 6H).

δ^{13}C (101 MHz, $CDCl_3$) 170.3, 144.7, 143.0, 138.9, 135.7, 134.6, 130.9, 129.7, 121.7, 118.4, 108.5, 64.4, 32.9, 19.3.

2-Bromo-*N*-(2-butyl-3-(4-(3-(dibutylamino)propoxy)benzoyl)benzofuran-5-yl)-2-methylpropanamide (**29-Br**)



29-Br

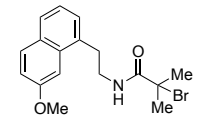
Synthesised according to General Procedure A using (5-amino-2-butylbenzofuran-3-yl)(4-(3-(dibutylamino)propoxy)phenyl)methanone (0.5 mmol, 239 mg), Et_3N (1.0 mmol, 140 µL), and 2-bromo-2-methylpropanoyl bromide (0.55 mmol, 68 µL). SiO_2 gel chromatography (50→100% EtOAc in hexanes) afforded **29-Br** as an orange oil (233 mg, 0.37 mmol, 74% yield).

HRMS m/z (ESI+) calculated for $[C_{34}H_{48}N_2O_4Br]^+$: 627.2792, found $[M+H]^+$: 627.2822.

δ^{1}H (400 MHz, $CDCl_3$) 8.47 (br s, 1H), 7.80 (d, 2H, *J* = 8.6 Hz), 7.56 (dd, 1H, *J* = 8.9, 2.1 Hz), 7.47 (d, 1H, *J* = 2.1 Hz), 7.40 (d, 1H, *J* = 8.9 Hz), 6.94 (d, 2H, *J* = 8.8 Hz), 4.11-4.06 (m, 2H), 2.79 (t, 2H, *J* = 7.2 Hz), 2.57 (t, 2H, *J* = 6.9 Hz), 2.41-2.37 (m, 4H), 1.99 (m, 6H), 1.91 (quintet, 2H, *J* = 6.5 Hz), 1.69 (quintet, 2H, *J* = 7.8 Hz), 1.43-1.20 (m, 10H), 0.88-0.82 (m, 9H).

δ^{13}C (101 MHz, $CDCl_3$) 190.2, 170.0, 164.9, 163.2, 151.0, 133.3, 131.7, 131.3, 127.7, 118.1, 116.9, 114.3, 113.3, 111.0, 66.5, 62.9, 54.0, 50.3, 32.5, 30.1, 29.4, 28.0, 27.1, 22.3, 20.7, 14.1, 13.7.

2-Bromo-*N*-(2-(7-methoxynaphthalen-1-yl)ethyl)-2-methylpropanamide (**30-Br**)



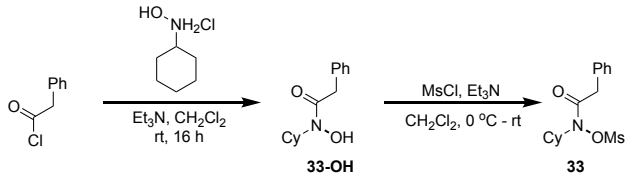
30-Br

Synthesised according to General Procedure A using 2-(7-methoxynaphthalen-1-yl)ethan-1-amine (0.5 mmol, 101 mg), Et_3N (1.0 mmol, 140 µL), and 2-bromo-2-methylpropanoyl bromide (0.55 mmol, 68 µL). SiO_2 gel chromatography (0→100% EtOAc in pentanes) afforded **30-Br** as a yellow solid (116 mg, 0.33 mmol, 66% yield).

HRMS m/z (ESI+) calculated for $[C_{17}H_{21}BrNO_2]^+$: 350.0750, found $[M+H]^+$: 350.0749.

δ^{1}H (499 MHz, $CDCl_3$) 7.78 (d, 1H, *J* = 8.9 Hz), 7.70 (d, 1H, *J* = 7.7 Hz), 7.44 (d, 1H, *J* = 2.2 Hz), 7.32-7.27 (m, 2H), 7.19 (dd, 1H, *J* = 8.9, 2.5 Hz), 6.82 (br m, 1H), 3.99 (s, 3H), 3.66 (q, 2H, *J* = 6.9 Hz), 3.28 (t, 2H, *J* = 7.0 Hz), 1.94 (s, 6H).
δ^{13}C (126 MHz, $CDCl_3$) 172.1, 158.1, 133.2, 133.1, 130.4, 129.4, 127.4, 127.2, 123.2, 118.2, 102.6, 63.0, 55.5, 40.7, 32.9, 32.6.

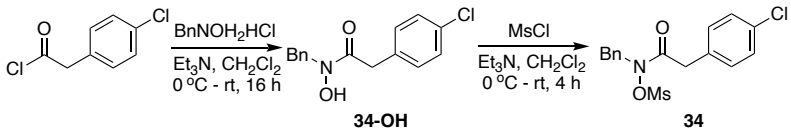
N-cyclohexyl-*N*-hydroxy-2-phenylacetamide (**33-OH**)[7]
N-cyclohexyl-*N*-((methylsulfonyl)oxy)-2-phenylacetamide (**33**)[7]



33-OH: At 0 °C under Ar, a solution of *N*-cyclohexylhydroxylamine hydrochloride (12 mmol, 1.2 equiv., 1.82 g), and Et_3N (22 mmol, 2.2 equiv. 3.1 mL) in CH_2Cl_2 (100 mL) was charged with 2-phenylacetyl chloride (10 mmol, 1.0 equiv., 1.5 mL) in CH_2Cl_2 (75 mL) dropwise over 1 h. The reaction mixture was warmed to room temperature and stirred overnight. The reaction was diluted with H_2O (100 mL) and washed with 1M HCl (2 x 25 mL), H_2O (25 mL), and brine (25 mL). The organic extract was dried over Na_2SO_4, filtered, and evaporated before purification with SiO_2 gel chromatography (0→100% EtOAc in hexanes), which afforded the hydroxamic acid as a white solid (1.10 g, 4.44 mmol, 47%). **33-OH** was obtained as a ca. 1.4:1 mixture of rotamers.
HRMS m/z (ESI+) calculated for $[C_{14}H_{20}NO_2]^+$: 234.1489, found $[M+H]^+$: 234.1500.
δ^{1}H (499 MHz, $CDCl_3$) 8.39 (br s, 1H), 7.34-7.19 (m, 5H), 4.27-4.22 (m, 0.6H), 3.74-3.70 (m, 2.7H), 1.81-1.72 (m, 3H), 1.63-1.45 (m, 4H), 1.31-1.01 (m, 3H)
δ^{13}C (126 MHz, $CDCl_3$) 172.0, 164.4, 135.5, 134.1, 129.4, 128.9, 128.6, 128.4, 127.3, 126.6, 58.8, 55.3, 39.8, 38.8, 30.0, 29.1, 25.5, 25.4, 25.4, 25.0.

33: At 0 °C under Ar, a solution of **33-OH** (2.5 mmol, 1.0 equiv, 2.5 mmol) and Et_3N (2.8 mmol, 1.1 equiv., 0.21 mL) in CH_2Cl_2 (12.5 mL) was charged with MsCl (2.5 mmol, 1.0 equiv., 0.35 mL) dropwise over 45 min. The reaction was stirred for 2 h at 0 °C and room temperature for 2 h before the addition of 5 mL H_2O and washing with H_2O (2 x 5 mL), 1M HCl (5 mL), and brine (5 mL). The organic layer was dried over Na_2SO_4, filtered, and evaporated before purification with SiO_2 gel chromatography (0→100% EtOAc in hexanes) to afford the *N*-mesyloxyamide as a white solid (669 mg, 2.15 mmol, 86%).
HRMS m/z (ESI+) calculated for $[C_{15}H_{22}NO_4S]^+$: 312.1264, found $[M+H]^+$: 312.1259.
δ^{1}H (499 MHz, $CDCl_3$) 7.37-7.25 (m, 5H), 3.93-3.87 (m, 1H), 3.79 (s, 2H), 3.32 (m, 3H), 1.82-1.59 (m, 7H), 1.27-1.06 (m, 3H).
δ^{13}C (126 MHz, $CDCl_3$) 171.3 (br), 133.3, 129.2, 129.0, 127.6, 62.5, 41.2, 39.4, 30.4, 25.8, 25.0.

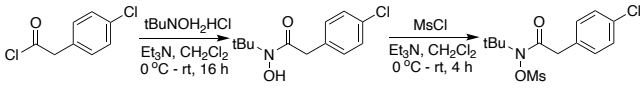
N-benzyl-2-(4-chlorophenyl)-*N*-hydroxyacetamide (**34-OH**)[7]
N-benzyl-2-(4-chlorophenyl)-*N*-((methylsulfonyl)oxy)acetamide (**34**)[7]



34-OH: At 0 °C under Ar, a solution of *N*-benzylhydroxylamine hydrochloride (2.5 mmol, 1.2 equiv., 400 mg), and Et_3N (5.5 mmol, 2.2 equiv. 0.77 mL) in CH_2Cl_2 (15 mL) was charged with 2-(4-chlorophenyl)acetyl chloride (2.1 mmol, 1.0 equiv., 0.37 mL) in CH_2Cl_2 (10 mL) dropwise over 1 h. The reaction mixture was warmed to room temperature and stirred overnight. The reaction was diluted with H_2O (15 mL) and washed with 1M HCl (2 x 10 mL), H_2O (15 mL), and brine (15 mL). The organic extract was dried over Na_2SO_4, filtered, and evaporated before purification with SiO_2 gel chromatography (0→40% EtOAc in hexanes), which afforded the hydroxamic acid **34-OH** as a white solid (183 mg, 0.66 mmol, 32%).
HRMS m/z (ESI+) calculated for $[C_{15}H_{15}NO_2Cl]^+$: 276.0786, found $[M+H]^+$: 276.0785.
δ^{1}H (499 MHz, MeOD) 7.32-7.23 (m, 9H), 4.76 (s, 2H), 3.81 (s, 2H).
δ^{13}C (126 MHz, MeOD) 173.5, 137.6, 135.4, 133.6, 132.1, 129.5, 129.4, 129.4, 128.6, 53.1, 39.3.

34: At 0 °C under Ar, a solution of **34-OH** (0.36 mmol, 1.0 equiv, 100 mg) and Et_3N (0.36 mmol, 1.0 equiv., 51 µL) in CH_2Cl_2 (2 mL) was charged with MsCl (0.40 mmol, 1.1 equiv., 31 µL) dropwise. The reaction was stirred for 2 h at 0 °C and room temperature for 2 h before the addition of 5 mL H_2O and washing with H_2O (2 x 2 mL), 1M HCl (2 mL), and brine (2 mL). The organic layer was dried over Na_2SO_4, filtered, and evaporated before purification with SiO_2 gel chromatography (0→100% EtOAc in hexanes) to afford the *N*-mesyloxyamide as a clear oil (98 mg, 0.28 mmol, 77%).
HRMS m/z (ESI+) calculated for $[C_{16}H_{17}ClNO_4S]^+$: 354.0561, found $[M+H]^+$: 354.0566.
δ^{1}H (499 MHz, $CDCl_3$) 7.34-7.33 (m, 3H), 7.28-7.26 (m, 4H), 7.11 (d, *J* = 8.4 Hz, 2H), 5.02 (s, 2H), 3.82 (s, 2H), 3.02 (s, 3H).
δ^{13}C (126 MHz, $CDCl_3$) 174.1, 134.6, 133.4, 131.5, 131.0, 129.0, 129.0, 128.9, 128.6, 55.4, 39.7, 38.1.

N-tert-butyl-2-(4-chlorophenyl)-*N*-hydroxyacetamide (**35-OH**)[7]
N-tert-butyl-2-(4-chlorophenyl)-*N*-((methylsulfonyl)oxy)acetamide (**35-OMs**)[7]

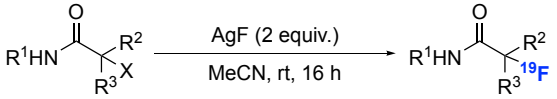


35-OH: At 0 °C under Ar, a solution of tertbutylhydroxylamine hydrochloride (2.5 mmol, 1.2 equiv., 314 mg), and Et_3N (5.5 mmol, 2.5 equiv., 0.77 mL) in CH_2Cl_2 (25 mL) was charged with 2-phenylacetyl chloride (2.1 mmol, 1.0 equiv., 0.37 mL) in CH_2Cl_2 (18 mL) dropwise over 1 h. The reaction mixture was warmed to room temperature and stirred overnight. The reaction was diluted with H_2O (100 mL) and washed with 1M HCl (2 x 25 mL), H_2O (25 mL), and brine (25 mL). The organic extract was dried over Na_2SO_4, filtered, and evaporated before purification with SiO_2 gel chromatography (0→30% EtOAc in hexanes), which afforded the hydroxamic acid **35-OH** as a white solid (167 mg, 0.69 mmol, 33%).
HRMS m/z (APCI+) calculated for $[C_{12}H_{17}NO_2Cl]^+$: 242.0942, found $[M+H]^+$: 242.0942.
δ^{1}H (499 MHz, MeOD) 7.35 (d, *J* = 8.5 Hz, 2H), 7.18 (d, *J* = 8.5 Hz, 2H), 3.71 (s, 2H), 1.39 (s, 9H).
δ^{13}C (126 MHz, MeOD) 174.5, 135.8, 133.3, 132.0, 129.3, 62.1, 41.9, 27.8.

35: At 0 °C under Ar, a solution of **35-OH** (0.41 mmol, 1.0 equiv, 100 mg) and Et_3N (0.41 mmol, 1.1 equiv., 57 µL) in CH_2Cl_2 (2 mL) was charged with MsCl (0.45 mmol, 1.1 equiv., 35 µL mL) dropwise. The reaction was stirred for 2 h at 0 °C and room temperature for 2 h before the addition of 5 mL H_2O and washing with H_2O (2 x 2 mL), 1M HCl (2 mL), and brine (2 mL). The organic layer was dried over Na_2SO_4, filtered, and evaporated before purification with SiO_2 gel chromatography (0→100% EtOAc in hexanes) to afford the *N*-mesyloxyamide as a white solid (104 mg, 0.33 mmol, 79%). **35-OMs** was isolated as a mixture of rotamers with ^{1}H and ^{13}C signals that coalesce at elevated temperature in d^8-PhMe.
HRMS m/z (ESI+) calculated for $[C_{13}H_{19}ClNO_4S]^+$: 320.0718, found $[M+H]^+$: 320.0714.
δ^{1}H (499 MHz, $CDCl_3$) 7.29 (d, *J* = 8.4 Hz, 2H), 7.15 (d, *J* = 8.4 Hz, 2H), 3.88 (s, 2H), 3.21 (s, 2H), 3.20-3.19 (m, 1H), 1.45 (s, 9H).
δ^{13}C (126 MHz, $CDCl_3$) 177.2, 133.1, 132.5, 131.2, 128.7, 128.7, 65.7, 41.7, 37.6, 37.6, 37.4, 37.2, 28.3.
δ^{1}H (400 MHz, PhMe, VT@95 °C) 7.10-7.08 (m, 3H), 7.00 (m, 2H), 3.70 (s, 2H), 2.37 (br m, 3H), 1.33 (s, 9H).
δ^{13}C (10 MHz, PhMe, VT@95 °C) 176.6, 138.0, 133.8, 133.7, 131.7, 65.5, 42.2, 37.2, 28.7.

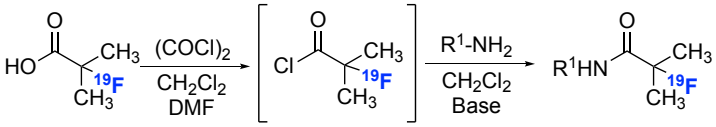
2.2 Synthesis of α-Fluoroamide Reference Standards

2.2.1 General Procedure B for the Synthesis of Fluorine-19 Reference Standards



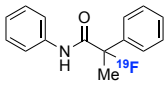
An α-haloamide (0.25 mmol, 1 equiv.) in anhydrous MeCN (0.1M) was stirred with AgF (63 mg, 0.50 mmol, 2 equiv.) at room temperature for 16 h according to a variation of Mizuta's procedure.[1] The reaction was filtered over Celite®, evaporated, and purified with SiO_2 gel chromatography.

2.2.2 General Procedure C for the Synthesis of Fluorine-19 Reference Standards



At 0 °C, a stirred solution of 2-fluoro-2-methylpropanoic acid (0.964 g, 9.09 mmol) in CH_2Cl_2 (10 mL) was treated with oxalyl dichloride (1.59 ml, 18.18 mmol), followed by 2 drops of DMF. The reaction mixture was heated at reflux overnight before atmospheric distillation of ca. 8 mL CH_2Cl_2 and the addition of CH_2Cl_2 (1.2 mL) to give a ca. 2.8M solution of crude 2-fluoro-2-methylpropanoyl chloride.[8] 100 µL of this stock solution (0.28 mmol, 1.1 equiv.) was added to a solution of amine (0.25 mmol, 1.0 equiv.) and Et_3N (0.5 mmol, 70 µL, 2 equiv.) in CH_2Cl_2 (0.4 mL) cooled in a brine/ice bath under Ar and stirred for 16 h. The volatiles were removed before purification with SiO_2 gel chromatography.

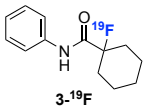
2-Fluoro-*N*,2-diphenylpropanamide (**2-^{19}F**)



2-^{19}F

Synthesised according to General Procedure B (with modifications) from **2-Cl** (0.13 mmol, 35 mg) and AgF (0.26 mmol, 33 mg). SiO_2 gel chromatography (0→100% EtOAc in hexanes) afforded **2-^{19}F** as a white solid (19 mg, 0.08 mmol, 60% yield).
HRMS m/z (ESI+) calculated for $[C_{15}H_{15}FNO]^+$: 244.1132, found $[M+H]^+$: 244.1130
δ^{1}H (499 MHz, $CDCl_3$) 8.19 (br, m), 7.61 (d, 2H, *J* = 7.2 Hz), 7.57 (d, 2H, *J* = 7.6 Hz), 7.40-7.32 (m, 5H), 7.14 (t, 1H, *J* = 7.6 Hz), 2.01 (d, 3H, *J* = 23.6 Hz).
δ^{19}F (470 MHz, $CDCl_3$) -149.38 (qd, *J* = 23.6, 7.6 Hz).
δ^{13}C (126 MHz, $CDCl_3$) 169.3 (d, *J* = 21 Hz), 139.5 (d, *J* = 22 Hz), 137.1, 129.2, 128.7 (d, *J* = 1.5 Hz), 128.6 (d, *J* = 1.0 Hz), 125.0, 124.6 (d, *J* = 9 Hz) 120.0, 97.9 (d, *J* = 188 Hz), 25.5 (d, *J* = 24 Hz).

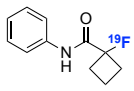
1-Fluoro-*N*-phenylcyclohexane-1-carboxamide (**3-^{19}F**)



3-^{19}F

Synthesised according to General Procedure B (with modifications) from **3-Br** (0.25 mmol, 71 mg) and AgF (0.50 mmol, 63 mg). SiO_2 gel chromatography (0→100% EtOAc in hexanes) afforded **3-^{19}F** as a white solid (42 mg, 0.19 mmol, 76% yield).
HRMS m/z (ESI+) calculated for $[C_{13}H_{17}FON]^+$: 222.1289, found $[M+H]^+$: 222.1280.
δ^{1}H (500 MHz, $CDCl_3$) 8.12 (br s, 1H), 7.57 (d, 2H, *J* = 7.7 Hz), 7.34 (t, 2H, *J* = 7.7 Hz), 7.14 (t, 1H, *J* = 7.7 Hz), 2.09-1.90 (m, 4H), 1.77-1.58 (m, 3H), 1.74-1.58 (m, 2H), 1.40-1.30 (m, 1H).
δ^{19}F (470 MHz, $CDCl_3$) -163.11 (s).
δ^{13}C (126 MHz, $CDCl_3$) 171.2 (d, *J* = 20 Hz), 137.3, 129.2, 124.8, 120.0, 98.0 (d, *J* = 189 Hz), 32.4 (d, *J* = 22 Hz), 24.5, 21.1.

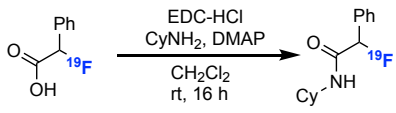
1-Fluoro-*N*-phenylcyclobutane-1-carboxamide (**4-^{19}F**)



4-^{19}F

Synthesised according to General Procedure B (with modifications) from **4-Br** (0.16 mmol, 40 mg) and AgF (0.32 mmol, 41 mg). SiO_2 gel chromatography (0→100% EtOAc in hexanes) afforded **4-^{19}F** as a white solid (9 mg, 0.05 mmol, 29% yield).
HRMS m/z (ESI+) calculated for $[C_{11}H_{13}FNO]^+$: 194.0976, found $[M+H]^+$: 194.0974.
δ^{1}H (500 MHz, $CDCl_3$) 7.92 (br s, 1H), 7.58 (d, 2H, *J* = 8.0 Hz), 7.34 (t, 2H, *J* = 7.7 Hz), 7.13 (t, 1H, *J* = 7.7 Hz), 2.80-2.71 (m, 2H), 2.53-2.41 (m, 2H), 2.07-1.99 (m, 2H).
δ^{19}F (470 MHz, $CDCl_3$) -143.4 to -143.6 (m).
δ^{13}C (126 MHz, $CDCl_3$) 169.8 (d, *J* = 20 Hz), 137.1, 129.2, 124.9, 120.0, 96.6 (d, *J* = 224 Hz), 33.0 (d, *J* = 21 Hz), 13.2 (d, *J* = 10 Hz).

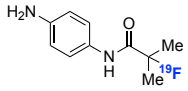
N-Cyclohexyl-2-fluoro-2-phenylacetamide (**6-^{19}F**)



6-^{19}F

To a solution of 2-fluoro-2-phenylacetic acid (0.2 mmol, 1.0 equiv., 31 mg), cyclohexylamine (0.2 mmol, 1.0 equiv., 23 µL), and *N*-(3-dimethylaminopropyl)-*N*'-ethylcarbodiimide hydrochloride (0.24 mmol, 1.2 equiv., 46 mg) in CH_2Cl_2 (2 mL) was added DMAP (0.04 mmol, 20 mol%, 5 mg) at room temperature. The reaction was stirred overnight, filtered over Celite®, and purified via SiO_2 gel chromatography (0→50% EtOAc in hexanes) to afford **6-^{19}F** as a white solid (28 mg, 0.12 mmol, 60%).
HRMS m/z (ESI+) calculated for $[C_{14}H_{19}FNO]^+$: 236.1445, found $[M+H]^+$: 236.1441.
δ^{1}H (499 MHz, $CDCl_3$) 7.46-7.36 (m, 5H), 6.38 (br s, 1H), 5.74 (d, 2H, *J* = 49.2 Hz) 3.88-3.80 (m, 1H), 2.00-1.89 (m, 2H), 1.77-1.70 (m, 2H), 1.66-1.61 (m, 1H), 1.41-1.35 (m, 2H), 1.28-1.16 (m, 3H).
δ^{19}F (470 MHz, $CDCl_3$) -175.56 (d, *J* = 49.2 Hz).
δ^{13}C (125 MHz, $CDCl_3$) 167.6 (d, *J* = 21 Hz), 135.1 (d, *J* = 19 Hz), 129.5 (d, *J* = 3 Hz), 128.8, 126.9 (d, *J* = 7 Hz), 91.9 (d, *J* = 187.9 Hz), 48.1, 33.2, 33.1, 25.6, 24.9. 24.9.

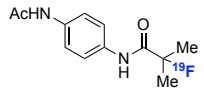
N-(4-Aminophenyl)-2-fluoro-2-methylpropanamide (**9-^{19}F**)



9-^{19}F

Synthesised according to General Procedure C (with modifications) using *tert*-butyl (4-aminophenyl)carbamate (0.25 mmol, 52 mg, 1.0 equiv.) and a solution of 2-fluoro-2-methylpropanoyl chloride (0.28 mmol, 35 mg, 1.1 equiv.) in CH_2Cl_2 (100 µL). After 16 h, HCl (8 mL, 2.0M in diethyl ether) was added, and the deprotection was left to stir overnight. The reaction was filtered, and the precipitate was rinsed with cold Et_2O (2 x 5 mL) before purification with SiO_2 gel chromatography (0→100% EtOAc in hexanes) to afford **9-^{19}F** as a white solid (23 mg, 0.12 mmol, 47%).
HRMS m/z (EI+) calculated for $[C_{10}H_{14}FON_2]^+$: 197.1085, found $[M+H]^+$: 197.1084.
δ^{1}H (500 MHz, $CDCl_3$) 7.93 (br s, 1H), 7.33 (d, 2H, *J* = 8.7 Hz), 6.66 (d, 2H, *J* = 8.7 Hz), 3.62 (br s, 2H), 1.64 (d, 6H, 21.9 Hz).
δ^{19}F (470 MHz, $CDCl_3$) -145.24 (heptet of doublets, *J* = 22.6, 8.3 Hz).
δ^{13}C (126 MHz, $CDCl_3$) 170.8 (d, *J* = 20 Hz), 143.7, 128.5, 121.8, 115.5, 96.7 (d, *J* = 183 Hz), 25.2 (d, *J* = 24 Hz).

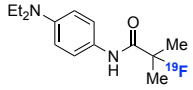
N-(4-Acetamidophenyl)-2-fluoro-2-methylpropanamide (**10-^{19}F**)



10-^{19}F

Synthesised according to General Procedure B using **10-Br** (0.25 mmol, 60 mg). SiO_2 gel chromatography (0→100% EtOAc in hexanes) afforded **10-^{19}F** as a white solid (31 mg, 0.13 mmol, 52% yield).
HRMS m/z (ESI+) calculated for $[C_{12}H_{16}N_2FO_2]^+$: 239.1190, found $[M+H]^+$: 239.1194.
δ^{1}H (500 MHz, DMSO) 9.88 (br s, 1H), 9.83 (br d, 1H, *J* = 3.3 Hz), 7.60 (d, 2H, *J* = 8.9 Hz), 7.50 (d, 2H, *J* = 8.9 Hz), 2.02 (s, 3H), 1.56 (d, 6H, *J* = 21.9 Hz).
δ^{19}F (470 MHz, DMSO) -144.30 (heptet of doublets, *J* = 21.9, 3.1 Hz).
δ^{13}C (126 MHz, DMSO) 170.6 (d, *J* = 22 Hz), 168.0, 135.5, 133.3, 120.9, 119.0, 95.3 (d, *J* = 182 Hz), 25.0 (d, *J* = 24 Hz), 23.9.

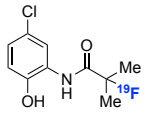
N-(4-(Diethylamino)phenyl)-2-fluoro-2-methylpropanamide (**11-^{19}F**)



11-^{19}F

Synthesised according to General Procedure C from *N*-(4-(diethylamino)phenyl)-2-fluoro-2-methylpropanamide (0.25 mmol, 40 µL). SiO_2 gel chromatography (0→50% EtOAc in hexanes) afforded **11-^{19}F** as a brown solid (56 mg, 0.22 mmol, 89% yield).
HRMS m/z (ESI+) calculated for $[C_{14}H_{22}FN_2O]^+$: 253.1711, found $[M+H]^+$: 253.1715.
δ^{1}H (400 MHz, $CDCl_3$) 7.92 (br d, 1H, *J* = 6.2 Hz), 7.39 (d, 2H, *J* = 8.8 Hz), 6.66 (d, 2H, *J* = 8.8 Hz), 3.33 (q, 4H, 7.1 Hz), 1.65 (d, 6H, *J* = 22.3 Hz), 1.14 (t, 6H, *J* = 7.1 Hz).
δ^{19}F (376 MHz, $CDCl_3$) -145.21 (heptet of doublets, *J* = 22.4, 7.5 Hz).
δ^{13}C (101 MHz, $CDCl_3$) 170.7 (d, *J* = 19 Hz), 145.4, 125.8, 121.9, 112.5, 97.6 (d, *J* = 182 Hz), 44.7, 25.2 (d, *J* = 24 Hz), 12.6.

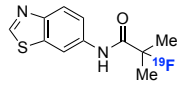
N-(5-Chloro-2-hydroxyphenyl)-2-fluoro-2-methylpropanamide (**12-^{19}F**)



12-^{19}F

At 0 °C under Ar, a stirred suspension of aqueous saturated Na_2CO_3 (0.9 mL) in $CHCl_3$ (1.5 mL) was charged with 2-amino-4-chlorophenol (74 mg, 0.25 mmol, 1.0 equiv.). A solution of 2-fluoro-2-methylpropanoyl chloride (0.28 mmol, 35 mg, 1.1 equiv.) in CH_2Cl_2 (100 µL) was added dropwise before removal of the ice bath and stirring overnight. The reaction was poured into H_2O (10 mL) and neutralized with 1M HCl before extraction with CH_2Cl_2 (3 x 10 mL). The combined organic layers were washed with brine (10 mL), dried with Na_2SO_4, filtered, and evaporated before purification with SiO_2 gel chromatography (0→100% EtOAc in hexanes) to obtain **12-^{19}F** as a brown solid (51 mg, 0.22 mmol, 88%).
HRMS m/z (ESI+) calculated for $[C_{10}H_{12}FNO_2Cl]^+$: 232.0535, found $[M+H]^+$: 232.0525.
δ^{1}H (499 MHz, $CDCl_3$) 8.75 (br s, 1H), 8.29 (br s, 1H), 7.04-7.03 (m, 2H), 6.87 (dd, 1H, *J* = 8.5, 2.2 Hz), 1.70 (d, 6H, *J* = 22.3 Hz).
δ^{19}F (470 MHz, $CDCl_3$) -143.76 (heptet of doublets, *J* = 22.3, 8.9 Hz)
δ^{13}C (126 MHz, $CDCl_3$) 170.2 (d, *J* = 20 Hz), 149.6, 132.7, 123.5, 123.2, 120.9, 120.2, 96.7 (d, *J* = 184 Hz), 25.2 (d, *J* = 24 Hz).

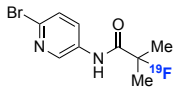
N-(Benzo[*d*]thiazol-6-yl)-2-fluoro-2-methylpropanamide (**13-^{19}F**)



13-^{19}F

Synthesised according to General Procedure C from benzo[*d*]thiazol-6-amine (0.25 mmol, 38 mg). SiO_2 gel chromatography (0→50% EtOAc in hexanes) afforded **13-^{19}F** as a yellow solid (25 mg, 0.11 mmol, 42% yield).
HRMS m/z (ESI+) calculated for $[C_{11}H_{12}N_2FSO]^+$: 239.0649, found $[M+H]^+$: 239.0654.
δ^{1}H (400 MHz, $CDCl_3$) 8.93 (s, 1H), 8.60 (d, 1H, *J* = 2.1 Hz), 8.33 (br d, 1H *J* = 7.5 Hz), 8.06 (d, 1H, *J* = 8.8 Hz), 7.41 (dd, 1H, *J* = 8.8, 2.1 Hz), 1.68 (d, 6H, *J* = 22.6 Hz).
δ^{19}F (470 MHz, $CDCl_3$) -145.25 (heptet of doublets, *J* = 22.6, 8.8 Hz)
δ^{13}C (101 MHz, $CDCl_3$) 171.4 (d, *J* = 20 Hz), 153.8 (d, *J* = 3 Hz), 150.3, 134.92, 134.87, 123.8 (d, *J* = 2 Hz), 119.2 (d, *J* = 5.5 Hz), 112.6 (d, *J* = 5.5 Hz), 96.7 (d, *J* = 183 Hz), 25.2 (dd, *J* = 24, 4.3 Hz).

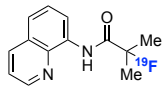
N-(6-Bromopyridin-3-yl)-2-fluoro-2-methylpropanamide (**14-^{19}F**)



14-^{19}F

Synthesised according to General Procedure C from 6-bromopyridin-3-amine (0.25 mmol, 43 mg). SiO_2 gel chromatography (0→40% EtOAc in hexanes) afforded **14-^{19}F** as a white solid (33 mg, 0.13 mmol, 50% yield).
HRMS m/z (ESI+) calculated for $[C_9H_{11}FBrN_2O]^+$: 261.0033, found $[M+H]^+$: 261.0038.
δ^{1}H (500 MHz, $CDCl_3$) 8.45 (d, 1H, *J* = 2.7 Hz), 8.15 (br d, 1H, *J* = 6.4 Hz), 8.06 (dd, 1H, *J* = 8.5, 2.7 Hz), 7.47 (d, 1H, *J* = 8.5 Hz), 1.67 (d, 6H, *J* = 22.4 Hz).
δ^{19}F (376 MHz, $CDCl_3$) -145.31 (heptet of doublets, *J* = 22.4, 8.5 Hz).
δ^{13}C (126 MHz, $CDCl_3$) 171.8 (d, *J* = 20 Hz), 141.5, 136.6, 133.6, 123.9, 128.3, 96.8 (d, *J* = 185 Hz), 25.1 (d, *J* = 24 Hz).

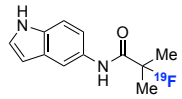
2-Fluoro-2-methyl-*N*-(quinolin-8-yl)propanamide (**15-^{19}F**)



15-^{19}F

Synthesised according to General Procedure B from **15-Br** (0.25 mmol, 73 mg). SiO_2 gel chromatography (0→50% EtOAc in pentanes) afforded **15-^{19}F** as a white solid (51 mg, 0.22 mmol, 88% yield).
HRMS m/z (ESI+) calculated for $[C_{13}H_{14}N_2FO]^+$: 233.1085, found $[M+H]^+$: 233.1090.
δ^{1}H (499 MHz, $CDCl_3$) 10.75 (br s, 1H), 8.86 (dd, 1H, *J* = 4.1, 1.4 Hz), 8.79 (t, 1H, *J* = 4.4 Hz), 8.17 (dd, 1H, *J* = 8.4, 1.4 Hz), 7.54 (d, 2H, *J* = 4.4 Hz), 7.47 (dd, 1H, *J* = 8.4, 4.4 Hz), 1.74 (d, 6H, *J* = 22.3 Hz).
δ^{19}F (470 MHz, $CDCl_3$) -145.76 (heptet of doublets, *J* = 22.3, 6.6 Hz).
δ^{13}C (126 MHz, $CDCl_3$) 171.9 (d, *J* = 20 Hz), 148.7, 139.0, 136.4, 134.0, 128.1, 127.3, 122.3, 121.9, 116.7, 96.6 (d, *J* = 183 Hz), 25.4 (d, *J* = 24 Hz).

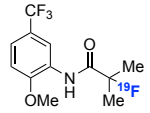
2-Fluoro-*N*-(1*H*-indol-5-yl)-2-methylpropanamide (**16-^{19}F**)



16-^{19}F

Synthesised according to General Procedure B (with modifications) from **16-Br** (0.13 mmol, 33 mg) and AgF (0.26 mmol, 33 mg). SiO_2 gel chromatography (0→100% EtOAc in hexanes) afforded **16-^{19}F** as a white solid (11 mg, 0.05 mmol, 38% yield).
HRMS m/z (ESI+) calculated for $[C_{12}H_{14}N_2FO]^+$: 221.1085, found $[M+H]^+$: 221.1096.
δ^{1}H (400 MHz, $CDCl_3$) 8.49 (br s, 1H), 8.16 (br d, 1H, *J* = 8.2 Hz), 7.92 (d, 1H, *J* = 0.6 Hz), 7.29-7.24 (m, 2H), 7.15 (t, 1H, *J* = 2.8 Hz), 6.49 (t, 1H, *J* = 2.8 Hz), 1.71 (d, 6H *J* = 22.4 Hz).
δ^{19}F (376 MHz, $CDCl_3$) -145.18 (heptet of doublets, *J* = 22.4, 8.2 Hz).
δ^{13}C (101 MHz, $CDCl_3$) 171.2 (d, *J* = 19 Hz), 133.6, 129.4, 128.1, 125.5, 116.1, 112.7, 111.4, 102.7, 96.7 (d, *J* = 182 Hz), 25.3 (d, *J* = 24 Hz).

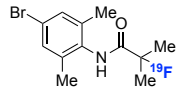
2-Fluoro-*N*-(2-methoxy-5-(trifluoromethyl)phenyl)-2-methylpropanamide (**17-^{19}F**)



17-^{19}F

Synthesised according to General Procedure C from 2-methoxy-5-(trifluoromethyl)aniline (0.25 mmol, 48 mg). SiO_2 gel chromatography (0→50% EtOAc in hexanes) afforded **17-^{19}F** as a white solid (44 mg, 0.16 mmol, 63% yield).
HRMS m/z (ESI+) calculated for $[C_{12}H_{14}NF_4O_2]^+$: 280.0955, found $[M+H]^+$: 280.0964.
δ^{1}H (499 MHz, $CDCl_3$) 8.82 (br d, 1H, *J* = 5.2 Hz), 8.75 (d, 1H, *J* = 1.6 Hz), 7.35 (d, 1H, *J* = 8.6 Hz), 6.95 (d, 1H, *J* = 8.6 Hz), 3.96 (s, 3H), 1.67 (d, 6H, *J* = 22.3 Hz).
δ^{19}F (470 MHz, $CDCl_3$) -67.14 (s, 3H), -145.99 (heptet of doublets, 1H, *J* = 22.3, 7.8 Hz).
δ^{13}C (126 MHz, $CDCl_3$) 171.5 (d, *J* = 20 Hz), 150.6, 127.3, 124.5 (q, *J* = 272 Hz), 123.5 (q, *J* = 33 Hz), 121.6 (q, *J* = 4 Hz), 116.7 (q, *J* = 4 Hz), 109.8, 96.6 (d, *J* = 182 Hz), 56.2, 25.2 (d, *J* = 24 Hz).

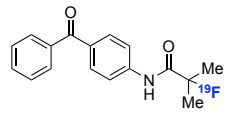
N-(4-Bromo-2,6-dimethylphenyl)-2-fluoro-2-methylpropanamide (**18-^{19}F**)



18-^{19}F

Synthesised according to General Procedure B (with modifications) from **18-Br** (0.20 mmol, 69 mg) and AgF (0.40 mmol, 51 mg). SiO_2 gel chromatography (0→50% EtOAc in hexanes) afforded **18-^{19}F** as a white solid (30 mg, 0.10 mmol, 52% yield).
HRMS m/z (ESI+) calculated for $[C_{11}H_{16}BrFNO]^+$: 288.0394, found $[M+H]^+$: 288.0398.
δ^{1}H (499 MHz, $CDCl_3$) 7.60 (br d, 1H, *J* = 4.2 Hz), 7.23 (s, 2H), 2.18 (s, 6H), 1.68 (d, 6H, *J* = 22.4 Hz).
δ^{19}F (470 MHz, $CDCl_3$) -145.15 (heptet of doublets, *J* = 22.4, 7.8 Hz).
δ^{13}C (126 MHz, $CDCl_3$) 171.6 (d, *J* = 20 Hz), 137.7, 132.0, 131.2, 121.1, 97.0 (d, *J* = 180 Hz), 25.3 (d, *J* = 24 Hz), 16.1.

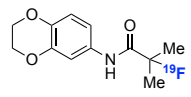
N-(4-Benzoylphenyl)-2-fluoro-2-methylpropanamide (**19-^{19}F**)



19-^{19}F

Synthesised according to General Procedure C from (4-aminophenyl)(phenyl)methanone (0.25 mmol, 49 mg). SiO_2 gel chromatography (0→50% EtOAc in hexanes) afforded **19-^{19}F** as a low melting, white solid (44 mg, 0.16 mmol, 63% yield).
HRMS m/z (ESI+) calculated for $[C_{17}H_{17}NFO_2]^+$: 286.1238, found $[M+H]^+$: 286.1245.
δ^{1}H (499 MHz, $CDCl_3$) 8.34 (br d, 1H, *J* = 8.5 Hz), 7.83 (d, 2H, *J* = 8.6 Hz), 7.76 (d, 2H, *J* = 7.5 Hz), 7.72 (d, 2H, *J* = 8.6 Hz), 7.58 (t, 1H, *J* = 7.5 Hz), 7.47 (t, 2H, *J* = 7.5 Hz), 1.67 (d, 6H, *J* = 22.0 Hz).
δ^{19}F (376 MHz, $CDCl_3$) -145.20 (heptet of doublets, *J* = 22.0, 8.6 Hz).
δ^{13}C (126 MHz, $CDCl_3$) 195.6, 171.6 (d, *J* = 20 Hz), 141.0, 137.9, 133.7, 132.4, 131.7, 130.0, 128.4, 119.2, 97.2 (d, *J* = 183 Hz), 25.1 (d, *J* = 24 Hz).

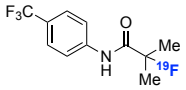
N-(2,3-Dihydrobenzo[*b*][1,4]dioxin-6-yl)-2-fluoro-2-methylpropanamide (**20-^{19}F**)



20-^{19}F

Synthesised according to General Procedure C from 2,3-dihydrobenzo[*b*][1,4]dioxin-6-amine (0.25 mmol, 30 mg). SiO_2 gel chromatography (0→50% EtOAc in hexanes) afforded **20-^{19}F** as a yellow solid (31 mg, 0.13 mmol, 50% yield).
HRMS m/z (ESI+) calculated for $[C_{12}H_{15}NFO_3]^+$: 240.1030, found $[M+H]^+$: 240.1038.
δ^{1}H (499 MHz, $CDCl_3$) 7.94 (br d, 1H, *J* = 6.5 Hz), 7.21 (d, 1H, *J* = 2.6 Hz), 6.95 (dd, 1H, *J* = 8.8, 2.6 Hz), 6.81 (d, 1H, *J* = 8.8 Hz), 4.25-4.22 (m, 4H), 1.64 (d, 6H, *J* = 22.4 Hz).
δ^{19}F (376 MHz, $CDCl_3$) -145.31 (heptet of doublets, *J* = 22.4, 8.8 Hz)
δ^{13}C (126 MHz, $CDCl_3$) 171.0 (d, *J* = 20 Hz), 143.7, 140.8, 130.8, 117.4, 113.6, 109.8, 96.7 (d, *J* = 186 Hz), 64.5, 64.6, 25.2 (d, *J* = 23 Hz).

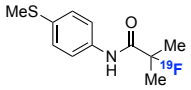
2-Fluoro-2-methyl-*N*-(4-(trifluoromethyl)phenyl)propanamide (**21-^{19}F**)



21-^{19}F

Synthesised according to General Procedure C from 4-(trifluoromethyl)aniline (0.25 mmol, 40 mg). SiO_2 gel chromatography (0→50% EtOAc in hexanes) afforded **21-^{19}F** as a white solid (33 mg, 0.13 mmol, 53% yield).
HRMS m/z (EI+) calculated for $[C_{11}H_{11}F_4NO]^+$: 249.0777, found $[M+H]^+$: 249.0772.
δ^{1}H (499 MHz, $CDCl_3$) 8.24 (br d, 1H, *J* = 6.0 Hz), 7.71 (d, 2H, *J* = 8.7 Hz), 7.60 (d, 2H, *J* = 8.7 Hz), 1.67 (d, 6H, *J* = 22.6 Hz).
δ^{19}F (470 MHz, $CDCl_3$) -62.24 (s, 3H), -145.27 (heptet of doublets, 1H, *J* = 22.6, 9.0 Hz).
δ^{13}C (126 MHz, $CDCl_3$) 171.6 (d, *J* = 20 Hz), 140.2, 126.7 (q, *J* = 32 Hz), 126.5 (q, *J* = 4Hz), 124.1 (q, *J* = 272 Hz), 119.7, 96.7 (d, *J* = 182 Hz), 25.1 (d, *J* = 24 Hz).

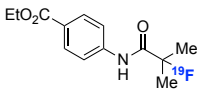
2-Fluoro-2-methyl-*N*-(4-(methylthio)phenyl)propanamide (**22-^{19}F**)



22-^{19}F

Synthesised according to General Procedure C from 4-(methylthio)aniline (0.25 mmol, 35 mg). SiO_2 gel chromatography (0→50% EtOAc in hexanes) afforded **22-^{19}F** as a white solid (39 mg, 0.17 mmol, 68% yield).
HRMS m/z (ESI+) calculated for $[C_{11}H_{15}FSNO]^+$: 228.0853, found $[M+H]^+$: 228.0855.
δ^{1}H (499 MHz, $CDCl_3$) 8.08 (br d, 1H, *J* = 6.5 Hz), 7.51 (d, 2H, *J* = 8.7 Hz), 7.25 (d, 2H, *J* = 8.7 Hz), 2.46 (s, 3H), 1.65 (d, 6H, *J* = 22.4 Hz).
δ^{19}F (376 MHz, $CDCl_3$) -145.21 (heptet of doublets, *J* = 22.4, 8.7 Hz).
δ^{13}C (126 MHz, $CDCl_3$) 171.2 (d, *J* = 20 Hz), 134.7, 134.3, 128.0, 120.6, 96.7 (d, *J* = 183 Hz), 25.2 (d, *J* = 24 Hz), 16.7.

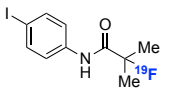
Ethyl 4-(2-fluoro-2-methylpropanamido)benzoate (**23-^{19}F**)



23-^{19}F

Synthesised according to General Procedure C from ethyl 4-aminobenzoate (0.25 mmol, 41 mg). SiO_2 gel chromatography (0→100% EtOAc in hexanes) afforded **23-^{19}F** as a white solid (46 mg, 0.18 mmol, 73% yield).
HRMS m/z (ESI+) calculated for $[C_{13}H_{17}FNO_3]^+$: 254.1187, found $[M+H]^+$: 254.1191.
δ^{1}H (499 MHz, $CDCl_3$) 8.27 (br d, 1H, *J* = 8.1 Hz), 8.03 (d, 2H, *J* = 8.7 Hz), 7.66 (d, 2H, *J* = 8.7 Hz), 4.34 (q, 2H, *J* = 7.1 Hz), 1.65 (d, 6H, *J* = 22.4 Hz), 1.38 (t, 3H, *J* = 7.1 Hz).
δ^{19}F (376 MHz, $CDCl_3$) -145.23 (heptet of doublets, *J* = 22.4, 8.9 Hz).
δ^{13}C (126 MHz, $CDCl_3$) 171.5 (d, *J* = 20 Hz), 166.1, 144.2, 130.9, 126.7, 119.1, 96.7 (d, *J* = 183 Hz), 61.0, 25.1 (d, *J* = 24 Hz), 14.5.

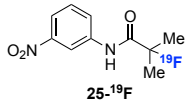
2-Fluoro-*N*-(4-iodophenyl)-2-methylpropanamide (**24-^{19}F**)



24-^{19}F

Synthesised according to General Procedure C from 4-iodoaniline (0.25 mmol, 55 mg). SiO_2 gel chromatography (0→50% EtOAc in hexanes) afforded **24-^{19}F** as a white solid (34 mg, 0.13 mmol, 54% yield).
HRMS m/z (ESI+) calculated for $[C_{10}H_{12}FINO]^+$: 307.9942, found $[M+H]^+$: 307.9935.
δ^{1}H (499 MHz, $CDCl_3$) 8.08 (br d, 1H, *J* = 6.4 Hz), 7.64 (d, 2H, *J* = 8.8 Hz), 7.36 (d, 2H, *J* = 8.8 Hz), 1.65 (d, 6H, *J* = 22.4 Hz).
δ^{19}F (470 MHz, $CDCl_3$) -145.22 (heptet of doublets, *J* = 22.4, 8.6 Hz).
δ^{13}C (126 MHz, $CDCl_3$) 171.3 (d, *J* = 20 Hz), 138.1, 136.9, 121.8, 96.7 (d, *J* = 183 Hz), 88.2, 25.1 (d, *J* = 24 Hz).

2-Fluoro-2-methyl-*N*-(3-nitrophenyl)propanamide (**25-^{19}F**)

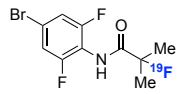


25-^{19}F

Synthesised according to General Procedure C from 3-nitroaniline (0.25 mmol, 35 mg). SiO_2 gel chromatography (0→50% EtOAc in hexanes) afforded **25-^{19}F** as a white solid (28 mg, 0.12 mmol, 50% yield).
HRMS m/z (ESI+) calculated for $[C_{10}H_{12}FN_2O_3]^+$: 227.0826, found $[M+H]^+$: 227.0831.
δ^{1}H (499 MHz, $CDCl_3$) 8.50 (t, 1H, *J* = 2.1 Hz), 8.35 (br d, 1H, *J* = 6.1 Hz), 8.00 (dd, 1H, *J* = 8.2, 1.6 Hz), 7.94 (dd, 1H, *J* = 8.2, 1.6 Hz), 7.52 (t, 1H, *J* = 8.2 Hz), 1.68 (d, 6H, *J* = 22.4 Hz).
δ^{19}F (470 MHz, $CDCl_3$) -145.54 (heptet of doublets, *J* = 22.4, 8.5 Hz).

δ^{13}C (126 MHz, $CDCl_3$) 171.8 (d, *J* = 20 Hz), 148.7, 138.2, 130.0, 125.6, 119.5, 114.9, 96.7 (d, *J* = 184 Hz), 25.1 (d, *J* = 24 Hz).

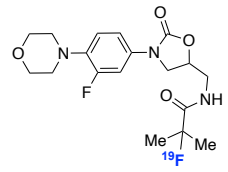
N-(4-Bromo-2,6-difluorophenyl)-2-fluoro-2-methylpropanamide (**26-^{19}F**)



26-^{19}F

Synthesised according to General Procedure C from 4-bromo-2,6-difluoroaniline (0.25 mmol, 52 mg). SiO_2 gel chromatography (0→50% EtOAc in hexanes) afforded **26-^{19}F** as a white solid (33 mg, 0.11 mmol, 45% yield).
HRMS m/z (ESI+) calculated for $[C_{10}H_{10}NF_3O]^+$: 295.9892, found $[M+H]^+$: 295.9889.
δ^{1}H (499 MHz, $CDCl_3$) 7.60 (br d, 1H, *J* = 4.6 Hz), 7.19-7.16 (m, 2H), 1.68 (d, 6H, *J* = 22.3 Hz).
δ^{19}F (470 MHz, $CDCl_3$) -115.84, (d, 2H, *J* = 7.1 Hz), -146.00 (heptet of doublets, 1H, *J* = 22.3, 7.1 Hz).
δ^{13}C (126 MHz, $CDCl_3$) 171.7 (d, *J* = 22 Hz), 157.9 (d, *J* = 255, 5 Hz), 120.2 (t, *J* = 11 Hz), 116.1-115.9 (m), 112.7, 97.0 (d, *J* = 182 Hz), 25.2 (d, *J* = 23 Hz).

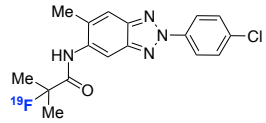
N-((3-(3-Fluoro-4-morpholinophenyl)-2-oxooxazolidin-5-yl)methyl)-2-fluoro-2-methylpropanamide (**27-^{19}F**)



27-^{19}F

Synthesised according to General Procedure B (with modifications) from **27-Br** (0.16 mmol, 70 mg) and AgF (0.32 mmol, 41 mg). SiO_2 gel chromatography (0→100% EtOAc in hexanes) afforded **27-^{19}F** as a white solid (33 mg, 0.09 mmol, 56% yield).
HRMS m/z (ESI+) calculated for $[C_{18}H_{24}O_4F_2N_3]^+$: 384.1729, found $[M+H]^+$: 384.1737.
δ^{1}H (700 MHz, $CDCl_3$) 7.41 (dd, 1H, *J* = 14.3Hz), 7.07 (d, 1H, *J* = 8.7 Hz), 6.94-6.89 (m, 2H), 4.77 (m, 1H), 4.03 (t, 1H, *J* = 8.8 Hz), 3.85 (m, 4H), 3.76-3.69 (m, 2H), 3.65-3.61 (m, 1H), 3.03 (m, 4H), 1.55 (d, 3H, *J* = 22.0 Hz), 1.46 (d, 3H, *J* = 22.0 Hz).
δ^{19}F (470 MHz, $CDCl_3$) -120.13 to -120.18, (m, 1H), -147.22 (heptet of doublets, 1H, *J* = 22.3, 5.8 Hz).
δ^{13}C (176 MHz, $CDCl_3$) 174.5 (d, *J* = 21 Hz), 155.6 (d, *J* = 246 Hz), 154.2, 136.7 (d, *J* = 21 Hz), 133.0 (d, *J* = 10 Hz), 118.9 (d, *J* = 4.1 Hz), 114.0 (d, *J* = 3.0 Hz), 107.6 (d, *J* = 26 Hz), 96.2 (d, *J* = 26 Hz), 71.7, 67.0, 51.1, 47.8, 42.0, 25.2 (d, *J* = 21 Hz), 25.0 (d, *J* = 24 Hz).

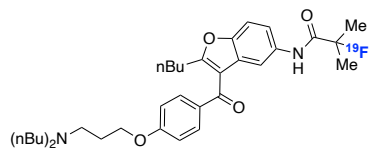
N-(2-(4-Chlorophenyl)-6-methyl-2*H*-benzo[*d*][1,2,3]triazol-5-yl)-2-fluoro-2-methylpropanamide (**28-^{19}F**)



28-^{19}F

Synthesised according to General Procedure B from **28-Br** (0.25 mmol, 100 mg). SiO_2 gel chromatography (0→100% EtOAc in hexanes) afforded **28-^{19}F** as a white solid (9 mg, 0.03 mmol, 10% yield).
HRMS m/z (ESI+) calculated for $[C_{17}H_{17}ClFN_4O]^+$: 347.1069, found $[M+H]^+$: 347.1067.
δ^{1}H (700 MHz, $CDCl_3$) 8.68 (s, 1H), 8.28-8.27 (m, 3H), 7.72 (s, 1H), 7.51 (d, 2H, *J* = 8.2 Hz), 2.47 (s, 3H), 1.73 (d, 6H, *J* = 22.4 Hz).
δ^{19}F (470 MHz, $CDCl_3$) -145.13 (heptet of doublets, *J* = 22.4, 9.8 Hz).
δ^{13}C (176 MHz, $CDCl_3$) 171.4 (d, *J* = 20 Hz), 144.7, 143.0, 139.0, 135.1, 134.6, 130.6, 129.7, 121.7, 118.4, 108.7, 97.2 (d, *J* = 182 Hz), 25.3 (d, *J* = 24 Hz), 18.98.

N-(2-Butyl-3-(4-(3-(dibutylamino)propoxy)benzoyl)benzofuran-5-yl)-2-fluoro-2-methylpropanamide (**29-^{19}F**)

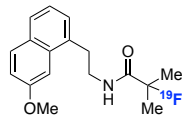


29-^{19}F

Synthesised according to General Procedure B (with modifications) from **29-Br** (0.11 mmol, 70 mg) and AgF (0.22 mmol, 28 mg). SiO_2 gel chromatography (0→100% EtOAc in hexanes) afforded **29-^{19}F** as a white solid (23 mg, 0.04 mmol, 37% yield).
HRMS m/z (ESI+) calculated for $[C_{34}H_{48}FN_2O_4]^+$: 567.3593, found $[M+H]^+$: 567.3614.

δ^{1}H (499 MHz, $CDCl_3$) 8.07 (br d, 1H, *J* = 7.7 Hz), 7.83 (d, 2H, *J* = 8.8 Hz), 7.70 (dd, 1H, *J* = 8.9, 2.2 Hz), 7.44 (d, 1H, *J* = 8.8 Hz), 7.40 (d, 1H, *J* = 2.4 Hz), 6.96 (d, 2H, *J* = 8.8 Hz), 4.11 (t, 2H, *J* = 6.3 Hz), 2.84 (t, 2H, *J* = 7.8 Hz), 2.60 (t, 2H, *J* = 6.7 Hz), 2.42 (t, 4H, *J* = 7.2 Hz), 1.94 (quintet, 2H, *J* = 6.5 Hz), 1.73 (quintet, 2H, *J* = 7.6 Hz), 1.64 (d, 6H, *J* = 22.4 Hz), 1.44-1.25 (m, 10H), 0.90-0.86 (m, 9H).
δ^{19}F (470 MHz, $CDCl_3$) -145.27 (heptet of doublets, *J* = 22.4, 8.5 Hz).
δ^{13}C (126 MHz, $CDCl_3$) 190.3, 171.2 (d, *J* = 20 Hz), 165.3, 163.4, 151.1, 133.0, 131.8, 131.5, 127.8, 117.8, 117.0, 114.4, 113.0, 111.3, 96.7 (d, *J* = 183 Hz), 66.7, 54.1, 50.5, 30.2, 29.5, 28.1, 27.2, 25.2 (d, *J* = 24 Hz), 22.5, 20.9, 14.2, 13.8.

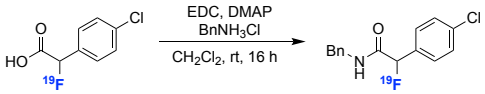
2-Fluoro-*N*-(2-(7-methoxynaphthalen-1-yl)ethyl)-2-methylpropanamide (**30-^{19}F**)



30-^{19}F

Synthesised according to General Procedure B (with modifications) from **30-Br** (0.20 mmol, 70 mg) and AgF (0.40 mmol, 51 mg). SiO_2 gel chromatography (0→100% EtOAc in hexanes) afforded **30-^{19}F** as a white solid (47 mg, 0.16 mmol, 81% yield).
HRMS m/z (ESI+) calculated for $[C_{17}H_{21}FO_2N]^+$: 290.1551, found $[M+H]^+$: 290.1555.
δ^{1}H (499 MHz, $CDCl_3$) 7.77 (d, 1H, *J* = 8.9 Hz), 7.70 (dd, 1H, *J* = 7.1, 2.2 Hz), 7.43 (d, 1H, *J* = 2.2 Hz), 7.29-7.26 (m, 2H), 7.18 (dd, 1H, *J* = 9.0, 2.5 Hz), 6.52 (br s, 1H), 3.99 (s, 3H), 3.67 (q, 2H, *J* = 6.7 Hz), 3.27 (t, 2H, *J* = 7.4 Hz), 1.56 (d, 6H, *J* = 22.3 Hz).
δ^{19}F (470 MHz, $CDCl_3$) -146.77 (heptet of doublets, *J* = 22.7, 6.3 Hz).
δ^{13}C (126 MHz, $CDCl_3$) 173.3 (d, *J* = 21 Hz),158.1, 133.3, 133.2, 130.4, 129.5, 127.31, 127.27, 123.3, 118.3, 102.5, 96.4 (d, *J* = 180 Hz). 55.6, 39.5, 33.2, 25.2 (d, *J* = 24 Hz).

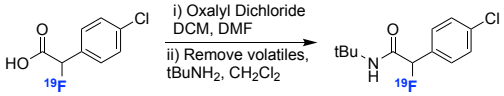
N-Benzyl-2-(4-chlorophenyl)-2-fluoroacetamide (**34-^{19}F**)



34-^{19}F

To a solution of 2-fluoro-2-(4-chlorophenyl)acetic acid (0.2 mmol, 1.0 equiv., 38 mg), benzylamine hydrochloride (0.2 mmol, 1.0 equiv., 35 mg), and *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (0.24 mmol, 1.2 equiv., 46 mg) in CH_2Cl_2 (1 mL) was added DMAP (0.04 mmol, 20 mol%, 5 mg) at room temperature. The reaction was stirred overnight, filtered over Celite®, and purified via SiO_2 gel chromatography (0→50% EtOAc in hexanes) to afford **34-^{19}F** as a white solid (27 mg, 0.09 mmol, 49%).
HRMS m/z (EI+) calculated for $[C_{15}H_{13}FOCl N]^+$: 277.0670, found $[M+H]^+$: 277.0670.
δ^{1}H (499 MHz, $CDCl_3$) 7.40-7.25 (m, 9H), 6.80 (br s, 1H), 6.29 (d, 1H, *J* = 47.9 Hz), 4.54-4.46 (m, 2H).
δ^{19}F (470 MHz, $CDCl_3$) -179.28 (dd, *J* = 48.3, 3.7 Hz).
δ^{13}C (126 MHz, $CDCl_3$) 168.1 (d, *J* = 22 Hz), 137.4, 135.6 (d, *J* = 3 Hz), 133.4 (d, *J* = 20 Hz), 129.0 (d, *J* = 6 Hz), 128.0, 128.0, 127.9, 91.3 (d, *J* = 189 Hz]), 43.4.

N-tert-Butyl-2-(4-chlorophenyl)-2-fluoroacetamide (**35-^{19}F**)



35-^{19}F

At 0 °C under Ar, a solution of 2-fluoro-2-(4-chlorophenyl)acetic acid (0.2 mmol, 1.0 equiv., 38 mg) in CH_2Cl_2 (1 mL) was charged with oxalyl dichloride (0.4 equiv., 34 µL) and one drop of DMF. The reaction was warmed to room temperature over 1 h before removal of the volatiles. The crude acid chloride was dissolved in CH_2Cl_2 (1 mL) and treated with tert-butylamine (0.4 mmol, 2.0 equiv., 42 µL) at 0 °C under Ar. After 3 h, the reaction was poured into sat. $NaHCO_3$ (5 mL) and extracted with CH_2Cl_2 (3 x 5 mL). The organic fractions were dried over Na_2SO_4, filtered and evaporated before purification with SiO_2 gel chromatography (0→50% EtOAc in hexanes), which afforded **35-^{19}F** as a white solid (36 mg, 0.15 mmol, 74%).
HRMS m/z (EI+) calculated for $[C_{12}H_{16}FOCl N]^+$: 243.0826, found $[M]^+$: 243.0821
δ^{1}H (499 MHz, $CDCl_3$) 7.39-7.35 (m, 4H), 6.29 (br s, 1H), 5.62 (d, 1H, *J* = 48.5 Hz), 1.40 (s, 9H).
δ^{19}F (470 MHz, $CDCl_3$) -174.96 (dd, *J* = 48.9, 5.1 Hz).
δ^{13}C (126 MHz, $CDCl_3$) 167.3 (d, *J* = 20 Hz), 135.4 (d, *J* = 3 Hz), 133.8 (d *J* = 20 Hz), 129.0, 128.1 (d, *J* = 7 Hz), 91.2 (d, *J* = 190 Hz), 51.8, 28.8.

3. Radiolabelling Procedures

3.1 Materials and Methods

See section 1.2 for a general description of materials and methods. Sterile product vials were purchased from Hollister-Stier. QMA-light (WAT023525), Sep-Pak cartridges, Alumina N Plus Light (WAT023561), Sep-Pak cartridges, and Oasis HLB 1 cc Vac (WAT094225) cartridges were purchased from Waters Corporation. QMA-light Sep-Paks were flushed with 10 mL of ethanol, 10 mL of aqueous 0.5M KOTf, and 10 mL of milli-Q water before use. Alumina N Plus Light Sep-Pak cartridges and Oasis HLB 1 cc Vac cartridges were flushed with 10 mL of ethanol and 10 mL of water before use.

3.2 General Procedure for the Preparation of [^{18}F]Fluoride Salts

[^{18}F]Fluoride salts were prepared using a TRACERlab FX$_{FN}$ automated radiochemistry synthesis module (General Electric, GE) with a glass reactor vial. [^{18}F]Fluoride was produced via the ^{18}O(p,n)^{18}F nuclear reaction using a GE PETTrace cyclotron (55 µA beam for ca. 1-2 min generating ca. 80-160 mCi of [^{18}F]fluoride). The [^{18}F]fluoride was transferred to the synthesis module and trapped on a QMA-light Sep-Pak (preconditioned with KOTf). [^{18}F]Fluoride was typically eluted into the reaction vessel using 26.5 µmol salt (usually a triflate) in 500 µL H_2O. A solution of base (3.6 µmol) in MeCN (1 mL) was added to the reaction vessel. The resulting solution was evaporated by heating the reaction vessel to 100 °C under vacuum for 5 min. Insoluble bases were instead added to the aqueous solution used for [^{18}F]fluoride elution. The reaction vessel was further dried under vacuum with a stream of Ar for an additional 8 min. The prepared [^{18}F]fluoride salts were cooled to 40 °C and dissolved in 5 mL solvent, which was transferred to a 10 mL vial. For example, 40.5 mCi [^{18}F]TMAF (derived from TMAOTf) in 5 mL of DMSO could be isolated with a 2 min GE PETtrace cyclotron beam.

3.3 HPLC Conditions

Analytical HPLC analysis was performed using a Shimadzu LC-20AD/T LPGEKIT system equipped with a CBM-20A controller, SIL 20AHT injector, SPD 20A UV detector, DGU 20A SR degasser, and CTO-20A column oven with an in-series B-FC-3300 radiation detector for observing gamma emissions. Radiochemical purities were approximated by comparison of integrated signals following the elution of inorganic [^{18}F]fluoride. Note: fluoride elution was sometimes streaky, possibly due to the formation of organic radiofluoride salts (e.g., guanidinium fluorides).

HPLC Conditions A

Column	Luna 5 µm C18 100 Å, 150 x 4.6 mm
Flow Rate	2 mL/min
Solvent A	0.1% TFA in H_2O
Solvent B	0.1% TFA in MeCN
Temperature	40 °C
Wavelength	254 nm
Method:	0-2 min 5% B 2-25 min 5-95% B 25-26.5 min 95% B 26.5-27 min 95-5% B 27-30 min 5% B

HPLC Conditions B

Column:	Luna 5 µm C18 100 Å, 150 x 4.6 mm
Flow Rate:	2 mL/min
Solvent A:	0.1% TFA in H_2O
Solvent B:	0.1% TFA in MeCN
Temperature	40 °C
Wavelength:	254 nm
Method:	0-2 min 5% B 2-24 min 5-95% B 24-27 min 95% B 27 min 5% B 27-30 min 5% B

HPLC Conditions C

Column:	Luna 5 µm C18 100 Å, 150 x 4.6 mm
Flow Rate:	1 mL/min

Solvent A:	0.2% AcOH in 10 mM Aqueous NH_4OAc
Solvent B:	EtOH
Temperature:	40 °C
Wavelength:	254 nm
Method:	0-12.8 min 40% B 12.8-13 min 40-95% B 13-14 min 95% B 14-14.2 min 95-5% B 14.2-16 min 5% B

HPLC Conditions D

Column:	Luna 10 µ C18(2), 100 Å, 250 x 10.0 mm
Flow Rate:	4 mL/min
Solvent A:	0.2% AcOH in 10 mM Aqueous NH_4OAc
Solvent B:	EtOH
Temperature:	40 °C
Wavelength:	254 nm
Method:	40% B

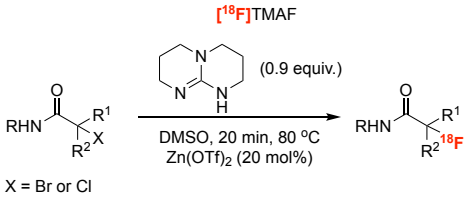
HPLC Conditions E

Column:	Luna 5 µm C18 100 Å, 150 x 4.6 mm
Flow Rate:	1 mL/min
Solvent A:	0.2% AcOH in 10 mM Aqueous NH_4OAc
Solvent B:	EtOH
Temperature:	40 °C
Wavelength:	254 nm
Method:	0-1 min 5% B 1-15.8 min 5-95% B 15.8-16 min 95-5% B 16-18 min 5% B

HPLC Conditions F

Column:	Luna 10 µ C18(2), 100 Å, 250 x 10.0 mm
Flow Rate:	4 mL/min
Solvent A:	0.2% AcOH in 10 mM Aqueous NH_4OAc
Solvent B:	EtOH
Temperature:	40 °C
Wavelength:	254 nm
Method:	35% B

3.4 General Procedure for the Radiofluorination of Amides



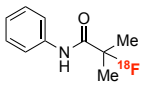
X = Br or Cl

To a 1-dram vial containing α-haloamide (or *N*-mesyloxyamide) precursor (5 µmol) in DMSO (200 µL) was added [^{18}F]TMAF in DMSO (100 µL, ca. 100 µCi), followed by a stock solution of TBD (0.63 mg, 4.5 µmol), and $Zn(OTf)_2$ (0.36 mg, 1 µmol), in anhydrous DMSO (200 µL). The vial was quickly capped with a Teflon-lined septa cap and stirred at 80 °C for 20 min. Radiochemical conversions (RCC) were obtained via rTLC analysis (1:1 Hex:EtOAc or 4:1 DCM:MeOH). RCC values indicate the conversion of inorganic fluorine-18 (R_f = 0) to organic products. Radiochemical identity and approximate radiochemical purities (RCP) were obtained via rHPLC analysis. The UV traces of the crude reaction mixtures with and without a coinjection of the fluorine-19 standard were compared to confirm product identity.

3.5 Analytical Data for the Radiolabelling of α-Haloamides

rHPLC chromatograms of the crude reaction mixtures were recorded to confirm compound identity and estimate RCP. Unless otherwise stated, all labelled compounds were prepared via the General Procedure described in Section 3.4.

2-(Fluoro-^{18}*F*)-2-methyl-*N*-phenylpropanamide (**1-^{18}F**)



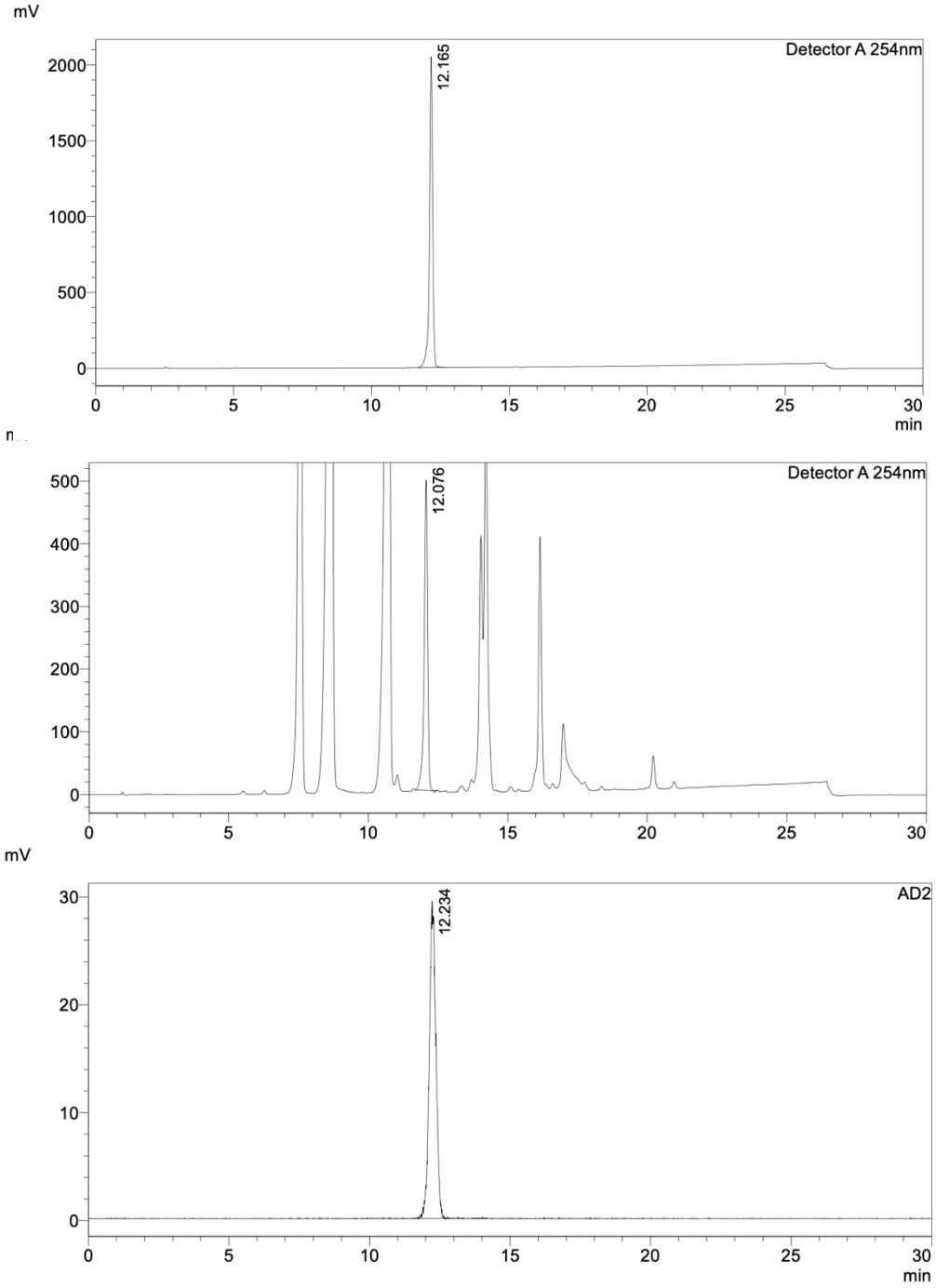
Synthesised from 2-bromo-2-methyl-*N*-phenylpropanamide **1-Br** (1.2 mg) or 2-chloro-2-methyl-*N*-phenylpropanamide **1-Cl** (1.0 mg).
From **1-Br**:

Entry	rTLC /%
1	80.05
2	94.54
3	80.50
4	84.93
5	88.03
6	89.66
7	85.72
8	91.48
9	95.03
10	96.00

RCC = **88.6 ± 5.5%** (n=10), RCP = **≥99%**
From **1-Cl**:

Entry	rTLC /%
1	41.47
2	41.53
3	43.95

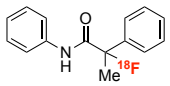
RCC = **42.3 ± 1.2%** (n=3) RCP = **≥99%**
HPLC Conditions A (prepared from **1-Br**):



Upper: UV (254 nm), chromatogram of independently synthesised **1-^{19}F** (12.165 min)
Middle: UV (254 nm), coinject chromatogram of crude reaction mixture showing **1-^{19}F** (12.076 min, prepared from **1-Br**)
Lower: Gamma chromatogram of crude reaction mixture showing **1-^{18}F** (12.234 min, prepared from **1-Br**)

SUPPORTING INFORMATION

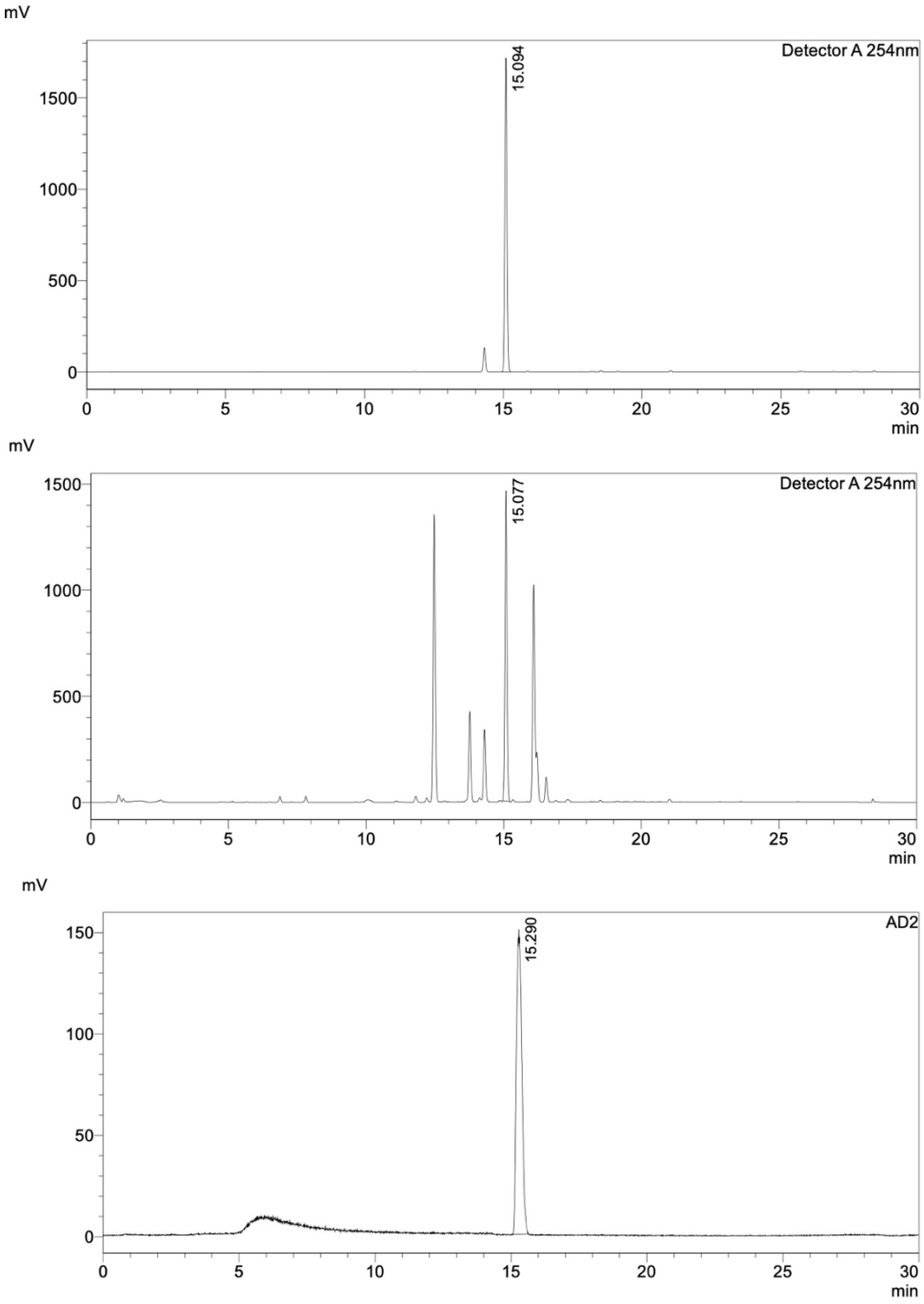
2-(Fluoro-^{18}F)-*N*,2-diphenylpropanamide (**2-^{18}F**)



Synthesised from 2-chloro-*N*,2-diphenylpropanamide **1-Cl** (1.3 mg).

Entry	rTLC /%
1	41.47
2	41.53
3	43.95

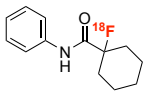
RCC = **42.3 ± 1.2%** (n=3) RCP **= ≥99%** HPLC Conditions B:



Upper: UV (254 nm), chromatogram of independently synthesised **2-^{19}F** (15.094 min)
Middle: UV (254 nm), coinject chromatogram of crude reaction mixture showing **2-^{19}F** (15.077 min)
Lower: Gamma chromatogram of crude reaction mixture showing **2-^{18}F** (15.290 min)

SUPPORTING INFORMATION

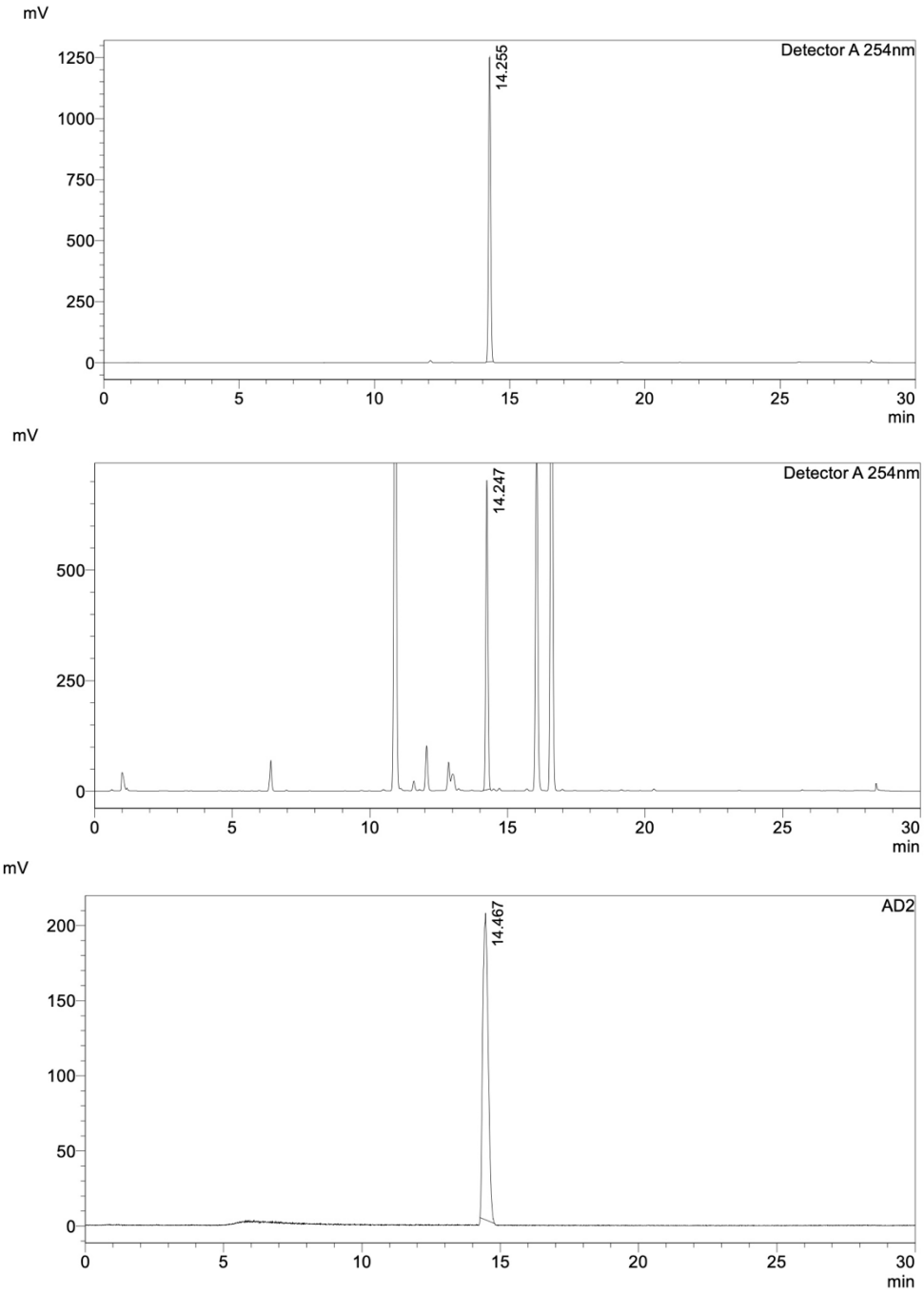
1-(Fluoro-^{18}F)-*N*-phenylcyclohexane-1-carboxamide (**3-^{18}F**)



Synthesised from 1-bromo-*N*-phenylcyclohexane-1-carboxamide **3-Br** (1.4 mg).

Entry	rTLC /%
1	77.77
2	79.41
3	56.77
4	47.82

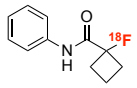
RCC = **65.4 ± 6.8%** (n=4), RCP = **≥99%** HPLC Conditions B:



Upper: UV (254 nm), chromatogram of independently synthesised **3-^{19}F** (14.255 min)
Middle: UV (254 nm), coinject chromatogram of crude reaction mixture showing **3-^{19}F** (14.247 min)
Lower: Gamma chromatogram of crude reaction mixture showing **3-^{18}F** (14.467 min)

SUPPORTING INFORMATION

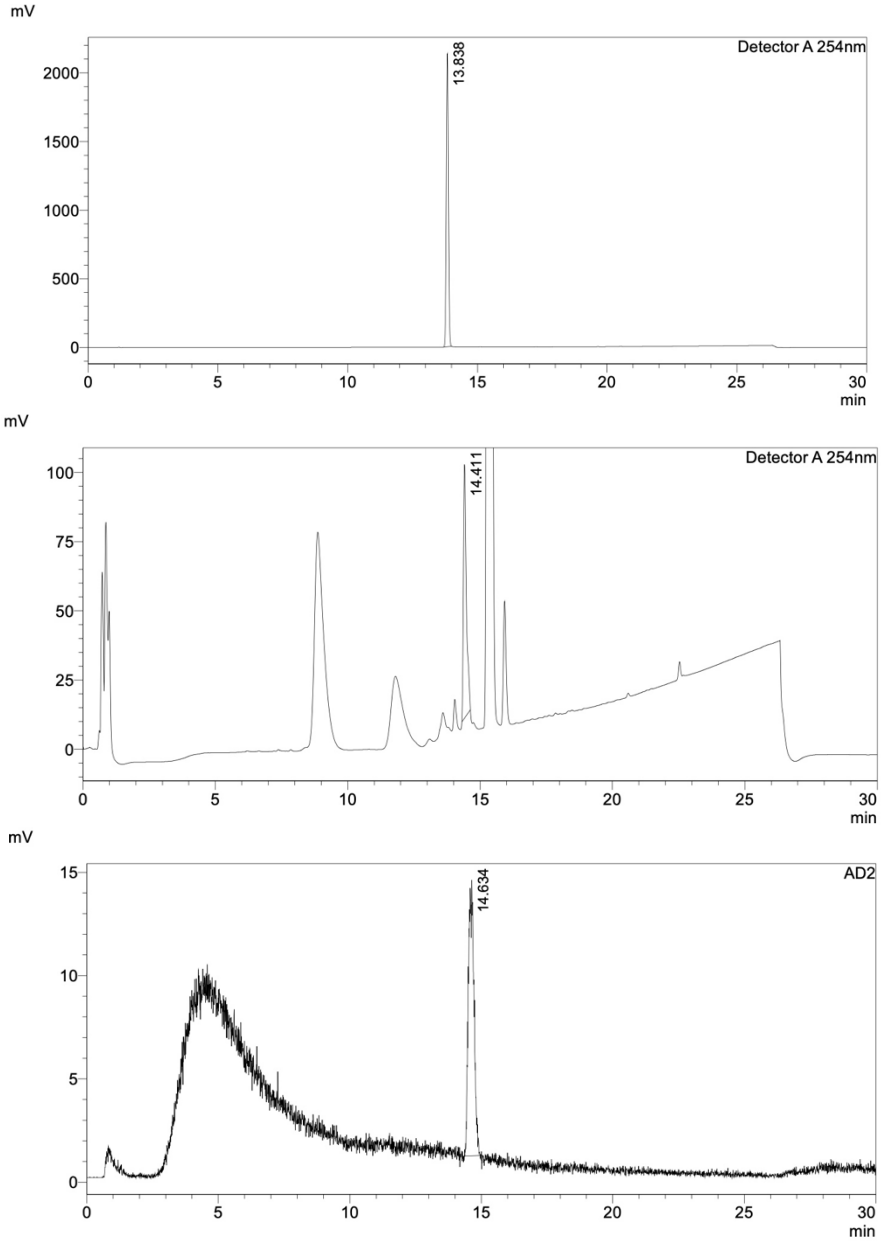
1-(Fluoro-^{18}F)-*N*-phenylcyclobutane-1-carboxamide (**4-^{18}F**)



Synthesised from 1-bromo-*N*-phenylcyclobutane-1-carboxamide **4-Br** (1.3 mg).

Entry	rTLC /%
1	7.71
2	5.31
3	6.74
4	8.52
5	3.91

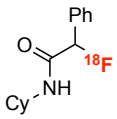
RCC = **6.4 ± 1.7%** (n=5), RCP = **≥99%** HPLC Conditions A:



Upper: UV (254 nm), chromatogram of independently synthesised **4-^{19}F** (13.838 min)
Middle: UV (254 nm), coinject chromatogram of crude reaction mixture showing **4-^{19}F** (14.411 min)
Lower: Gamma chromatogram of crude reaction mixture showing **4-^{18}F** (14.634 min)

SUPPORTING INFORMATION

N-Cyclohexyl-2-(fluoro-^{18}F)-2-phenylacetamide (**6-^{18}F**)



Synthesised from *N*-cyclohexyl-*N*-((methylsulfonyl)oxy)-2-phenylacetamide **33** (1.6 mg) using MeCN instead of DMSO solvent.

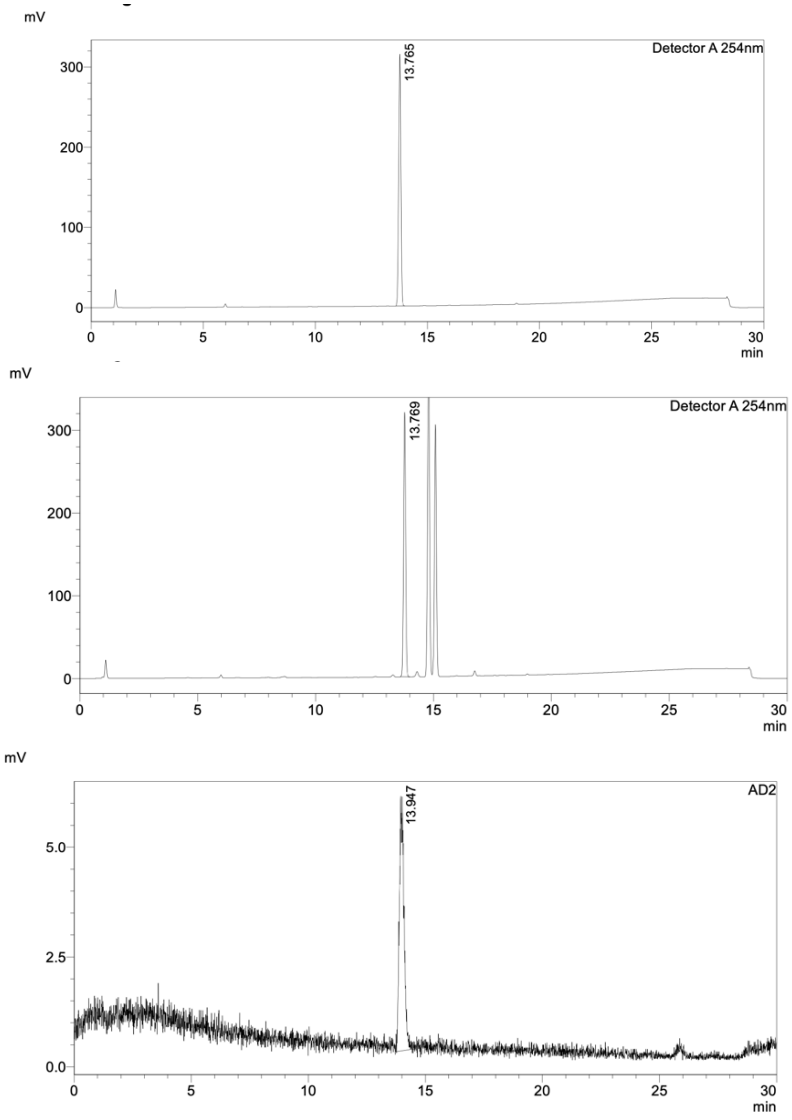
Entry	rTLC /%
1	17.32
2	16.27
3	26.83
4	26.23

RCC = **21.6 ± 4.9%** (n=4), RCP = **≥99%** HPLC Conditions A.

Also synthesised from 2-bromo-*N*-cyclohexyl-2-phenylacetamide **6-Br** (1.5 mg) using MeCN instead of DMSO solvent.

Entry	rTLC /%
1	1.18
2	1.87

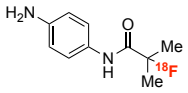
RCC = **1.5 ± 0.3%** (n=2). Owing to low conversion, the reaction was reformulated by passing through a Waters Al_2O_3 Sep-Pak cartridge. The eluted product was diluted in 9.5 mL H_2O and trapped on a Waters C-18 Sep-Pak Cartridge. The C-18 cartridge was eluted with 0.5 mL EtOH and analyzed with HPLC Conditions A (shown below):



Upper: UV (254 nm), chromatogram of independently synthesised **6-^{19}F** (13.765 min)
Middle: UV (254 nm), coinject chromatogram of crude reaction mixture showing **6-^{19}F** (13.769 min)
Lower: Gamma chromatogram of crude reaction mixture showing **6-^{18}F** (13.947 min)

SUPPORTING INFORMATION

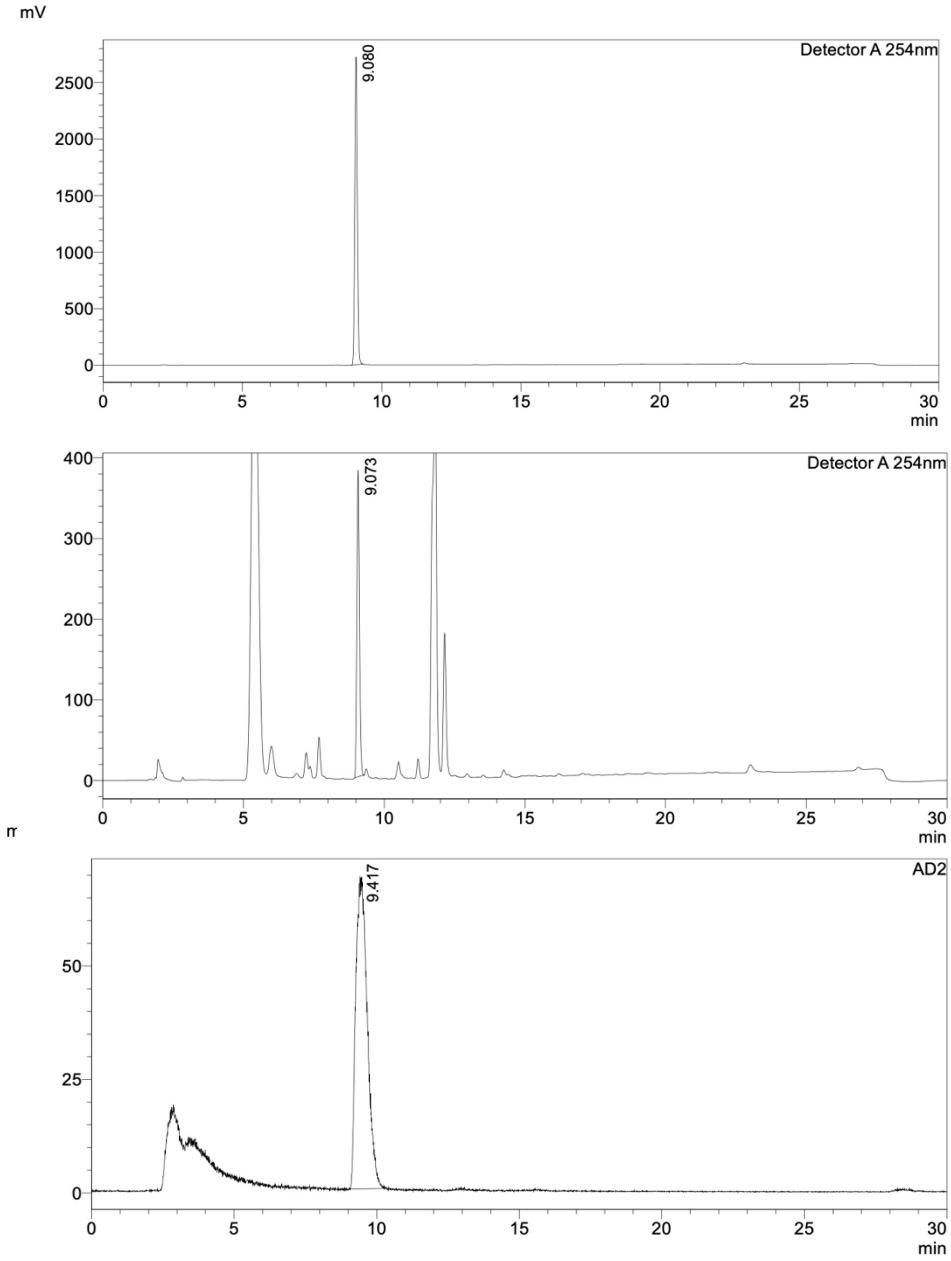
N-(4-Aminophenyl)-2-(fluoro-^{18}*F*)-2-methylpropanamide (**9-^{18}F**)



Synthesised from *N*-(4-aminophenyl)-2-bromo-2-methylpropanamide **9-Br** (1.3 mg).

Entry	rTLC /%
1	50.55
2	50.88
3	47.57
4	36.94

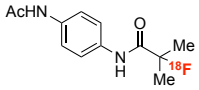
RCC = **46.5 ± 5.7%** (n=4), RCP = **≥99%** HPLC Conditions E:



Upper: UV (254 nm), chromatogram of independently synthesised **9-^{19}F** (9.080 min)
Middle: UV (254 nm), coinject chromatogram of crude reaction mixture showing **9-^{19}F** (9.073 min)
Lower: Gamma chromatogram of crude reaction mixture showing **9-^{18}F** (9.417 min)

SUPPORTING INFORMATION

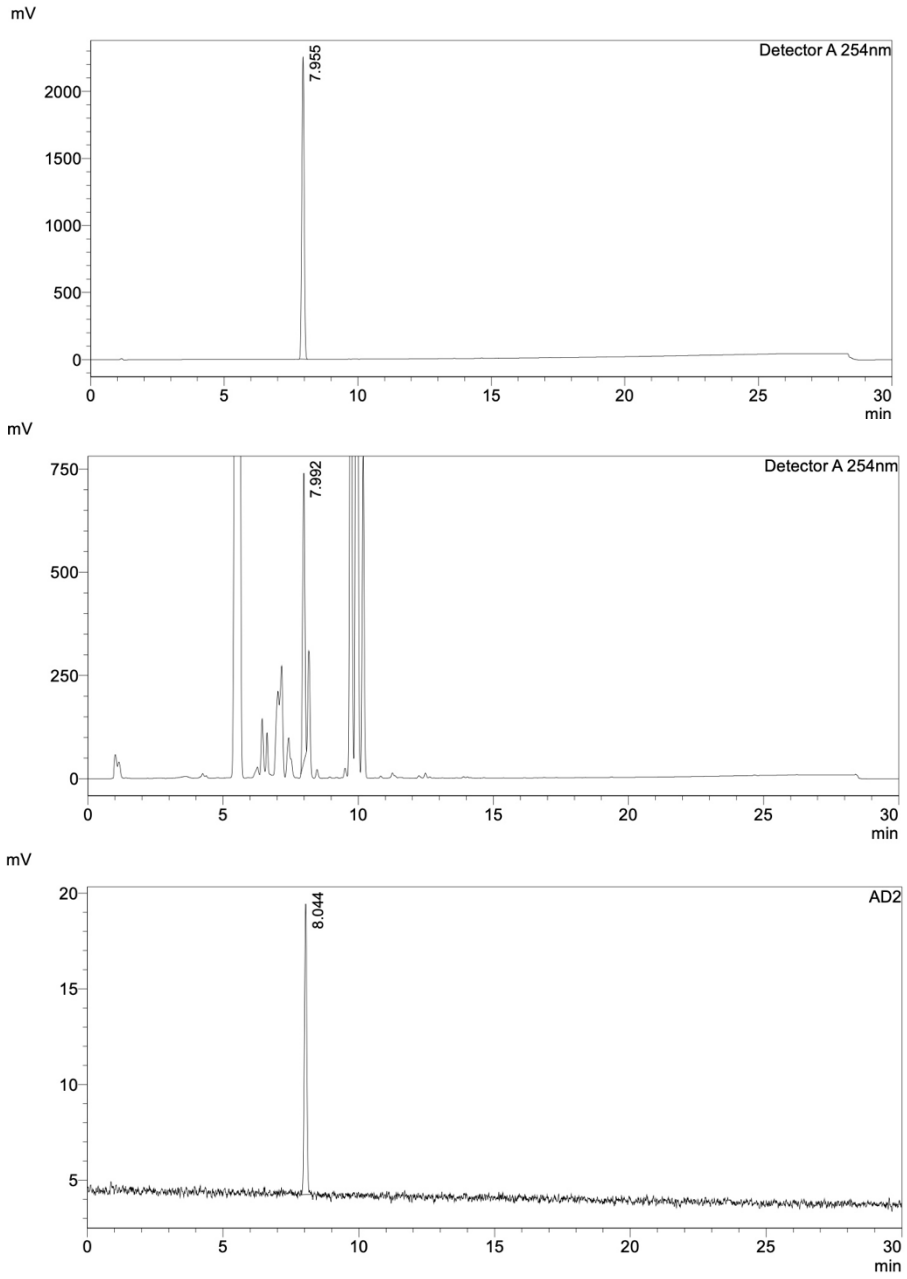
N-(4-Acetamidophenyl)-2-(fluoro-^{18}F)-2-methylpropanamide (**10-^{18}F**)



Synthesised from *N*-(4-acetamidophenyl)-2-bromo-2-methylpropanamide **10-Br** (1.5 mg).

Entry	rTLC /%
1	76.15
2	82.09
3	76.40

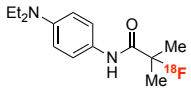
RCC = **78.2 ± 2.7%** (n=3) RCP = **≥99%** HPLC Conditions B:



Upper: UV (254 nm), chromatogram of independently synthesised **10-^{19}F** (7.955 min)
Middle: UV (254 nm), coinject chromatogram of crude reaction mixture showing **10-^{19}F** (7.992 min)
Lower: Gamma chromatogram of crude reaction mixture showing **10-^{18}F** (8.044 min)

SUPPORTING INFORMATION

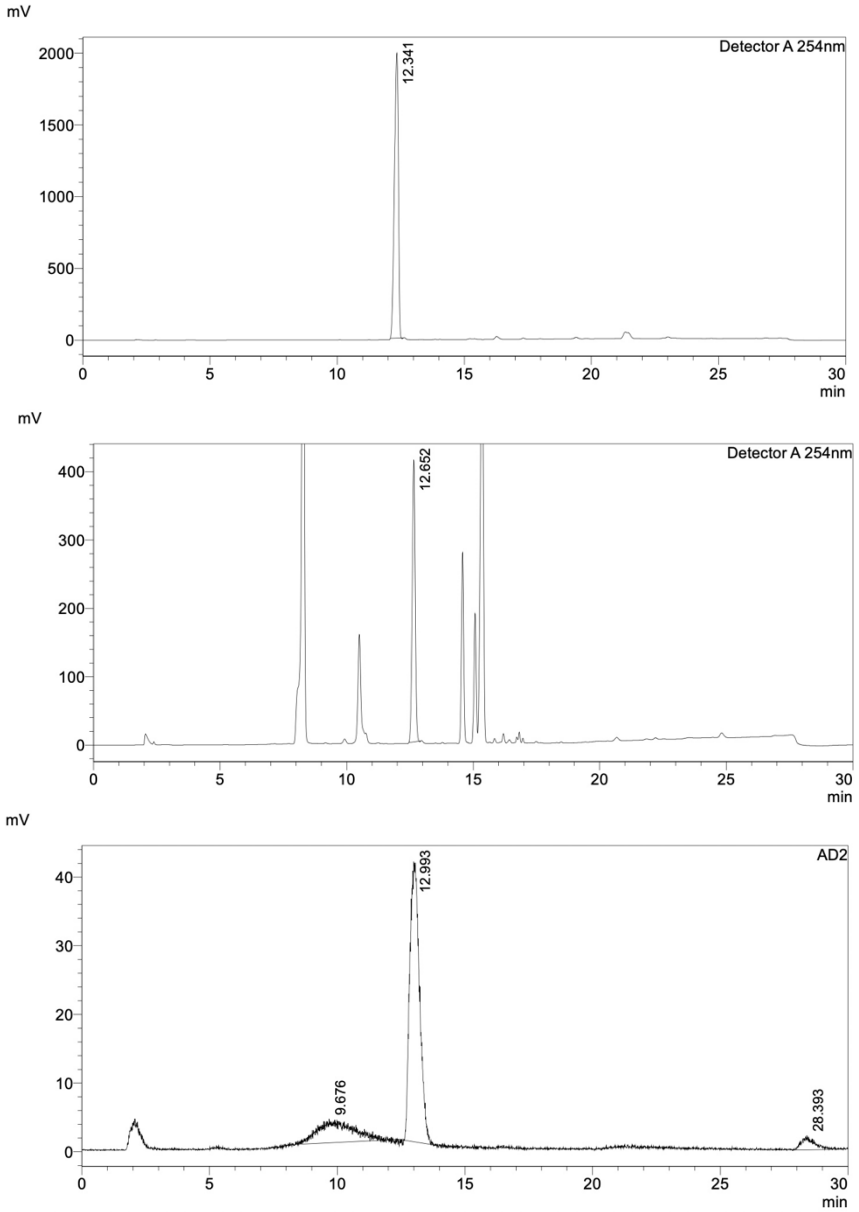
N-(4-(Diethylamino)phenyl)-2-(fluoro-^{18}F)-2-methylpropanamide (**11-^{18}F**)



Synthesised from 2-bromo-*N*-(4-(diethylamino)phenyl)-2-methylpropanamide **11-Br** (1.6 mg).

Entry	rTLC /%
1	50.38
2	45.45
3	42.13

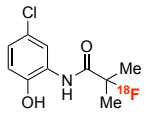
RCC = **46.0 ± 3.4%** (n=3) RCP = **74.7%** HPLC Conditions C:



Upper: UV (254 nm), chromatogram of independently synthesised **11-^{19}F** (12.341 min)
Middle: UV (254 nm), coinject chromatogram of crude reaction mixture showing **11-^{19}F** (12.652 min)
Lower: Gamma chromatogram of crude reaction mixture showing **11-^{18}F** (12.993 min)

SUPPORTING INFORMATION

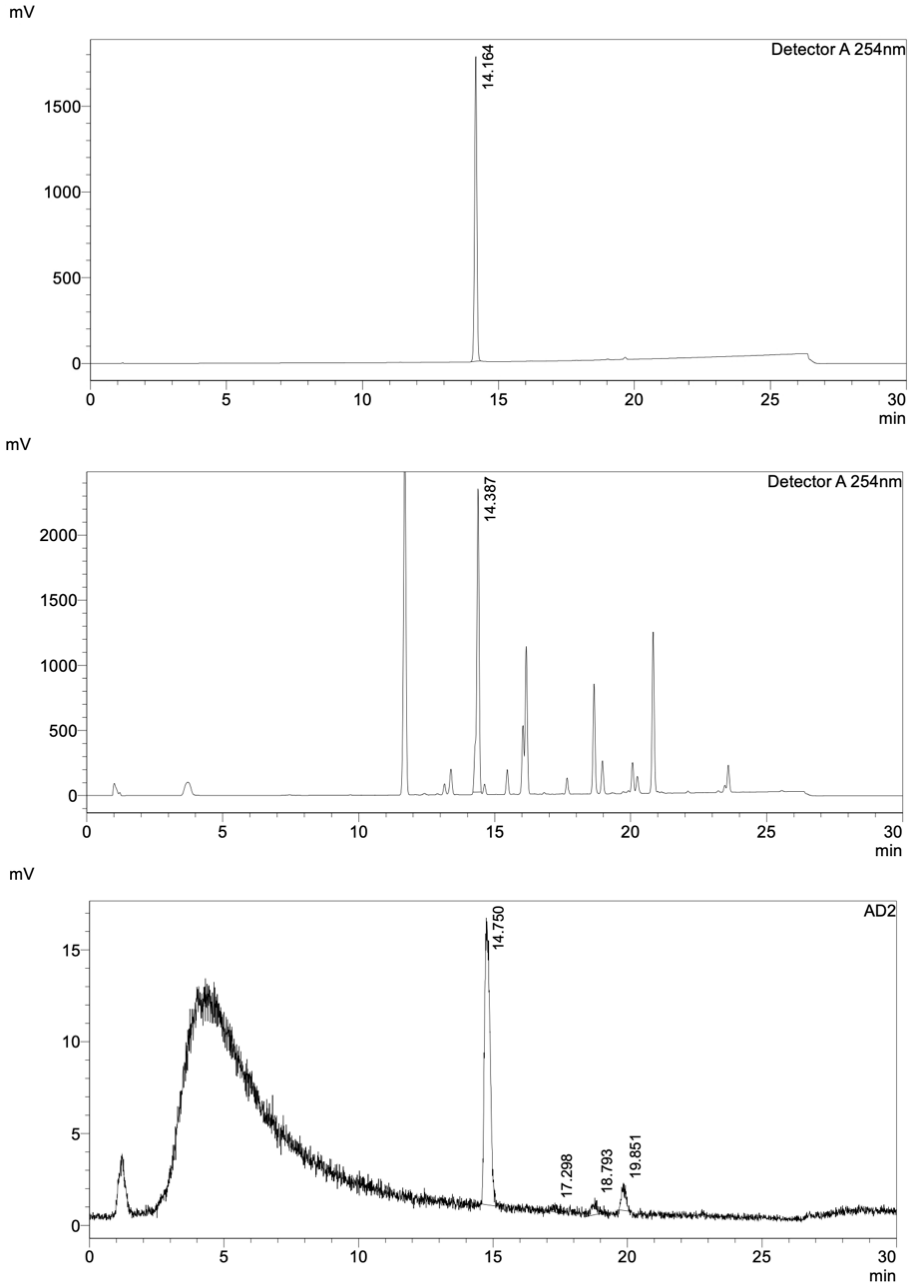
N-(5-Chloro-2-hydroxyphenyl)-2-(fluoro-^{18}*F*)-2-methylpropanamide (**12-^{18}F**)



Synthesised from 2-bromo-*N*-(5-chloro-2-hydroxyphenyl)-2-methylpropanamide **12-Br** (1.5 mg).

Entry	rTLC /%
1	7.55
2	9.56
3	11.13

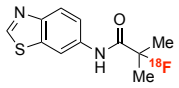
RCC = **9.4 ± 1.5%** (n=3) RCP = **87.8%** HPLC Conditions A:



Upper: UV (254 nm), chromatogram of independently synthesised **12-^{19}F** (14.164 min)
Middle: UV (254 nm), coinject chromatogram of crude reaction mixture showing **12-^{19}F** (14.387 min)
Lower: Gamma chromatogram of crude reaction mixture showing **12-^{18}F** (14.750 min)

SUPPORTING INFORMATION

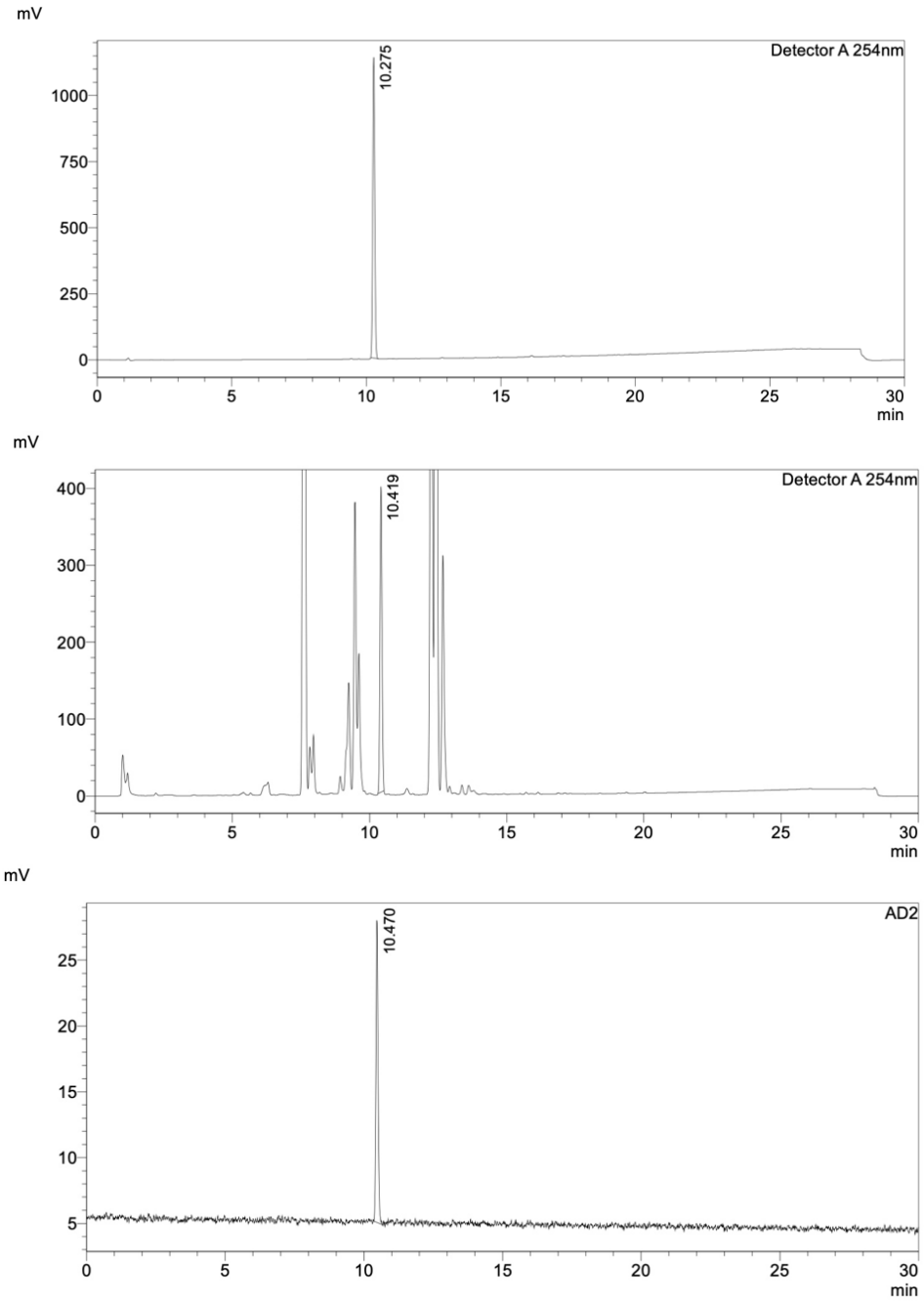
N-(Benzo[*d*]thiazol-6-yl)-2-(fluoro-^{18}*F*)-2-methylpropanamide (**13-^{18}F**)



Synthesised from *N*-(benzo[*d*]thiazol-6-yl)-2-bromo-2-methylpropanamide **13-Br** (1.5 mg).

Entry	rTLC /%
1	78.51
2	77.93
3	83.82

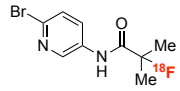
RCC = **80.1 ± 2.7%** (n=3) RCP = **≥99%** HPLC Conditions B:



Upper: UV (254 nm), chromatogram of independently synthesised **13-^{19}F** (10.275 min)
Middle: UV (254 nm), coinject chromatogram of crude reaction mixture showing **13-^{19}F** (10.419 min)
Lower: Gamma chromatogram of crude reaction mixture showing **13-^{18}F** (10.470 min)

SUPPORTING INFORMATION

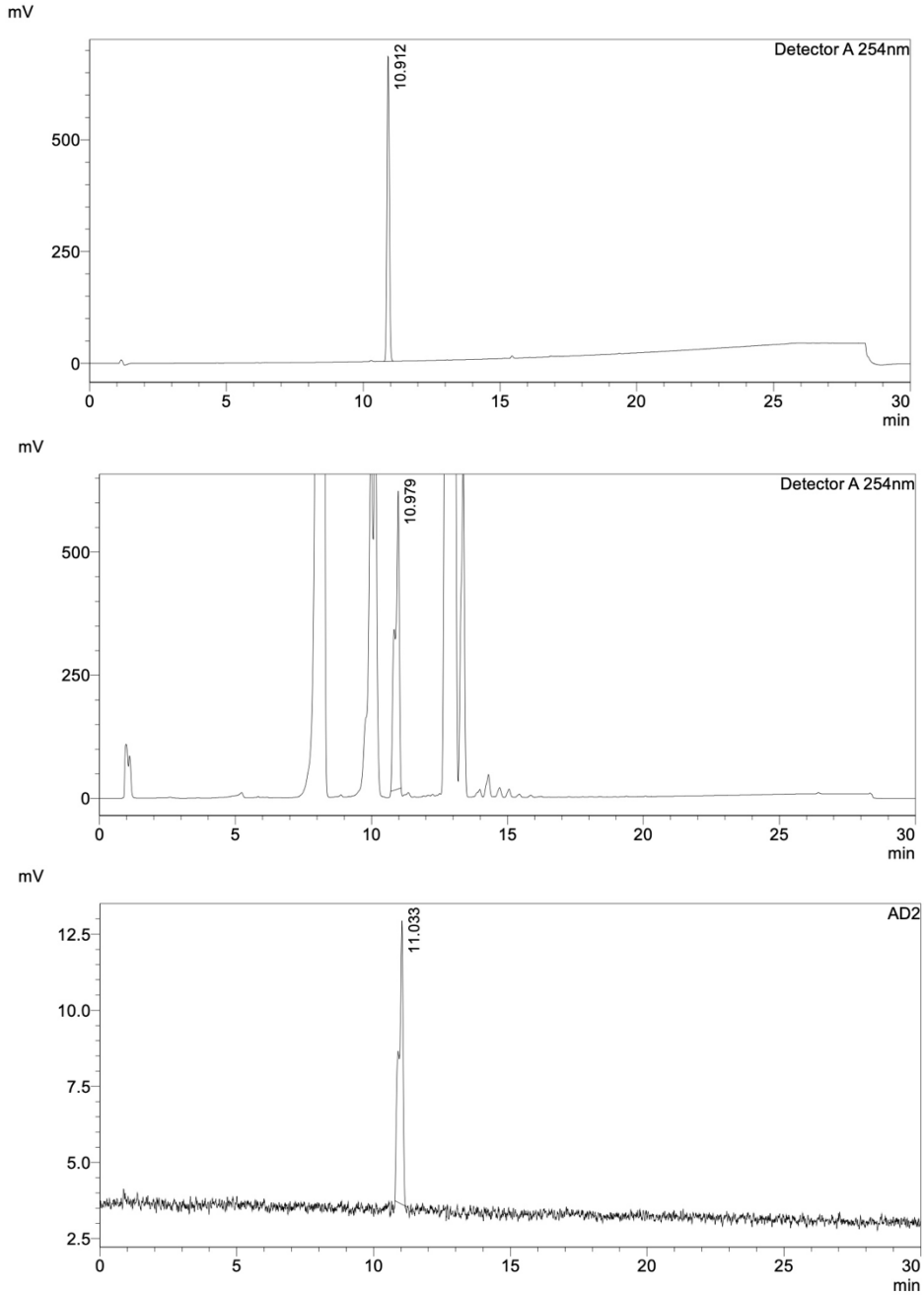
N-(6-Bromopyridin-3-yl)-2-(fluoro-^{18}*F*)-2-methylpropanamide (**14-^{18}F**)



2-bromo-*N*-(6-bromopyridin-3-yl)-2-methylpropanamide **14-Br** (1.6 mg).

Entry	rTLC /%
1	67.05
2	78.04
3	66.24

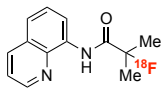
RCC = **70.4 ± 5.4%** (n=3) RCP = **≥99%** HPLC Conditions B:



Upper: UV (254 nm), chromatogram of independently synthesised **14-^{19}F** (10.912 min)
Middle: UV (254 nm), coinject chromatogram of crude reaction mixture showing **14-^{19}F** (10.979 min)
Lower: Gamma chromatogram of crude reaction mixture showing **14-^{18}F** (11.033 min)

SUPPORTING INFORMATION

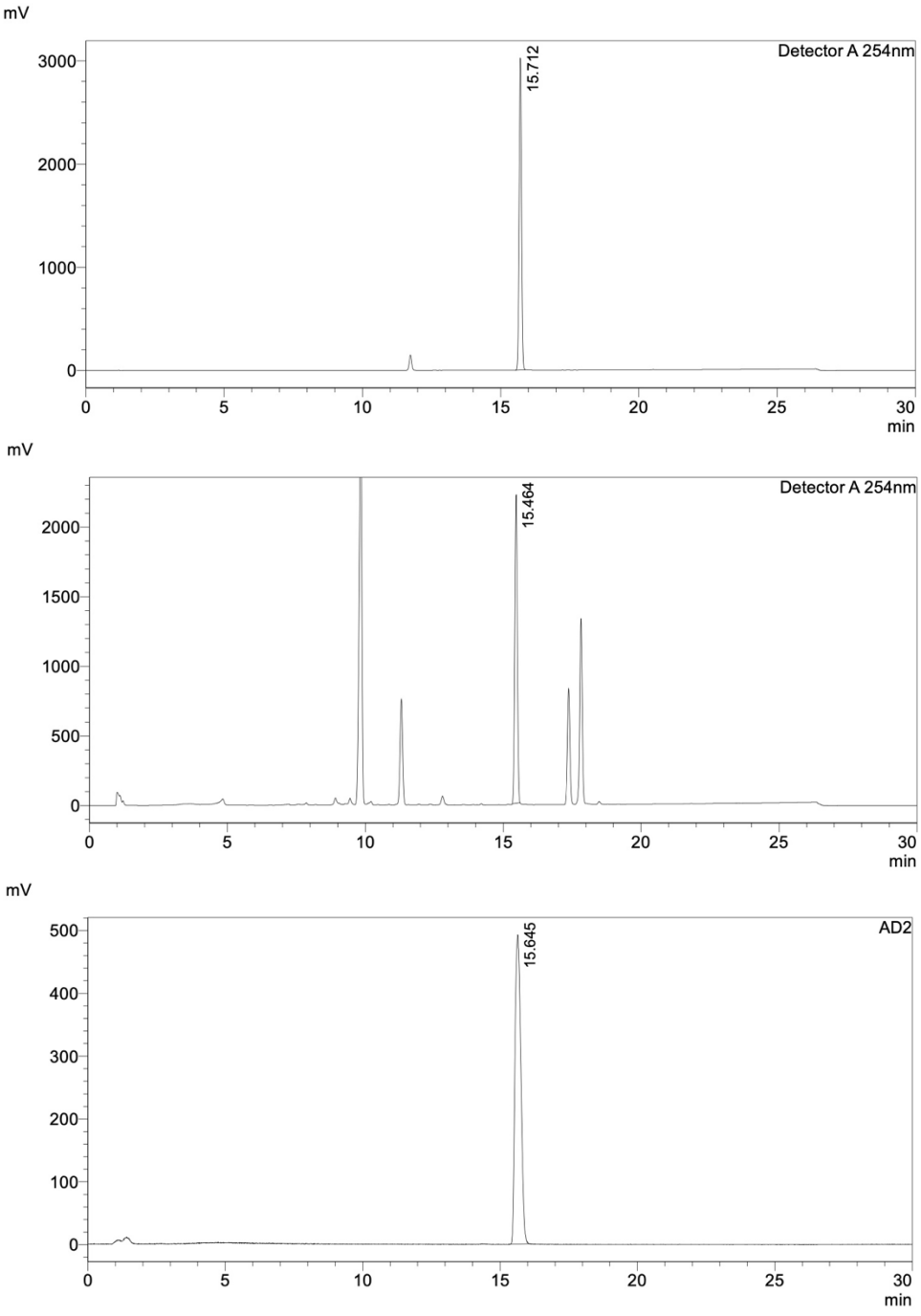
2-(Fluoro-^{18}F)-2-methyl-*N*-(quinolin-8-yl)propanamide (**15-^{18}F**)



Synthesised from 2-bromo-2-methyl-*N*-(quinolin-8-yl)propenamide **15-Br** (1.6 mg).

Entry	rTLC /%
1	93.22
2	89.19
3	94.04

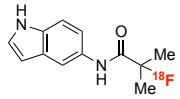
RCC = **92.2 ± 2.1%** (n=3) RCP = **≥99%** HPLC Conditions A:



Upper: UV (254 nm), chromatogram of independently synthesised **15-^{19}F** (15.172 min)
Middle: UV (254 nm), coinject chromatogram of crude reaction mixture showing **15-^{19}F** (15.464 min)
Lower: Gamma chromatogram of crude reaction mixture showing **15-^{18}F** (15.654 min)

SUPPORTING INFORMATION

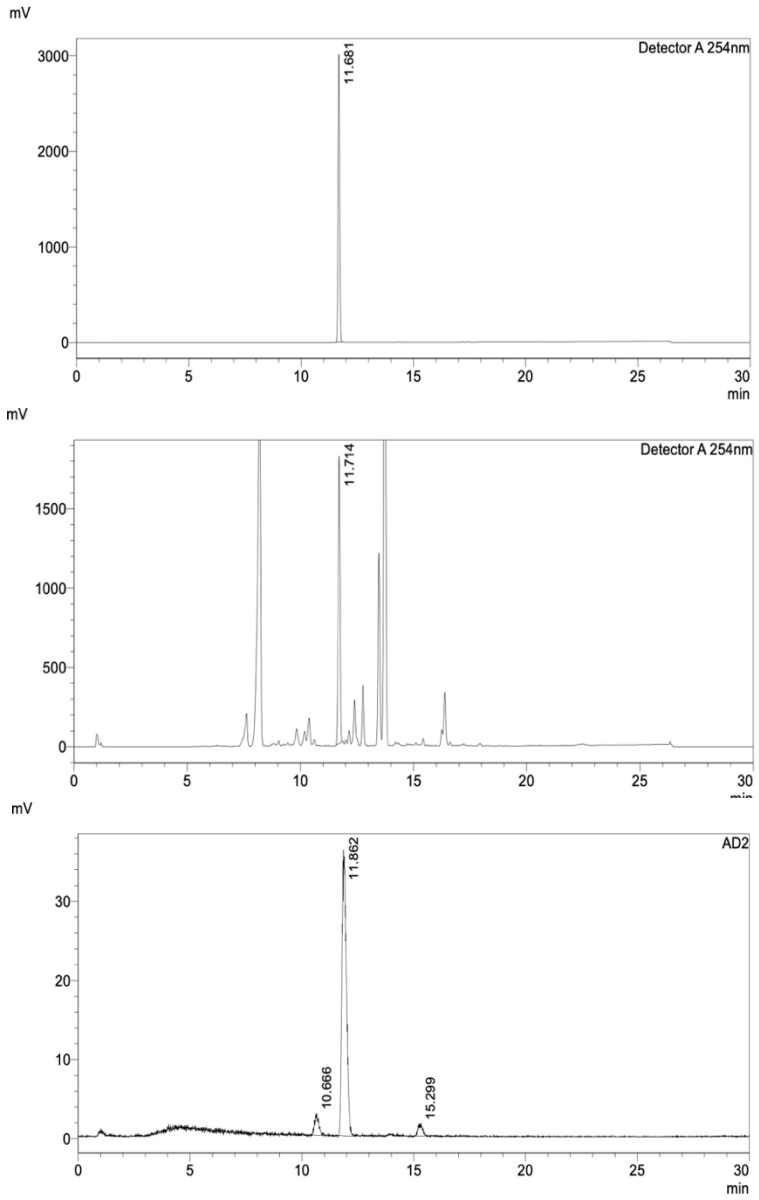
2-(Fluoro-^{18}*F*)-N-(1H-indol-5-yl)-2-methylpropanamide (**16-^{18}F**)



Synthesised from 2-bromo-*N*-(1H-indol-5-yl)-2-methylpropanamide **16-Br** (1.4 mg).

Entry	rTLC /%
1	81.28
2	60.74
3	72.50
4	73.18
5	66.45
6	69.01
7	57.71

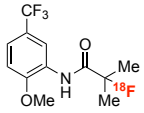
RCC = **68.7 ± 7.4%** (n=7), RCP = **90.1%** HPLC Conditions A:



Upper: UV (254 nm), chromatogram of independently synthesised **16-^{19}F** (11.681 min)
Middle: UV (254 nm), coinject chromatogram of crude reaction mixture showing **16-^{19}F** (11.714 min)
Lower: Gamma chromatogram of crude reaction mixture showing **16-^{18}F** (11.862 min)

SUPPORTING INFORMATION

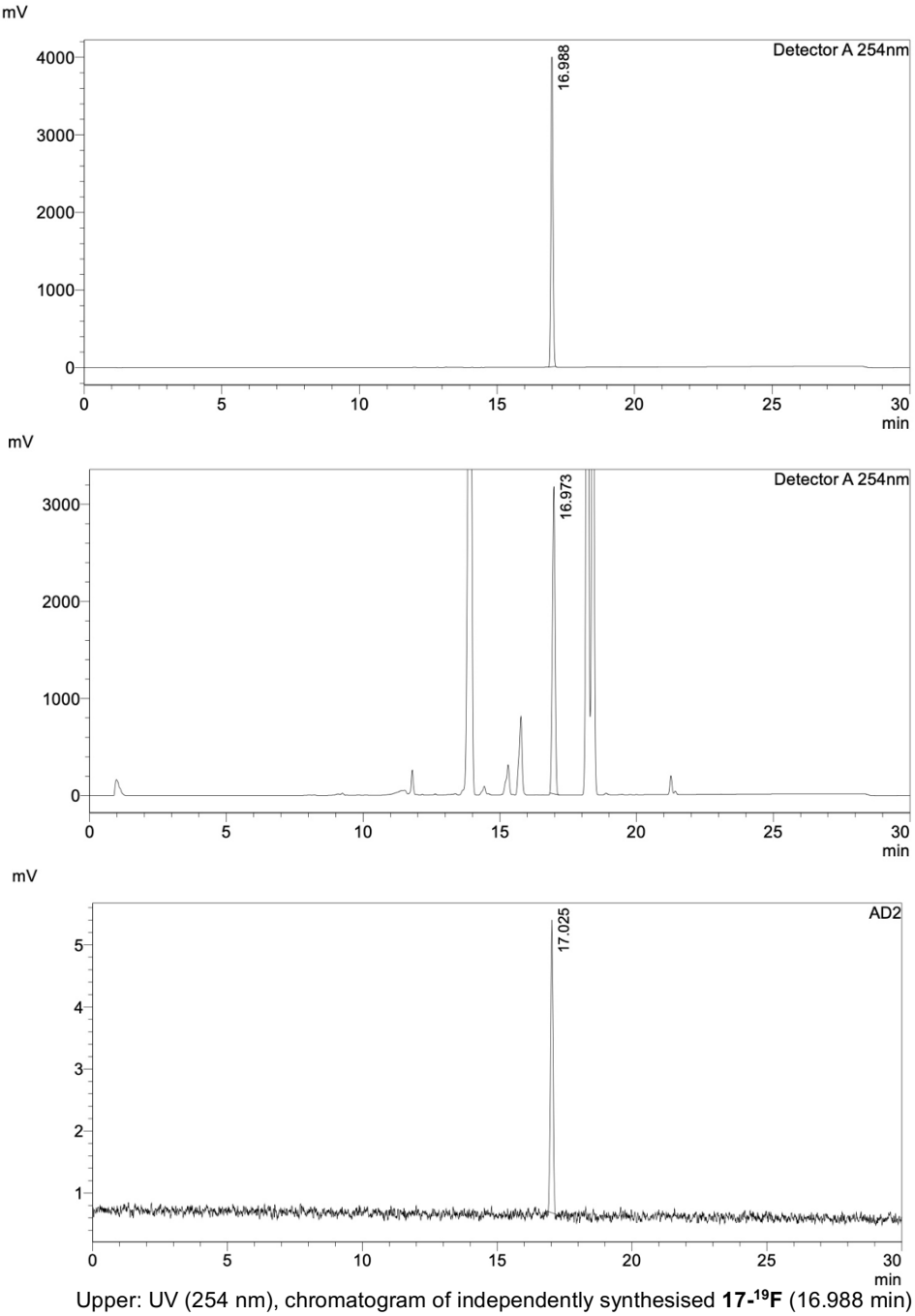
2-(Fluoro-^{18}F)-*N*-(2-methoxy-5-(trifluoromethyl)phenyl)-2-methylpropanamide (**17-^{18}F**)



Synthesised from 2-bromo-*N*-(2-methoxy-5-(trifluoromethyl)phenyl)-2-methylpropanamide **17-Br** (1.7 mg).

Entry	rTLC /%
1	75.41
2	88.47
3	84.21

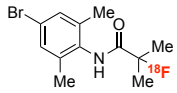
RCC = **82.7 ± 5.4%** (n=3) RCP = **≥99%** HPLC Conditions B:



Upper: UV (254 nm), chromatogram of independently synthesised **17-^{19}F** (16.988 min)
Middle: UV (254 nm), coinject chromatogram of crude reaction mixture showing **17-^{19}F** (16.973 min)
Lower: Gamma chromatogram of crude reaction mixture showing **17-^{18}F** (17.025 min)

SUPPORTING INFORMATION

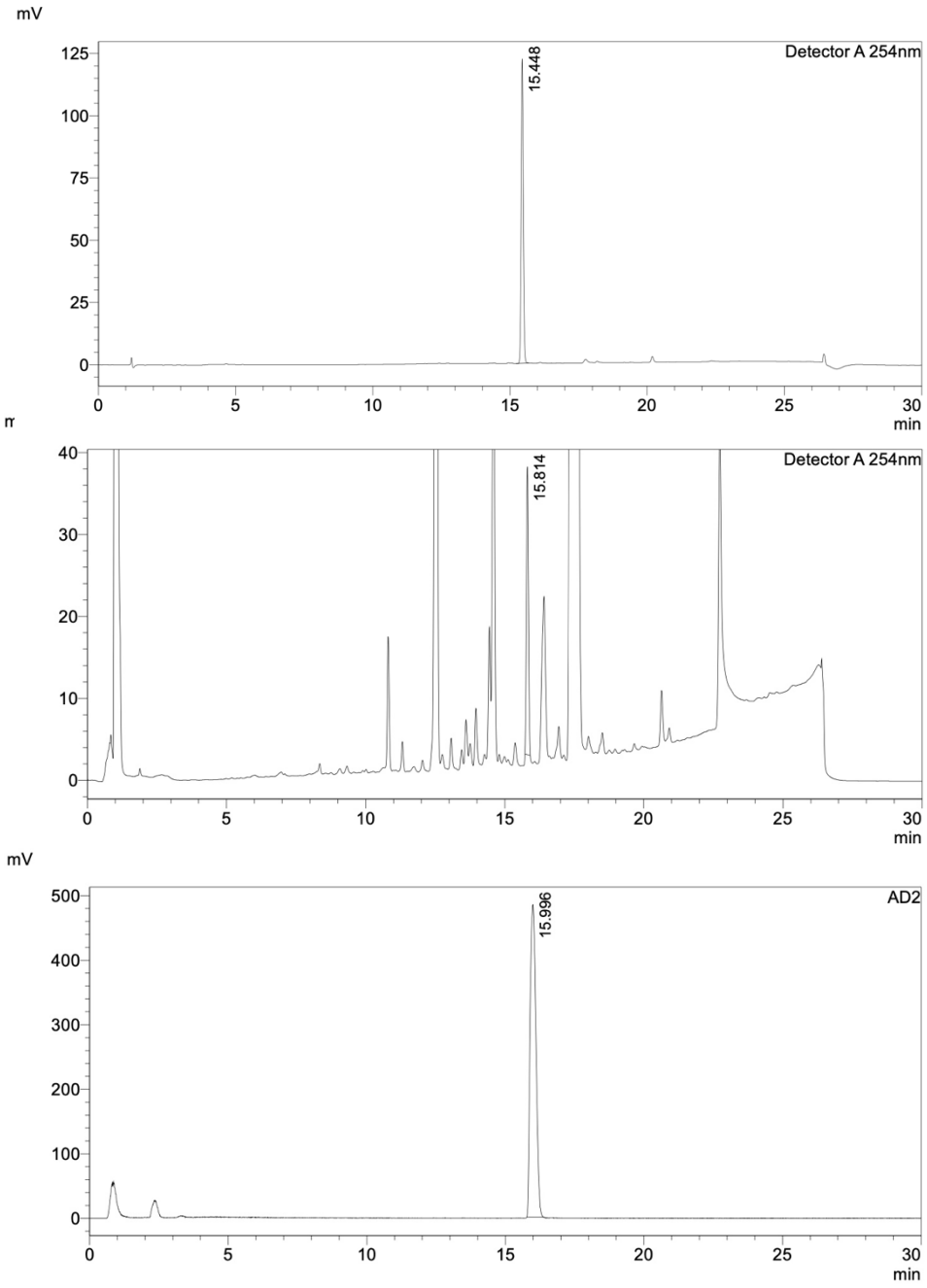
N-(4-Bromo-2,6-dimethylphenyl)-2-(fluoro-^{18}F)-2-methylpropanamide (**18-^{18}F**)



Synthesised from 2-bromo-*N*-(4-bromo-2,6-dimethylphenyl)-2-methylpropanamide **18-Br** (1.7 mg).

Entry	rTLC /%
1	82.70
2	82.31
3	85.59
4	86.21

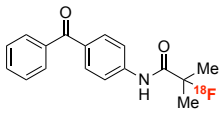
RCC = **84.2 ± 1.7%** (n=3) RCP = **≥99%** HPLC Conditions A:



Upper: UV (254 nm), chromatogram of independently synthesised **18-^{19}F** (15.448 min)
Middle: UV (254 nm), coinject chromatogram of crude reaction mixture showing **18-^{19}F** (15.814 min)
Lower: Gamma chromatogram of crude reaction mixture showing **18-^{18}F** (15.996 min)

SUPPORTING INFORMATION

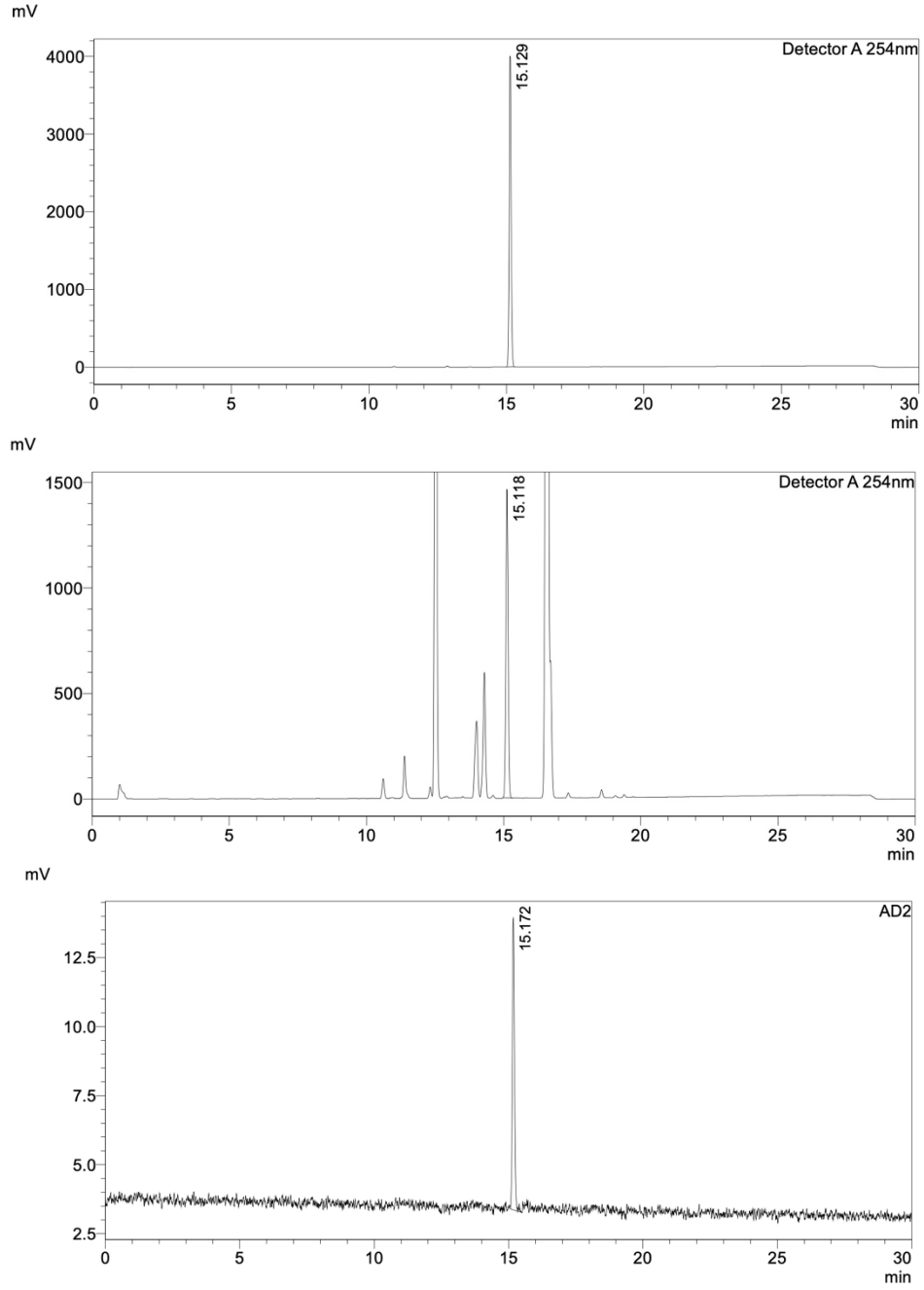
N-(4-benzoylphenyl)-2-(fluoro-^{18}*F*)-2-methylpropanamide (**19-^{18}F**)



Synthesised from *N*-(4-benzoylphenyl)-2-bromo-2-methylpropanamide **19-Br** (1.7 mg).

Entry	rTLC /%
1	75.72
2	76.31
3	80.29

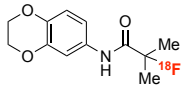
RCC = **77.1 ± 2.0%** (n=3) RCP = **≥99%** HPLC Conditions B:



Upper: UV (254 nm), chromatogram of independently synthesised **19-^{19}F** (15.129 min)
Middle: UV (254 nm), coinject chromatogram of crude reaction mixture showing **19-^{19}F** (15.118 min)
Lower: Gamma chromatogram of crude reaction mixture showing **19-^{18}F** (15.172 min)

SUPPORTING INFORMATION

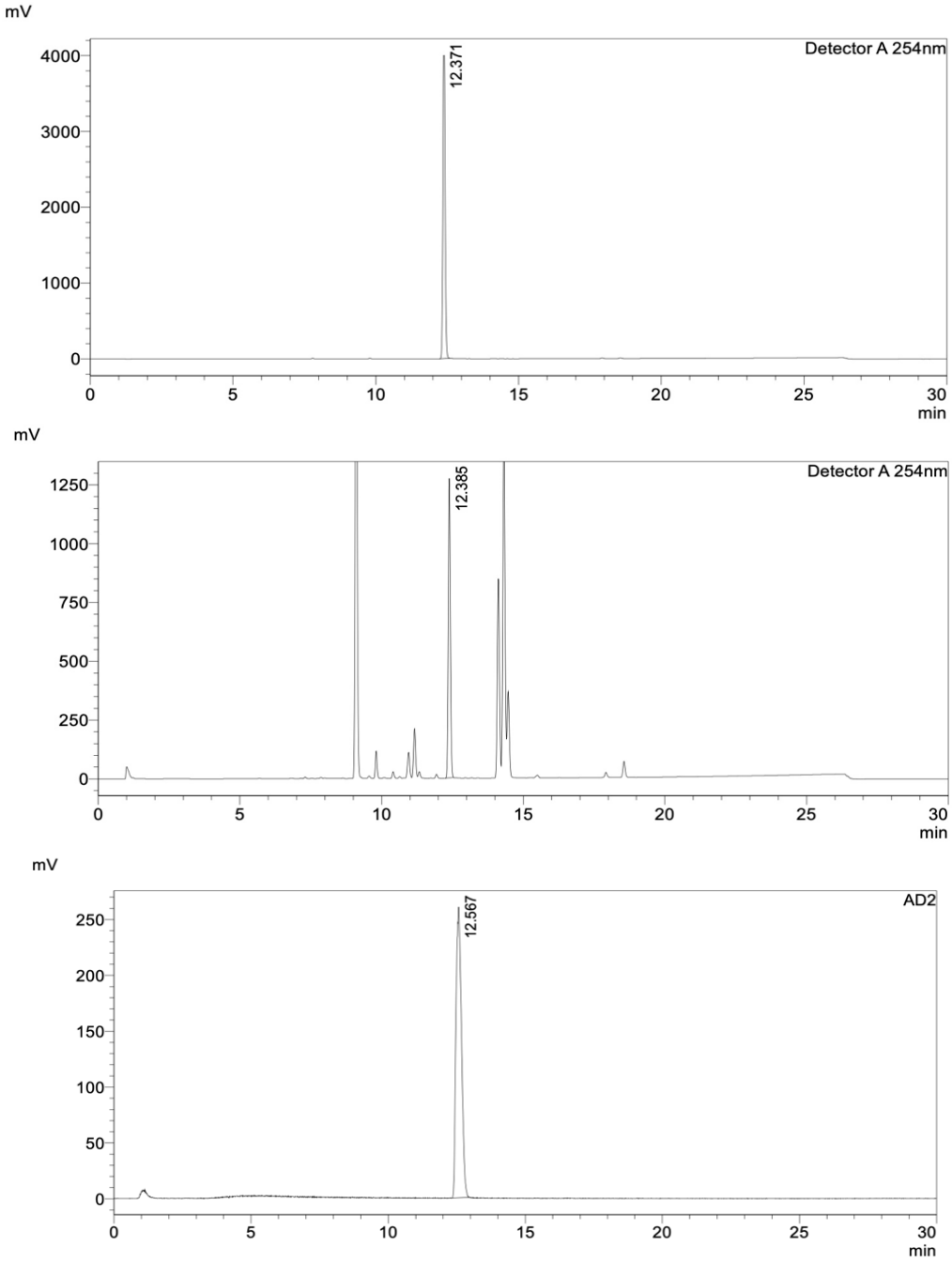
N-(2,3-Dihydrobenzo[*b*]1,4dioxin-6-yl)-2-(fluoro-^{18}*F*)-2-methylpropanamide (**20-^{18}F**)



Synthesised from 2-bromo-*N*-(2,3-dihydrobenzo[*b*][1,4]dioxin-6-yl)-2-methylpropanamide **20-Br** (1.5 mg).

Entry	rTLC /%
1	77.70
2	78.97
3	82.52

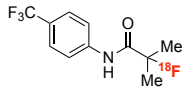
RCC = **79.7 ± 2.0%** (n=3) RCP = **≥99%** HPLC Conditions A



Upper: UV (254 nm), chromatogram of independently synthesised **20-^{19}F** (12.371 min)
Middle: UV (254 nm), coinject chromatogram of crude reaction mixture showing **20-^{19}F** (12.385 min)
Lower: Gamma chromatogram of crude reaction mixture showing **20-^{18}F** (12.567 min)

SUPPORTING INFORMATION

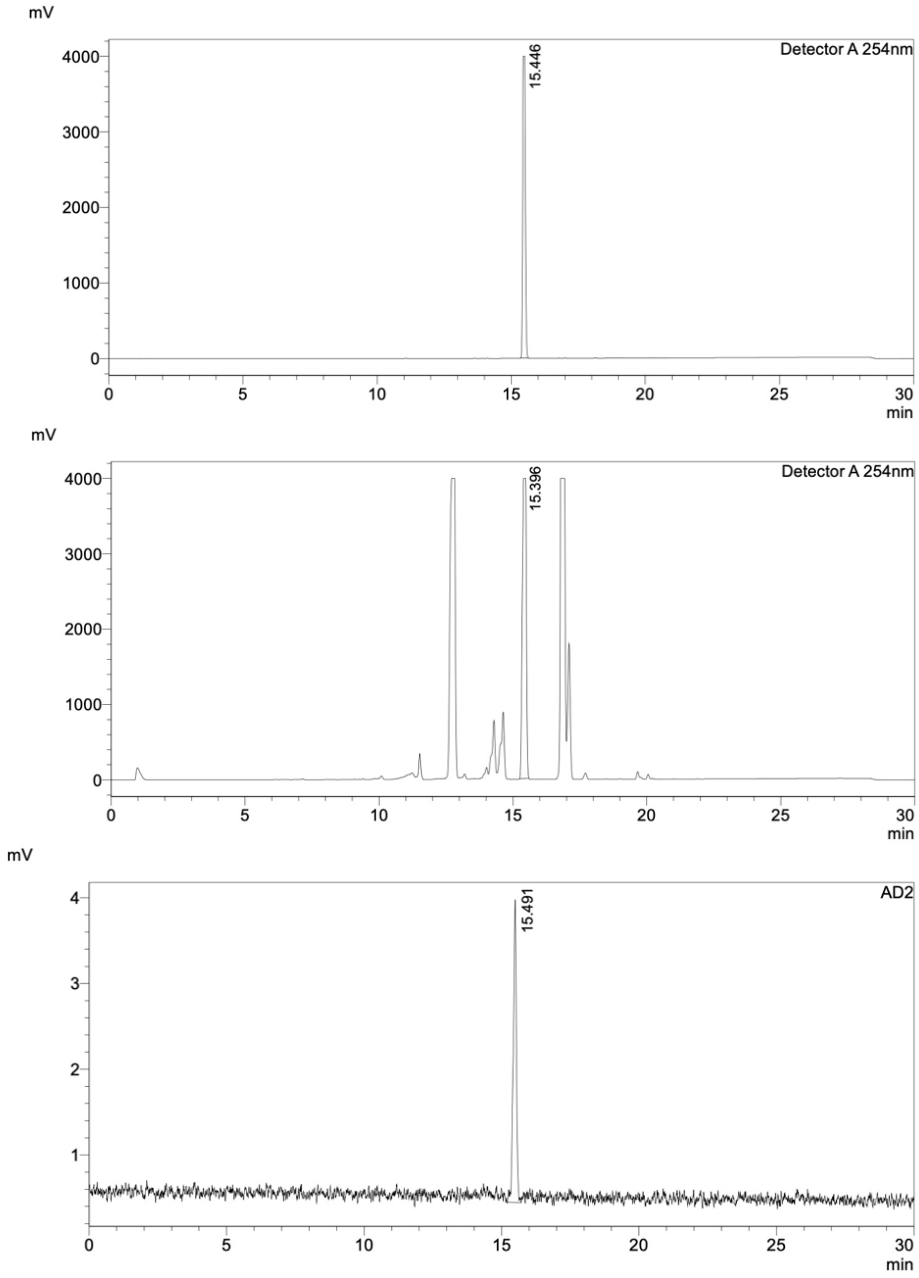
2-(Fluoro-^{18}F)-2-methyl-*N*-(4-(trifluoromethyl)phenyl)propanamide (**21-^{18}F**)



Synthesised from 2-bromo-2-methyl-*N*-(4-(trifluoromethyl)phenyl)propenamide **21-Br** (1.6 mg).

Entry	rTLC /%
1	85.56
2	85.15
3	83.81

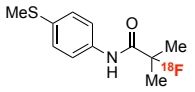
RCC = **84.8 ± 0.7%** (n=3) RCP = **≥99%** HPLC Conditions A



Upper: UV (254 nm), chromatogram of independently synthesised **21-^{19}F** (15.446 min)
Middle: UV (254 nm), coinject chromatogram of crude reaction mixture showing **21-^{19}F** (15.396 min)
Lower: Gamma chromatogram of crude reaction mixture showing **21-^{18}F** (15.491 min)

SUPPORTING INFORMATION

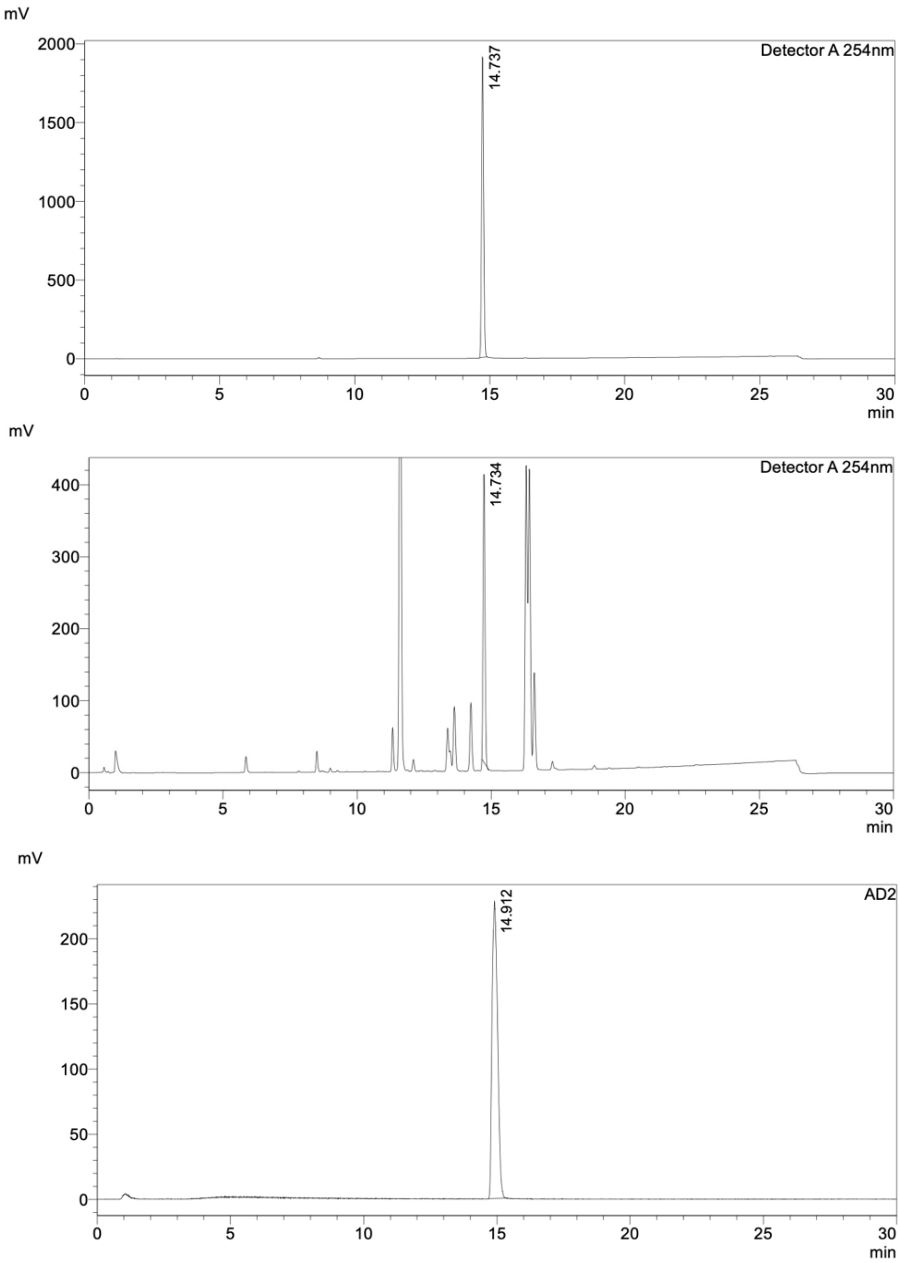
2-(Fluoro-^{18}F)-2-methyl-*N*-(4-(methylthio)phenyl)propanamide (**22-^{18}F**)



Synthesised from 2-bromo-2-methyl-N-(4-(methylthio)phenyl)propenamide **22-Br** (1.4 mg).

Entry	rTLC /%
1	81.00
2	82.64
3	82.86

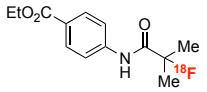
RCC = **82.2 ± 0.8%** (n=3) RCP = **≥99%** HPLC Conditions A:



Upper: UV (254 nm), chromatogram of independently synthesised **22-^{19}F** (14.737 min)
Middle: UV (254 nm), coinject chromatogram of crude reaction mixture showing **22-^{19}F** (14.734 min)
Lower: Gamma chromatogram of crude reaction mixture showing **22-^{18}F** (14.912 min)

SUPPORTING INFORMATION

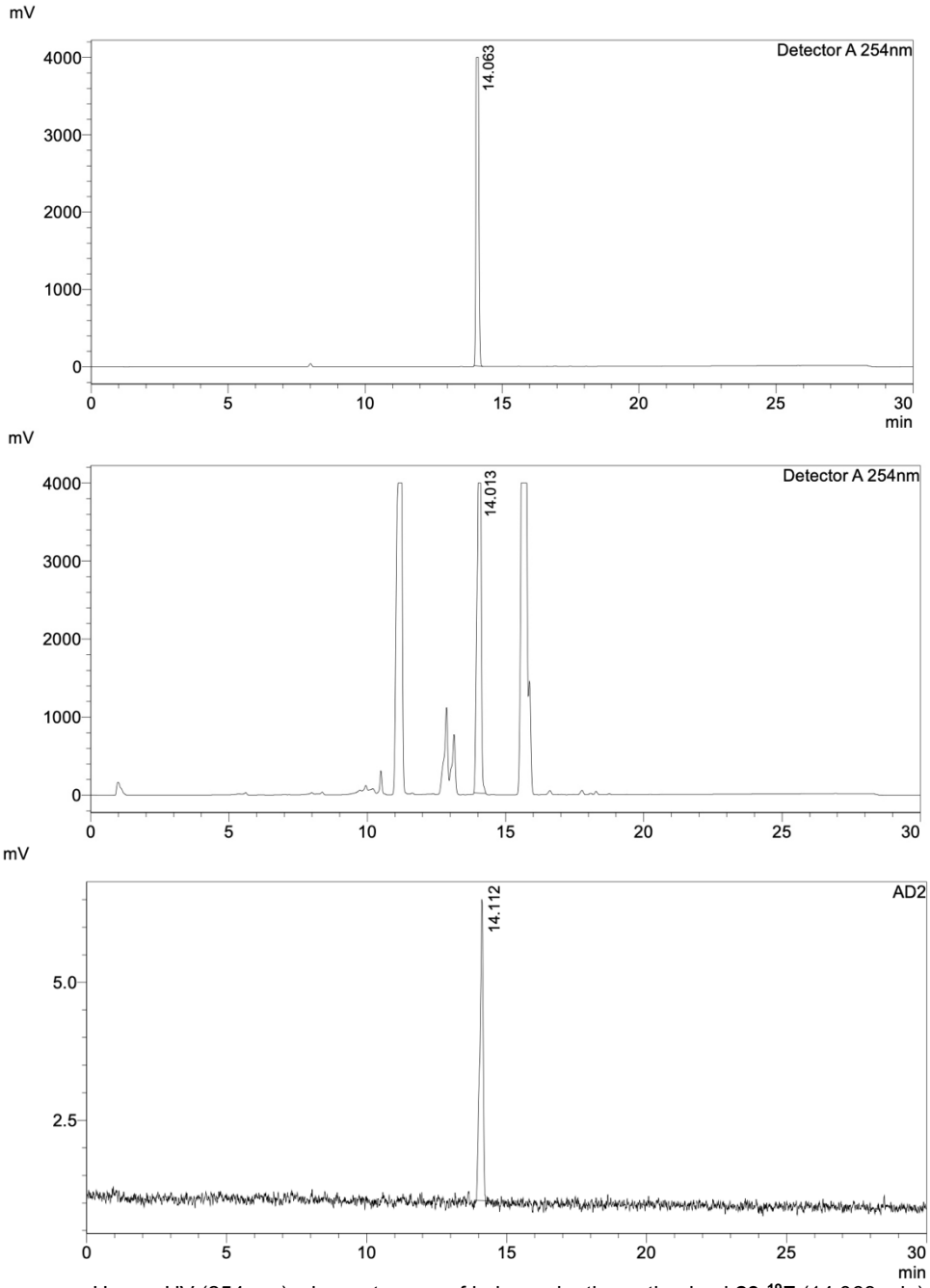
Ethyl 4-(2-(fluoro-^{18}F)-2-methylpropanamido)benzoate (**23-^{18}F**)



Synthesised from ethyl 4-(2-bromo-2-methylpropanamido)benzoate **23-Br** (1.6 mg).

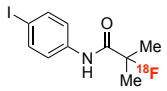
Entry	rTLC /%
1	81.40
2	65.12
3	81.40
4	82.37

RCC = **77.6 ± 7.2%** (n=4), RCP = **≥99%** HPLC Conditions B:



Upper: UV (254 nm), chromatogram of independently synthesised **23-^{19}F** (14.063 min)
Middle: UV (254 nm), coinject chromatogram of crude reaction mixture showing **23-^{19}F** (14.013 min)
Lower: Gamma chromatogram of crude reaction mixture showing **23-^{18}F** (14.112 min)

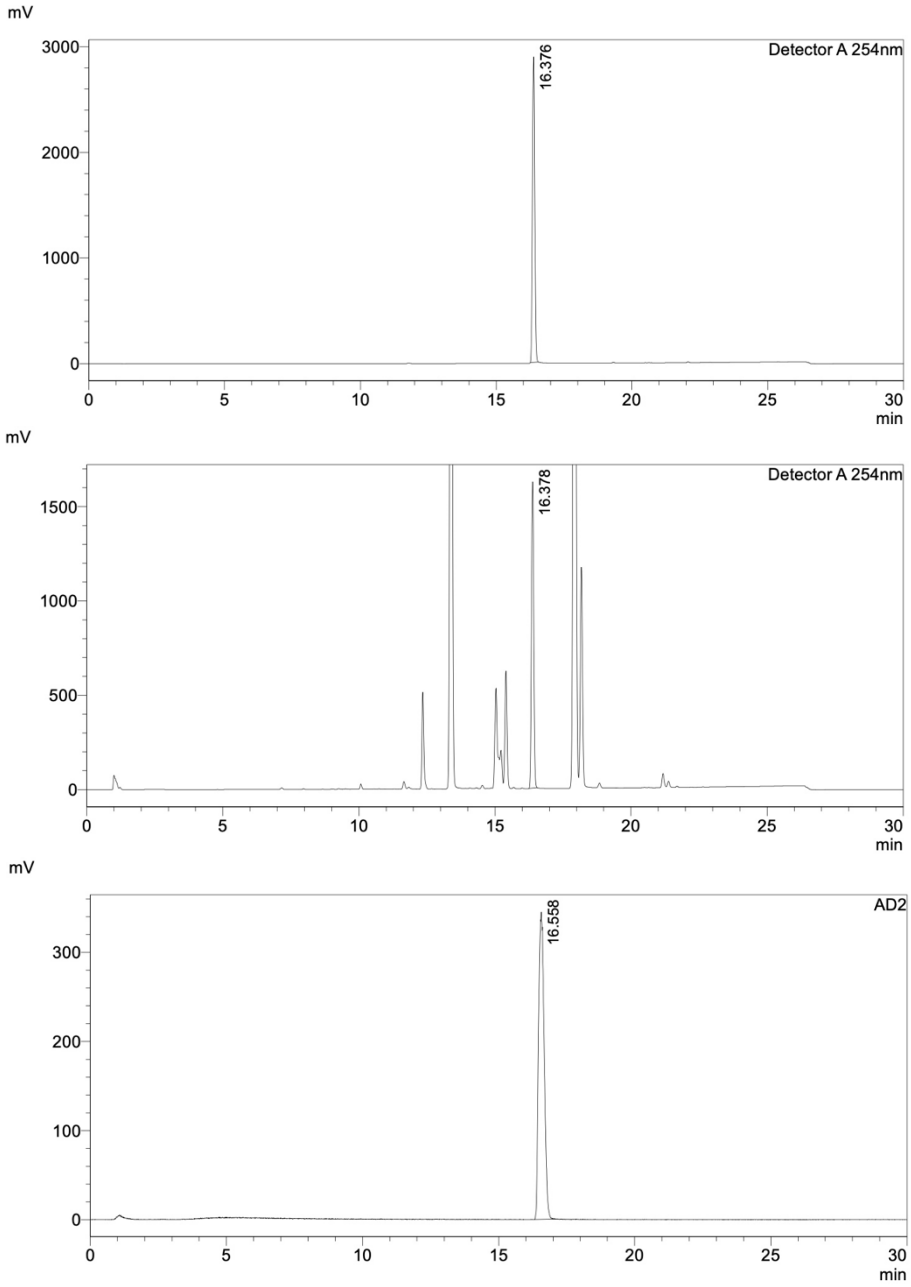
2-(Fluoro-^{18}F)-*N*-(4-iodophenyl)-2-methylpropanamide (**24-^{18}F**)



Synthesised from 2-bromo-*N*-(4-iodophenyl)-2-methylpropanamide **24-Br** (1.8 mg).

Entry	rTLC /%
1	87.53
2	84.61
3	87.07

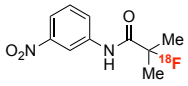
RCC = **86.4 ± 1.3%** (n=3) RCP = **≥99%** HPLC Conditions A:



Upper: UV (254 nm), chromatogram of independently synthesised **24-^{19}F** (16.376 min)
Middle: UV (254 nm), coinject chromatogram of crude reaction mixture showing **24-^{19}F** (16.378 min)
Lower: Gamma chromatogram of crude reaction mixture showing **24-^{18}F** (16.558 min)

SUPPORTING INFORMATION

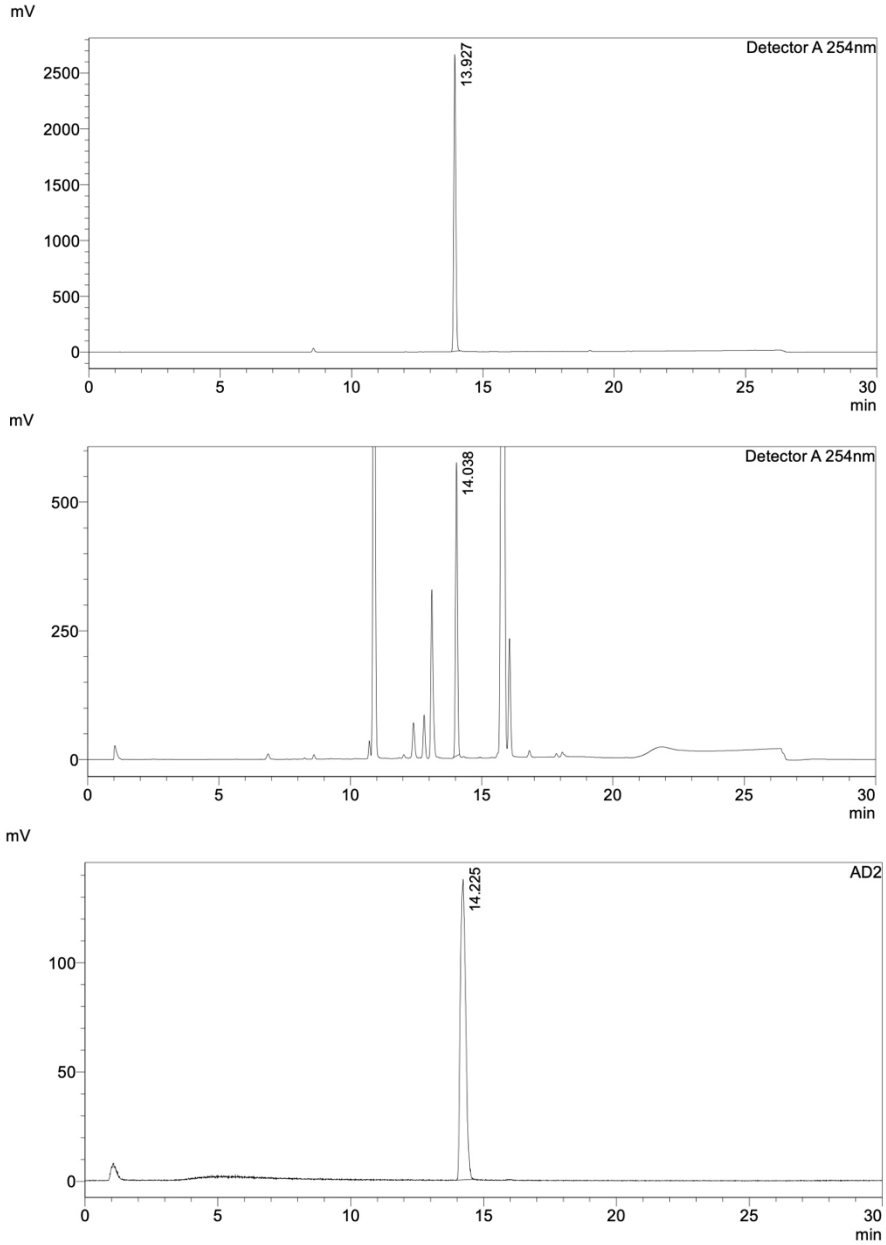
N-(4-Bromo-2,6-difluorophenyl)-2-(fluoro-^{18}*F*)-2-methylpropanamide (**25-^{18}F**)



Synthesised from 2-bromo-2-methyl-*N*-(3-nitrophenyl)propenamide **25-Br** (1.4 mg).

Entry	rTLC /%
1	67.72
2	69.22
3	74.75

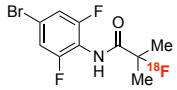
RCC = **70.6 ± 3.0%** (n=3) RCP = **≥99%** HPLC Conditions A:



Upper: UV (254 nm), chromatogram of independently synthesised **25-^{19}F** (13.927 min)
Middle: UV (254 nm), coinject chromatogram of crude reaction mixture showing **25-^{19}F** (14.038 min)
Lower: Gamma chromatogram of crude reaction mixture showing **25-^{18}F** (14.225 min)

SUPPORTING INFORMATION

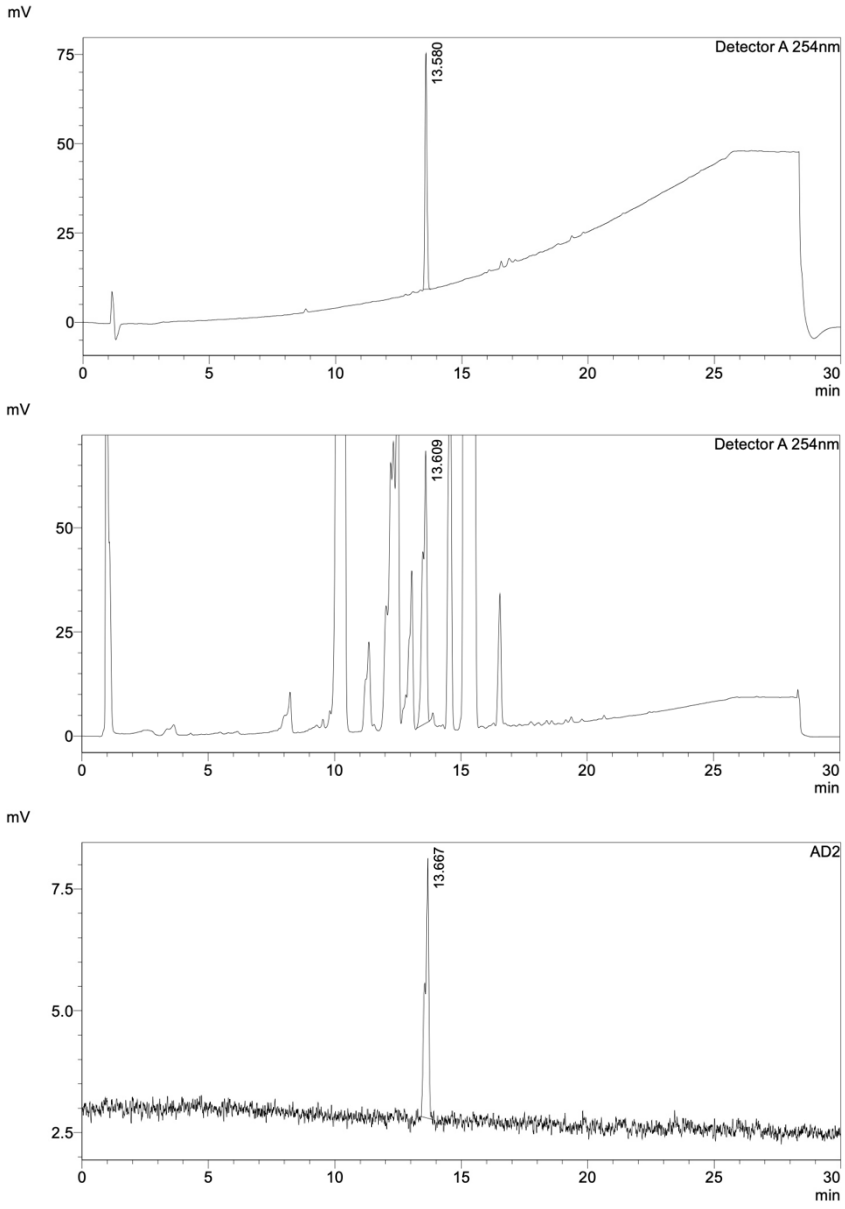
N-(4-Bromo-2,6-difluorophenyl)-2-(fluoro-^{18}*F*)-2-methylpropanamide (**26-^{18}F**)



Synthesised from 2-bromo-*N*-(4-bromo-2,6-difluorophenyl)-2-methylpropanamide **26-Br** (1.8 mg).

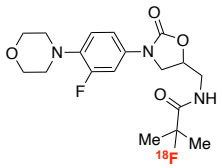
Entry	rTLC /%
1	36.68
2	45.27
3	17.35

RCC = **33.1 ± 11.7%** (n=3) RCP = **≥99%** HPLC Conditions A:



Upper: UV (254 nm), chromatogram of independently synthesised **26-^{19}F** (13.580 min)
Middle: UV (254 nm), coinject chromatogram of crude reaction mixture showing **26-^{19}F** (13.609 min)
Lower: Gamma chromatogram of crude reaction mixture showing **26-^{18}F** (13.667 min)

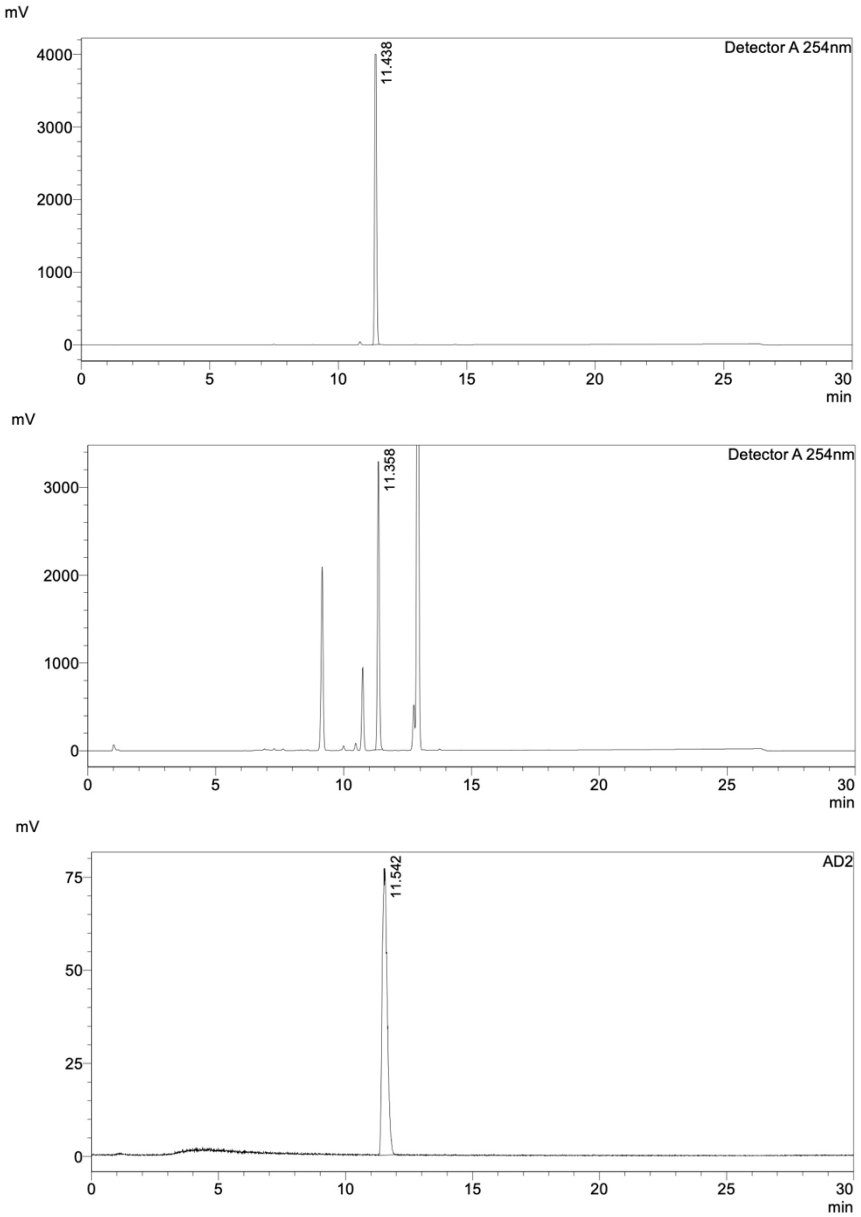
N-((3-(3-Fluoro-4-morpholinophenyl)-2-oxooxazolidin-5-yl)methyl)-2-(fluoro-^{18}*F*)-2-methylpropanamide (**27-^{18}F**)



Synthesised from 2-bromo-*N*-((3-(3-fluoro-4-morpholinophenyl)-2-oxooxazolidin-5-yl)methyl)-2-methylpropanamide **27-Br** (2.2 mg).

Entry	rTLC /%
1	77.78
2	65.08
3	61.85
4	62.90

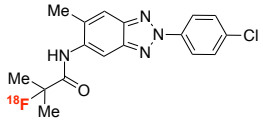
RCC = **66.9 ± 6.4%** (n=4), RCP = **≥99%** HPLC Conditions A:



Upper: UV (254 nm), chromatogram of independently synthesised **27-^{19}F** (11.438 min)
Middle: UV (254 nm), coinject chromatogram of crude reaction mixture showing **27-^{19}F** (11.358 min)
Lower: Gamma chromatogram of crude reaction mixture showing **27-^{18}F** (11.542 min)

SUPPORTING INFORMATION

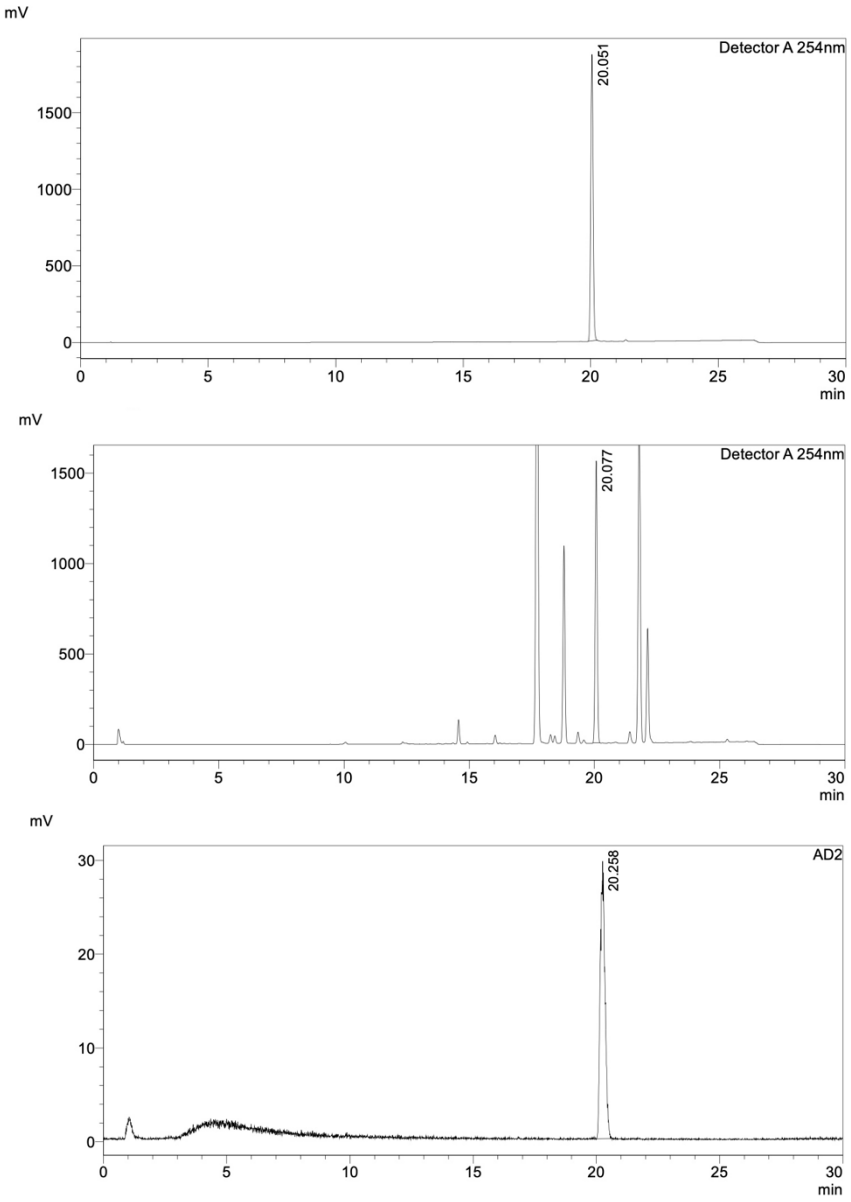
N-(2-(4-Chlorophenyl)-6-methyl-2*H*-benzo[*d*]1,2,3triazol-5-yl)-2-(fluoro-^{18}*F*)-2-methylpropanamide (**28-^{18}F**)



Synthesised from 2-bromo-*N*-(2-(4-chlorophenyl)-6-methyl-2*H*-benzo[*d*]1,2,3triazol-5-yl)-2-methylpropanamide **28-Br** (2.0 mg).

Entry	rTLC /%
1	52.62
2	38.64
3	40.48

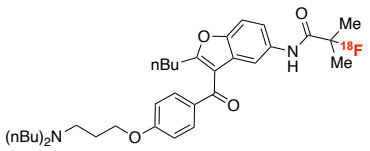
RCC = **43.9 ± 6.2%** (n=3) RCP = **≥99%** HPLC Conditions A:



Upper: UV (254 nm), chromatogram of independently synthesised **28-^{19}F** (20.051 min)
Middle: UV (254 nm), coinject chromatogram of crude reaction mixture showing **28-^{19}F** (20.077 min)
Lower: Gamma chromatogram of crude reaction mixture showing **28-^{18}F** (20.258 min)

SUPPORTING INFORMATION

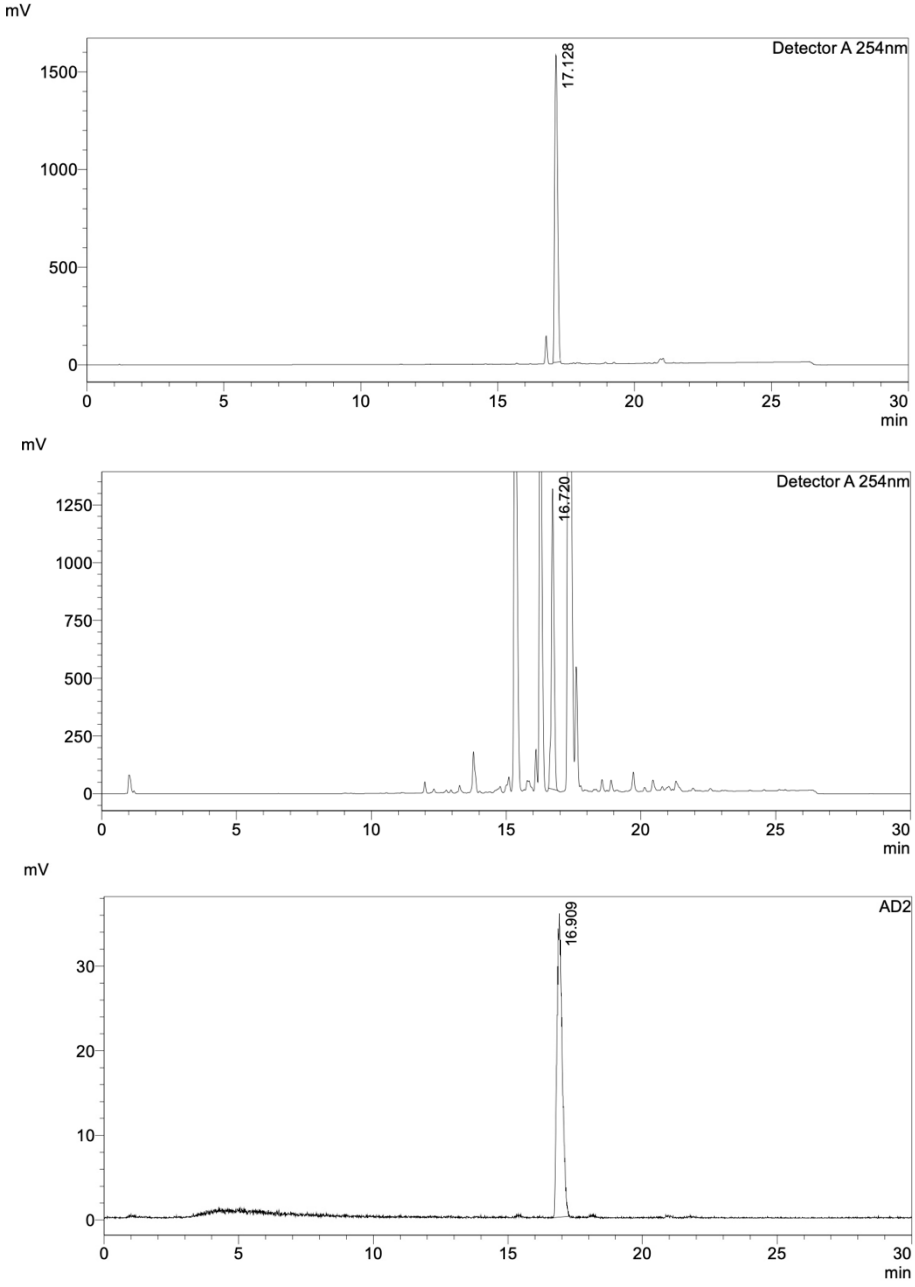
N-(2-Butyl-3-(4-(3-(dibutylamino)propoxy)benzoyl)benzofuran-5-yl)-2-(fluoro-^{18}F)-2-methylpropanamide (**29-^{18}F**)



Synthesised from 2-bromo-*N*-(2-butyl-3-(4-(3-(dibutylamino)propoxy)benzoyl)benzofuran-5-yl)-2-methylpropanamide **29-Br** (3.1 mg).

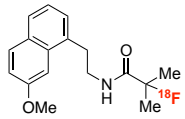
Entry	rTLC /%
1	81.43
2	60.32
3	81.22
4	51.22

RCC = **68.5 ± 13.2%** (n=4), RCP = **≥99%** HPLC Conditions A:



Upper: UV (254 nm), chromatogram of independently synthesised **29-^{19}F** (17.128 min)
Middle: UV (254 nm), coinject chromatogram of crude reaction mixture showing **29-^{19}F** (16.720 min)
Lower: Gamma chromatogram of crude reaction mixture showing **29-^{18}F** (16.909 min)

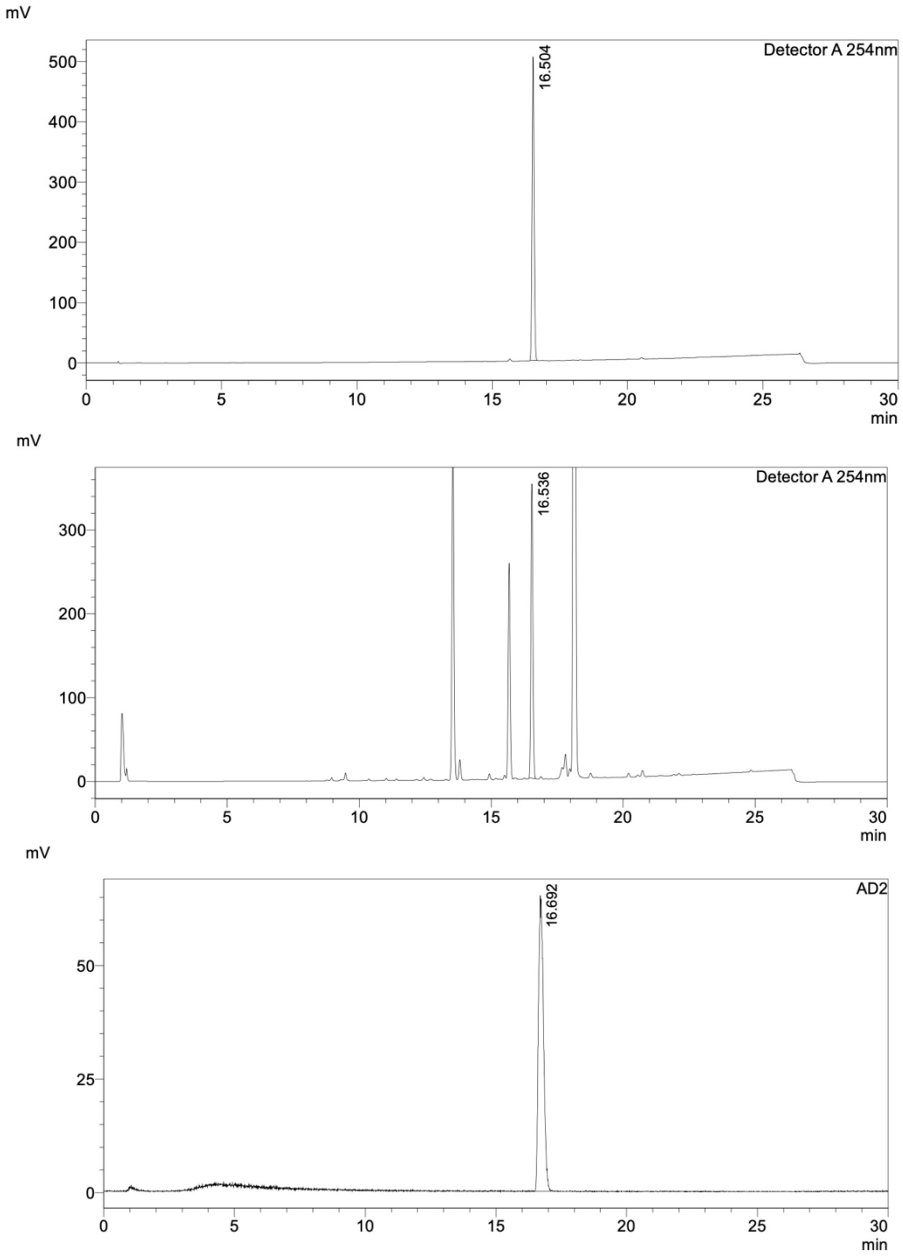
2-(Fluoro-^{18}*F*)-*N*-(2-(7-methoxynaphthalen-1-yl)ethyl)-2-methylpropanamide (**30-^{18}F**)



Synthesised from 2-bromo-*N*-(2-(7-methoxynaphthalen-1-yl)ethyl)-2-methylpropanamide **30-Br** (1.8 mg).

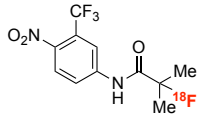
Entry	rTLC /%
1	70.01
2	72.58
3	62.31

RCC = **68.3 ± 4.4%** (n=3) RCP = **≥99%** HPLC Conditions A:



Upper: UV (254 nm), chromatogram of independently synthesised **30-^{19}F** (16.504 min)
Middle: UV (254 nm), coinject chromatogram of crude reaction mixture showing **30-^{19}F** (16.536 min)
Lower: Gamma chromatogram of crude reaction mixture showing **30-^{18}F** (16.692 min)

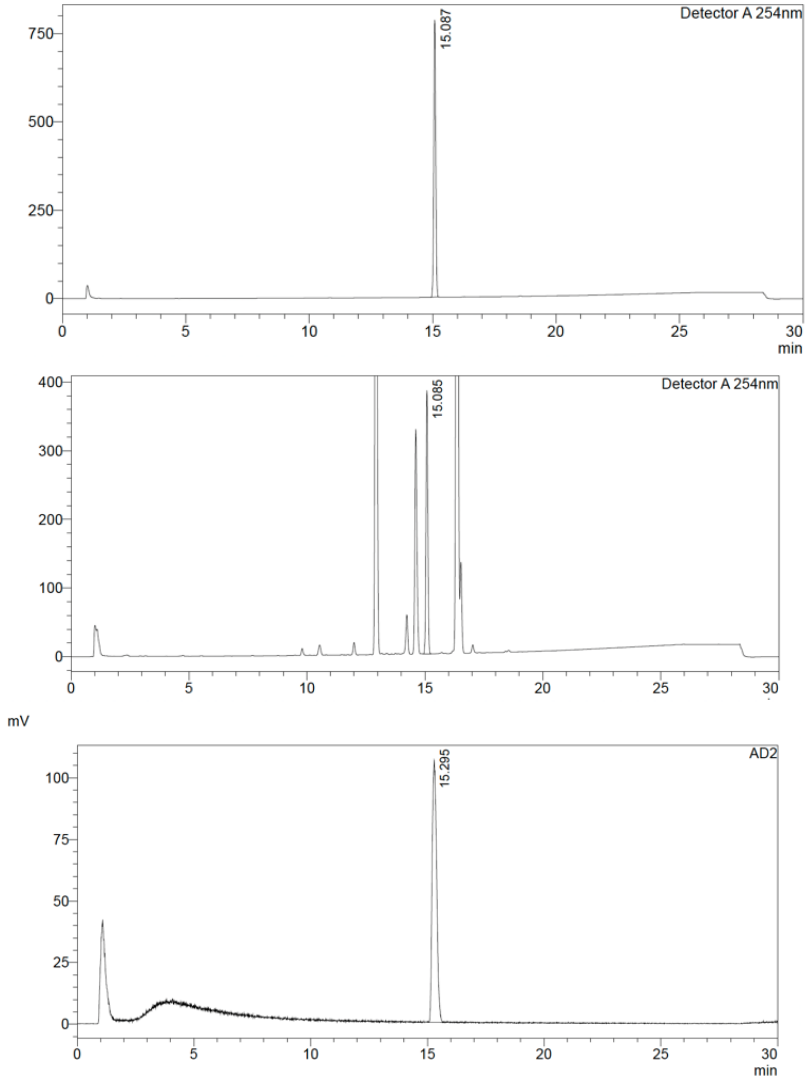
2-(Fluoro-^{18}F)-2-methyl-*N*-(4-nitro-3-(trifluoromethyl)phenyl)propanamide (**31-^{18}F**)



Synthesised from 2-bromo-2-methyl-*N*-(4-nitro-3-(trifluoromethyl)phenyl)propanamide **31-Br** (1.8 mg).

Entry	rTLC /%
1	21.18
2	27.24

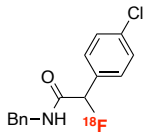
RCC = **24.2 ± 3.0%** (n=2) RCP = **≥99%** HPLC Conditions A



Upper: UV (254 nm), chromatogram of independently synthesised **31-^{19}F** (15.087 min)
Middle: UV (254 nm), coinject chromatogram of crude reaction mixture showing **31-^{19}F** (15.085 min)
Lower: Gamma chromatogram of crude reaction mixture showing **31-^{18}F** (15.295 min)

SUPPORTING INFORMATION

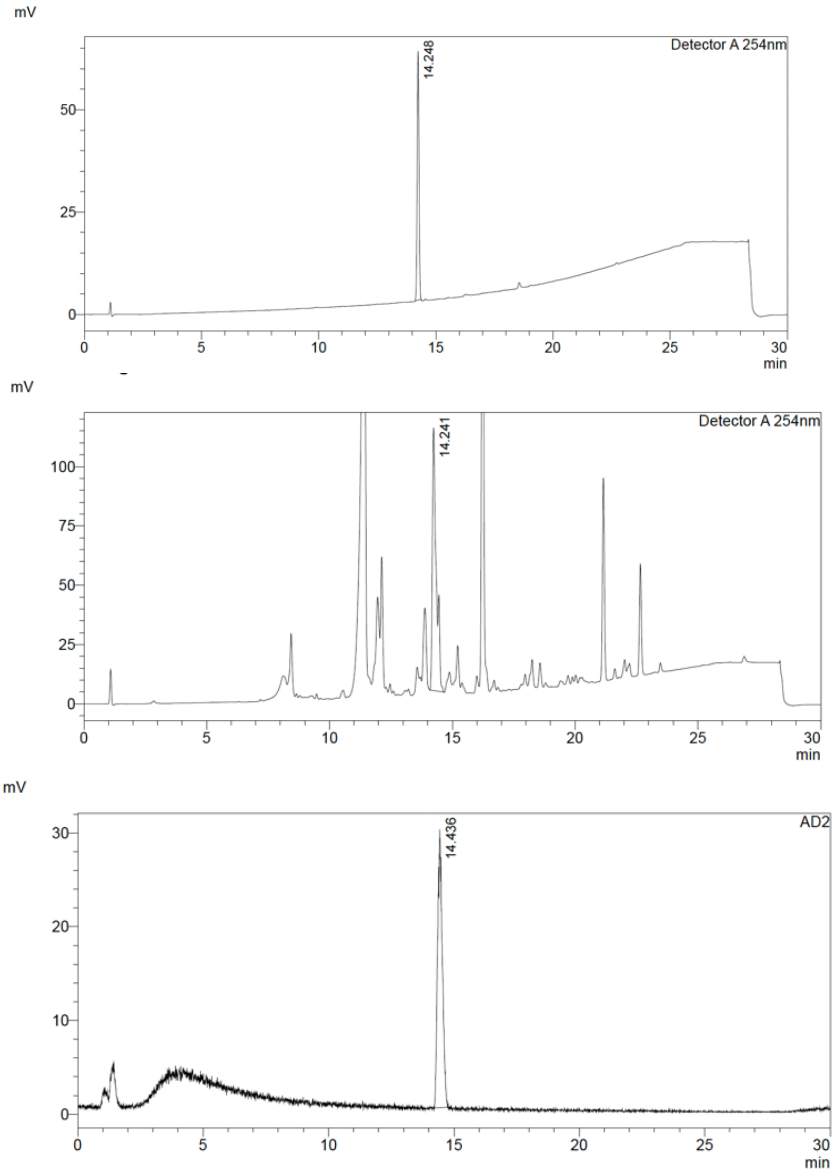
2-(Fluoro-^{18}F)-*N*-(2-(7-methoxynaphthalen-1-yl)ethyl)-2-methylpropanamide (**34-^{18}F**)



Synthesised from *N*-benzyl-2-(4-chlorophenyl)-*N*-((methylsulfonyl)oxy)acetamide **34** (1.8 mg) using MeCN instead of DMSO solvent.

Entry	rTLC /%
1	13.42
2	13.46

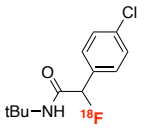
RCC = **13.4 ± 0.0%** (n=2) RCP = **≥99%** HPLC Conditions A



Upper: UV (254 nm), chromatogram of independently synthesised **34-^{19}F** (14.248 min)
Middle: UV (254 nm), coinject chromatogram of crude reaction mixture showing **34-^{19}F** (14.241 min)
Lower: Gamma chromatogram of crude reaction mixture showing **34-^{18}F** (14.436 min)

SUPPORTING INFORMATION

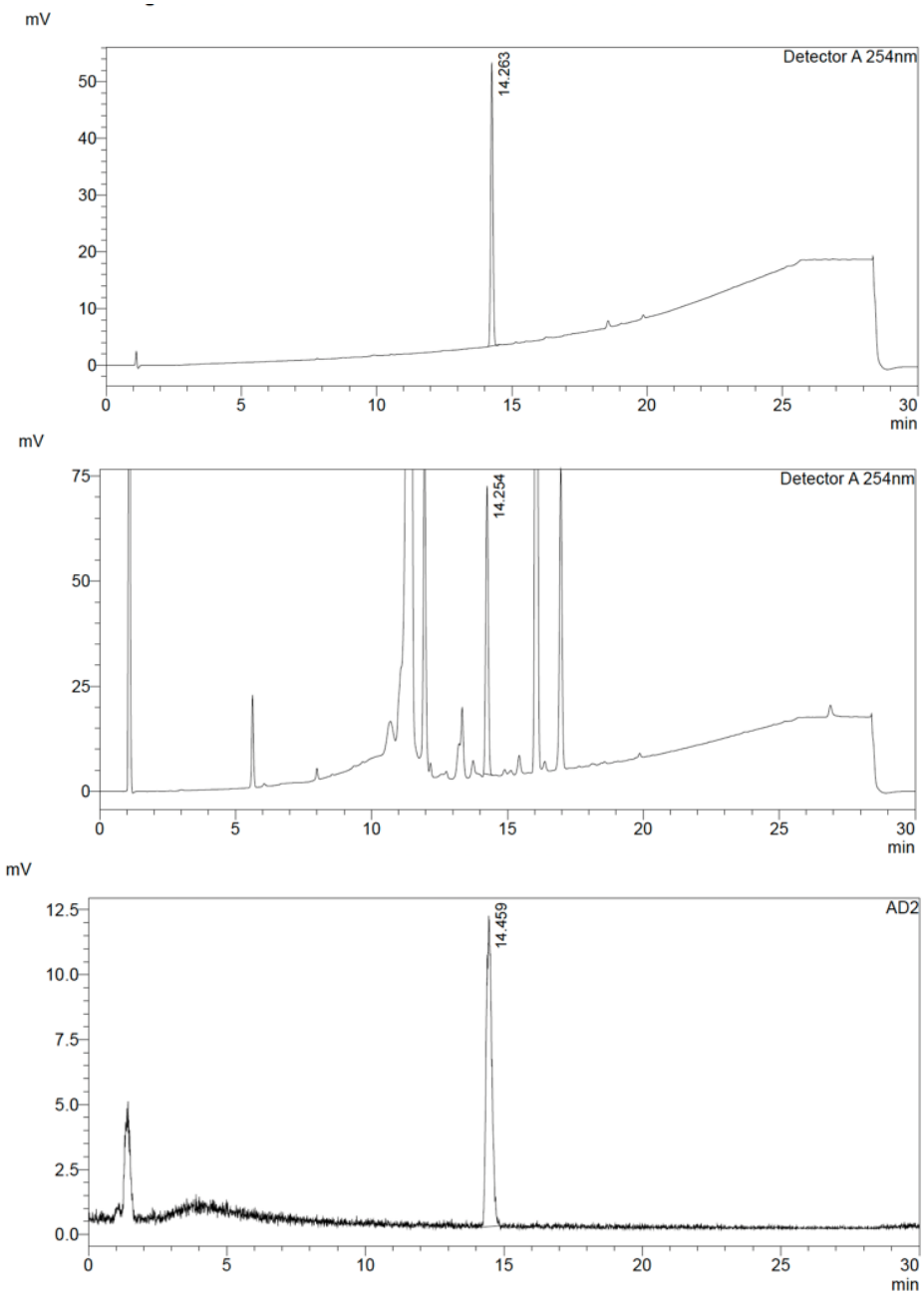
N-(tert-butyl)-2-(4-chlorophenyl)-2-(fluoro-^{18}F)acetamide (**35-^{18}F**)



Synthesised from *N*-(*tert*-butyl)-2-(4-chlorophenyl)-*N*-((methylsulfonyl)oxy)acetamide **35** (1.6 mg) using MeCN instead of DMSO solvent.

Entry	rTLC /%
1	8.55
2	10.98

RCC = **9.8 ± 1.2%** (n=2) RCP = **≥99%** HPLC Conditions A:

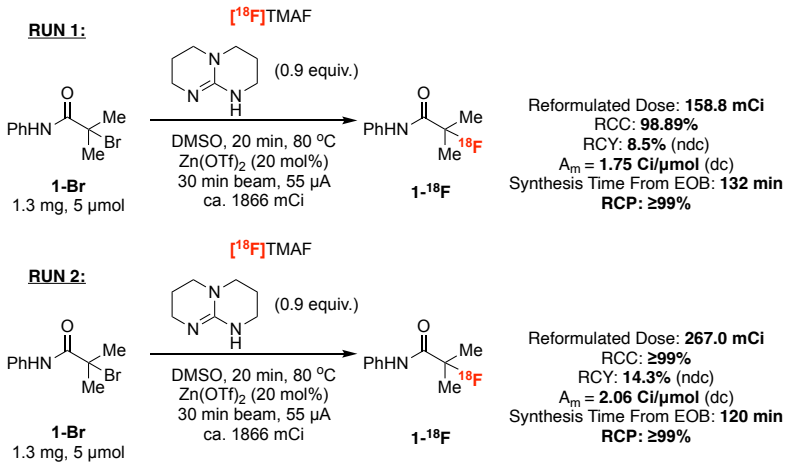


Upper: UV (254 nm), chromatogram of independently synthesised **35-^{19}F** (14.263 min)
Middle: UV (254 nm), coinject chromatogram of crude reaction mixture showing **35-^{19}F** (14.254 min)
Lower: Gamma chromatogram of crude reaction mixture showing **35-^{18}F** (14.459 min)

3.6 General Procedure for Automated Synthesis

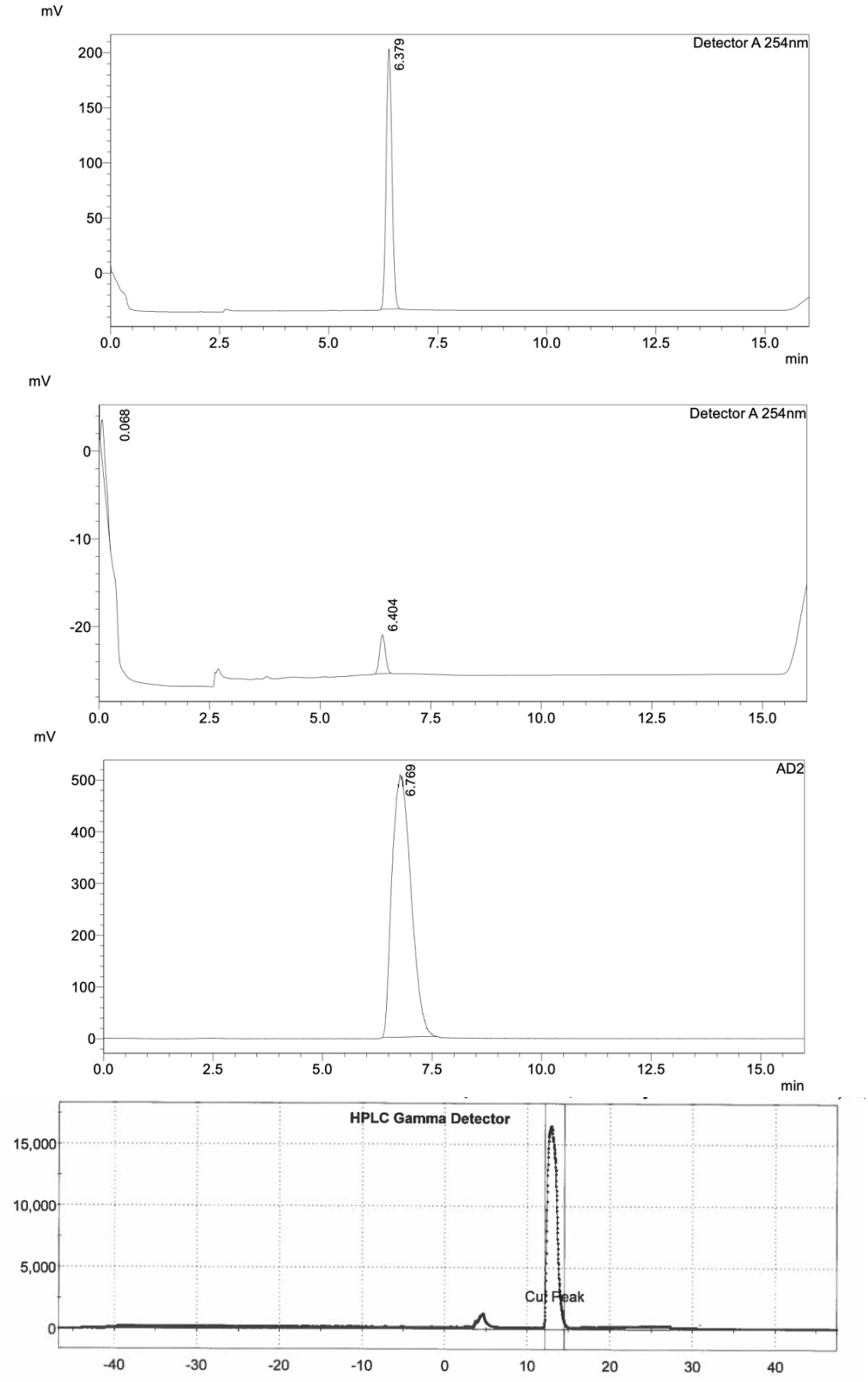
Automated syntheses were conducted using a TRACERlab FX_{FN} automated radiochemistry synthesis module (General Electric, GE) equipped with a glass reactor vial. [^{18}F]Fluoride was produced via the $^{18}O(p,n)^{18}F$ nuclear reaction using a GE PETTrace cyclotron (55 µA beam for 30 min generated ca. 1866 mCi of [^{18}F]fluoride). The [^{18}F]fluoride was transferred to the synthesis module and trapped on a QMA-light Sep-Pak preconditioned with 0.5M aqueous KOTf. The [^{18}F]fluoride was transferred to the synthesis module and trapped on a QMA-light Sep-Pak cartridge. [^{18}F]Fluoride was eluted into the reaction vessel using Me_4NOTf (5.9 mg, 26.5 µmol) in 500 µL H_2O. A solution of K_{222} (1.4 mg, 3.6 µmol) in MeCN (1 mL) was added to the reaction vessel. The solution was evaporated by heating the reaction vessel to 100 °C under vacuum for 5 min. The reaction vessel was further dried under vacuum with a stream of Ar for an additional 8 min. The reactor was cooled to 60 °C before the sequential addition of a solution of TBD (0.63 mg, 4.5 µmol) and $Zn(OTf)_2$ (0.36 mg, 1 µmol) in DMSO (500 µL), followed by a solution of the substrate (5 µmol), in DMSO (500 µL). The reactor was sealed and heated to 80 °C for 20 min before being cooled to 40 °C and diluted with 3.5 mL HPLC buffer solution (EtOH/10 mM NH_4OAc w/ 0.2% AcOH) and passed through a Sep-Pak Alumina N Plus Light (WAT023561) cartridge. This solution was loaded onto a 5 mL injection loop for purification by semi-preparative HPLC. The purified radiolabeled product was collected and diluted in H_2O (corresponding to 5% v/v of organic solvent) and trapped on an Oasis HLB 1 cc 30 mg (WAT094225), Vac cartridge, which was rinsed with H_2O (10 mL). The cartridge was rinsed with EtOH (0.5 mL) and 0.9% saline solution (6.5 mL) into a vial containing 3.5 mL 0.9% saline solution. The reformulated dose was transferred to a 10 mL bolus for further analysis by rTLC and rHPLC. **1-^{18}F** and **27-^{18}F** were purified via semi-preparative HPLC with a Phenomenex Luna 10 µ C18(2), 100 Å, 250 x 10.0 mm, 4 mL min^{-1}, EtOH/Aqueous 10 mM NH_4OAc w/ 0.2% AcOH using an isocratic method (vide infra). Excellent resolution (ca. >3 min separation) was obtained from the respective haloamide precursors for both compounds.

3.6.1 2-(fluoro-^{18}F)-2-methyl-N-phenylpropanamide (**1-^{18}F**)



The automated protocol afforded 212.9 ± 54.1 mCi of reformulated **1-^{18}F** from 2-bromo-2-methyl-*N*-phenylpropanamide **1-Br** (1.2 mg) in **99%** RCC, **11.4 ± 2.9%** non-decay-corrected (ndc) isolated RCY, **1.91 ± 0.16** decay-corrected (dc), A_m, and **≥99%** RCP (n=2).

Data obtained from Run 1 with HPLC Conditions C or D is depicted.

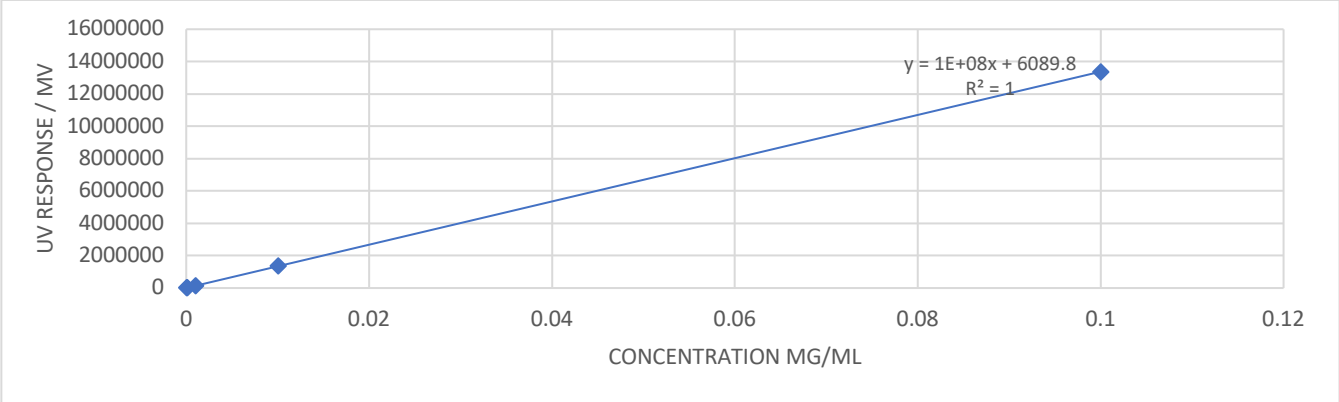


Upper: UV (254 nm), chromatogram of independently synthesised **1-^{19}F** (6.379 min, HPLC Conditions C)
Middle-1: UV (254 nm), coinject chromatogram of reformulated dose showing **1-^{19}F (**6.404 min, HPLC Conditions C)
Middle-2: Gamma chromatogram of reformulated dose showing **1-^{19}F** (6.769 min, HPLC Conditions C)
Lower: Gamma chromatogramfrom semi-preparative rHPLC recorded during automated radiosynthesis of **1-^{18}F** (HPLC Conditions D)

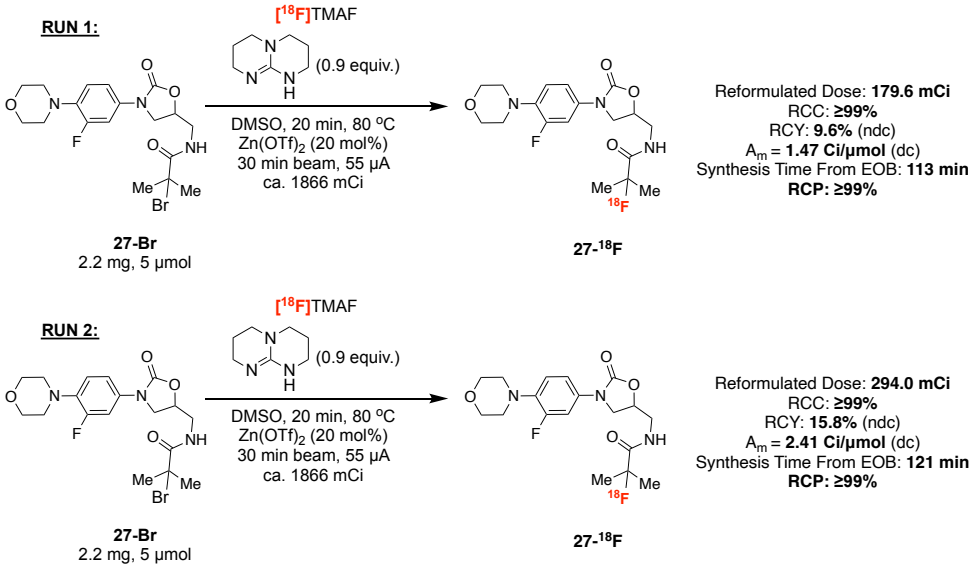
Example Molar Activity Calculation for **1-^{18}F** (Run 1)

Concentration **1-^{19}F** /mg ml^{-1}	UV Response /mV
0.1	13375600
0.01	1362216
0.001	136643
0.0001	11631
0.00001	1287

Reformulated Dose **1-^{18}F** UV Response: 383558 mV

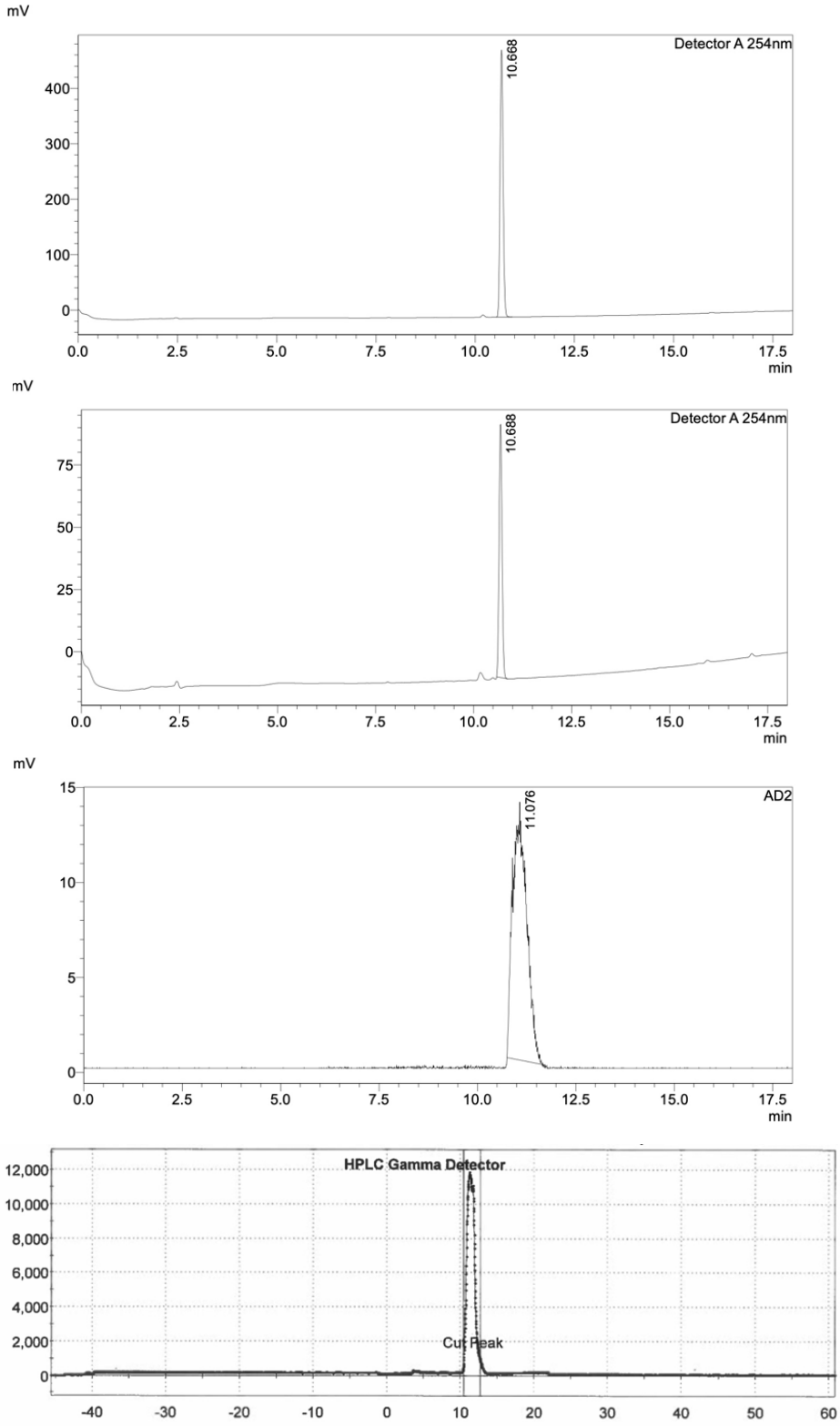


3.6.2 N-((3-(3-fluoro-4-morpholinophenyl)-2-oxooxazolidin-5-yl)methyl)-2-(fluoro-^{18}F)-2-methylpropanamide (**27-^{18}F**)



The automated protocol afforded 236.8 ± 57.2 mCi of reformulated **27-^{18}F** from 2-bromo-*N*-((3-(3-fluoro-4-morpholinophenyl)-2-oxooxazolidin-5-yl)methyl)-2-methylpropanamide **27-Br** (2.2 mg), in **≥99%** RCC, **12.7 ± 3.1** non-decay-corrected (ndc), isolated RCY, **1.94 ± 0.47** decay-corrected (dc), A_m, and **≥99%** RCP (n=2).

Data obtained from Run 1 with HPLC conditions E or F is depicted:

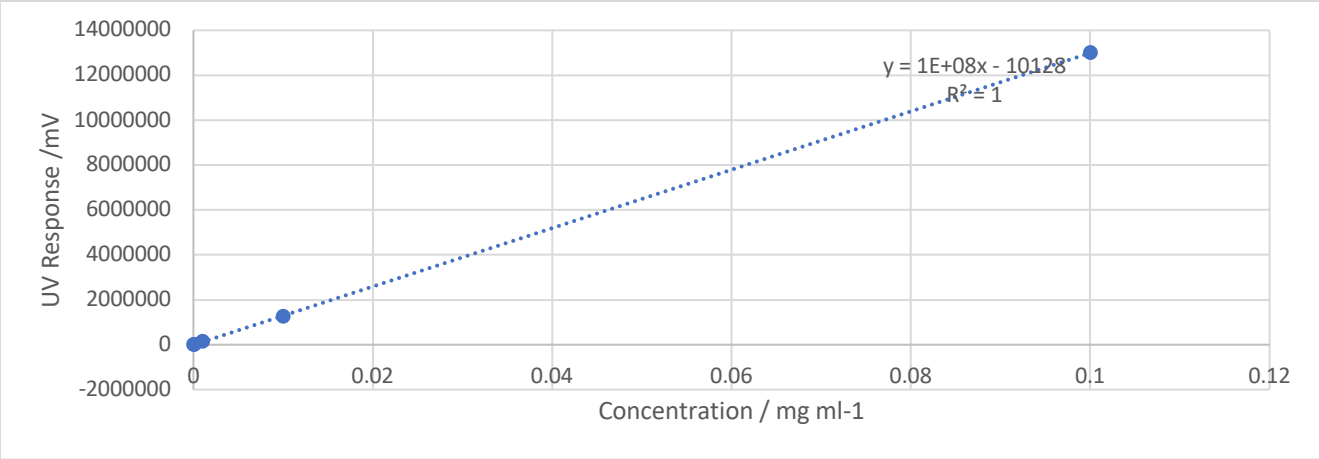


Upper: UV (254 nm), chromatogram of independently synthesised **27-^{19}F** (10. 668 min, HPLC Conditions E)
Middle-1: UV (254 nm), coinject chromatogram of reformulated dose showing **27-^{19}F** (10.688 min, HPLC Conditions E)
Middle-2: Gamma chromatogram of reformulated dose showing **27-^{18}F** (11.076 min, HPLC Conditions E)
Lower: Gamma chromatogram from semi-preparative rHPLC recorded during automated radiosynthesis of **27-^{18}F** (HPLC Conditions F)

Example Molar Activity Calculation for **27-^{18}F** (Run 1)

Concentration **1-^{19}F** /mg ml^{-1}	UV Response /mV
0.1	12994354
0.01	1258701
0.001	134126
0.0001	7756
0.00001	389

Reformulated Dose **27-^{18}F** UV Response: 952357 mV



4. Stability Studies

4.1 1-^{18}F and 27-^{18}F Buffer and Radiolytic Stability Analysis

Aliquots of isolated and purified **1-^{18}F** and **27-^{18}F** obtained from automated radiosynthesis protocols (t=0 min, **≥99%** RCP) for both samples), described in Section 3.6 were each incubated in HPLC buffers (35% or 40% EtOH/10mM NH_4OAc). After 8 h, no radiolytic or buffer degradation was observed (t = 8 h, **≥99%** RCP).

4.2 Plasma Stability Analysis

4.2.1 General Considerations

All animal imaging experiments were conducted under the supervision of the University of Michigan and its Institutional Animal Care and Use Committee (IACUC, accreditation number PRO00010019) according to approved protocols and all applicable federal, state, local and institutional laws and guidelines governing animal research.

4.2.2 Rodent Plasma Metabolite Study

Approximately 1 mL of blood was collected from a female Sprague-Dawley rat into a centrifuge tube preloaded with 10 mg anticoagulant ethylenediaminetetraacetic acid disodium dihydrate. A solution of *N*-((3-(3-fluoro-4-morpholinophenyl)-2-oxooxazolidin-5-yl)methyl)-2-(fluoro-^{18}*F*)-2-methylpropanamide **27-^{18}F** (803 µCi in 0.2 mL 35% EtOH/0.2% AcOH/10 mM Aqueous NH_4OAc), was added to the blood. The solution was agitated with a vortex mixer before maintaining the temperature at 37 °C in a water bath. At each time point, a 0.3 mL aliquot was transferred to a new centrifuge tube and spun at 13000 rpm for ca. 30 s. The plasma was transferred to a new centrifuge tube, and the radioactive contents of the plasma and pellet were measured using a Capintec dose calibrator. Ice cold MeCN (150 µL) was added to the plasma, which was then agitated and centrifuged at 13000 rpm for ca. 30 s. A sample of the resulting supernatant was assayed via analytical HPLC (Conditions E).

Table S1. Plasma Timepoint Stability Study of **27-^{18}F**

Time/ min	Plasma/ µCi	Pellet/ µCi	Plasma Activity %	Pellet Activity %	RCP %
30	84	62	58%	42%	≥99%
60	60	37	62%	38%	≥99%
180	29	17	63%	37%	≥99%

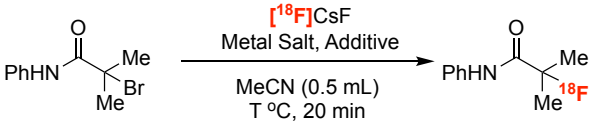
5. Reaction Development

5.1 Radiochemical Corrections

The final, optimised reaction conditions described in the manuscript afford homogenous reaction mixtures and can, therefore, be measured with rTLC without correction. A small number of reactions conducted during reaction development required RCC corrections owing to reproducibility issues. For example, this was necessary when large amounts of insoluble metal reagents/products were used (e.g., AgOTf) since precipitation of fluorine-18 could inflate RCC values (which measures primarily soluble fluorine-18). In a typical procedure, the radioactivity of heterogeneous final reaction mixtures was measured (Capintec dose calibrator) before removing and filtering the supernatant with a 0.22 µm Merck Millex^{TM} GV membrane filter. The remaining precipitate was rinsed with 1 mL MeCN and filtered. The inorganic fluorine-18 content of the resulting homogenous solution was measured via rTLC. Corrected RCCs were recorded as the quotient of the organic fraction in the final filtered solution and the total activity measured from the initial reaction vial. Unless

otherwise stated, all RCCs are corrected or did not require correction. **Note**: *Most reaction conditions, including the optimised reaction conditions described in the manuscript, afford homogenous final reaction mixtures and do not require correction.*

5.2 Screening Data

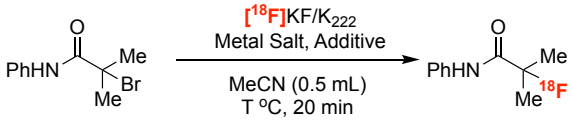


1-Br
12 mg, 50 µmol

1-^{18}F

Table S2. Screening studies for the labelling of **1-Br**. [^{18}F]CsF was prepared from CsOTf (7.5 mg, 26.5 µmol) and Cs_2CO_3 (1.2 mg, 3.6 µmol) (See Section 3.2). Entries 7 and 8 gave significant precipitation and could not be reliably corrected (see section 5.1)

Entry	Additive	Metal Salt	T/ °C	RCC %
1	Phenanthroline (50 µmol, 9 mg)	$CuBr_2$ (50 µmol, 11.2 mg)	80	0
2	Phenanthroline (25 µmol, 4.5 mg)	$CuBr_2$ (25 µmol, 5.6 mg)	80	0
3	Phenanthroline (5 µmol, 0.9 mg)	$CuBr_2$ (5 µmol, 1.1 mg)	80	0
4	Phenanthroline (50 µmol, 9 mg)	$CuBr_2$ (50 µmol, 11.2 mg)	rt	0
5	Phenanthroline (25 µmol, 4.5 mg)	$CuBr_2$ (25 µmol, 5.6 mg)	rt	0
6	Phenanthroline (5 µmol, 0.9 mg)	$CuBr_2$ (5 µmol, 1.1 mg)	rt	0
7		$AgBF_4$ (100 µmol, 19.5 mg)	rt	0
8	-	$AgBF_4$ (100 µmol, 19.5 mg)	80	0
7	-	AgOTf (100 µmol, 25.7 mg)	rt	10 (NOT CORRECTED)
8		AgOTf (100 µmol, 25.7 mg)	80	27 (NOT CORRECTED)
9	Phenanthroline (50 µmol, 9 mg)	-	80	0
10	-	$CuBr_2$ (50 µmol, 11.2 mg)	80	0
11	-	-	rt	0
13	-	-	80	0



1-Br
12 mg, 50 µmol

1-^{18}F

Table S3. Screening studies for the labelling of **1-Br**. [^{18}F]KF was prepared from KOTf (5 mg, 26.5 µmol), K_{222} (15 mg, 40 µmol), and K_2CO_3 (0.5 mg, 3.6 µmol) (See Section 3.2). Entries 4, 5, and 6 gave significant precipitates and were not corrected (see Section 5.1).

Entry	Additive	Metal Salt	T/ °C	RCC %
1	Phenanthroline (50 µmol, 9 mg)	$CuBr_2$ (50 µmol, 11.2 mg)	80	0
2	Phenanthroline (50 µmol, 9 mg)	$CuBr_2$ (50 µmol, 11.2 mg)	rt	0
3	-	AgOTf (100 µmol, 25.7 mg)	rt	<1
4	-	AgOTf (100 µmol, 25.7 mg)	80	21.7 (UNCORRECTED)
5	DIPEA (1 equiv. 9 uL)	AgOTf (100 µmol, 25.7 mg)	rt	49.3 (UNCORRECTED)
6	DIPEA (1 equiv. 9 uL)	AgOTf (100 µmol, 25.7 mg)	80	78 (UNCORRECTED)

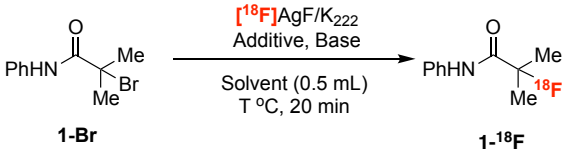


Table S4. Screening studies for the labelling of **1-Br**. [^{18}F]AgF was prepared from AgOTf (6.8 mg, 26.5 µmol) and K_{222} (15 mg, 40 µmol) (See Section 3.2). N-IMTA = N-Isopropyl-N-methyl-tert-butylamine.

Entry	Substrate Quantity	Additive	Base	Solvent	T/ °C	RCC %
1	50 µmol	-	-	MeCN	rt	0
2	50 µmol	-	-	MeCN	80	0
3	25 µmol	$Zn(OTf)_2$ (20 mol%)	TBD (0.9 eq.)	DMSO	80	54.83
4	25 µmol	$Zn(OTf)_2$ (20 mol%)	TBD (0.9 eq.)	DMSO	80	62.68
5	25 µmol	$Fe(II)OTf_2$ (20 mol%, 1.8 mg),	TBD (0.9 eq.)	DMSO	80	0
6	25 µmol	$Fe(II)OTf_2$ (20 mol%, 1.8 mg),	TBD (0.9 eq.)	DMSO	80	0
7	25 µmol	-	TBD (0.9 eq.)	DMSO	80	2.31
8	25 µmol	-	TBD (0.9 eq.)	DMSO	80	2.19
9	25 µmol	$Zn(OTf)_2$ (20 mol%)	-	DMSO	80	0
10	25 µmol	$Zn(OTf)_2$ (20 mol%)		DMSO	80	0
11	25 µmol	-	-	DMSO	80	0
12	25 µmol	-	-	DMSO	80	0
13	25 µmol	$Zn(OTf)_2$ (20 mol%)	N-IMTA (1 equiv. 4.8 uL),	DMSO	80	33.29
14	25 µmol	$Zn(OTf)_2$ (20 mol%)	N-IMTA (1 equiv. 4.8 uL)	DMSO	80	30.72

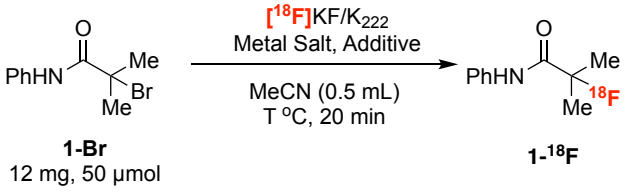


Table S5. Screening studies for the labelling of **1-Br**. [^{18}F]KF was prepared from KOTf (5 mg, 26.5 µmol) and K_{222} (15 mg, 40 µmol) (See Section 3.2). DBU = 1,8-Diazabicyclo[5.4.0]undec-7-ene.

Entry	Additive	Metal Salt	T/ °C	RCC %
1	Hünig's Base (1 equiv. 9 uL)	-	rt	4
2	Hünig's Base (1 equiv. 9 uL)	-	80	0
3	DBU (1 equiv. 7.5 uL)	-	rt	<1
4	DBU (1 equiv. 7.5 uL)	-	80	8
5	KOtBu (1 equiv. 5.6 mg)	-	rt	0
6	KOtBu (1 equiv. 5.6 mg)	-	80	1

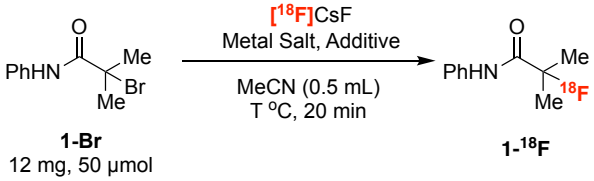


Table S6. Screening studies for the labelling of **1-Br**. [^{18}F]CsF was prepared from CsOTf (7.5 mg, 26.5 µmol) and K_{222} (15 mg, 40 µmol) (See Section 3.2). DBU = 1,8-Diazabicyclo[5.4.0]undec-7-ene.

Entry	Additive	Metal Salt	T/ °C	RCC %
1	Hünig's Base (1 equiv. 9 uL)	-	80	0
2	Hünig's Base (1 equiv. 9 uL)	-	80	0
3	DBU (1 equiv. 7.5 uL)	-	80	<1
4	DBU (1 equiv. 7.5 uL)	-	rt	7.2
5	Hünig's Base (2 equiv. 18 uL)	-	rt	0
6	Hünig's Base (2 equiv. 18 uL)	-	rt	0
7	DBU (2 equiv. 15 uL)	-	rt	<1
8	DBU (2 equiv. 15 uL)	-	80	8
9	Hünig's Base (5 equiv. 18 uL)	-	80	0
10	Hünig's Base (5 equiv. 18 uL)	-	80	0
11	DBU (5 equiv. 45 uL)	-	rt	2.1
12	DBU (5 equiv. 45 uL)	-	80	5.1
13	Et_4NHCO_3 (1 equiv, 9.6 mg)	-		0
14	Et_4NHCO_3 (1 equiv. 9.6 mg)	-		2.3
15	Et_4NHCO_3 (1 equiv, 9.6 mg), + nBuOH (1 equiv, 5 uL)	-		0
16	Et_4NHCO_3 (1 equiv, 9.6 mg), + nBuOH (5 uL)	-		1.2

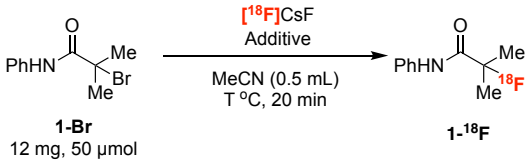
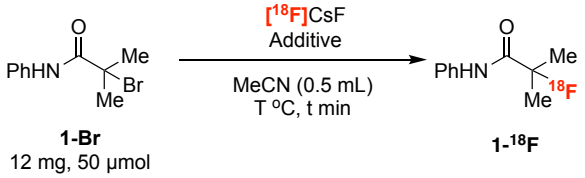


Table S7. Screening studies for the labelling of **1-Br**. [^{18}F]CsF was prepared from CsOTf (7.5 mg, 26.5 µmol), K_{222} (1.4 mg, 3.6 µmol), and 3,4-Dibenzo-21-crown-7 (16 mg), (See Section 3.2). DBU = 1,8-Diazabicyclo[5.4.0]undec-7-ene. TMPH = 2,2,6,6-Tetramethylpiperidine. TBD = 1,5,7-Triazabicyclo[4.4.0]dec-5-ene. MTBD = 7-Methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene. PMP = 1,2,2,6,6-Pentamethylpiperidine. DABCO = 1,4-diazabicyclo[2.2.2]octane). N-IMTA = N-Isopropyl-N-methyl-tert-butylamine.

Entry	Additive	T/ °C	RCC %
1	Hünig's Base (1 equiv. 9 uL)	rt	0
2	Hünig's Base (1 equiv. 9 uL)	80	0
3	Et_3N (1 equiv. 7 uL)	rt	0
4	Et_3N (1 equiv. 7 uL)	80	0
5	Barton's Base (1 equiv. 10 uL)	rt	<1
6	Barton's Base (1 equiv. 10 uL)	80	15
7	TMPH (1 equiv. 8.5 uL)	rt	0

8	TMPH (1 equiv. 8.5 uL)	80	0
9	TBD (1 equiv. 7 mg)	rt	4
10	TBD (1 equiv. 7 mg)	80	22.75
11	MTBD (1 equiv. 7 uL)	rt	2
12	MTBD (1 equiv. 7 uL)	80	9
13	PMP (1 equiv. 9 uL)	rt	0
14	PMP (1 equiv. 9 uL)	80	0
15	2,6-Lutidine (1 equiv. 6 uL)	rt	0
16	2,6-Lutidine (1 equiv. 6 uL)	80	0
17	Proton-sponge® (1 equiv. 11 mg)	rt	0
18	Proton Sponge® (1 equiv. 11 mg)	80	0
29	DABCO (1 equiv. 5.6 mg)	rt	0
30	DABCO (1 equiv. 5.6 mg)	80	0
34	N-IMTA (1 equiv. 8.4 uL),	rt	0
35	N-IMTA (1 equiv. 8.4 uL)	80	0

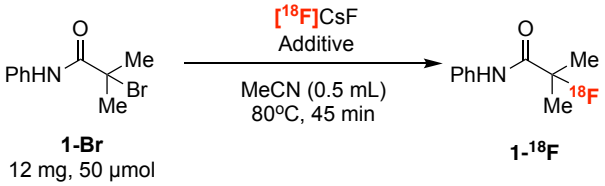


1-Br
12 mg, 50 µmol

1-^{18}F

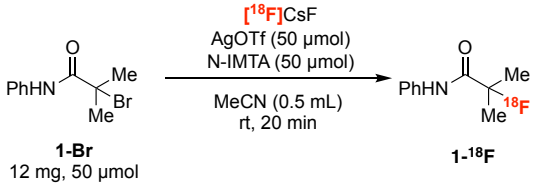
Table S8. Screening studies for the labelling of **1-Br**. [^{18}F]CsF was prepared from Cs_2CO_3 (8.6 mg, 26.5 µmol), and 3,4-Dibenzo-21-crown-7 (16 mg), (See Section 3.2), TBD = 1,5,7-Triazabicyclo[4.4.0]dec-5-ene.

Entry	Additive	Time/ min	T/ °C	RCC %
1	TBD (1 equiv. 7 mg),	1	80	8.7
2	TBD (1 equiv. 7 mg),	5	80	18.5
3	TBD (1 equiv. 7 mg),	10	80	13.4
4	TBD (1 equiv. 7 mg),	20	80	15.3
5	TBD (1 equiv. 7 mg),	30	80	26.7
6	TBD (1 equiv. 7 mg),	45	80	39.8
7	TBD (1 equiv. 7 mg),	60	80	32.8
8	TBD (1 equiv. 7 mg),	1	110	15
9	TBD (1 equiv. 7 mg),	5	110	26
10	TBD (1 equiv. 7 mg),	10	110	24
11	TBD (1 equiv. 7 mg),	20	110	34.6
12	TBD (1 equiv. 7 mg),	30	110	38.4
13	TBD (1 equiv. 7 mg),	45	110	41
14	TBD (1 equiv. 7 mg),	60	110	33



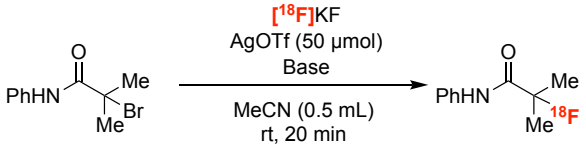
S8. Screening studies for the labelling of **1-Br**. [^{18}F]CsF was prepared from CsOTf (7.5 mg, 26.5 µmol) and K_{222} (15 mg) (See Section 3.2). TBD = 1,5,7-Triazabicyclo[4.4.0]dec-5-ene. Verkade-iPr = 2,8,9-Triisopropyl-2,5,8,9-tetraaza-1-phosphabicyclo[3,3,3]undecane. Phosphazene base P1-t-Oct = tert-Octylimino-tris(dimethylamino)phosphorane. Phosphazene base P1-H = Imino-tris(dimethylamino)phosphorane. Phosphazene base P2-Et = 1-Ethyl-2,2,4,4,4-pentakis(dimethylamino)-2λ^5,4λ^5-catenadi(phosphazene). TMG = *N*,*N*,*N*',*N*'-Tetramethylguanidine. BTMGN = 1,8-Bis(tetramethylguanidino)naphthalene. MTBD = 7-Methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene.

Entry	Additive	RCC %
1	TBD (1 equiv. 7 mg)	17.9
2	TBD (1 equiv. 7 mg) PRE-STIR 5 min	18.5
3	TBD (1 equiv. 7 mg) + 2 equiv. H_2O (1.8 uL)	22.5
4	Verkade-iPr (1 equiv. 15 mg)	0
5	Phosphazene base P1-t-Oct (1 equiv. 14.5 mg)	2.4
6	Phosphazene base P1-H (1 equiv. 9 mg)	15.9
7	Phosphazene base P2-Et (1 equiv. 17 mg)	1.2
8	Barton's Base (1 equiv. 6 uL)	3.4
9	TMG (1 equiv. 10 uL)	0
10	DMAP (1 equiv. 6 mg)	0
11	BTMGN (1 equiv. 17.7 mg)	1.58
13	MTBD (1 equiv. 7 uL)	3
14	Hünig's Base (1 equiv. 9 uL)	0
15	*N*-Isopropyl-*N*-methyl-tert-butylamine (1 equiv. 8.4 uL)	0
16	Tridodecylamine (1 equiv, 32 uL)	0



S9. Screening studies for the labelling of **1-Br**. [^{18}F]CsF was prepared from CsOTf (7.5 mg, 26.5 µmol), K_{222} (1.4 mg, 3.6 µmol), and 3,4-Dibenzo-21-crown-7 (16 mg), (See Section 3.2). N-IMTA = N-Isopropyl-N-methyl-tert-butylamine.

Entry	Change from Conditions	RCC %
1	No N-IMTA or Ag	0
2	No N-IMTA, 80 °C	0
3	No Base	0
4	No Base, 80 °C	0
5	**None** (Order of Addition is: (a), Fluoride (b), N-IMTA (c), Bromide)	38
6	Order of Addition: (a), Bromide (b), Fluoride (c), N-IMTA	47
7	Order of Addition: (a), Fluoride (b), N-IMTA (c), Bromide + 10 equiv. H_2O	27

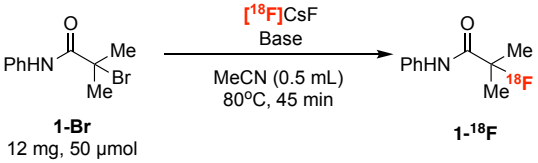


1-Br
12 mg, 50 μmol

1-^{18}F

S10. Screening studies for the labelling of **1-Br**. [^{18}F]KF was prepared from KOTf (5 mg, 26.5 μmol) and 15 mg Kryptofix (See Section 3.2). TBD = 1,5,7-Triazabicyclo[4.4.0]dec-5-ene. Verkade-iPr = 2,8,9-Triisopropyl-2,5,8,9-tetraaza-1-phosphabicyclo[3,3,3]undecane. Phosphazene base P1-t-Oct = tert-Octylimino-tris(dimethylamino)phosphorane. Phosphazene base P1-H = Imino-tris(dimethylamino)phosphorane. Phosphazene base P2-Et = 1-Ethyl-2,2,4,4,4-pentakis(dimethylamino)-2λ^5,4λ^5-catenadi(phosphazene). TMG = *N*,*N*,*N'*,*N'*-Tetramethylguanidine. BTMGN = 1,8-Bis(tetramethylguanidino)naphthalene. MTBD = 7-Methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene. TMPH = 2,2,6,6-Tetramethylpiperidine. MTBD = 7-Methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene. PMP = 1,2,2,6,6-Pentamethylpiperidine. DABCO = 1,4-diazabicyclo[2.2.2]octane). N-IMTA = N-Isopropyl-N-methyl-tert-butylamine. HMDS = Hexamethyldisilazane.

Entry	Base	RCC %
1	TBD (1 equiv. 7 mg)	2.99
2	Et_3N (1 equiv. 7 uL)	4.67[3]
3	2,6-Lutidine (1 equiv. 6 uL)	<1%
4	Verkade-iPr (1 equiv. 15 mg)	0
5	Phosphazene base P1-t-Oct (1 equiv. 16 uL mg)	1.88
6	Phosphazene base P1-H (1 equiv. 9 uL)	1.12
7	Phosphazene base P2-Et (1 equiv. 17 uL)	9.42
8	Barton's Base (1 equiv. 6 uL)	2.36
9	TMG (1 equiv. 10 uL)	2.78
10	DMAP (1 equiv. 6 mg)	1.57
11	BTMGN (1 equiv. 17.7 mg)	2.06
12	Phosphazene base P1-t-Bu-tris(tetramethylene), (1 equiv., 15 uL)	2.43
13	MTBD (1 equiv. 7 uL)	3.44
14	Hünig's Base (1 equiv. 9 uL)	8.74
15	N-Isopropyl-N-methyl-tert-butylamine (1 equiv. 8.4 uL)	15.74
16	Tridodecylamine (1 equiv, 32 uL)	3.65
17	DABCO (1 equiv. 5.6 mg)	1.02
18	Proton Sponge (1 equiv. 11 mg)	<1
19	PMP (1 equiv. 9 uL)	13.1
20	TMPH (1 equiv. 8.5 uL)	8.47
21	HMDS (1 equiv. 10 uL)	1.93
22	None (Only AgOTf)	0



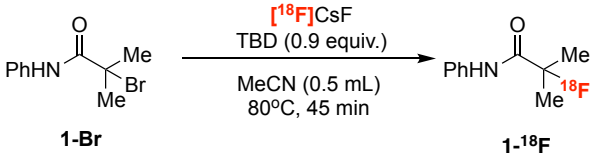
1-Br
12 mg, 50 μmol

1-^{18}F

S11. Screening studies for the labelling of **1-Br**. [^{18}F]CsF was prepared from CsOTf (7.5 mg, 26.5 μmol), K_{222} (1.4 mg, 3.6 μmol), and 3,4-Dibenzo-21-crown-7 (16 mg), (See Section 3.2). TBD = 1,5,7-Triazabicyclo[4.4.0]dec-5-ene.

Entry	Base	RCC %

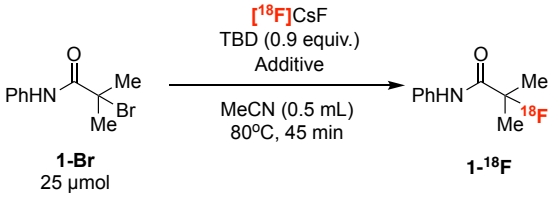
1	TBD (1 equiv. 7 mg),	45
2	TBD (1 equiv. 7 mg), + 2 equiv. H_2O (1.8 uL)	33
3	TBD (1 equiv. 7 mg), + 5 equiv. H_2O (4.5 uL)	29
4	TBD (1 equiv. 7 mg), + 10 equiv. H_2O (9 uL)	18
5	TBD (5 mol% 0.35 mg),	14
6	TBD (10 mol% 0.7 mg),	27
7	TBD (20 mol% 1.4 mg),	35
8	TBD (0.5 equiv 3.5 mg),	25
9	TBD (0.75 equiv 5.3 mg),	32
10	TBD (0.9 equiv 6.3 mg),	44
11	TBD (1.1 equiv. 7.7 mg),	29
12	TBD (1.5 equiv. 10.5 mg),	20
13	TBD (2 equiv. 14 mg),	11
14	TBD (5 equiv. 35 mg),	4



S11. Screening studies for the labelling of **1-Br**. [^{18}F]CsF was prepared from CsOTf (7.5 mg, 26.5 μmol), K_{222} (1.4 mg, 3.6 μmol), and 3,4-Dibenzo-21-crown-7 (16 mg), (See Section 3.2). TBD = 1,5,7-Triazabicyclo[4.4.0]dec-5-ene.

Entry	Substrate Quantity	RCC %
1	50 μmol	58.34
2	100 μmol	61.45
3	40 μmol	34.85
4	30 μmol	59.45
5	20 μmol	65.95
6	15 μmol	39.04
7	10 μmol	33.78
8	5 μmol	32.22
9	1 μmol	12.71
10	50 μmol	51.00
11	100 μmol	43.24
12	40 μmol	50.32
13	30 μmol	44.97
14	20 μmol	55.43
15	15 μmol	26.21
16	10 μmol	38.54
17	5 μmol	19.36

18	1 µmol	26.80

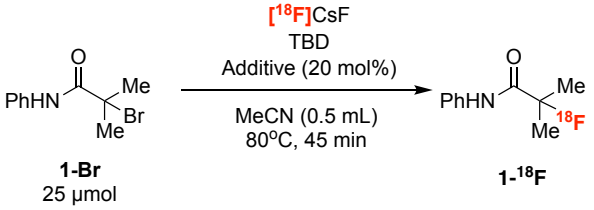


S11. Screening studies for the labelling of **1-Br**. [^{18}F]CsF was prepared from CsOTf (7.5 mg, 26.5 µmol), K_{222} (1.4 mg, 3.6 µmol), and 3,4-Dibenzo-21-crown-7 (16 mg), (See Section 3.2). TBD = 1,5,7-Triazabicyclo[4.4.0]dec-5-ene. RCC values in this table are uncorrected and therefore are likely inflated since many reactions gave highly heterogeneous solutions. [1] Trace product observed via rHPLC, $(Et_4N)_2SO_2$ is highly insoluble.

Entry	Additive	RCC % UNCORRECTED
1	$Fe(acac)_3$ (20 mol%, 1.8 mg)	3.69
2	$Cu(MeCN)_4OTf$ (20 mol%, 1.9 mg)	28.29
3	$Cu(OTf)_2$ (20 mol%, 1.8 mg)	46.87
4	$Ti(Cp)_2(OTf)_2$ (20 mol%, 2.4 mg)	Trace
5	LiOTf (20 mol%, 0.8 mg)	0
6	KI (20 mol%, 0.9 mg)	1.96
7	None	15.74
8	Me_4NOTf (1 equiv. 5.6 mg)	17.75
9	Et_4NOTf (1 equiv. 7 mg)	5.3
10	Bu_4NOTf (1 equiv. 9.8 mg),	12.4
11	$Fe(acac)_3$ (20 mol%, 1.8 mg)	2.74
12	$Cu(MeCN)_4OTf$ (20 mol%, 1.9 mg)	27.79
13	$Cu(OTf)_2$ (20 mol%, 1.8 mg)	41.65
14	$Ti(Cp)_2(OTf)_2$ (20 mol%, 2.4 mg)	Trace
15	LiOTf (20 mol%, 0.8 mg)	0
16	KI (20 mol%, 0.9 mg)	2.93[1]
17	None	7.49
18	Me_4NOTf (1 equiv. 5.6 mg)	13.31
19	Et_4NOTf (1 equiv. 7 mg)	6.17
20	Bu_4NOTf (1 equiv. 9.8 mg),	15.72
21	Bu_4NI (20 mol%, 1.9 mg)	11.37
22	Bu_4NI (20 mol%, 1.9 mg)	13.12
23	Me_4NI (20 mol%, 1 mg)	16.4
24	Me_4NI (20 mol%, 1 mg)	16.97
25	Ph_4PI (20 mol%, 2.3 mg)	13.09

26	Ph_4PI (20 mol%, 2.3 mg)	17.08
27	$Fe(acac)_3$ (20 mol%, 1.8 mg)	3.69
28	$Cu(MeCN)_4OTf$ (20 mol%, 1.9 mg)	28.29
29	$Cu(OTf)_2$ (20 mol%, 1.8 mg)	46.87
30	$Ti(Cp)_2(OTf)_2$ (20 mol%, 2.4 mg)	Trace
31	LiOTf (20 mol%, 0.8 mg)	0
32	KI (20 mol%, 0.9 mg)	1.96
33	None	15.74
34	Me_4NOTf (1 equiv. 5.6 mg)	17.75
35	Et_4NOTf (1 equiv. 7 mg)	5.3
36	Bu_4NOTf (1 equiv. 9.8 mg),	12.4
37	$Fe(acac)_3$ (20 mol%, 1.8 mg)	2.74
38	$Cu(MeCN)_4OTf$ (20 mol%, 1.9 mg)	27.79
39	$Cu(OTf)_2$ (20 mol%, 1.8 mg)	41.65
40	$Ti(Cp)_2(OTf)_2$ (20 mol%, 2.4 mg)	Trace
41	LiOTf (20 mol%, 0.8 mg)	0
42	KI (20 mol%, 0.9 mg)	2.93
43	None	7.49
44	Me_4NOTf (1 equiv. 5.6 mg)	13.31
45	Et_4NOTf (1 equiv. 7 mg)	6.17
46	Bu_4NOTf (1 equiv. 9.8 mg),	15.72
47	Bu_4NI (20 mol%, 1.9 mg)	11.37
48	Bu_4NI (20 mol%, 1.9 mg)	13.12
49	Me_4NI (20 mol%, 1 mg)	16.4
50	Me_4NI (20 mol%, 1 mg)	16.97
51	Ph_4PI (20 mol%, 2.3 mg)	13.09
52	Ph_4PI (20 mol%, 2.3 mg)	17.08
53	$(Et_4N)_2SO_2$	52.79[1]
54	$(Et_4N)_2SO_2$	75.60[1]
56	$Fe(OTs)_3$ (20 mol%)	2.25
57	$Fe(OTf)_3$ (20 mol%, 2.5 mg)	1.78
58	$Fe(OTf)_3$ (20 mol%, 2.5 mg)	2.37
59	$Sc(OTf)_3$ (20 mol%, 2.5 mg)	4.16
60	$Sc(OTf)_3$ (20 mol%, 2.5 mg)	2.10
61	$Ga(OTf)_3$ (20 mol%, 2.6 mg)	4.88
62	$Ga(OTf)_3$ (20 mol%, 2.6 mg)	0.94
63	$Mg(OTf)_2$ (20 mol%, 1.6 mg)	Trace
64	$Mg(OTf)_2$ (20 mol%, 1.6 mg)	0

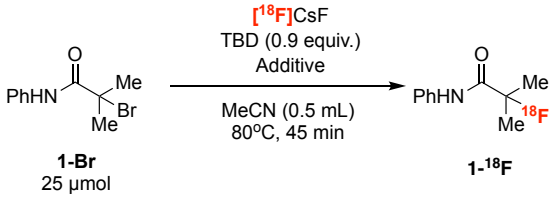
65	$Al(OTf)_3$ (20 mol%, 2.4 mg)	0
66	$Al(OTf)_3$ (20 mol%, 2.4 mg)	0



S12. Screening studies for the labelling of **1-Br**. [^{18}F]CsF was prepared from CsOTf (7.5 mg, 26.5 µmol), K_{222} (1.4 mg, 3.6 µmol), and 3,4-Dibenzo-21-crown-7 (16 mg), (See Section 3.2). TBD = 1,5,7-Triazabicyclo[4.4.0]dec-5-ene.

Entry	Additive	Substrate Quantity/ µmol	TBD Quantity/ µmol	RCC %
1	None	50 (12.2 mg)	45 (6.3 mg)	20.7
2	$Cu(OTf)_2$ (20 mol%, 3.6 mg)	50 (12.2 mg)	45 (6.3 mg)	40.76
3	None	40 (9.6 mg)	36 (5.0 mg)	19.45
4	$Cu(OTf)_2$ (20 mol%, 2.9 mg)	40 (9.6 mg)	36 (5.0 mg)	37.3
5	None	30 (7.3 mg)	27 (3.8mg)	16.71
6	$Cu(OTf)_2$ (20 mol%, 2.2 mg)	30 (7.3 mg)	27 (3.8mg)	34.18
7	None	25 (6.1 mg)	22.5 (3.2 mg)	24.01
8	$Cu(OTf)_2$ (20 mol%, 1.8 mg)	25 (6.1 mg)	22.5 (3.2 mg)	20.88
9	None	50 (12.2 mg)	45 (6.3 mg)	36.26
10	$Cu(OTf)_2$ (20 mol%, 3.6 mg)	50 (12.2 mg)	45 (6.3 mg)	23.07
11	None	40 (9.6 mg)	36 (5.0 mg)	30.63
12	$Cu(OTf)_2$ (20 mol%, 2.9 mg)	40 (9.6 mg)	36 (5.0 mg)	28.69
13	None	30 (7.3 mg)	27 (3.8mg)	18.28
14	$Cu(OTf)_2$ (20 mol%, 2.2 mg)	30 (7.3 mg)	27 (3.8mg)	18.53
15	None	25 (6.1 mg)	22.5 (3.2 mg)	22.26
16	$Cu(OTf)_2$ (20 mol%, 1.8 mg)	25 (6.1 mg)	22.5 (3.2 mg)	35.81
17	None	25 (6.1 mg)	25 (3.5 mg)	19.5
18	$Cu(OTf)_2$ (20 mol%, 1.8 mg)	25 (6.1 mg)	25 (3.5 mg)	21.48
19	None	25 (6.1 mg)	25 (3.5 mg)	32.26
20	$Cu(OTf)_2$ (20 mol%, 1.8 mg)	25 (6.1 mg)	25 (3.5 mg)	29.18
21	None	50 (12.2 mg)	50 (7 mg)	31.96
22	$Cu(OTf)_2$ (20 mol%, 3.6 mg)	50 (12.2 mg)	50 (7 mg)	28.40
23	None	50 (12.2 mg)	50 (7 mg)	37.3
24	$Cu(OTf)_2$ (20 mol%, 3.6 mg)	50 (12.2 mg)	50 (7 mg)	37.55

25	None	25 (6.1 mg)	22.5 (3.2 mg)	31.41
26	None	25 (6.1 mg)	22.5 (3.2 mg)	26.19
27	None	25 (6.1 mg)	22.5 (3.2 mg)	22.9
28	$Cu(OTf)_2$ (20 mol%, 1.8 mg)	25 (6.1 mg)	22.5 (3.2 mg)	41.29
29	None	25 (6.1 mg)	22.5 (3.2 mg)	34.06
30	$Cu(OTf)_2$ (20 mol%, 1.8 mg)	25 (6.1 mg)	22.5 (3.2 mg)	28.88
32	$Cu(OTf)_2$ (20 mol%, 1.8 mg)	25 (6.1 mg)	None	2.4
33	$Cu(OTf)_2$ (20 mol%, 1.8 mg)	25 (6.1 mg)	None	2.3



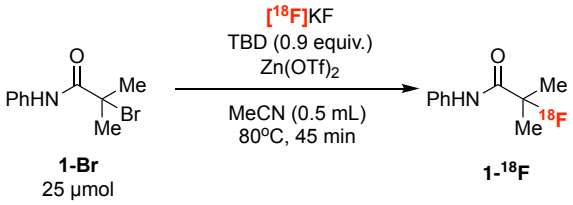
1-Br
25 µmol

1-^{18}F

S13. Screening studies for the labelling of **1-Br**. [^{18}F]CsF was prepared from CsOTf (7.5 mg, 26.5 µmol), K_{222} (1.4 mg, 3.6 µmol), and 3,4-Dibenzo-21-crown-7 (16 mg), (See Section 3.2). TBD = 1,5,7-Triazabicyclo[4.4.0]dec-5-ene.

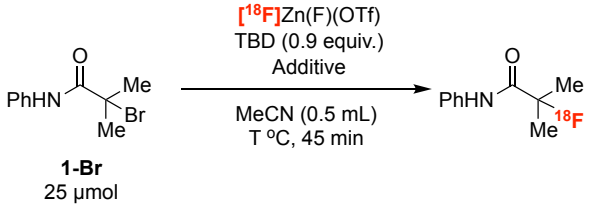
Entry	Additive	Substrate Quantity/ µmol	TBD Quantity/ µmol	RCC %
1	t-AmOH (1 equiv., 2.8 uL)	50 (12.2 mg)	45 (6.3 mg)	62.76
2	t-AmOH (2 equiv., 5.5 uL)	50 (12.2 mg)	45 (6.3 mg)	56.48
3	t-AmOH (5 equiv., 14 uL)	40 (9.6 mg)	36 (5.0 mg)	51.88
4	t-AmOH (10 equiv., 28 uL)	40 (9.6 mg)	36 (5.0 mg)	45.54
6	$LiClO_4$ (20 mol%, 0.6 mg)	30 (7.3 mg)	27 (3.8mg)	0
7	$Yb(OTf)_3$ (20 mol%, 3.1 mg)	25 (6.1 mg)	22.5 (3.2 mg)	<1
8	$Y(OTf)_3$ (20 mol%, 2.7 mg)	25 (6.1 mg)	22.5 (3.2 mg)	<1
10	$Zn(OTf)_2$ (20 mol%, 1.8 mg)	50 (12.2 mg)	45 (6.3 mg)	85.64
11	t-AmOH (1 equiv., 2.8 uL)	40 (9.6 mg)	36 (5.0 mg)	64.87
12	t-AmOH (2 equiv., 5.5 uL)	40 (9.6 mg)	36 (5.0 mg)	58.62
13	t-AmOH (5 equiv., 14 uL)	30 (7.3 mg)	27 (3.8mg)	38.21
14	t-AmOH (10 equiv., 28 uL)	30 (7.3 mg)	27 (3.8mg)	33.80
16	$LiClO_4$ (20 mol%, 0.6 mg)	25 (6.1 mg)	22.5 (3.2 mg)	0
17	$Yb(OTf)_3$ (20 mol%, 3.1 mg)	25 (6.1 mg)	25 (3.5 mg)	0
18	$Y(OTf)_3$ (20 mol%, 2.7 mg)	25 (6.1 mg)	25 (3.5 mg)	0
20	$Zn(OTf)_2$ (20 mol%, 1.8 mg)	25 (6.1 mg)	25 (3.5 mg)	85.29
21	Ti(itBuO)4 (20 mol%, 1.9 uL)	50 (12.2 mg)	50 (7 mg)	16.65
22	$Ti(itBuO)_4$ (20 mol%, 1.9 uL)	50 (12.2 mg)	50 (7 mg)	11.76
23	tAmOH (1 equiv. 2.8 uL)	25 (6.1 mg)	22.5 (3.2 mg)	38.68
24	tAmOH (1 equiv. 2.8 uL)	25 (6.1 mg)	22.5 (3.2 mg)	30.03
25	$Zn(OTf)_2$ (20 mol%, 1.8 mg)	25 (6.1 mg)	22.5 (3.2 mg)	63.96
26	$Zn(OTf)_2$ (20 mol%, 1.8 mg)	25 (6.1 mg)	22.5 (3.2 mg)	77

27	$Zn(OTf)_2$ (20 mol%, 1.8 mg), + tAmOH (1 equiv. 2.8 uL)	25 (6.1 mg)	22.5 (3.2 mg)	66.9
28	$Zn(OTf)_2$ (20 mol%, 1.8 mg), + tAmOH (1 equiv. 2.8 uL)	25 (6.1 mg)	22.5 (3.2 mg)	70.75
29	$Cu(OTf)_2$ (20 mol%, 18 mg)	25 (6.1 mg)	22.5 (3.2 mg)	38.11
30	$Cu(OTf)_2$ (20 mol%, 18 mg)	25 (6.1 mg)	22.5 (3.2 mg)	41.63
31	$Cu(OTf)_2$ (20 mol%, 18 mg), + tAmOH (1 equiv. 2.8 uL)	25 (6.1 mg)	22.5 (3.2 mg)	42.11
32	$Cu(OTf)_2$ (20 mol%, 18 mg), + tAmOH (1 equiv. 2.8 uL)	25 (6.1 mg)	22.5 (3.2 mg)	41.37
33	None	25 (6.1 mg)	22.5 (3.2 mg)	27.52
34	None	25 (6.1 mg)	22.5 (3.2 mg)	43.35



S14. Screening studies for the labelling **1-Br**. [^{18}F]KF was prepared from KOTf (5 mg, 26.5 µmol) and K_2CO_3 (0.5 mg) (see Section 3.2). TBD = 1,5,7-Triazabicyclo[4.4.0]dec-5-ene.

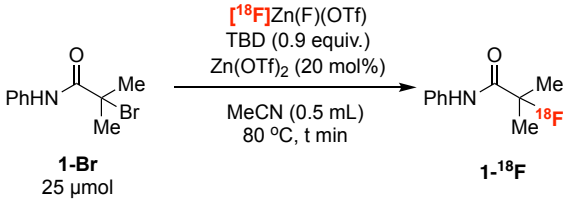
Entry	$Zn(OTf)_2$ (x mol%)	RCC %
1	1 (0.1 mg)	4.19
2	5 (0.5 mg)	11.5
3	10 (0.9 mg)	27.03
4	20 (1.8 mg)	42.28
6	50 (4.5 mg)	<1
7	100 (9 mg)	1.35
8	1 (0.1 mg)	3.5
10	5 (0.5 mg)	11.47
11	10 (0.9 mg)	22.46
12	20 (1.8 mg)	32.92
13	50 (4.5 mg)	<1
14	100 (9 mg)	<1



S15. Screening studies for the labelling of **1-Br**. [^{18}F]Zn(F)(OTf) was prepared from $Zn(OTf)_2$ (9.6 mg, 26.5 µmol) and K_{222} (1.4 mg),(See Section 3.2). TBD = 1,5,7-Triazabicyclo[4.4.0]dec-5-ene.

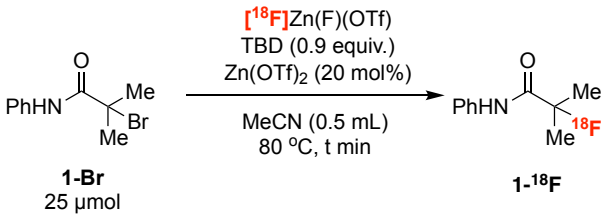
Entry	Additive	T/ °C	RCC %

1	-	rt	2.20
2	-	50	7.25
3	-	80	51.40
4	-	rt	2.70
5	-	50	7.42
6	-	80	51.20
7	$Zn(OTf)_2$ (20 mol%, 1.8 mg)	rt	0
8	$Zn(OTf)_2$ (20 mol%, 1.8 mg)	50	8.57
9	$Zn(OTf)_2$ (20 mol%, 1.8 mg)	80	61.63
10	$Zn(OTf)_2$ (20 mol%, 1.8 mg)	rt	0
11	$Zn(OTf)_2$ (20 mol%, 1.8 mg)	50	13.7
12	$Zn(OTf)_2$ (20 mol%, 1.8 mg)	80	55.53



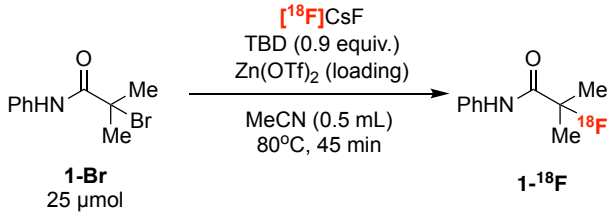
S16. Screening studies for the labelling of **1-Br**. [^{18}F]Zn(F)(OTf), as prepared from $Zn(OTf)_2$ (9.6 mg, 26.5 µmol), ad K_{222} (1.4 mg) (see Section 3.2). TBD = 1,5,7-Triazabicyclo[4.4.0]dec-5-ene.

Entry	Time / min	RCC %
1	5	12.99
2	10	13.71
3	20	46.21
4	45	53.79
5	30	55.96
6	5	17.59
7	10	37.1
8	20	39.08
9	30	50.44
10	45 (No Zn)	45.83
11	45 (No Zn)	37.58
12	45 (No Zn)	12.99



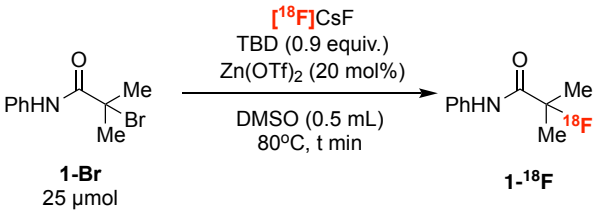
S17. Screening studies for the labelling of **1-Br**. [^{18}F]Zn(F)(OTf), as prepared from $Zn(OTf)_2$ (9.6 mg, 26.5 μmol), benzo-12-crown-4 (8.9 mg, 39.5 μmol), and K_{222} (1.4 mg, 3.6 μmol), (See Section 3.2). TBD = 1,5,7-Triazabicyclo[4.4.0]dec-5-ene.

Entry	Time/min	RCC %
1	20	60.77
2	30	51.13
5	20	48.67
6	30	58.89
7	45	53.15
8	60	71.99



S18. Screening studies for the labelling of **1-Br**. [^{18}F]CsF was prepared from CsOTf (7.5 mg, 26.5 μmol) and K_{222} (1.4 mg, 3.6 μmol), Se Section 3.2). TBD = 1,5,7-Triazabicyclo[4.4.0]dec-5-ene.

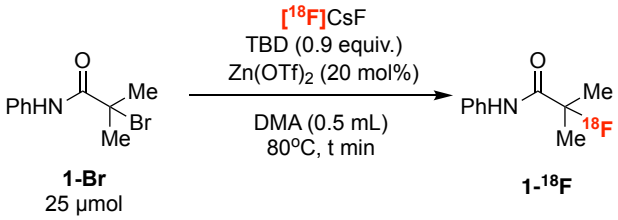
Entry	Zn Loading	RCC %
1	$Zn(OTf)_2$ (20 mol%, 1.8 mg)	69.6
2	$Zn(OTf)_2$ (20 mol%, 1.8 mg)	87.3
3	$Zn(OTf)_2$ (30 mol%, 2.7 mg)	70.5
4	$Zn(OTf)_2$ (30 mol%, 2.7 mg)	83.03
5	$Zn(OTf)_2$ (40 mol%, 3.6 mg)	76.76
6	$Zn(OTf)_2$ (40 mol%, 3.6 mg)	85.18



S19. Screening studies for the labelling of **1-Br**. [^{18}F]CsF was prepared from CsOTf (7.5 mg, 26.5 μmol), K_{222} (1.4 mg, 3.6 μmol), and 3,4-Dibenzo-21-crown-7 (16 mg), (See Section 3.2). TBD = 1,5,7-Triazabicyclo[4.4.0]dec-5-ene.

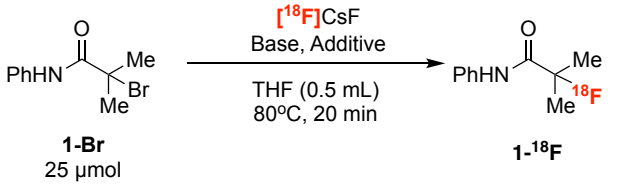
Entry	Time/min	RCC %
1	5	47.00
2	10	62.21
3	20	76.85
4	30	50.36
5	45	80.93
6	5	47.05

7	10	63.21
8	20	73.22
9	30	79.14
10	45	78.22



S20. Screening studies for the labelling of **1-Br**. [^{18}F]CsF was prepared from CsOTf (7.5 mg, 26.5 μmol), and K_{222} (1.4 mg, 3.6 μmol) (see Section 3.2). TBD = 1,5,7-Triazabicyclo[4.4.0]dec-5-ene.

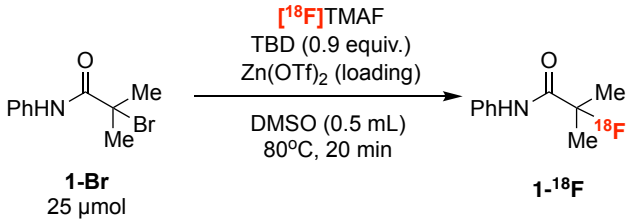
Entry	Time/min	RCC %
1	5	21.14
2	10	28.03
3	20	41.28
4	30	60
5	45	51.86
6	5	8.11
7	10	27.34
8	20	33.89
9	30	51.30



S21. Screening studies for the labelling of **1-Br**. [^{18}F]CsF was prepared from CsOTf (7.5 mg, 26.5 μmol), and K_{222} (1.4 mg, 3.6 μmol) (see section 3.2). TBD = 1,5,7-Triazabicyclo[4.4.0]dec-5-ene. N-IMTA = N-Isopropyl-N-methyl-tert-butylamine. phen = 1,10-phenanthroline.

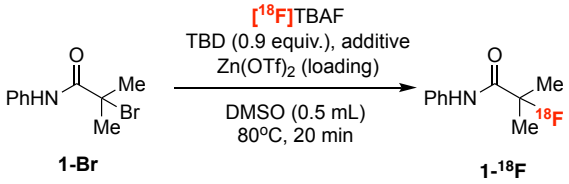
Entry	Base	Additive	RCC %
1	-	phen (10 mol%, 0.5 mg), $CuBr_2$ (10 mol%, 0.4 mg)	0
2	N-IMTA (2 equiv, 8.4 uL)	phen (10 mol%, 0.5 mg), $CuBr_2$ (10 mol%, 0.4 mg)	0
3	TBD (2 equiv, 7 mg)	phen (10 mol%, 0.5 mg), $CuBr_2$ (10 mol%, 0.4 mg)	2.39
4	N-IMTA (2 equiv, 8.4 uL)	phen (10 mol%, 0.5 mg), $CuBr_2$ (10 mol%, 0.4 mg)	0
5	TBD (0.9 equiv, 3.1 mg)	phen (10 mol%, 0.5 mg), $CuBr_2$ (10 mol%, 0.4 mg)	1.59
6	-	phen (2 equiv., 9 mg), $CuBr_2$ (2 equiv., 11.2 mg)	0
7	N-IMTA (2 equiv, 8.4 uL)	phen (2 equiv., 9 mg), $CuBr_2$ (2 equiv., 11.2 mg)	0
8	TBD (2 equiv, 7 mg)	phen (2 equiv., 9 mg), $CuBr_2$ (2 equiv., 11.2 mg)	0

9	N-IMTA (0.9 equiv, 3.8 uL)	phen (2 equiv., 9 mg), $CuBr_2$ (2 equiv., 11.2 mg)	0
10	TBD (0.9 equiv, 3.1 mg)	phen (2 equiv., 9 mg), $CuBr_2$ (2 equiv., 11.2 mg)	0
11	TBD (0.9 equiv, 3.1 mg)	-	0
12	TBD (0.9 equiv, 3.1 mg)	$Zn(OTf)_2$ (20 mol%, 1.8 mg)	0
13	-	-	0



S22. Screening studies for the labelling of **1-Br**. [^{18}F]TMAF was prepared from TMAOTf (5.9 mg, 26.5 µmol), and K_{222} (1.4 mg, 3.6 µmol), (See Section 3.2). TBD = 1,5,7-Triazabicyclo[4.4.0]dec-5-ene.

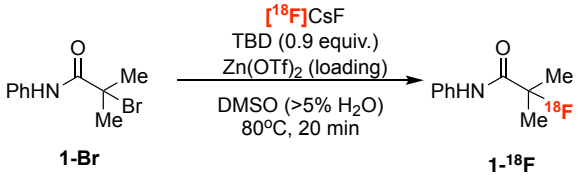
Entry	Zn Loading	RCC %
1	1 mol%	40.64
2	5 mol%	66.86
3	10 mol%	73.61
4	20 mol%	87.26
5	40 mol%	52.42
6	50 mol%	39.80
7	60 mol%	54.91
8	70 mol%	54.20
9	80 mol%	54.68
10	90 mol%	51.89
11	1 equiv.	43.07
12	2 equiv.	39.26
13	5 equiv.	44.29
14	None	5.84



S23. Screening studies for the labelling of **1-Br**. [^{18}F]TMAF was prepared from TBAOTf (10.4 mg, 26.5 µmol), and K_{222} (1.4 mg, 3.6 µmol), (See Section 3.2). TBD = 1,5,7-Triazabicyclo[4.4.0]dec-5-ene.

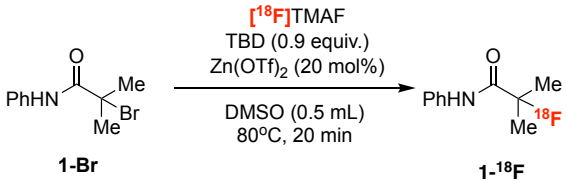
Entry	Substrate Quantity	Zn Quantity	TBD Quantity	Additive	RCC %
1	1 µmol (0.2 mg)	0.07 mg	0.9 µmol (0.13 mg)	-	40.4
2	5 µmol (1.2 mg)	0.36 mg	4.5 µmol (0.63 mg)	-	60.53
3	10 µmol (2.4 mg)	0.73 mg	9 µmol (1.23 mg)	-	59.32

4	25 µmol (6.1 mg)	1.8 mg	22.5 µmol (3.1 mg)	-	61.74
5	50 µmol (12.2 mg)	3.63 mg	45 µmol (6.3 mg)	-	64.76
6	1 µmol (0.2 mg)	0.07 mg	0.9 µmol (0.13 mg)	-	37.25
7	5 µmol (1.2 mg)	0.36 mg	4.5 µmol (0.63 mg)	-	54.44
8	10 µmol (2.4 mg)	0.73 mg	9 µmol (1.23 mg)	-	56.73
9	25 µmol (6.1 mg)	1.8 mg	22.5 µmol (3.1 mg)	-	61.45
10	50 µmol (12.2 mg)	3.63 mg	45 µmol (6.3 mg)	-	56.06
11	25 µmol (6.1 mg)	1.8 mg	22.5 µmol (3.1 mg)	H_2O (1 equiv. 1.8 uL)	45.83
12	25 µmol (6.1 mg)	1.8 mg	22.5 µmol (3.1 mg)	H_2O (2 equiv. 3.6 uL)	50.68
13	25 µmol (6.1 mg)	1.8 mg	22.5 µmol (3.1 mg)	H_2O (5 equiv. 9 uL)	37.78
14	25 µmol (6.1 mg)	1.8 mg	22.5 µmol (3.1 mg)	H_2O (10 equiv. 18 uL)	23.55
15	25 µmol (6.1 mg)	1.8 mg	22.5 µmol (3.1 mg)	H_2O (1 equiv. 1.8 uL)	52.01
16	25 µmol (6.1 mg)	1.8 mg	22.5 µmol (3.1 mg)	H_2O (2 equiv. 3.6 uL)	56.17
17	25 µmol (6.1 mg)	1.8 mg	22.5 µmol (3.1 mg)	H_2O (5 equiv. 9 uL)	40.66



S24. Screening studies for the labelling of **1-Br**. [^{18}F]CsF was prepared from CsOTf (7.5 mg, 26.5 µmol), and K_{222} (1.4 mg, 3.6 µmol), (See Section 3.2). TBD = 1,5,7-Triazabicyclo[4.4.0]dec-5-ene.

Entry	Substrate Quantity	Additives	RCC %
1	1 µmol (0.2 mg)	-	0
2	5 µmol (1.2 mg)	-	21.7
3	10 µmol (2.4 mg)	-	31.89
4	25 µmol (6.1 mg)	-	45.71
5	1 µmol (0.2 mg)	-	15.47
6	25 µmol (6.1 mg)	-	34.66
7	25 µmol (6.1 mg)	^{19}F-CsF (20 mol%, 0.8 mg), + Dibenzo-21-C-7 (2 mg)	13.55
8	25 µmol (6.1 mg)	^{19}F-CsF (20 mol%, 0.8 mg), + Dibenzo-21-C-7 (2 mg)	3.85
9	25 µmol (6.1 mg)	^{19}F-CsF (20 mol%, 0.8 mg), + Dibenzo-21-C-7 (2 mg)	3.85

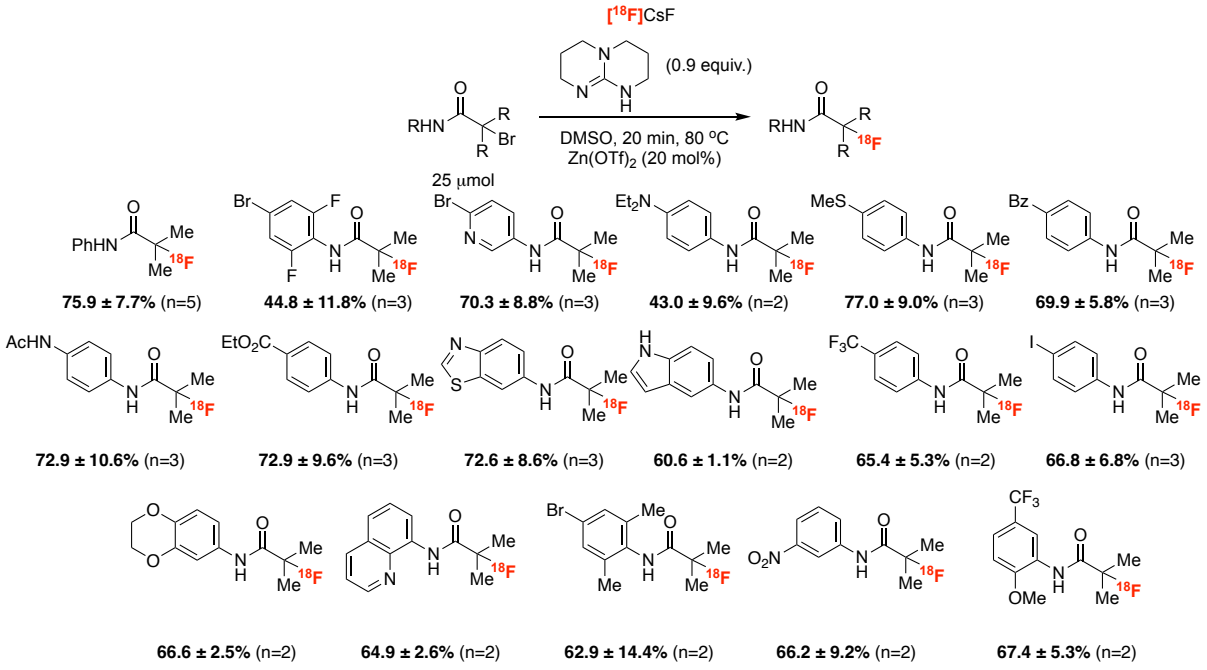


S25. Screening studies for the labelling of **1-Br**. [^{18}F]TMAF was prepared from TMAOTf (5.9 mg, 26.5 µmol) and K_{222} (1.4 mg, 3.6 µmol) (See Section 3.2). TBD = 1,5,7-Triazabicyclo[4.4.0]dec-5-ene.

Entry	Substrate Quantity	Additives	RCC %
1	0.02 µmol (0.048 mg),	-	55.84
2	0.5 µmol (0.12 mg),	-	93.58
3	1 µmol (0.24 mg),	-	76.99
4	5 µmol (1.21 mg),	-	95.03
5	10 µmol (2.42 mg),	-	91.93
6	0.02 µmol (0.048 mg),	-	32.61
7	0.5 µmol (0.12 mg),	^{19}F-CsF (20 mol%, 0.8 mg), + Dibenzo-21-C-7 (2 mg)	72.48
8	1 µmol (0.24 mg),	^{19}F-CsF (20 mol%, 0.8 mg), + Dibenzo-21-C-7 (2 mg)	79.28
9	5 µmol (1.21 mg),	^{19}F-CsF (20 mol%, 0.8 mg), + Dibenzo-21-C-7 (2 mg)	91.48
10	10 µmol (2.42 mg),	-	69.59 (Wet DMSO)

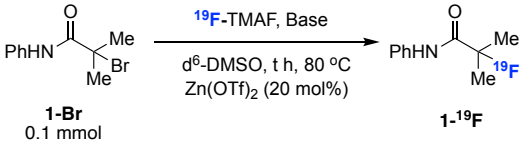
5.3 Reaction Scope with [^{18}F]CsF

To a 1-dram vial containing α-bromoamide precursor (25 µmol) in DMSO (200 µL), was added [^{18}F]CsF in DMSO (100 µL, ca. 100 µCi), followed by a stock solution of TBD (3.2 mg, 22.5 µmol), and $Zn(OTf)_2$ (1.8 mg, 5 µmol), in anhydrous DMSO (200 µL). The vial was quickly capped with a Teflon-lined septa cap and stirred at 80 °C for 20 min. Radiochemical conversions (RCC) were obtained via rTLC analysis (4:1 DCM:MeOH). RCC values indicate the conversion of inorganic fluorine-18 to organic products. Radiochemical identity and approximate radiochemical purities (RCP) were obtained via rHPLC analysis (Section 3.3).



5.4 ^{19}F-Fluorination of α-Haloamides

TMAF tetrahydrate was charged into a 1-dram vial and azeotropically dried with MeCN (3 x 2 mL) before being dried under high vacuum (10^{-2} mbar) at 120 °C for 16 h. The vial was quickly charged in air with a solution of TBD (0.9 equiv.) and $Zn(OTf)_2$ (20 mol%) in

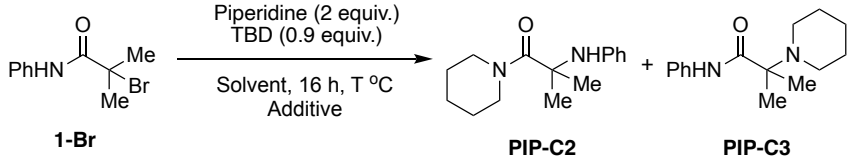


anhydrous d^6-DMSO (400 µL), followed by a solution of **1-Br** (0.1 mmol), in anhydrous d^6-DMSO (100 µL). The vial was quickly capped with a Teflon-lined septa cap and stirred at 80 °C for the allotted time. Yields were obtained with ^{19}F NMR spectroscopy via comparison to an internal standard.

S26. Fluorination of **1-Br** with ^{19}F-TMAF

Entry	TMAF Quantity	Base	Time	^{19}F NMR Yield 1-^{19}F
1	0.9 equiv.	TBD (0.9 equiv.)	20 min	11
2	0.9 equiv.	TBD (0.9 equiv.)	1 h	17
3	0.9 equiv.	TBD (0.9 equiv.)	3 h	20
4	0.9 equiv.	TBD (0.9 equiv.)	5 h	21
5	0.9 equiv.	TBD (0.9 equiv.)	16 h	21
6	2.0 equiv.	TBD (0.9 equiv.)	20 min	19
7	2.0 equiv.	TBD (0.9 equiv.)	1 h	21
8	2.0 equiv.	TBD (0.9 equiv.)	3 h	23
9	2.0 equiv.	TBD (0.9 equiv.)	5 h	22
10	2.0 equiv.	TBD (0.9 equiv.)	16 h	23

5.5 Amination of 1-Br



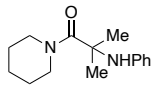
S27. Regiochemical outcomes of the amination of **1-Br** with piperidine.[1] 4 equiv. piperidine [2] 3 equiv. piperidine

Entry	Substrate/ mmol	Additive	Solvent	T/ °C	PIP-C2:PIP-C3	Isolated Yield PIP-C2	Isolated Yield PIP-C3
1	0.1	-	MeCN-H3	rt	1:4	-	-
2	0.1	-	MeCN-H3	80	1:2.9	-	-
3	0.1	-	DMSO-d6	rt	1:2.6	-	-
4	0.1	-	DMSO-d6	80	Inconclusive, both detected	-	-
5	0.1	$Zn(OTf)_2$ (7.3 mg)	MeCN-H3	rt	1:2.6	-	-
6	0.1	$Zn(OTf)_2$ (7.3 mg)	MeCN-H3	80	1:3.3	-	-
7	0.1	$Zn(OTf)_2$ (7.3 mg)	DMSO-d6	rt	1:3.3	-	-
8	0.1	$Zn(OTf)_2$ (7.3 mg)	DMSO-d6	80	1:1	-	-
9[1]	0.1	AgOTf (51.4 mg)	MeCN-H3	rt	1:3	-	4 mg (containing 4% **PIP-C2**), 0.016 mmol, 16%
10[2]	0.1	CuBr-DMS (1.5 mg) PPh_3 (0.3 mg)	PhMe	rt	only **PIP-C3** observed	-	5 mg, 0.02 mol, 20%

		K_3PO_4 (27 mg)					
11	0.5	-	MeCN-H3	80	1:3.1	-	-
12	0.5	$Zn(OTf)_2$ (36.5 mg)	MeCN-H3	80	1:5.2	12 mg, 0.05 mmol, 10% (containing 7% **PIP-C3)**	32 mg, 0.13 mmol, 26%

Amination Procedure: A 1-dram vial was charged with a solution of **1-Br** and additive (where applicable) in anhydrous solvent followed by piperidine (2 equiv.) and a solution of TBD (0.9 equiv.) in anhydrous solvent. The reaction (0.2M for 0.1 mmol scale, 0.5M for 0.5 mmol scale) was capped with a Teflon-lined septa cap and stirred at 80 °C for 16 h. Reactions in MeCN or PhMe were evaporated *in vacuo* and analyzed via NMR spectroscopy ($CDCl_3$). Reactions in d6-DMSO were analyzed with NMR spectroscopy directly. Entries 9, 10, and 12 were purified via SiO_2 gel chromatography (hexanes/EtOAc) to obtain **PIP-C2** and/or **PIP-C3**. Independent syntheses of these compounds are reported.[10]

2-Methyl-*N*-phenyl-2-(piperidin-1-yl)propenamide[9]



PIP-C2

Synthesised from **1-Br** (121 mg, 0.5 mmol, 1.0 equiv.), see Table **S27** Entry 12. SiO_2 gel chromatography (0→20% EtOAc in Hexanes) afforded **PIP-C2** as a light brown solid containing 7% **PIP-C3** (12 mg, 0.05 mmol, 10% yield). Variable temperature (VT) NMR recorded @ 50 °C in DMSO to reduce line broadening observed from piperidinyl protons.

HRMS m/z (ESI+) calculated for $[C_{15}H_{23}N_2O]^+$: 247.1805, found $[M+H]^+$: 247.1809.

δ^{1}H (400 MHz, $CDCl_3$) 7.15-7.11 (m, 2H), 6.70 (t, 1H, J = 7.4 Hz), 6.54 (d, 2H, *J* = 7.4 Hz), 4.10-3.40 (br m, 5H), 1.55 (s, 6H), 1.53-1.20 (br m, 6H).

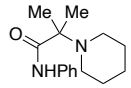
Entry	Substrate	Nucleophile	Base	Solvent	Additive (eq.)	**C2:C3**	**Yield C2/%**	**Yield C3/%**
1[a]	**1-Br** (0.1 mmol)	^{19}F-NMe_4F (2 equiv)	TBD	d^6-DMSO	$Zn(OTf)_2$ (0.2)	C3 only	-	23[c]
2[a]	**1-Br** (0.5 mmol)	Piperidine (2 equiv)	TBD	MeCN	$Zn(OTf)_2$ (0.2)	1:5.2	10[d]	26
3[a]	**1-Br** (0.1 mmol)	Piperidine (2 equiv)	TBD	d^6-DMSO	$Zn(OTf)_2$ (0.2)	1:1	-	-
4[b]	**1-Br** (0.1 mmol)	Piperidine (4 equiv)	-	MeCN	AgOTf (2)	1:3	-	16[e]

δ^{13}C (101 MHz, $CDCl_3$) 172.6, 145.7, 129.3, 117.9, 114.3, 58.4, 46.2 (br), 27.4, 26.2, 24.8.

δ^{1}H (500 MHz, DMSO, VT @ 50 °C) 7.02 (t, 2H, *J* = 7.7 Hz), 6.53-6.48 (m, 3H), 5.77 (br s, 1H), 3.63 (br s, 4H), 1.42 (br s, 8H), 1.25 (br s, 4H).

δ^{13}C (126 MHz, DMSO, VT @ 50 °C) 171.9, 146.4, 128.4, 120.5, 115.7, 113.0, 57.0, 26.4, 25.4, 23.9.

2-Methyl-2-(phenylamino)-1-(piperidin-1-yl)propan-1-one



PIP-C3

Synthesised from **1-Br** (121 mg, 0.5 mmol, 1.0 equiv.), see Table **S27** Entry 12. SiO_2 gel chromatography (0→20% EtOAc in Hexanes) afforded **PIP-C3** as a white solid (32 mg, 0.13 mmol, 26% yield).

Alternatively synthesised from **1-Br** (24 mg, 0.1 mmol, 1.0 equiv.) under Mizuta's conditions without fluoride,[1] see Table **S27** Entry 9. SiO_2 gel chromatography (5→15% EtOAc in Hexanes) afforded **PIP-C3** as a light brown solid containing 4% **PIP-C2** (4 mg, 0.02 mmol, 16% yield).

Alternatively synthesised from **1-Br** (24 mg, 0.1 mmol, 1.0 equiv.) under Nishikata's conditions,[10] see Table **S27** Entry 10. SiO_2 gel chromatography (5→15% EtOAc in Hexanes) afforded **PIP-C3** as a light brown solid (5 mg, 0.02 mmol, 20% yield).

HRMS m/z (ESI+) calculated for $[C_{15}H_{23}N_2O]^+$: 247.1805, found $[M+H]^+$: 247.1808.

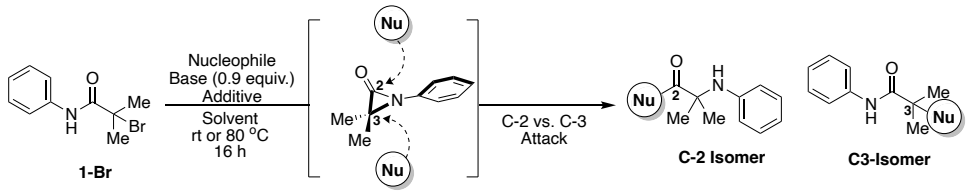
δ^{1}H (499 MHz, $CDCl_3$) 9.51 (br s, 1H), 7.57 (d, 2H, *J* = 7.5 Hz), 7.32 (t, 2H, *J* = 7.5 Hz), 7.07 (t, 1H, *J* = 7.1 Hz), 2.49 (br s, 4H), 1.65-1.63 (m, 4H), 1.51 (br s, 2H), 1.26 (s, 6H).

δ^{13}C (126 MHz, $CDCl_3$) 176.0, 138.5, 129.1, 123.7, 119.2, 64.7, 48.2, 27.2, 24.9, 20.7.

δ^{1}H (400 MHz, DMSO) 9.58 (br s, 1H), 7.62 (dd, 2H, *J* = 8.7, 1.1 Hz), 7.30, (t, 2H, *J* = 7.6 Hz), 7.06-7.02 (m, 1H), 2.39 (br s, 4H), 1.60 (quintet, 4H, *J* = 5.6 Hz), 1.44-1.42 (m 2H), 1.16 (s, 6H).

δ^{13}C (101 MHz, DMSO) 175.3, 138.7, 128.7, 123.2, 119.3, 64.0, 47.5, 26.2, 24.5, 20.2.

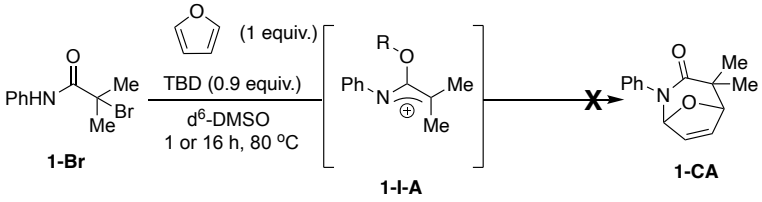
The reaction of **1-Br** with piperidine was conducted in d^6-DMSO or MeCN owing to their comparably high performance as solvents in the radiolabelling reaction. As shown in Table 2, entries 2 and 3 afforded the corresponding C-2 and C-3 piperidinyl isomers in a 1:5.2 and 1:1 ratio, respectively, as determined by ^{1}H NMR spectroscopy. Importantly, these aminated C-2 isomers could not be formed via



S28. Summary of key substitution reactions of **1-Br** with different nucleophiles. Nu = Nucleophile. [a] 80 °C [b] rt [c] Determined by ^{19}F NMR spectroscopy [d] Isolated in 93% purity with 7% **C-3** isomer [e] Isolated in 96% purity with 4% **C-2** isomer.

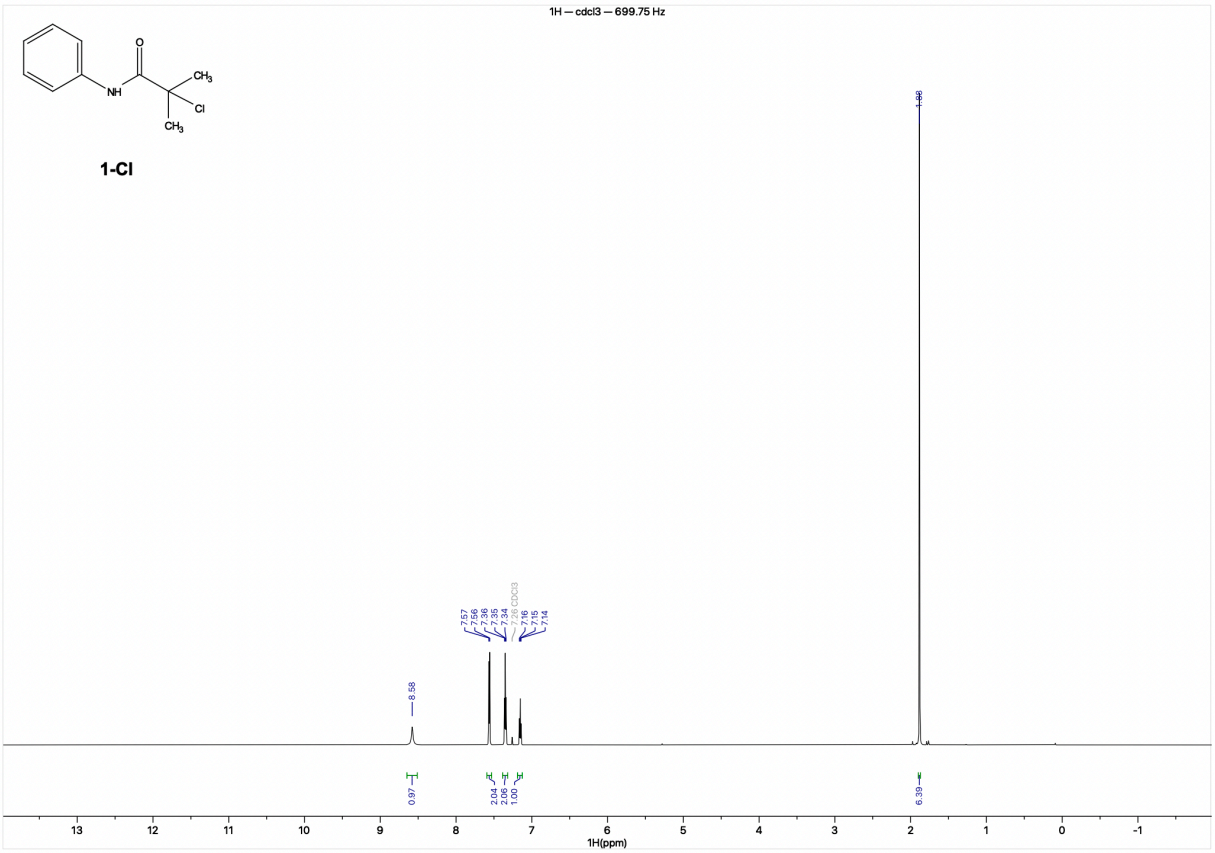
attack of iminolactone **1-I-B** or aza-oxyallyl cation **1-I-A**. Iminolactones **1-I-B** are less likely to be the reactive intermediate since they have been reported to isomerise rapidly to the corresponding α-lactam.[11] In analogy, Mizuta's silver-mediated reaction was also conducted using piperidine as a replacement nucleophile for ^{19}F-fluoride and resulted in a similar mixture of C-2 and C-3 piperidinyl isomers, suggesting that this process may occur through a related mechanism (see Table **S27**, entry 9). Although **PIP-C2** and **PIP-C3** exhibit comparable polarities, SiO_2 gel chromatography afforded samples of sufficient purity for comparison to analytical spectra obtained from independent sources, confirming product identities. The disparities between product ratios recorded with ^{1}H NMR vs isolated yields are explained by purification efficiency.

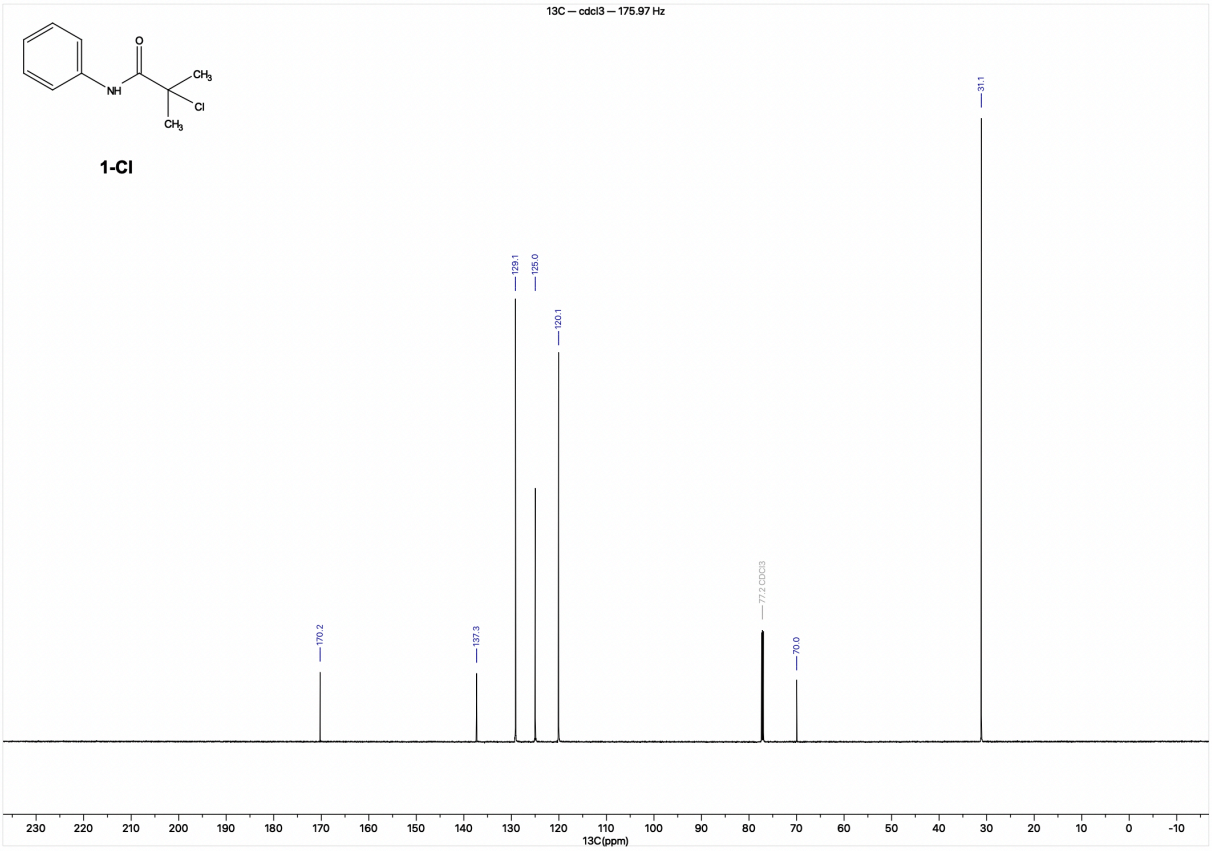
5.6 Attempted Cycloaddition Reaction of 1-Br

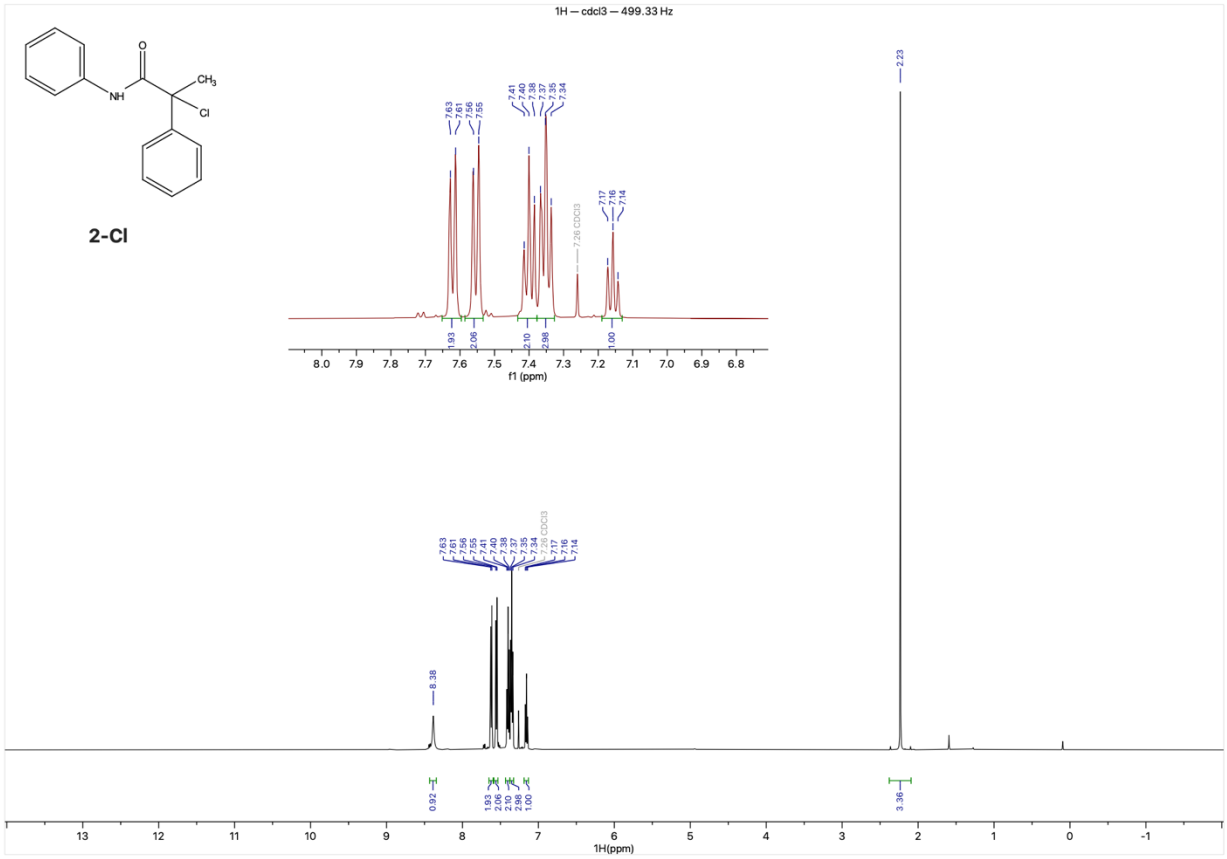


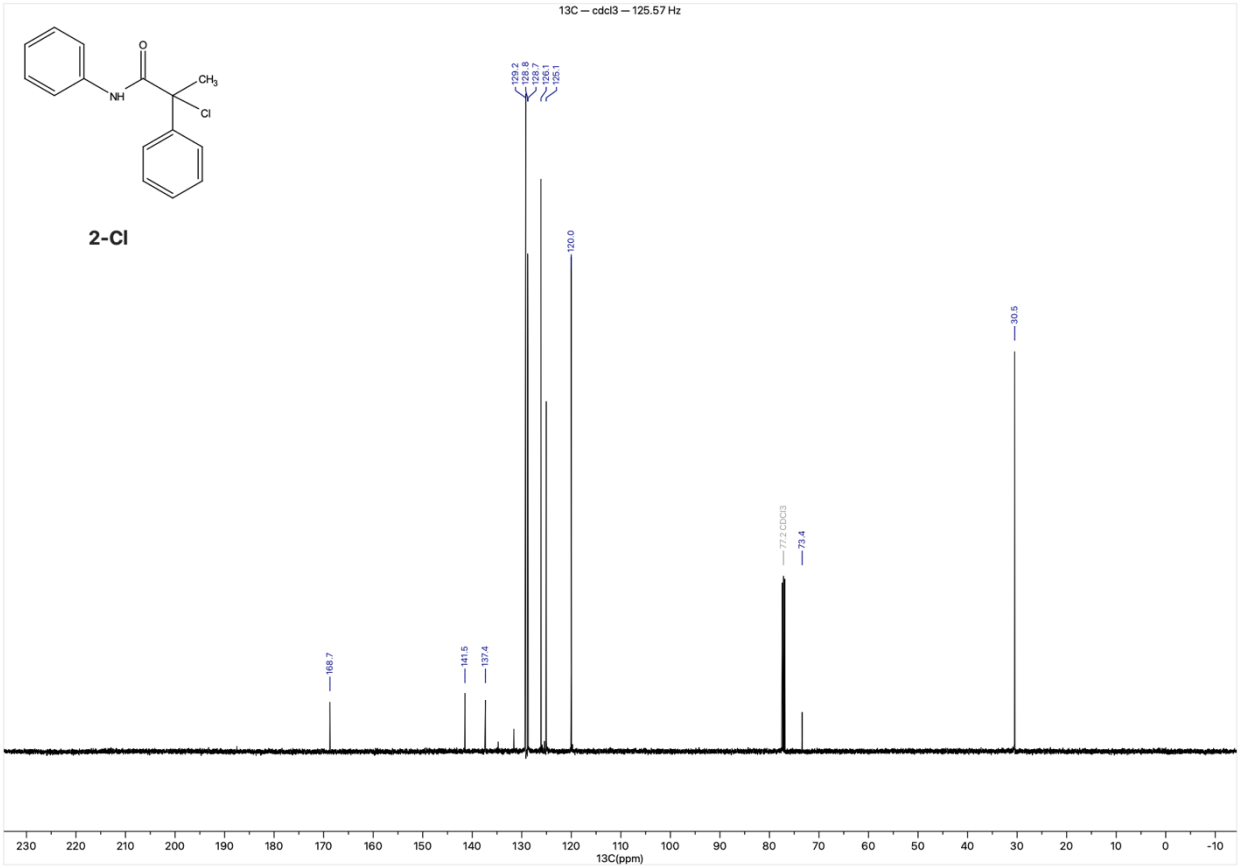
Derivatives of aza-oxyallyl cation **1-I-A** undergo aza-[4+3] cycloaddition with dienes such as furan.[12] However, under the optimized reaction conditions (replacing fluoride with furan), cycloaddition adduct **1-CA** was not detected by ^{1}H NMR spectroscopy or electrospray ionisation high-resolution mass spectrometry after 1 or 16 h.

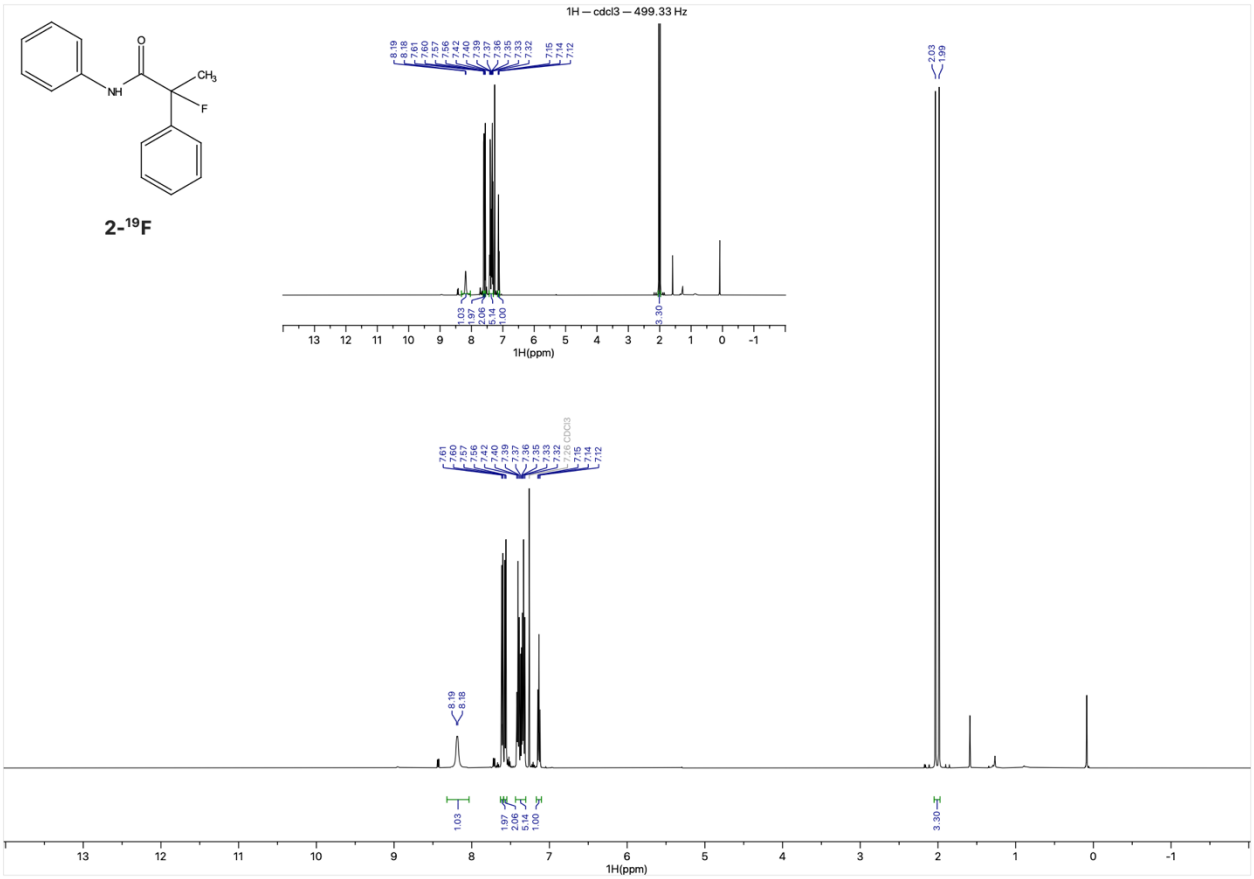
6. NMR Spectra

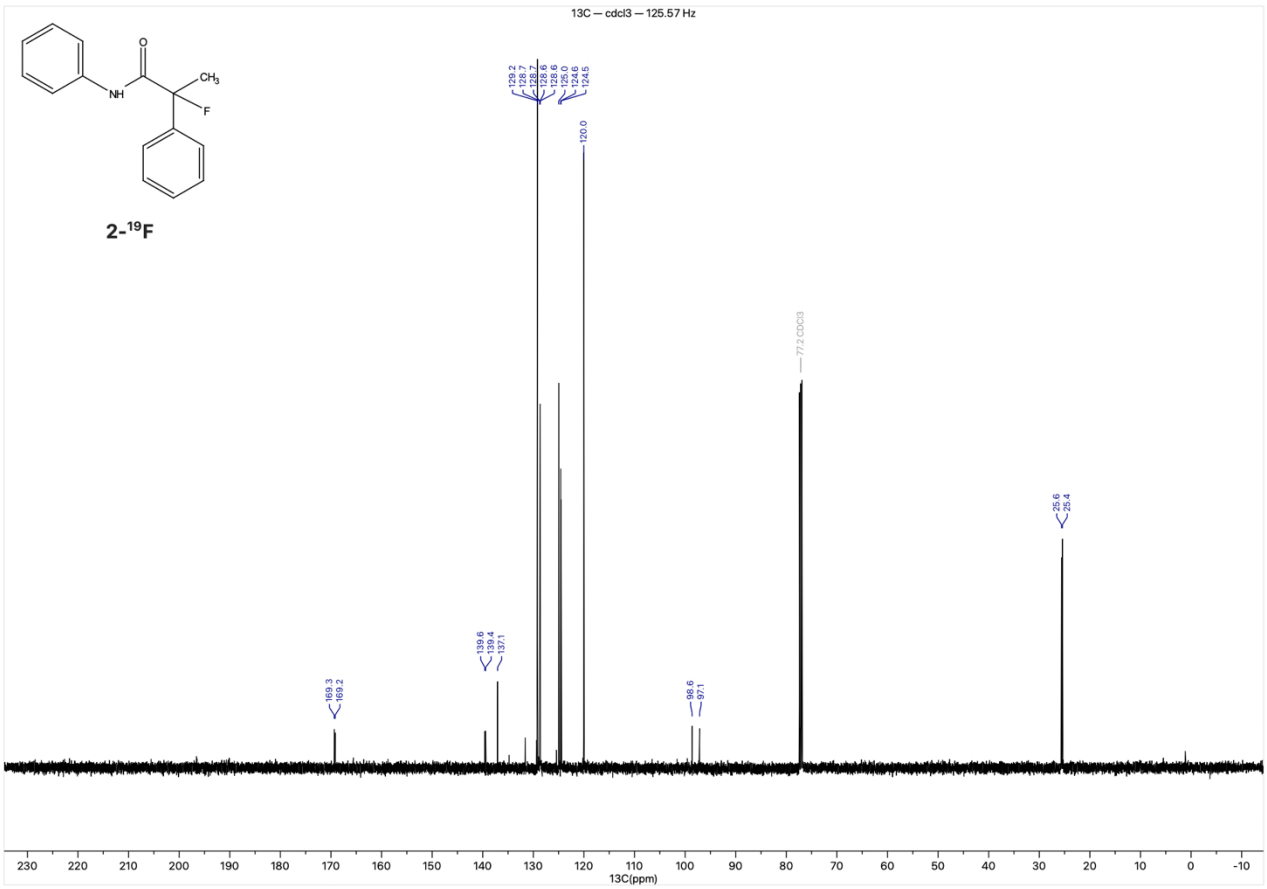

1H — cdcl3 — 699.75 Hz
1-Cl
8.58
7.57
7.56
7.36
7.35
7.34
7.33
7.16
7.15
7.14
0.97
2.04
2.06
1.00
6.39
1H(ppm)

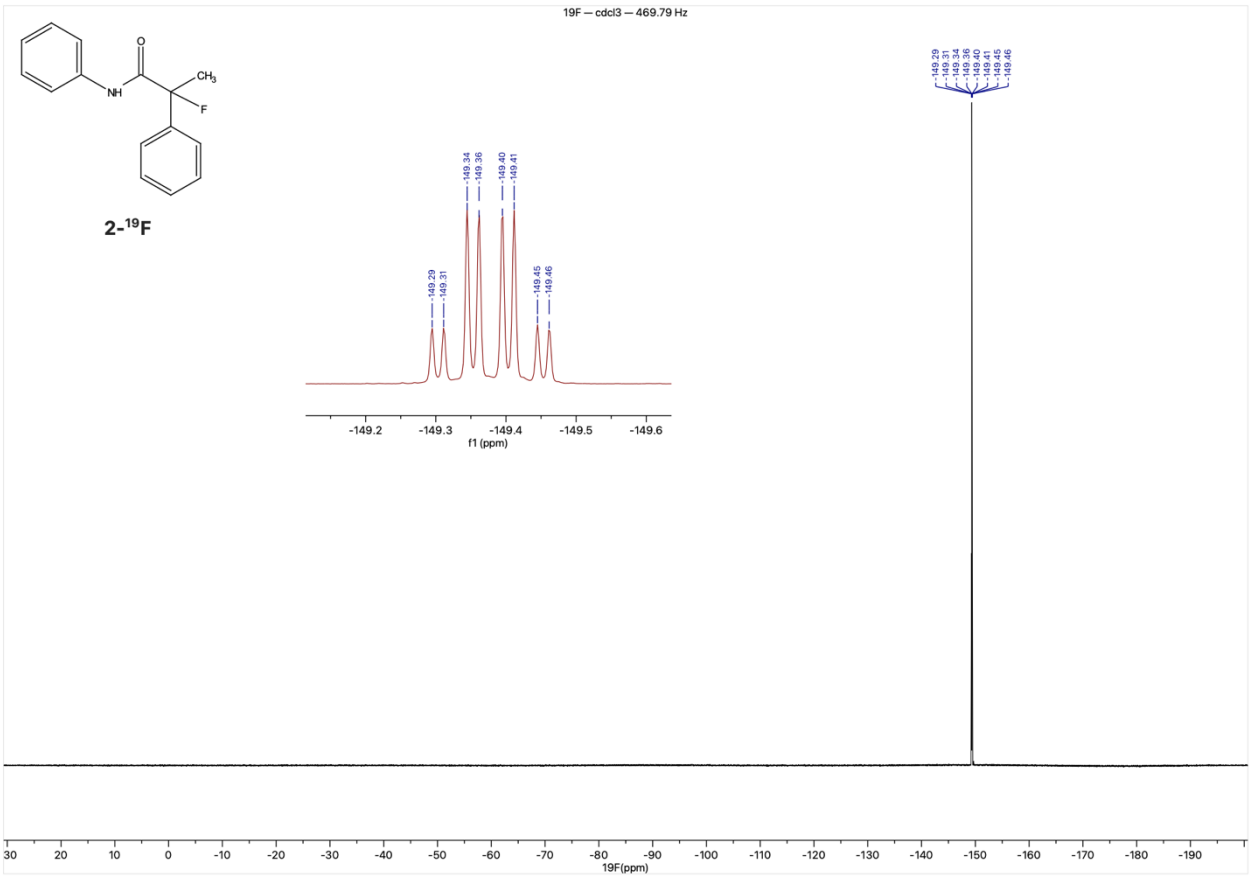

13C — cdcl3 — 175.97 Hz
1-Cl
170.2
137.3
129.1
125.0
120.1
77.2 CDCl3
70.0
31.1
13C(ppm)

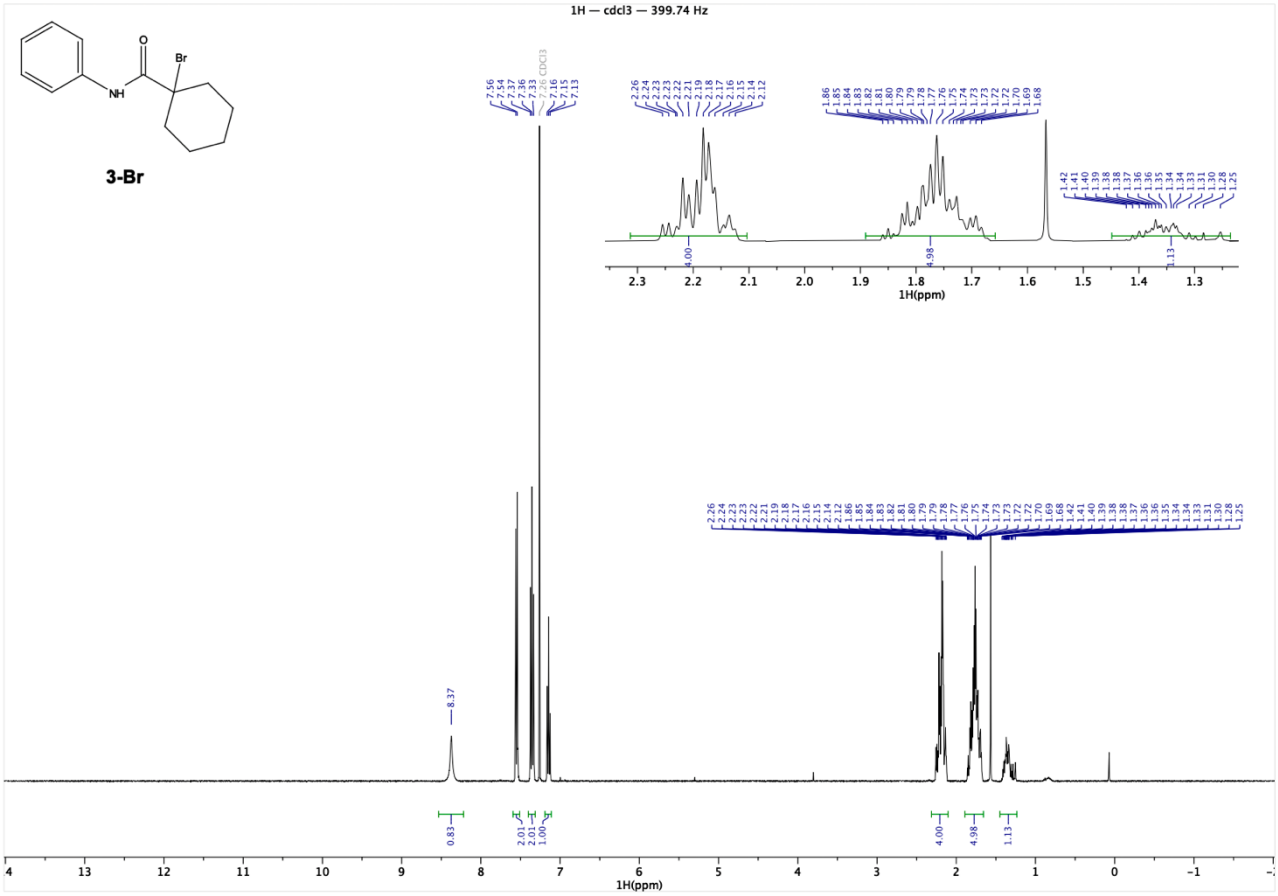

1H — cdcl3 — 499.33 Hz
2-Cl
f1 (ppm)
1H(ppm)

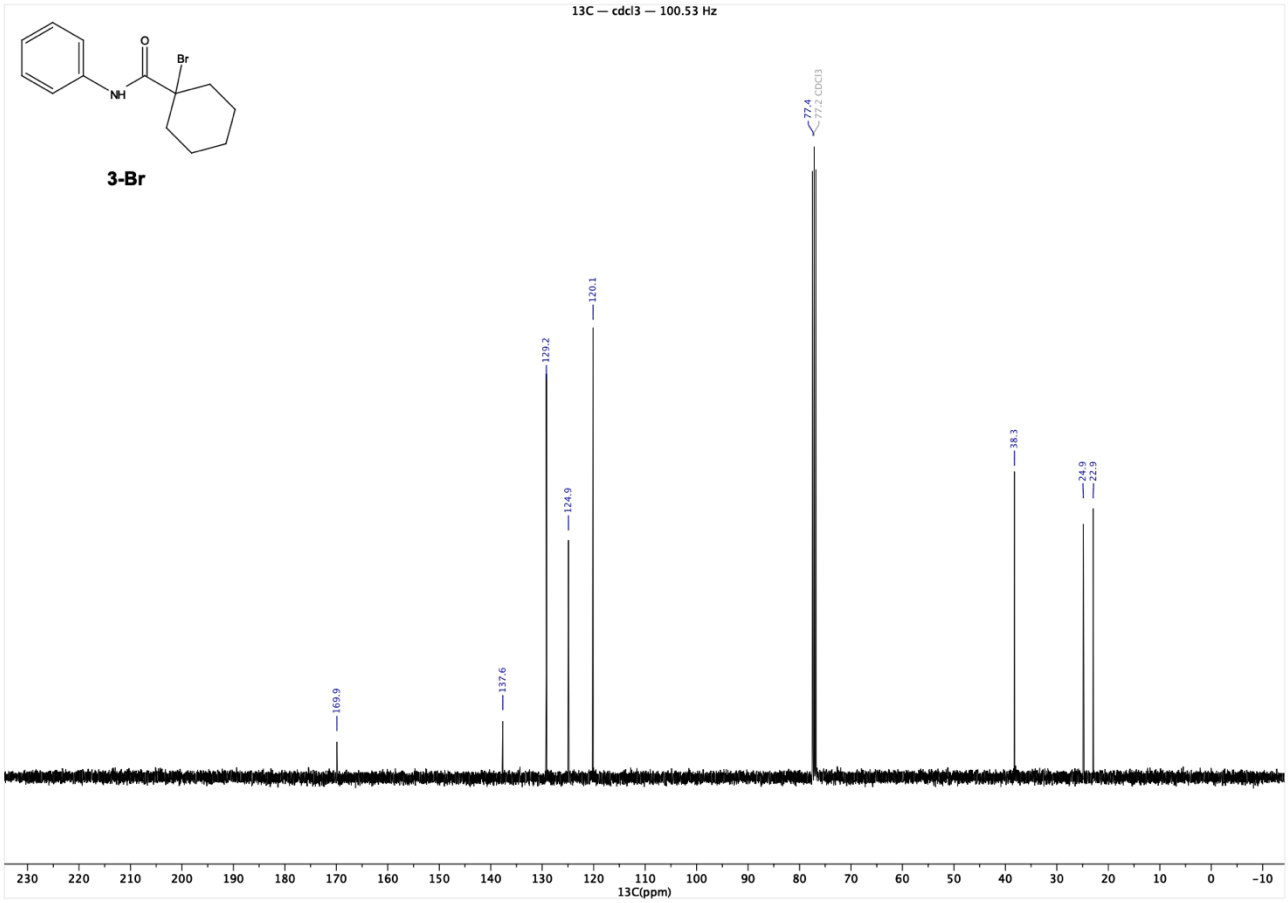

13C — cdcl3 — 125.57 Hz
2-Cl
13C(ppm)

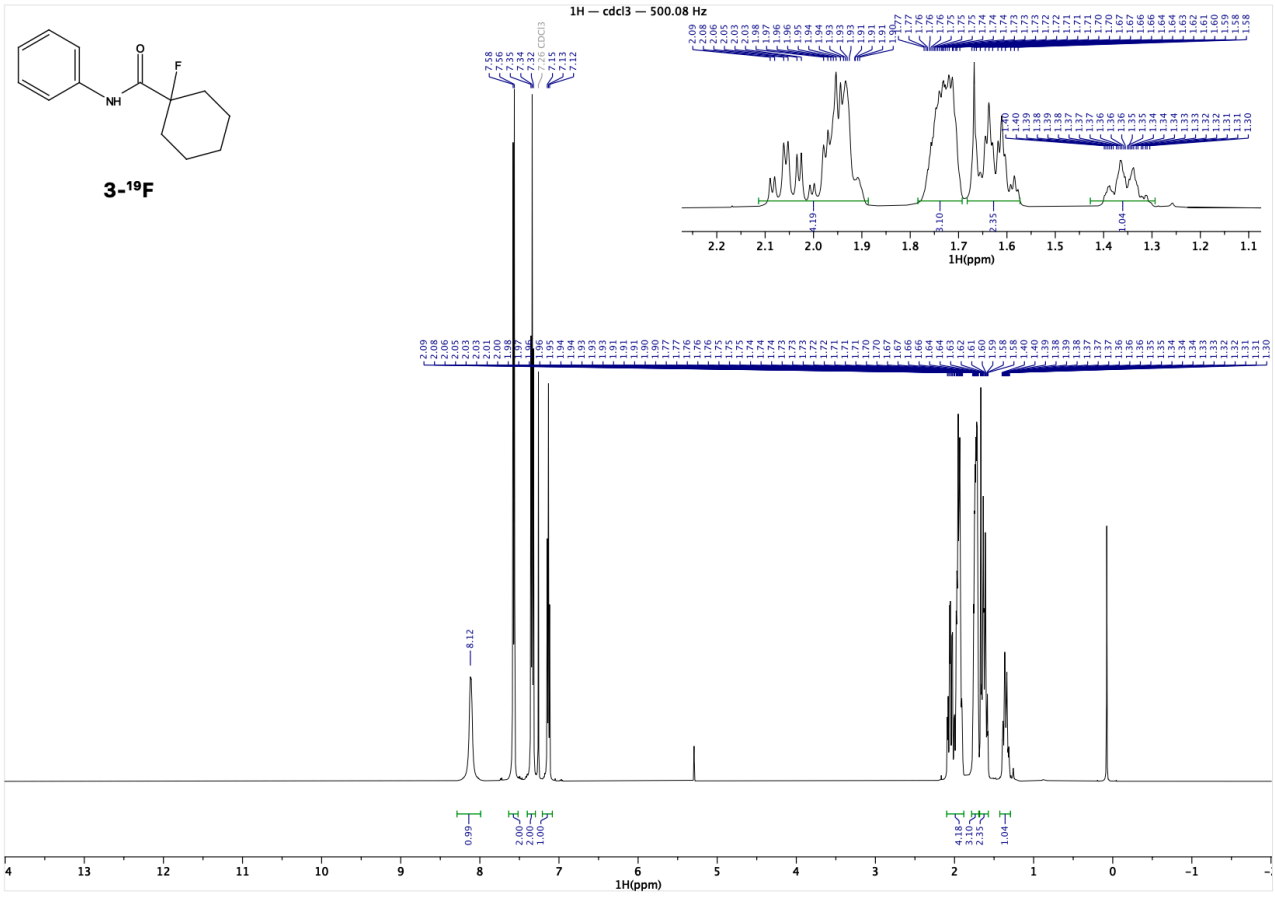

1H — cdcl3 — 499.33 Hz
2-19F
1H(ppm)

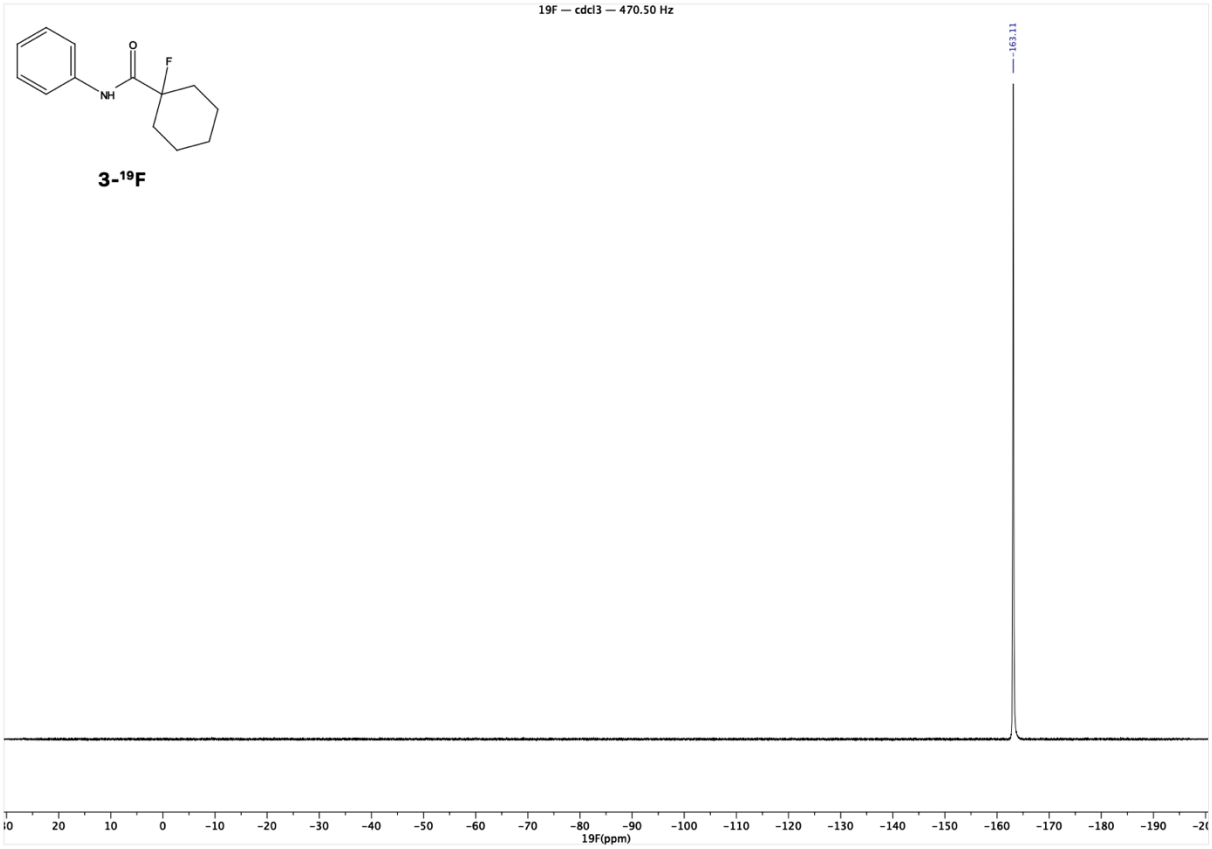

13C — cdcl3 — 125.57 Hz
2-19F
13C(ppm)

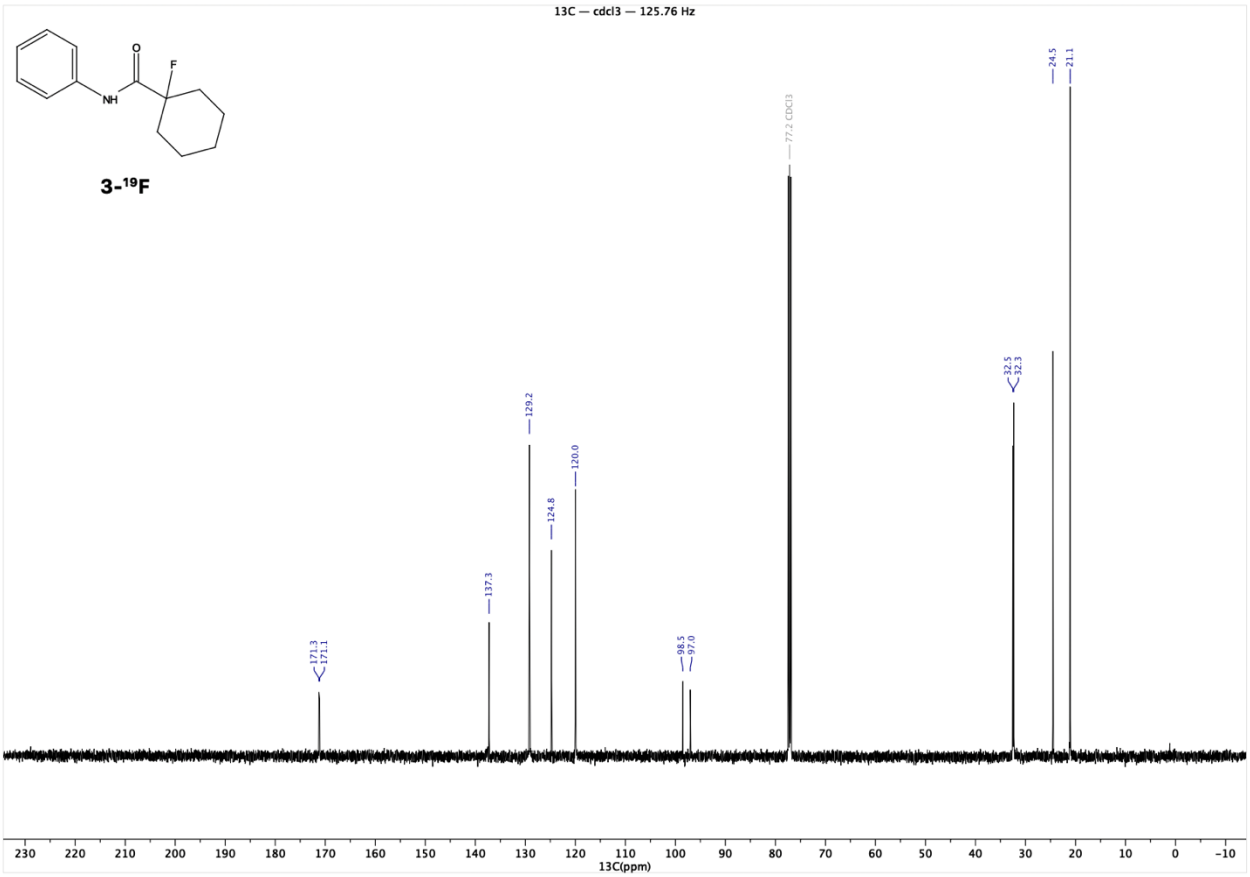

19F — cdcl3 — 469.79 Hz
2-19F
f1 (ppm)
19F(ppm)

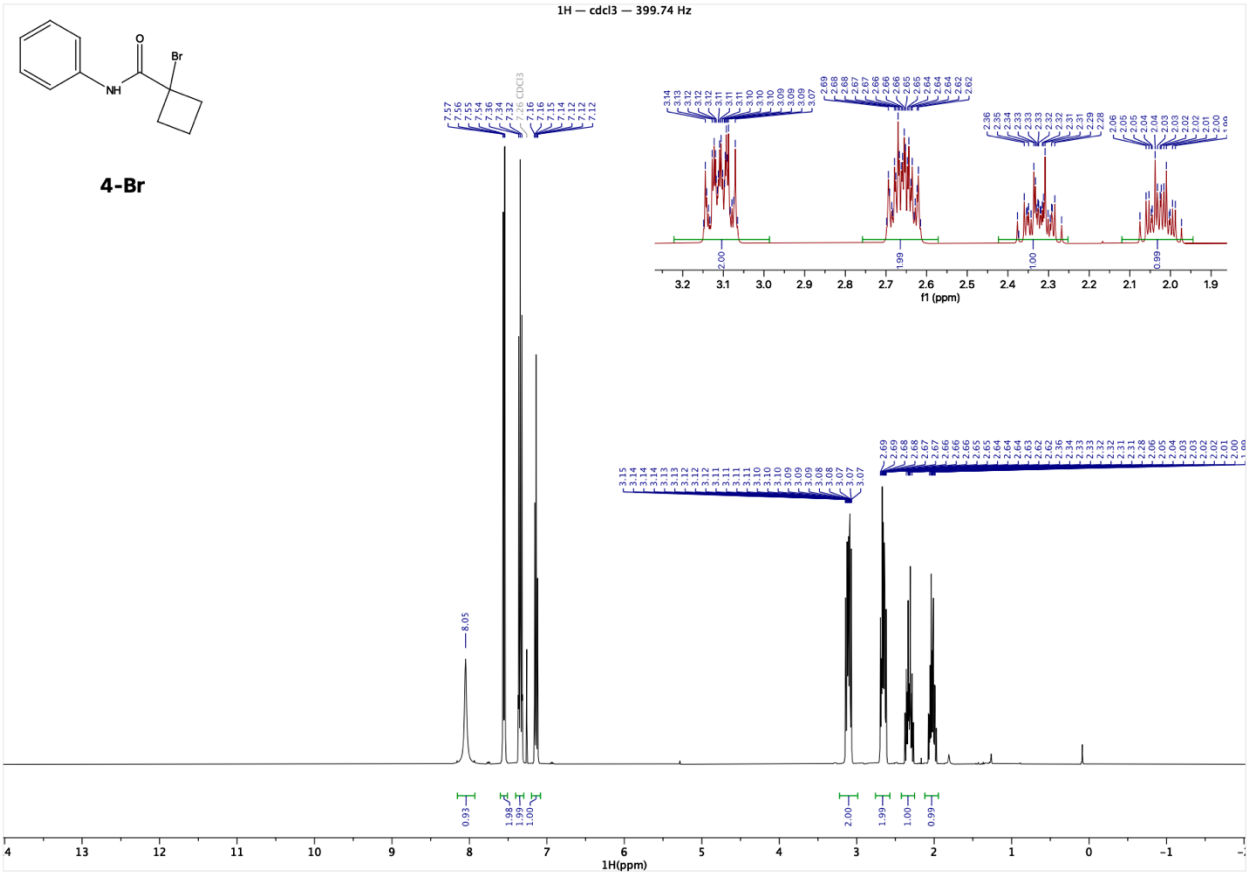

1H — cdcl3 — 399.74 Hz
3-Br
1H(ppm)

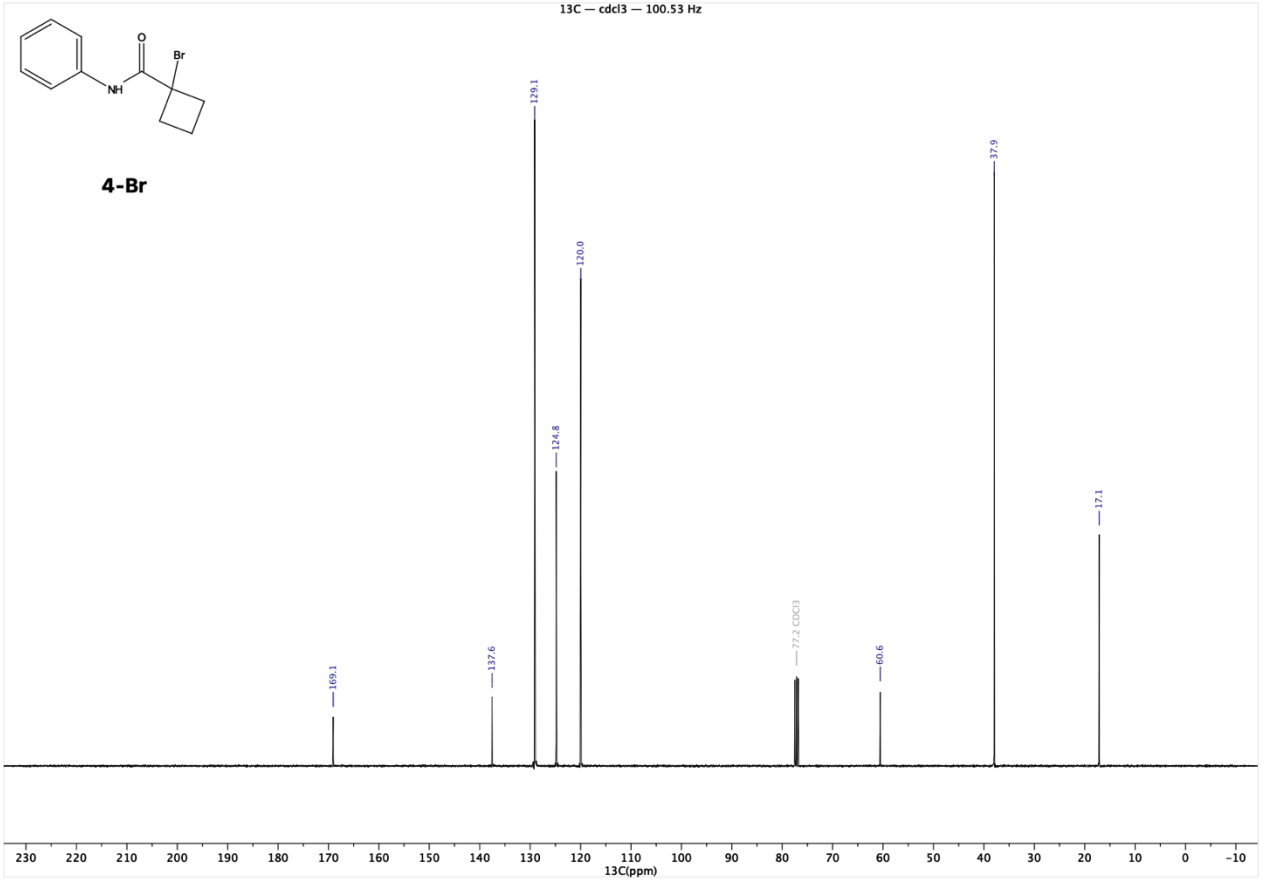

13C — cdcl3 — 100.53 Hz
3-Br
77.4
77.2 CDCl3
129.2
120.1
124.9
38.3
24.9
22.9
169.9
137.6
13C(ppm)

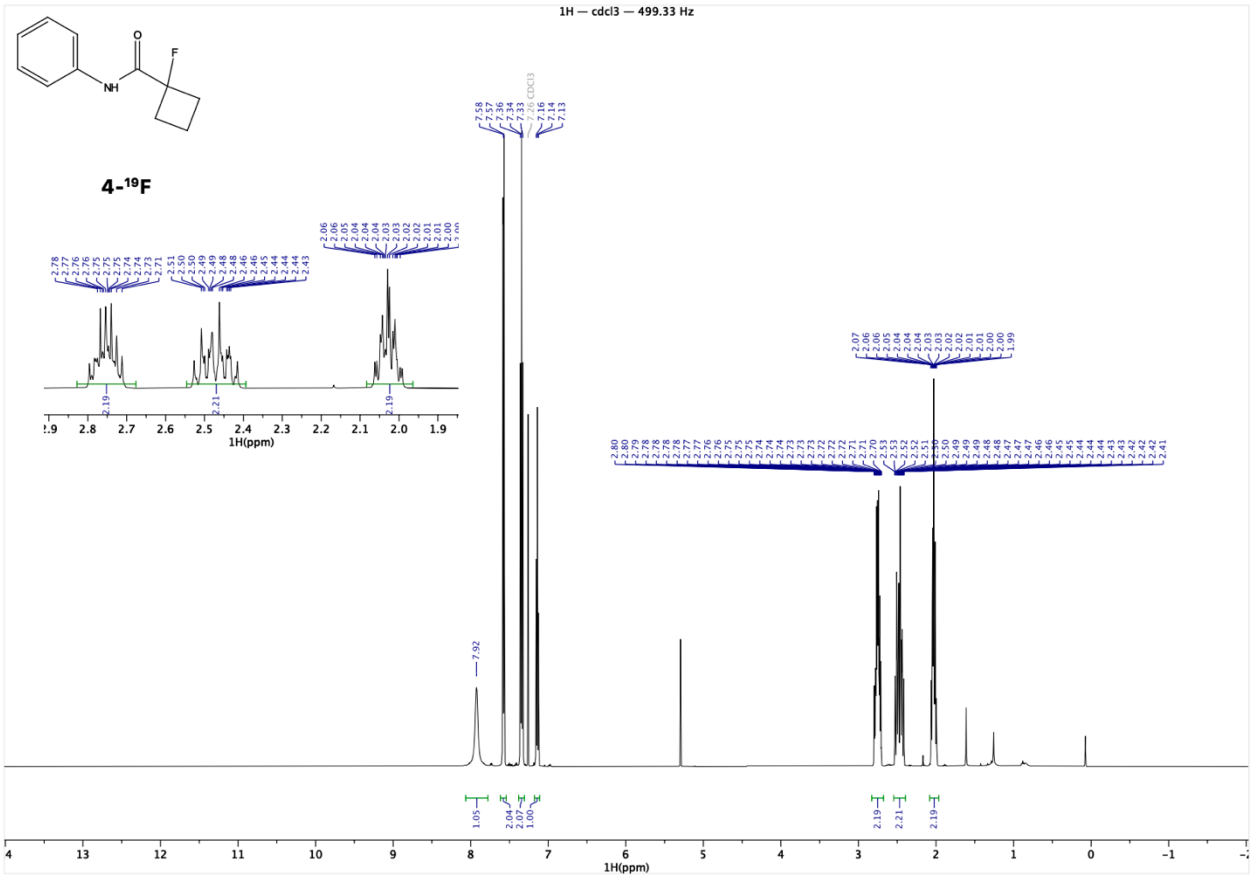

1H — cdcl3 — 500.08 Hz
3-19F
7.26 CDCl3
8.12
1H(ppm)

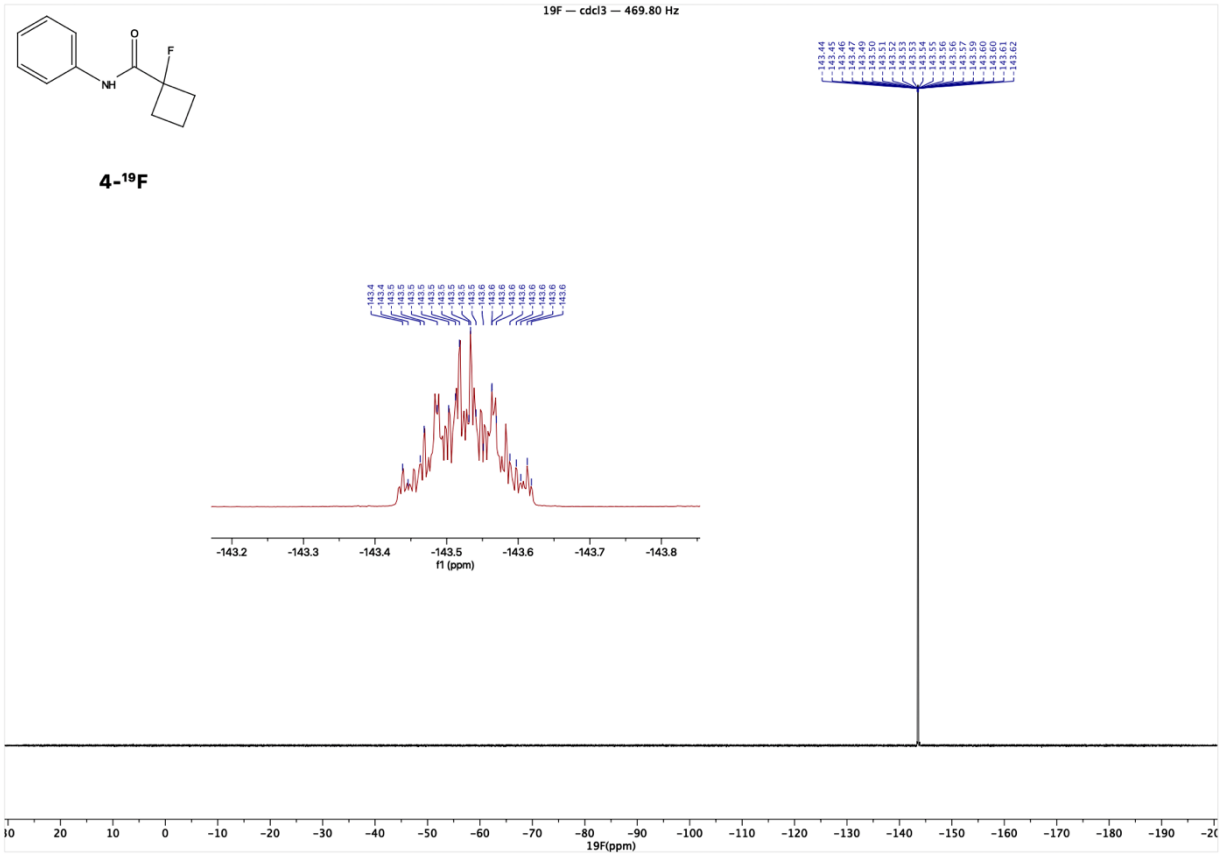

19F — cdcl3 — 470.50 Hz
-163.11
O
F
NH
3-19F
19F(ppm)

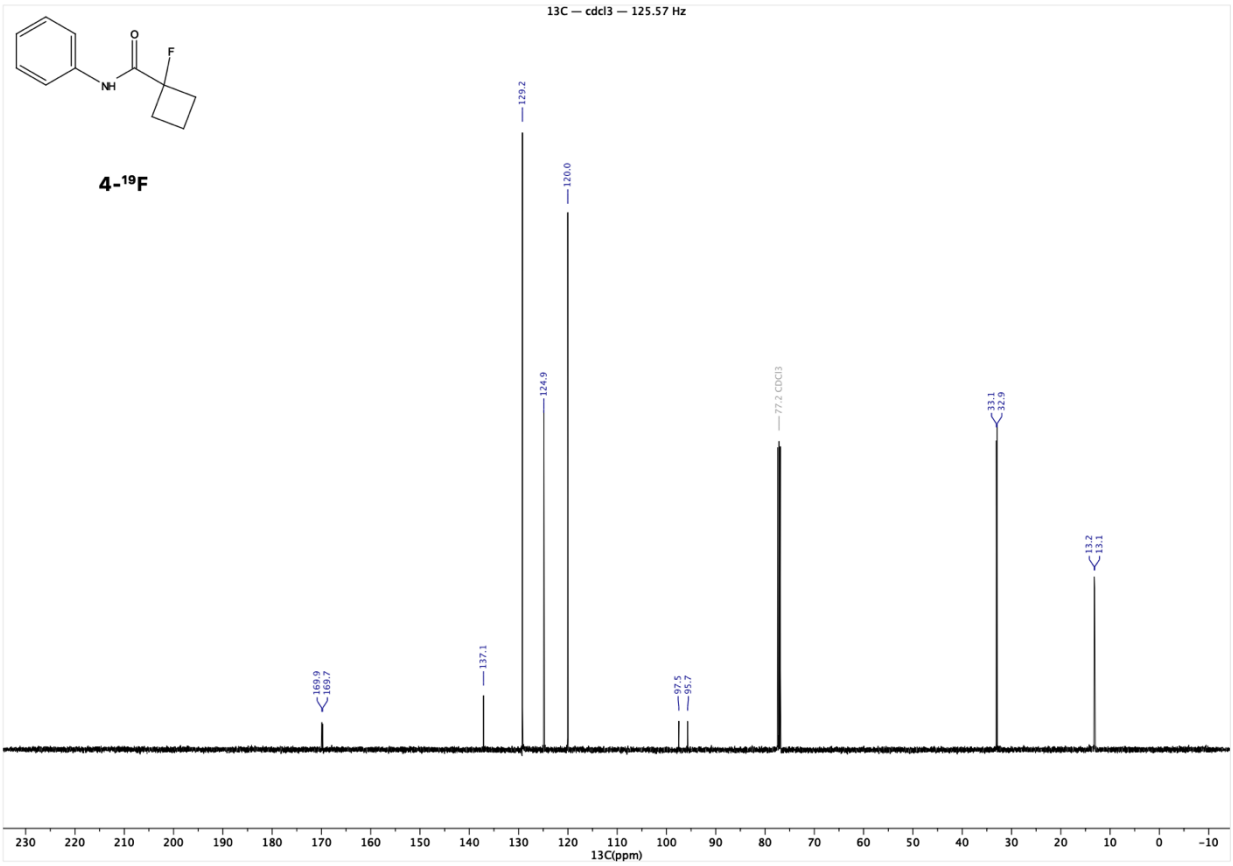

13C — cdcl3 — 125.76 Hz
O
F
NH
3-19F
171.3
171.1
137.3
129.2
124.8
120.0
98.5
97.0
77.2 CDCl3
32.5
32.3
24.5
21.1
13C(ppm)

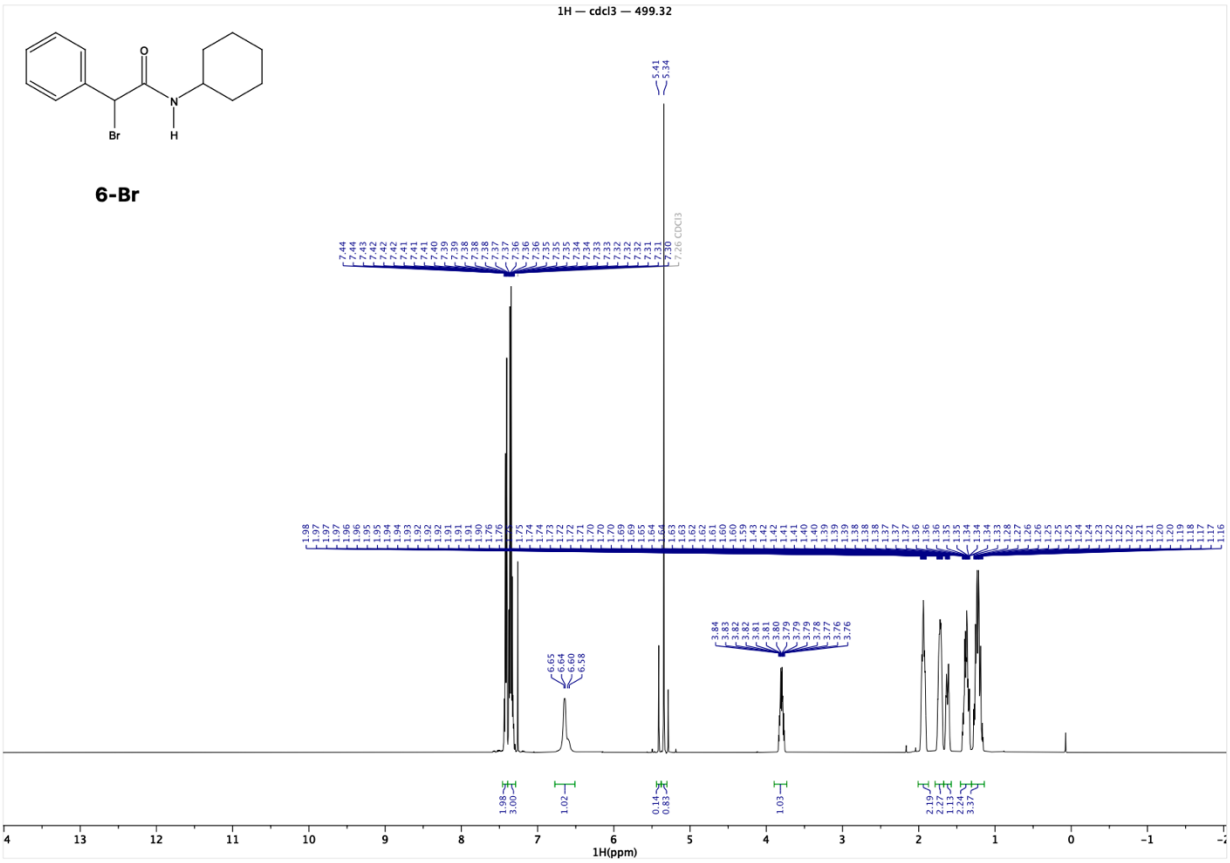

1H — cdcl3 — 399.74 Hz
4-Br
f1 (ppm)
1H(ppm)

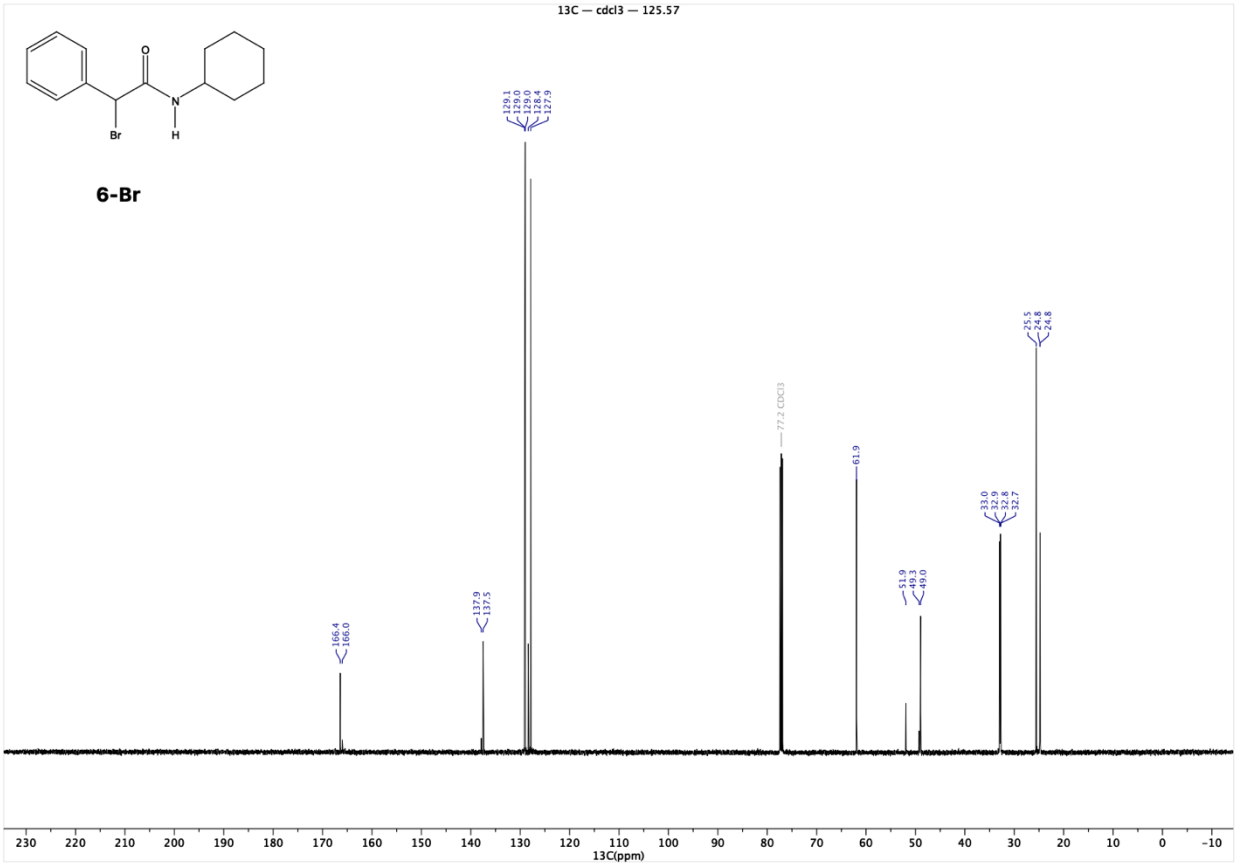

13C — cdcl3 — 100.53 Hz
4-Br
13C(ppm)

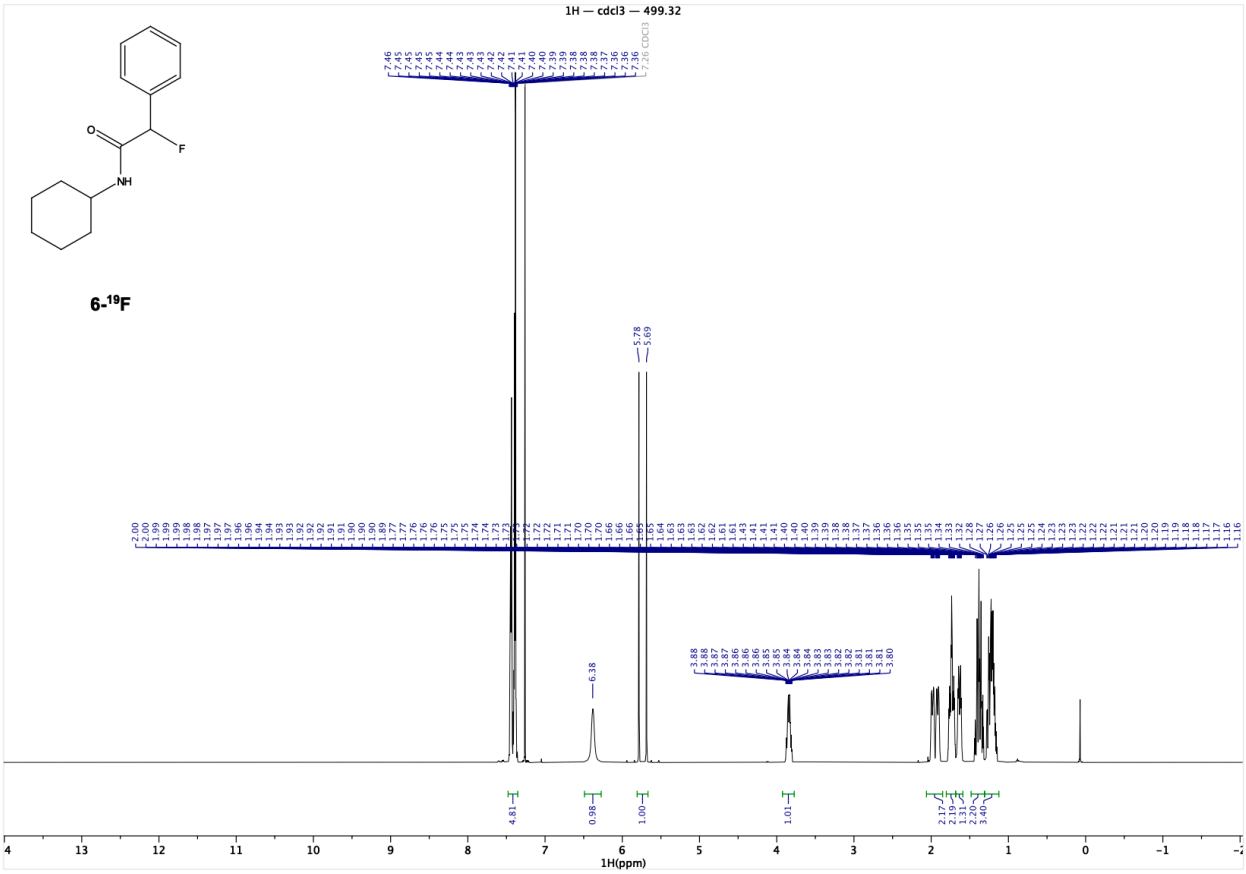

1H — cdcl3 — 499.33 Hz
4-19F
1H(ppm)

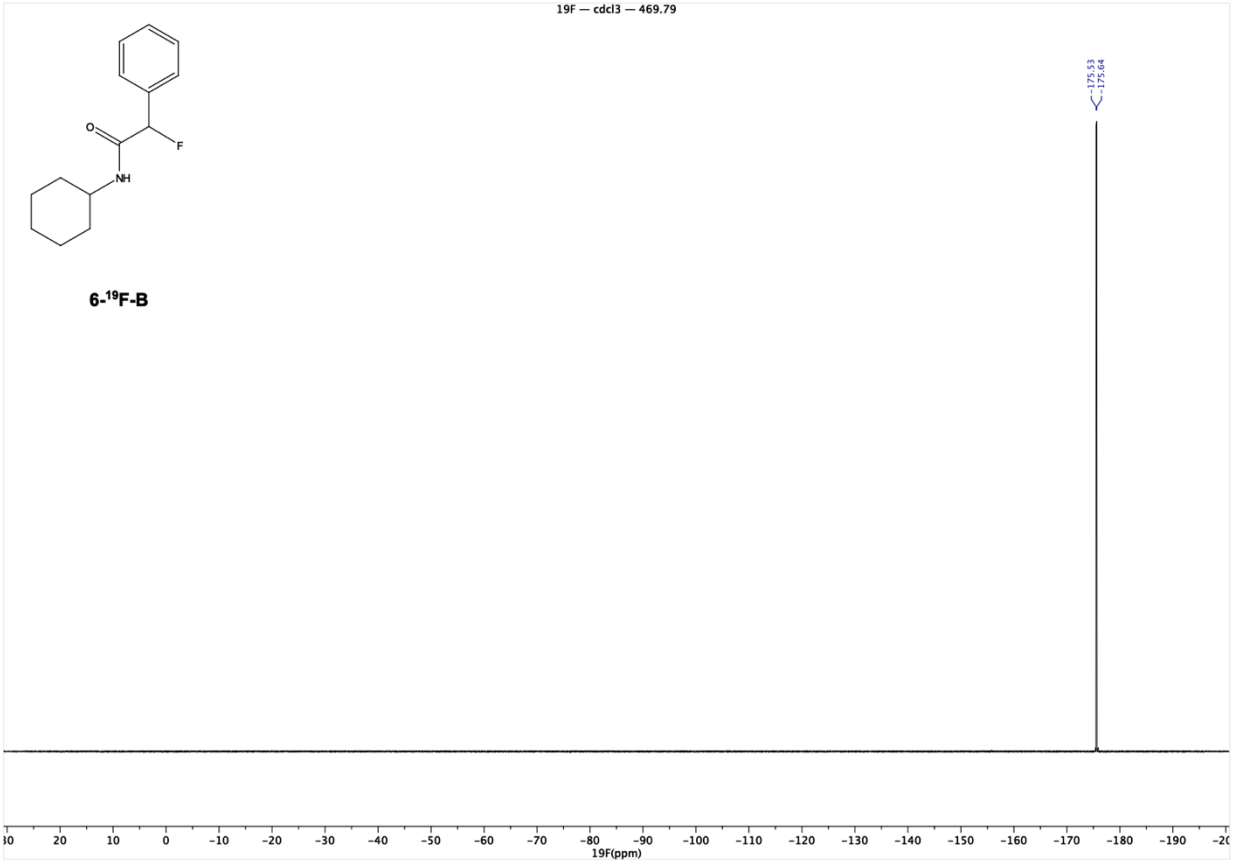

19F — cdcl3 — 469.80 Hz
4-19F
f1 (ppm)
19F(ppm)

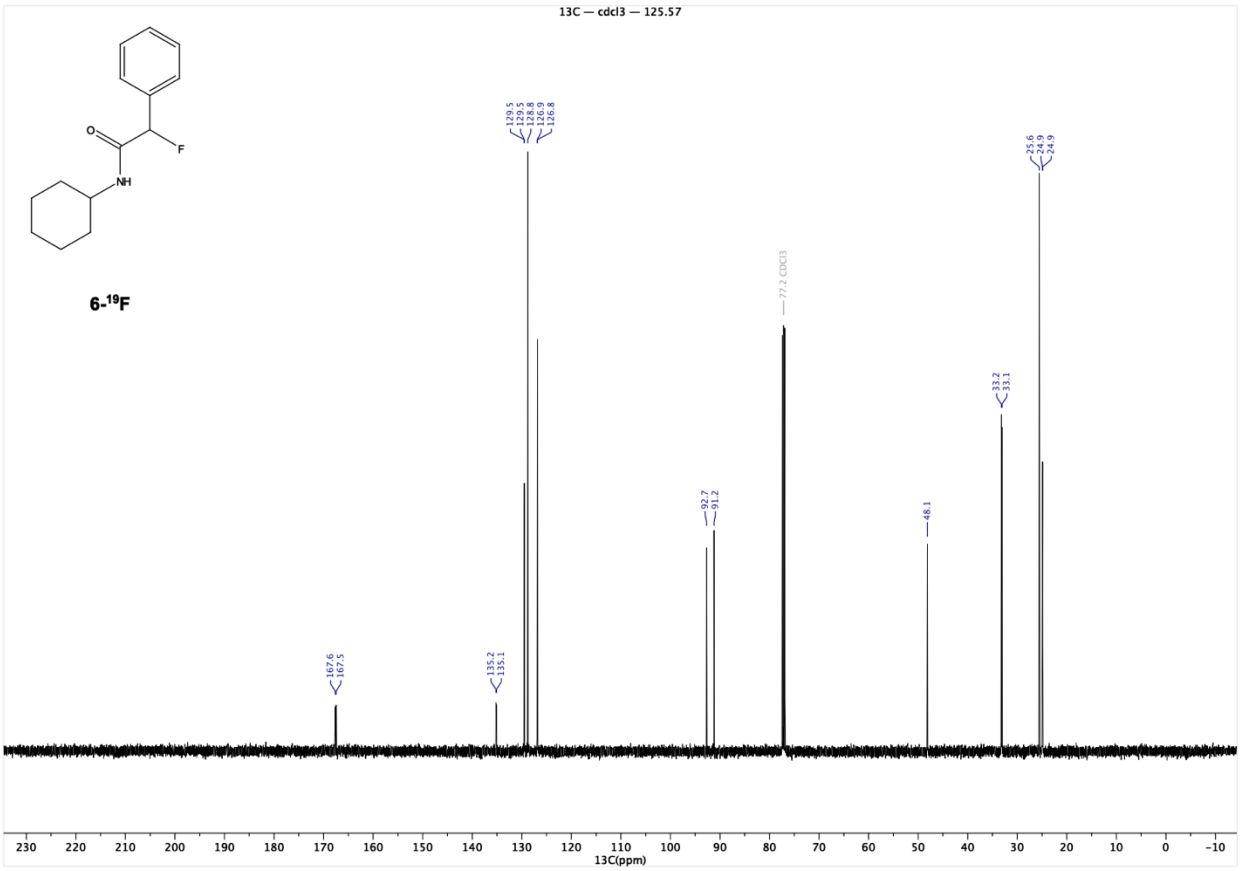

13C — cdcl3 — 125.57 Hz
4-19F
129.2
120.0
124.9
77.2 CDCl3
33.1
32.9
13.2
13.1
169.9
169.7
137.1
97.5
95.7
13C(ppm)

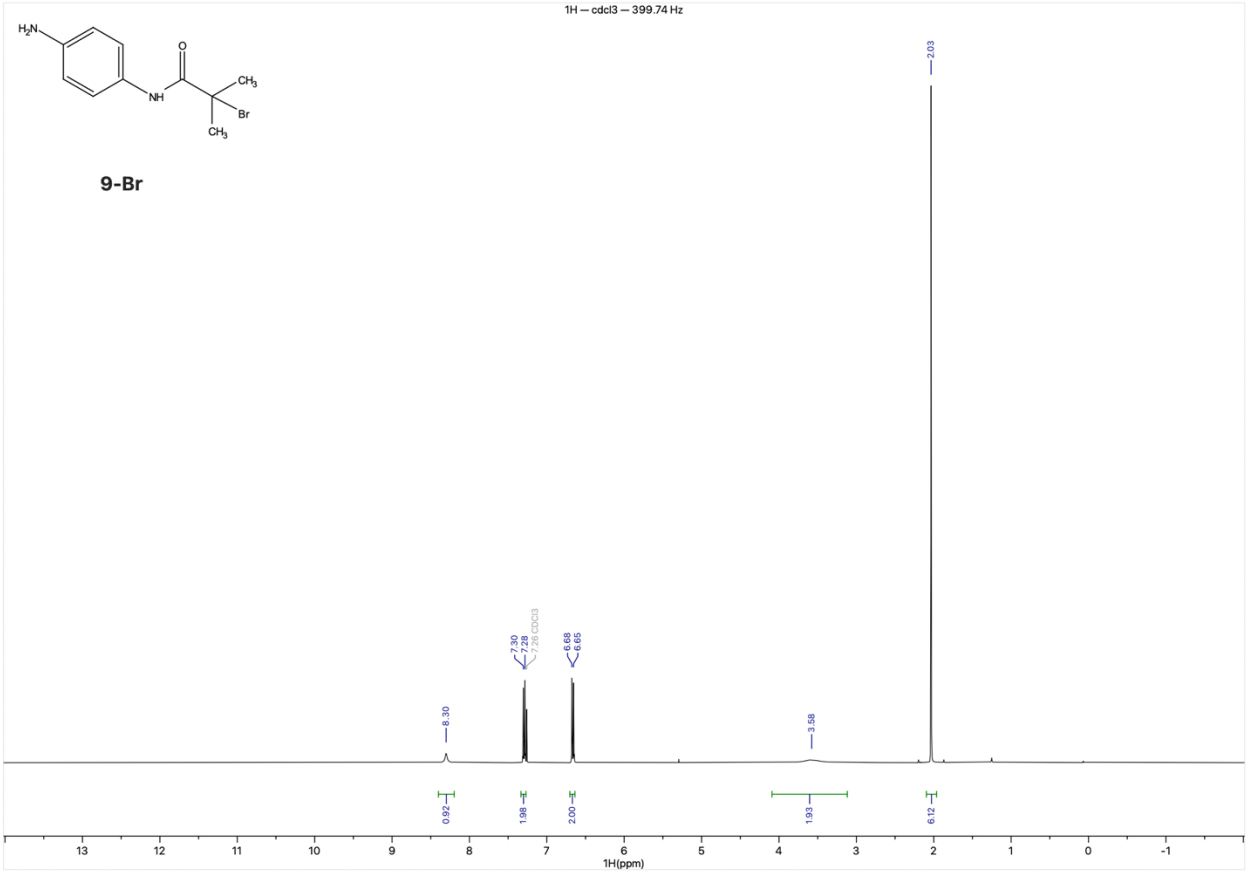

1H — cdcl3 — 499.32
6-Br
5.41
5.34
7.26 CDCl3
6.65
6.64
6.60
6.58
1.98
3.00
1.02
0.14
0.83
1.03
2.19
2.27
1.13
2.14
3.37
1H(ppm)

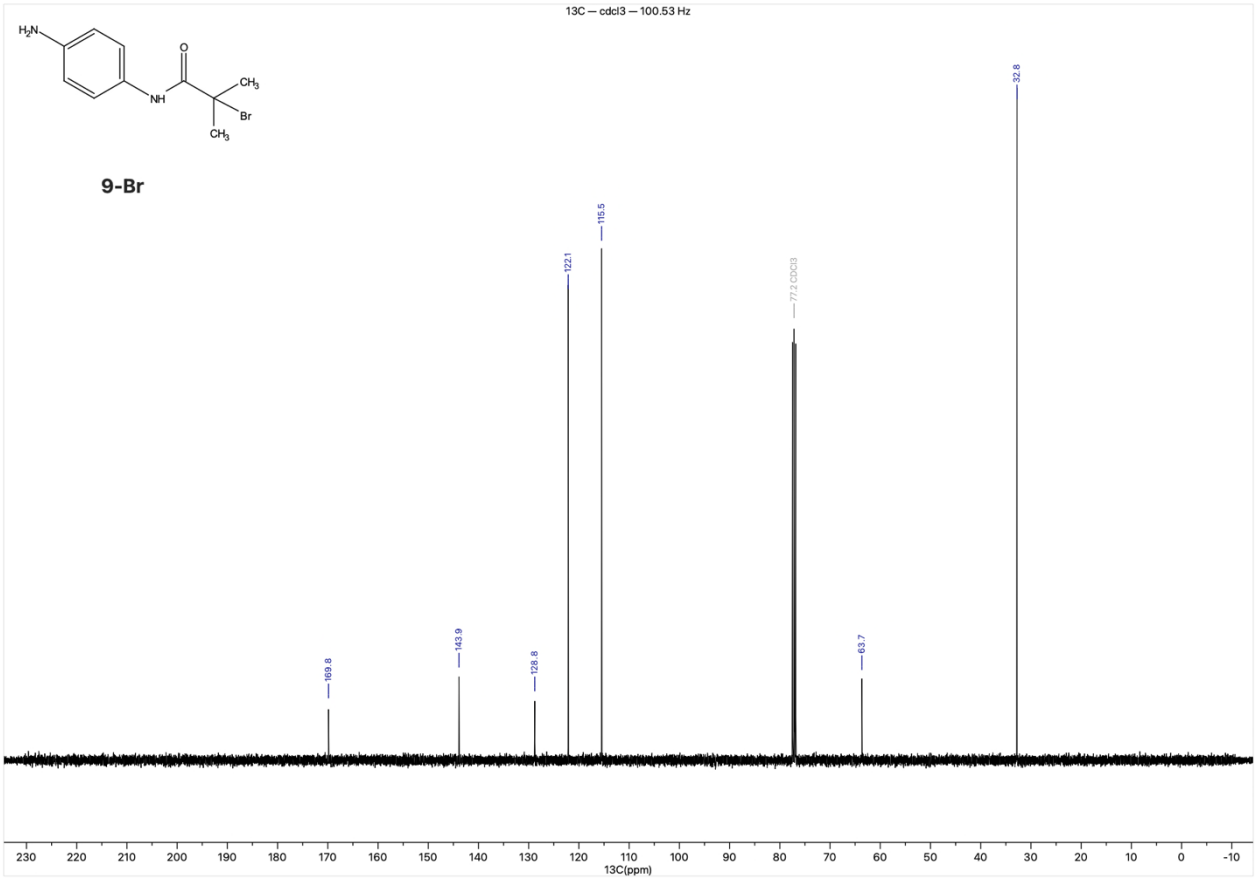

13C — cdcl3 — 125.57
6-Br
13C(ppm)

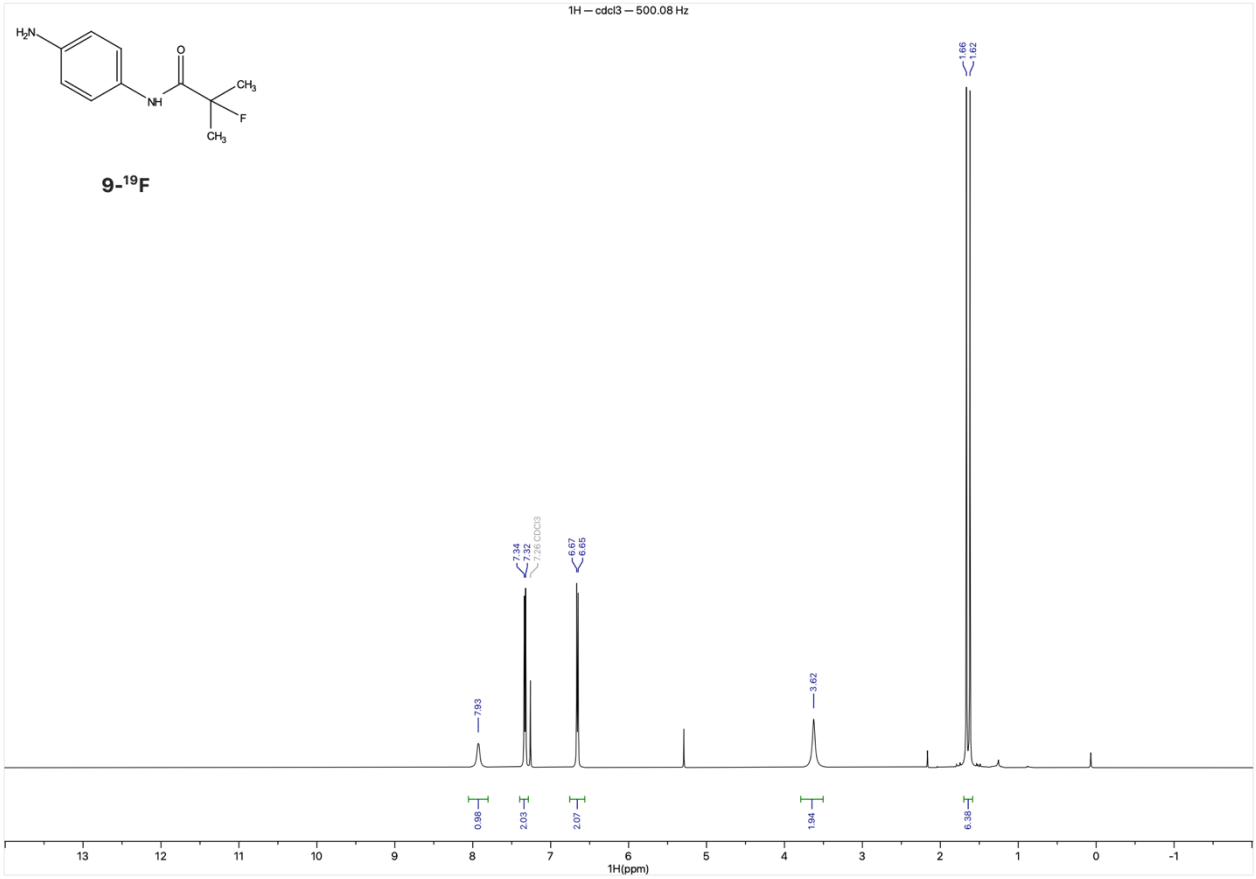

1H — cdcl3 — 499.32
6-19F
1H(ppm)

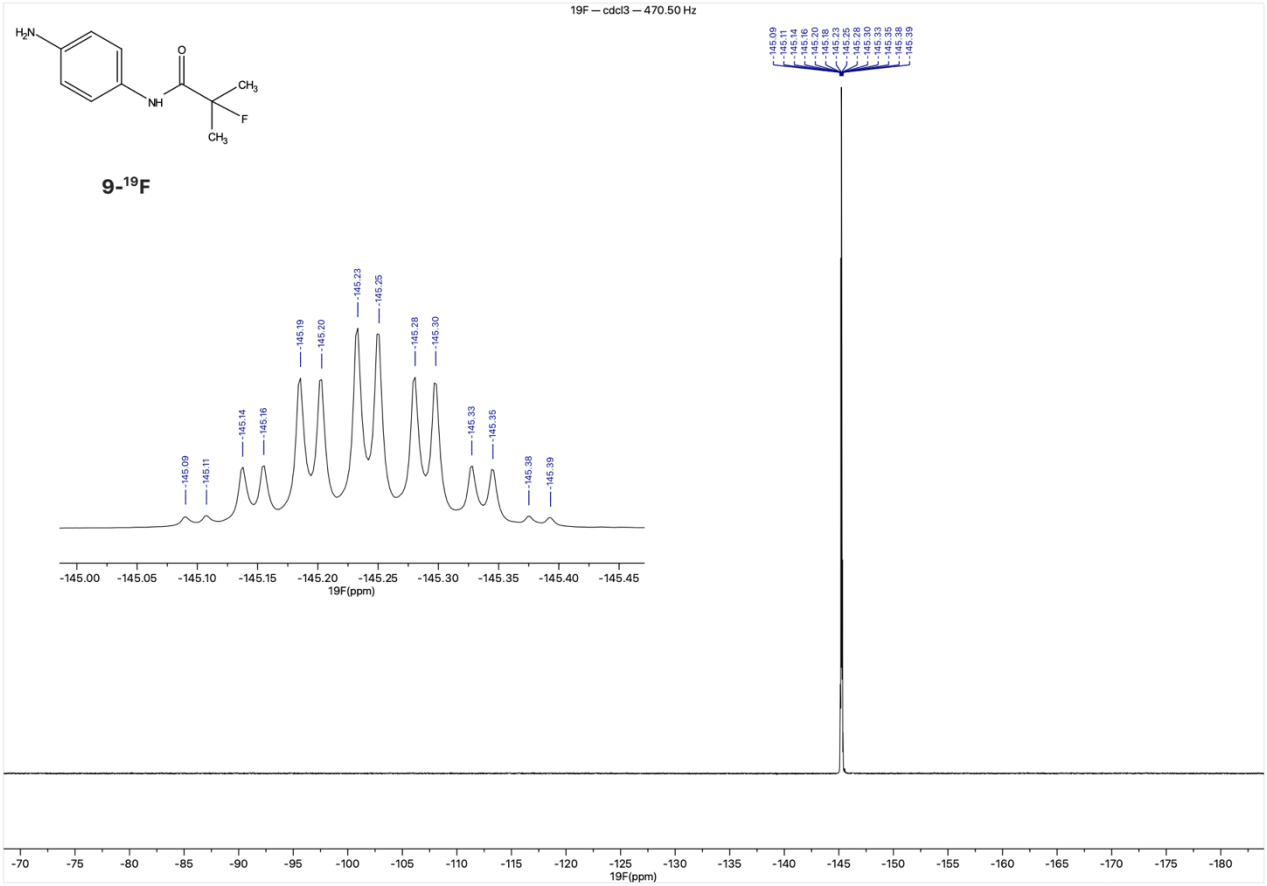

19F — cdcl3 — 469.79
O
F
NH
6-19F-B
175.53
175.64
19F(ppm)

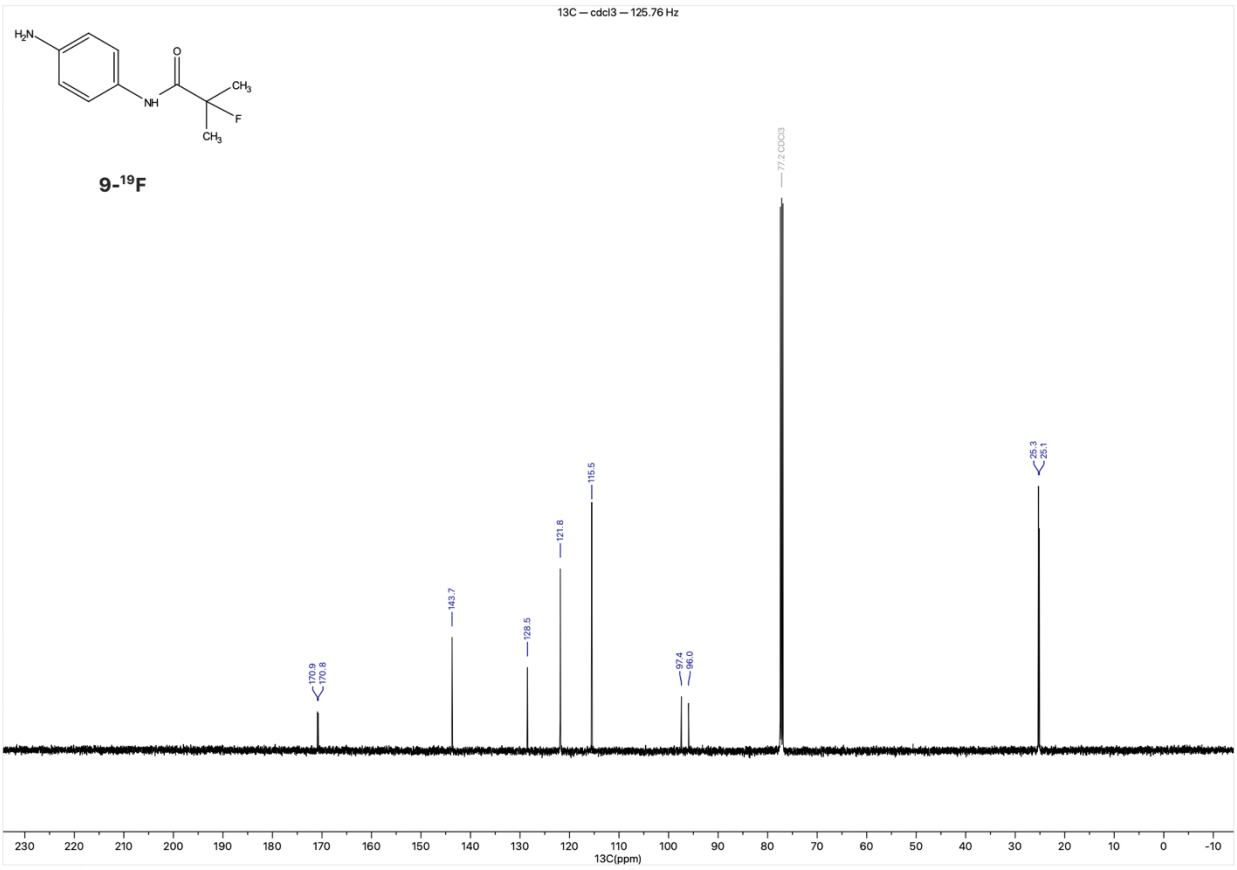

13C — cdcl3 — 125.57
O
F
NH
6-19F
129.5
129.5
128.8
126.9
126.8
77.2 CDCl3
92.7
91.2
48.1
33.2
33.1
25.6
24.9
24.9
167.6
167.5
135.2
135.1
13C(ppm)

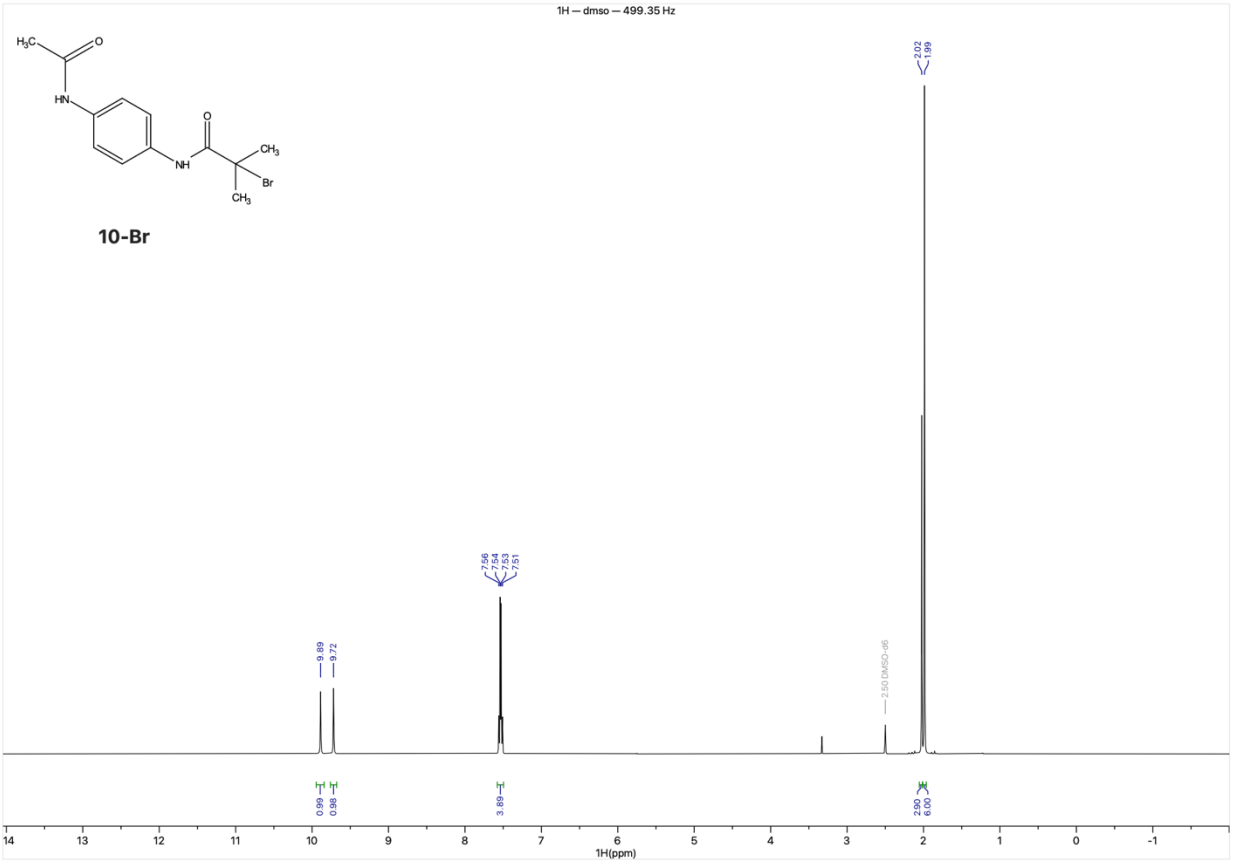

1H — cdcl3 — 399.74 Hz
9-Br
2.03
7.30
7.28
7.26 CDCl3
6.68
6.66
8.30
3.58
0.92
1.98
2.00
1.93
6.12
1H(ppm)

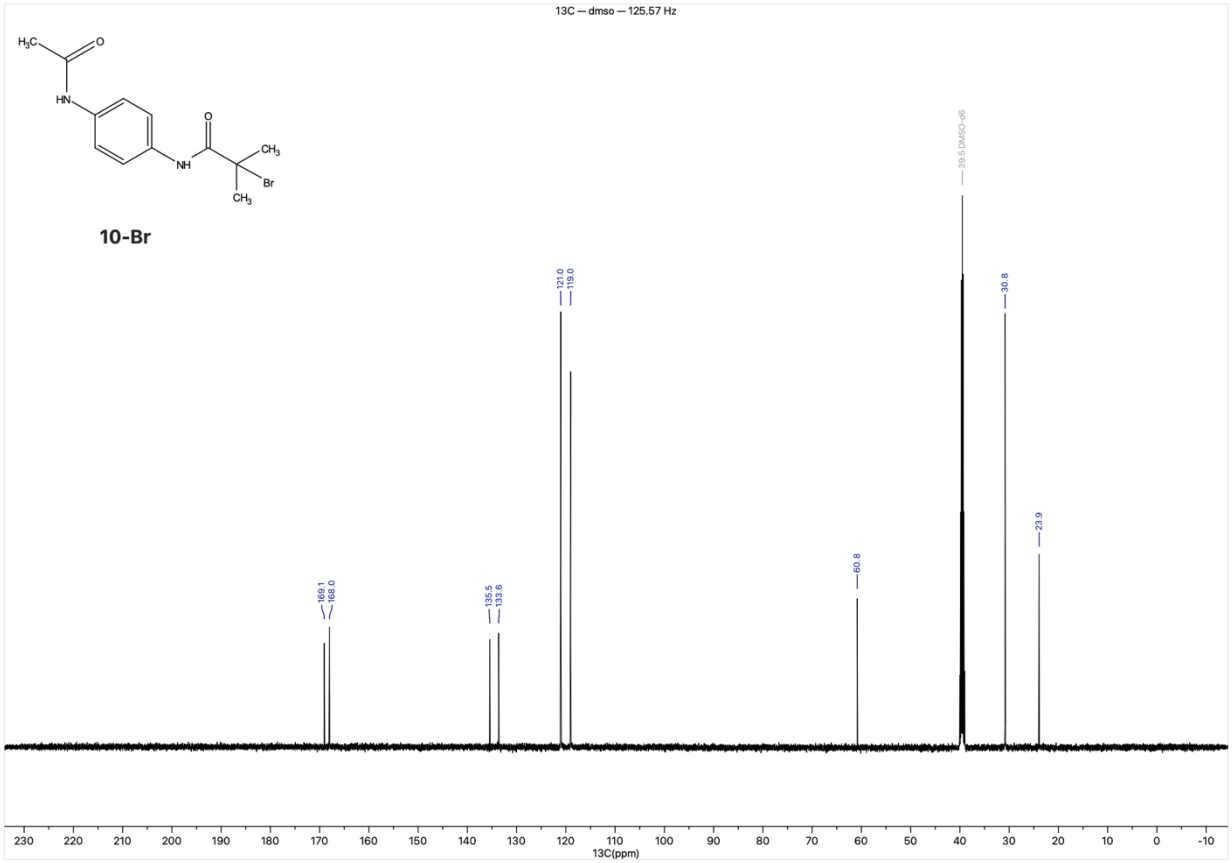

13C — cdcl3 — 100.53 Hz
9-Br
32.8
115.5
122.1
77.2 CDCl3
169.8
143.9
128.8
63.7
13C(ppm)

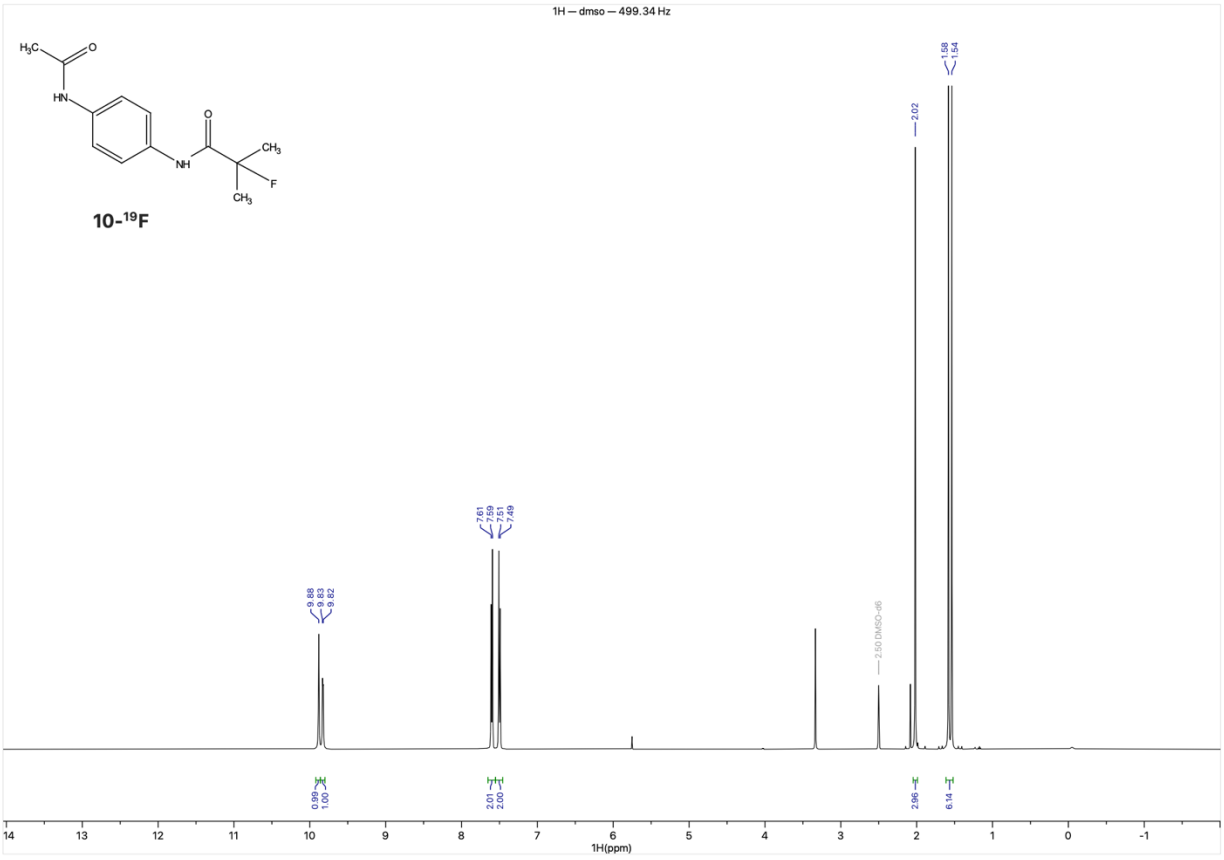

1H — cdcl3 — 500.08 Hz
9-19F
7.93
7.34
7.32
7.26 CDCl3
6.67
6.65
3.62
1.66
1.62
0.98
2.03
2.07
1.94
6.38
1H(ppm)

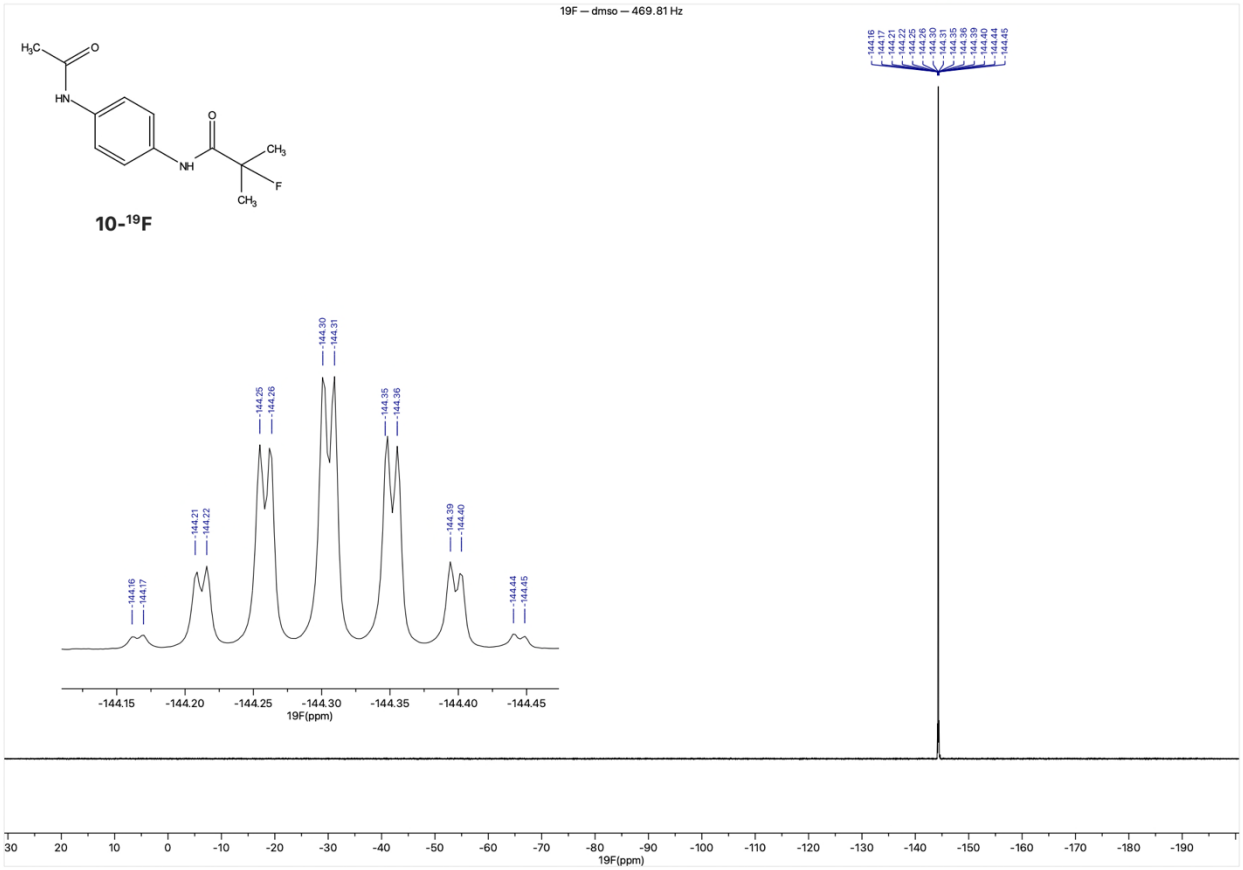

19F — cdcl3 — 470.50 Hz
9-19F
-145.09
-145.11
-145.14
-145.16
-145.19
-145.20
-145.23
-145.25
-145.28
-145.30
-145.33
-145.35
-145.38
-145.39
19F(ppm)

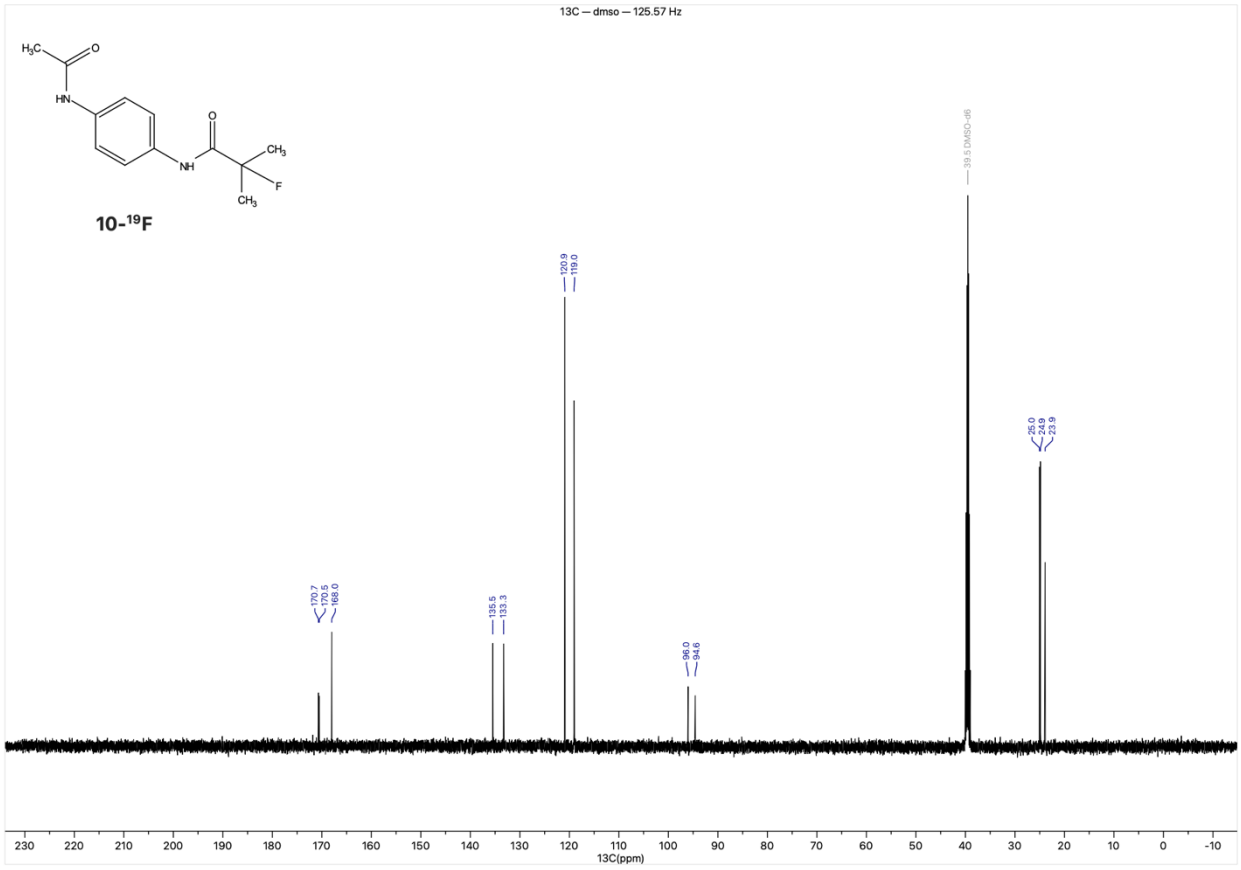

13C — cdcl3 — 125.76 Hz
H2N
O
NH
CH3
F
CH3
9-19F
77.2 CDCl3
170.9
170.8
143.7
128.5
121.8
115.5
97.4
96.0
25.3
25.1
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
13C(ppm)

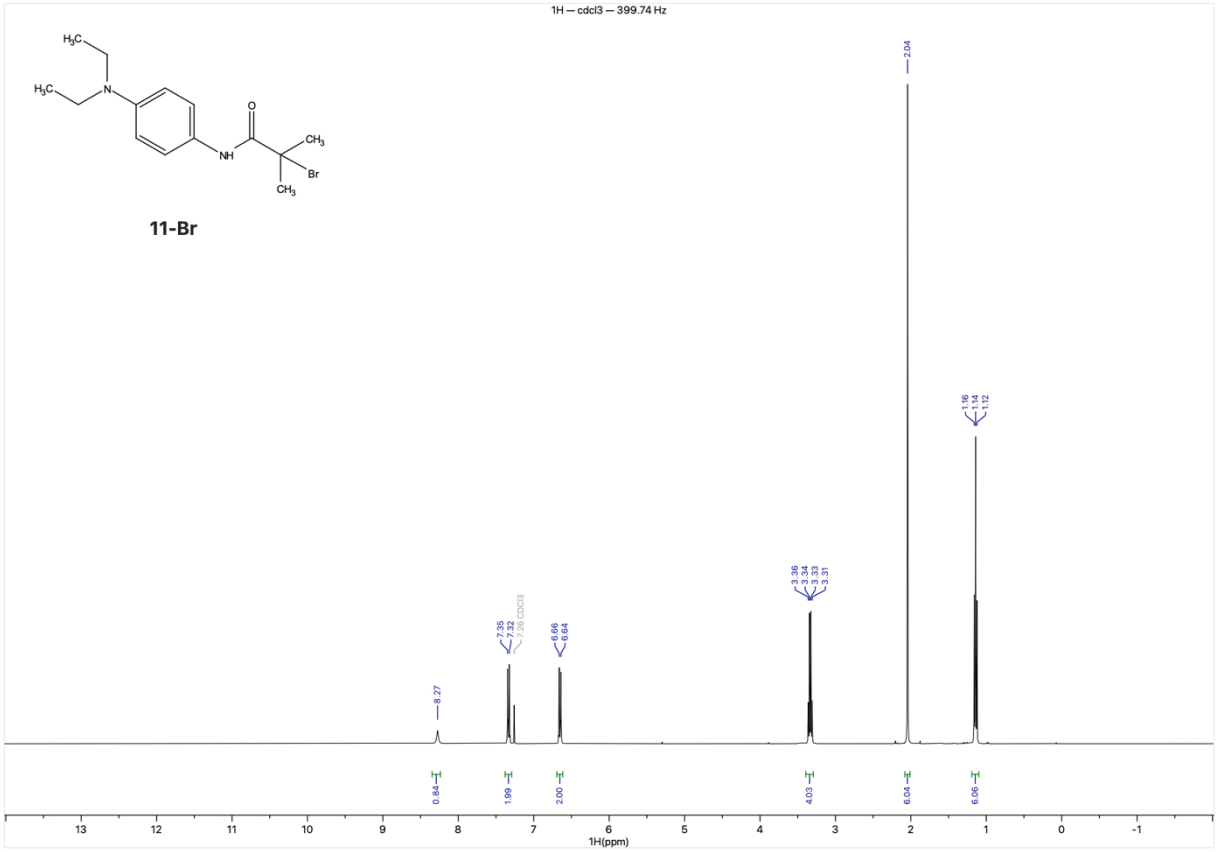

1H — dmso — 499.35 Hz
H3C
O
HN
O
NH
CH3
Br
CH3
10-Br
2.02
1.99
7.56
7.54
7.53
7.51
9.89
9.72
2.50 DMSO-d6
0.99
0.98
3.89
2.90
6.00
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
1H(ppm)

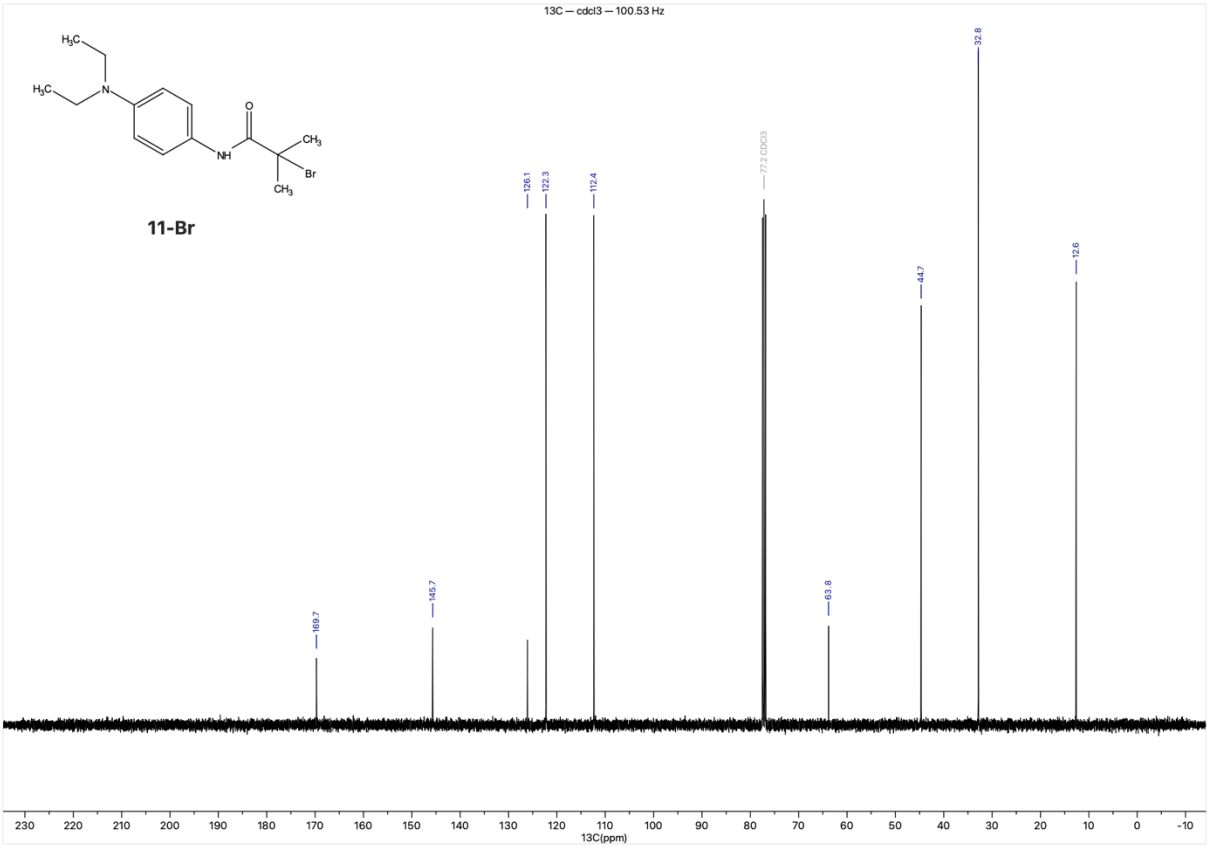

13C — dmso — 125.57 Hz
10-Br
169.1
168.0
135.5
133.6
121.0
119.0
60.8
39.5 DMSO-d6
30.8
23.9
13C(ppm)

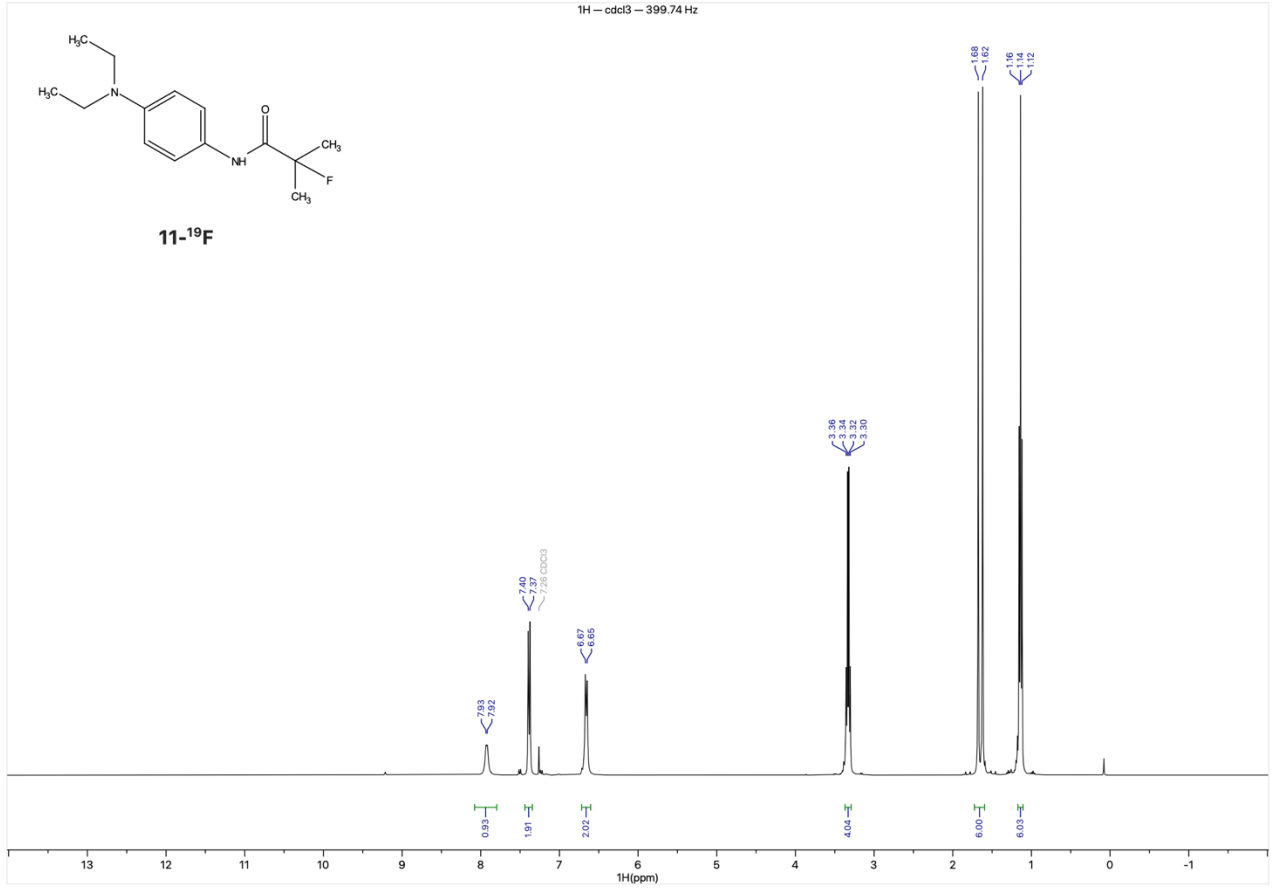

1H — dmso — 499.34 Hz
10-19F
9.88
9.83
9.82
7.61
7.59
7.51
7.49
2.50 DMSO-d6
2.02
1.58
1.54
0.99
1.00
2.01
2.00
2.96
6.14
1H(ppm)

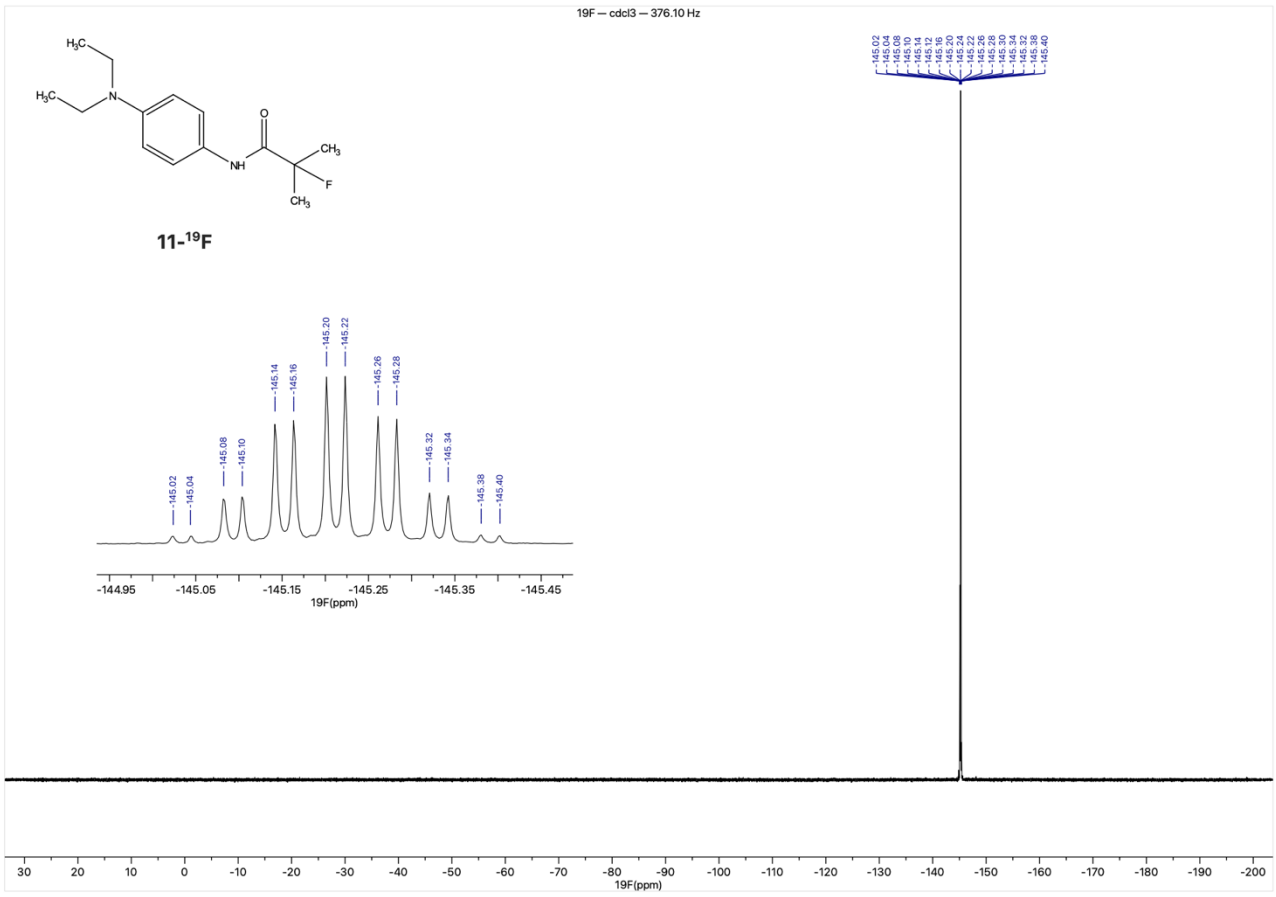

19F — dmso — 469.81 Hz
10-19F
19F(ppm)

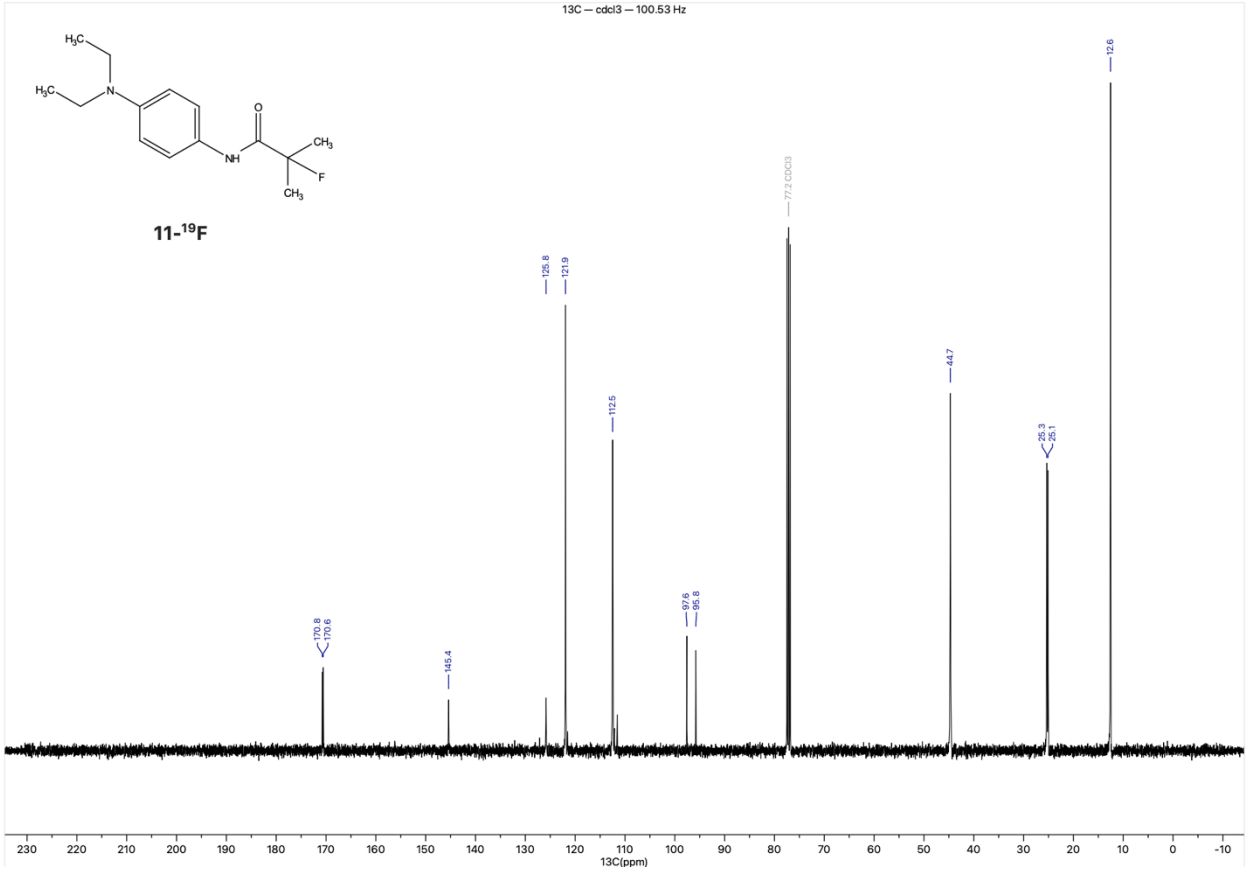

13C — dmso — 125.57 Hz
10-19F
13C(ppm)

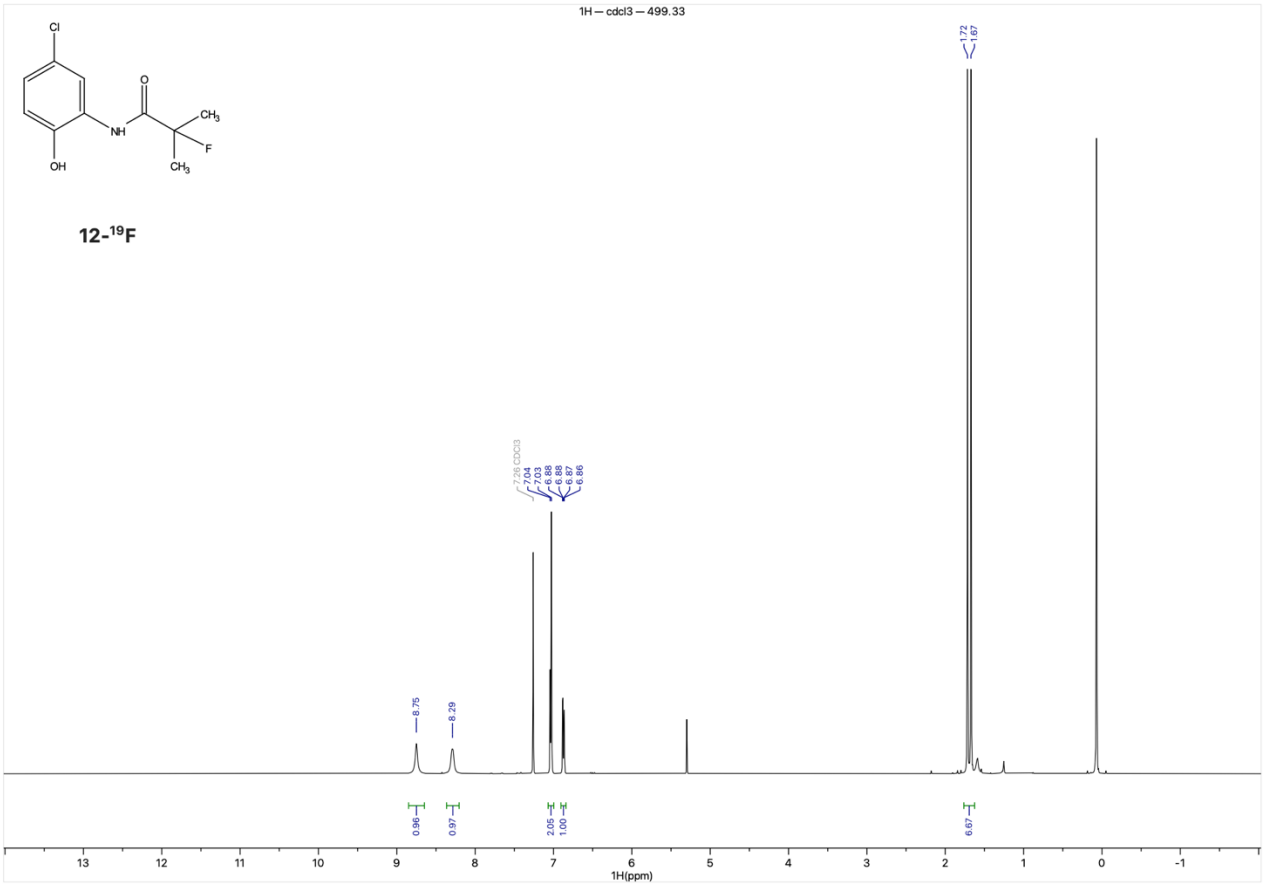

1H — cdcl3 — 399.74 Hz
11-Br
8.27
7.35
7.33
7.24 CDCl3
6.66
6.64
3.36
3.34
3.33
3.31
2.04
1.16
1.14
1.12
0.84
1.99
2.00
4.03
6.04
6.06
1H(ppm)

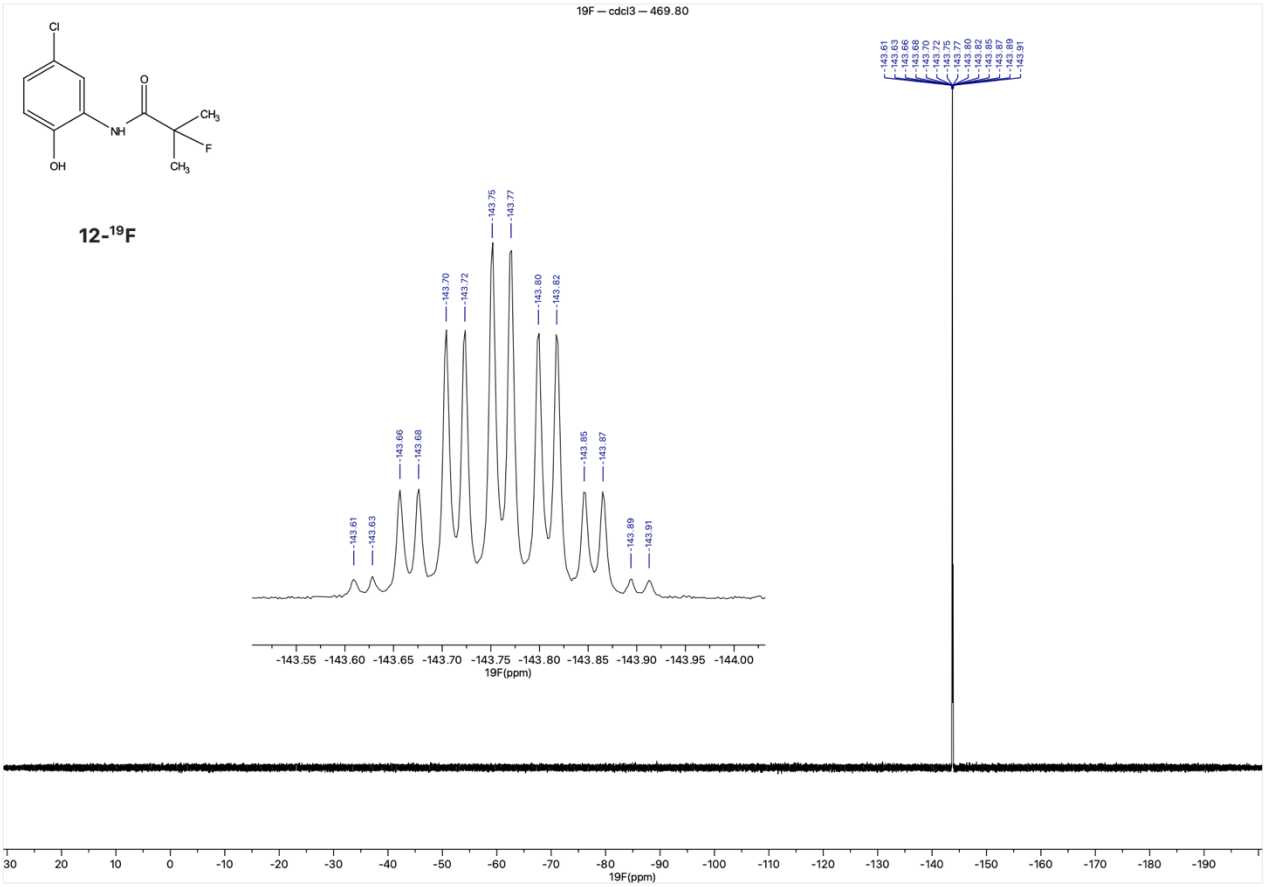

13C — cdcl3 — 100.53 Hz
11-Br
169.7
145.7
126.1
122.3
112.4
77.2 CDCl3
63.8
44.7
32.8
12.6
13C(ppm)

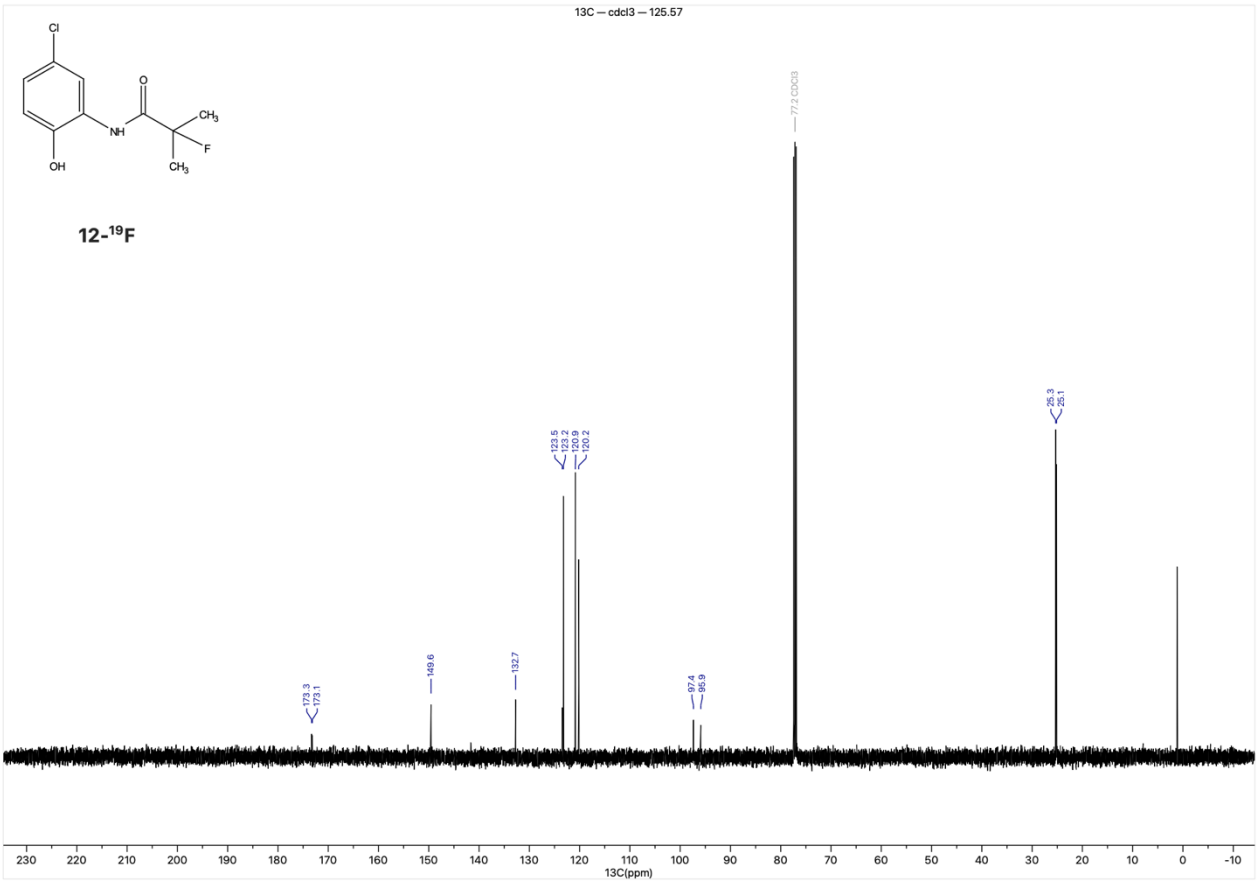

1H — cdcl3 — 399.74 Hz
11-19F
1H(ppm)

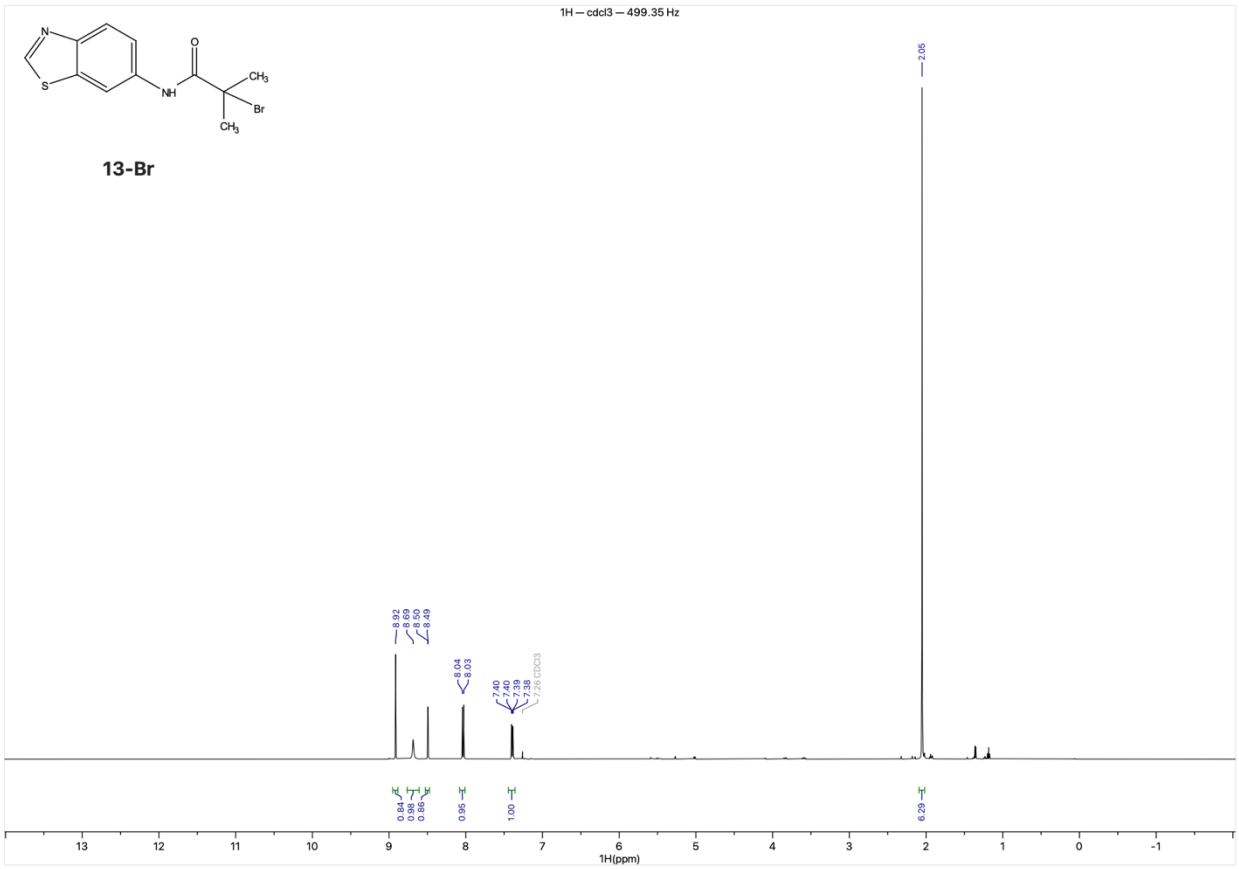

19F — cdcl3 — 376.10 Hz
11-19F
19F(ppm)

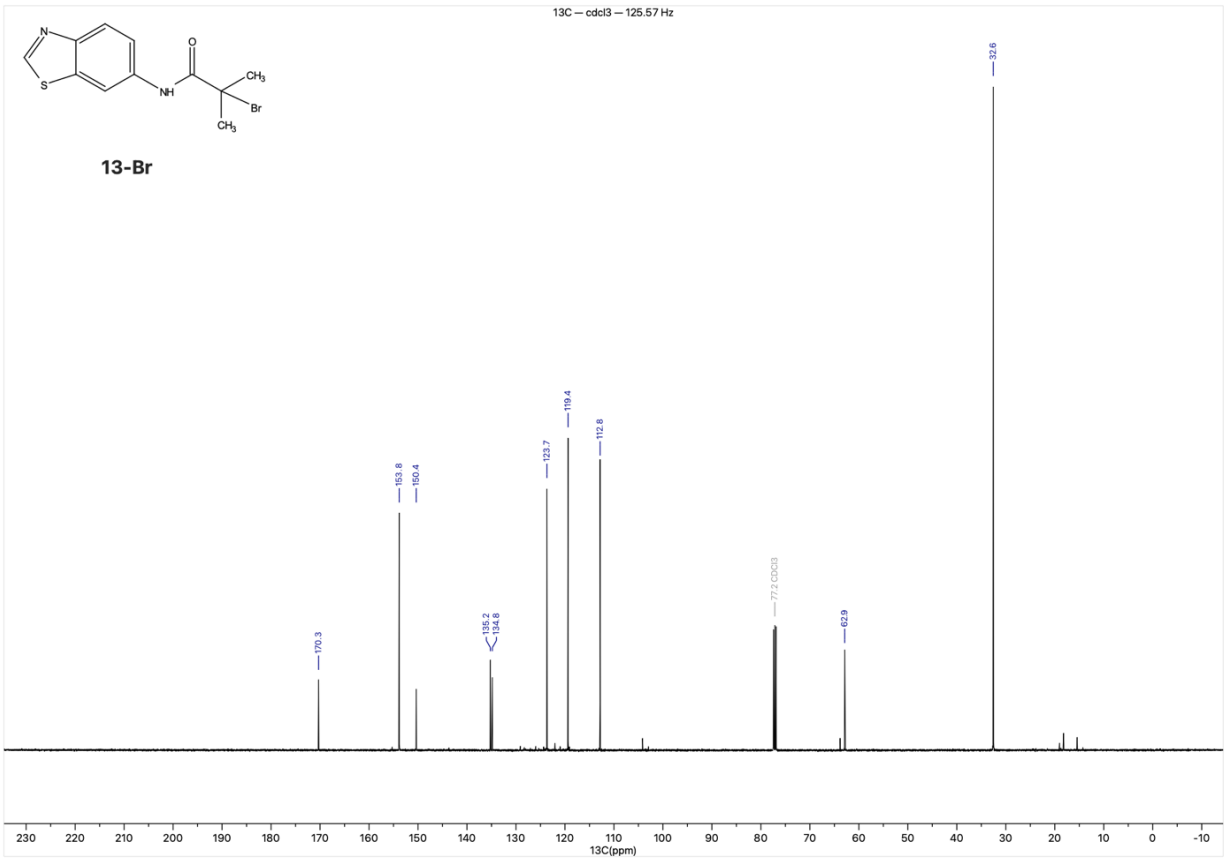

13C — cdcl3 — 100.53 Hz
11-19F
170.8
170.6
145.4
125.8
121.9
112.5
97.6
95.8
77.2 CDCl3
44.7
25.3
25.1
12.6
13C(ppm)

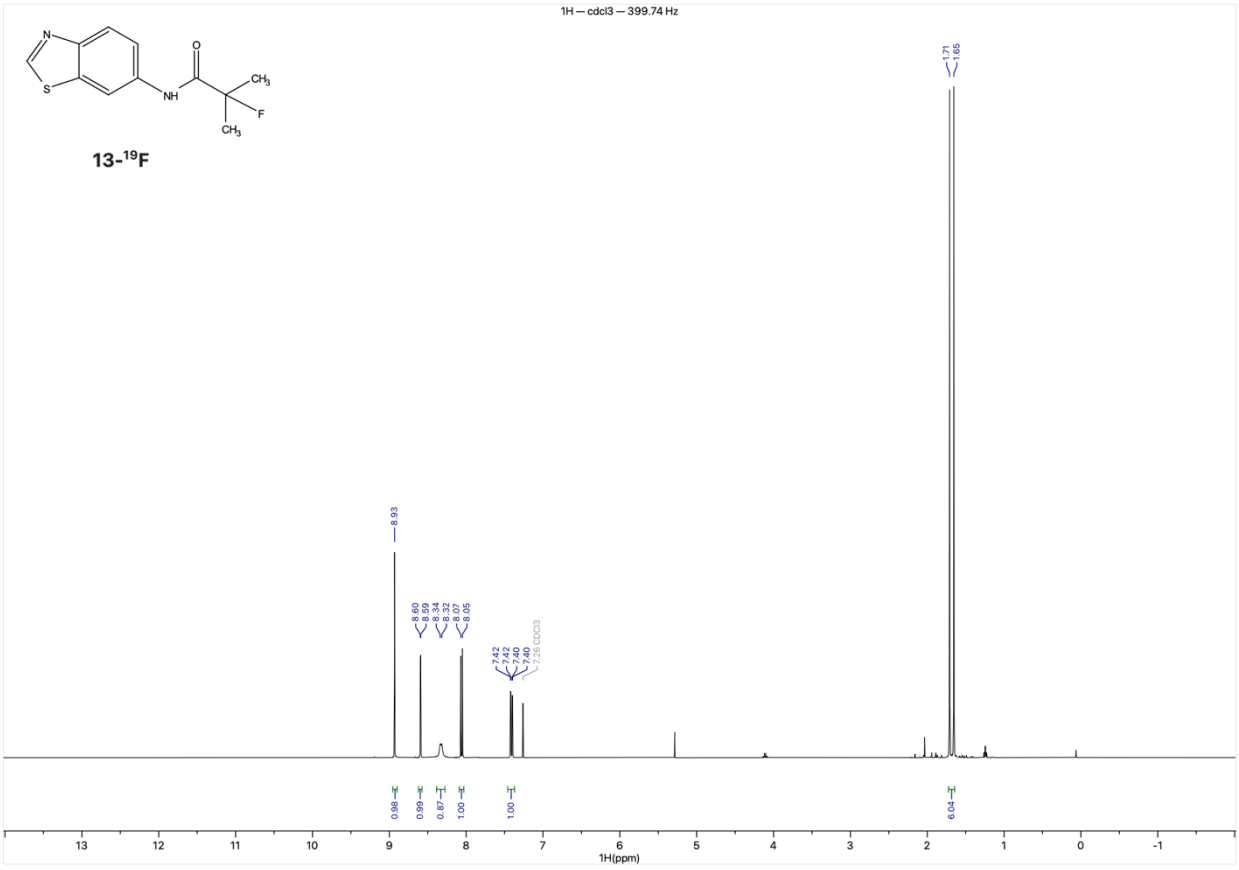

1H — cdcl3 — 499.33
12-19F
8.75
8.29
7.26 CDCl3
7.04
7.03
6.88
6.88
6.87
6.86
1.72
1.67
0.96
0.97
2.05
1.00
6.67
1H(ppm)

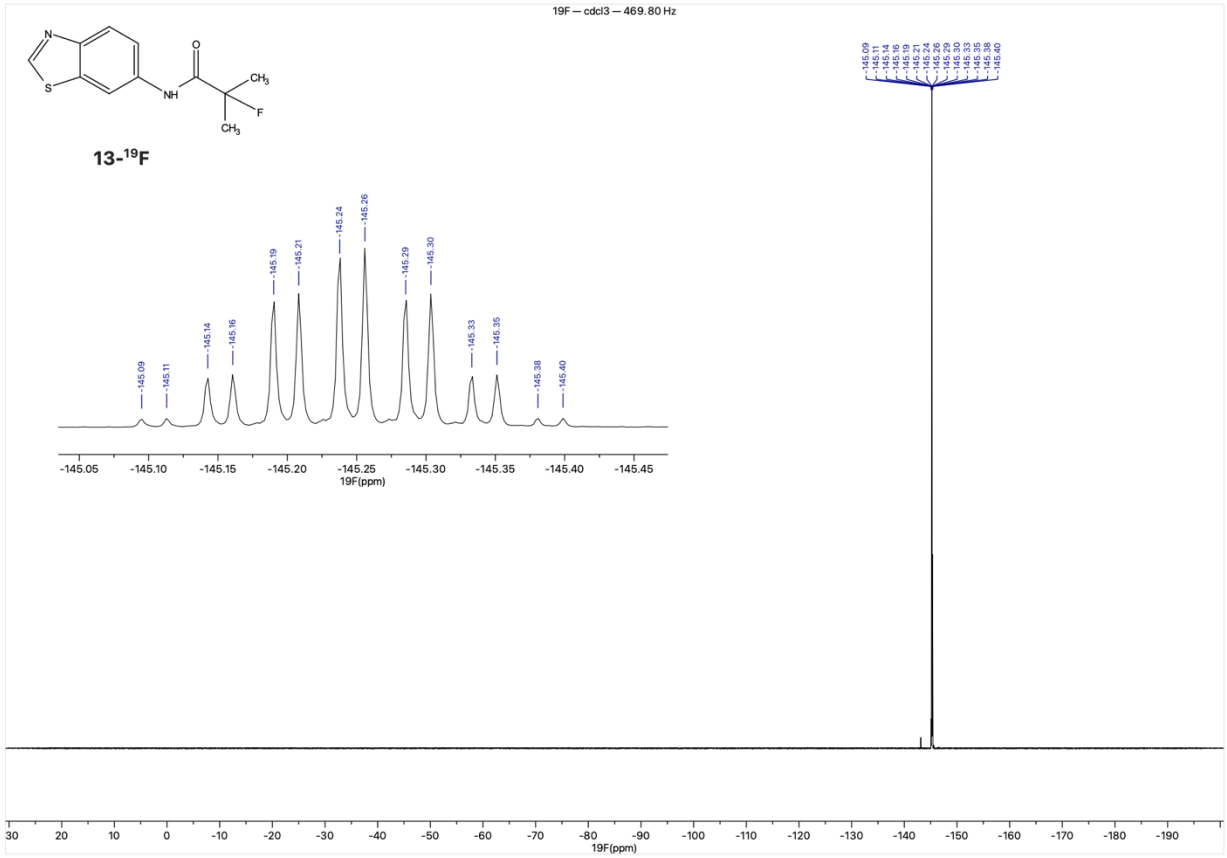

19F — cdcl3 — 469.80
Cl
NH
O
OH
CH3
F
CH3
12-19F
-143.61
-143.63
-143.66
-143.68
-143.70
-143.72
-143.75
-143.77
-143.80
-143.82
-143.85
-143.87
-143.89
-143.91
-143.55 -143.60 -143.65 -143.70 -143.75 -143.80 -143.85 -143.90 -143.95 -144.00
19F(ppm)
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
19F(ppm)


13C — cdcl3 — 125.57
Cl
NH
O
OH
CH3
F
CH3
12-19F
77.2 CDCl3
173.3
173.1
149.6
132.7
123.5
123.2
120.9
120.2
97.4
96.9
25.3
25.1
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
13C(ppm)

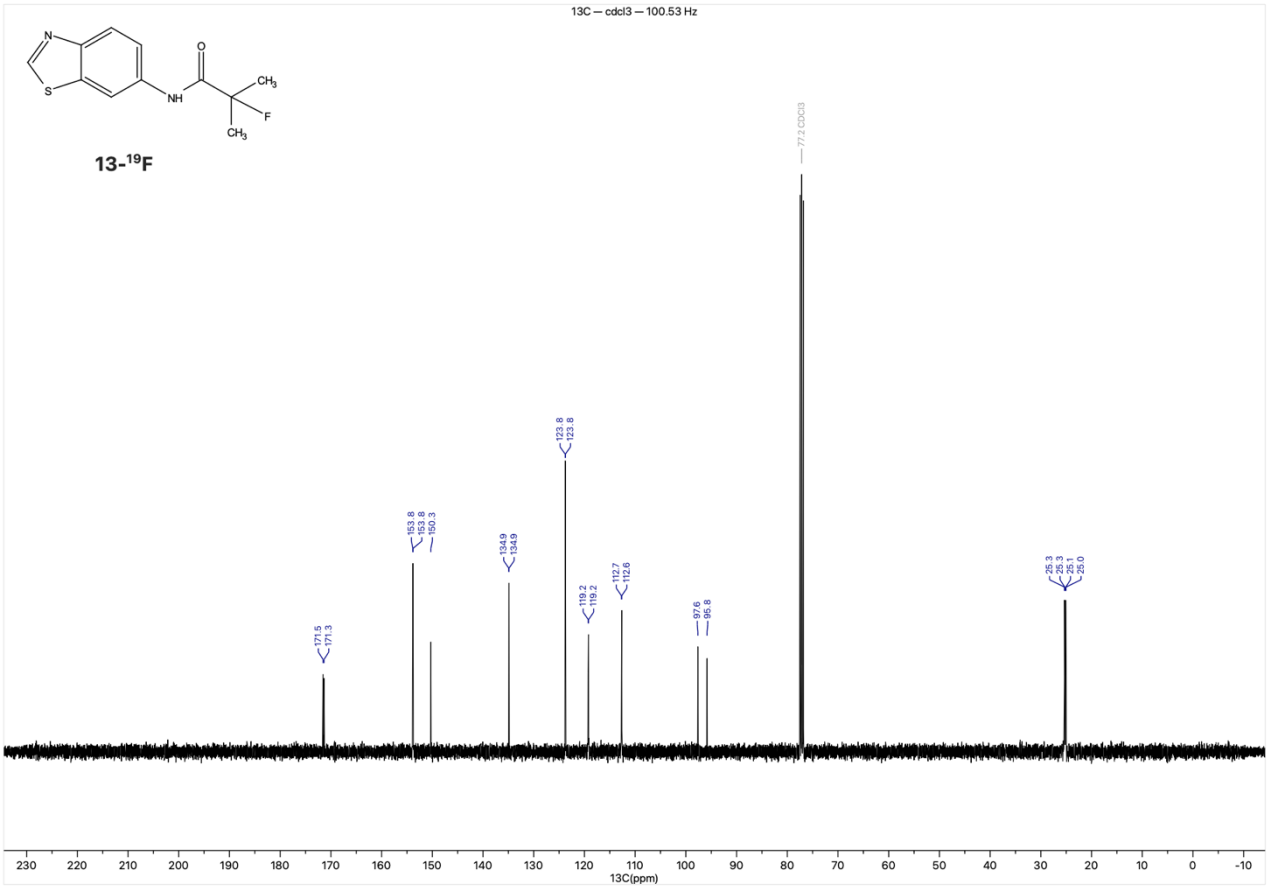

1H — cdcl3 — 499.35 Hz
13-Br
8.92
8.69
8.50
8.49
8.04
8.03
7.40
7.40
7.39
7.38
2.05
0.84
0.98
0.86
0.95
1.00
6.29
1H(ppm)

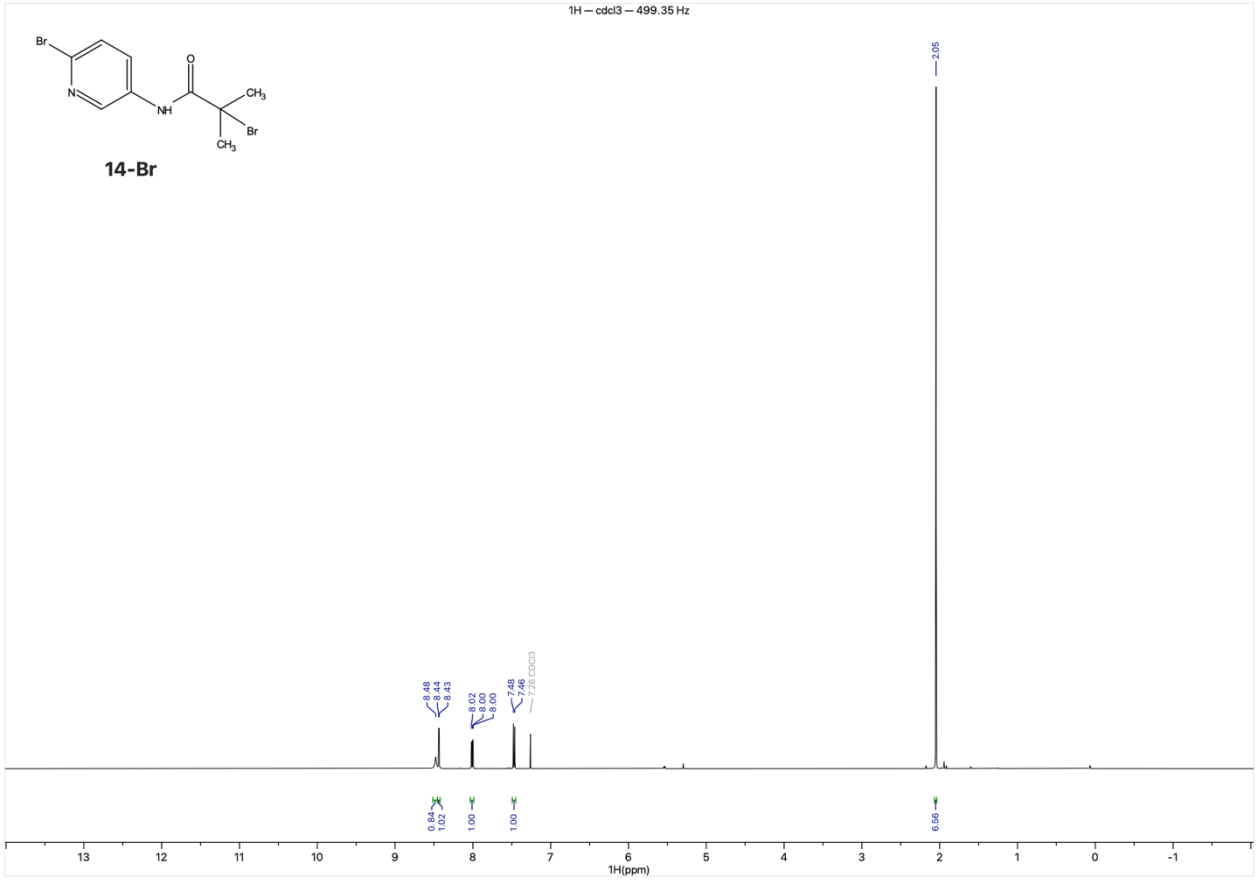

13C — cdcl3 — 125.57 Hz
13-Br
170.3
153.8
150.4
135.2
134.8
123.7
119.4
112.8
77.2 CDCl3
62.9
32.6
13C(ppm)

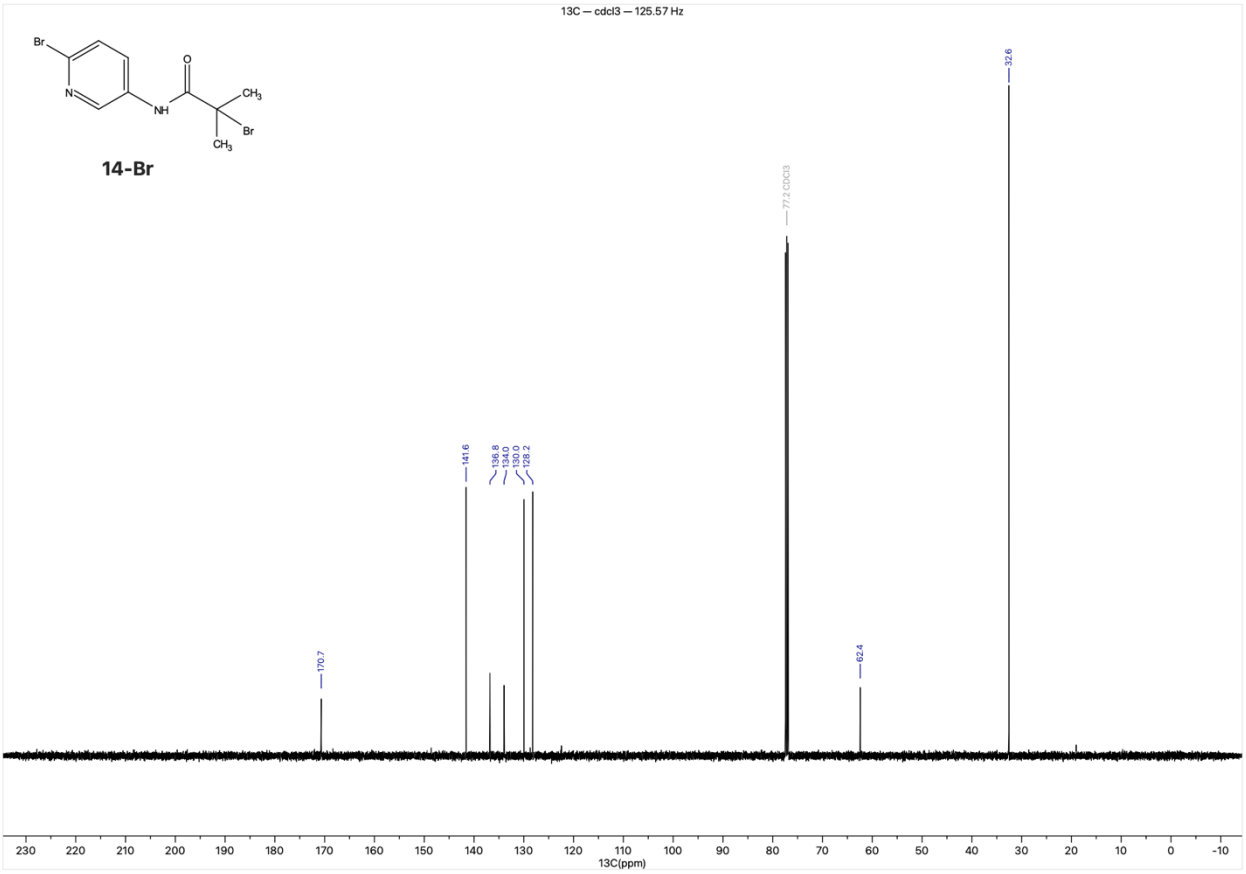

1H — cdcl3 — 399.74 Hz
13-19F
8.93
8.60
8.59
8.34
8.32
8.07
8.05
7.42
7.42
7.40
7.40
7.26 CDCl3
1.71
1.65
0.98
0.99
0.87
1.00
1.00
6.04
1H(ppm)

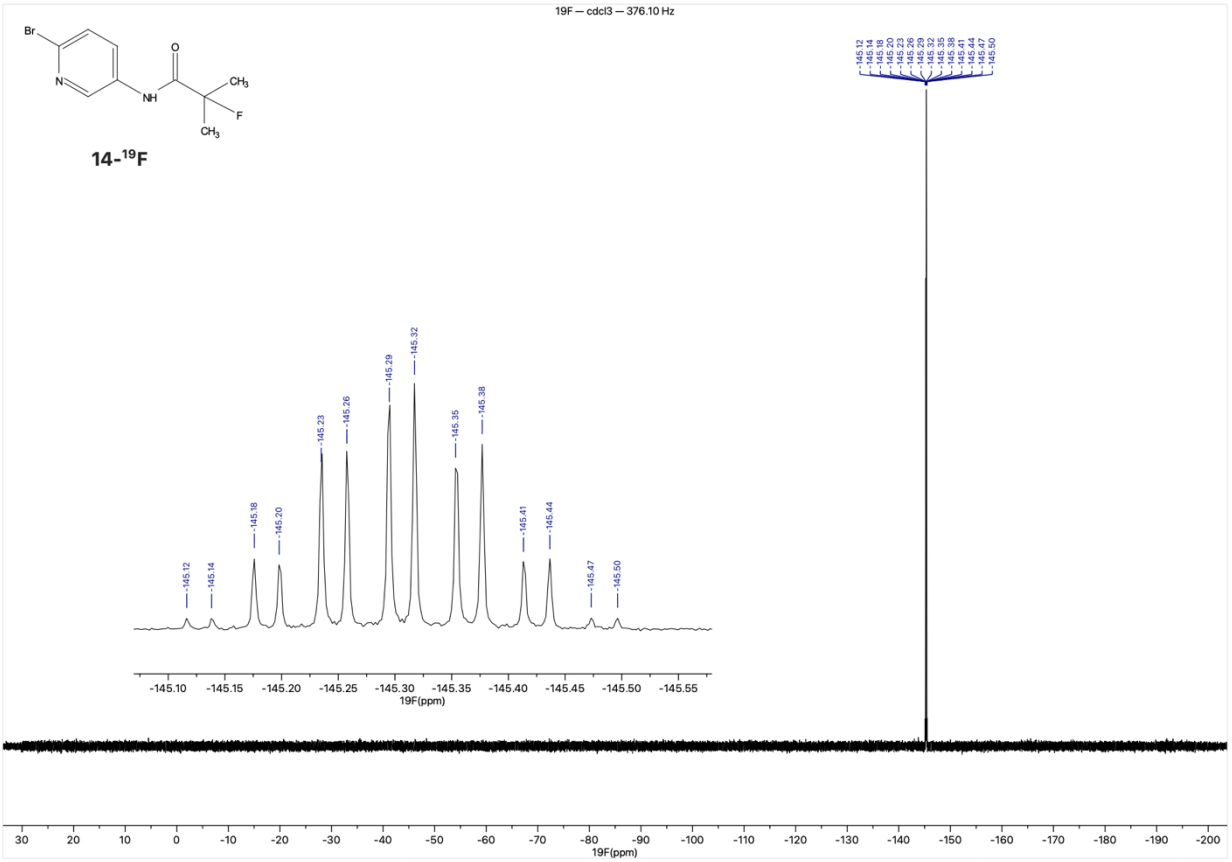

19F — cdcl3 — 469.80 Hz
13-19F
-145.09
-145.11
-145.14
-145.16
-145.19
-145.21
-145.24
-145.26
-145.29
-145.30
-145.33
-145.35
-145.38
-145.40
19F(ppm)

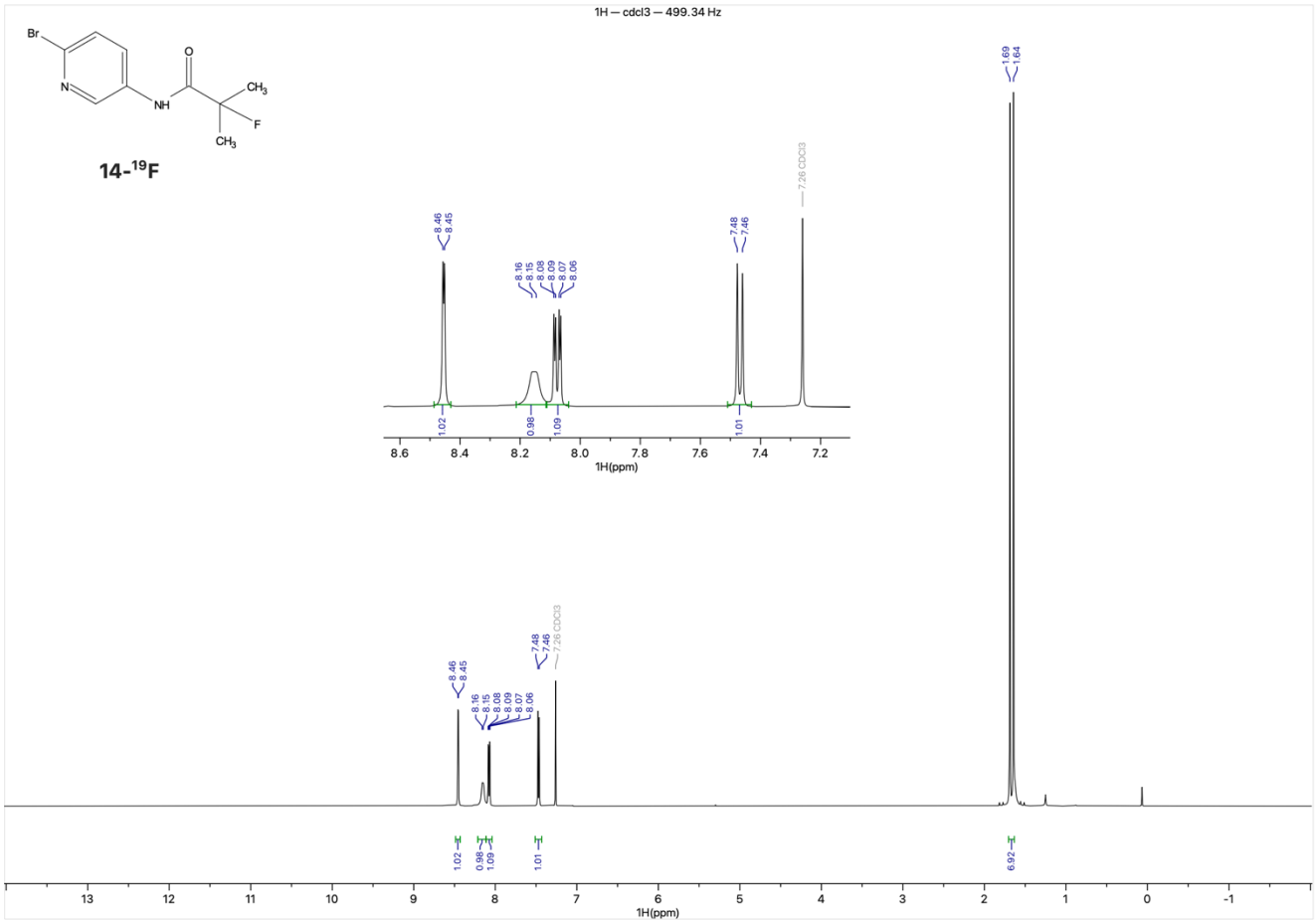
SUPPORTING INFORMATION

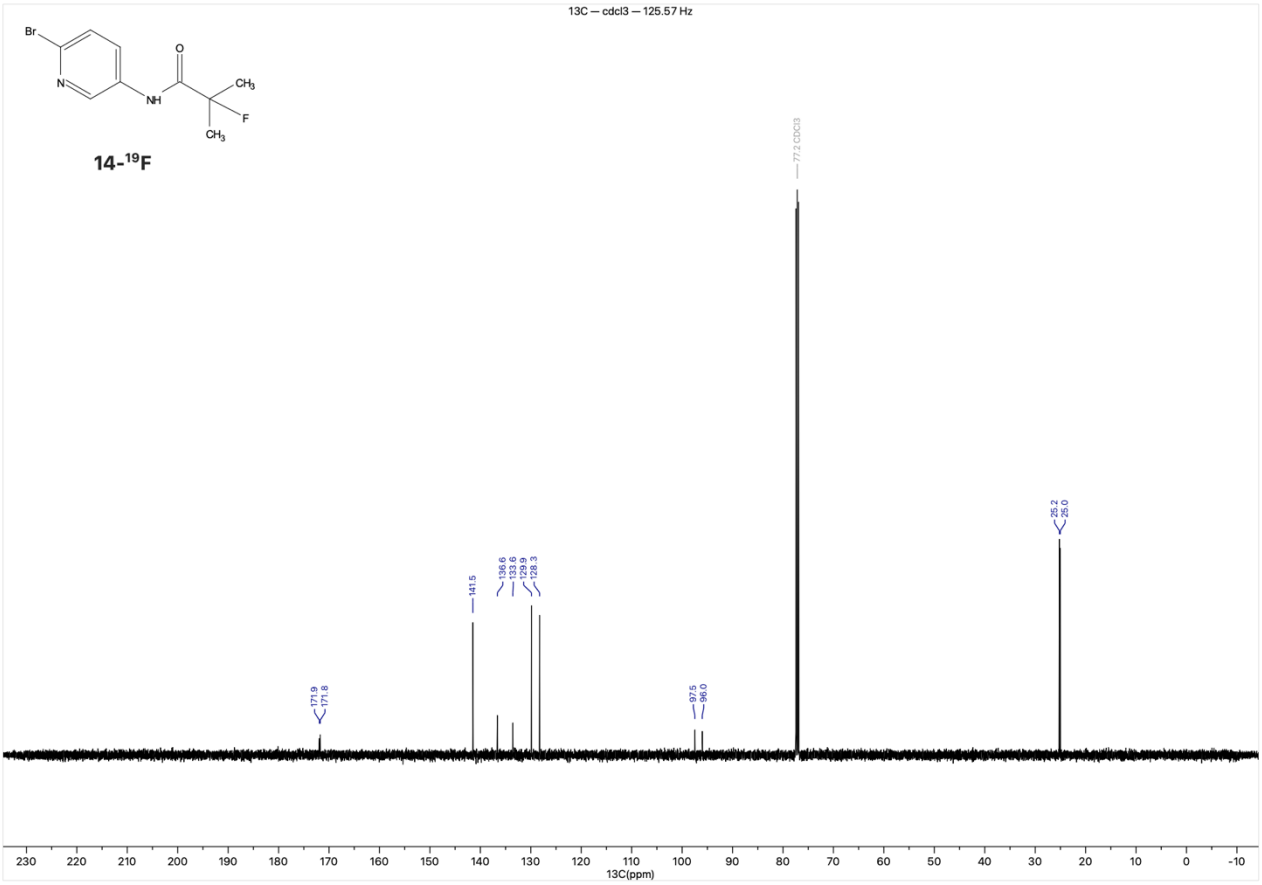


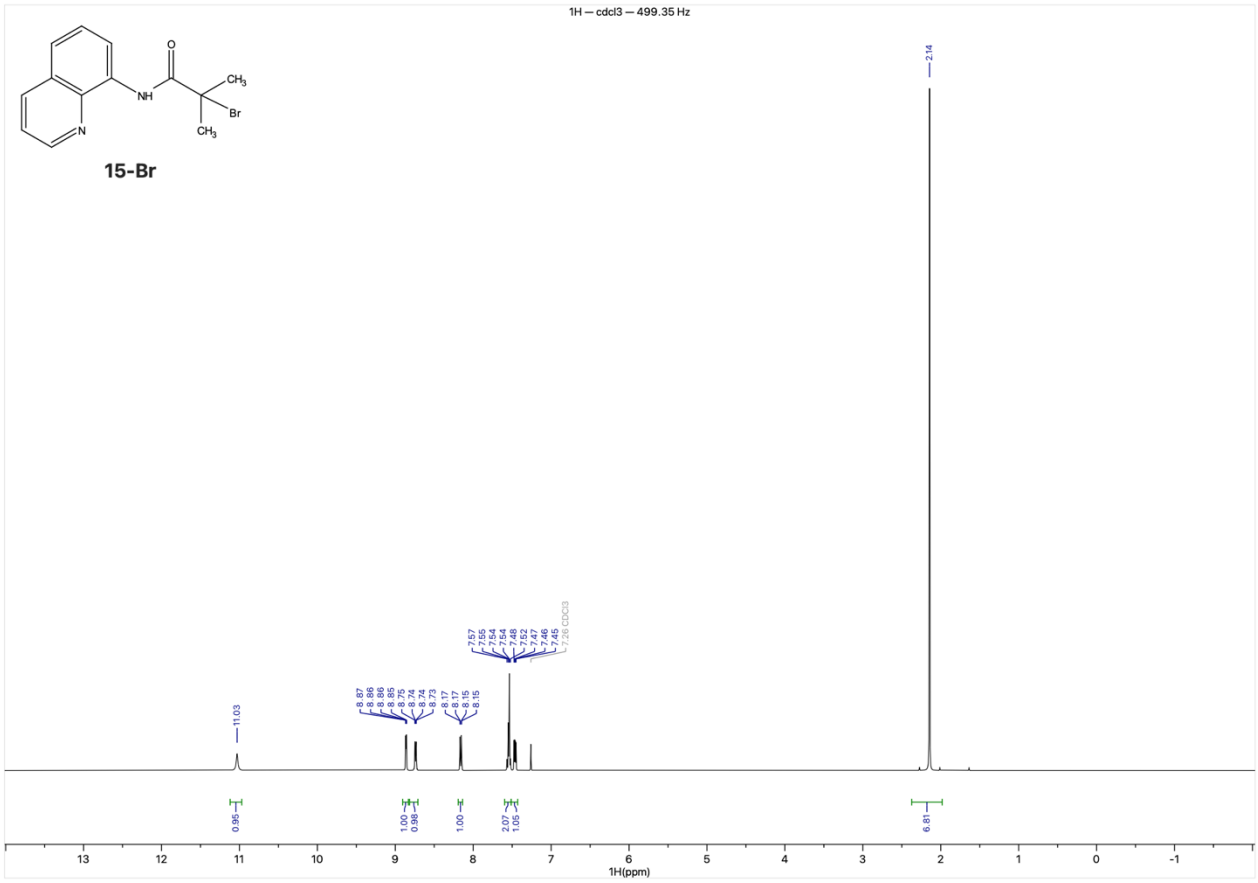


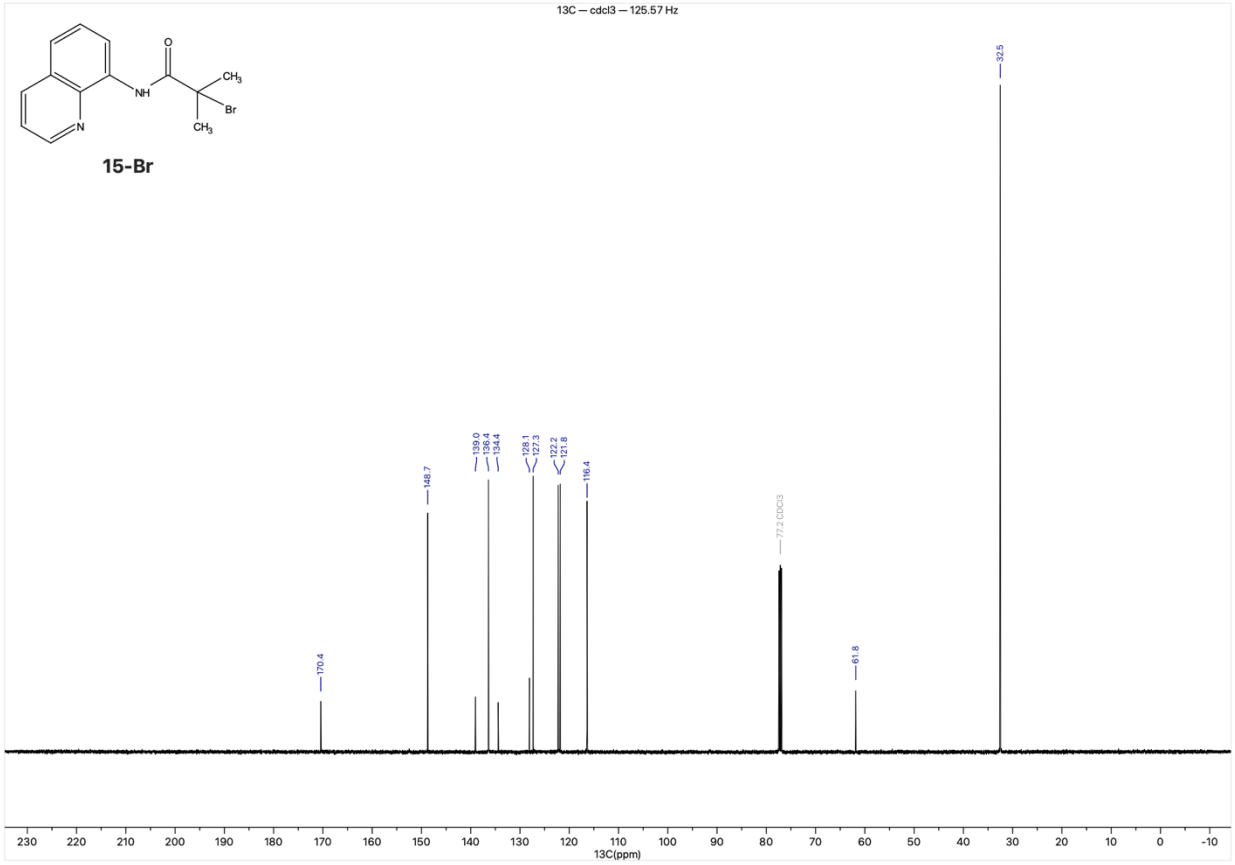

13C — cdcl3 — 125.57 Hz
14-Br
170.7
141.6
136.8
134.0
130.0
128.2
77.2 CDCl3
62.4
32.6
13C(ppm)

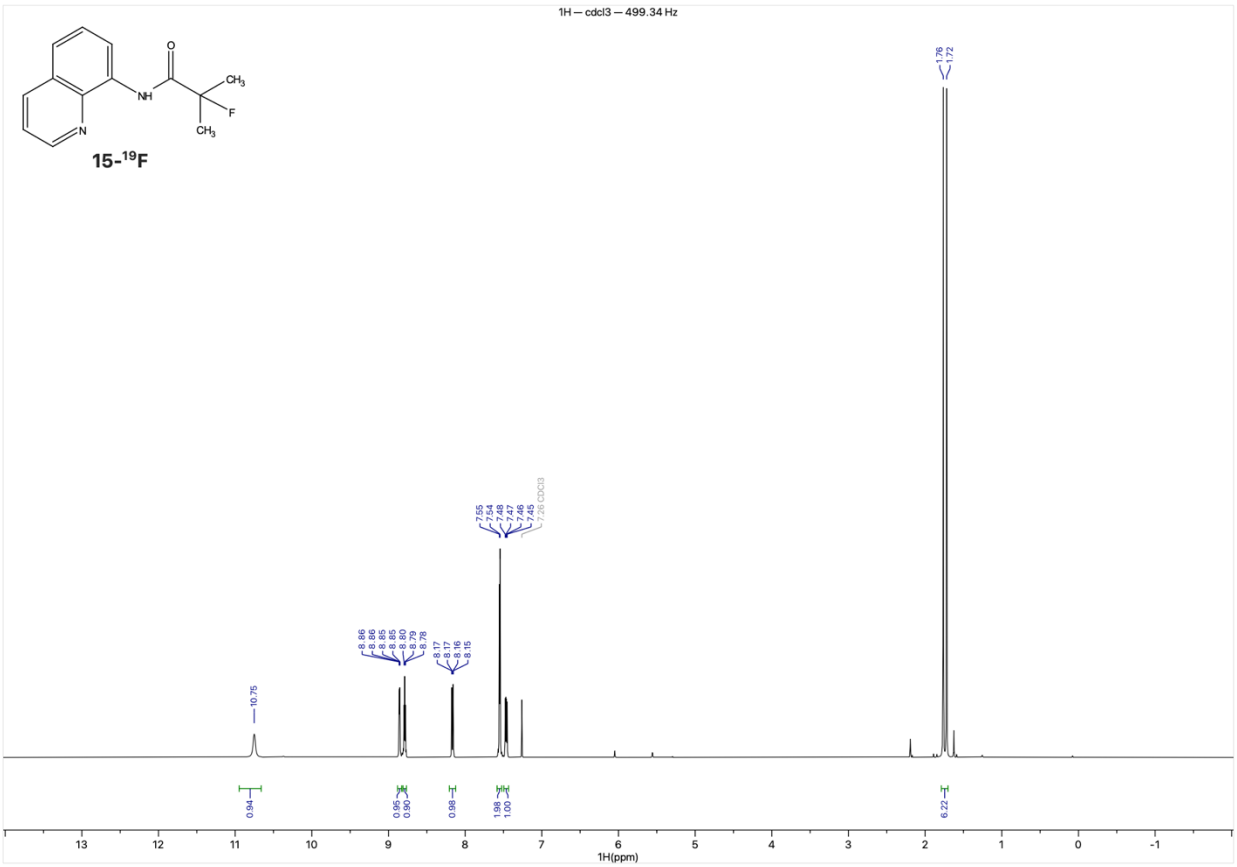

19F — cdcl3 — 376.10 Hz
14-19F
-145.12
-145.14
-145.18
-145.20
-145.23
-145.26
-145.29
-145.32
-145.35
-145.38
-145.41
-145.44
-145.47
-145.50
19F(ppm)

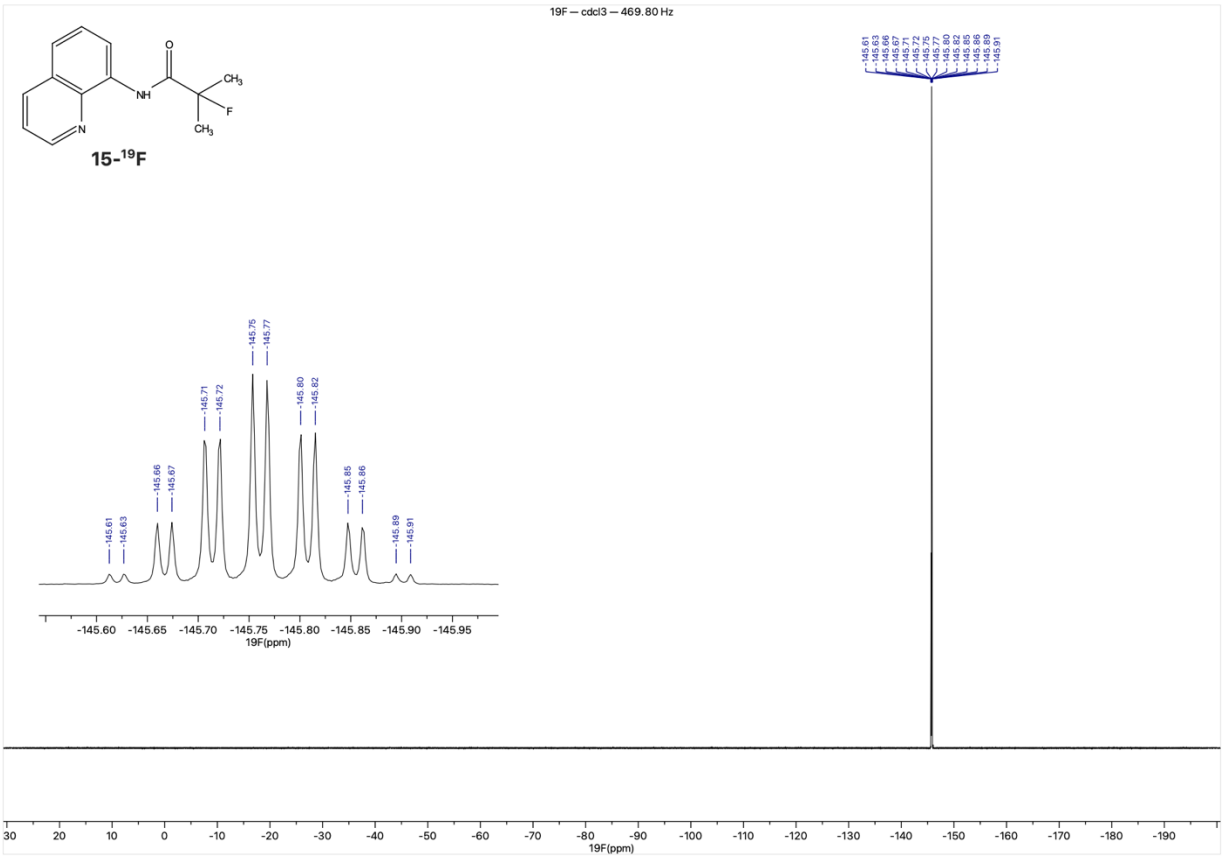

1H — cdcl3 — 499.34 Hz
Br
N
NH
O
CH3
F
CH3
14-19F
8.46
8.45
8.16
8.15
8.08
8.09
8.07
8.06
7.48
7.46
7.26 CDCl3
1.69
1.64
1.02
0.98
1.09
1.01
6.92
1H(ppm)

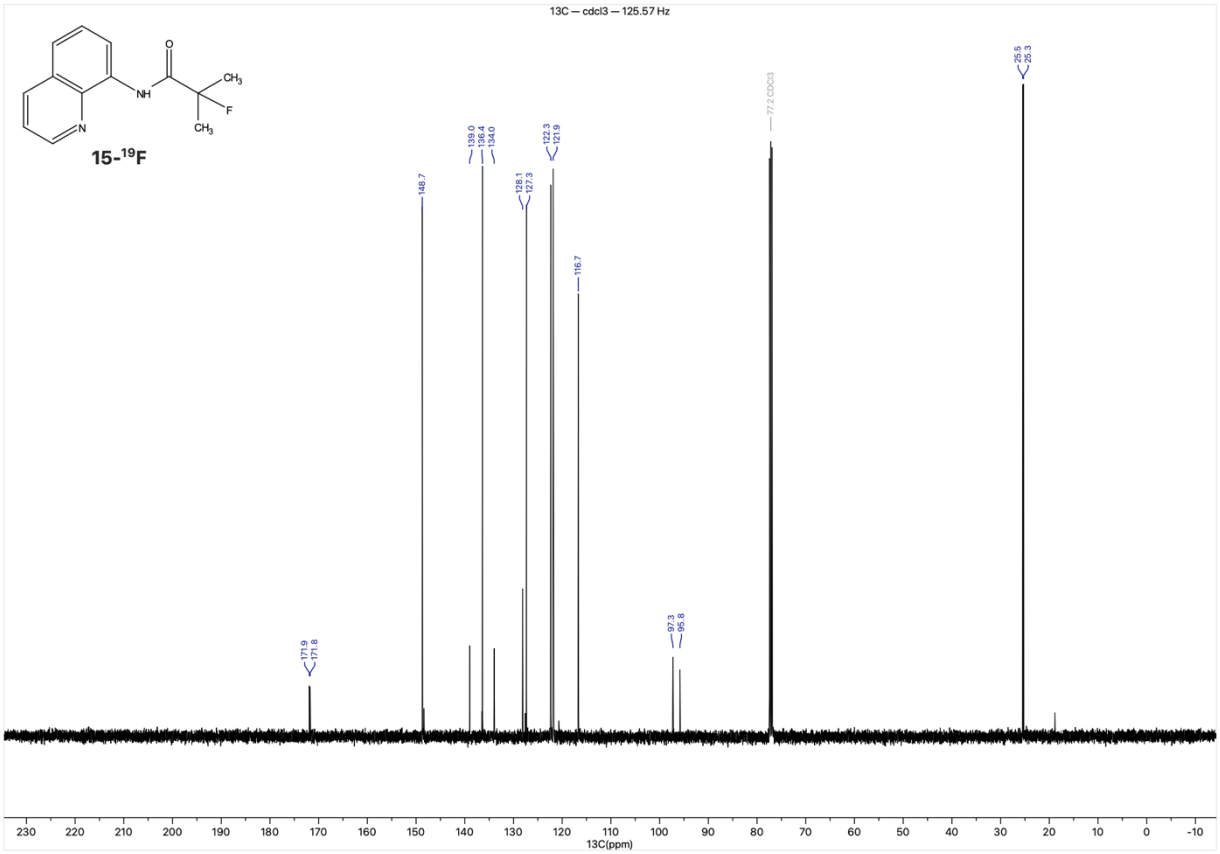

13C — cdcl3 — 125.57 Hz
Br
N
O
NH
CH3
F
CH3
14-19F
77.2 CDCl3
171.9
171.8
141.5
136.6
133.6
129.9
128.3
97.5
96.0
25.2
25.0
13C(ppm)

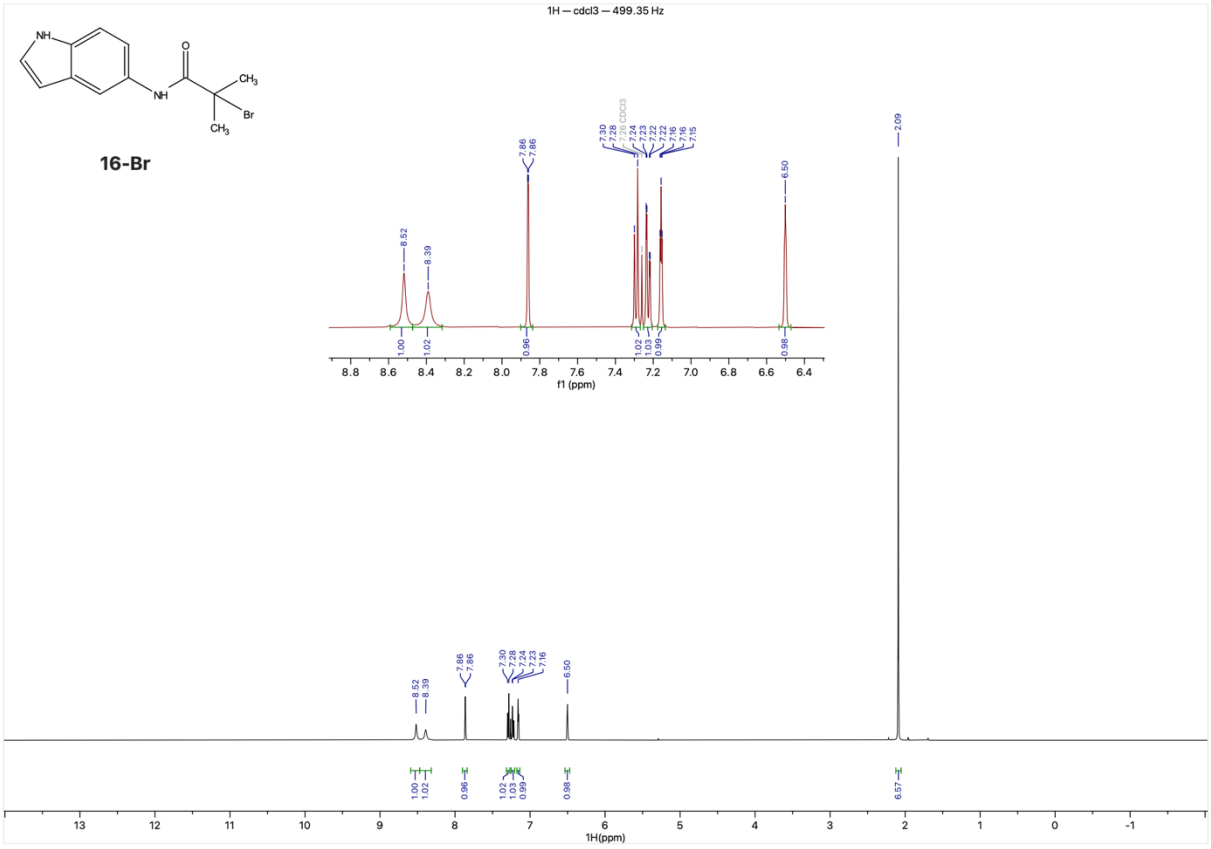

1H — cdcl3 — 499.35 Hz
O
NH
CH3
Br
CH3
N
15-Br
2.14
7.57
7.55
7.54
7.54
7.48
7.52
7.47
7.46
7.45
7.26 CDCl3
8.87
8.86
8.86
8.85
8.75
8.74
8.74
8.73
8.17
8.17
8.15
8.15
11.03
0.95
1.00
0.98
1.00
2.07
1.05
6.81
1H(ppm)

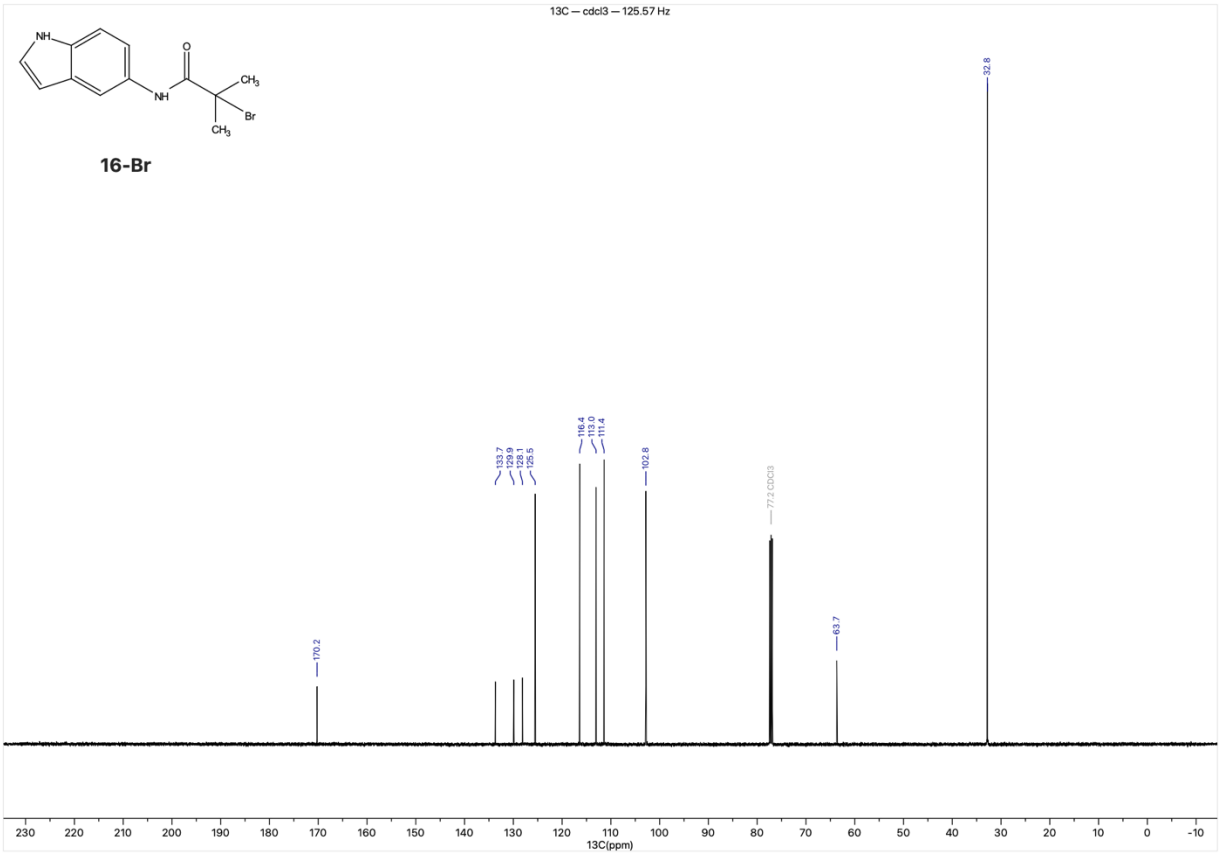

13C — cdcl3 — 125.57 Hz
15-Br
170.4
148.7
139.0
138.4
134.4
128.1
127.3
122.2
121.8
116.4
77.2 CDCl3
61.8
32.5
13C(ppm)

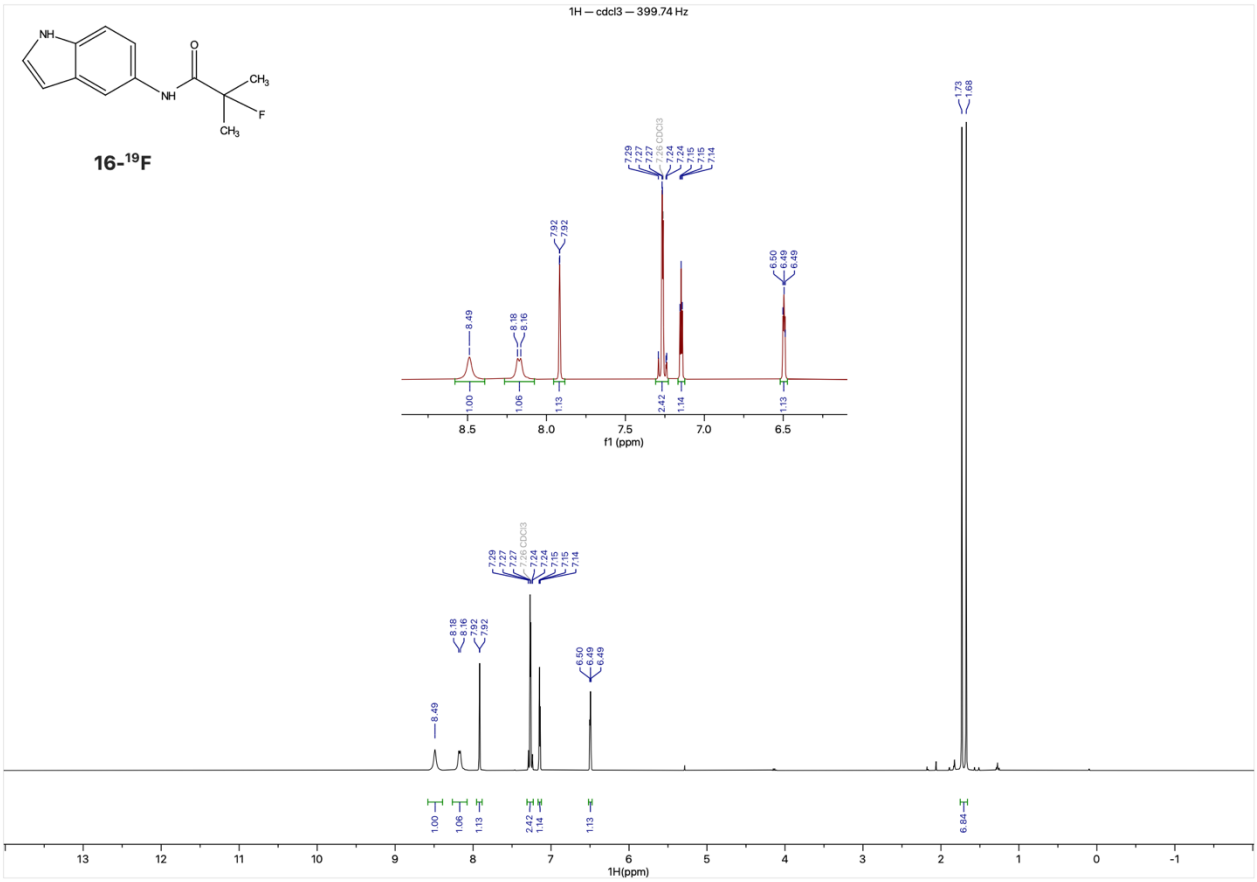

1H — cdcl3 — 499.34 Hz
15-19F
10.75
8.86
8.86
8.85
8.85
8.80
8.79
8.78
8.17
8.17
8.16
8.15
7.55
7.54
7.48
7.47
7.46
7.45
7.26 CDCl3
1.76
1.72
0.94
0.95
0.90
0.98
1.98
1.00
6.22
1H(ppm)

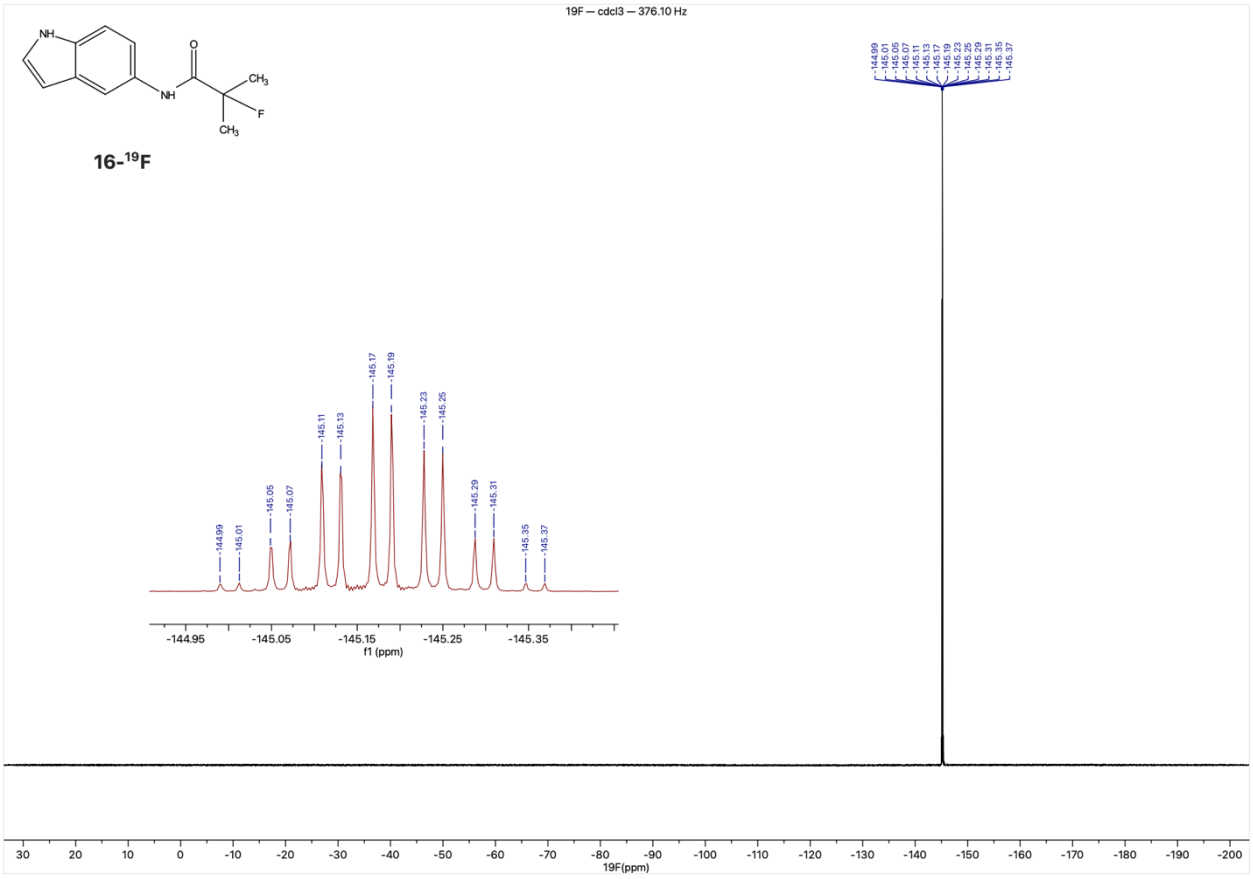

19F — cdcl3 — 469.80 Hz
15-19F
-145.61
-145.63
-145.66
-145.67
-145.71
-145.72
-145.75
-145.77
-145.80
-145.82
-145.85
-145.86
-145.89
-145.91
19F(ppm)

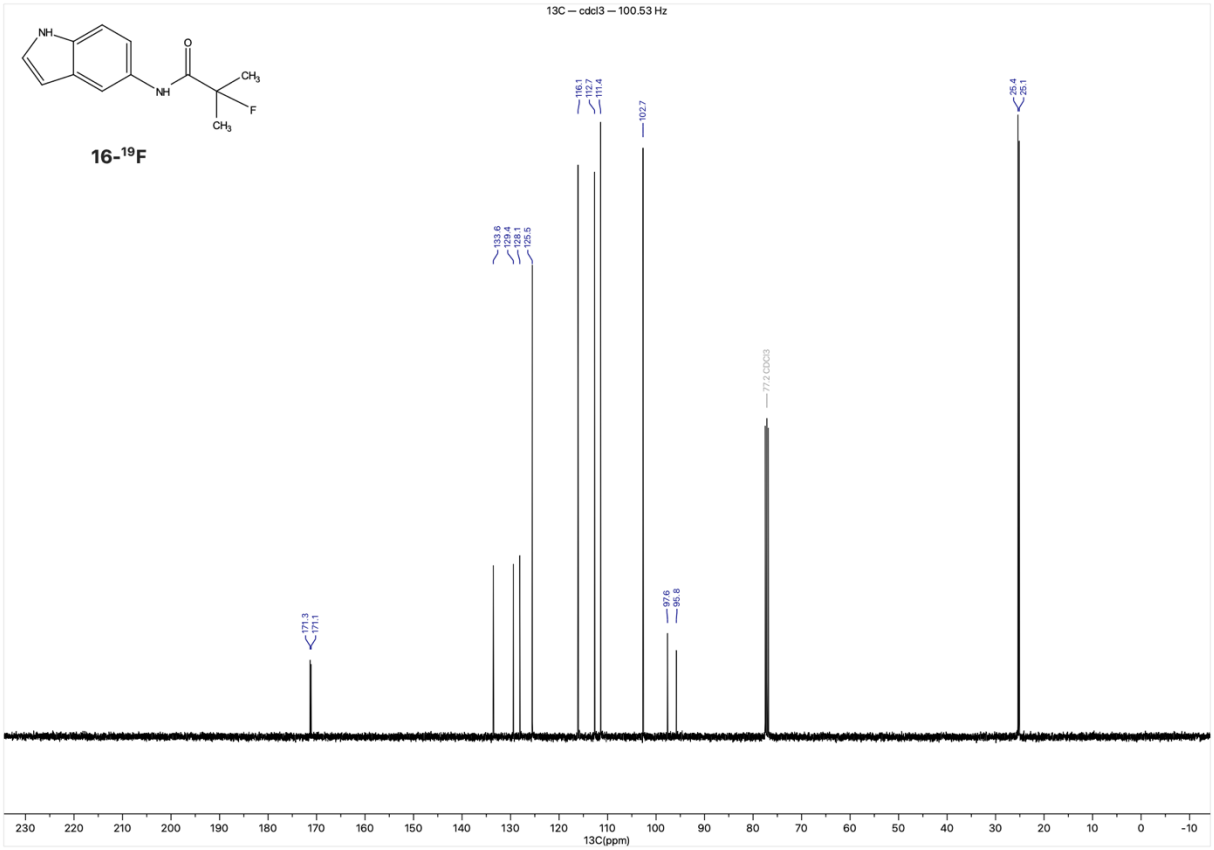

13C — cdcl3 — 125.57 Hz
15-19F
171.9
171.8
148.7
139.0
136.4
134.0
128.1
127.3
122.3
121.9
116.7
97.3
95.8
77.2 CDCl3
25.5
25.3
13C(ppm)

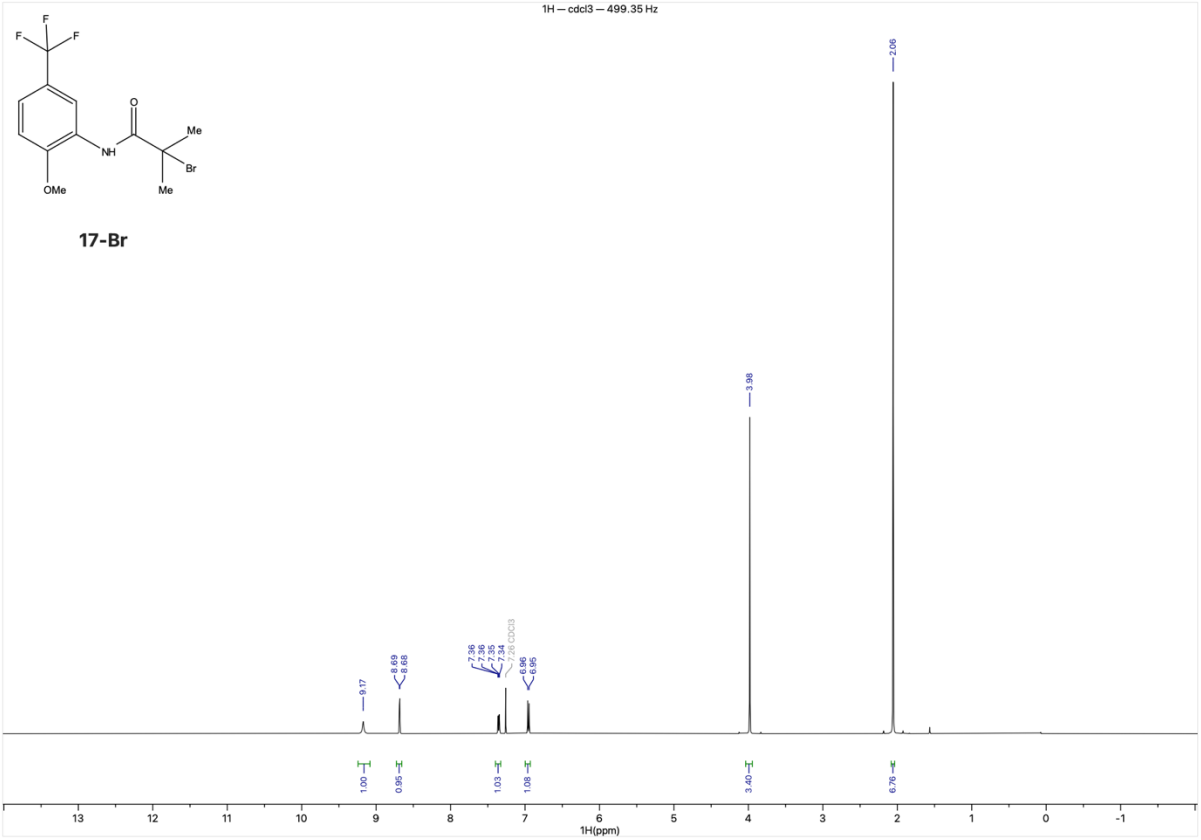

1H — cdcl3 — 499.35 Hz
16-Br
f1 (ppm)
1H(ppm)

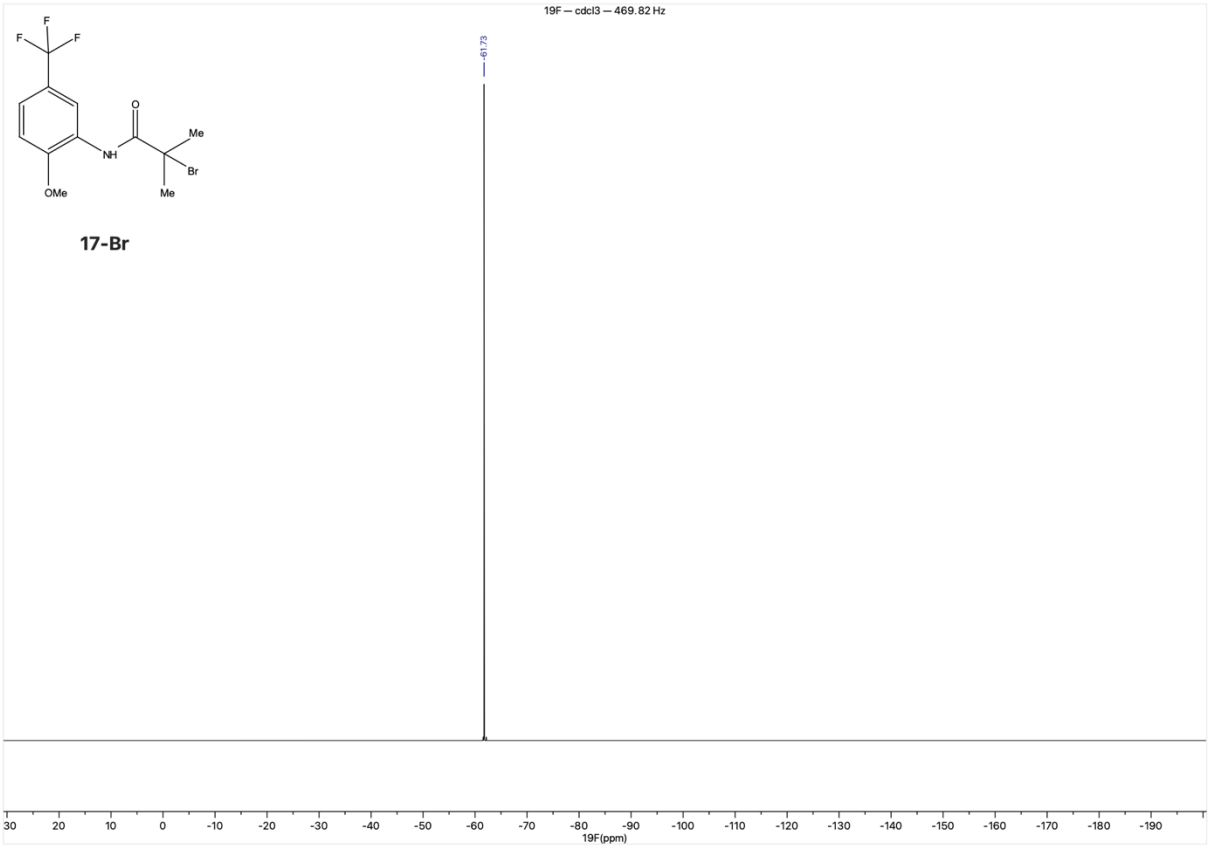

13C — cdcl3 — 125.57 Hz
16-Br
13C(ppm)

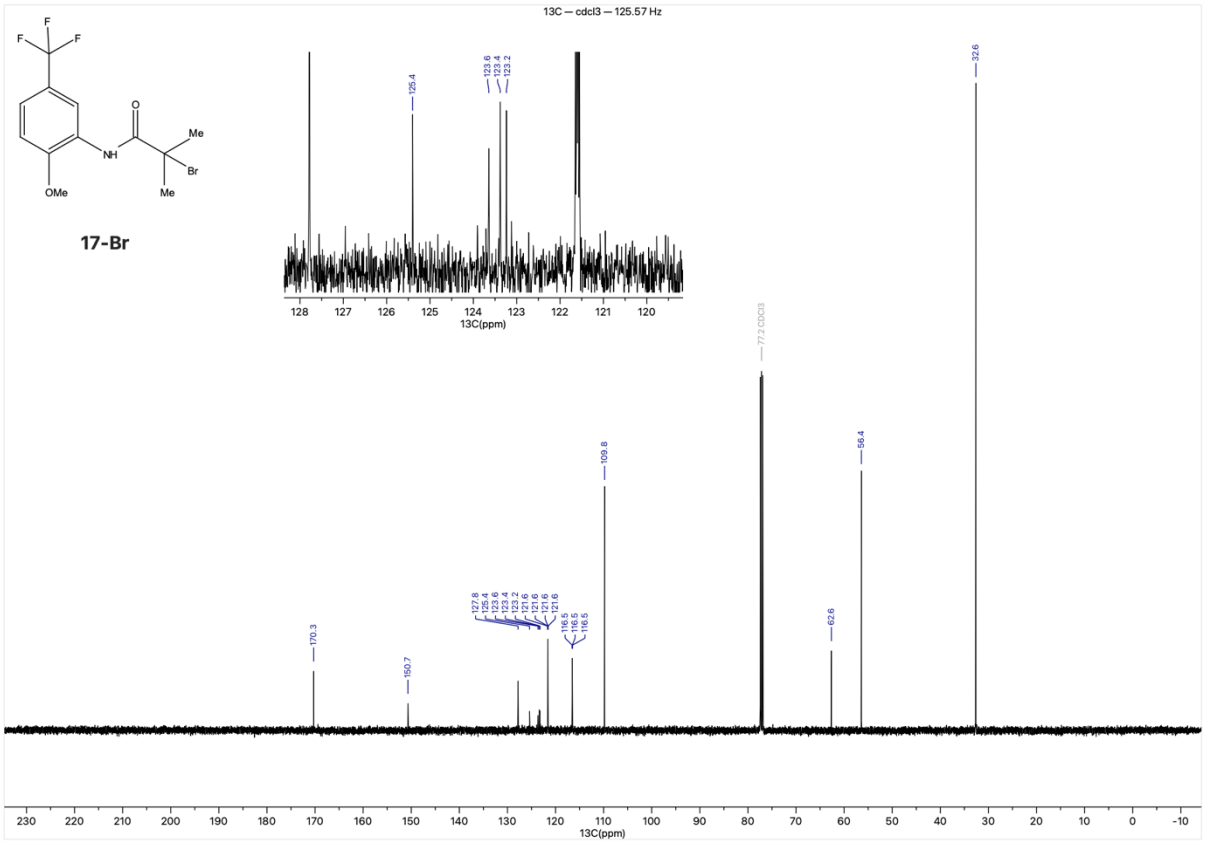

1H — cdcl3 — 399.74 Hz
16-19F
f1 (ppm)
1H(ppm)

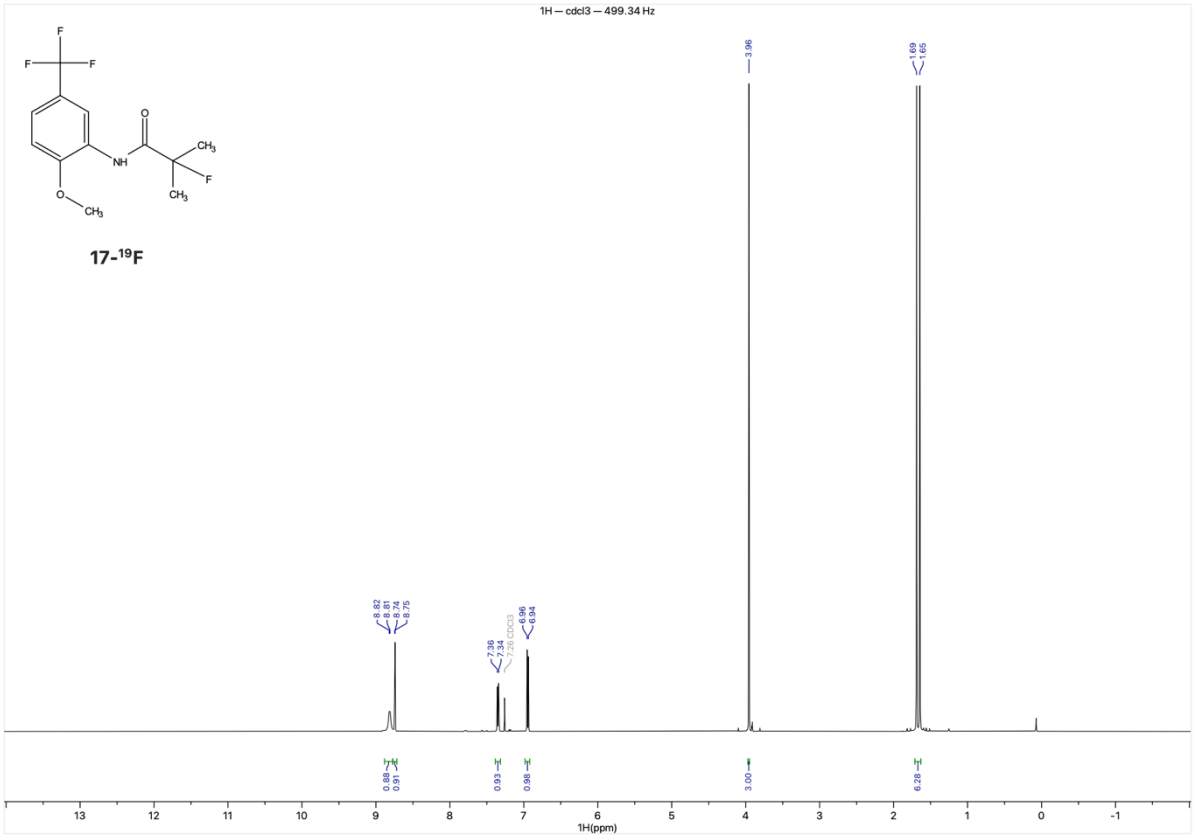

19F — cdcl3 — 376.10 Hz
16-19F
f1 (ppm)
19F(ppm)


13C — cdcl3 — 100.53 Hz
16-19F
171.3
171.1
133.6
129.4
128.1
125.5
116.1
112.7
111.4
102.7
97.6
95.8
77.2 CDCl3
25.4
25.1
13C(ppm)

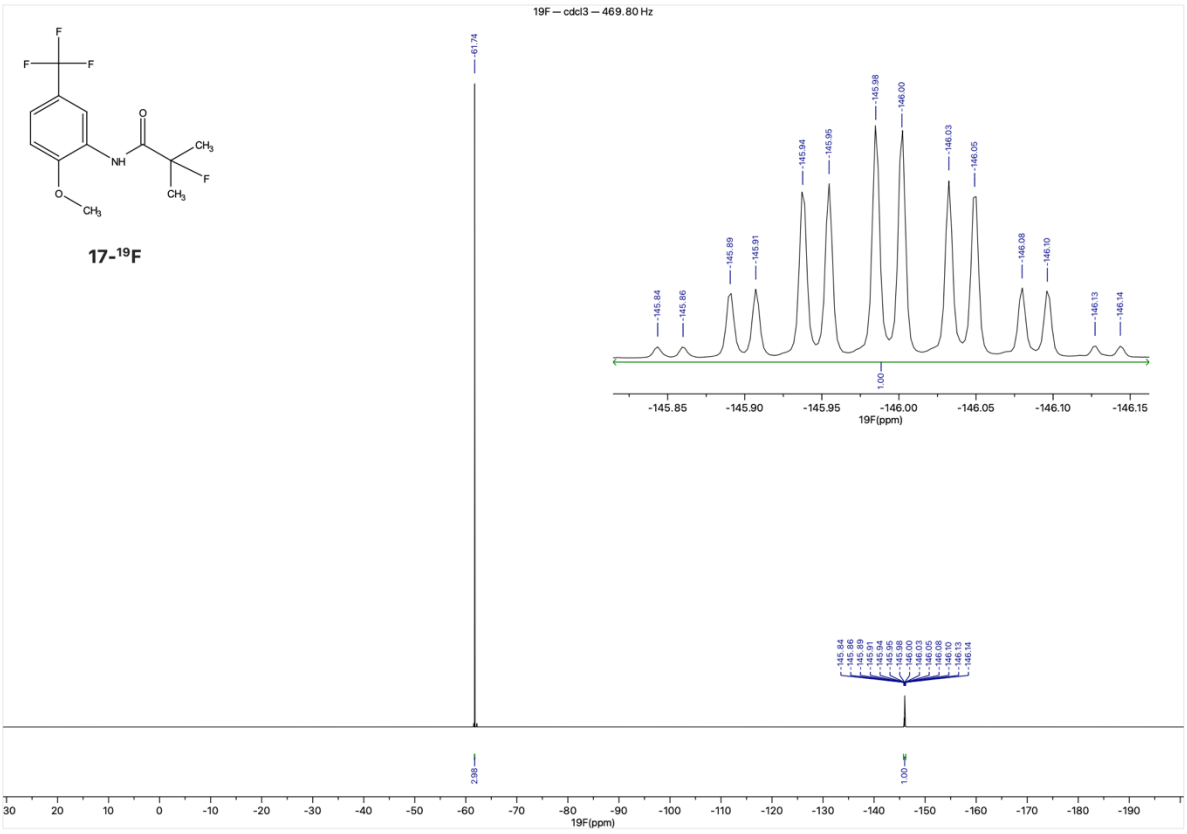

1H — cdcl3 — 499.35 Hz
17-Br
9.17
8.69
8.68
7.36
7.36
7.35
7.34
7.26 CDCl3
6.96
6.95
3.98
2.06
1.00
0.95
1.03
1.08
3.40
6.76
1H(ppm)


19F — cdcl3 — 469.82 Hz
-61.73
F
F
F
O
NH
Me
Br
Me
OMe
17-Br
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
19F(ppm)

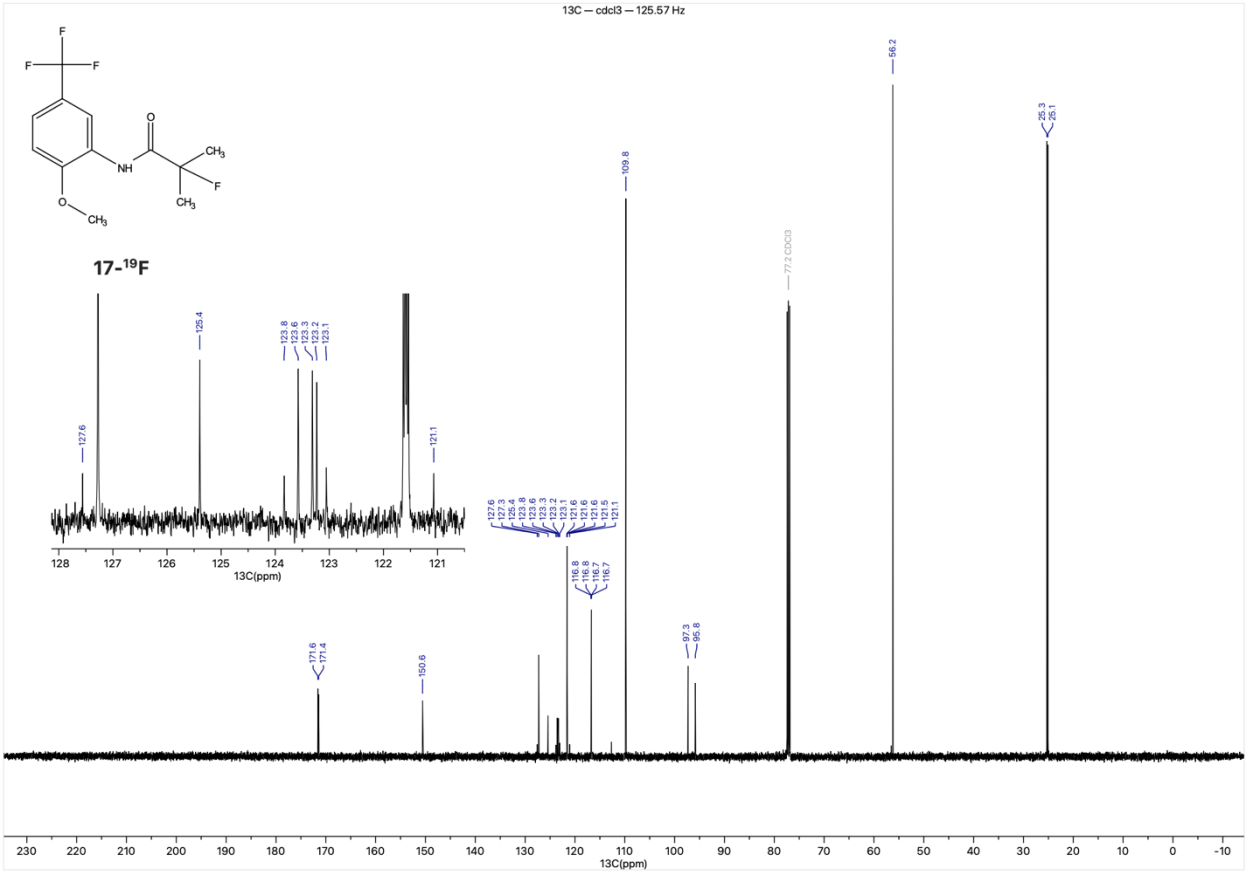

13C — cdcl3 — 125.57 Hz
F
F
F
O
NH
Me
Br
Me
OMe
17-Br
126.4
123.6
123.4
123.2
32.6
77.2 CDCl3
109.8
56.4
62.6
170.3
150.7
127.8
125.4
123.6
123.4
123.2
121.6
121.6
121.6
116.5
116.5
116.5
128 127 126 125 124 123 122 121 120
13C(ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
13C(ppm)

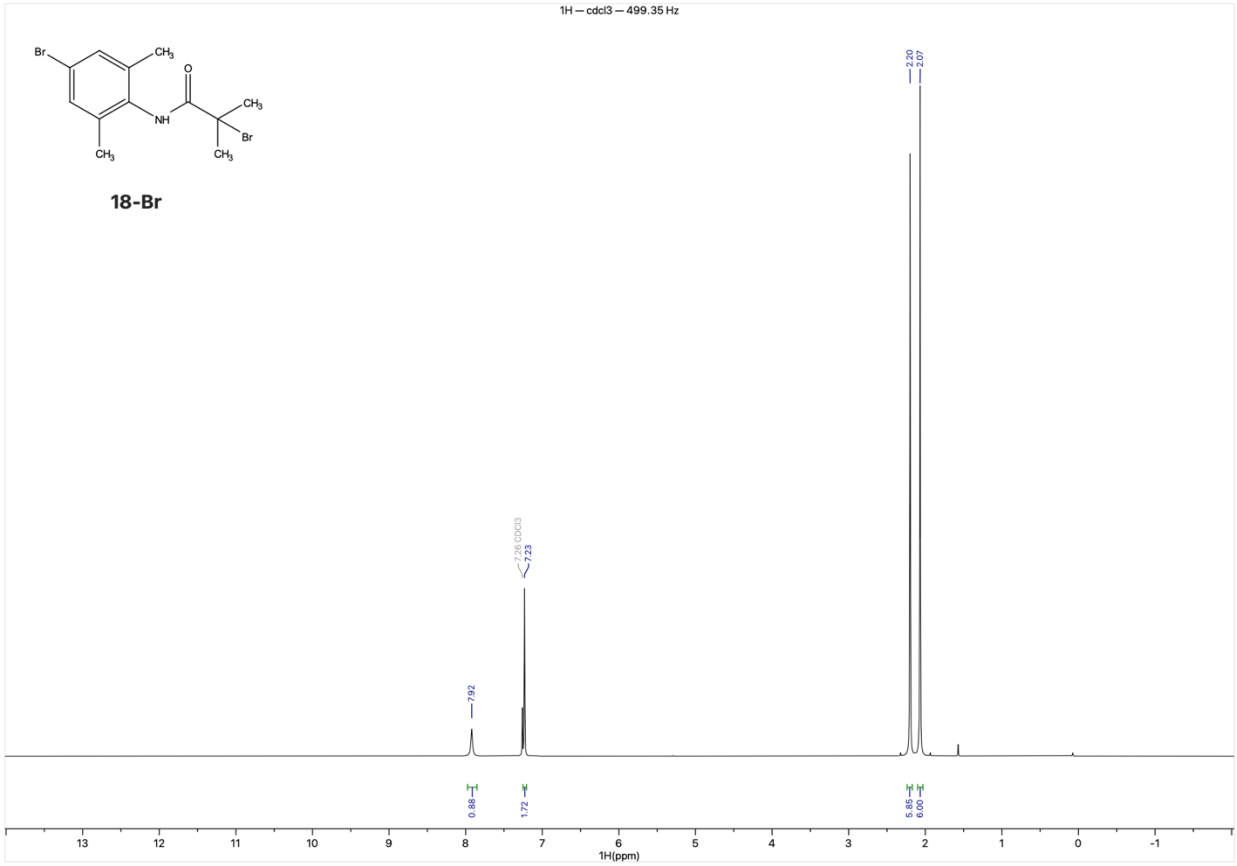

1H — cdcl3 — 499.34 Hz
3.96
1.69
1.65
8.82
8.81
8.76
8.75
7.36
7.34
7.26 CDCl3
6.96
6.94
0.88
0.91
0.93
0.98
3.00
6.28
1H(ppm)

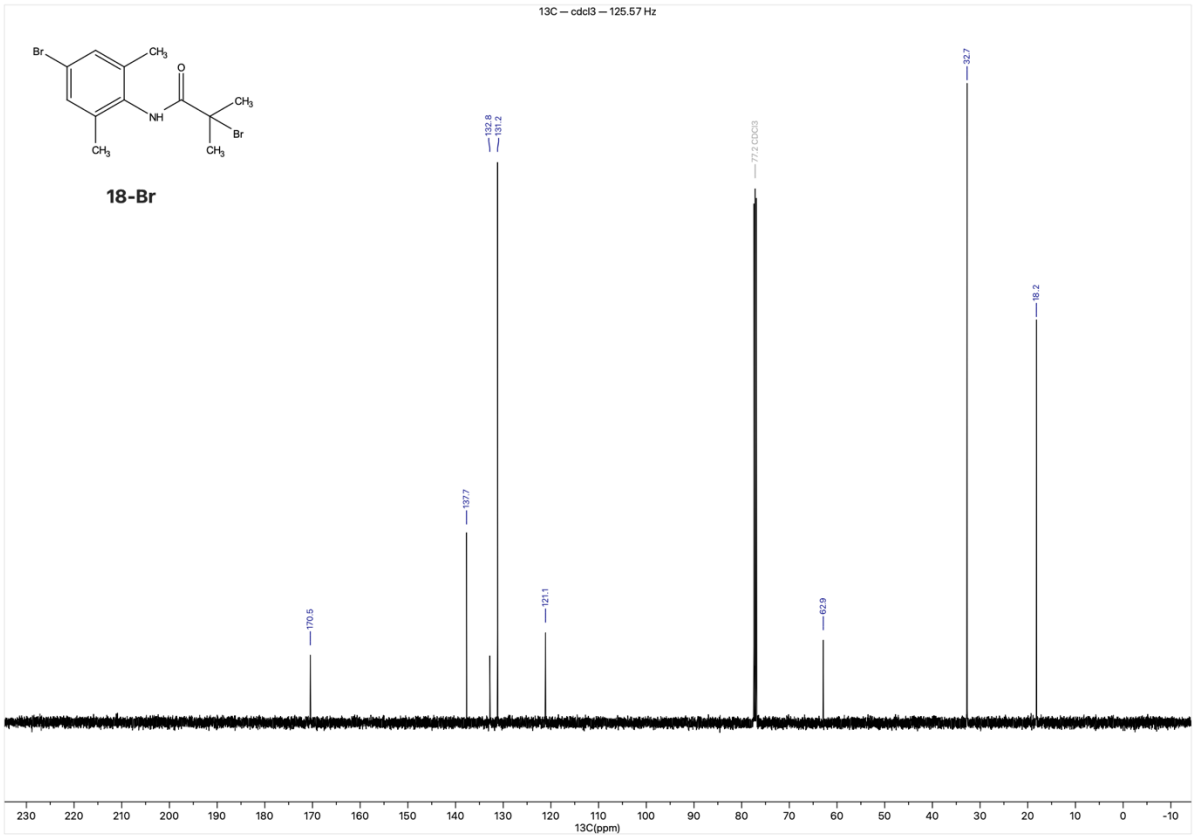
17-^{19}F

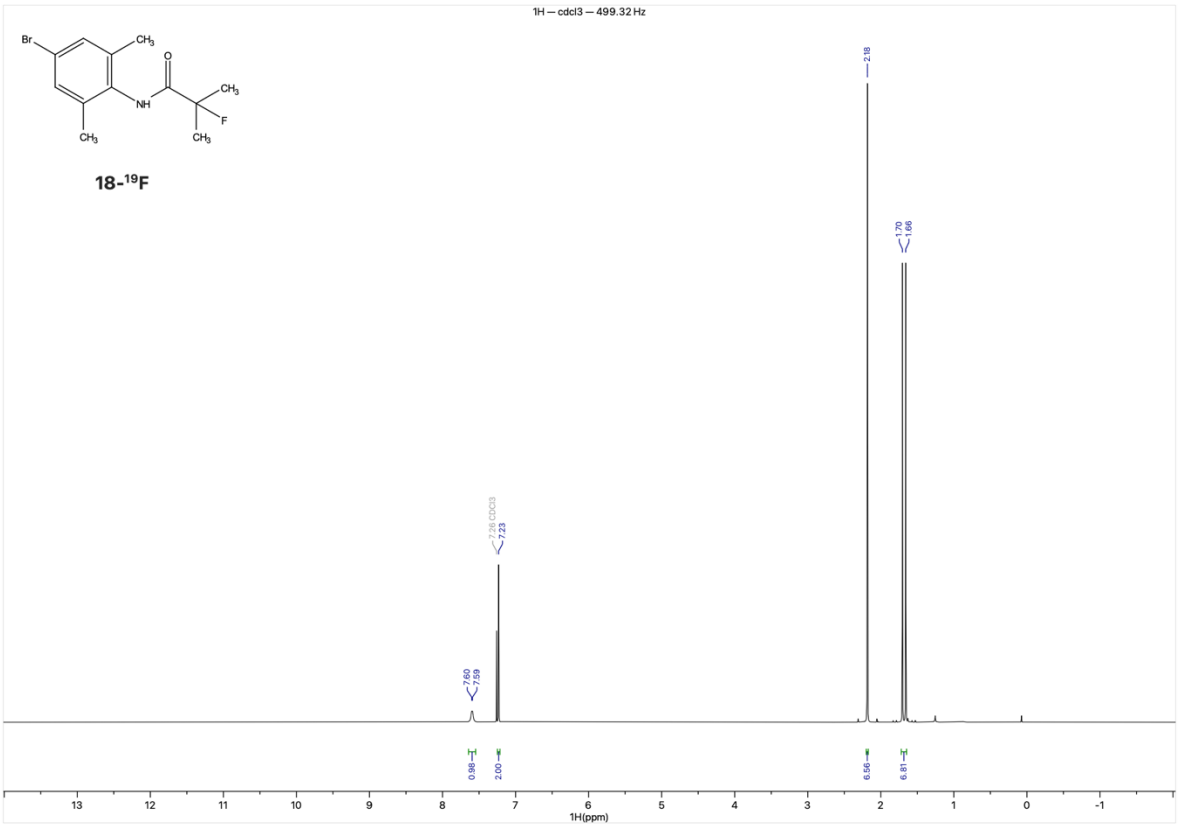

19F — cdcl3 — 469.80 Hz
-61.74
-145.98
-146.00
-145.94
-145.95
-146.03
-146.05
-145.89
-145.91
-146.08
-146.10
-145.84
-145.86
-146.13
-146.14
1.00
-145.85
-145.90
-145.95
-146.00
-146.05
-146.10
-146.15
19F(ppm)
2.98
1.00
19F(ppm)

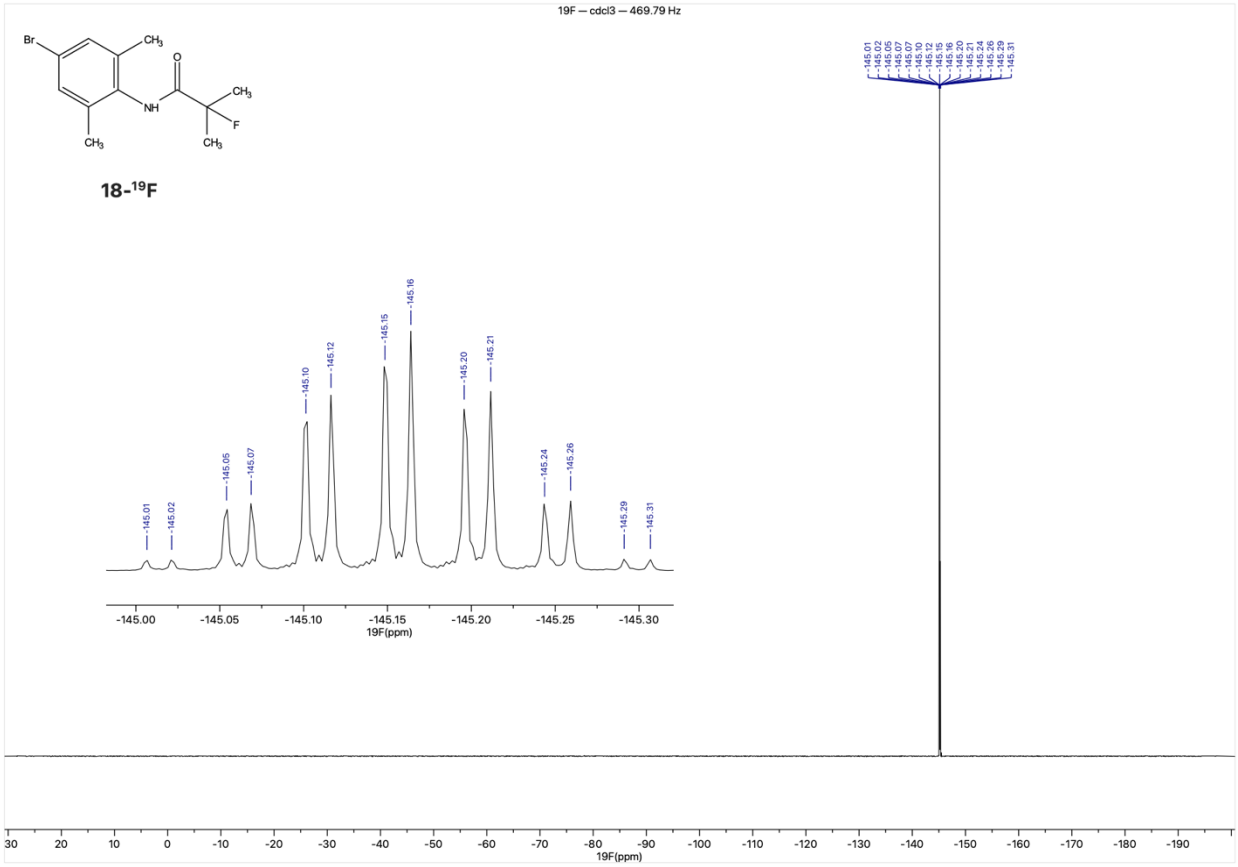
17-^{19}F

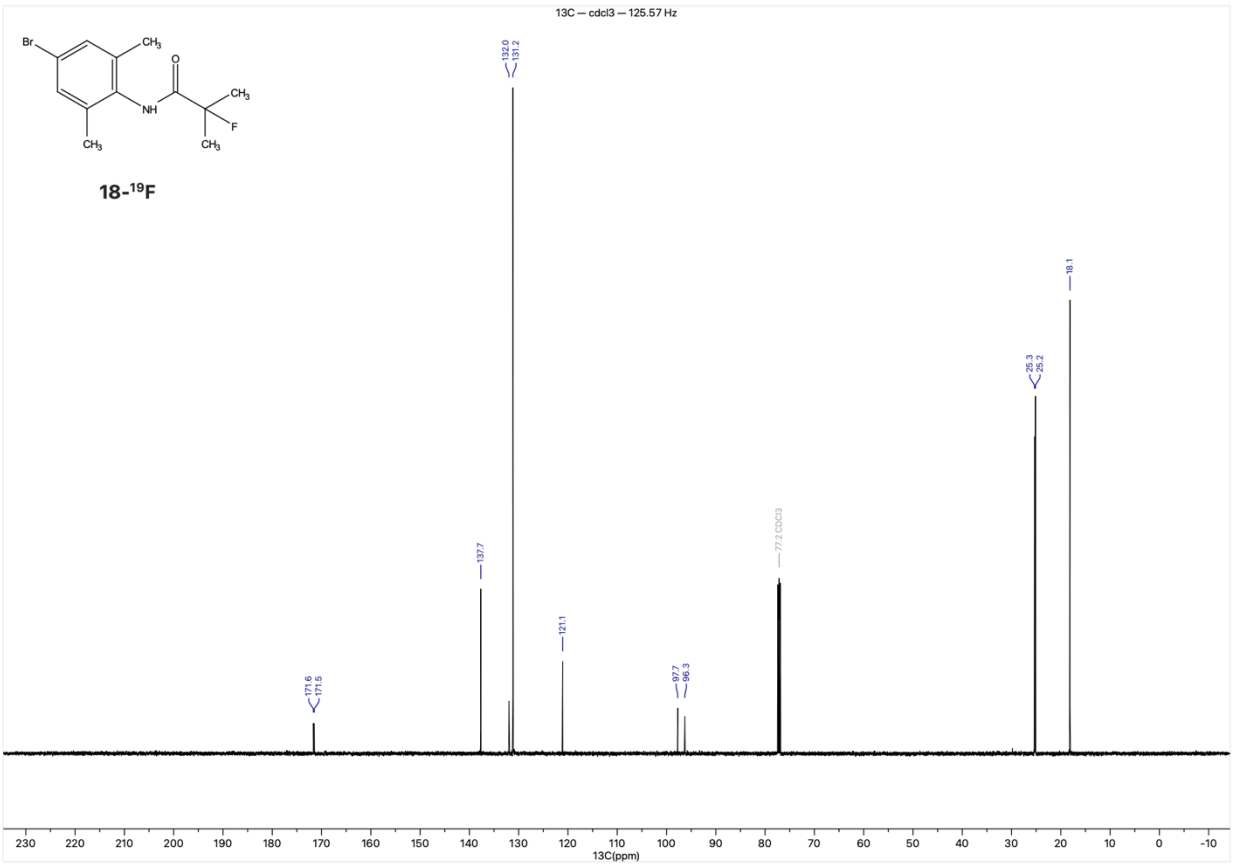

13C — cdcl3 — 125.57 Hz
17-19F
13C(ppm)

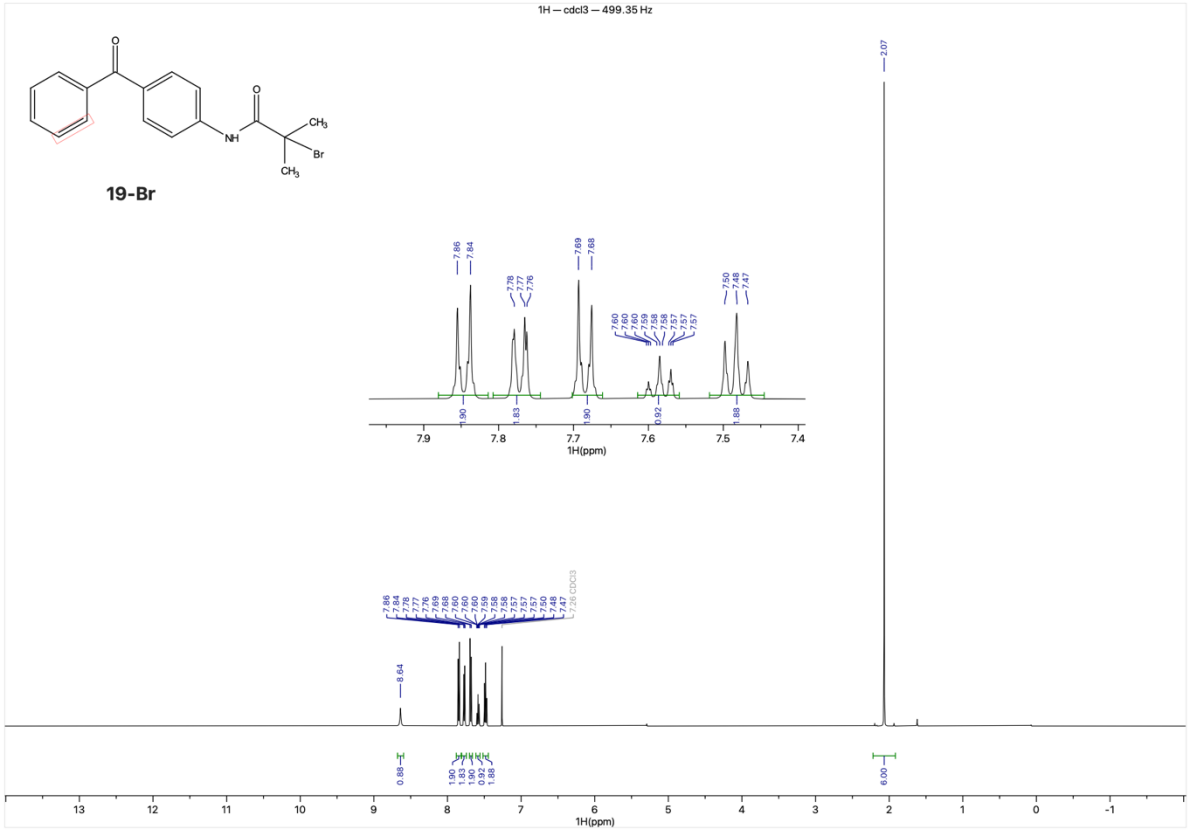

1H — cdcl3 — 499.35 Hz
18-Br
1H(ppm)

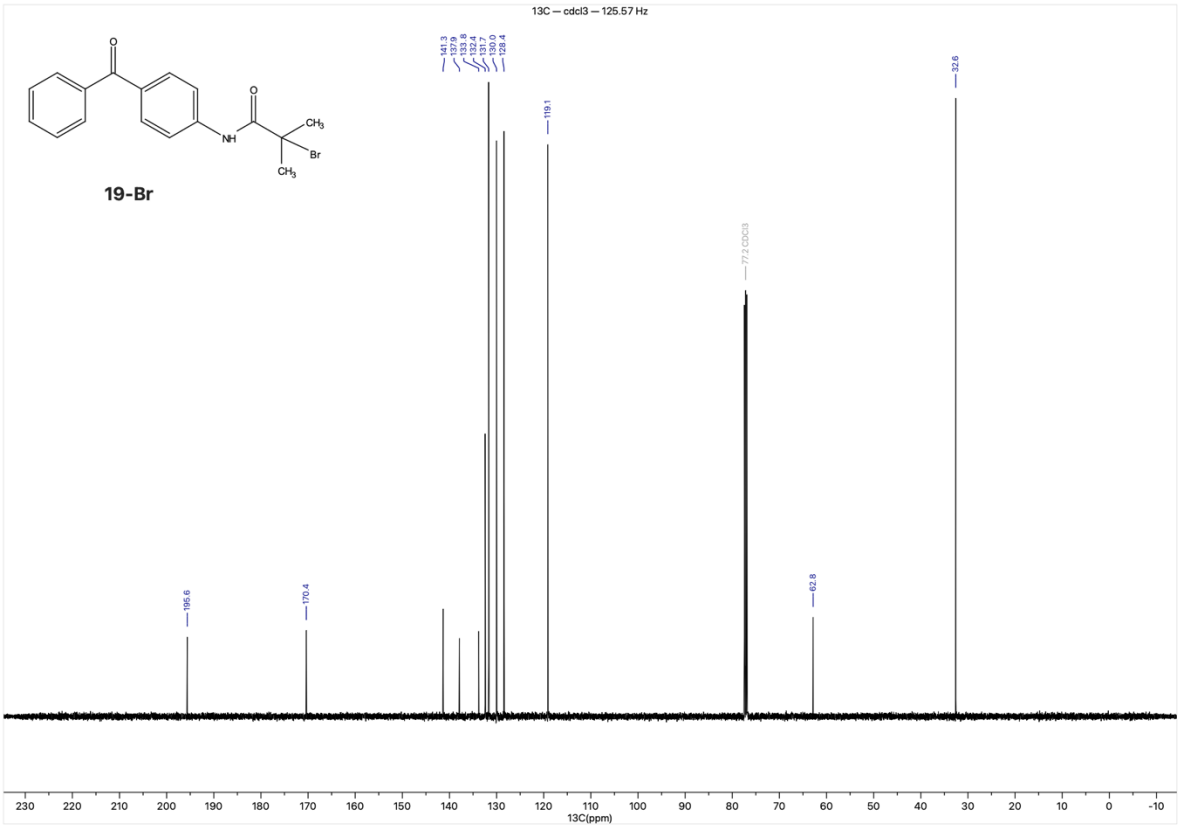

13C — cdcl3 — 125.57 Hz
Br
CH3
O
NH
CH3
Br
CH3
CH3
18-Br
132.8
131.2
77.2 CDCl3
32.7
18.2
137.7
170.5
121.1
62.9
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
13C(ppm)

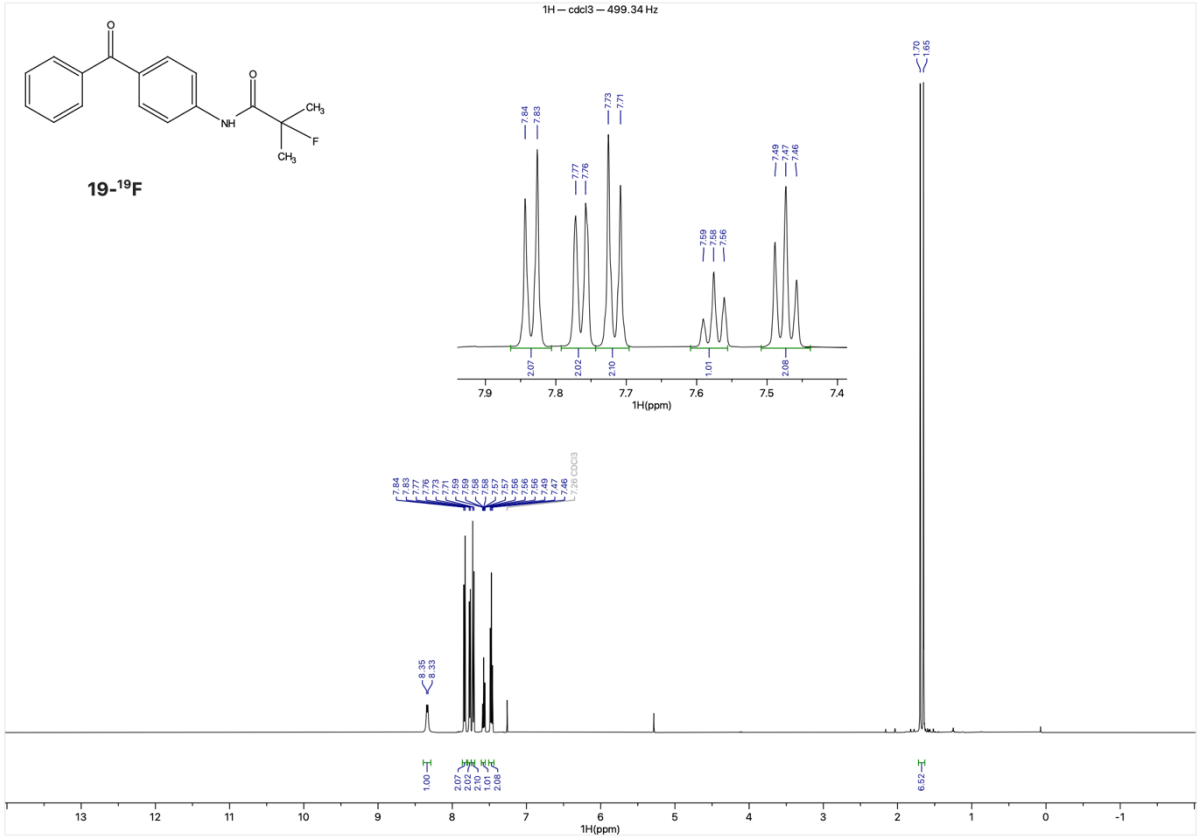

1H — cdcl3 — 499.32 Hz
Br
CH3
O
NH
CH3
F
CH3
CH3
18-19F
2.18
1.70
1.66
7.26 CDCl3
7.23
7.60
7.59
0.98
2.00
6.56
6.81
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
1H(ppm)

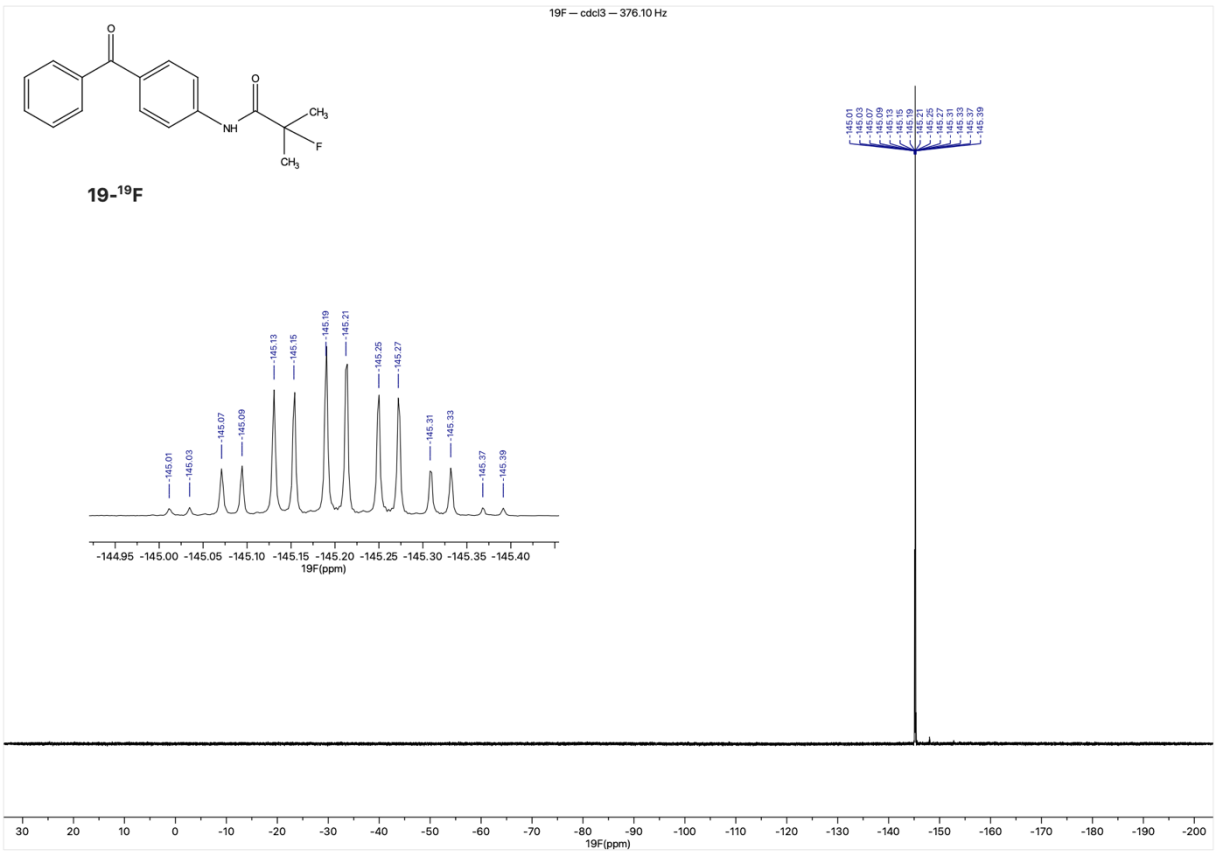

19F — cdcl3 — 469.79 Hz
18-19F
-145.01
-145.02
-145.05
-145.07
-145.10
-145.12
-145.15
-145.16
-145.20
-145.21
-145.24
-145.26
-145.29
-145.31
-145.00
-145.05
-145.10
-145.15
-145.20
-145.25
-145.30
19F(ppm)
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
19F(ppm)

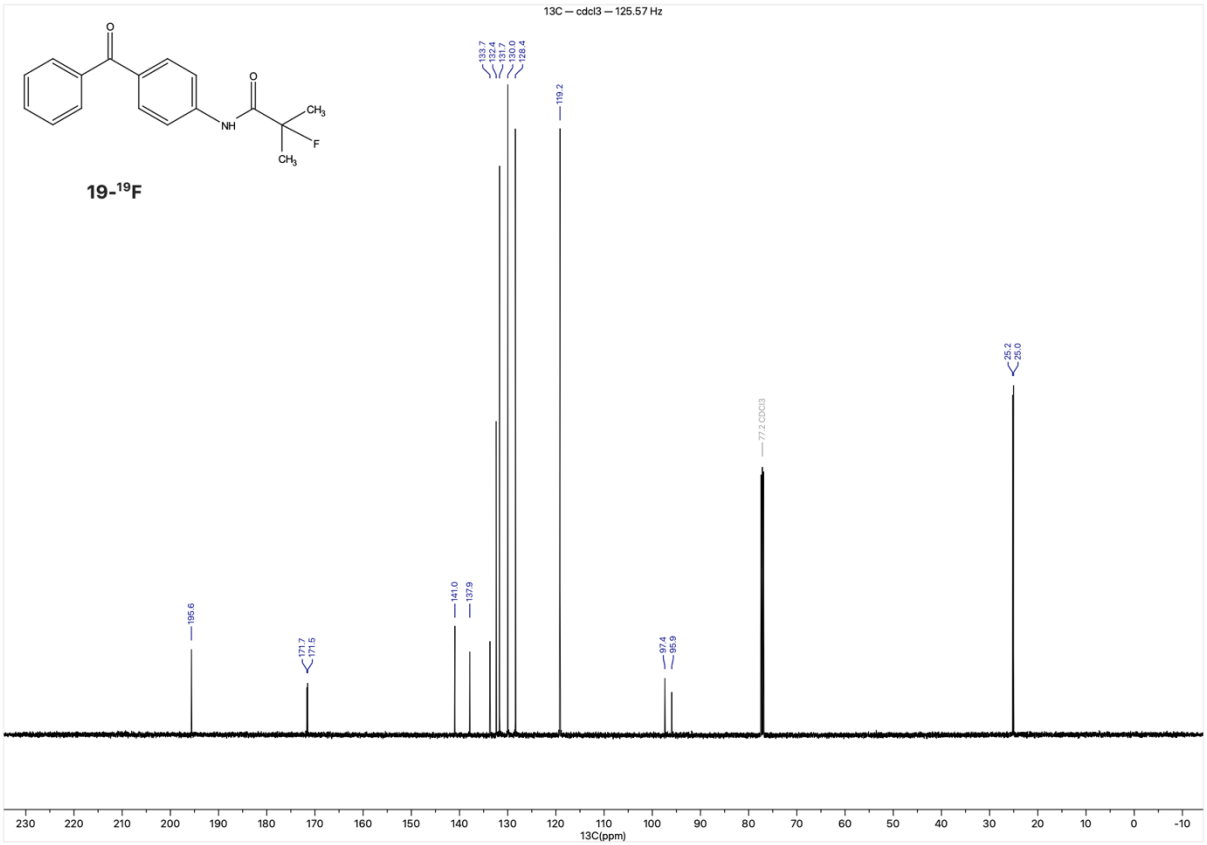

13C — cdcl3 — 125.57 Hz
18-19F
132.0
131.2
137.7
121.1
97.7
96.3
77.2 CDCl3
25.3
25.2
18.1
171.6
171.5
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
13C(ppm)

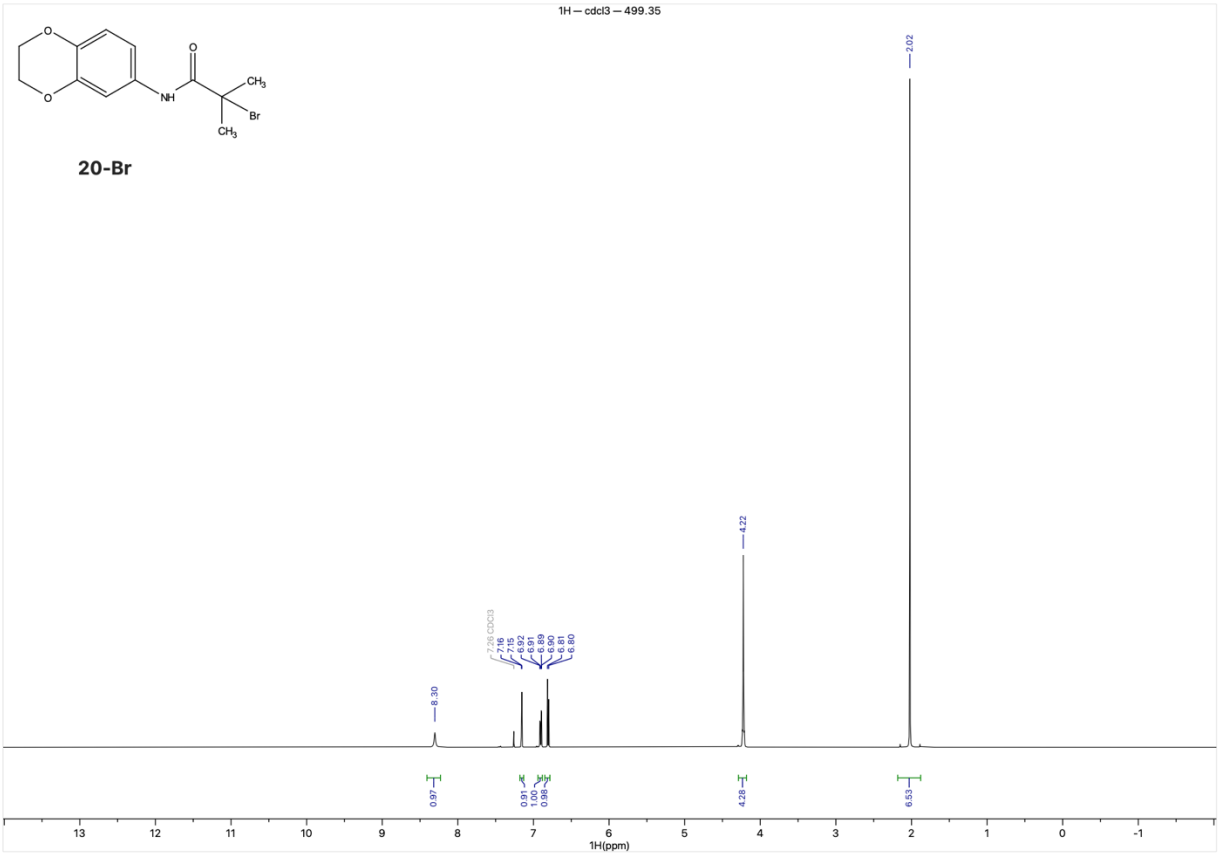

1H — cdcl3 — 499.35 Hz
19-Br
1H(ppm)

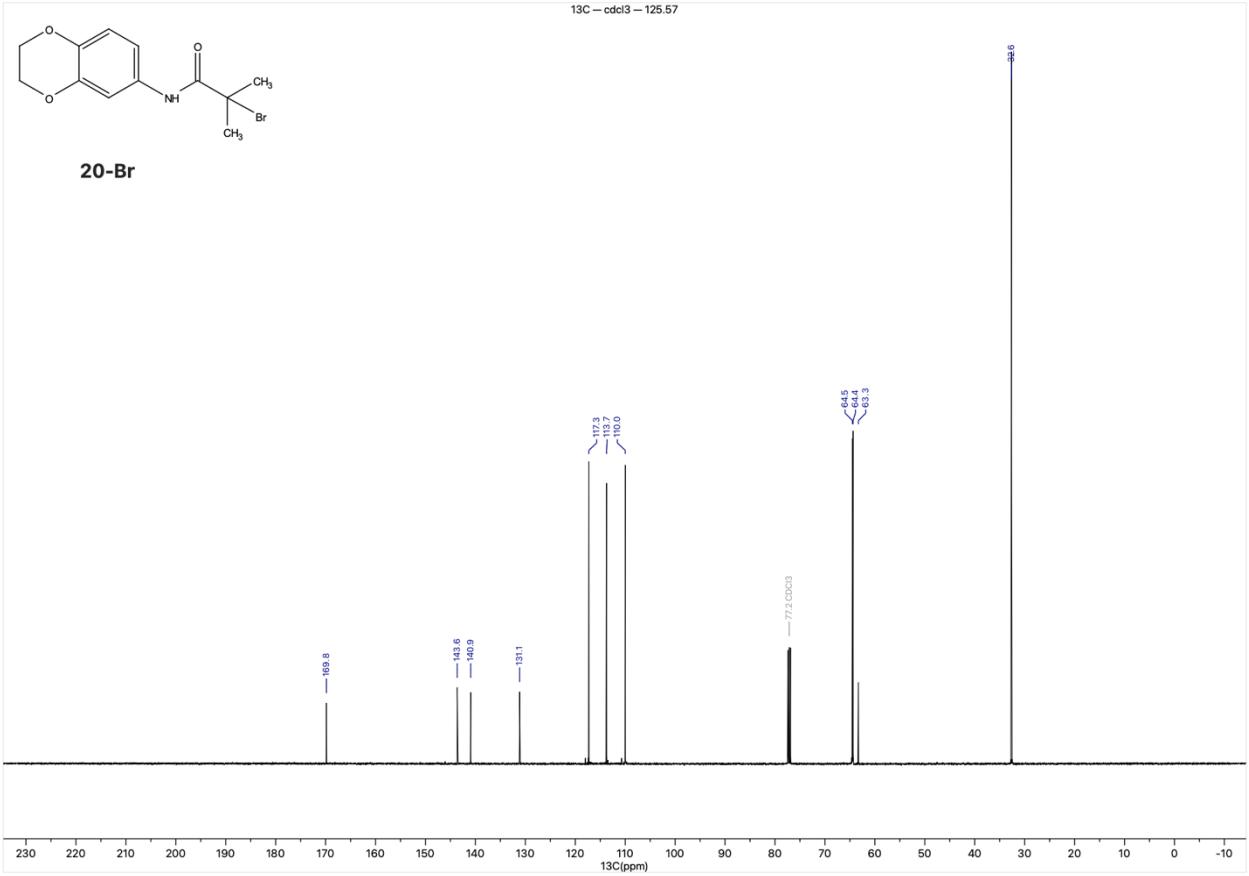

13C — cdcl3 — 125.57 Hz
19-Br
13C(ppm)

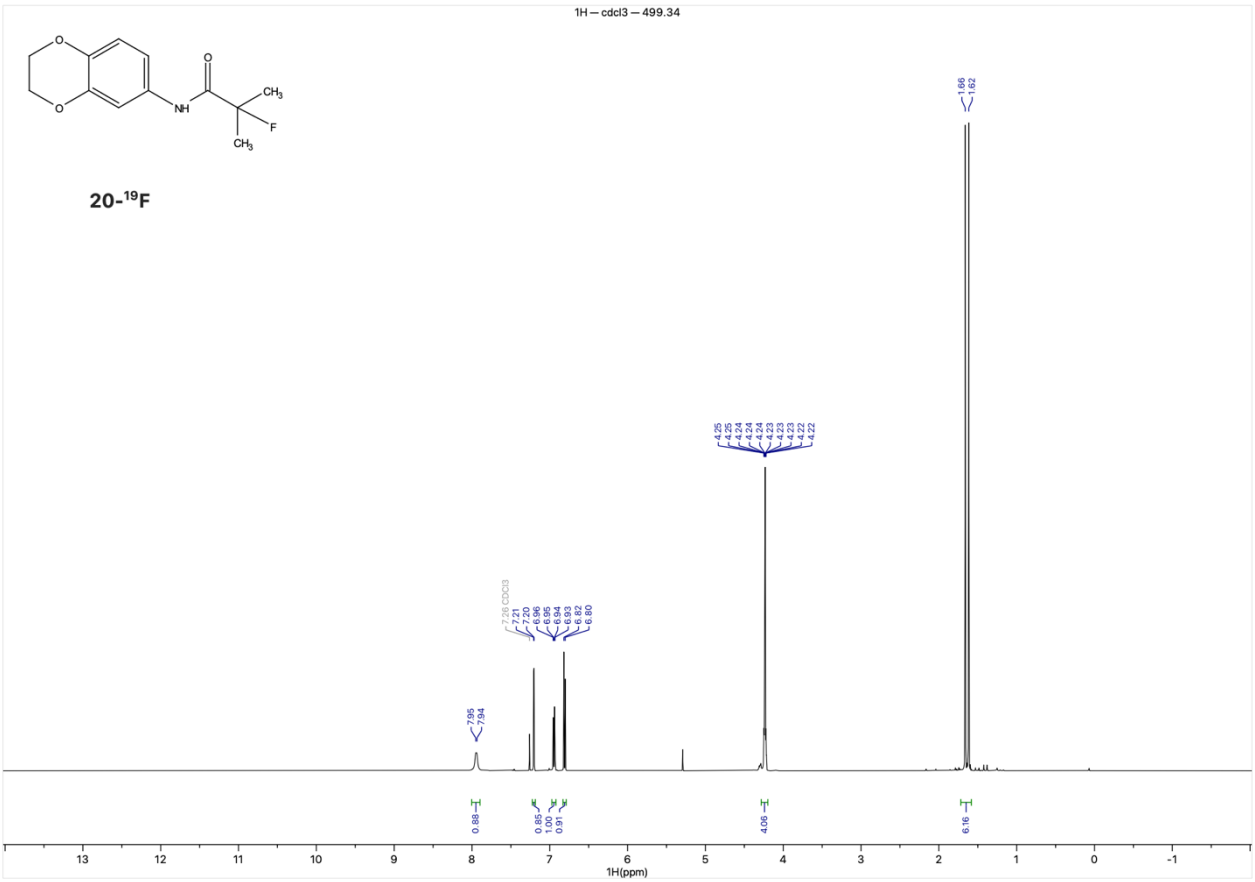

1H — cdcl3 — 499.34 Hz
19-19F
1H(ppm)

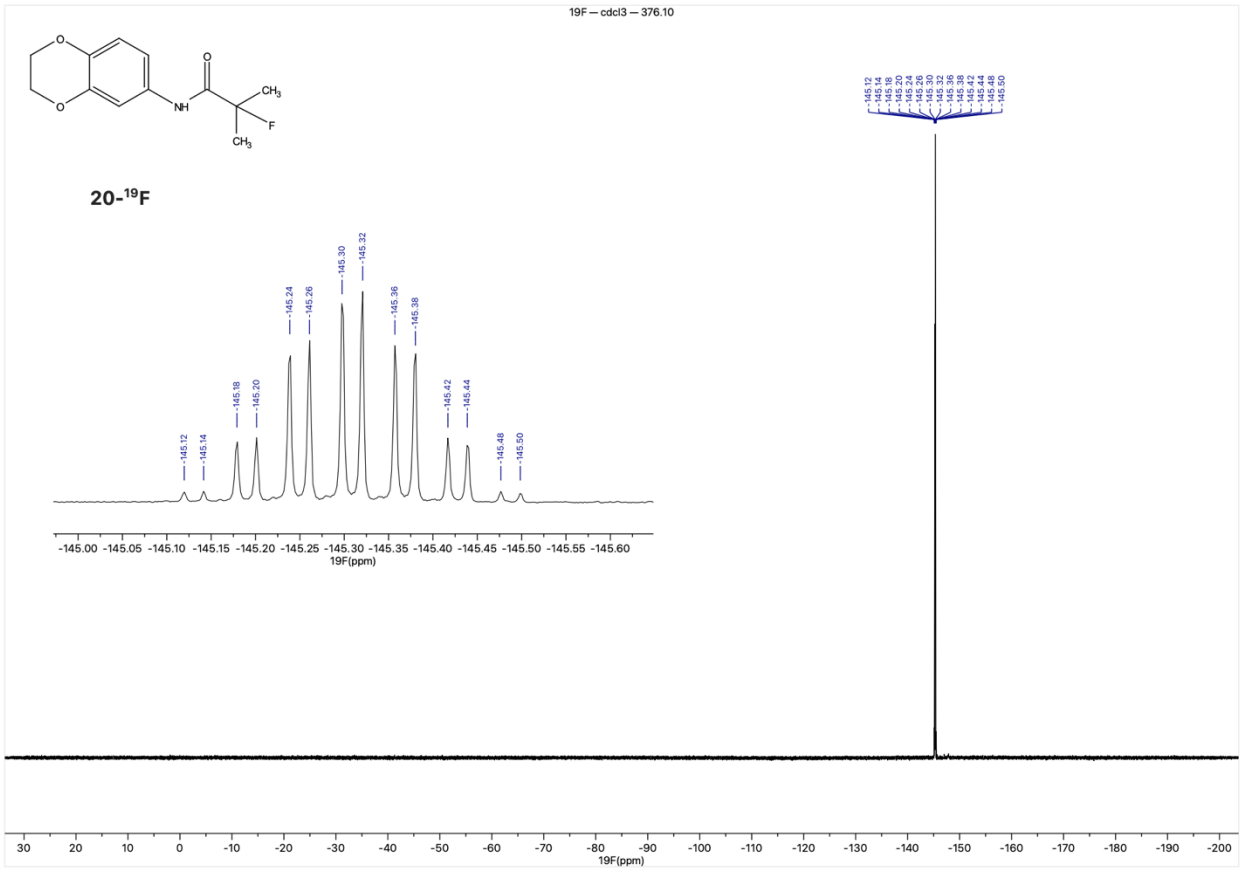

19F — cdcl3 — 376.10 Hz
19-19F
19F(ppm)

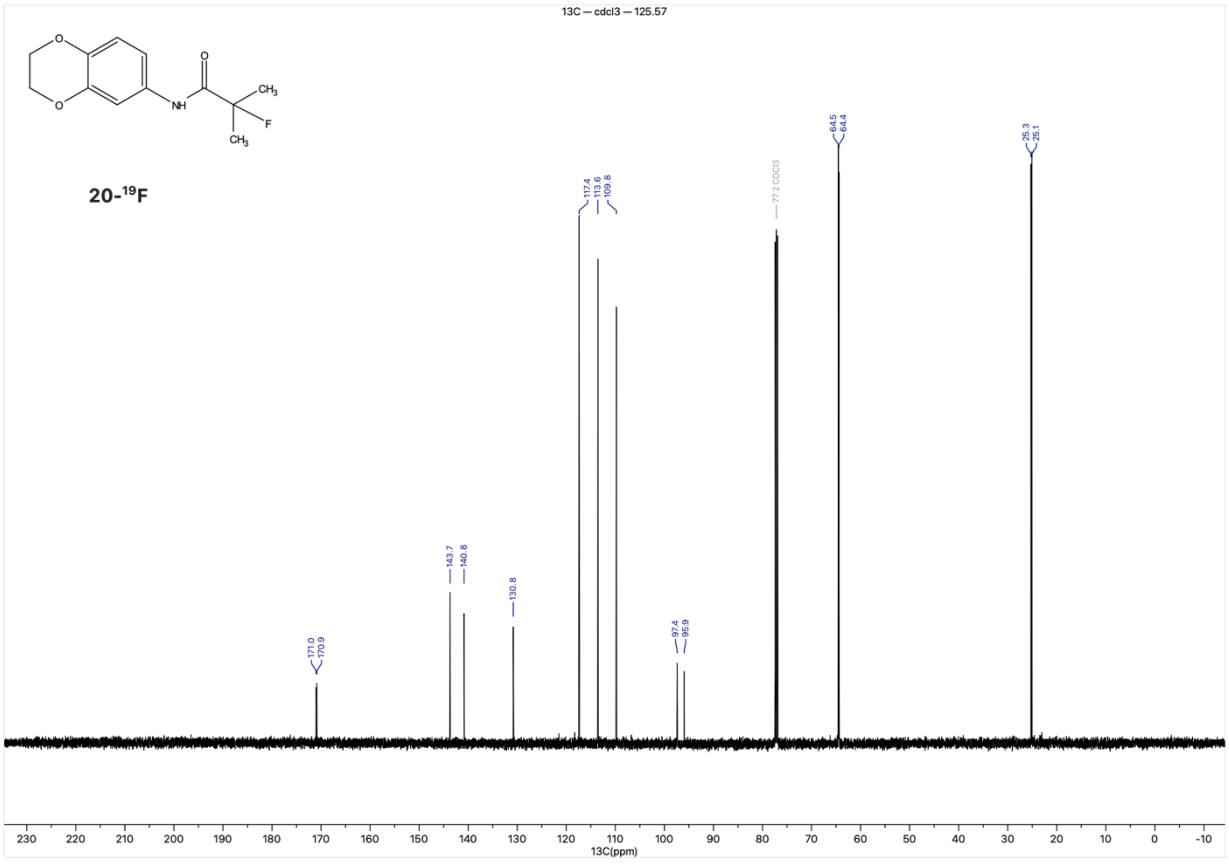

13C — cdcl3 — 125.57 Hz
19-19F
133.7
132.4
131.7
130.0
128.4
119.2
77.2 CDCl3
26.2
25.0
196.6
171.7
171.5
141.0
137.9
97.4
95.9
13C(ppm)

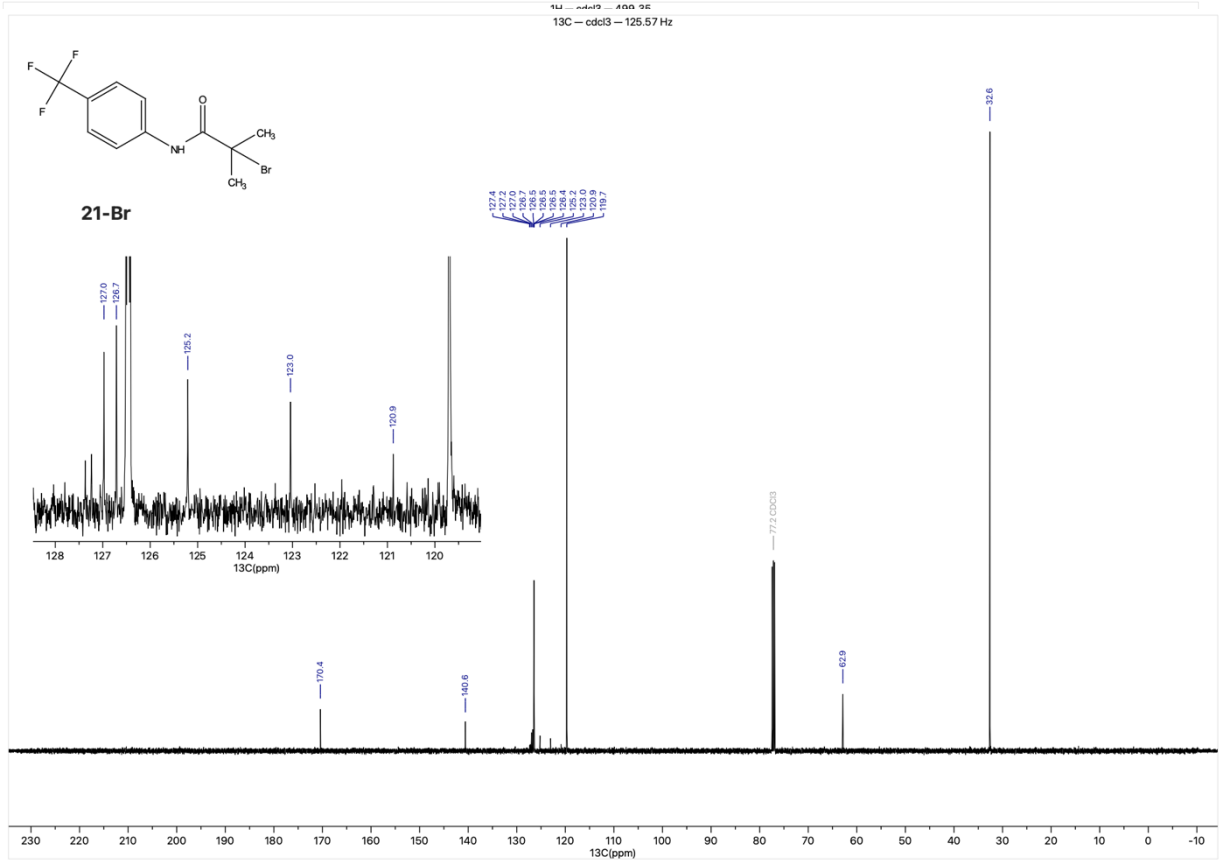

1H — cdcl3 — 499.35
20-Br
2.02
4.22
7.26 CDCl3
7.16
7.15
6.92
6.91
6.89
6.80
6.81
6.80
8.30
0.97
0.91
1.00
0.98
4.28
6.53
1H(ppm)

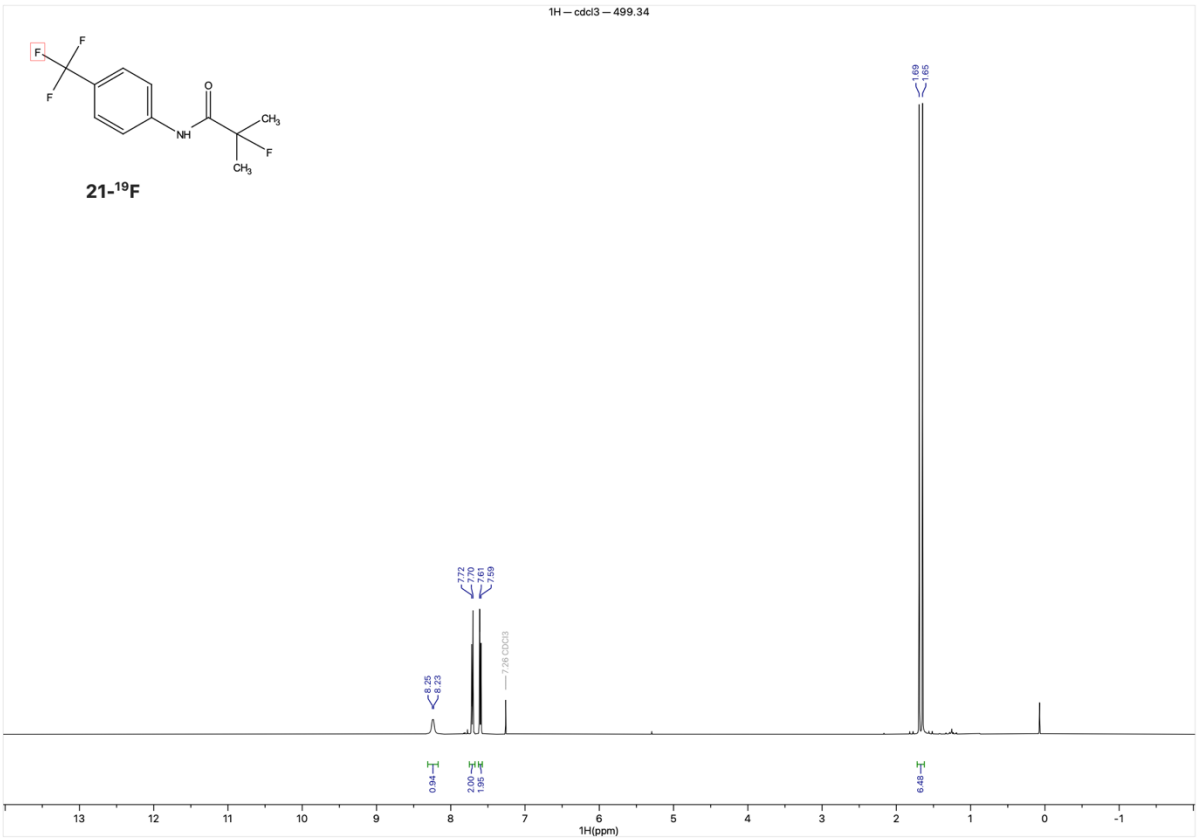

13C — cdcl3 — 125.57
20-Br
169.8
143.6
140.9
131.1
117.3
113.7
110.0
77.2 CDCl3
64.5
64.4
63.3
28.8
13C(ppm)

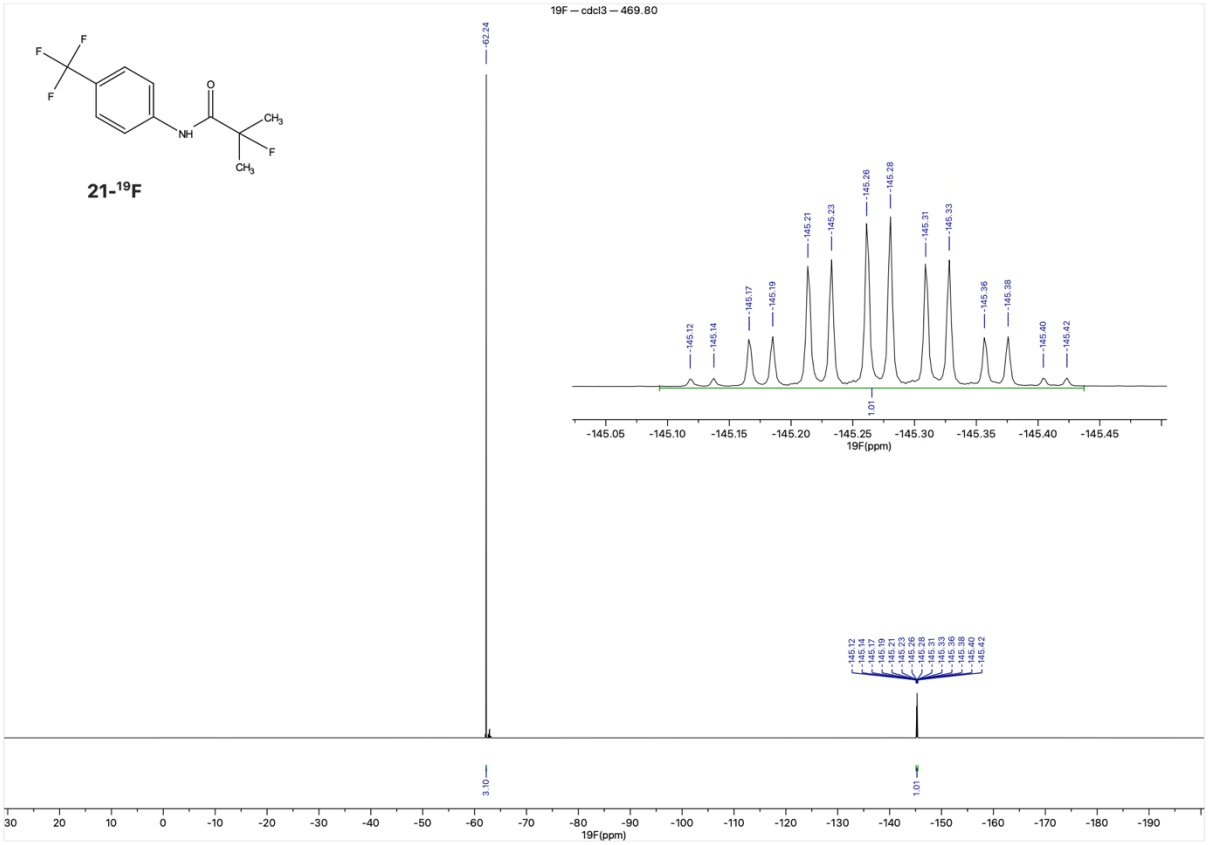

1H — cdcl3 — 499.34
20-19F
7.95
7.94
7.26 CDCl3
7.21
7.20
6.96
6.95
6.94
6.93
6.82
6.80
4.25
4.25
4.24
4.24
4.24
4.24
4.23
4.23
4.23
4.22
4.22
4.22
1.66
1.62
0.88
0.85
1.00
0.97
4.06
6.16
1H(ppm)

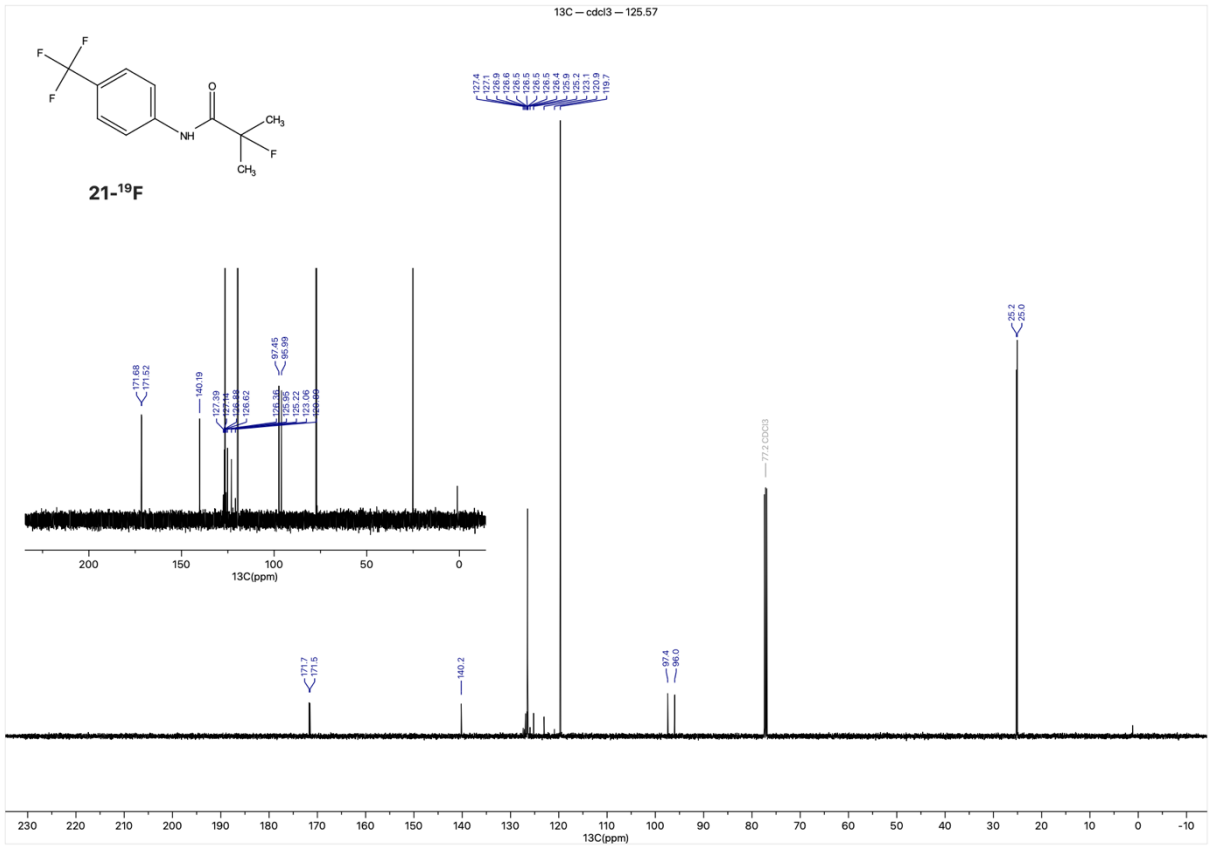

19F — cdcl3 — 376.10
20-19F
-145.12
-145.14
-145.18
-145.20
-145.24
-145.26
-145.30
-145.32
-145.36
-145.38
-145.42
-145.44
-145.48
-145.50
-145.00 -145.05 -145.10 -145.15 -145.20 -145.25 -145.30 -145.35 -145.40 -145.45 -145.50 -145.55 -145.60
19F(ppm)
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
19F(ppm)

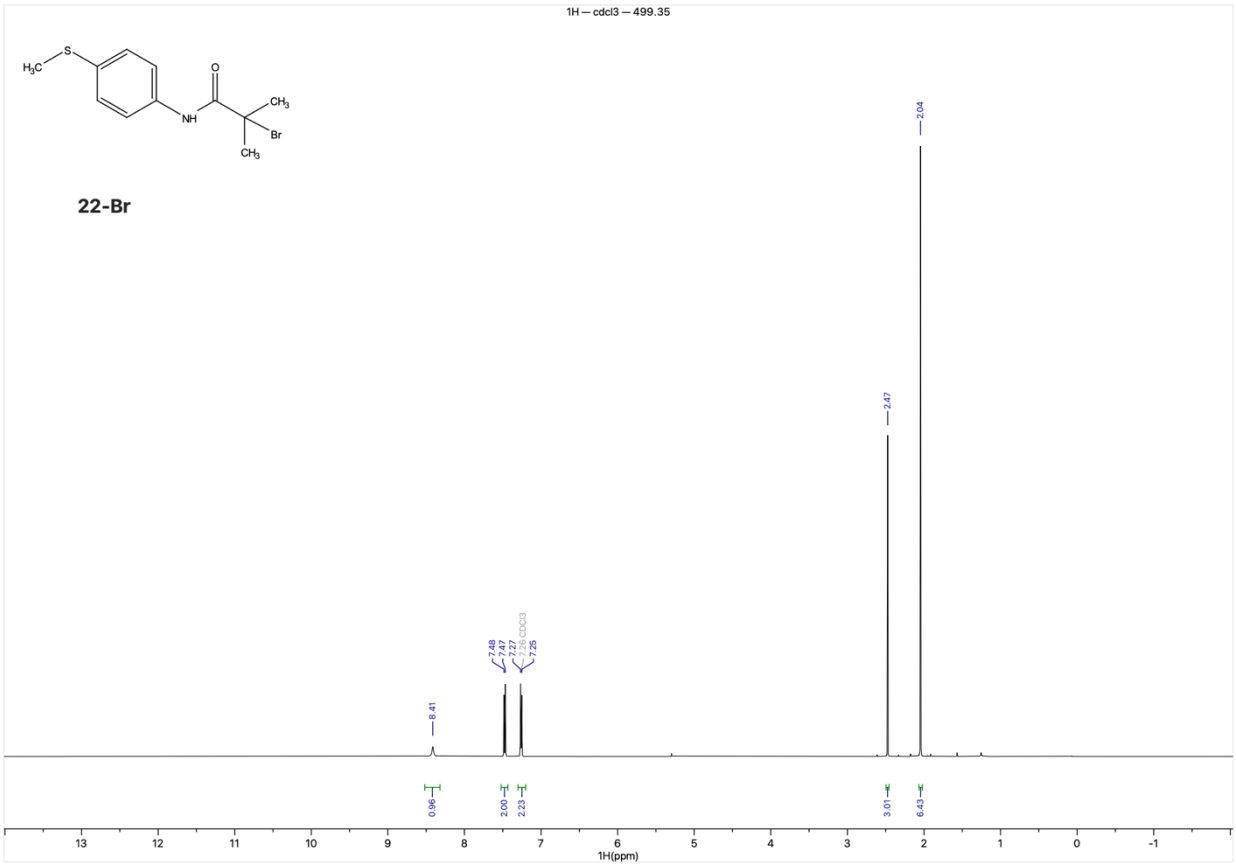

13C — cdcl3 — 125.57
20-19F
171.0
170.9
143.7
140.8
130.8
117.4
113.6
109.8
97.4
95.9
77.2 CDCl3
64.5
64.4
25.3
25.1
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
13C(ppm)

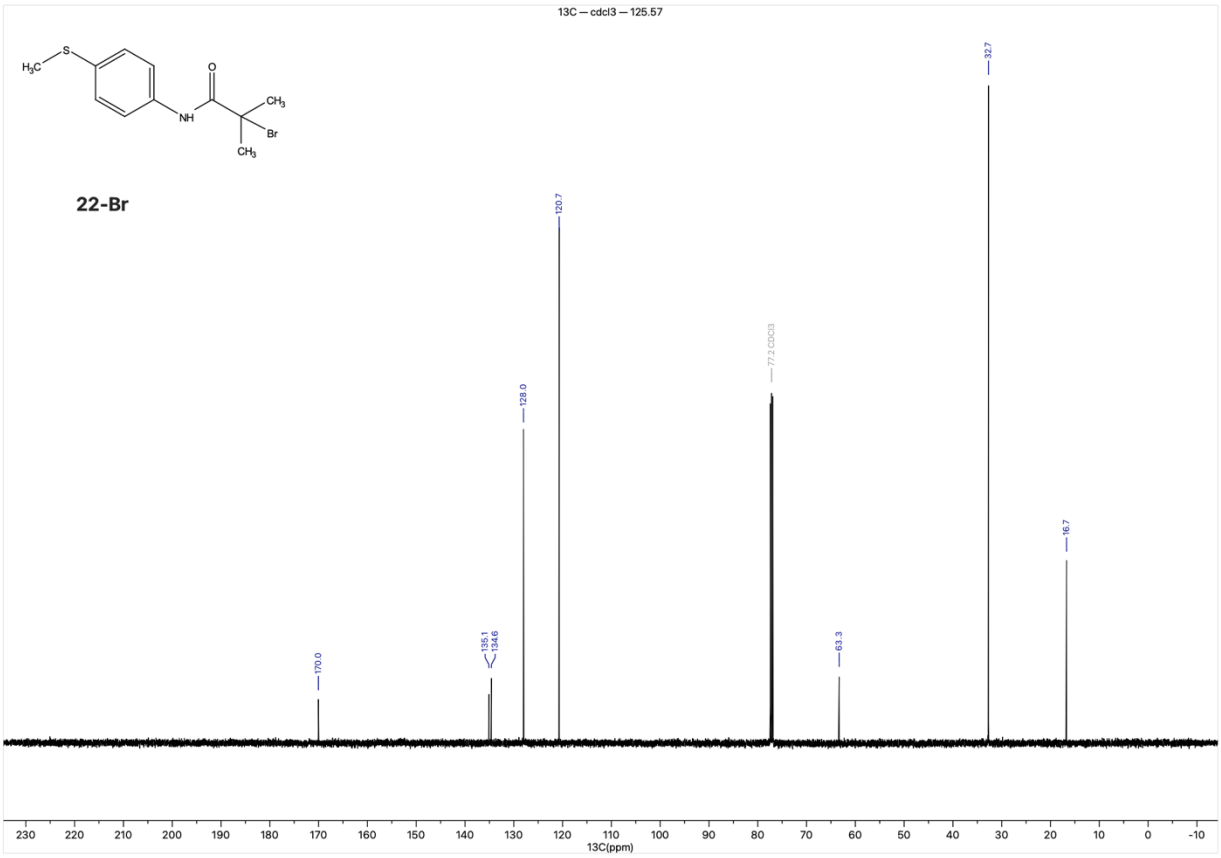

13C — cdcl3 — 125.57 Hz
21-Br
13C(ppm)

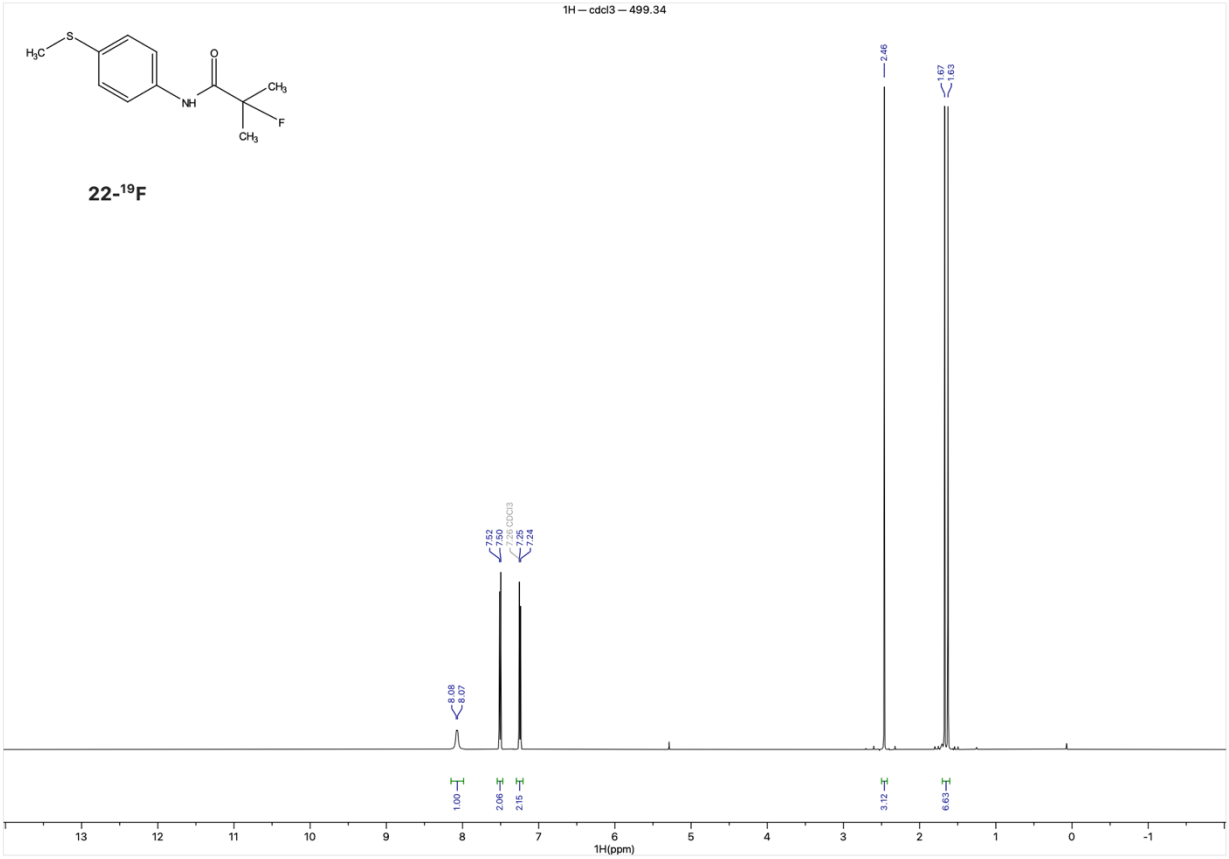

1H — cdcl3 — 499.34
21-19F
1H(ppm)

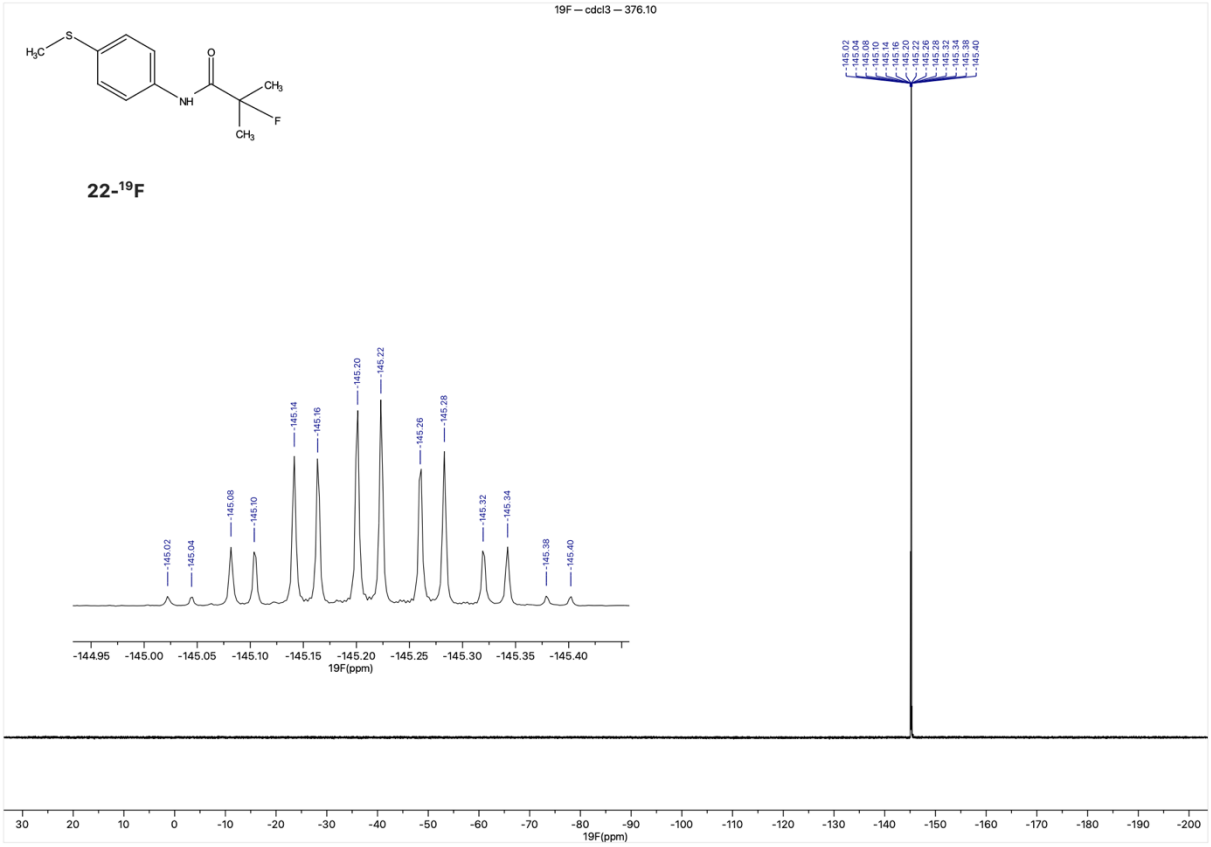

19F — cdcl3 — 469.80
-62.24
-145.12
-145.14
-145.17
-145.19
-145.21
-145.23
-145.26
-145.28
-145.31
-145.33
-145.36
-145.38
-145.40
-145.42
1.01
-145.05
-145.10
-145.15
-145.20
-145.25
-145.30
-145.35
-145.40
-145.45
19F(ppm)
3.10
1.01
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
19F(ppm)
21-19F

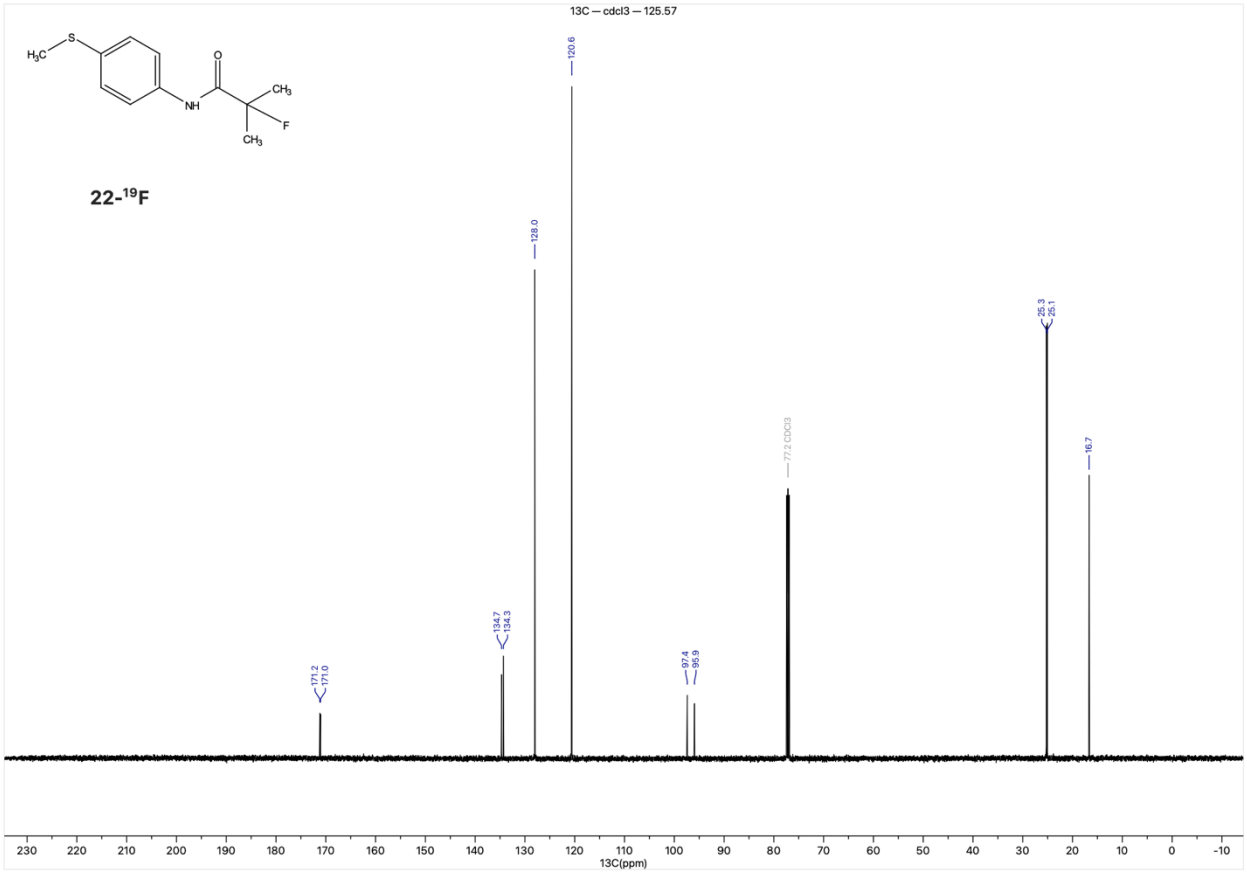

13C — cdcl3 — 125.57
171.68
171.52
140.19
127.39
97.45
95.99
126.62
126.36
125.95
125.22
26.2
25.0
77.2 CDCl3
171.7
171.5
140.2
97.4
96.0
200
150
100
50
0
13C(ppm)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
13C(ppm)
21-19F


1H — cdcl3 — 499.35
22-Br
8.41
7.48
7.47
7.27
7.26 CDCl3
7.25
2.47
2.04
0.96
2.00
2.23
3.01
6.43
1H(ppm)

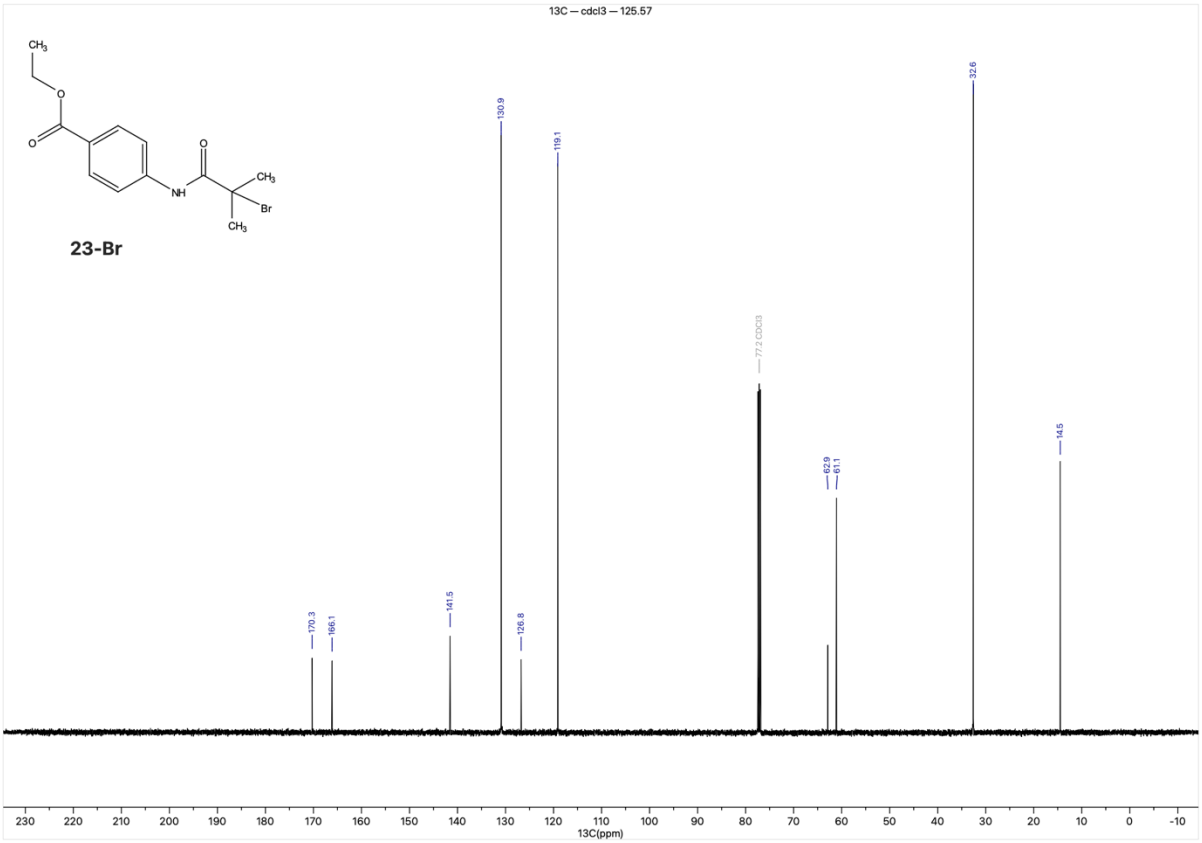

13C — cdcl3 — 125.57
22-Br
170.0
135.1
134.6
128.0
120.7
77.2 CDCl3
63.3
32.7
16.7
13C(ppm)

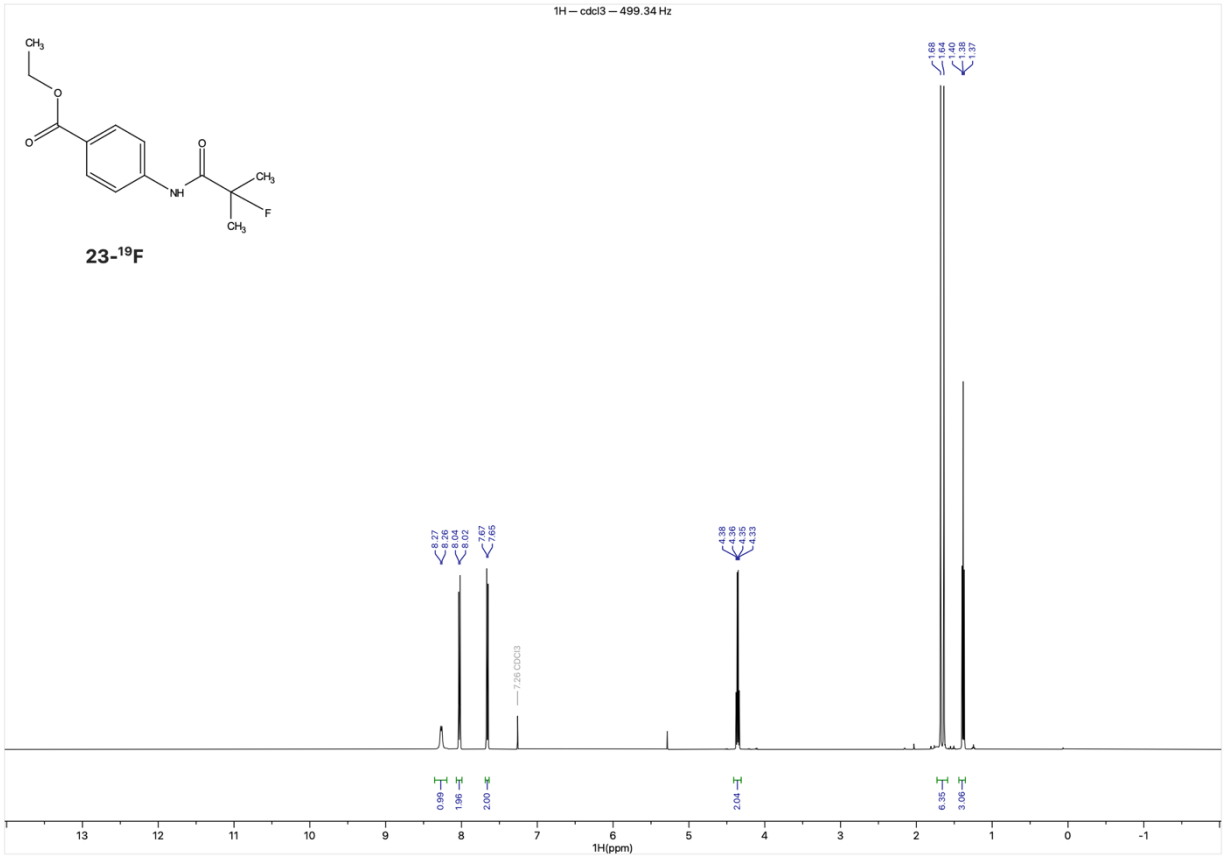

1H — cdcl3 — 499.34
22-19F
2.46
1.67
1.63
7.52
7.50
7.26 CDCl3
7.25
7.24
8.08
8.07
1.00
2.06
2.15
3.12
6.63
1H(ppm)

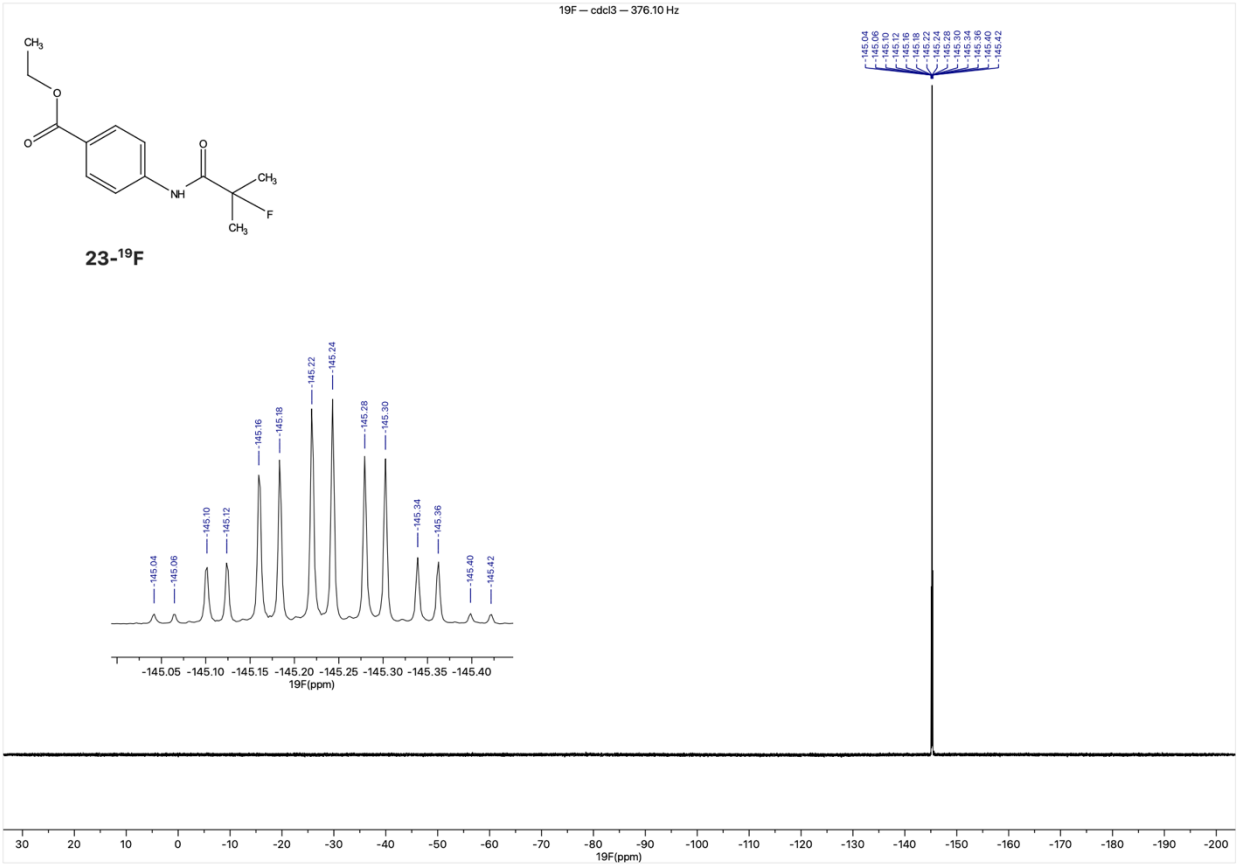

19F — cdcl3 — 376.10
22-19F
-145.02
-145.04
-145.08
-145.10
-145.14
-145.16
-145.20
-145.22
-145.26
-145.28
-145.32
-145.34
-145.38
-145.40
19F(ppm)

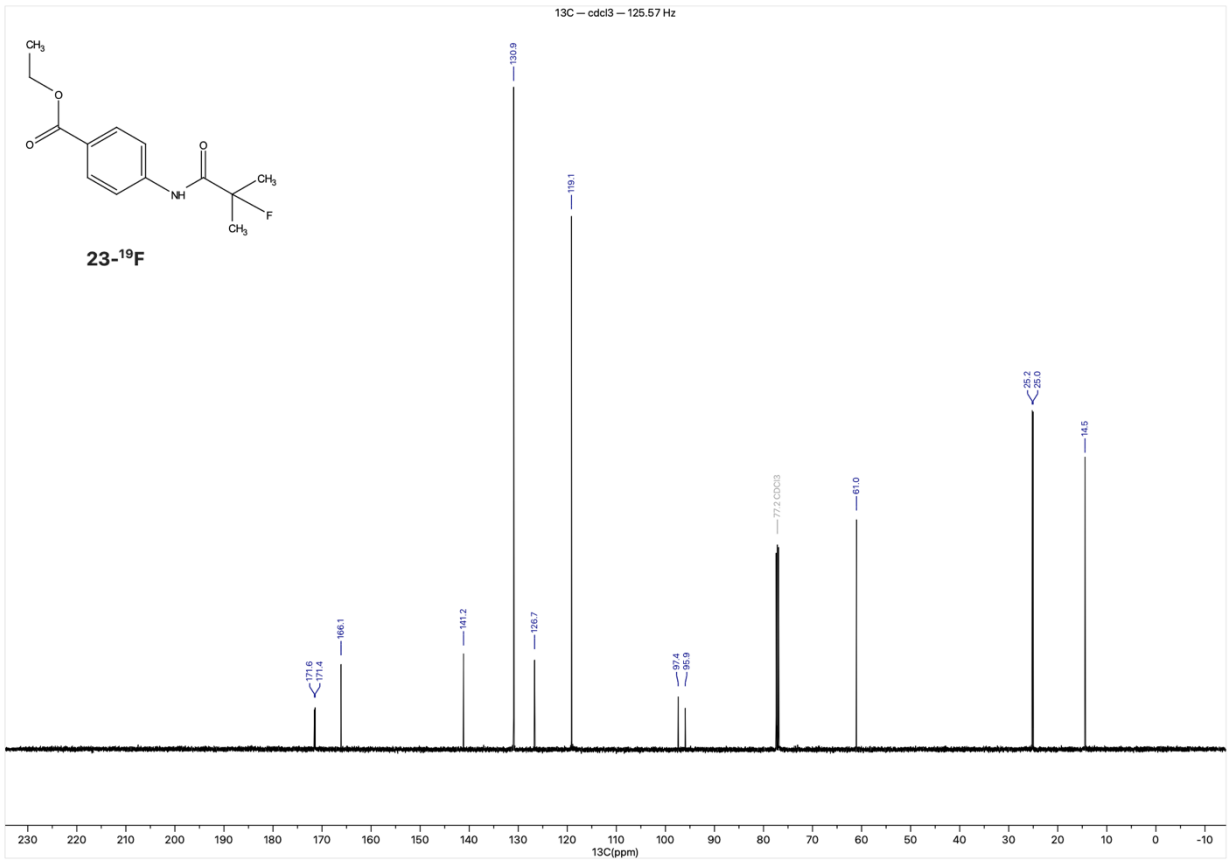

13C — cdcl3 — 125.57
22-19F
171.2
171.0
134.7
134.3
128.0
120.6
97.4
96.9
77.2 CDCl3
25.3
25.1
16.7
13C(ppm)

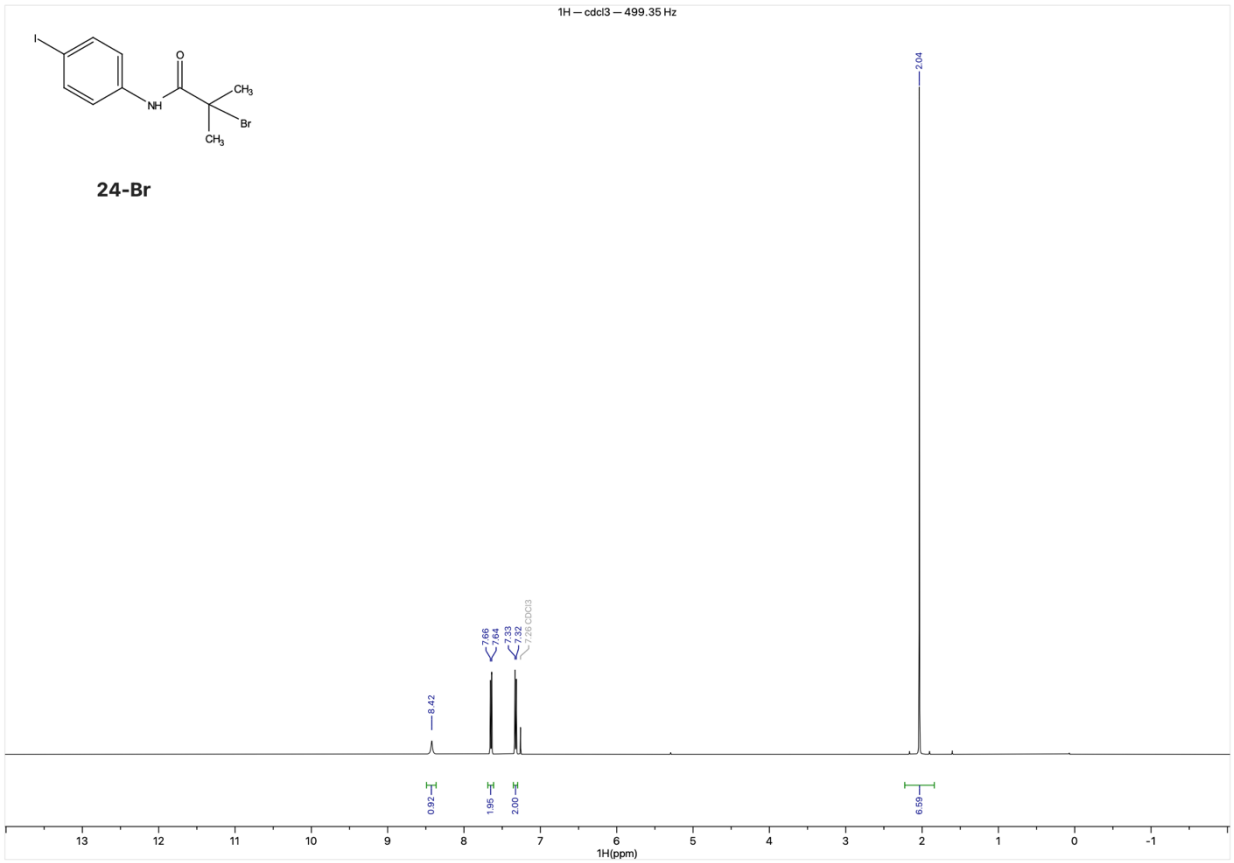

1H — cdcl3 — 499.35
23-Br
8.59
8.04
8.03
7.64
7.62
7.26 CDCl3
4.38
4.37
4.36
4.34
2.05
1.40
1.38
1.37
1.00
1.98
2.03
2.06
6.31
3.09
1H(ppm)

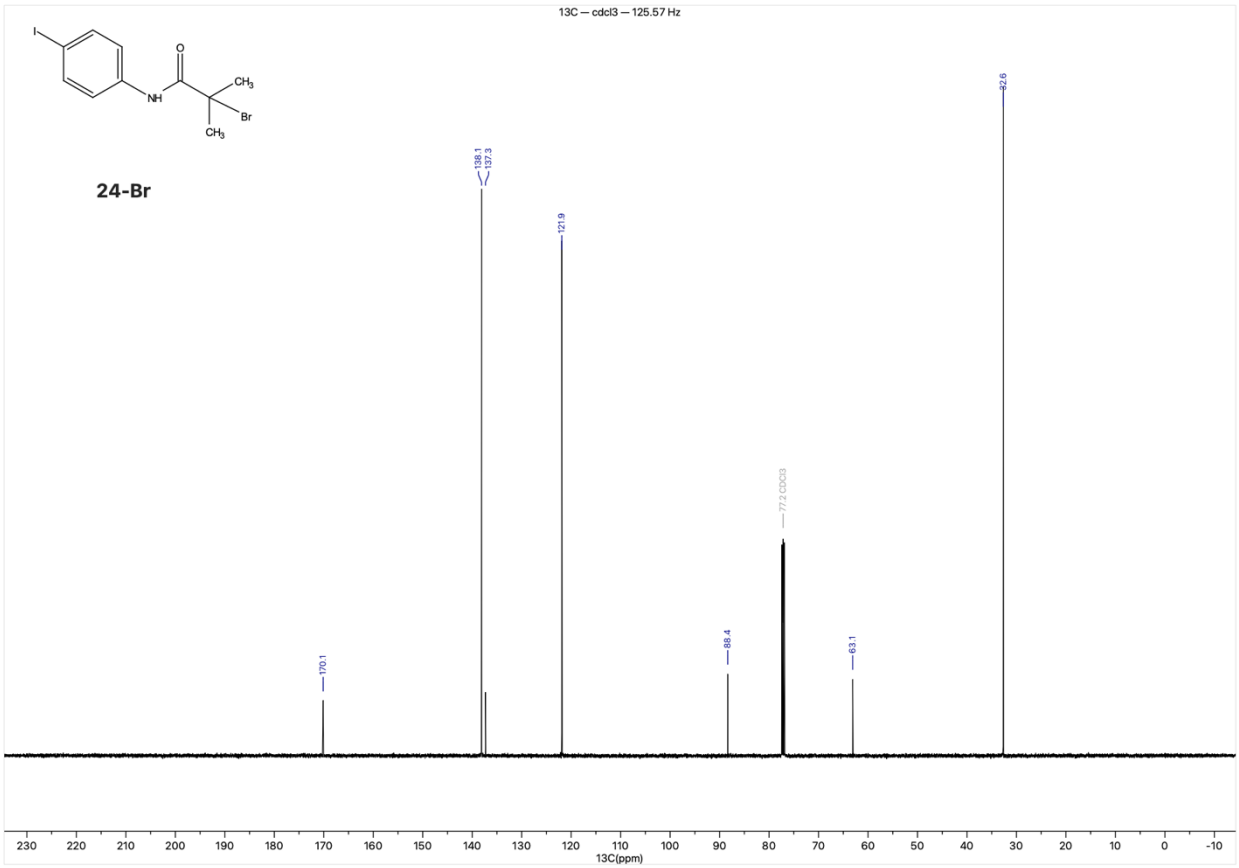

13C — cdcl3 — 125.57
23-Br
170.3
166.1
141.5
130.9
126.8
119.1
77.2 CDCl3
62.9
61.1
32.6
14.5
13C(ppm)

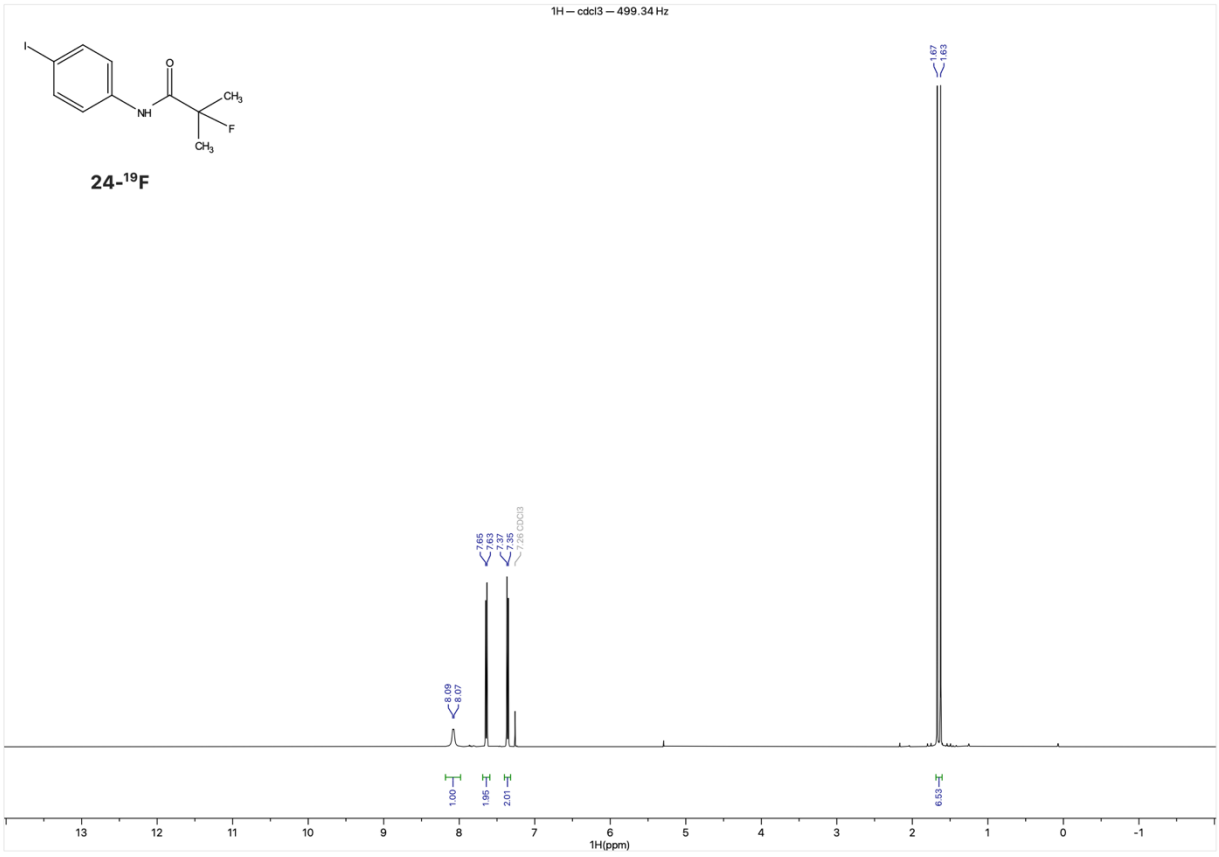

1H — cdcl3 — 499.34 Hz
23-19F
8.27
8.26
8.04
8.02
7.67
7.65
7.26 CDCl3
4.38
4.36
4.35
4.33
1.68
1.64
1.40
1.38
1.37
0.99
1.96
2.00
2.04
6.35
3.06
1H(ppm)

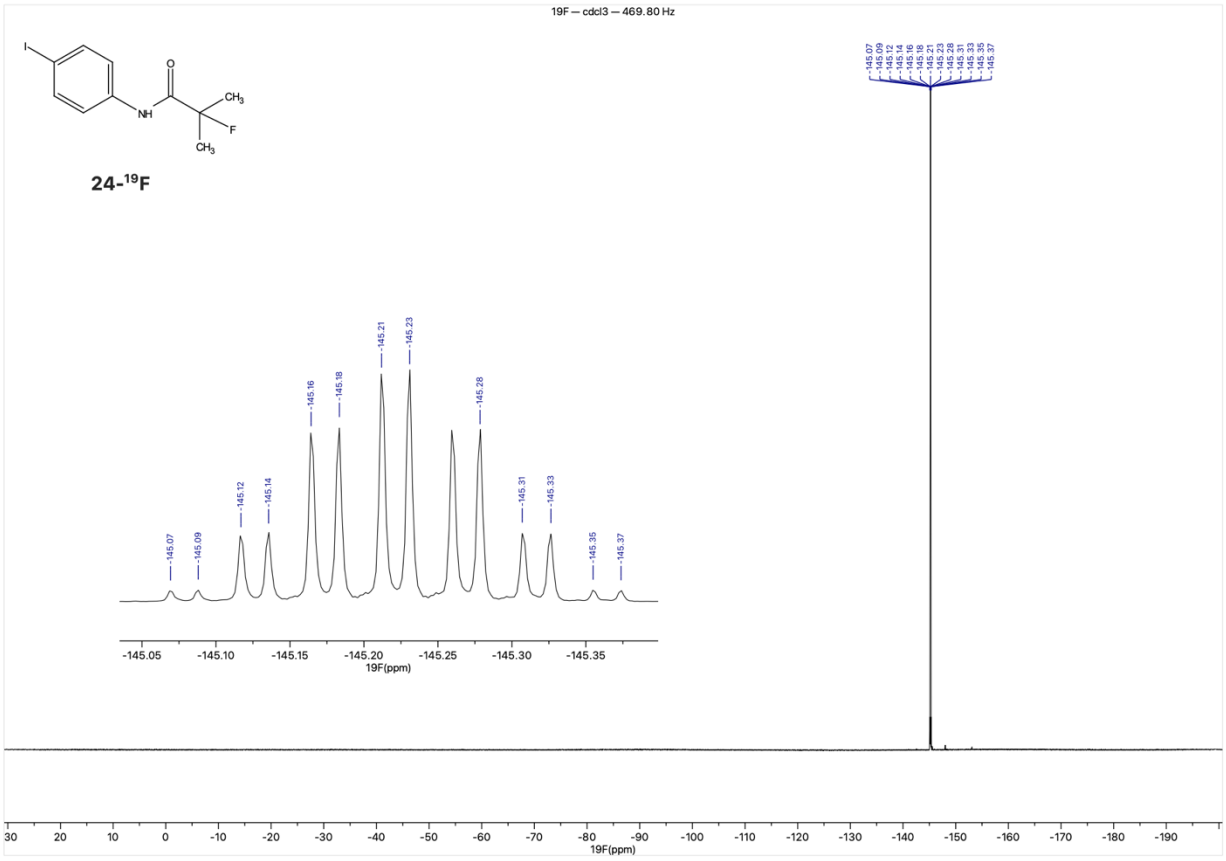

19F — cdcl3 — 376.10 Hz
23-19F
-145.04
-145.06
-145.10
-145.12
-145.16
-145.18
-145.22
-145.24
-145.28
-145.30
-145.34
-145.36
-145.40
-145.42
-145.05 -145.10 -145.15 -145.20 -145.25 -145.30 -145.35 -145.40
19F(ppm)
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
19F(ppm)

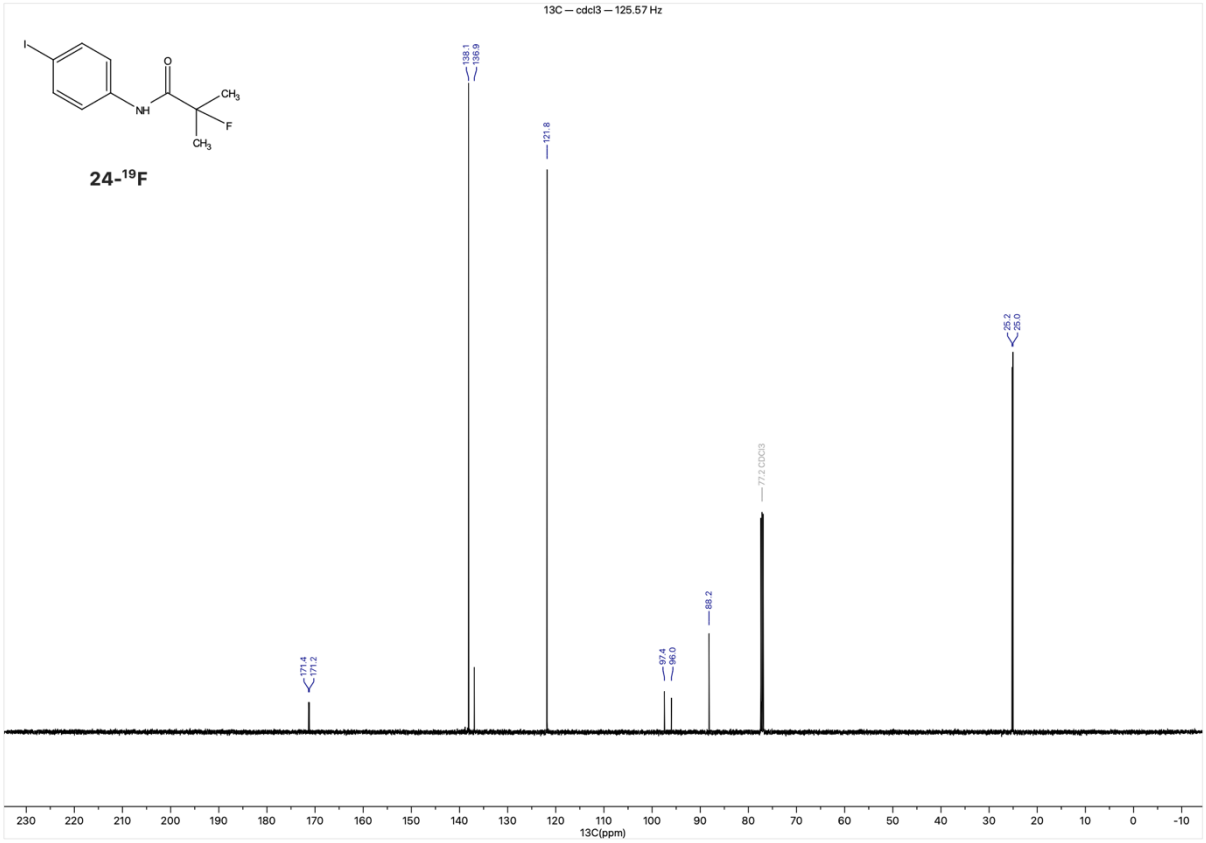

13C — cdcl3 — 125.57 Hz
23-19F
171.6
171.4
166.1
141.2
130.9
126.7
119.1
97.4
96.9
77.2 CDCl3
61.0
25.2
25.0
14.5
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
13C(ppm)

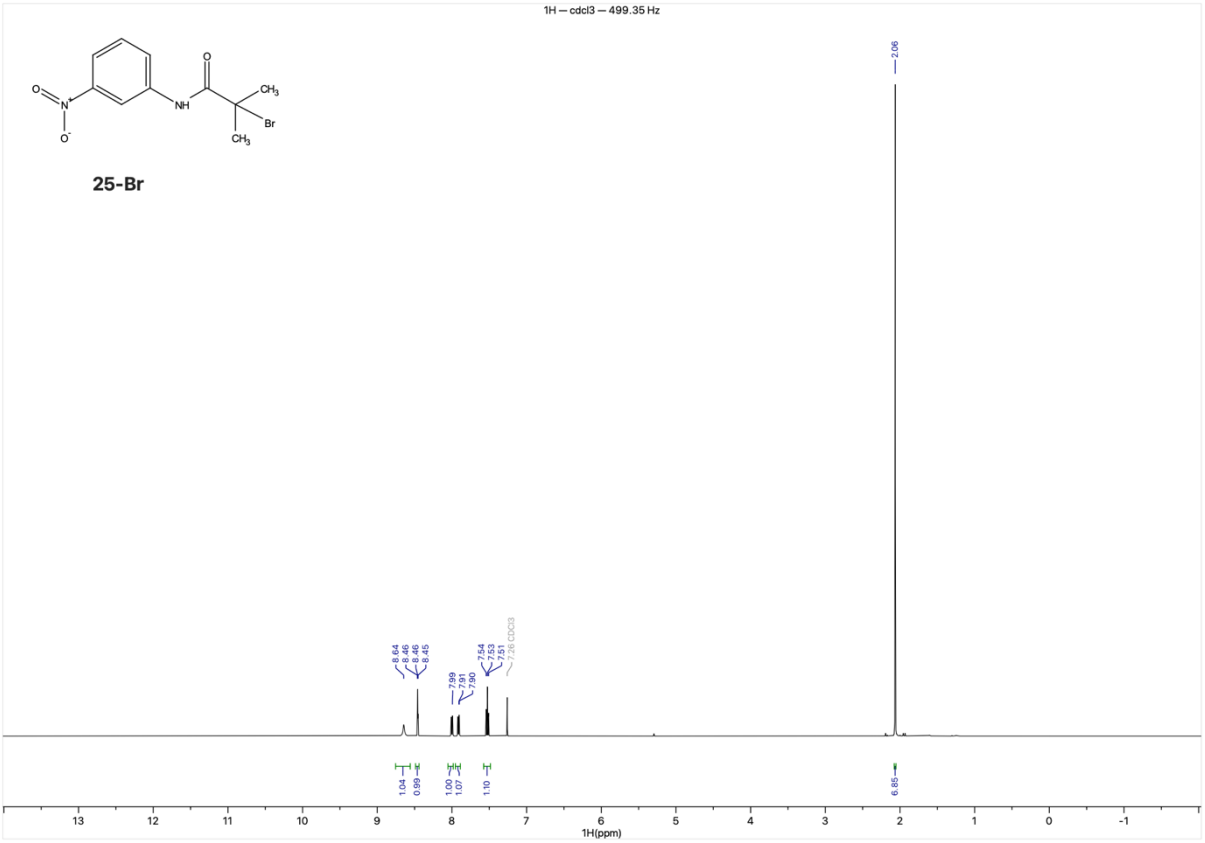

1H — cdcl3 — 499.35 Hz
24-Br
8.42
7.66
7.64
7.33
7.32
7.26 CDCl3
2.04
0.92
1.95
2.00
6.59
1H(ppm)

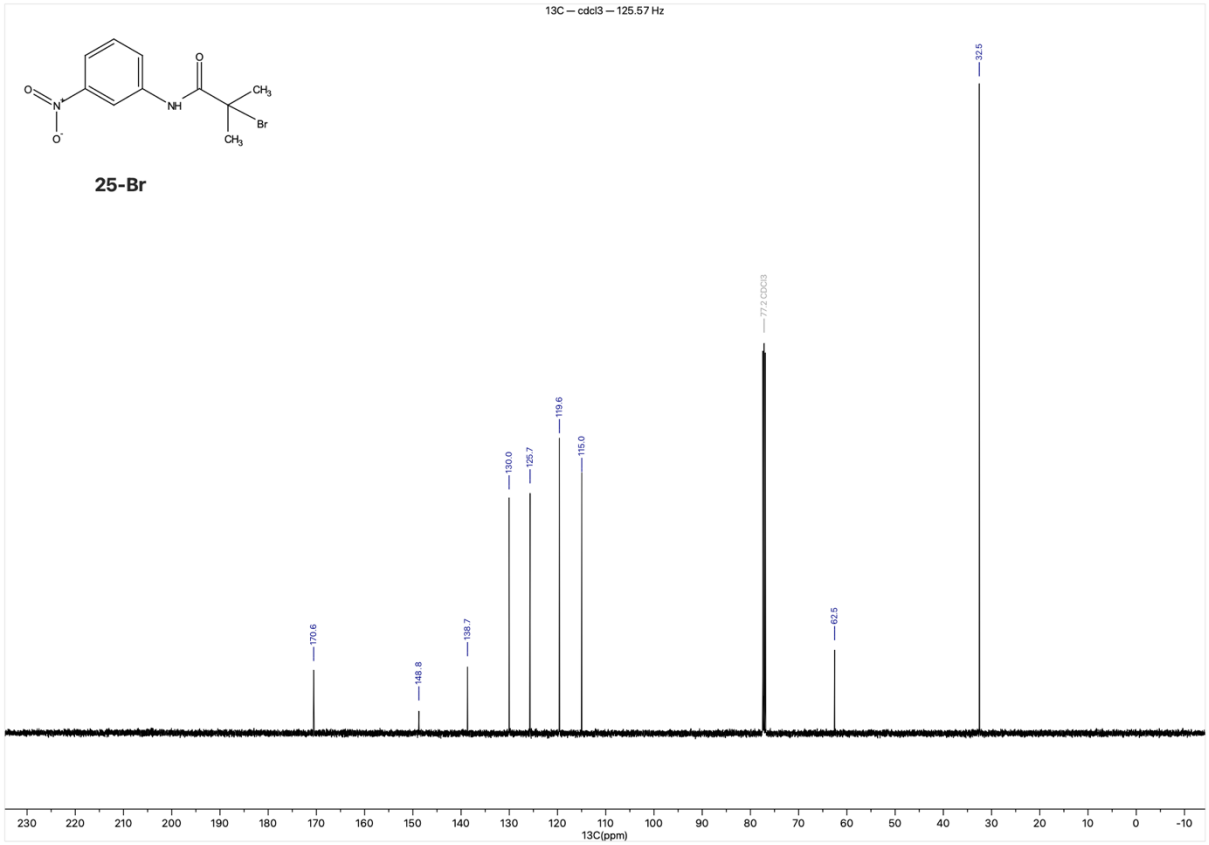

13C — cdcl3 — 125.57 Hz
24-Br
170.1
138.1
137.3
121.9
88.4
77.2 CDCl3
63.1
42.6
13C(ppm)

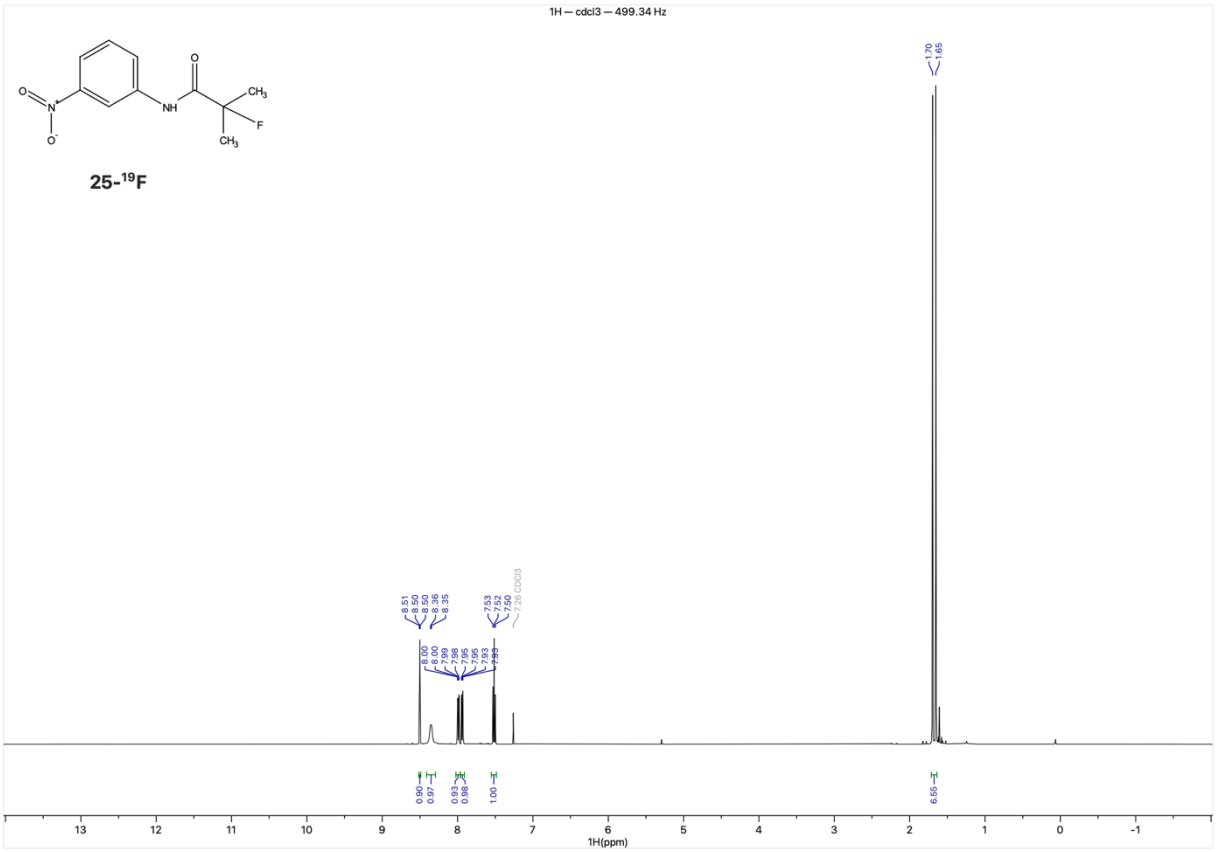

1H — cdcl3 — 499.34 Hz
24-19F
1.67
1.63
7.65
7.63
7.37
7.35
7.26 CDCl3
8.09
8.07
1.00
1.95
2.01
6.53
1H(ppm)

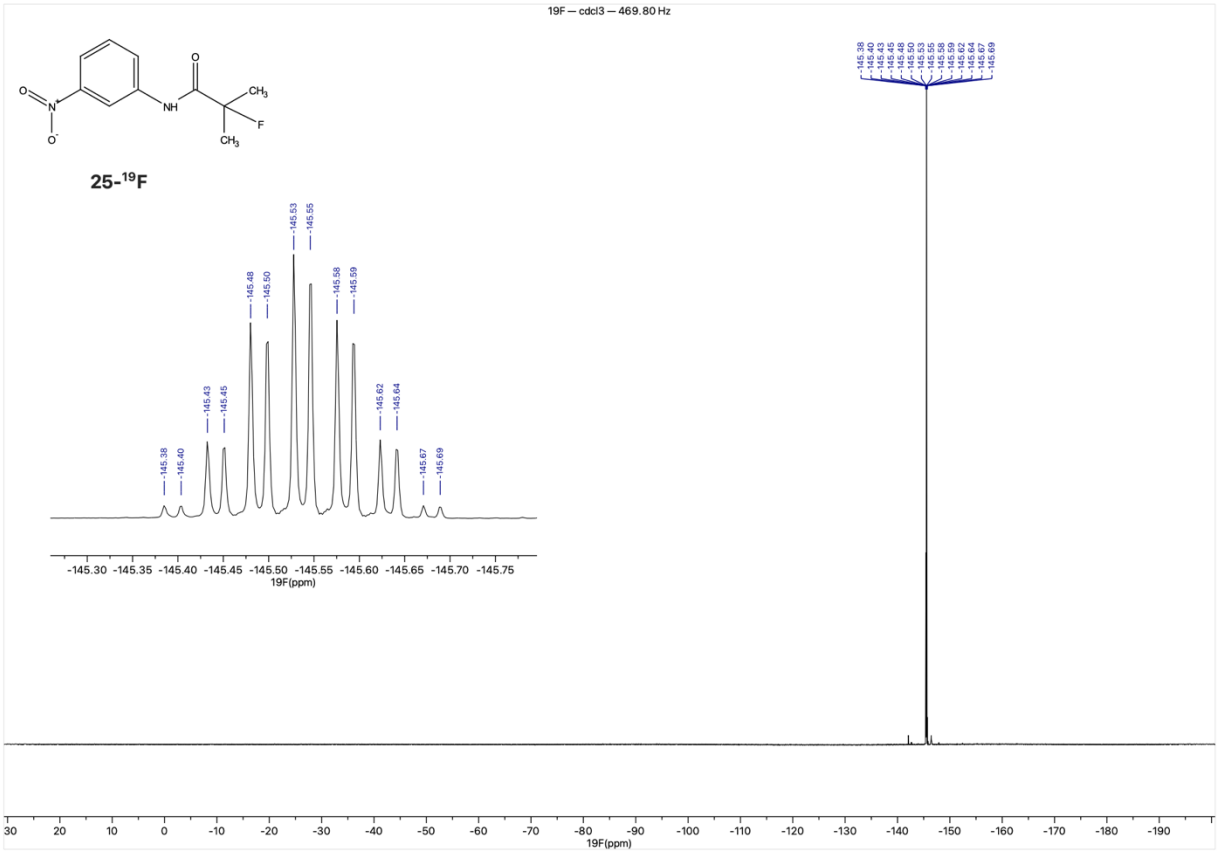

19F — cdcl3 — 469.80 Hz
24-19F
-145.07
-145.09
-145.12
-145.14
-145.16
-145.18
-145.21
-145.23
-145.28
-145.31
-145.33
-145.35
-145.37
19F(ppm)

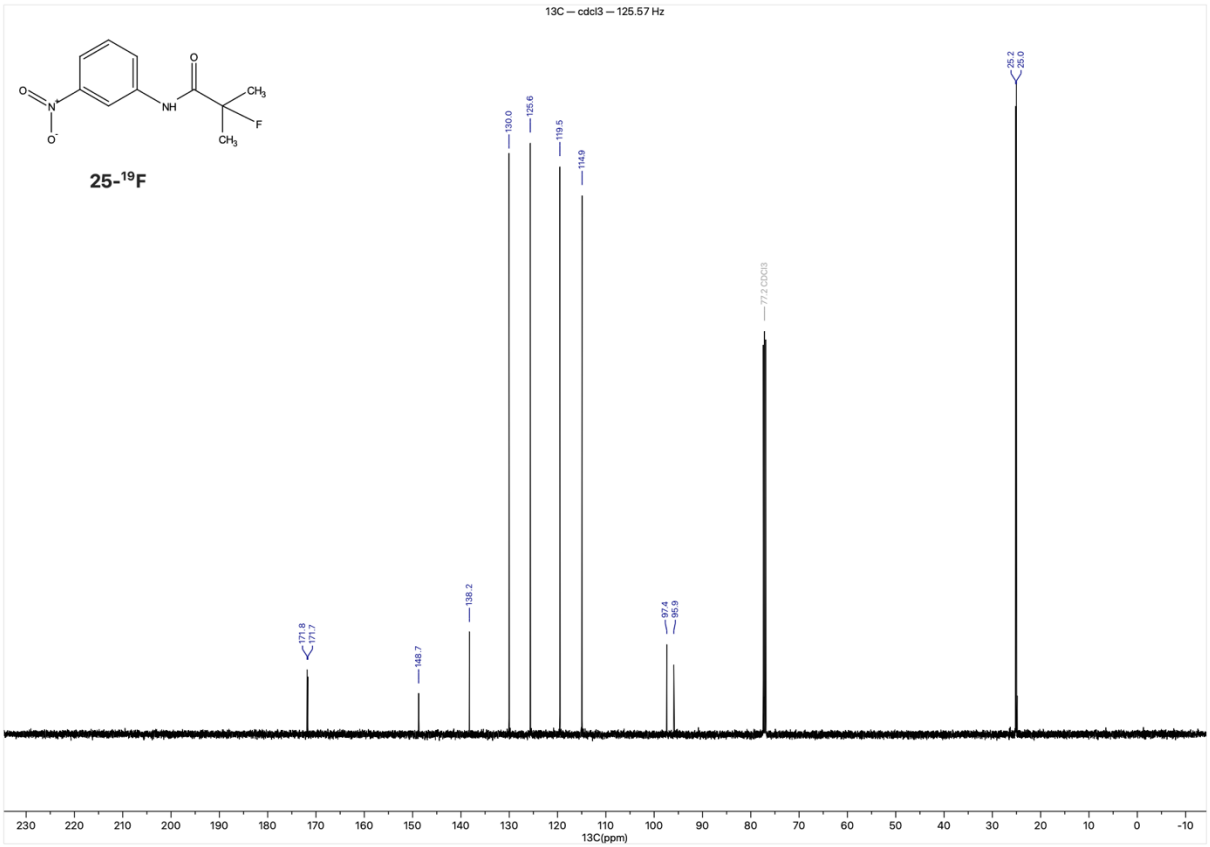

13C — cdcl3 — 125.57 Hz
24-19F
138.1
136.9
121.8
77.2 CDCl3
25.2
25.0
88.2
97.4
96.0
171.4
171.2
13C(ppm)

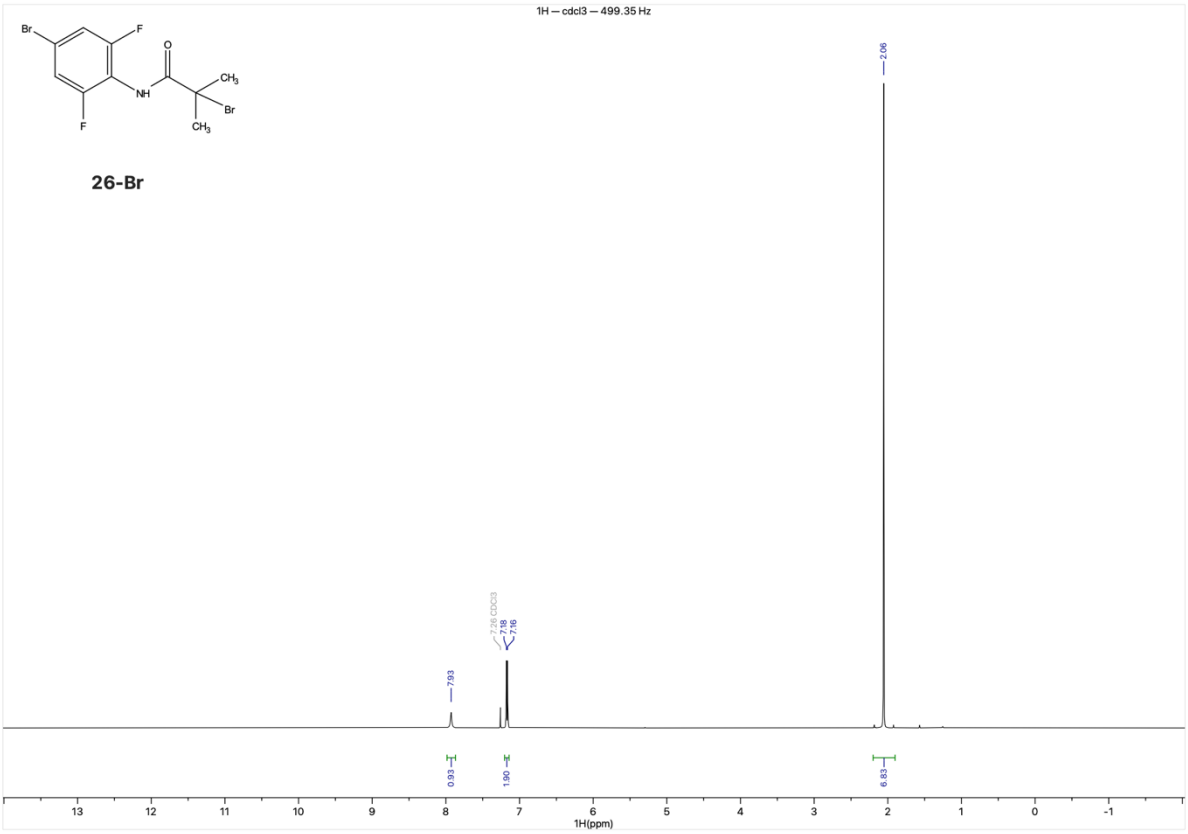

1H — cdcl3 — 499.35 Hz
25-Br
2.06
8.64
8.46
8.46
8.45
7.99
7.91
7.90
7.54
7.53
7.51
7.26 CDCl3
1.04
0.99
1.00
1.07
1.10
6.85
1H(ppm)

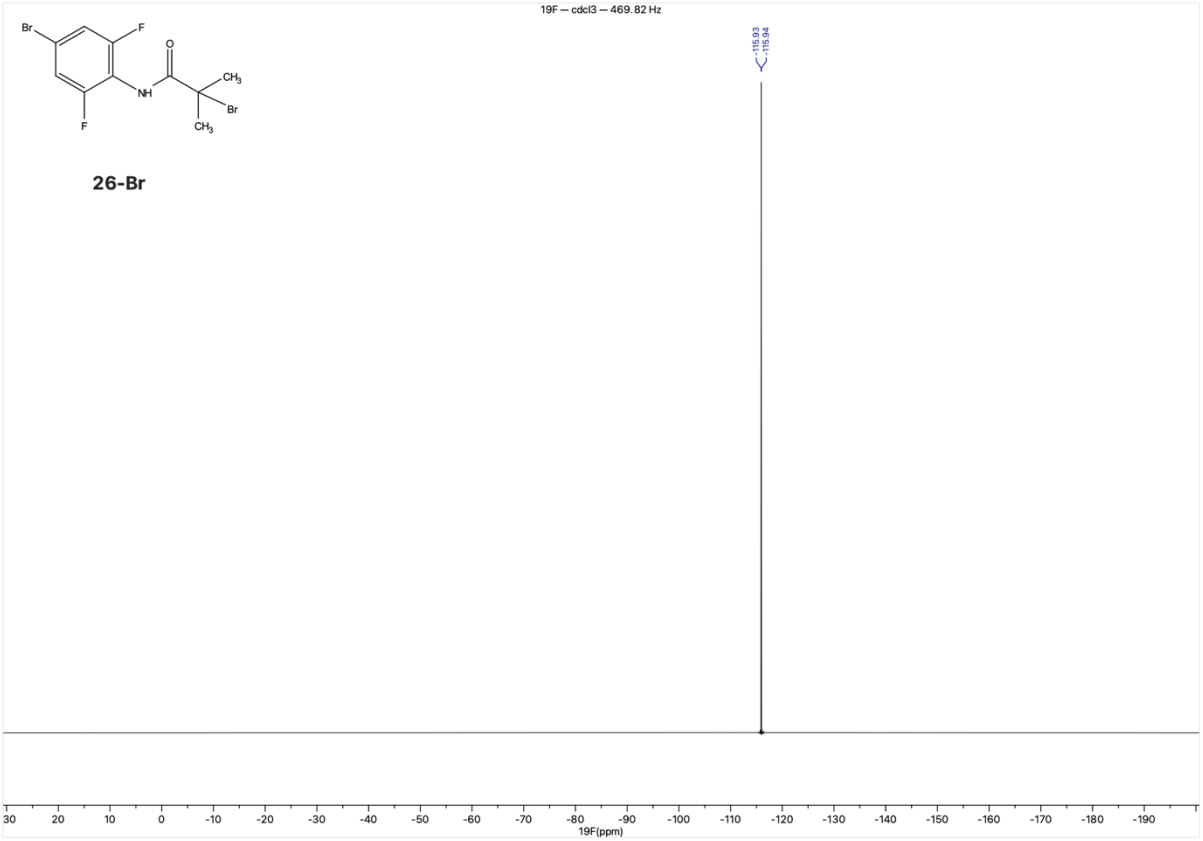

13C — cdcl3 — 125.57 Hz
25-Br
32.5
77.2 CDCl3
119.6
130.0
125.7
115.0
62.5
170.6
148.8
138.7
13C(ppm)

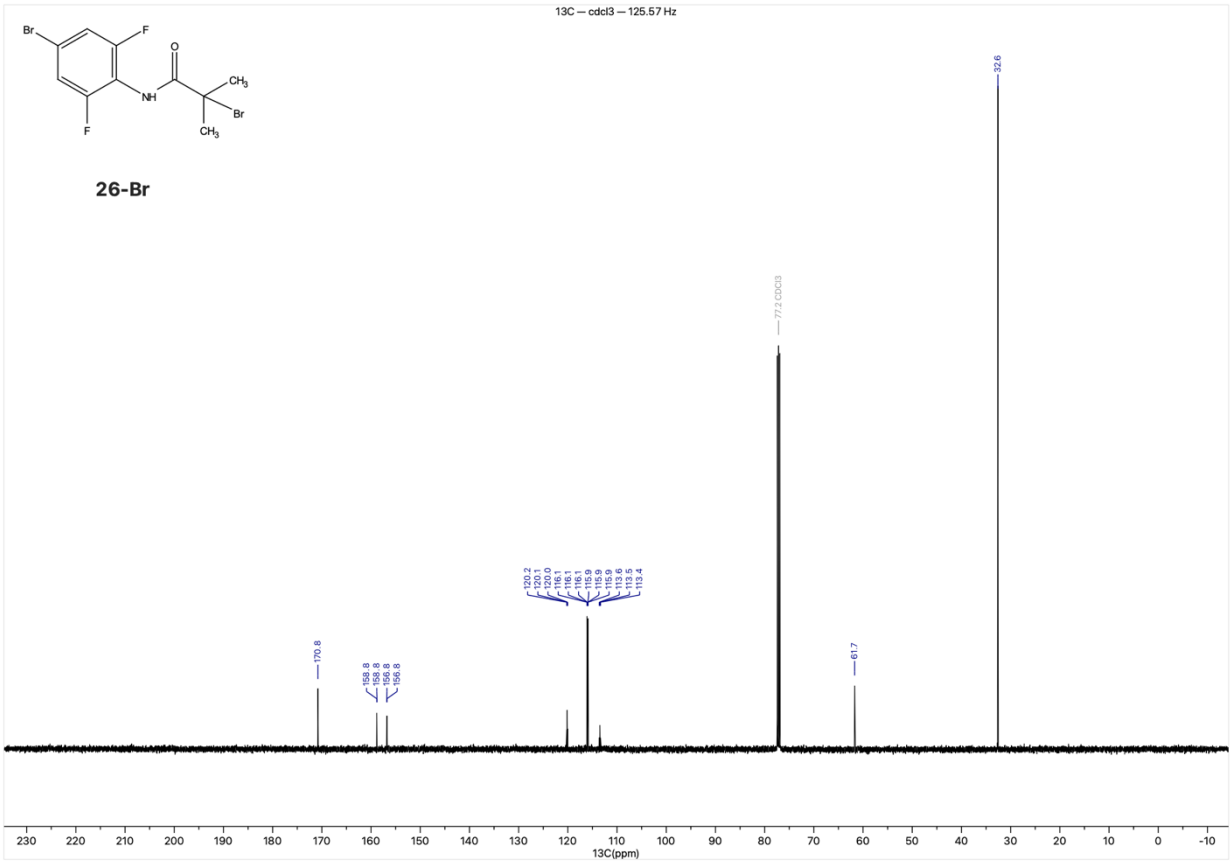

1H — cdcl3 — 499.34 Hz
25-19F
1.70
1.65
8.51
8.50
8.50
8.36
8.35
8.00
8.00
7.99
7.98
7.96
7.95
7.93
7.93
7.53
7.52
7.52
7.26 CDCl3
0.90
0.97
0.83
0.98
1.00
6.55
1H(ppm)

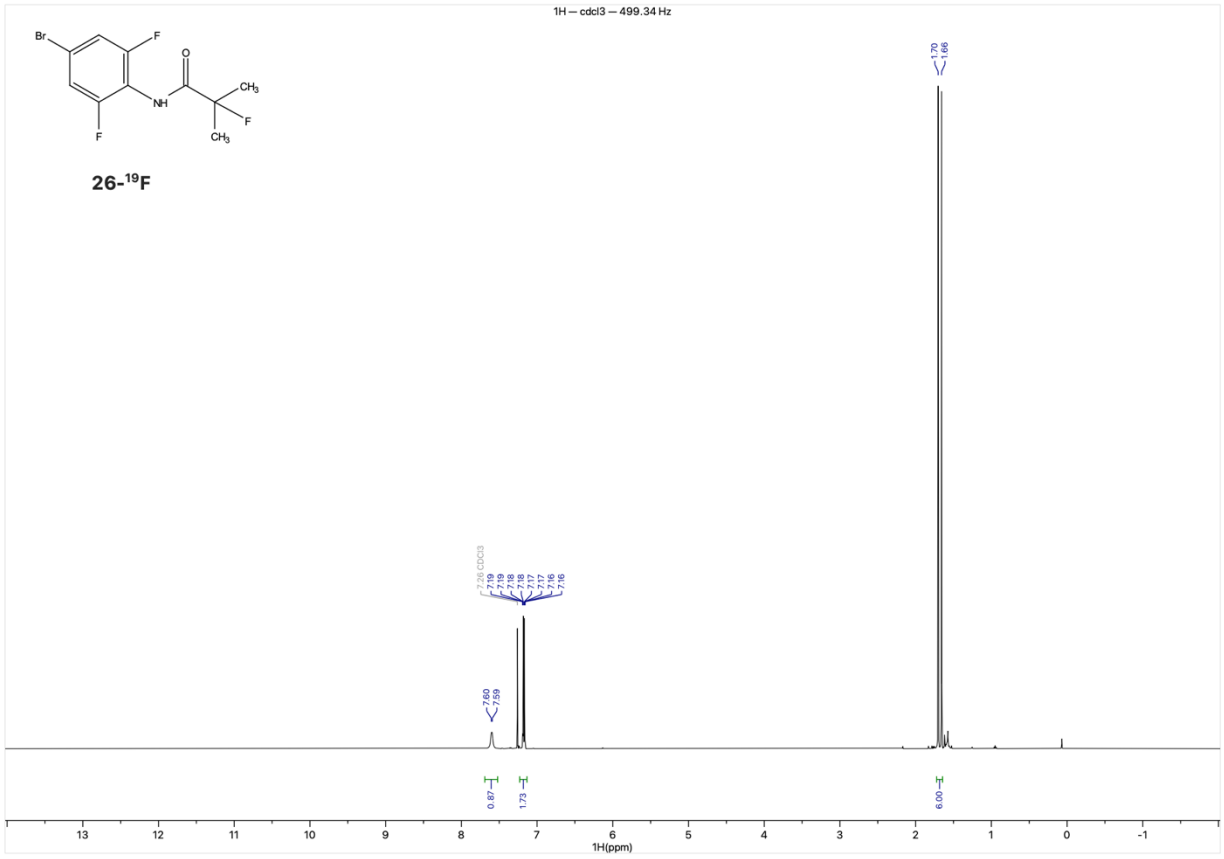

19F — cdcl3 — 469.80 Hz
25-19F
-145.38
-145.40
-145.43
-145.45
-145.48
-145.50
-145.53
-145.55
-145.58
-145.59
-145.62
-145.64
-145.67
-145.69
-145.30 -145.35 -145.40 -145.45 -145.50 -145.55 -145.60 -145.65 -145.70 -145.75
19F(ppm)
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
19F(ppm)

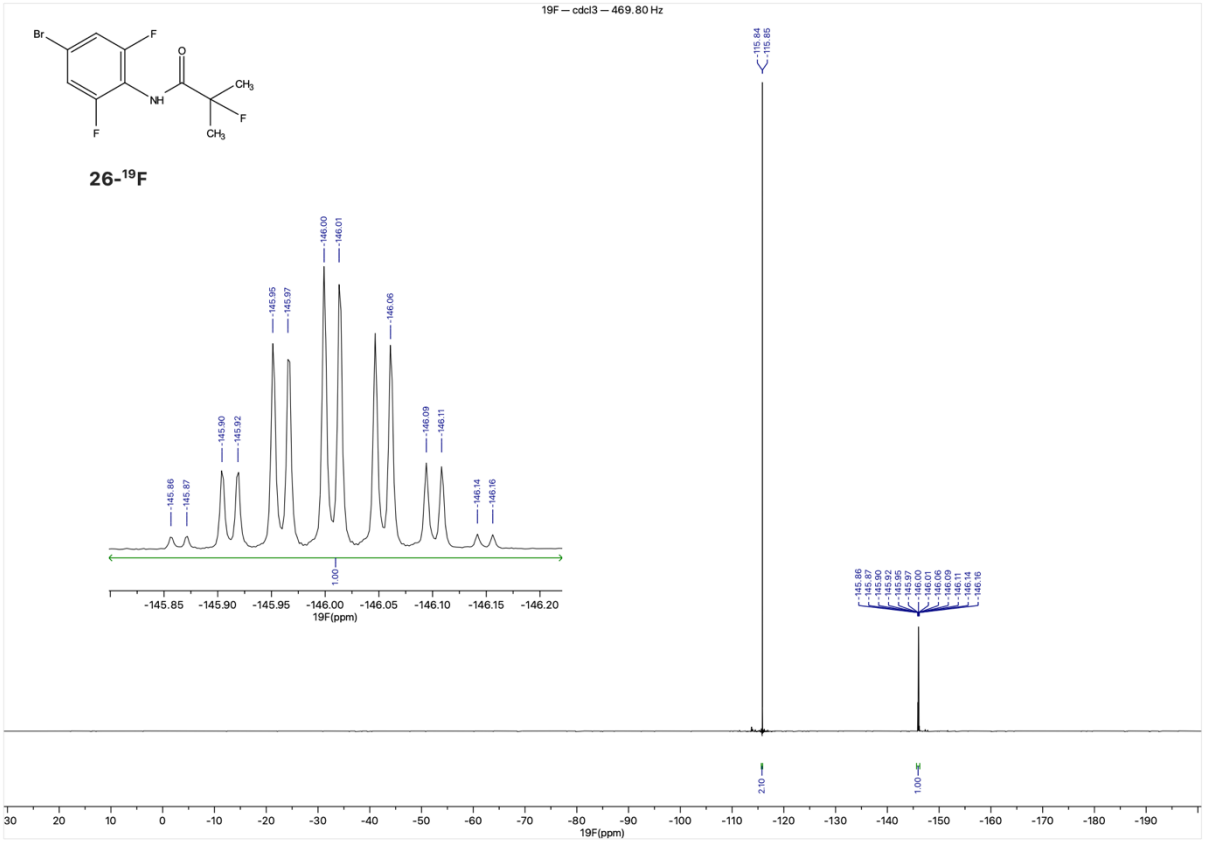

13C — cdcl3 — 125.57 Hz
25-19F
171.8
171.7
148.7
138.2
130.0
125.6
119.5
114.9
97.4
95.9
77.2 CDCl3
25.2
25.0
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
13C(ppm)

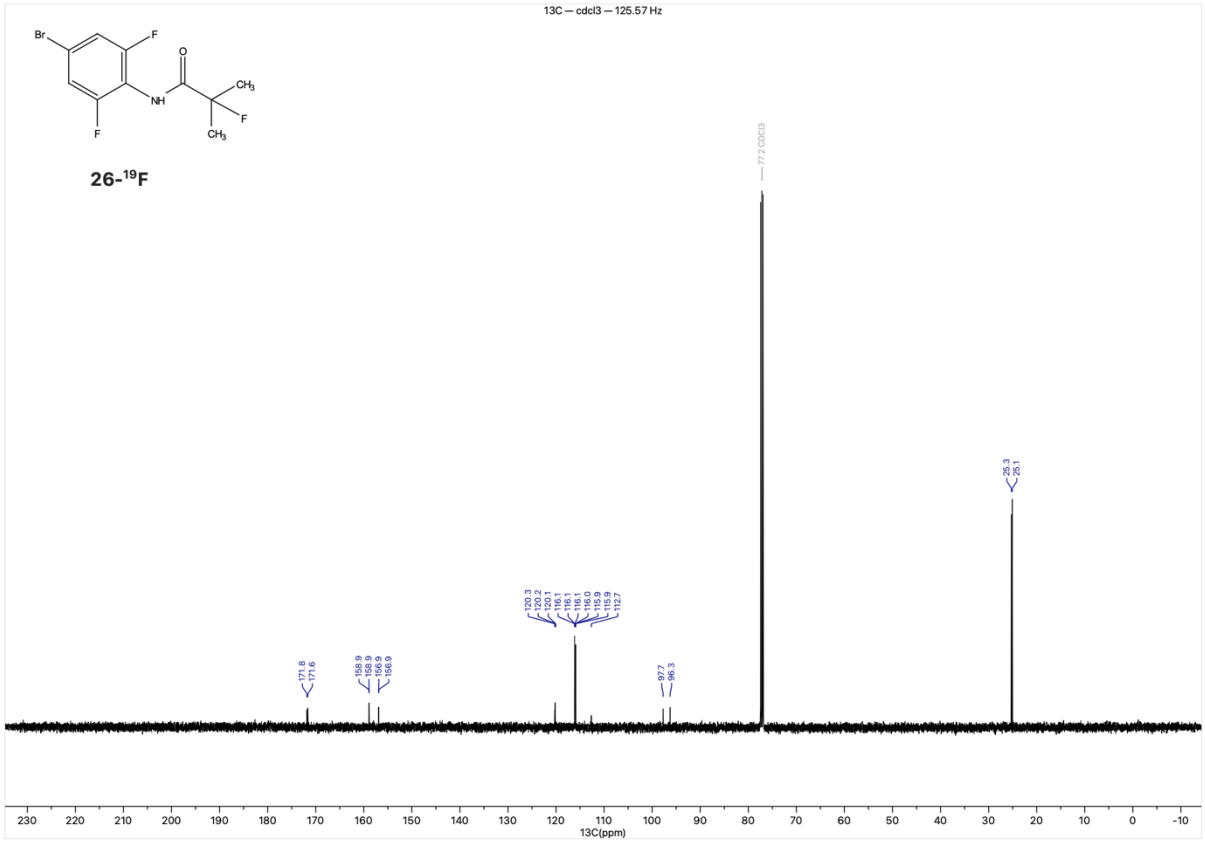

1H — cdcl3 — 499.35 Hz
Br
F
O
NH
CH3
Br
F
CH3
26-Br
2.06
7.93
7.26 CDCl3
7.18
7.16
0.93
1.90
6.83
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
1H(ppm)


19F — cdcl3 — 469.82 Hz
Br
F
O
NH
CH3
Br
F
CH3
26-Br
-115.93
-115.94
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
19F(ppm)

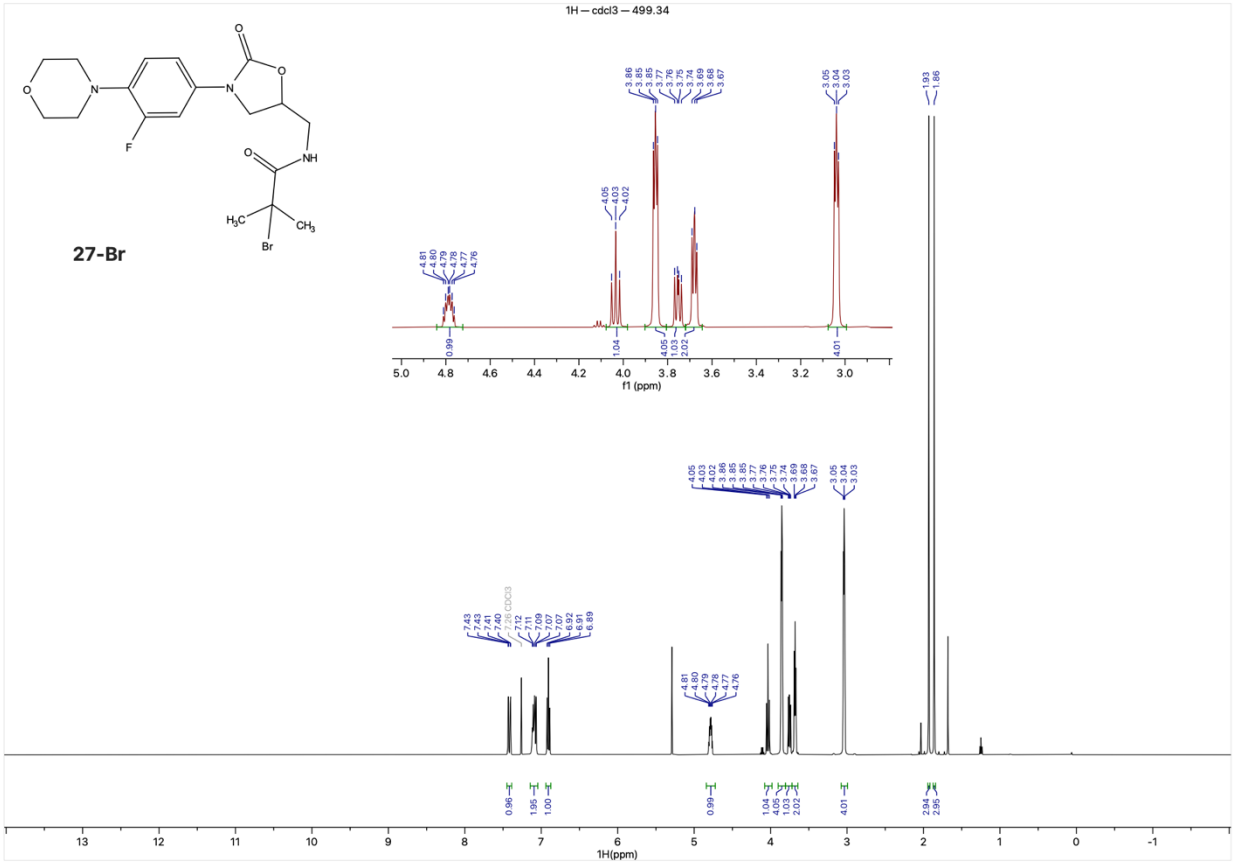

13C — cdcl3 — 125.57 Hz
Br
F
O
NH
CH3
Br
CH3
F
26-Br
32.6
77.2 CDCl3
170.8
158.8
158.8
156.8
156.8
120.2
120.1
120.0
116.1
116.1
115.9
115.9
115.9
115.9
113.6
113.5
113.4
61.7
13C(ppm)

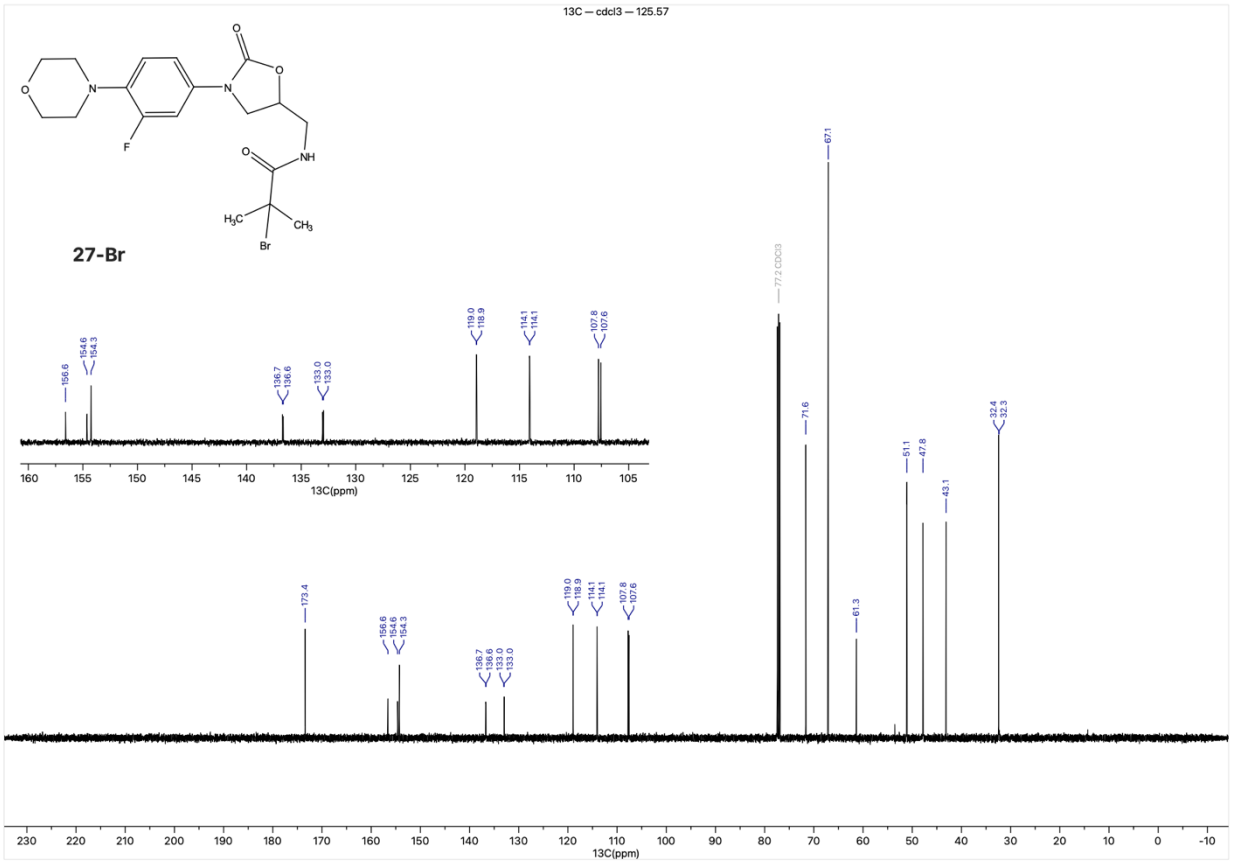

1H — cdcl3 — 499.34 Hz
Br
F
O
NH
CH3
F
CH3
F
26-19F
1.70
1.66
7.26 CDCl3
7.19
7.19
7.18
7.18
7.17
7.17
7.16
7.16
7.60
7.59
0.87
1.73
6.00
1H(ppm)

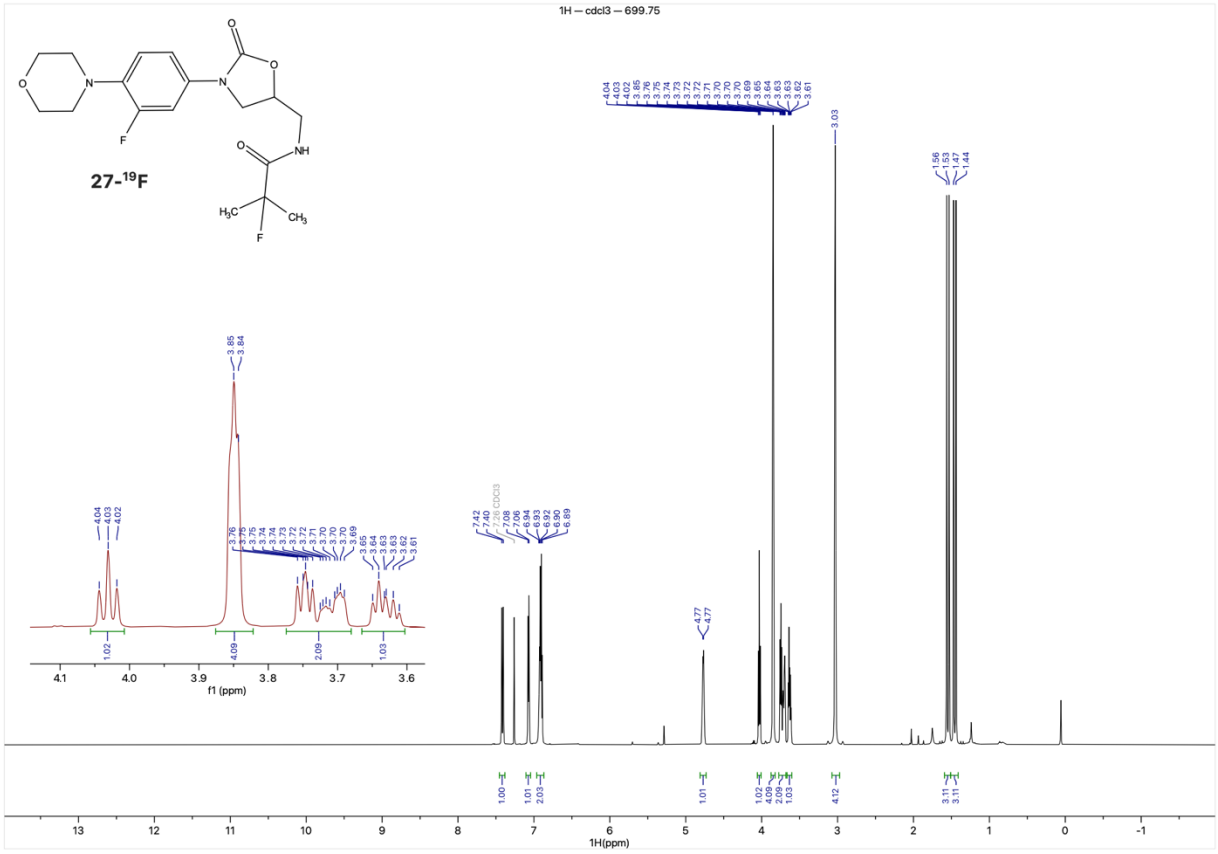

19F — cdcl3 — 469.80 Hz
Br
F
O
NH
CH3
F
F
CH3
26-19F
-115.84
-115.85
-145.86
-145.87
-145.90
-145.92
-145.95
-145.97
-146.00
-146.01
-146.06
-146.09
-146.11
-146.14
-146.16
1.00
-145.85
-145.90
-145.95
-146.00
-146.05
-146.10
-146.15
-146.20
19F(ppm)
2.10
1.00
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
19F(ppm)

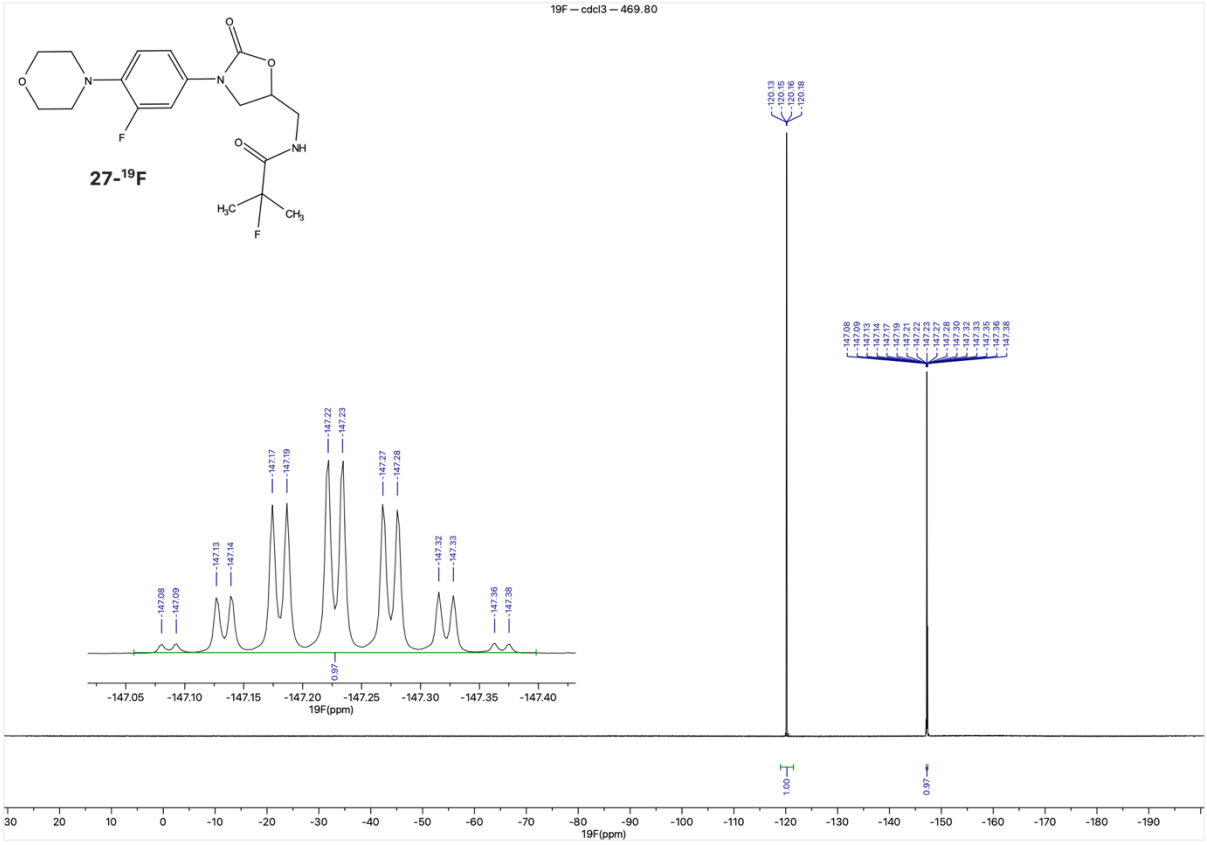

13C — cdcl3 — 125.57 Hz
Br
F
O
NH
CH3
F
F
CH3
26-19F
77.2 CDCl3
171.8
171.6
158.9
158.9
156.9
156.9
120.3
120.2
120.1
116.1
116.1
116.1
116.0
115.9
115.9
112.7
97.7
96.3
28.3
28.1
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
13C(ppm)

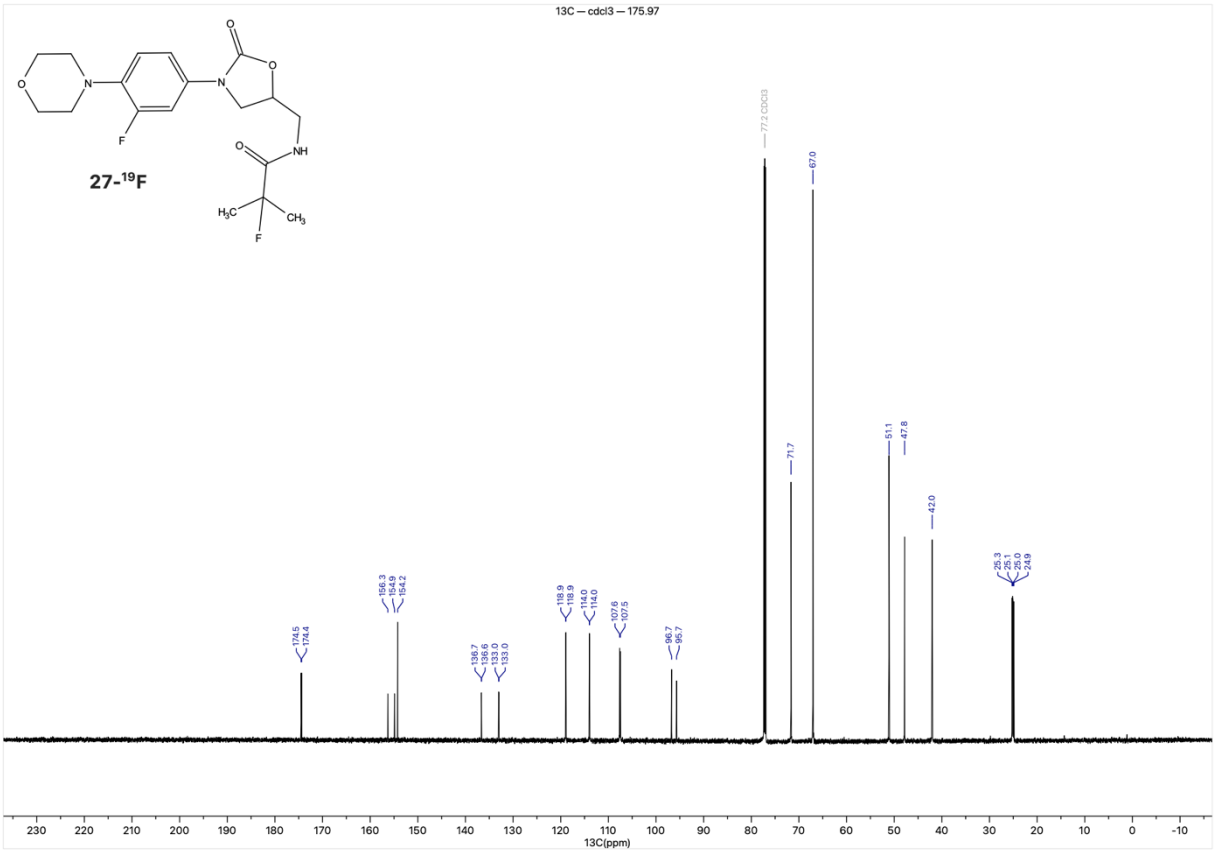
SUPPORTING INFORMATION

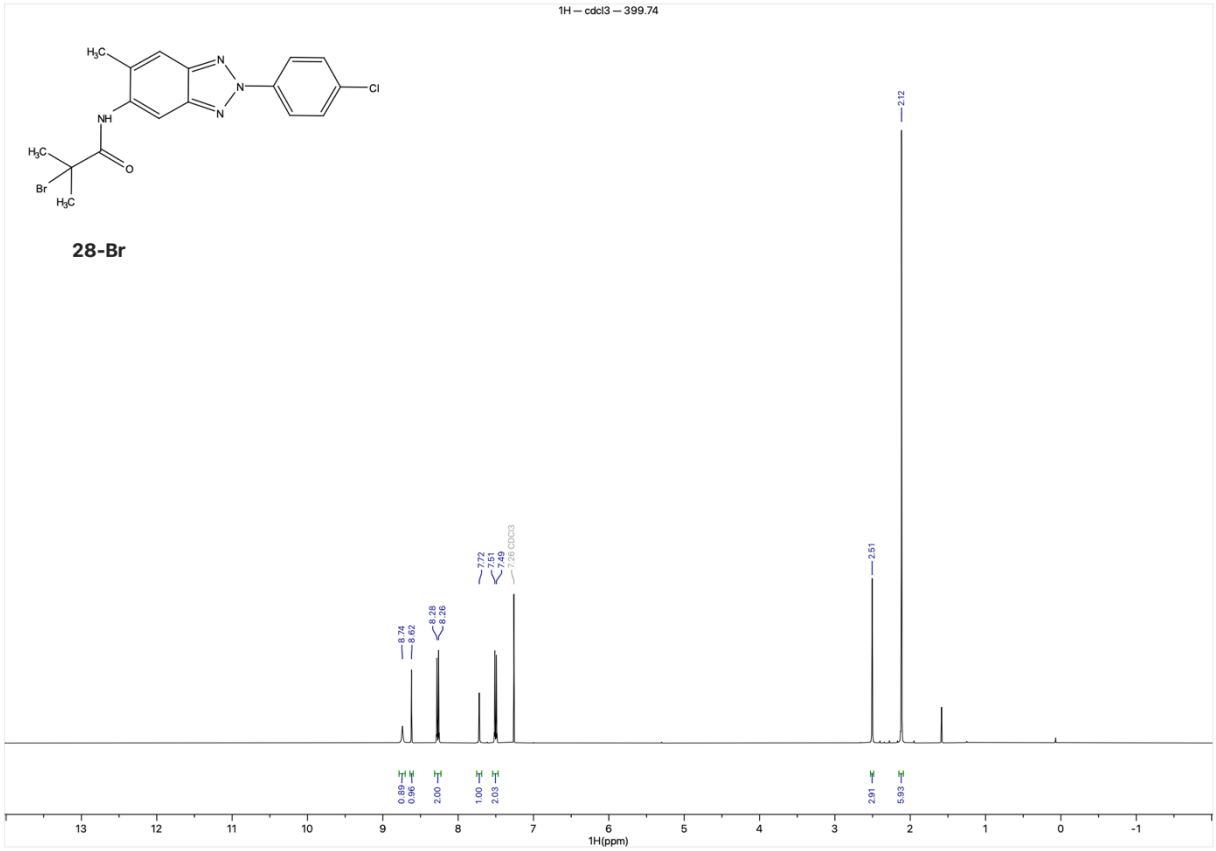


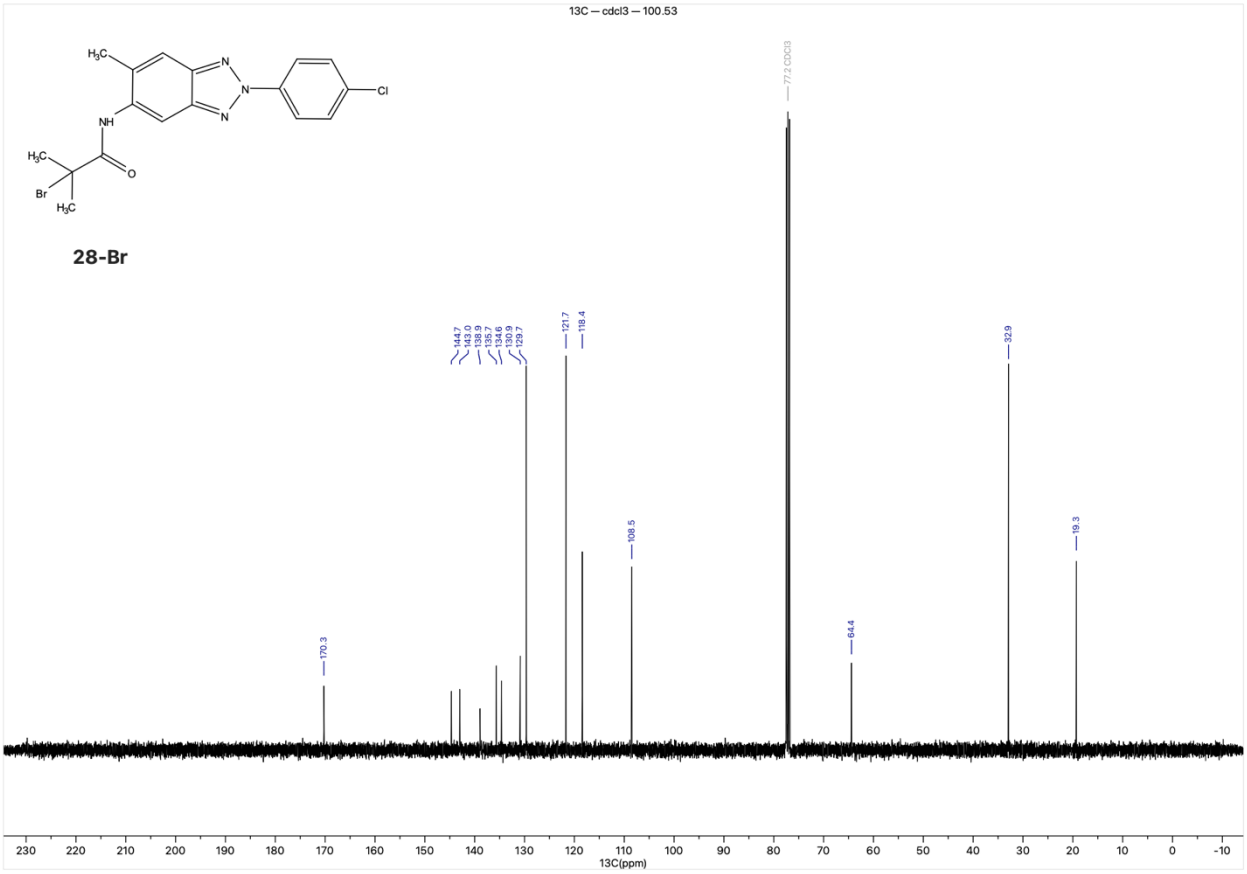


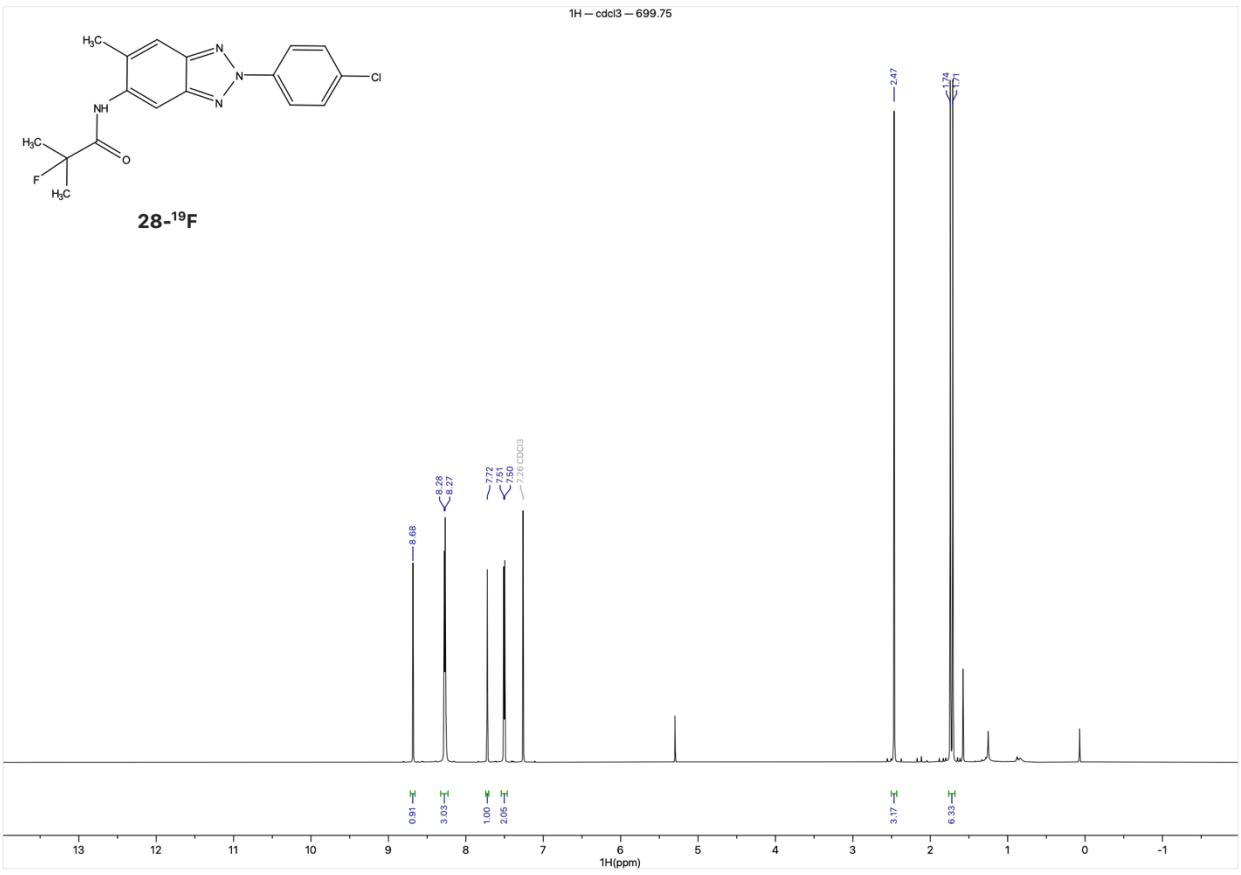

1H — cdcl3 — 699.75
27-19F
1H(ppm)
f1 (ppm)

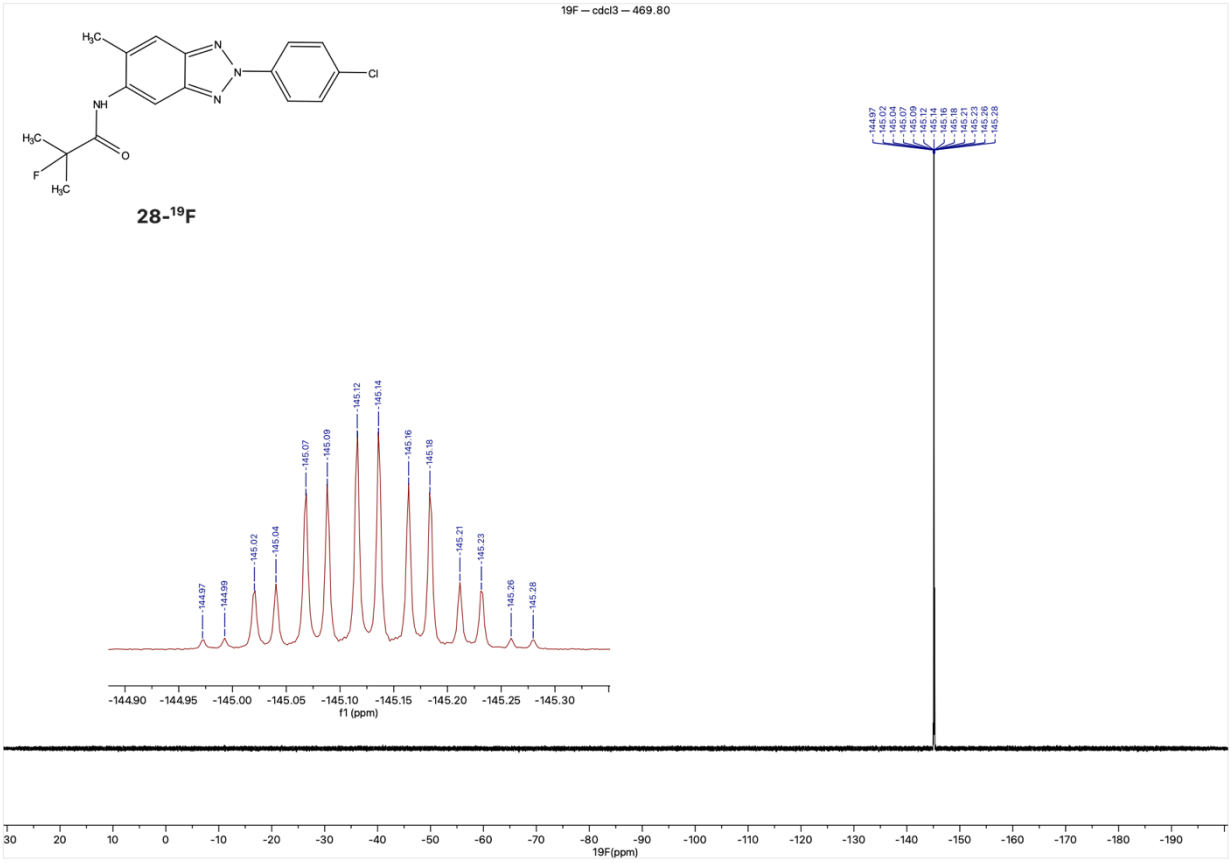

19F — cdcl3 — 469.80
27-19F
19F(ppm)

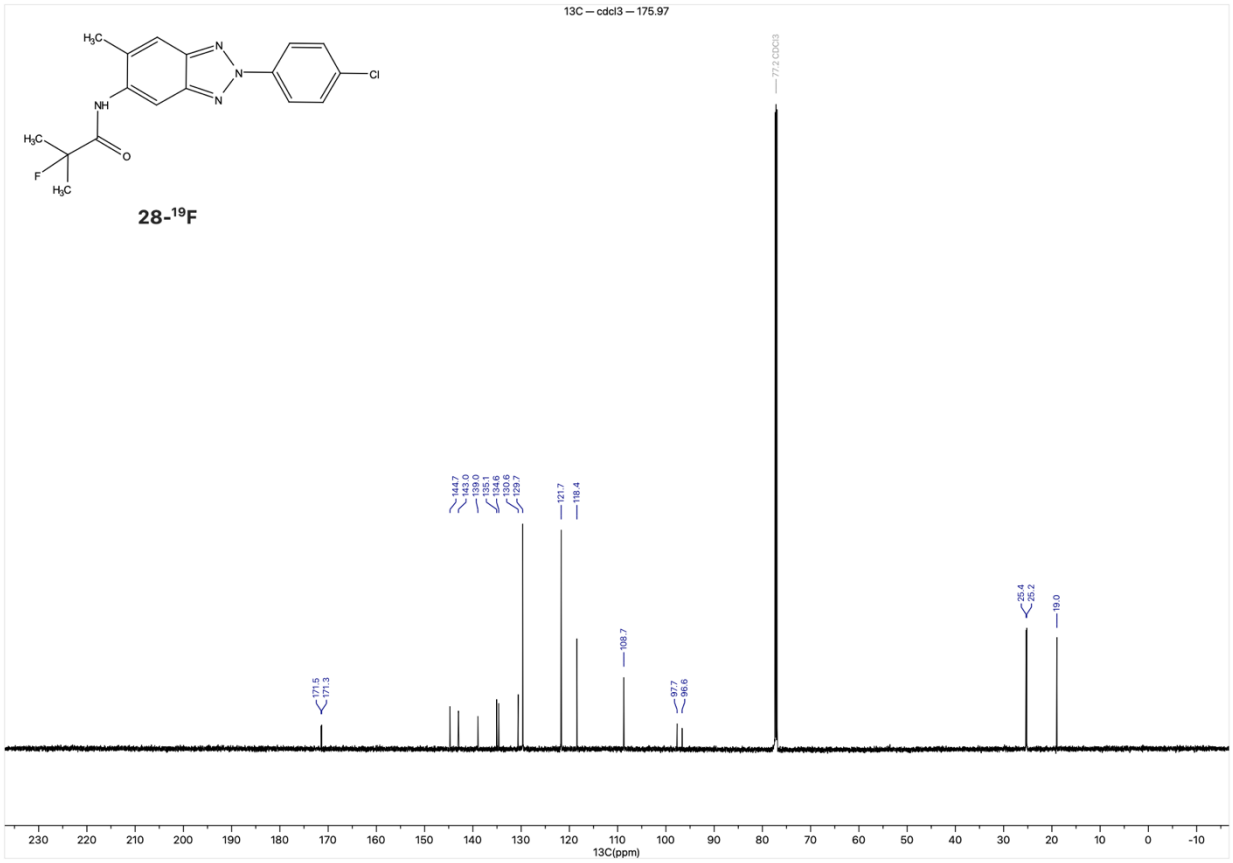

13C — cdcl3 — 175.97
27-19F
13C(ppm)

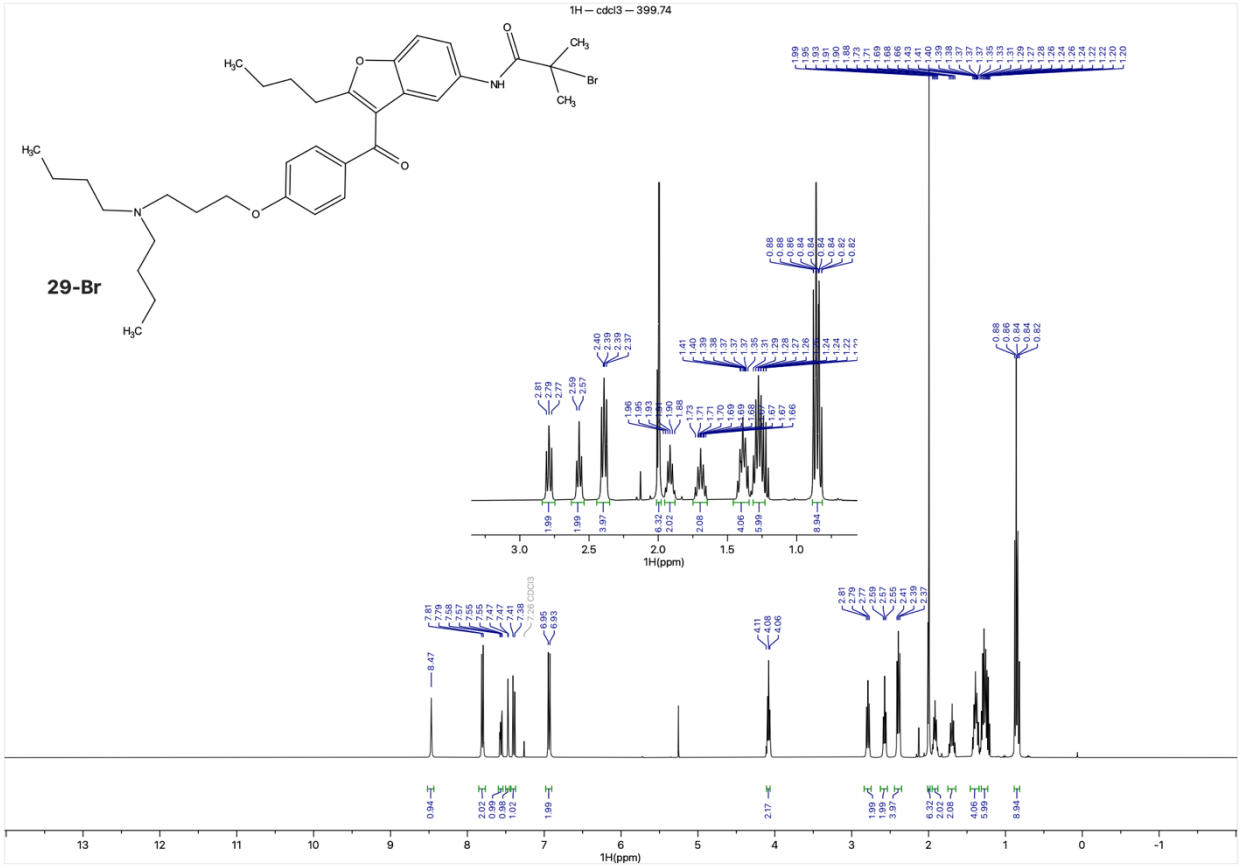

1H — cdcl3 — 399.74
28-Br
1H(ppm)

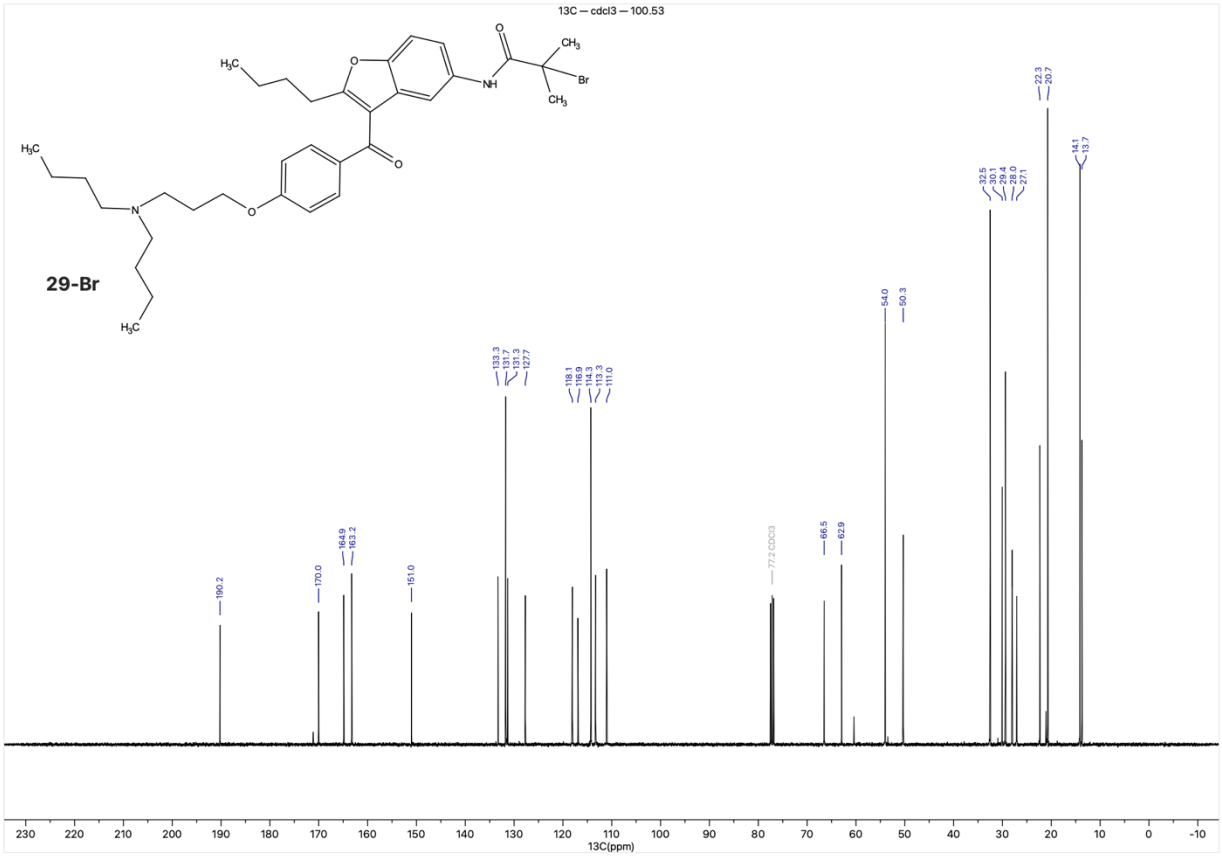

13C — cdcl3 — 100.53
28-Br
144.7
143.0
139.8
138.7
134.6
130.9
129.7
121.7
118.4
108.5
77.2 CDCl3
64.4
32.9
19.3
170.3
13C(ppm)

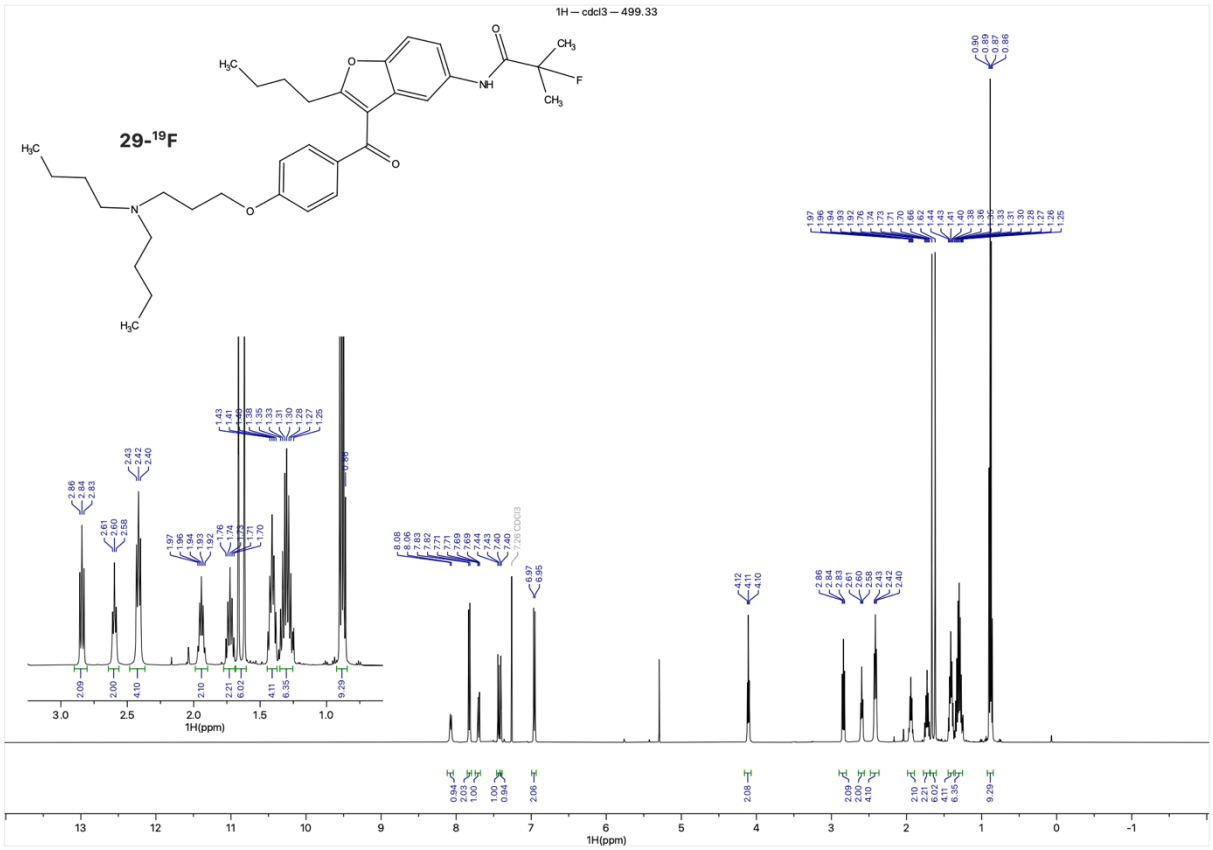

1H — cdcl3 — 699.75
28-19F
8.68
8.28
8.27
7.72
7.51
7.50
7.26 CDCl3
2.47
1.74
0.91
3.03
1.00
2.06
3.17
6.33
1H(ppm)

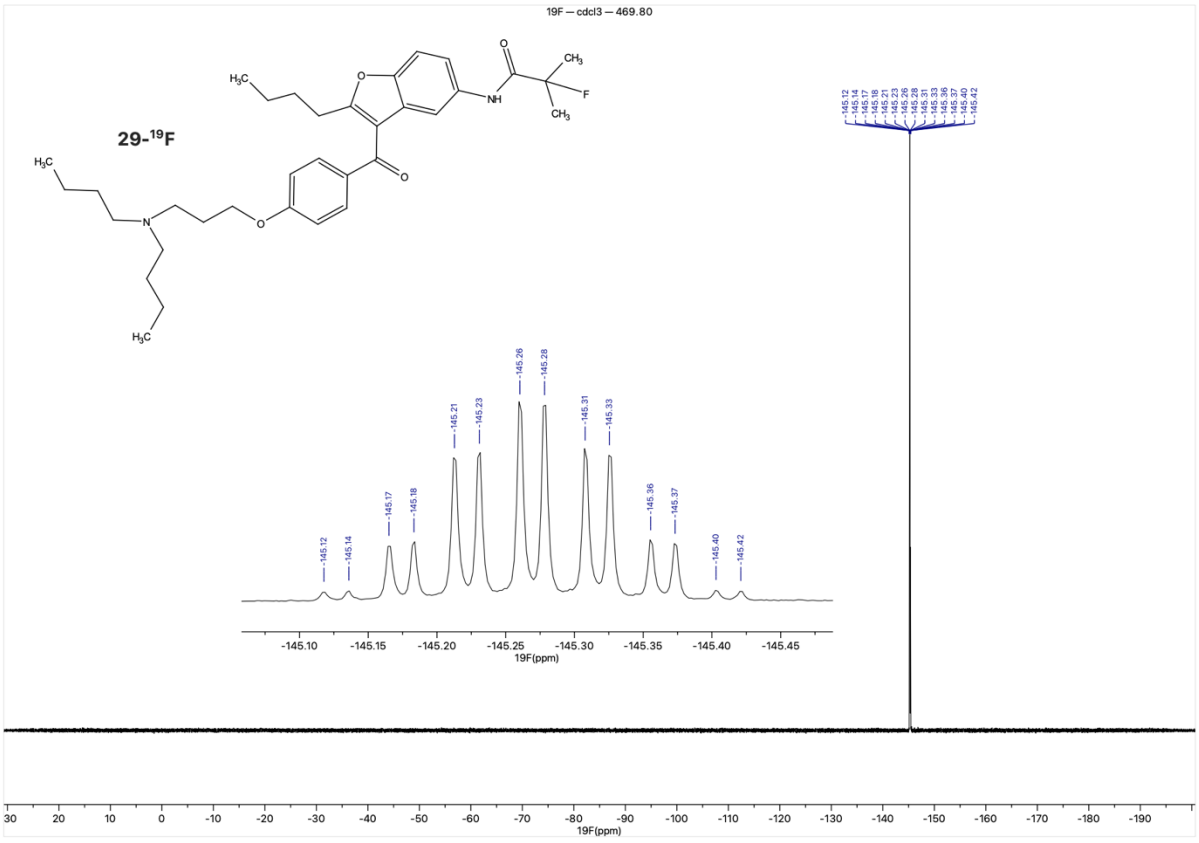

19F — cdcl3 — 469.80
28-19F
-144.97
-144.99
-145.02
-145.04
-145.07
-145.09
-145.12
-145.14
-145.16
-145.18
-145.21
-145.23
-145.26
-145.28
f1 (ppm)
19F(ppm)

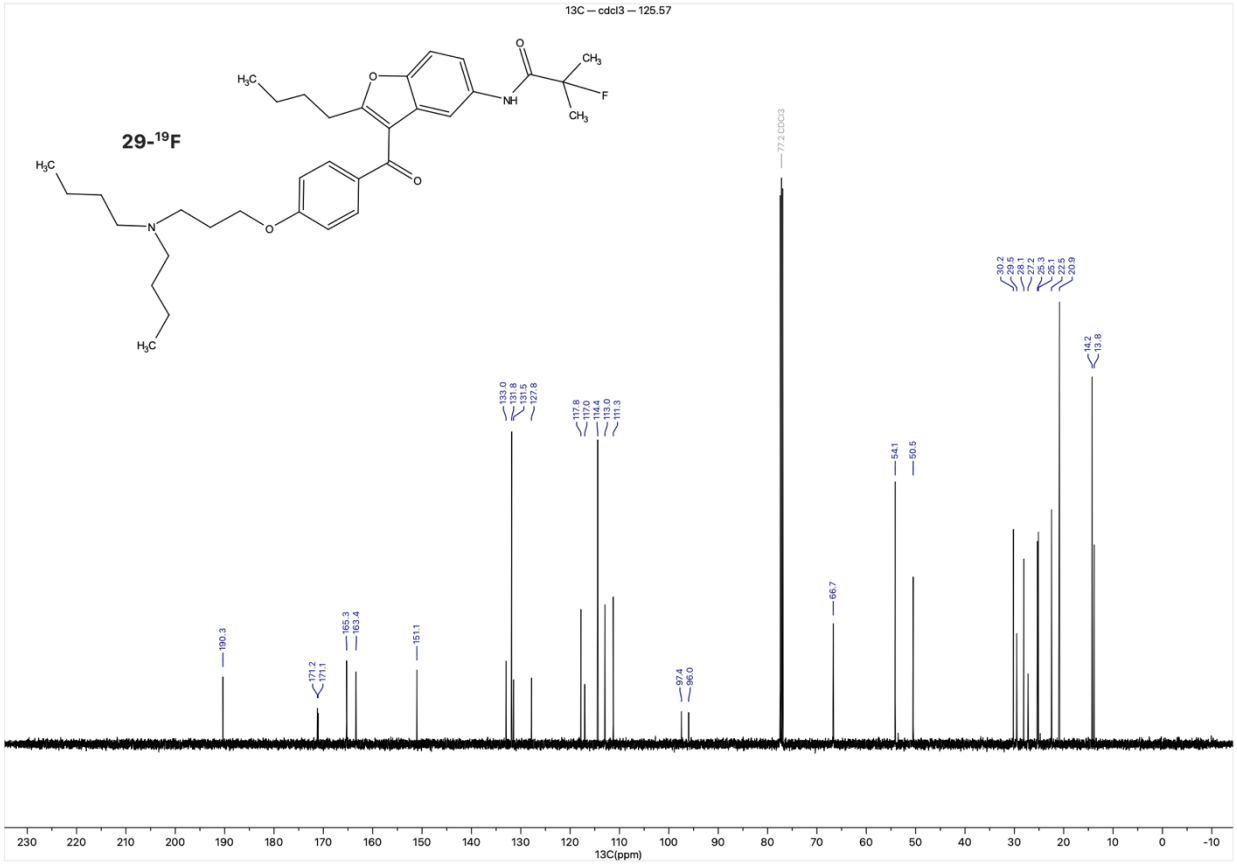

13C — cdcl3 — 175.97
28-19F
77.2 CDCl3
144.7
143.0
139.0
135.1
134.6
130.6
129.7
121.7
119.4
108.7
97.7
96.6
171.5
171.3
25.4
25.2
19.0
13C(ppm)

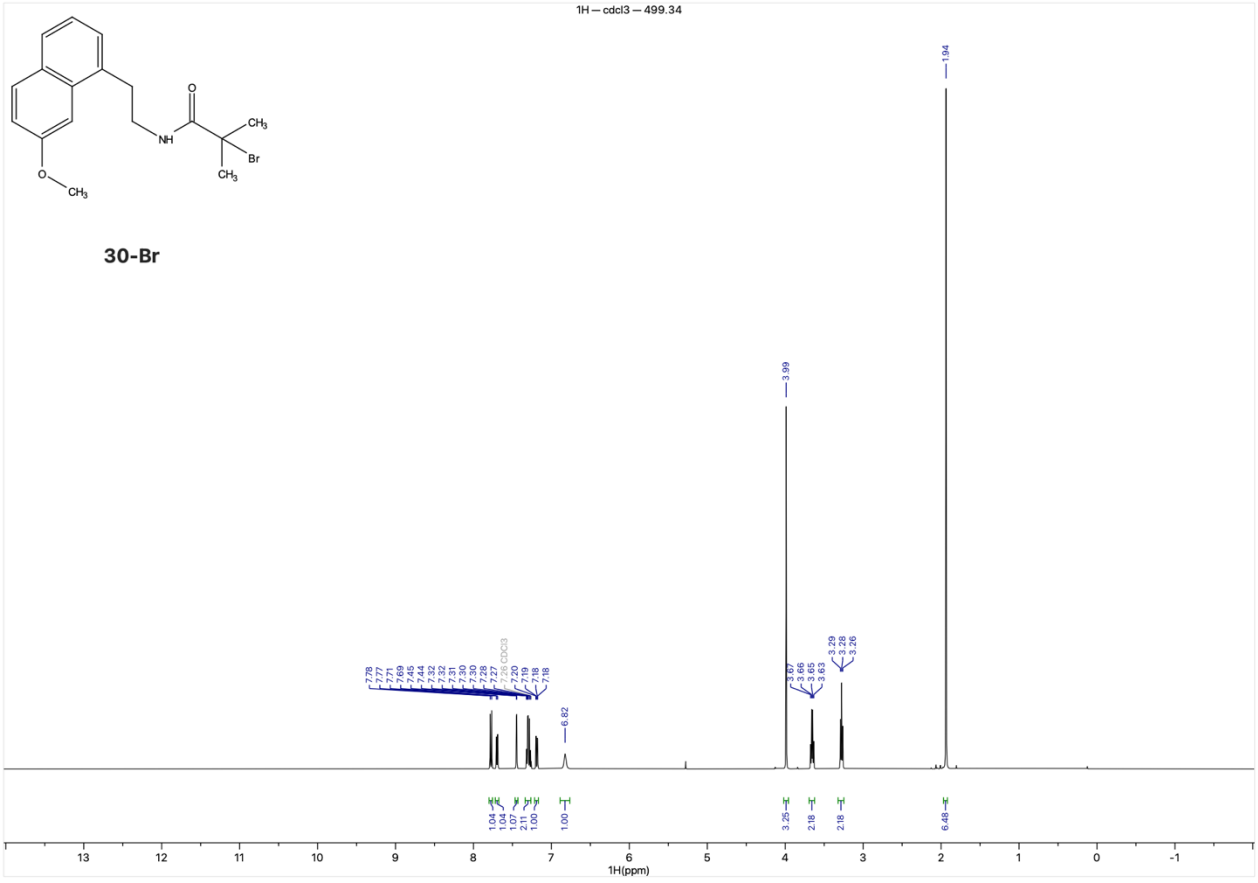

1H — cdcl3 — 399.74
29-Br
1H(ppm)

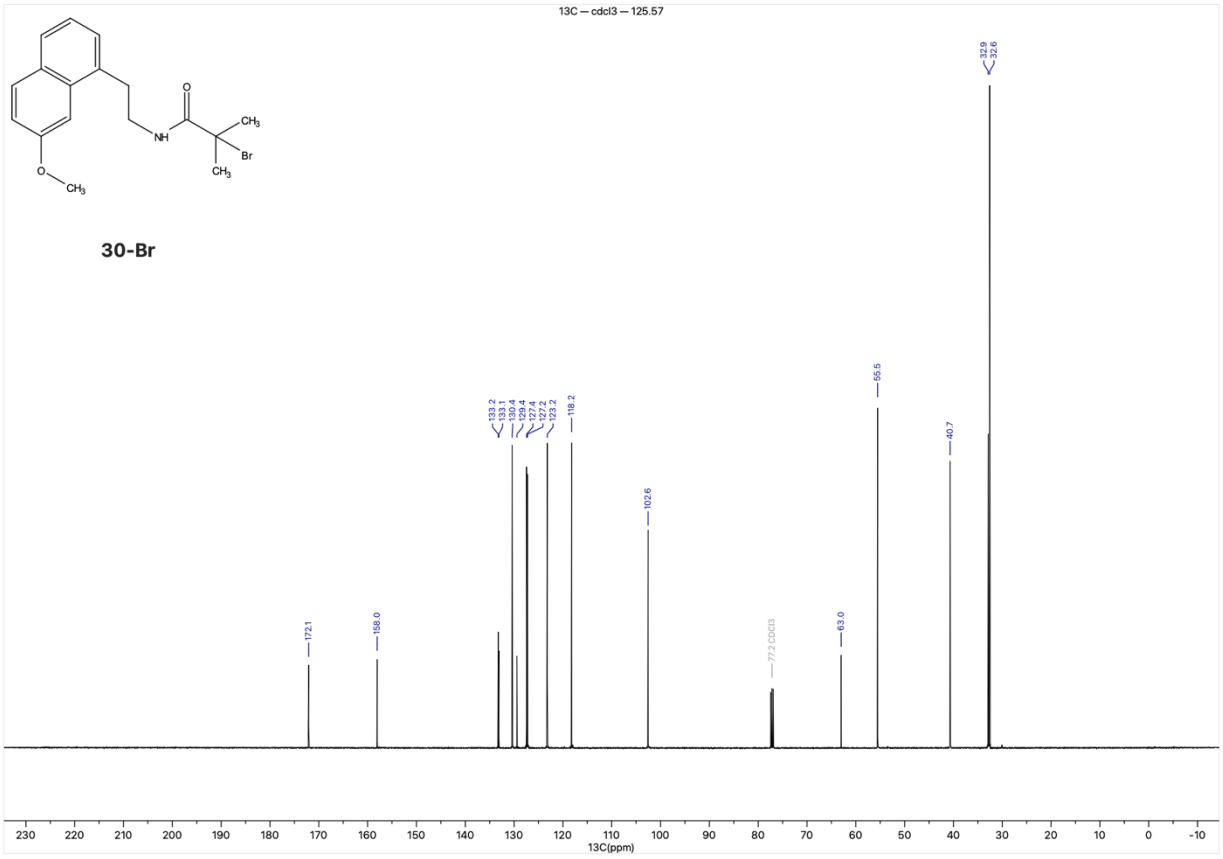

13C — cdcl3 — 100.53
29-Br
13C(ppm)

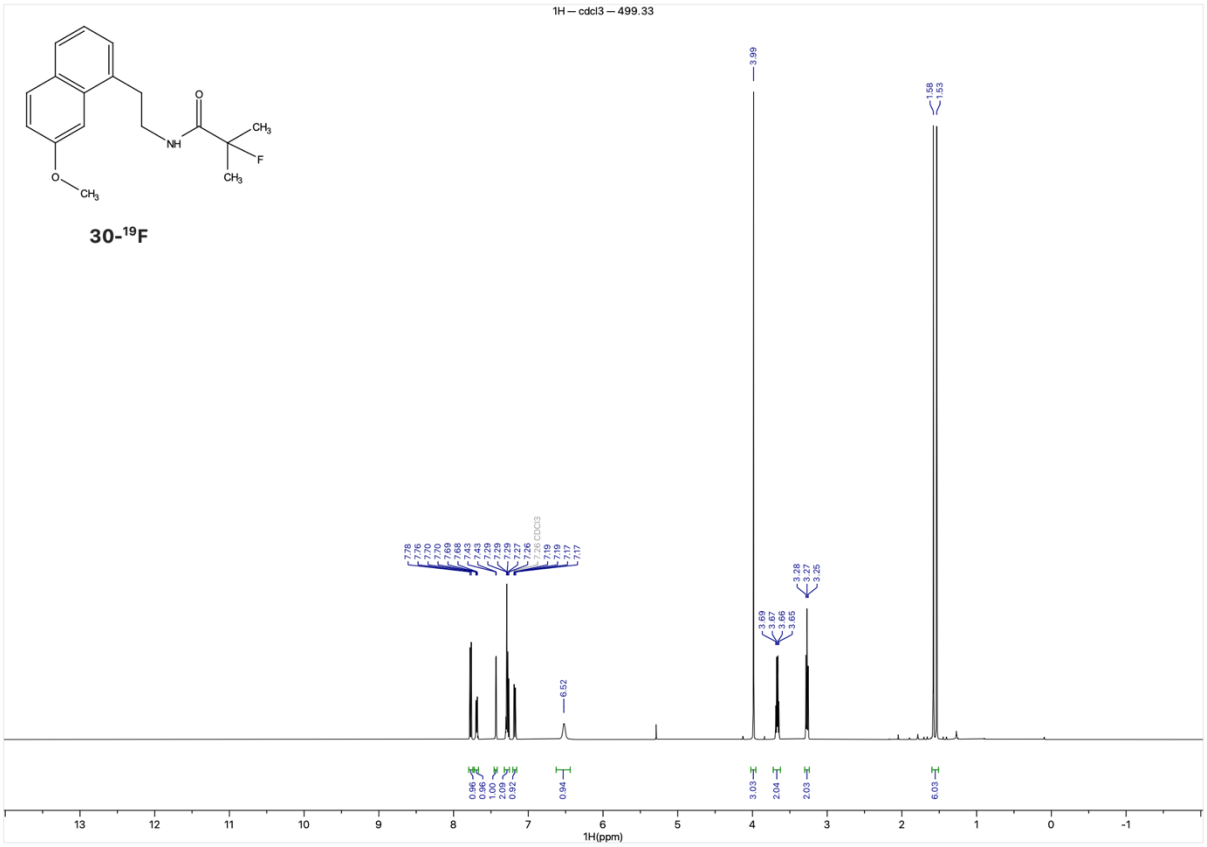

1H — cdcl3 — 499.33
29-19F
1H(ppm)

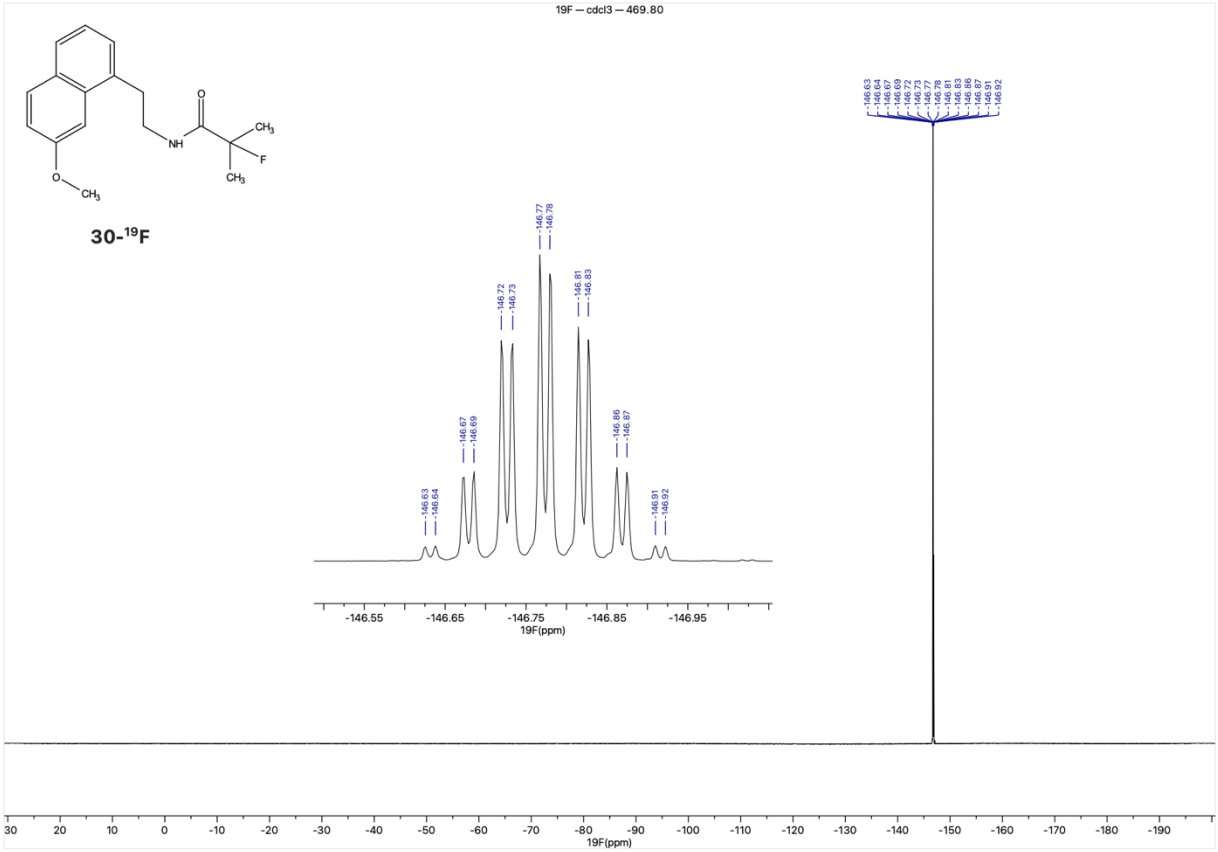

19F — cdcl3 — 469.80
29-19F
19F(ppm)

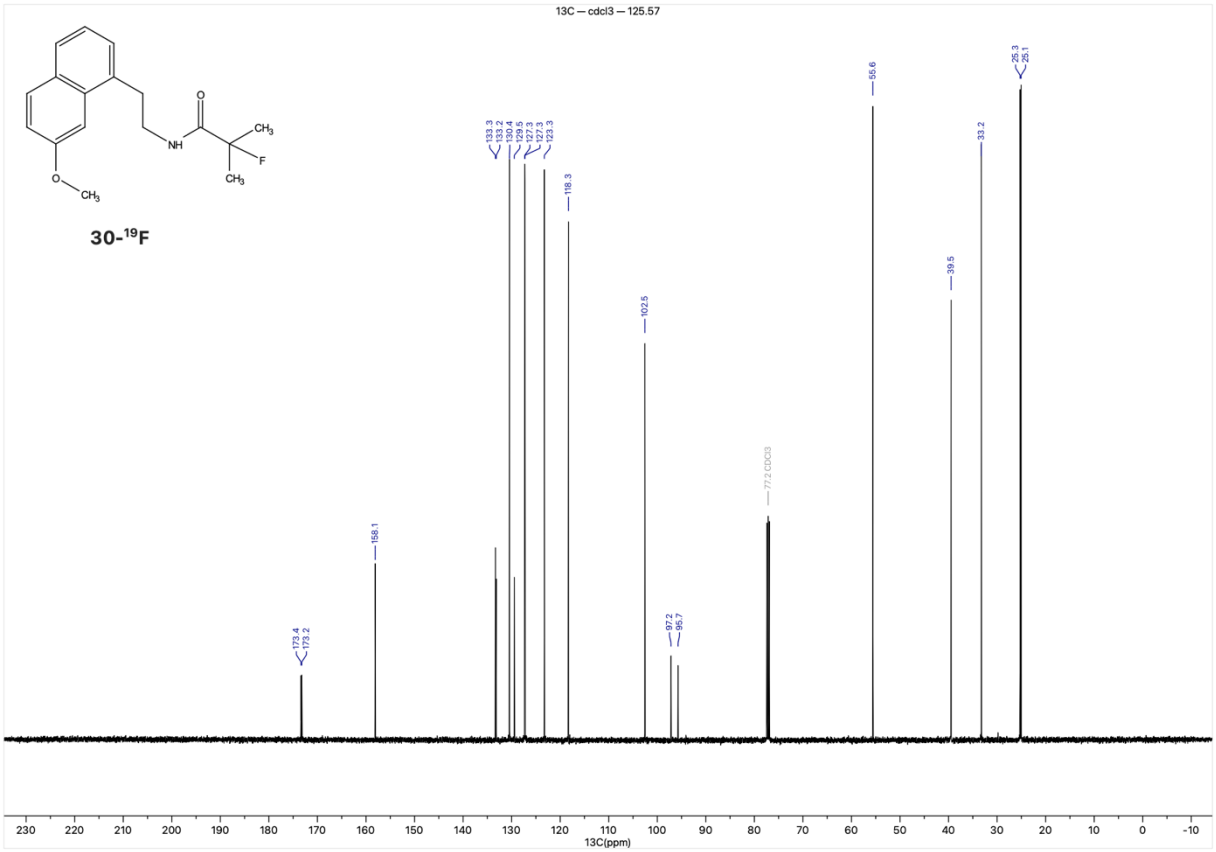

13C — cdcl3 — 125.57
29-19F
77.2 CDCl3
190.3
171.2
171.1
165.3
163.4
151.1
133.0
131.8
131.5
127.8
117.8
117.0
114.4
113.0
111.3
97.4
96.0
66.7
54.1
50.5
30.2
29.5
29.1
27.2
25.3
25.1
23.5
20.9
14.2
13.8
13C(ppm)

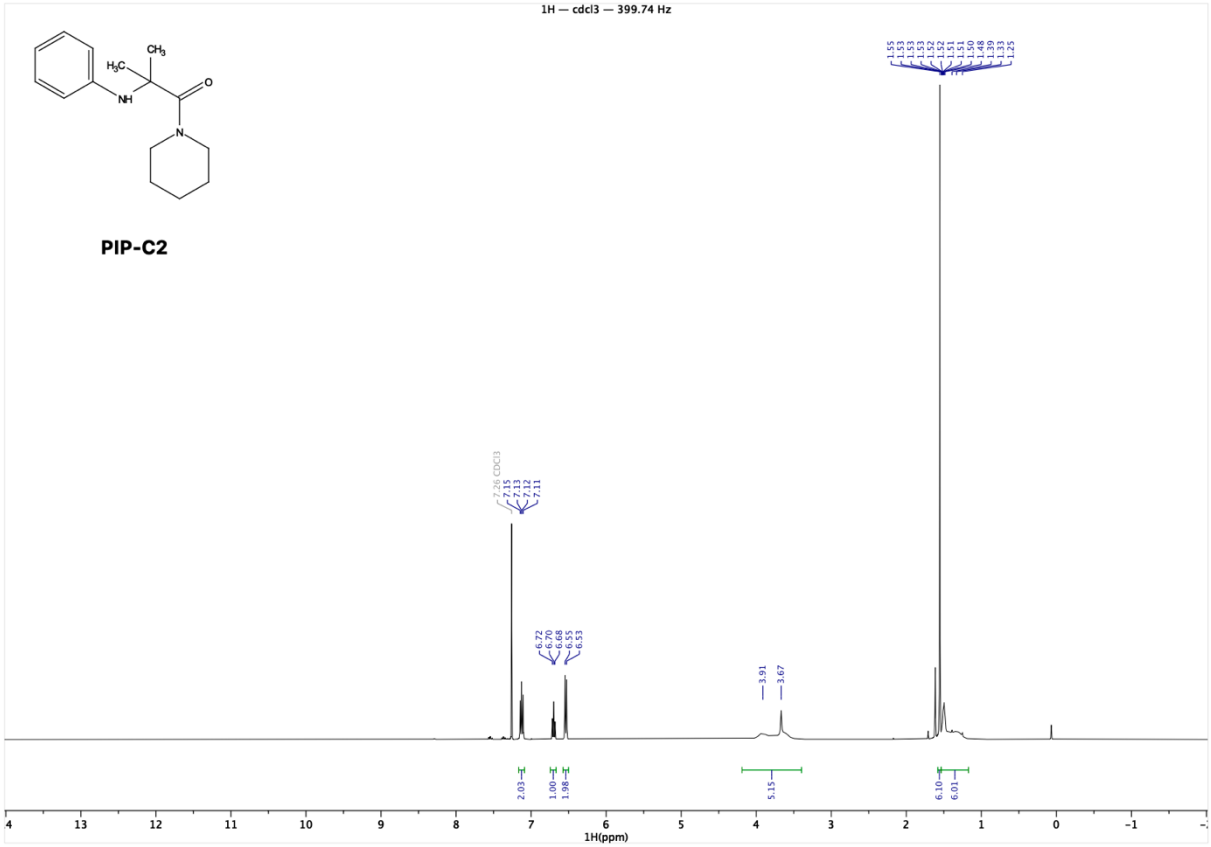

1H — cdcl3 — 499.34
30-Br
1.94
3.99
7.78
7.77
7.71
7.69
7.45
7.44
7.32
7.31
7.30
7.28
7.27
7.26 CDCl3
7.20
7.19
7.18
6.82
3.67
3.66
3.65
3.63
3.29
3.28
3.26
1.04
1.04
1.07
2.11
1.00
1.00
3.25
2.18
2.18
6.48
1H(ppm)

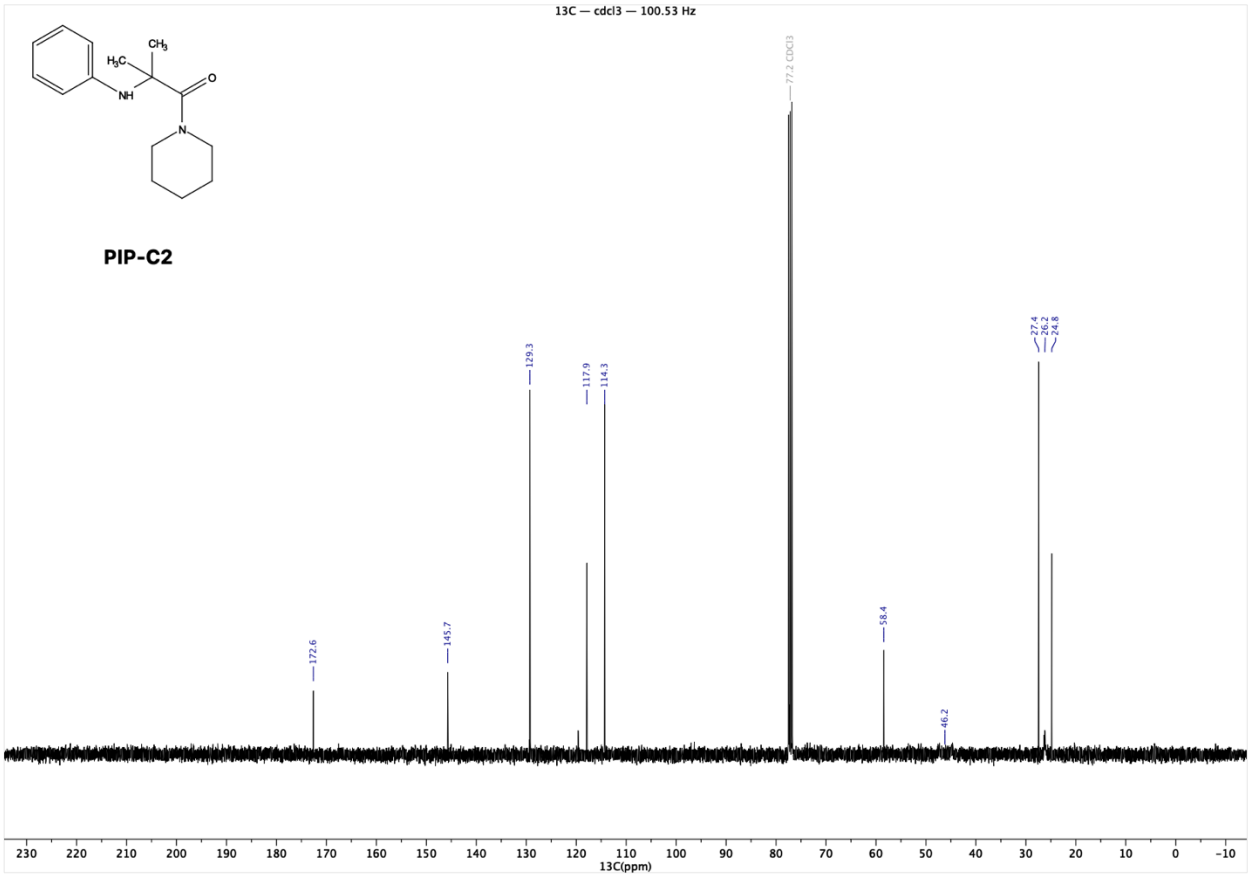

13C — cdcl3 — 125.57
30-Br
172.1
158.0
133.2
133.1
130.4
129.4
127.4
127.2
123.2
118.2
102.6
77.2 CDCl3
63.0
55.5
40.7
32.9
32.6
13C(ppm)

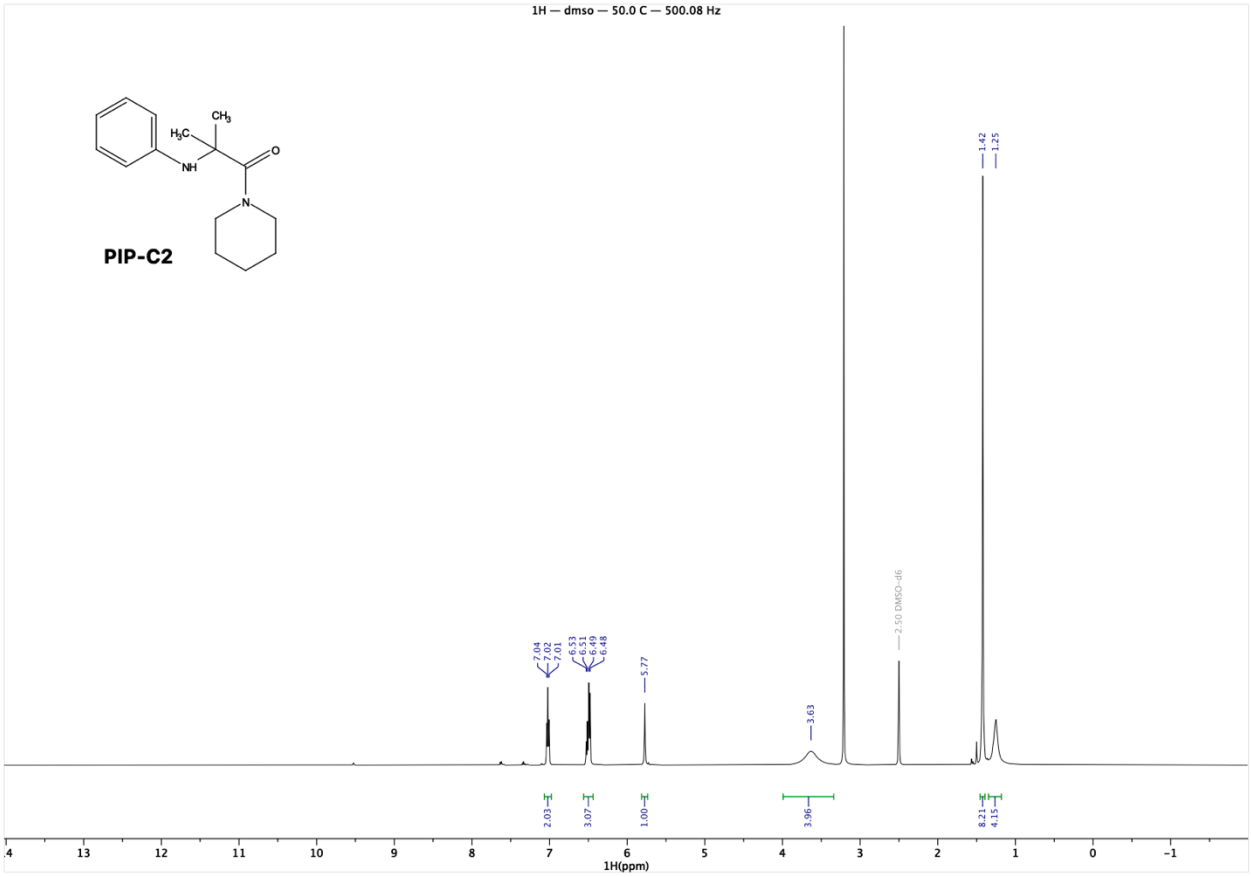

1H — cdcl3 — 499.33
30-19F
3.99
1.58
1.53
7.78
7.76
7.70
7.70
7.70
7.68
7.43
7.43
7.29
7.29
7.27
7.26
7.26 CDCl3
7.19
7.17
7.17
6.52
3.69
3.67
3.66
3.65
3.28
3.27
3.25
0.96
0.96
1.00
1.15
2.09
0.92
0.94
3.03
2.04
2.03
6.03
1H(ppm)

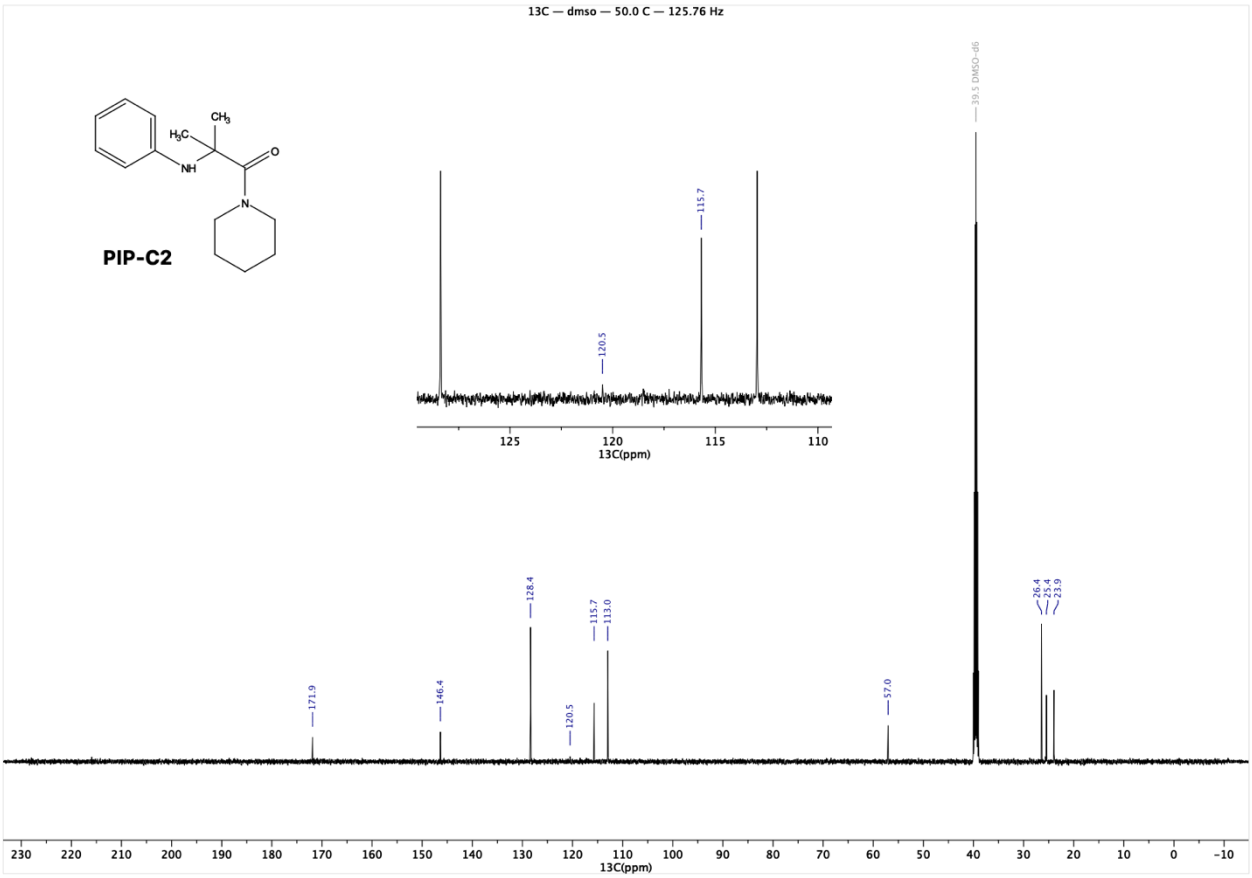

19F — cdcl3 — 469.80
30-19F
-146.63
-146.64
-146.67
-146.69
-146.72
-146.73
-146.77
-146.78
-146.81
-146.83
-146.86
-146.87
-146.91
-146.92
-146.55
-146.65
-146.75
-146.85
-146.95
19F(ppm)
19F(ppm)

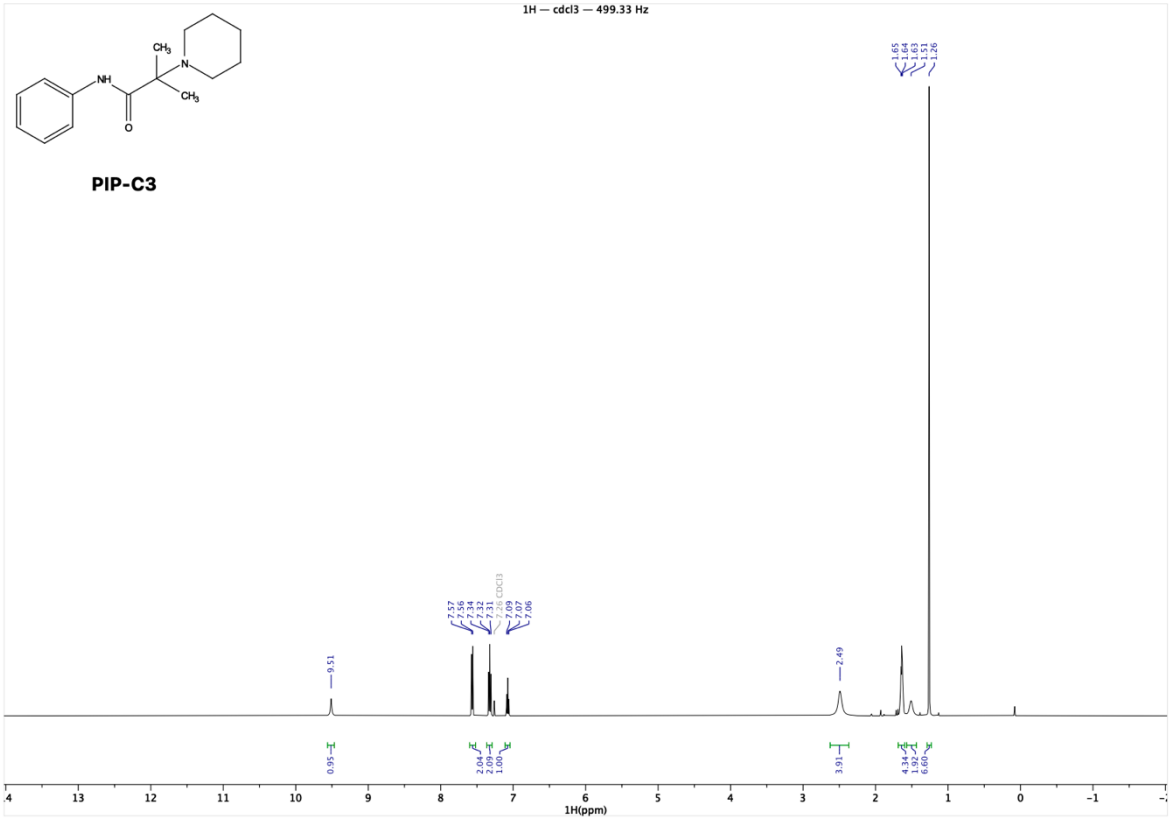

13C — cdcl3 — 125.57
30-19F
133.3
133.2
130.4
129.5
127.5
127.3
123.3
118.3
102.5
77.2 CDCl3
55.6
39.5
33.2
25.3
25.1
97.2
95.7
158.1
173.4
173.2
13C(ppm)

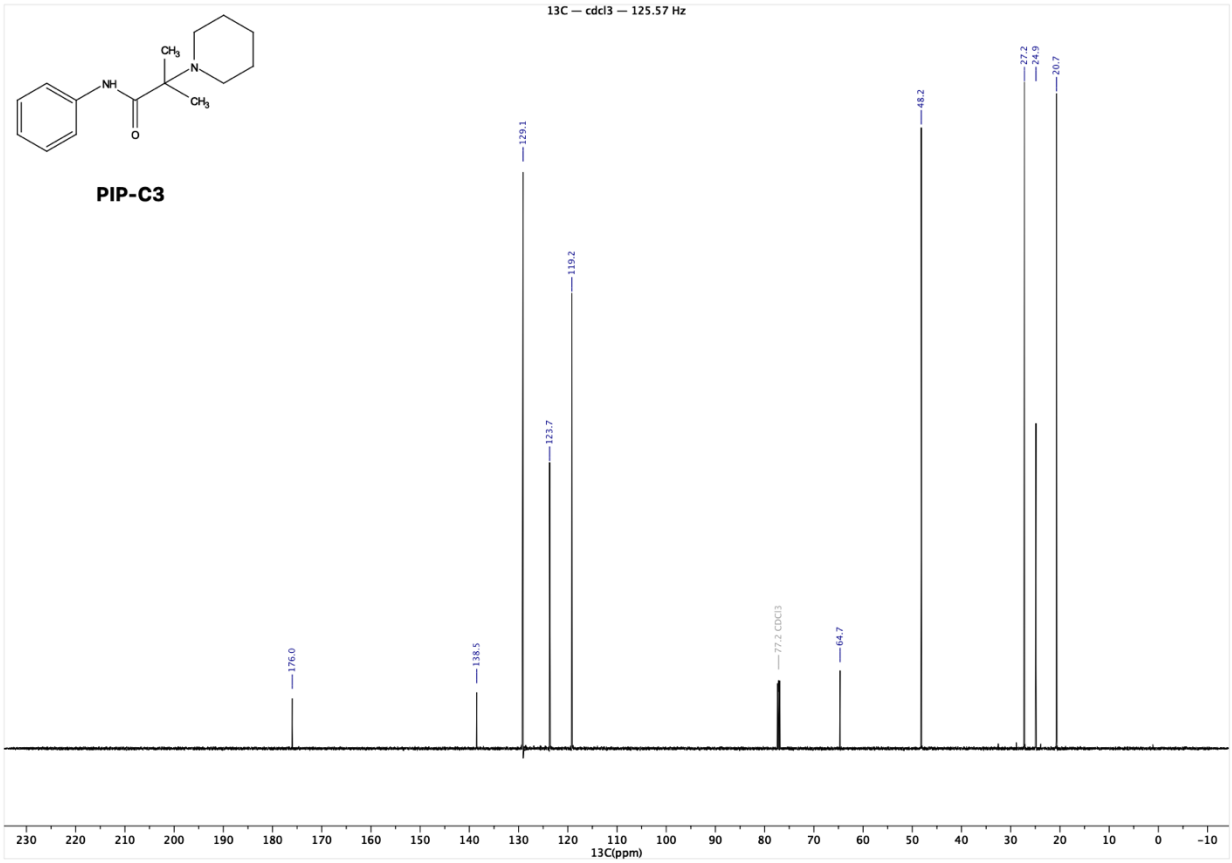

1H — cdcl3 — 399.74 Hz
PIP-C2
1H(ppm)

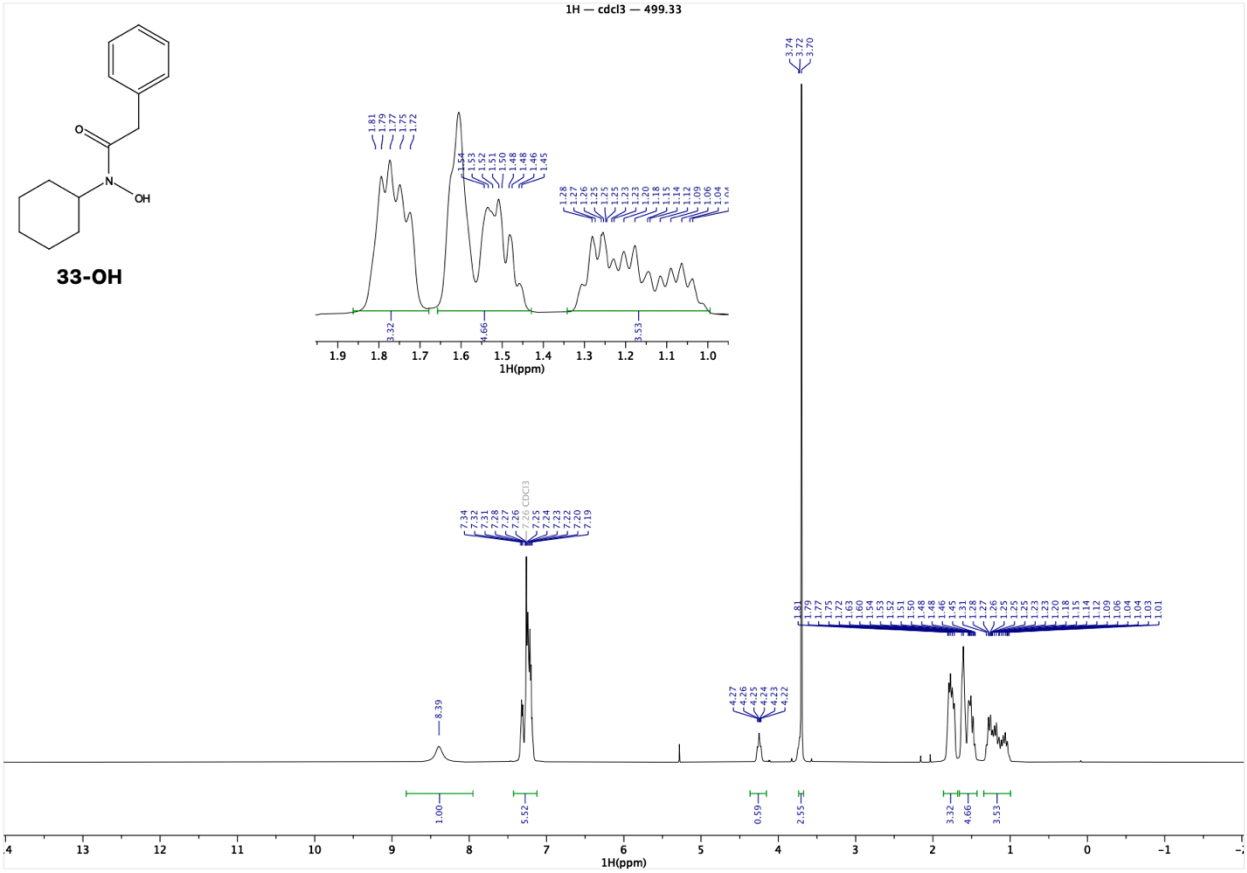

13C — cdcl3 — 100.53 Hz
PIP-C2
13C(ppm)

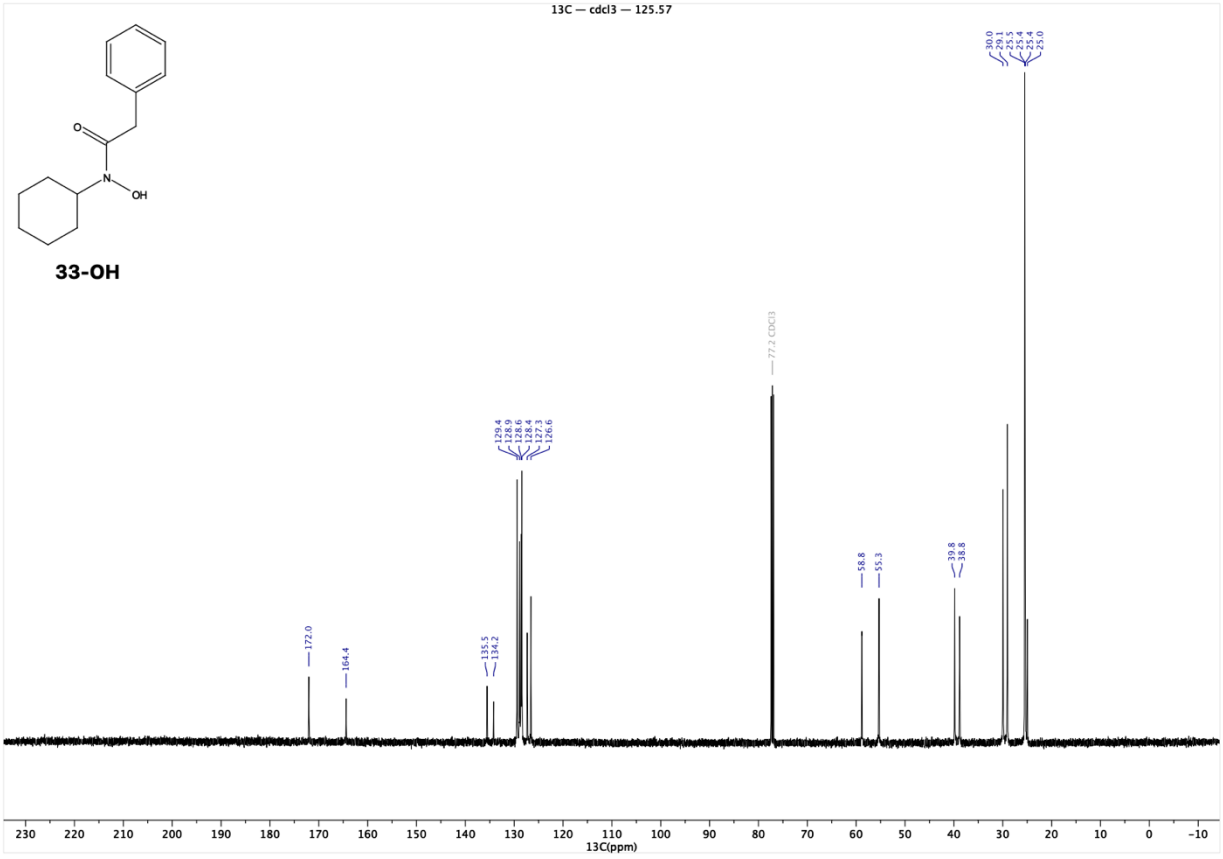

1H — dmso — 50.0 C — 500.08 Hz
PIP-C2
7.04
7.02
7.01
6.53
6.51
6.49
6.48
5.77
3.63
2.50 DMSO-d6
1.42
1.25
2.03
3.07
1.00
3.96
8.21
4.15
1H(ppm)

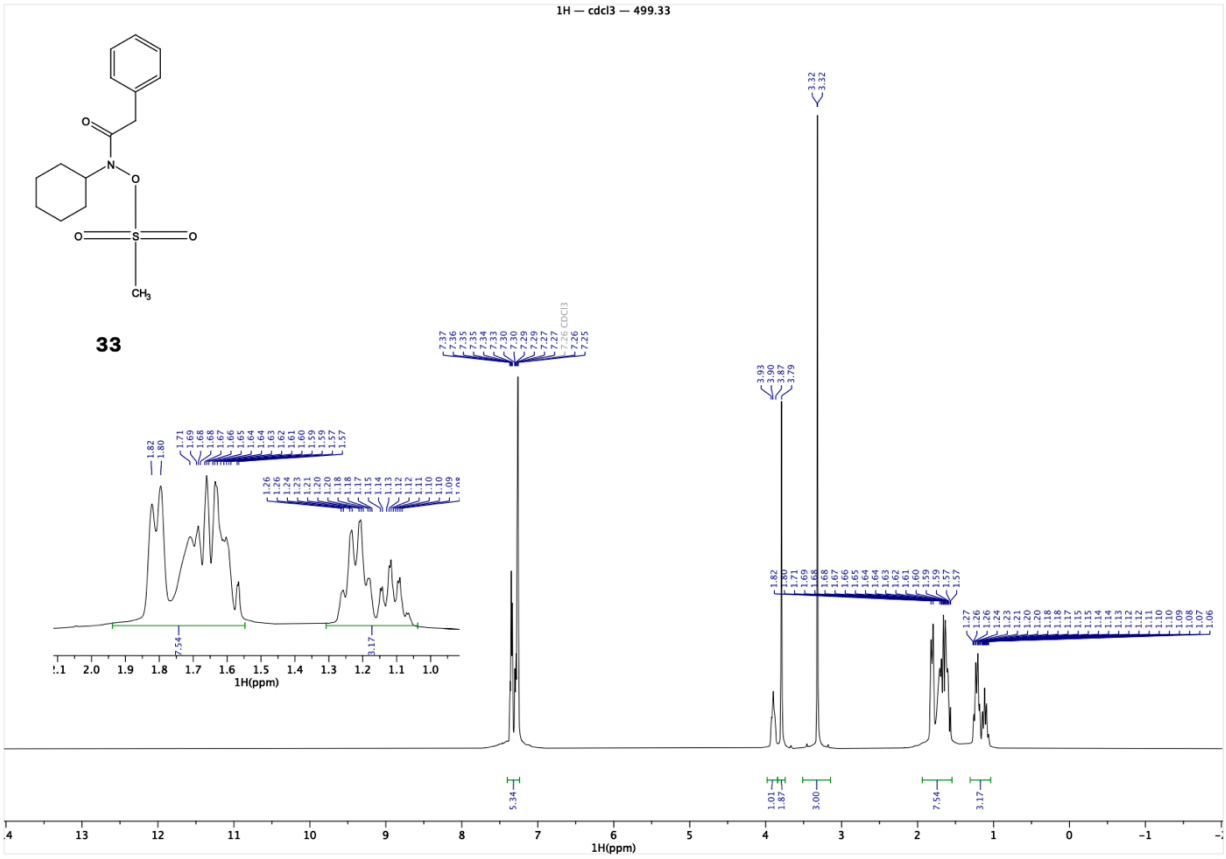

13C — dmso — 50.0 C — 125.76 Hz
PIP-C2
115.7
120.5
13C(ppm)
39.5 DMSO-d6
171.9
146.4
128.4
115.7
113.0
120.5
57.0
26.4
25.4
23.9
13C(ppm)

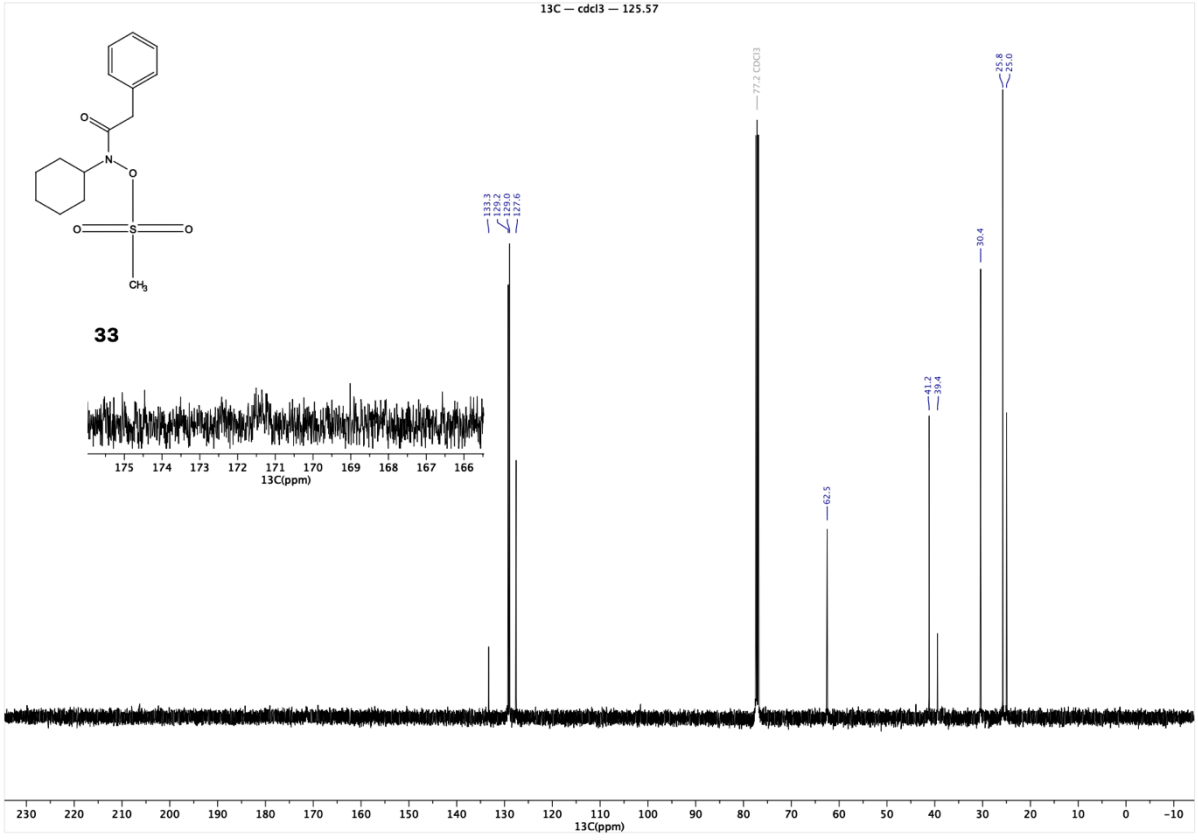

1H — cdcl3 — 499.33 Hz
PIP-C3
1H(ppm)

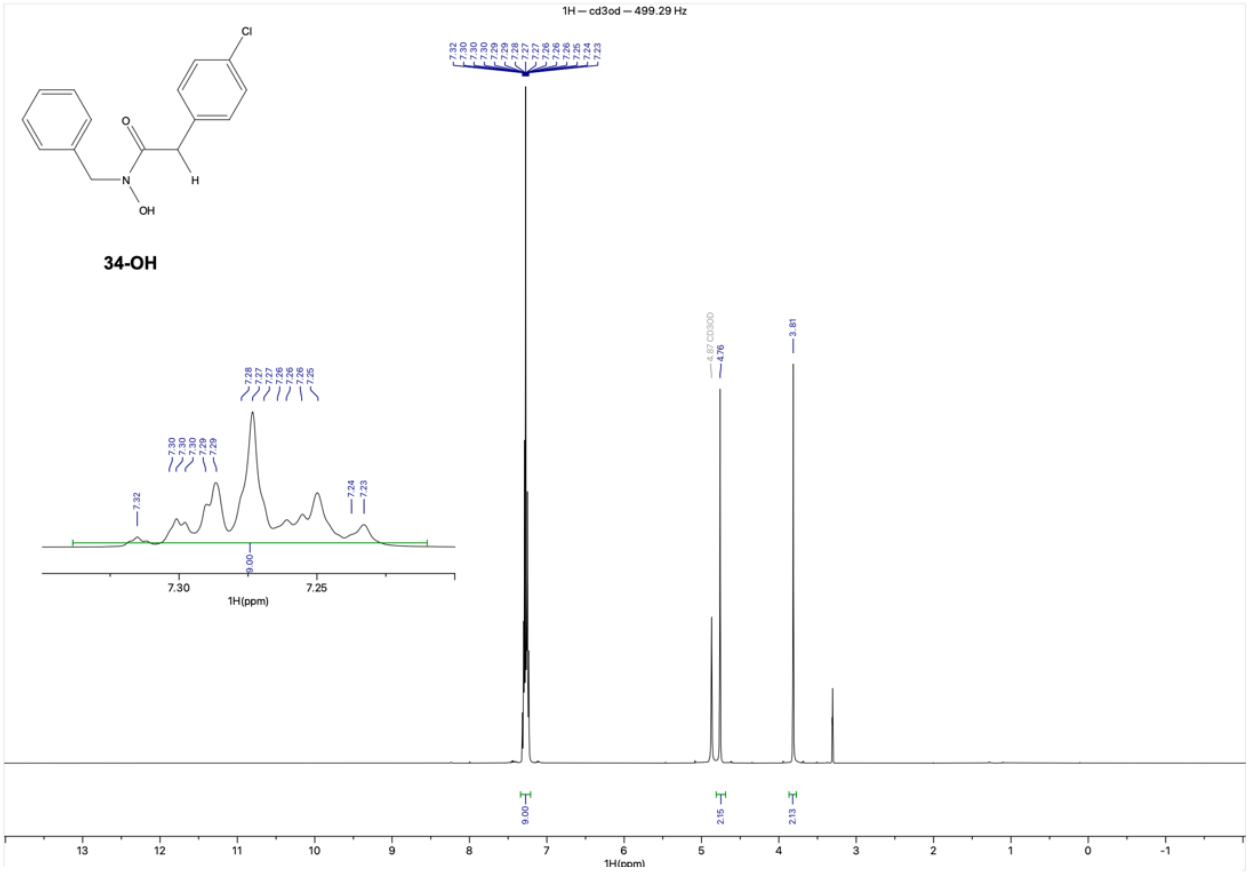

13C — cdcl3 — 125.57 Hz
PIP-C3
13C(ppm)

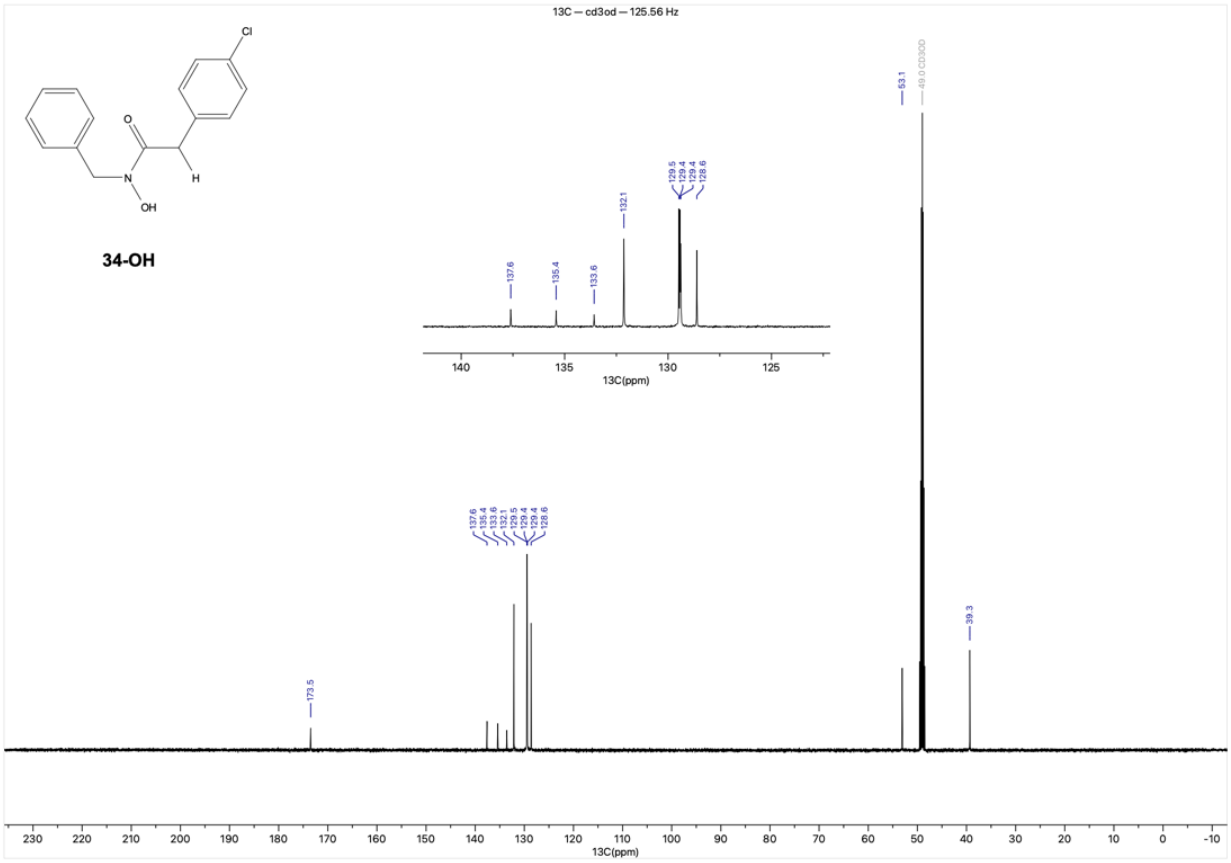

1H — cdcl3 — 499.33
33-OH
1H(ppm)

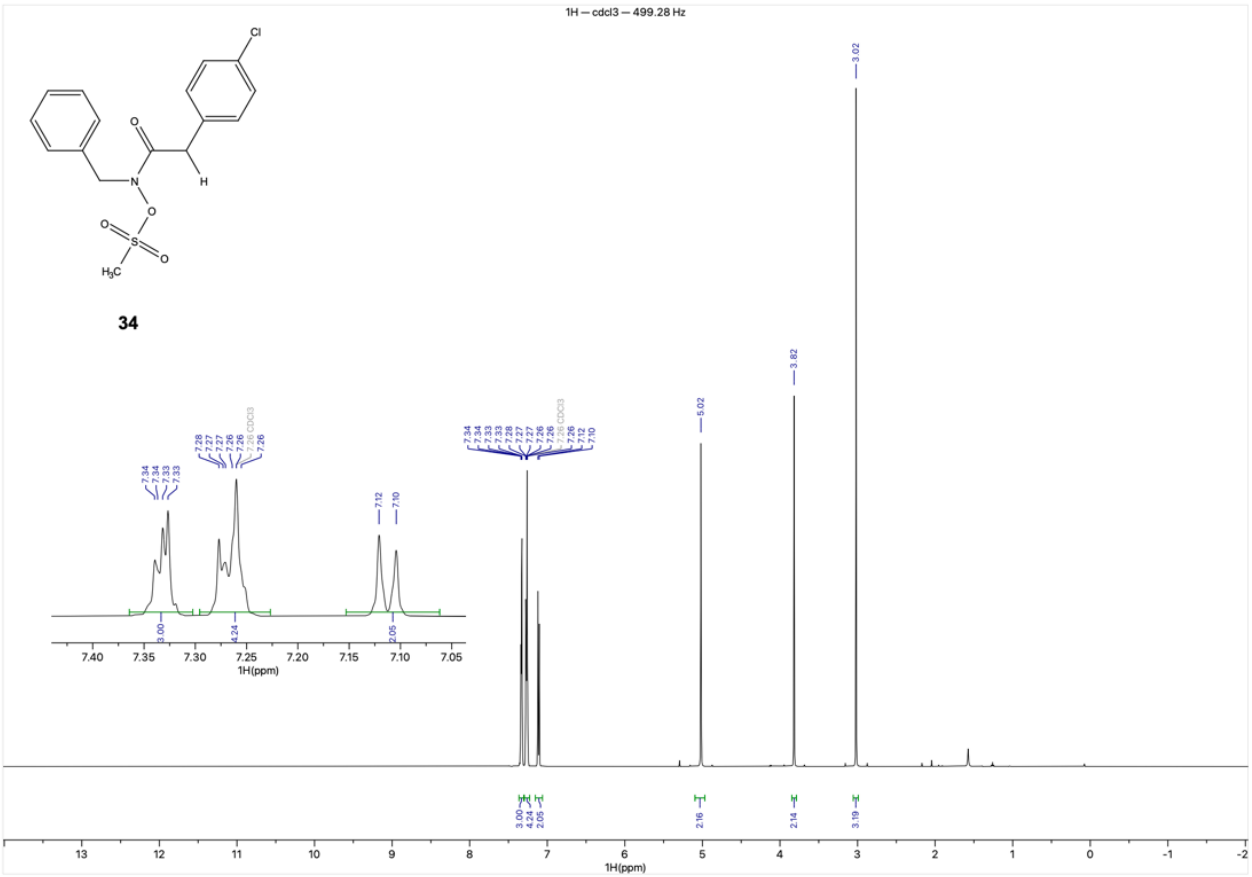

13C — cdcl3 — 125.57
33-OH
13C(ppm)

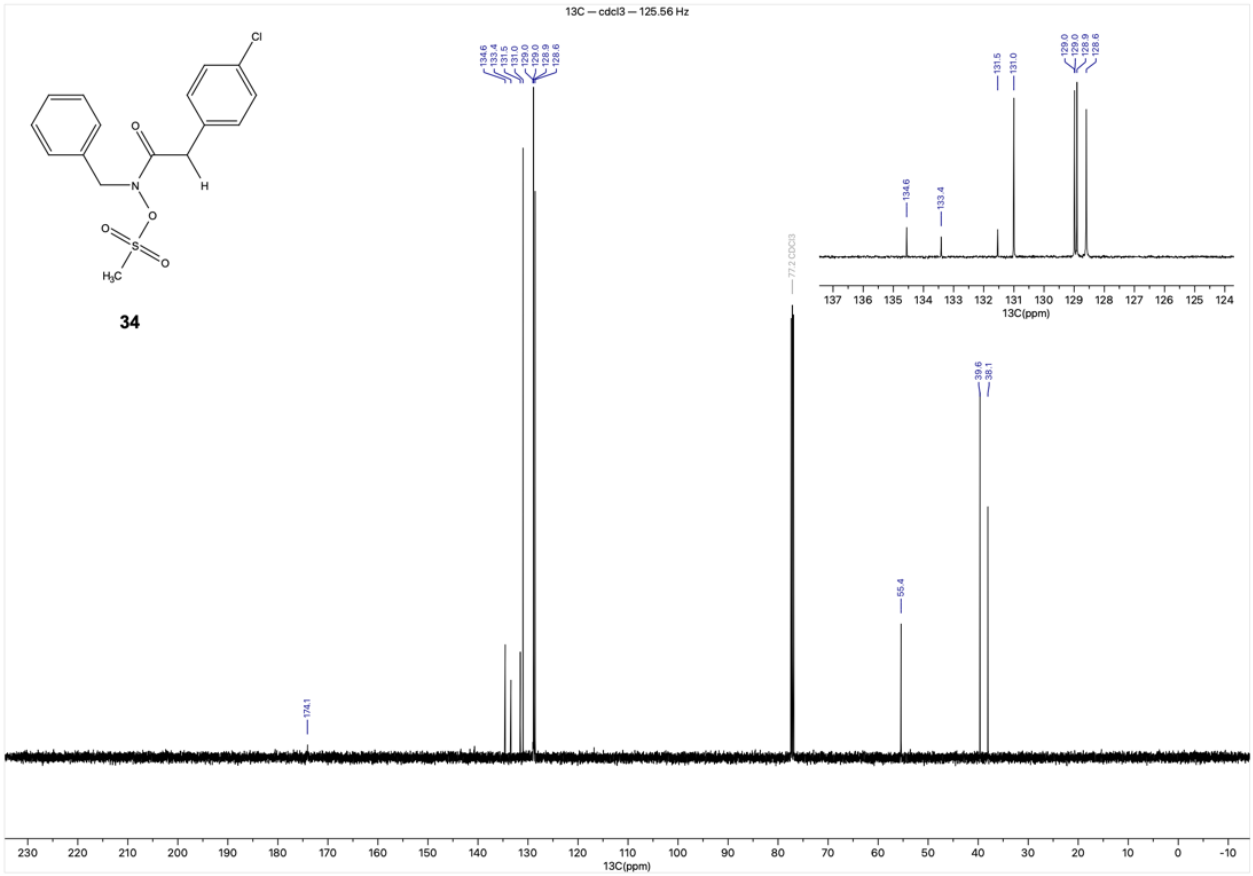

1H — cdcl3 — 499.33
33
1H(ppm)

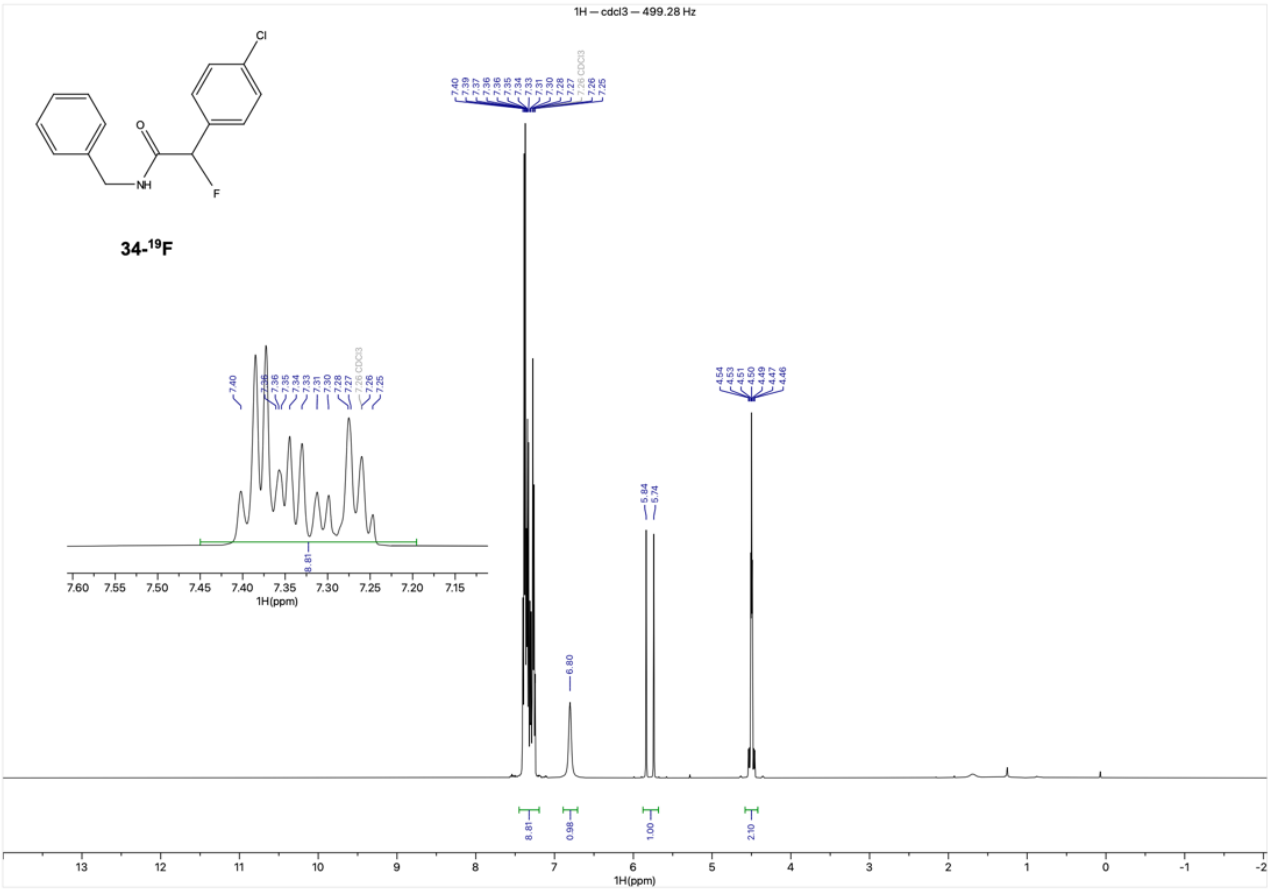

13C — cdcl3 — 125.57
33
13C(ppm)

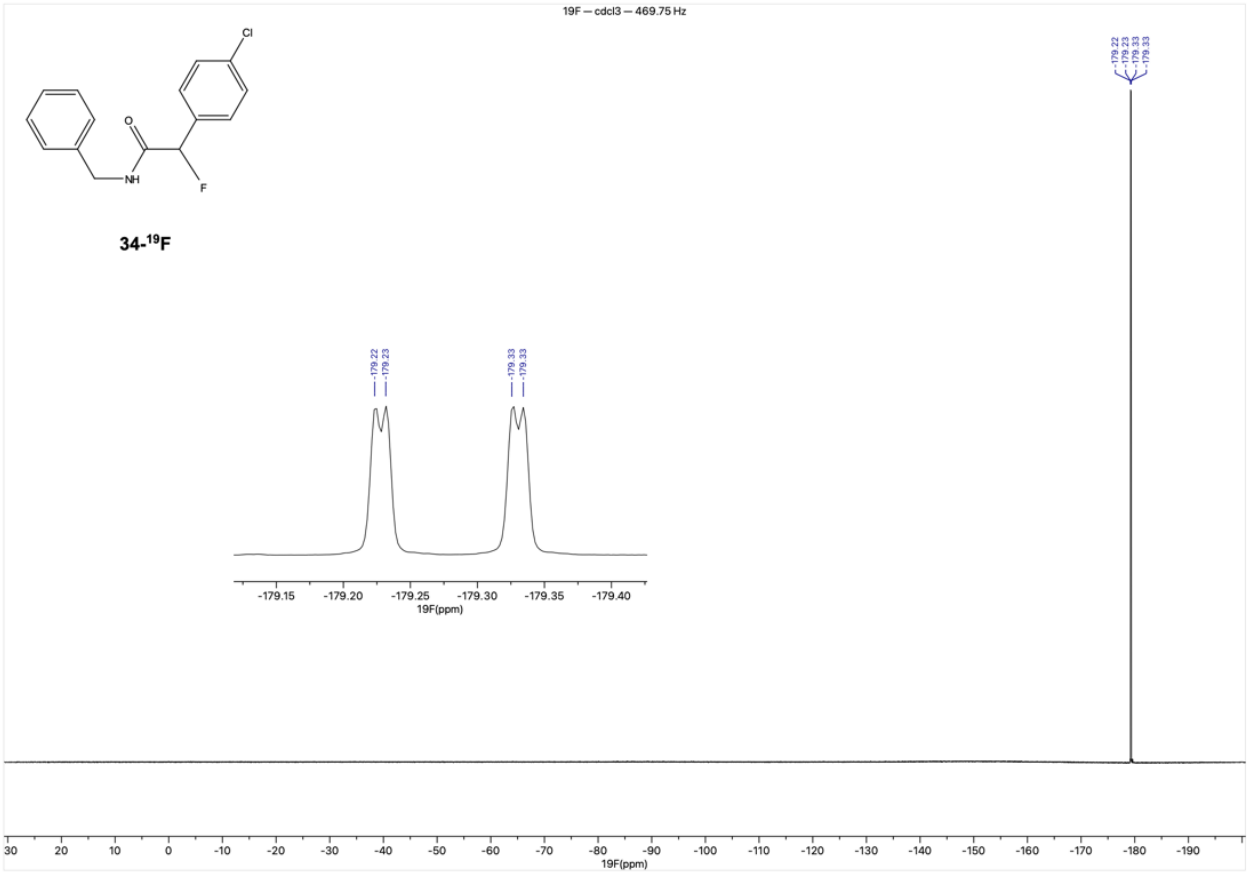

1H — cd3od — 499.29 Hz
34-OH
1H(ppm)

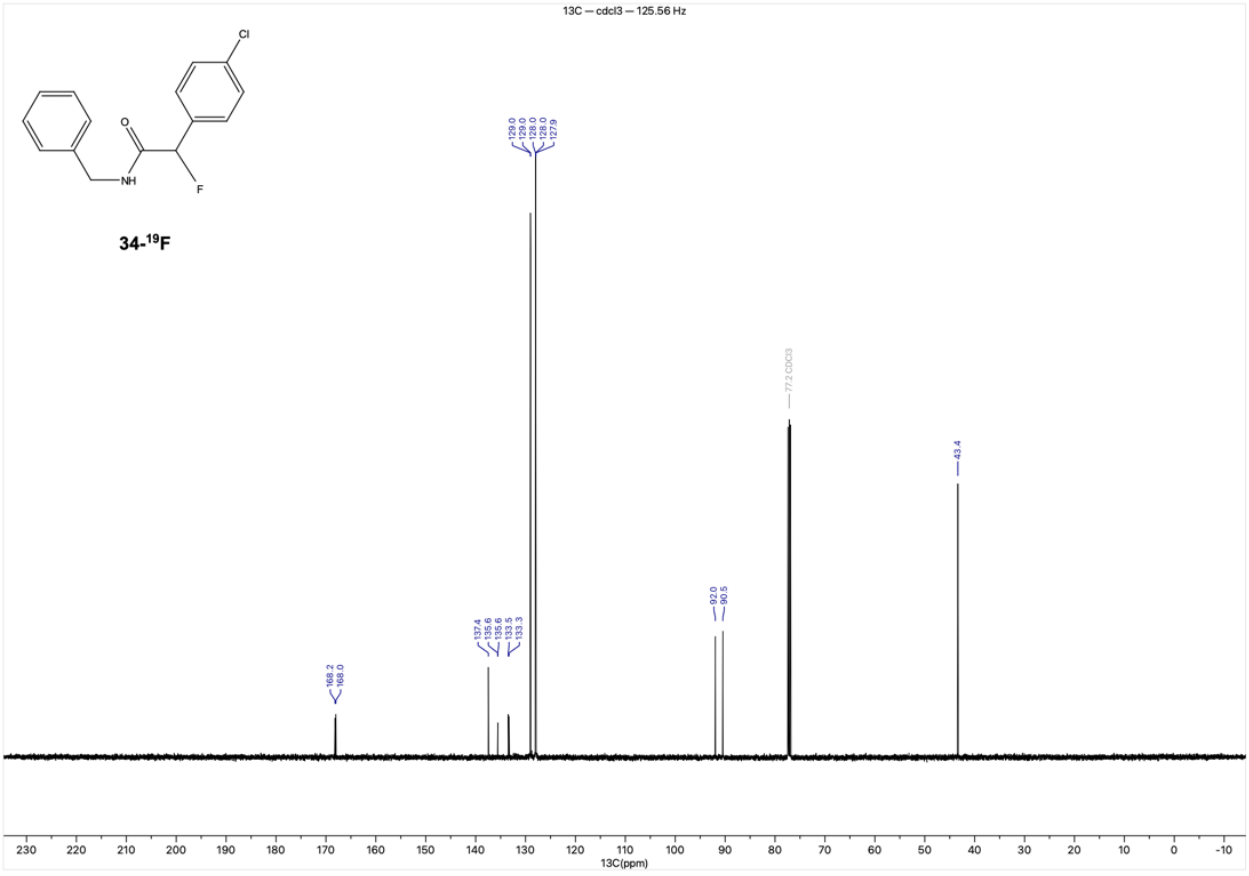

13C — cd3od — 125.56 Hz
34-OH
13C(ppm)

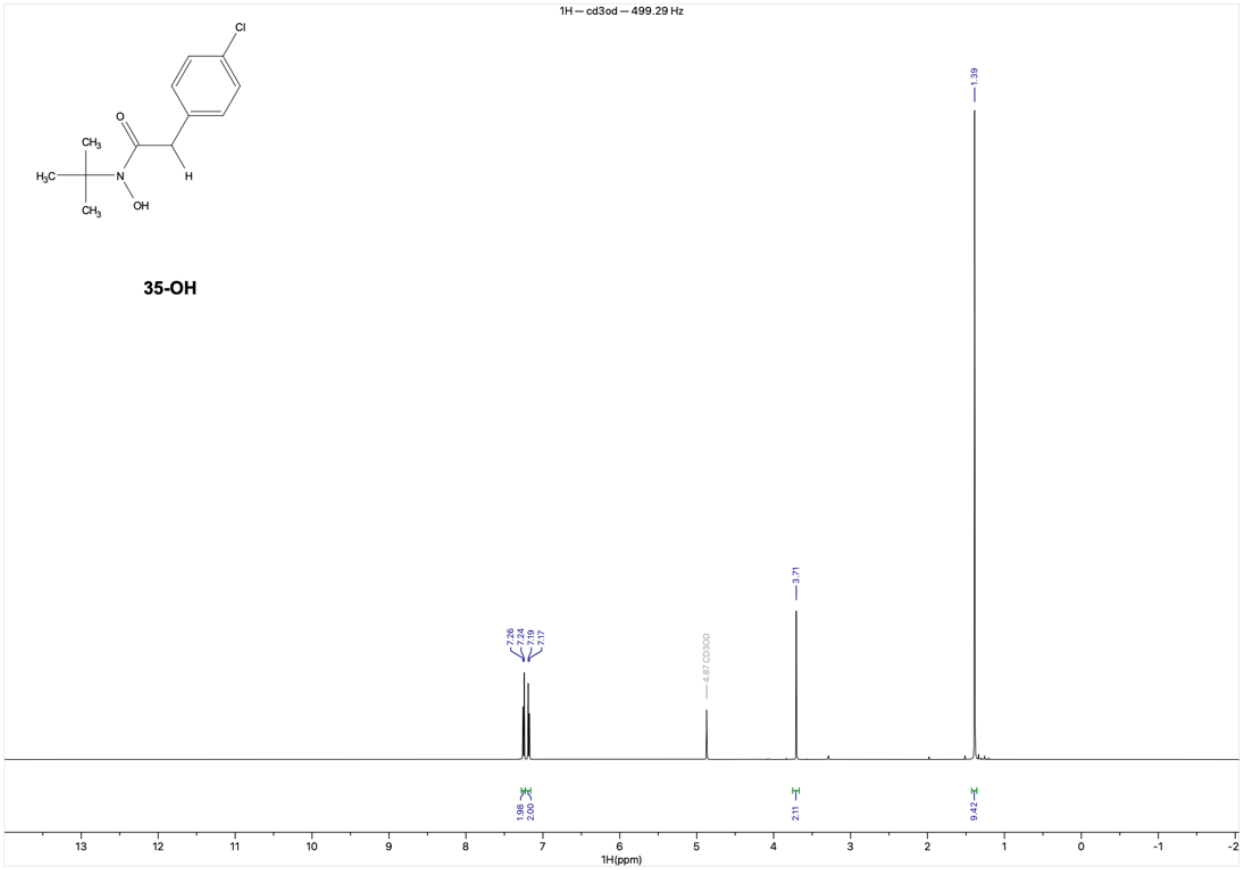

1H — cdcl3 — 499.28 Hz
34
1H(ppm)

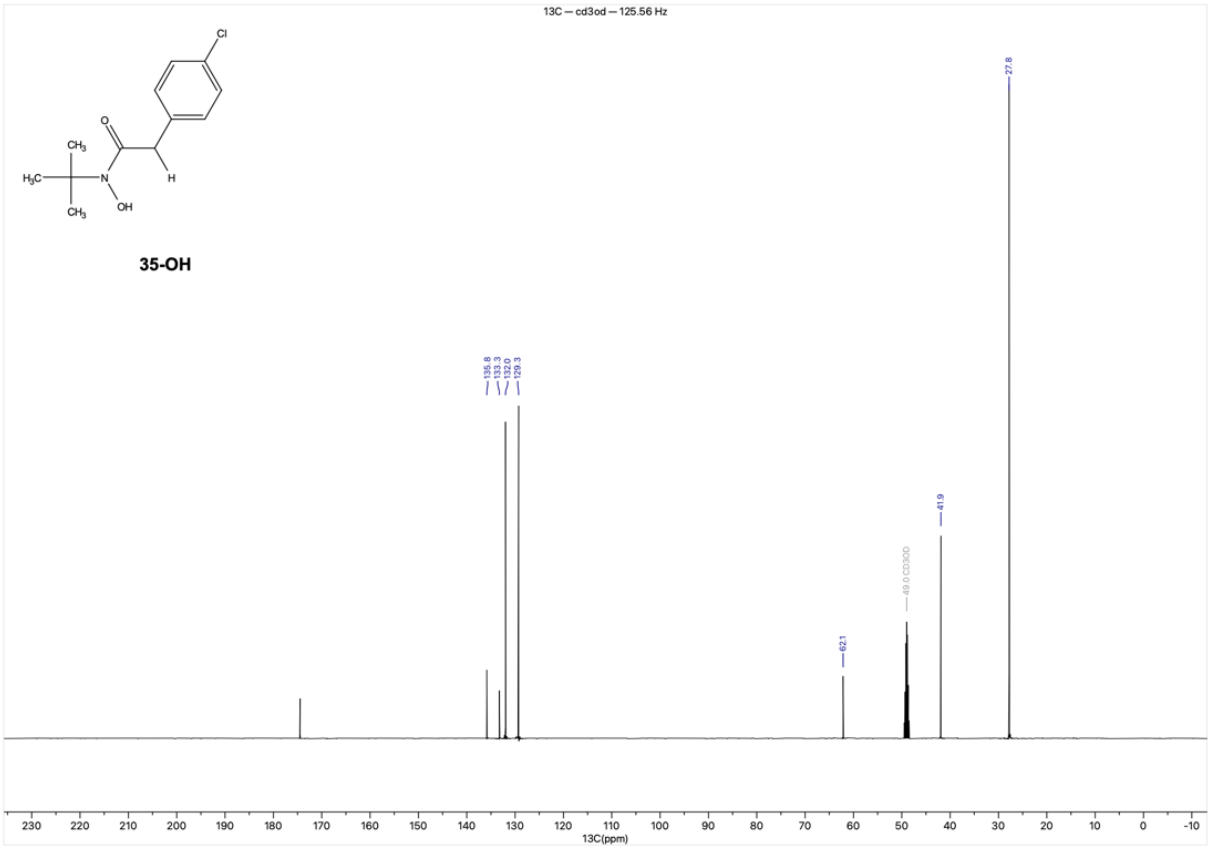

13C — cdcl3 — 125.56 Hz
34
13C(ppm)

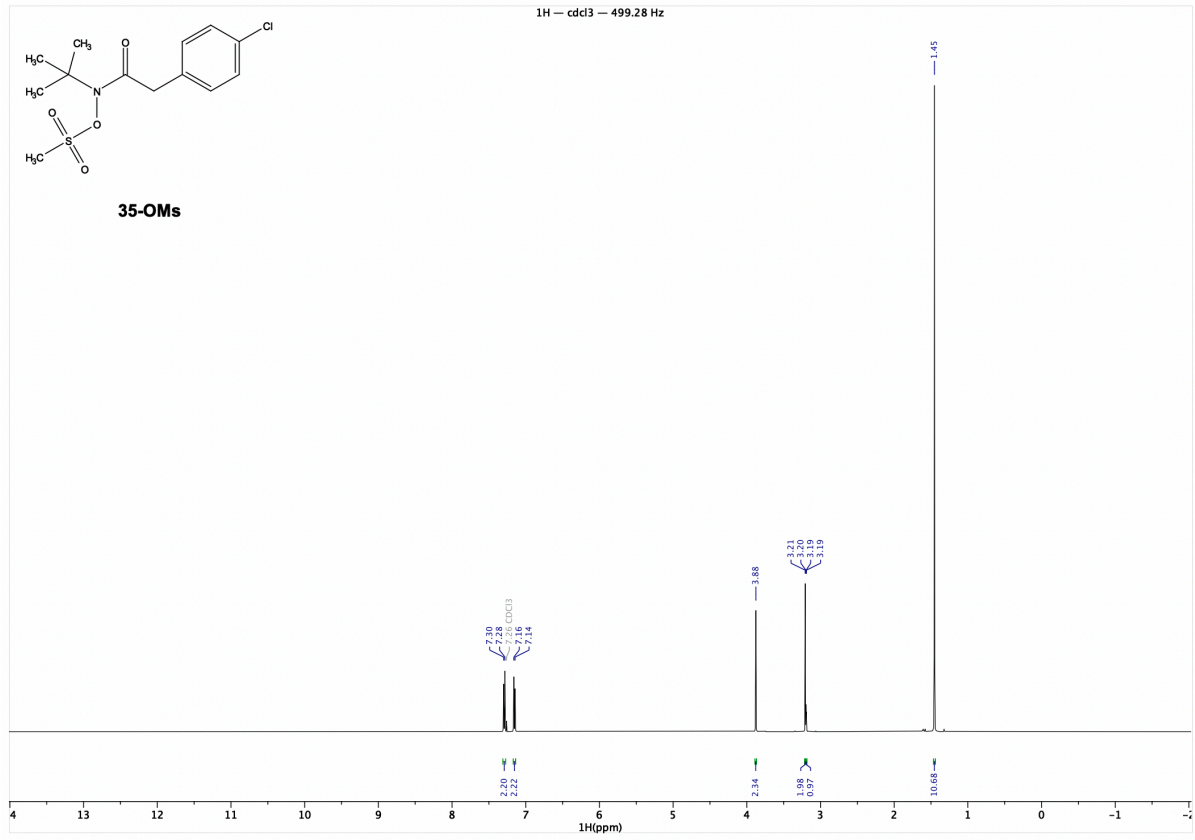

1H — cdcl3 — 499.28 Hz
Cl
O
NH
F
34-19F
7.40
7.39
7.37
7.36
7.35
7.34
7.33
7.31
7.30
7.28
7.27
7.26 CDCl3
7.25
4.54
4.53
4.51
4.50
4.49
4.47
4.46
5.84
5.74
6.80
8.81
0.98
1.00
2.10
1H(ppm)

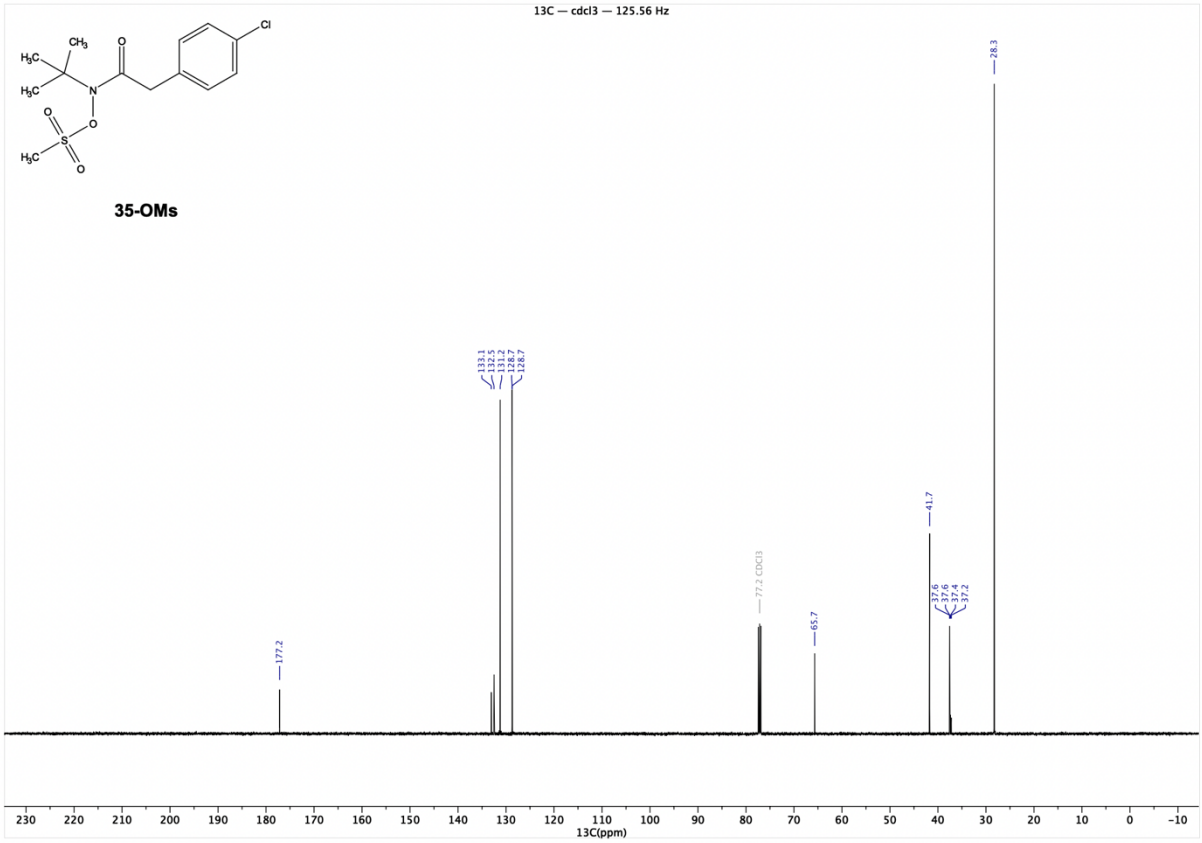

19F — cdcl3 — 469.75 Hz
Cl
O
NH
F
34-19F
-179.22
-179.23
-179.33
-179.33
19F(ppm)

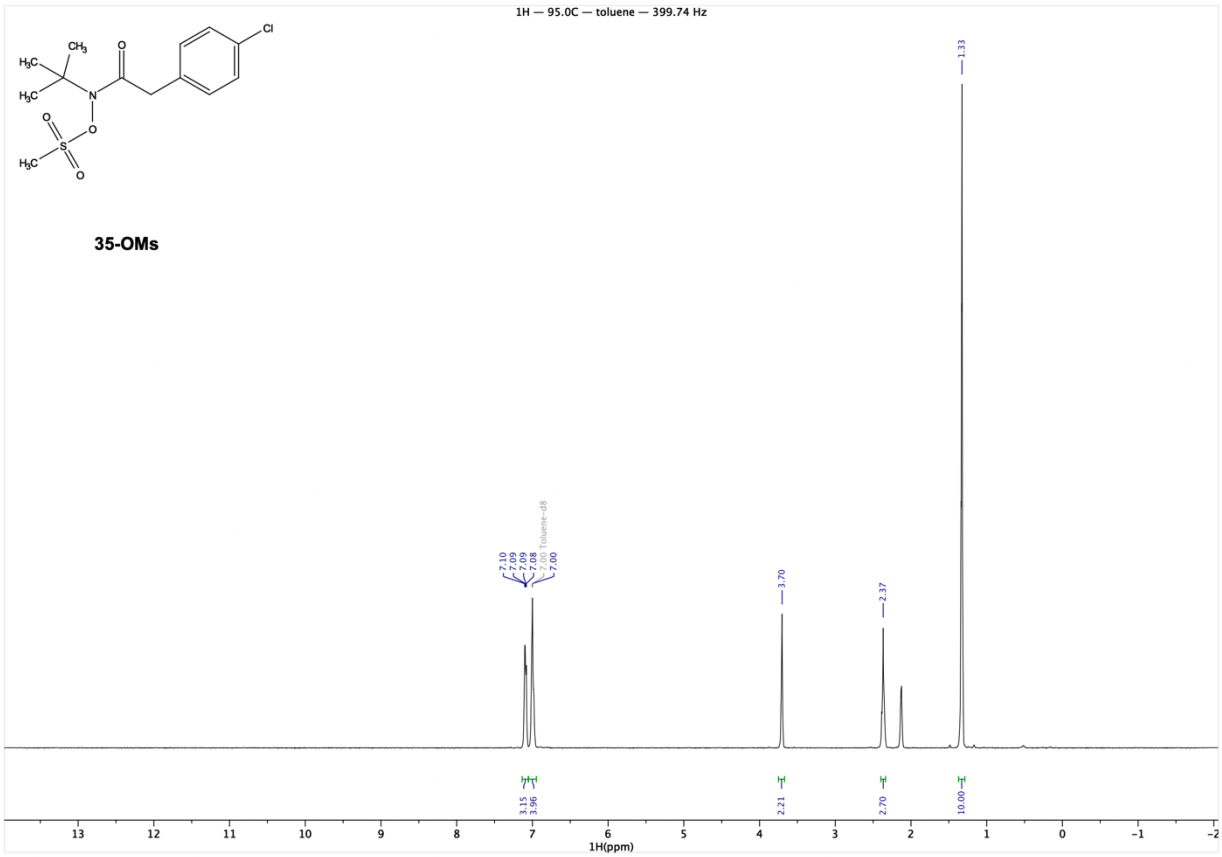

13C — cdcl3 — 125.56 Hz
Cl
O
NH
F
34-19F
129.0
128.8
128.0
127.9
77.2 CDCl3
43.4
92.0
90.5
137.4
135.6
135.5
133.3
168.2
160.0
13C(ppm)

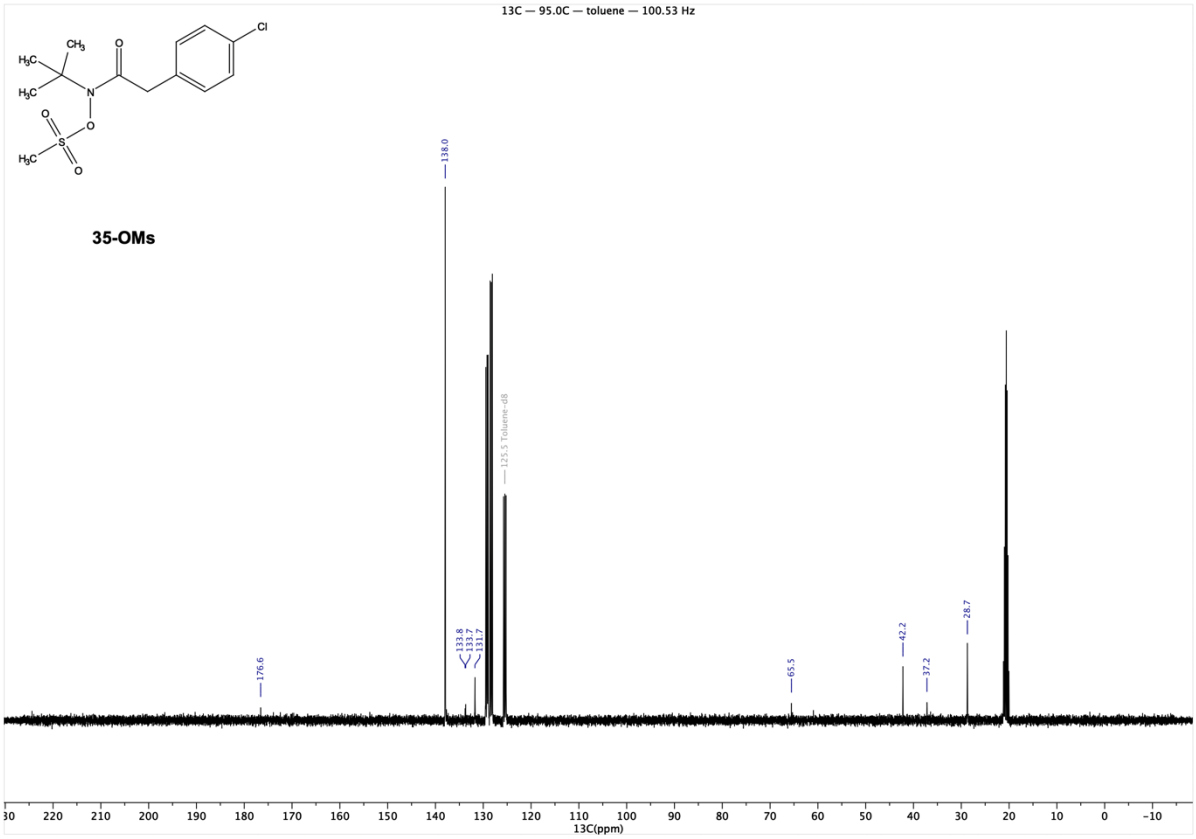

1H — cd3od — 499.29 Hz
Cl
O
CH3
H3C
N
OH
CH3
H
35-OH
1.39
3.71
7.26
7.24
7.19
7.17
4.87 CD3OD
1.98
2.00
2.11
9.42
1H(ppm)

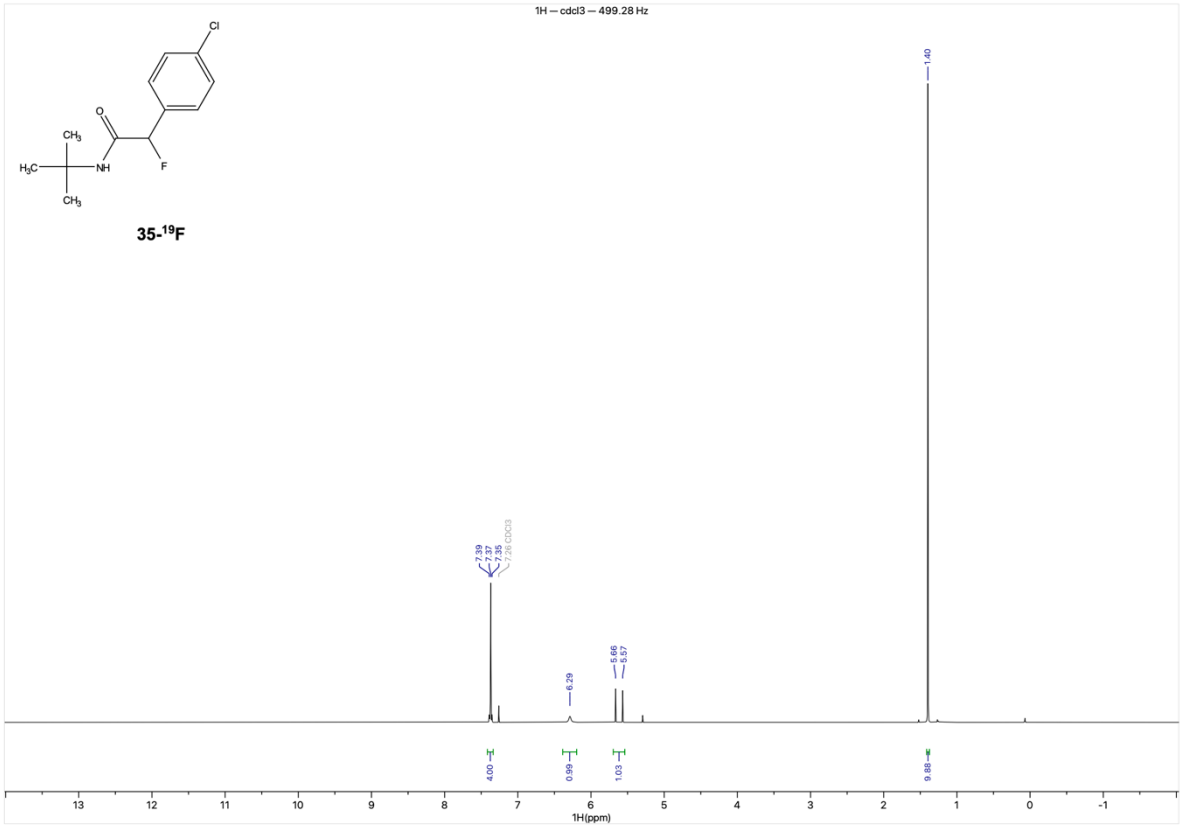

13C — cd3od — 125.56 Hz
35-OH
135.8
133.3
132.0
129.3
62.1
49.0 CD3OD
41.9
27.8
13C(ppm)

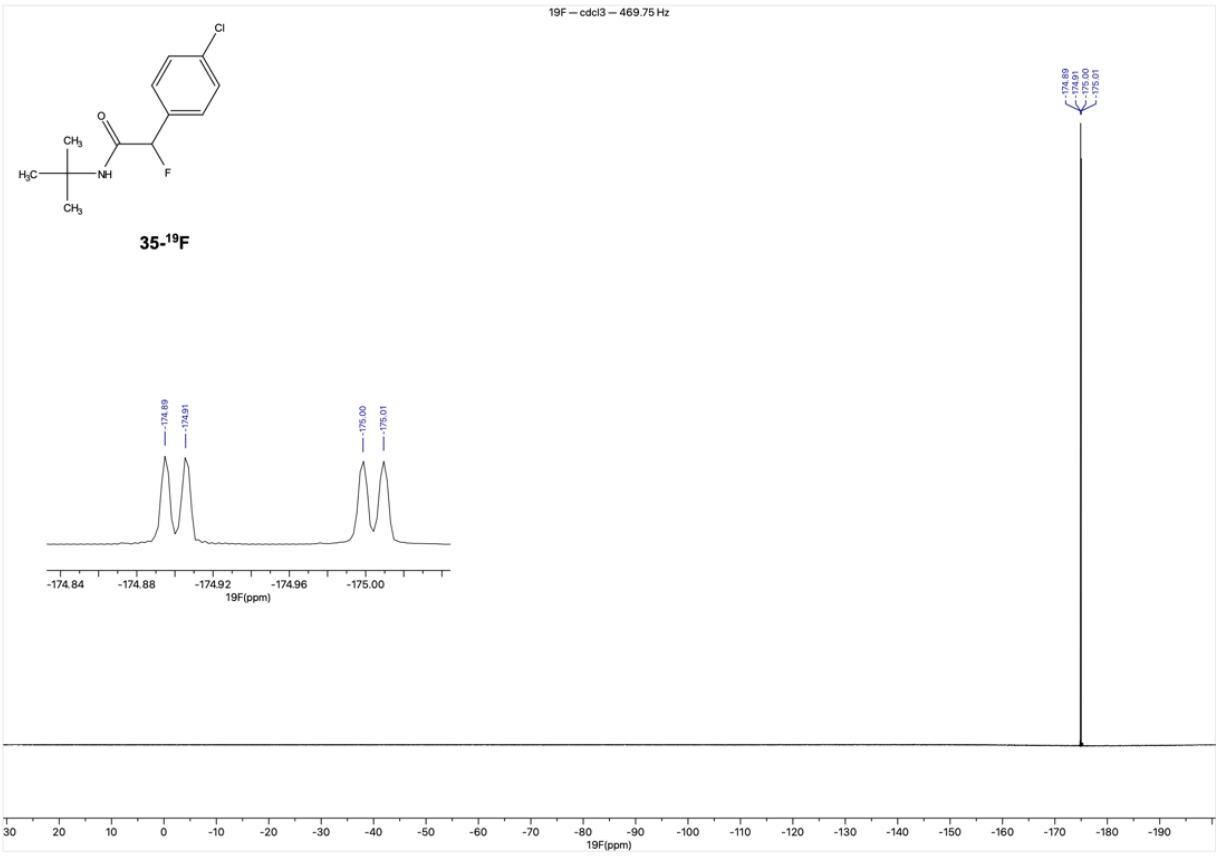

1H — cdcl3 — 499.28 Hz
35-OMs
7.30
7.28
7.26 CDCl3
7.15
7.14
3.88
3.21
3.20
3.19
3.19
1.45
2.20
2.22
2.34
1.98
0.97
10.68
1H(ppm)

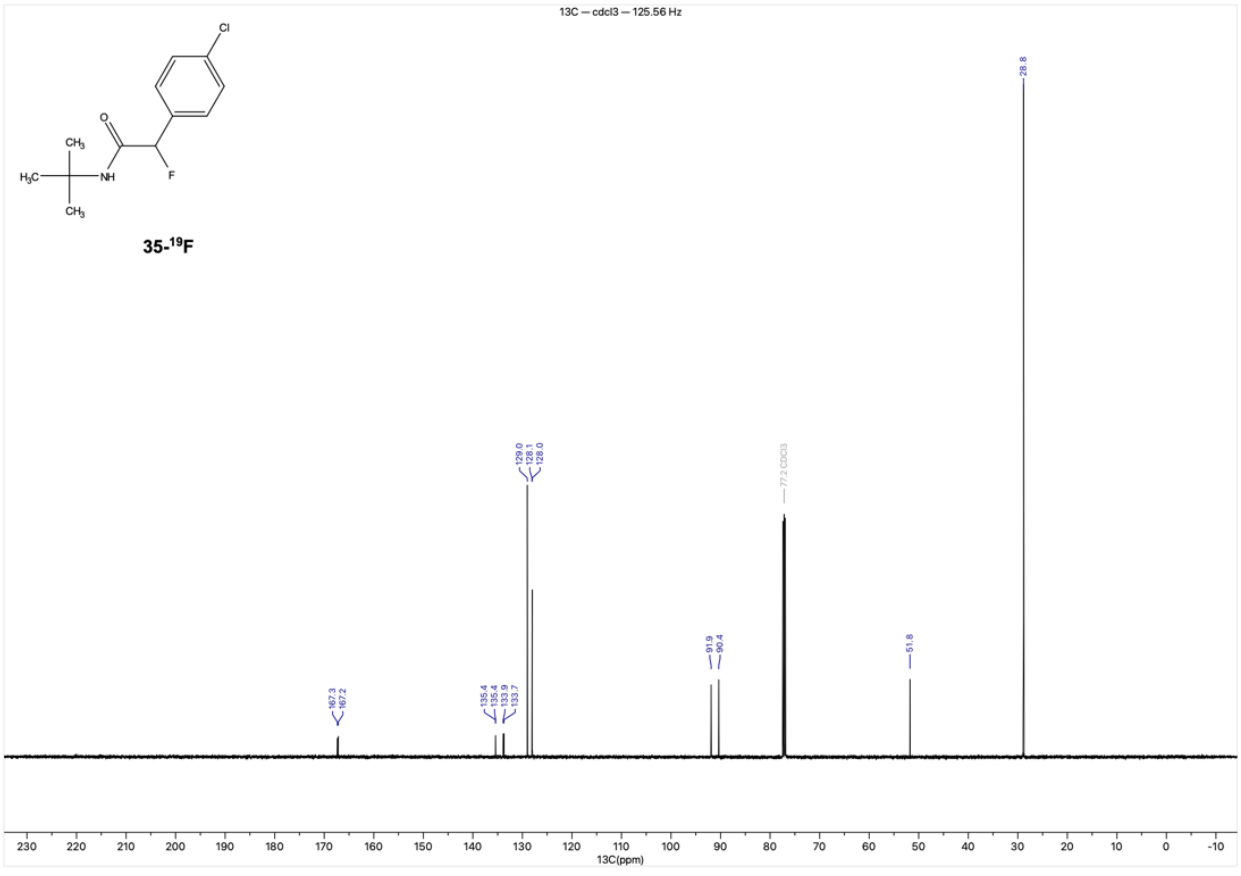

13C — cdcl3 — 125.56 Hz
35-OMs
177.2
133.1
132.5
132.2
128.8
128.7
77.2 CDCl3
65.7
41.7
37.6
37.6
37.4
37.2
28.3
13C(ppm)


1H — 95.0C — toluene — 399.74 Hz
35-OMs
7.10
7.09
7.09
7.08
7.08 Toluene-d8
7.00
3.70
2.37
1.33
3.15
3.96
2.21
2.70
10.00
1H(ppm)


13C — 95.0C — toluene — 100.53 Hz
35-OMs
138.0
133.8
133.7
131.7
125.5 Toluene-d8
176.6
65.5
42.2
37.2
28.7
13C(ppm)


1H — cdcl3 — 499.28 Hz
35-19F
1.40
7.39
7.37
7.35
7.26 CDCl3
6.29
5.66
5.57
4.00
0.99
1.03
9.88
1H(ppm)


19F — cdcl3 — 469.75 Hz
35-19F
-174.89
-174.91
-175.00
-175.01
-174.84
-174.88
-174.92
-174.96
-175.00
19F(ppm)
19F(ppm)


13C — cdcl3 — 125.56 Hz
35-19F
167.3
167.2
135.4
135.4
133.9
133.7
129.0
128.1
128.0
91.9
90.4
77.2 CDCl3
51.8
28.8
13C(ppm)

7. References

[1] S. Mizuta, K. Kitamura, A. Kitagawa, T. Yamaguchi, T. Ishikawa, *Chem. Eur. J.* **2021**, *27*, 5930–5935.
[2] P. Sokołowska, K. Dąbrowa, S. Jarosz, *Org. Lett.* **2021**, *23*, 2687–2692.
[3] J. M. S. Toro, T. Den Hartog, P. Chen, *Chem. Commun.* **2014**, *50*, 10608–10610.
[4] D. J. Sagl, J. C. Martin, *J. Am. Chem. Soc.* **1988**, *110*, 5827–5833.
[5] T. Den Hartog, J. M. S. Toro, E. P. A. Couzijn, P. Chen, *Chem. Commun.* **2014**, *50*, 10604–10607.
[6] H. Pracejus, *Justus Liebigs Ann. Chem.* **1960**, *634*, 9–22.
[7] R. V. Hoffman, N. K. Nayyar, W. Chen, *J. Org. Chem* **1992**, *57*, 5700–5707.
[8] C. Zehe, M. Schmidt, R. Siegel, K. Kreger, V. Daebel, S. Ganzleben, H. W. Schmidt, J. Senker, *CrystEngComm* **2014**, *16*, 9273–9283.
[9] D. J. Fisher, G. L. Burnett, R. Velasco, J. Read De Alaniz, *J. Am. Chem. Soc.* **2015**, *137*, 11614–11617.
[10] S. Ishida, K. Takeuchi, N. Taniyama, Y. Sunada, T. Nishikata, *Angew. Chem. Int. Ed.* **2017**, *56*, 11610–11614.
[11] A. D. Cohen, B. M. Showalter, J. P. Toscano, *Org. Lett.* **2004**, *6*, 401–403.
[12] C. S. Jeffrey, K. L. Barnes, J. A. Eickhoff, C. R. Carson, *J. Am. Chem. Soc.* **2011**, *133*, 7688–7691.

8. Acknowledgements

Image graphics were obtained from https://www.macrovector.com brgfx at https://freepik.com and Vecteezy.com.
This work was supported by the NIH Award Number 559 R01EB021155 (PJHS and MSS).
JSW acknowledges the NIH for funding Award Number K99EB031564.

9. Author Contributions

JSW wrote the manuscript/SI and designed/performed all experiments. RM and EWW performed chemistry experiments and assisted with the manuscript review. AFB assisted with the manuscript review. WW and JS performed preclinical experiments. MSS and PJHS reviewed and edited the manuscript/SI.