Electronic Supplementary Material (ESI) for Chemical Science.

Synthesis of secondary and tertiary amides without coupling agents from amines and potassium acyltrifluoroborates (KATs)

Anne Schuhmacher,[a] Tomoya Shiro,[a,c] Sarah J. Ryan,[b] and Jeffrey W. Bode[a]*

a Laboratory of Organic Chemistry, Department of Chemistry and Applied Biosciences, ETH Zurich
Vladimir-Prelog-Weg 3, 8093 Zurich, Switzerland
Email: bode@org.chem.ethz.ch, Homepage: http://www.bode.ethz.ch

b Eli Lilly and Company, Indianapolis IN 46285 U.S.A.
Homepage: http://www.lilly.com

c Current address: Sumitomo Dainippon Pharma Co., Ltd.
3-1-98 Kasugade-naka, Konohana-ku, Osaka 554-0022, Japan

Table of Contents

1. General information

1.1. Materials

Compounds that are not described in the experimental part were synthesized according to literature procedures. Unless otherwise stated, chemicals were purchased from ABCR, Acros, Alfa Aesar, Apollo Scientific, Fluorochem, Merck, Sigma-Aldrich, or TCI, and were used without further purification. Common organic solvents were used as supplied (ACS or HPLC grade). For reactions requiring anhydrous solvents, CH_3CN, CH_2Cl_2, THF, and DMF (HPLC grade) were freshly dried by passage over activated alumina under an inert atmosphere of N_2.

1.2. Reaction monitoring and purification

Thin layer chromatography (TLC) was performed on glass-backed plates pre-coated with silica gel (*Merck*, Silica Gel 60 F254) and visualized by UV quenching and oxidative staining with basic $KMnO_4$ solution. Flash column chromatography was performed on Sigma-Aldrich Silica Gel (high purity grade, 60 Å, 230–400 mesh) using a forced flow of eluent at 0.4–0.5 bar at room temperature. Organic solutions were concentrated at 40 °C under reduced pressure on a rotary evaporator.

1.3. Characterization instruments

NMR spectra were recorded on Bruker Avance 400 MHz, Bruker Avance 500 MHz, and Bruker Avance 600 MHz spectrometers using chloroform-*d* or acetone-*d6* as the solvent unless indicated otherwise. The residual signal of the chloroform-*d* (7.26 ppm for ^1H and 77.16 ppm for ^{13}C NMR) or acetone-*d6* (2.05 ppm for ^1H and 29.8 ppm for ^{13}C NMR) was used as the internal standard. ^{19}F NMR spectra were referenced to an external sample of trifluoroacetic acid, ^{11}B NMR were referenced to an external sample of BF_3-OEt_2. ^1H-NMR was reported as follows: chemical shift in ppm, multiplicity (s = singlet, d = doublet, t =

triplet, q = quadruplet, m = multiplet and br = broad singlet), coupling constant (*J* values) in Hz and integration. Infrared (IR) data were obtained on a *JASCO* FT-IR-4100 spectrometer with only major peaks being reported. Melting points (m.p.) were measured on an *OptiMelt* melting point apparatus and are reported uncorrected. High resolution mass spectra were measured by the Molecular and Biomolecular Analytical Service (MoBiAS) at ETH Zurich on a Bruker Daltonics maXis ESI-QTOF mass spectrometer.

1.4. Peptide synthesis, HPLC analysis and purification and analysis

a) Peptide synthesis

Peptides were synthesized on a CS Bio 136X synthesizer using Fmoc SPPS chemistry. The following Fmoc amino acids with side-chain protecting groups were used: Fmoc-Ala-OH, Fmoc-Arg(Pbf)-OH, Fmoc-Asp(OtBu)-OH, Fmoc-Gln(Trt)-OH, Fmoc-Glu(OtBu)-OH, Fmoc-Gly-OH, Fmoc-His(1-Trt)-OH, Fmoc-Ile-OH, Fmoc-Leu-OH, Fmoc-Lys(Boc)-OH, Fmoc-Met-OH, Fmoc-Phe-OH, Fmoc-Ser(tBu)-OH, Fmoc-Thr(tBu)-OH, Fmoc-Trp(Boc)-OH, Fmoc-Tyr(tBu)-OH, Fmoc-Val-OH. SPPS was performed on HMPB ChemMatrix® or MBHA Rink amide resin. Fmoc deprotections were performed with 20% piperidine in DMF (2 x 8 min). Couplings were performed with Fmoc amino acids (4.0 equiv to resin substitution), HCTU (3.9 equiv) and *N,N*-diisopropylethylamine (8.0 equiv) in DMF for 45 min. Double coupling was used for each coupling. After coupling, the resin was treated with 20% acetic anhydride in DMF for capping of unreacted free amine.

b) General HPLC analysis and purification

The peptide reactions were analyzed and purified by reverse phase high performance liquid chromatography (RP-HPLC) on Jasco analytical and preparative instruments equipped with UV2077 plus detector, PU 2080 Plus and PU 2087 Plus pumps for analytical and preparative HPLC, respectively. The mobile phase for RP-HPLC were

Millipore-H_2O containing 0.1% (v/v) TFA and HPLC grade CH_3CN containing 0.1% (v/v) TFA. Analytical HPLC was performed on a Shiseido Capcell pak C18 UG80 (5 μm, 4.6 mm I.D. x 250 mm column at a flow rate of 1 mL/min. Preparative HPLC was performed on a YMC C18 (5 μm, 20 mm I.D. x 250 mm) column at a flowrate of 10 mL/min, or on Shiseido Capcell pak C18 UG80 column (5 μm, 50 mm I.D. x 250 mm) at a flow rate of 40 mL/min.

c) Characterization

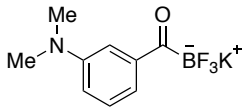
High-resolution mass spectra were recorded by the Molecular and Biomolecular Analytical Service (MoBiAS) at ETH Zurich on a Bruker maXis instrument (ESI-QTOF MS) equipped with an ESI source and a Qq-TOF detector or with a Bruker solariX instrument (MALDI FTMS) with a FT-ICR detector using 4-hydroxy-α-cyanocinnamic acid as the matrix. MALDI-MS data were obtained on a Bruker Microflex MALDI-TOF spectrometer using 4-hydroxy-α-cyanocinnamic acid as the matrix. UV–Vis absorption spectroscopy was carried out on an Agilent 8453 UV–Vis spectrophotometer with a 1 cm path length quartz cuvette.

2. Preparation of potassium acyltrifluoroborates (KATs)

2.1. General procedure

KATs that are not commercially available were prepared following the general procedure published by Bode and co-workers in 2014 from the commercially available KAT transfer reagent.[1] Only the synthesis of unpublished KATs is reported here.

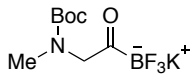
2.2. Synthesis of potassium acyltrifluoroborates (KATs)



Potassium 3-(dimethylamino)benzoyltrifluoroborate was prepared from 3-iodo-*N,N*-dimethylaniline[2] (0.74 g, 3.0 mmol) by the general procedure and obtained as a pale yellow solid (0.61 g, 2.4 mmol, 79%).

m.p.: 219 °C (decomposition); **^{1}H NMR** (500 MHz, acetone-*d6*): 7.53 – 7.47 (m, 2 H), 7.23 – 7.17 (m, 1 H), 6.85 – 6.83 (m, 1 H), 2.93 (s, 6 H); **^{13}C NMR** (150 MHz, acetone-*d6*): 236.8, 151.4, 143.0, 129.0, 118.7, 116.3, 113.2, 40.8; **^{19}F NMR** (470 MHz, acetone-*d6*): –144.3 (dd, *J* = 102.0, 47.6 Hz); **^{11}B NMR** (160 MHz, acetone-*d6*): –0.82 (q, *J* = 52.6 Hz); **IR** (v/cm^{-1}, neat): 1627, 1600, 1567, 1494, 1351, 1075, 1002, 983, 883, 712; **HRMS** (ESI neg.): calculated for $C_9H_{10}BF_3NO$ [M – K]$^-$: 216.0815, found: 216.0818.

2.3. Synthesis of *N*-methylglycine KAT analogues

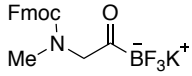


Potassium (*N*-(tert-butoxycarbonyl)-*N*-methylglycyl)trifluoroborate was synthesized by a modified procedure for the synthesis of KATs from cuprates.[3] The cuprate was prepared based on a procedure reported by Dieter and co-workers in 2000.[4] In a flame-dried round-bottom flask under an atmosphere of dry N_2, tert-

[1] G. Erős, Y. Kushida and J. W. Bode, *Angew. Chem. Int. Ed.*, 2014, **53**, 7604–7607.
[2] P. M. Liu and C. G. Frost, *Org. Lett.*, 2013, **15**, 5862–5865.
[3] S. M. Liu, D. Wu and J. W. Bode, *Org. Lett.*, 2018, **20**, 2378–2381.
[4] R. K. Dieter, C. W. Alexander and L. E. Nice, *Tetrahedron*, 2000, **56**, 2767–2778.

butyl methyl((tributylstannyl)methyl)carbamate [5] (0.31 g, 0.71 mmol, 2.5 equiv) was dissolved in dry THF (4 mL) and cooled down to –78 ºC. n-Butyllithium (1.41 M (titrated), 0.47 mL, 0.66 mmol, 2.3 equiv) was added dropwise and the solution was stirred for 1 h. Dry CuCN (27.5 mg, 0.31 mmol, 1.1 equiv) and dry LiCl (27 mg, 0.62 mmol, 2.2 equiv) dissolved in THF (1 mL) were added dropwise and the solution was warmed up to –60 ºC. The reaction mixture was allowed to slowly warm up for 30 min reaching a temperature of –45 °C. The cuprate solution was cooled down to –78 ºC and neat (ethylthiotrifluoroborate)methane dimethyliminium (52 mg, 0.28 mmol, 1.0 equiv) was added. After 1 h, the reaction mixture was quenched with aqueous KF solution (6.5 M, 0.5 mL) and stirred for additional 5 min. The solvent was removed in vacuo and the resulting solid was suspended in hexane (10 mL). The suspension was filtered and washed with hexane (3 x 50 mL). The product was extracted from the filter cake with CH_2Cl_2 and dried in vacuo to give the product as a white solid (67 mg, 0.24 mmol, 86%, mixture of rotamers 2:3).

m.p.: 91 °C; **^{1}H NMR** (600 MHz, acetone-*d6*): 4.11 (s, 0.8H), 4.05 (s, 1.2H), 2.73 (s, 1.2H), 2.69 (s, 1.8H), 1.41 (s, 3.6H), 1.33 (s, 5.4H); **^{13}C NMR** (151 MHz, acetone-*d6*): 240.8 (br), 156.9, 156.4, 78.6, 78.4, 61.6, 60.9, 35.7, 35.6, 28.7, 28.5; **^{19}F NMR** (470 MHz, acetone-*d6*): –150.4 – –150.8; **^{11}B NMR** (160 MHz, acetone-*d6*): −1.13 – –2.11; **IR** (v/cm^{-1}, thin film): 2977, 1690, 1670, 1483, 1453, 1393, 1366, 1172, 1149, 1011; **HRMS** (ESI neg.): calculated for $C_8H_{14}BF_3NO_3$ [M – K]$^-$: 240.1026, found: 240.1032.



Potassium (*N*-(fluorenylmethoxycarbonyl)-*N*-methylglycyl)trifluoroborate (10) was synthesized from **potassium (*N*-(tert-butoxycarbonyl)-*N*-methylglycyl)trifluoroborate**. Potassium (*N*-(tert-butoxycarbonyl)-*N*-methylglycyl)trifluoroborate (100 mg, 0.358 mmol, 1.00 equiv) was dissolved in 2 M aq. HCl / CH_3CN (4:1, 1.8 mL, 0.2 M), the reaction was stirred for 30 min, and the solvent was

[5] Literature procedure for the synthesis of tert-butyl methyl((tributylstannyl)methylcarbamate: L. Strekowski, K. Van Aken and Y. Gulevich, *J. Heterocyclic Chem.*, 2000, **37**, 1495–1499.

evaporated. The residue was suspended in THF (3.6 mL, 0.1 M), 9-fluorenylmethyl chloroformate (186 mg, 0.718 mmol, 2.00 equiv) and *N,N*-diisopropylethylamine (244 μL, 1.43 mmol, 4.00 equiv) were added and the reaction mixture was stirred at rt for 1 h. Another portion of 9-fluorenylmethyl chloroformate (186 mg, 0.718 mmol, 2.00 equiv) was added, the reaction was stirred at rt for 14 h and evaporated. The residue was washed with hexanes/Et_2O (2:1) and the crude product was extracted with CH_2Cl_2. Purification by flash column chromatography (hexanes/acetone 3:1 to 1:1) gave the product as a white solid (71.3 mg, 0.177 mmol, 49%, mixture of rotamers).

m.p.: 94 °C; **^{1}H NMR** (600 MHz, acetone-*d6*): 7.87 (d, *J* = 7.5 Hz, 1 H), 7.83 (d, *J* = 7.5 Hz, 1 H), 7.72 (d, *J* = 7.4 Hz, 1 H), 7.63 (d, *J* = 7.5 Hz, 1 H), 7.45 – 7.27 (m, 4 H), 4.43 – 4.11 (m, 5 H), 2.87 (d, *J* = 5.3 Hz, 3 H); **^{13}C NMR** (151 MHz, acetone-*d6*): 243.2 (br), 157.3, 157.0, 145.3, 145.2, 142.1, 141.9, 128.5, 128.4, 128.1, 128.0, 126.5, 126.1, 120.8, 120.7, 68.1, 67.9, 60.9, 48.1, 36.2, 35.6; **^{19}F NMR** (470 MHz, acetone-*d6*): –153.7; **^{11}B NMR** (160 MHz, acetone-*d6*): −1.01; **IR** (v/cm^{-1}, neat): 3154, 1702, 1685, 1447, 1231, 1037, 1007, 756, 737; **HRMS** (ESI neg.): calculated for $C_{18}H_{16}BF_3NO_3$ [M – K]$^-$: 362.1184, found: 362.1180.

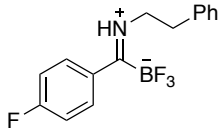
3. Preparation of trifluoroborate iminiums (TIMs)

Previously reported TIMs were prepared following the general procedure published by Bode and co-workers in 2018 from KATs.[6] Only the synthesis of unpublished TIMs is reported here.

3.1. General procedure

The KAT (1.0 equiv) was suspended in CH_3CN (0.2 M – 0.5 M). AcOH (2.0 equiv) and amine (1.5 equiv) were added and the reaction mixture was stirred at rt for 14 h. The solvent was evaporated and the crude product was purified by flash column chromatography.

3.2. Synthesis of TIMs

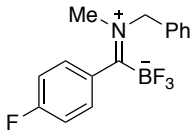


S1 was prepared from potassium 4-fluorobenzoyltrifluoroborate (0.15 g, 0.65 mmol, 1.0 equiv) by the general procedure. Purification by flash column chromatography (hexanes/acetone 2:1) gave the product as a white solid (0.15 mg, 0.52 mmol, 79%, mixture of E and Z isomer).

m.p.: 148 °C; **^{1}H NMR** (600 MHz, acetone-*d6*): 7.90 – 7.84 (m, 1.1 H), 7.43 – 7.38 (m, 0.9 H), 7.36 – 7.22 (m, 6.1 H), 7.19 – 7.15 (m, 0.9 H), 4.41 – 4.34 (m, 1.1 H), 4.11 (q, *J* = 6.7 Hz, 0.9 H), 3.25 – 3.16 (m, 2 H); **^{13}C NMR** (151 MHz, acetone-*d6*): 208.4 (m), 166.3 (d, *J* = 252.3 Hz), 165.0 (d, *J* = 250.3 Hz), 138.5, 137.9, 134.3, 132.3 (d, *J* = 8.9 Hz), 130.7 (d, *J* = 8.9 Hz), 130.2, 129.8, 129.7, 129.6, 129.6, 127.8, 127.7, 116.6 (d, *J* = 22.2 Hz), 116.5 (d, *J* = 22.2 Hz), 52.2, 50.7, 36.2, 35.0; **^{19}F NMR** (376 MHz, acetone-*d6*): –107.7 (tt, *J* = 8.9, 5.3 Hz), –110.0 (tt, *J* = 8.9, 5.3 Hz), –139.1 (dd, *J* = 78.7, 39.3 Hz), –149.2 (dd, *J* = 76.6, 37.8 Hz); **^{11}B NMR** (128 MHz, acetone-*d6*): 0.09 (q, *J* = 39.6 Hz), –0.33 (q, *J* = 39.6

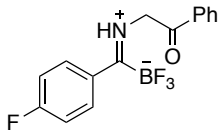
[6] T. Shiro, A. Schuhmacher, M. K. Jackl and J. W. Bode, *Chem. Sci.*, 2018, **9**, 5191–5196; M. K. Jackl, A. Schuhmacher, T. Shiro and J. W. Bode, *Org. Lett.*, 2018, **20**, 4044–4047.

Hz); **IR** (v/cm^{-1}, neat): 3278, 3202, 1596, 1246, 1061, 1045, 976, 966, 892, 836, 748, 698; **HRMS** (ESI pos.): calculated for $C_{15}H_{14}BF_4NNa$ [M + Na]$^+$: 318.1050, found: 318.1049.



S2 was prepared from potassium 4-fluorobenzoyltrifluoroborate (0.20 g, 0.87 mmol, 1.0 equiv) by the general procedure. Purification by flash column chromatography (hexanes/acetone 2:1) gave the product as a white solid (0.15 g, 0.49 mmol, 57%, mixture of E and Z isomers).

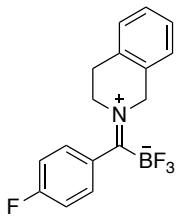
m.p.: 136 °C; **^{1}H NMR** (500 MHz, acetone-*d6*): 7.65 – 7.61 (m, 1.6 H), 7.51 – 7.37 (m, 5 H), 7.34 – 7.26 (m, 2.4 H), 5.51 (s, 1.6 H), 5.07 (0.4 H), 3.79 (s, 0.6 H), 3.03 (s, 2.4 H); **^{13}C NMR** (151 MHz, acetone-*d6*): 211.3 (m), 164.1 (d, *J* = 248.1 Hz), 164.0 (d, *J* = 22.4 Hz), 134.5, 134.4, 134.1, 133.4, 130.2, 130.0, 129.8, 129.7, 128.9 (d, *J* = 8.9 Hz), 128.8, 128.5 (d, *J* = 8.6 Hz), 116.5 (d, *J* = 22.3 Hz), 116.3 (d, *J* = 22.4 Hz), 63.2, 61.8, 44.7, 43.7; **^{19}F NMR** (470 MHz, acetone-*d6*): –112.5 (tt, *J* = 9.0, 5.3 Hz), –112.7 (tt, *J* = 9.0, 5.3 Hz), –139.6 (dd, *J* = 76.0, 37.8 Hz), –141.6 (dd, *J* = 76.0, 37.9 Hz); **^{11}B NMR** (160 MHz, acetone-*d6*): –0.19 (q, *J* = 38.0 Hz), –0.32 (q, *J* = 38.0 Hz); **IR** (v/cm^{-1}, neat): 3024, 1630, 1605, 1504, 1452, 1229, 1047, 998, 891, 741; **HRMS** (ESI pos.): calculated for $C_{15}H_{14}BF_4NNa$ [M + Na]$^+$: 318.1050, found: 318.1050.



S3 was prepared from potassium 4-fluorobenzoyltrifluoroborate (0.20 g, 0.87 mmol, 1.0 equiv) by the general procedure with a slight modification. As the amine hydrochloride salt was used, no additional AcOH was added. Purification by flash column chromatography (hexanes/acetone 2:1) gave the product as a orange oil (0.23 g, 0.74 mmol, 86%, mixture of E and Z isomer).

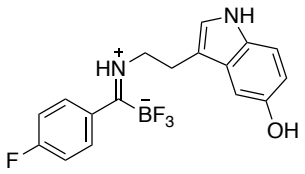
^{1}H NMR (500 MHz, acetone-*d6*): 11.21 (br, 1 H), 8.13 – 8.02 (m, 3 H), 7.94 – 7.86 (m, 1 H), 7.78 – 7.70 (m, 1 H), 7.66 – 7.56 (m, 2 H), 7.44 – 7.34 (m, 2 H), 5.70 (d, *J* = 74.9 Hz, 2 H); **^{13}C NMR** (151 MHz, acetone-*d6*): 207.6 (m), 192.8, 192.4, 166.8 (d, *J* = 253.6 Hz),

165.9 (d, *J* = 252.4 Hz), 167.6, 166.7, 165.9, 165.0, 135.5, 135.3, 132.7 (d, *J* = 9.3 Hz), 132.4 (d, *J* = 9.3 Hz), 130.0, 129.9, 129.2, 129.0, 117.0 (d, *J* = 2.1 Hz), 116.9 (d, *J* = 1.9 Hz), 56.2, 54.3; **^{19}F NMR** (470 MHz, acetone-*d6*): –106.6, –107.9, –139.4 (dd, *J* = 77.9, 38.5 Hz), –148.9 (dd, *J* = 75.6, 37.5 Hz); **^{11}B NMR** (160 MHz, acetone-*d6*): –0.03 (q, *J* = 39.1 Hz), –0.09 (q, *J* = 38.1 Hz); **IR** (v/cm^{-1}, neat): 3286, 1692, 1596, 1227, 1044, 1000, 978, 888, 837, 755, 687; **HRMS** (ESI pos.): calculated for $C_{15}H_{12}BF_4NNaO$ [M + Na]$^+$: 332.0843, found: 332. 0839.



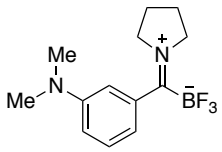
S4 was prepared from potassium 4-fluorobenzoyltrifluoroborate (0.20 g, 0.87 mmol, 1.0 equiv) by the general procedure. Purification by flash column chromatography (hexanes/acetone 2:1) gave the product as a white solid (0.12 g, 0.39 mmol, 45%, mixture of E and Z isomers).

m.p.: 171 °C; **^{1}H NMR** (400 MHz, acetone-*d6*): 7.46 – 7.36 (m, 2 H), 7.36 – 7.18 (m, 5.4 H), 7.11 – 7.02 (m, 0.6 H), 5.50 (s, 0.85 H), 5.15 (s, 1.15 H), 4.71 (t, *J* = 6.1 Hz, 1.15 H), 4.16 (t, *J* = 6.3 Hz, 0.85 H), 3.32 (t, *J* = 6.1 Hz, 1.15 H), 3.19 (t, *J* = 6.3 Hz, 0.85 H); **^{13}C NMR** (151 MHz, acetone-*d6*): 209.1 (m), 164.3 (d, *J* = 248.3 Hz), 164.1 (d, *J* = 247.7 Hz), 134.0, 134.0, 133.8, 133.6, 132.2, 131.6, 129.4, 129.3 (d, *J* = 8.7 Hz), 129.2, 128.6, 128.5 (d, *J* = 8.6 Hz), 127.9, 127.8, 127.4, 127.1, 116.4 (d, *J* = 22.2 Hz), 116.3 (d, *J* = 22.3 Hz), 57.5, 56.8, 54.7, 53.3, 30.7, 30.2; **^{19}F NMR** (470 MHz, acetone-*d6*): –112.2 (tt, *J* = 8.9, 5.3 Hz), –112.9 (tt, *J* = 8.9, 5.3 Hz), –141.1 (ddd, *J* = 76.8, 39.1, 38.9 Hz); **^{11}B NMR** (160 MHz, acetone-*d6*): –0.26 (q, *J* = 38.5 Hz), –0.32 (q, *J* = 38.4 Hz); **IR** (v/cm^{-1}, neat): 2956, 2925, 2869, 1599, 1506, 1232, 1069, 1040, 1009, 977, 896, 816, 753; **HRMS** (ESI pos.): calculated for $C_{16}H_{14}BF_4NNa$ [M + Na]$^+$: 330.1051, found: 330.1050.



S5 was prepared from potassium 4-fluorobenzoyltrifluoroborate (0.20 g, 0.87 mmol, 1.0 equiv) by the general procedure. Purification by flash column chromatography (hexanes/acetone 2:1) gave the product as a white solid (0.28 g, 0.81 mmol, 93%, mixture of E and Z isomers).

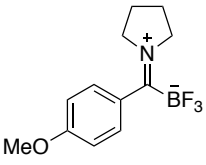
m.p.: 52 °C; **^{1}H NMR** (500 MHz, acetone-*d6*): 11.03 (br, 1 H), 9.87 (d, *J* = 14.3 Hz, 1 H), 7.89 – 7.80 (m, 1.1 H), 7.73 (s, 0.6 H), 7.56 (s, 0.4 H), 7.40 – 7.34 (m, 0.9 H), 7.32 – 7.25 (m, 1 H), 7.24 – 7.18 (m, 1.6 H), 7.16 – 7.09 (m, 1.4 H), 7.05 (dt, *J* = 2.3, 0.6 Hz, 0.6 H), 6.80 (dt, *J* = 2.3, 0.6 Hz, 0.4 H), 6.75 – 6.69 (m, 1 H), 4.39 (q, *J* = 7.1 Hz, 1.1 H), 4.11 (q, *J* = 6.6 Hz, 0.9 H), 3.31 – 3.19 (m, 2 H); **^{13}C NMR** (151 MHz, acetone-*d6*): 204.6 (m), 166.2 (d, *J* = 252.3 Hz), 164.9 (d, *J* = 250.3 Hz), 151.8, 151.7, 134.4, 132.3 (d, *J* = 9.2 Hz), 130.6 (d, *J* = 8.9 Hz), 130.2, 129.1, 128.7, 125.0, 124.6, 116.5 (d, *J* = 22.2 Hz), 116.3 (d, *J* = 22.2 Hz), 112.7, 112.7, 112.7, 110.6, 109.8,103.4, 103.1, 51.6, 49.4, 26.3, 25.2; **^{19}F NMR** (470 MHz, acetone-*d6*): –108.1 (tt, *J* = 8.7, 5.3 Hz), –110.3 (tt, *J* = 8.9, 5.3 Hz), –139.1 (dd, *J* = 79.0, 39.2 Hz), –149.3 (dd, *J* = 76.6, 37.5 Hz); **^{11}B NMR** (160 MHz, acetone-*d6*): –0.10 (dq, *J* = 76.4, 38.7 Hz); **IR** (v/cm^{-1}, neat): 3427, 3286, 3069, 1599, 1231, 1163, 1042, 977, 888, 833, 798; **HRMS** (ESI neg.): calculated for $C_{17}H_{14}BF_4N_2O$ [M – H]$^-$: 349.1144, found: 349.1144.



S6 was prepared from potassium 3-(dimethylamino)benzoyltrifluoroborate (0.10 g, 0.39 mmol, 1.0 equiv) by the general procedure. Purification by flash column chromatography (hexanes/acetone 1:1) gave the product as a yellow solid (70 mg, 0.26 mmol, 66%).

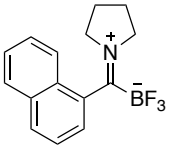
m.p.: 139 °C; **^{1}H NMR** (500 MHz, acetone-*d6*): 7.33 – 7.22 (m, 1 H)., 6.85 – 6.75 (m, 1 H), 6.69 – 6.52 (m, 1 H), 4.31 – 4.24 (m, 2 H), 3.85 – 3.78 (m, 2 H) , 2.95 (s, 6 H), 2.19 – 2.14

(m, 2 H), 2.07 – 1.99 (m, 2 H); **^{13}C NMR** (151 MHz, acetone-*d6*): 206.8 (m), 151.3, 139.9, 129.8, 114.0, 113.0, 109.0, 56.3, 56.1, 40.4, 25.1, 24.6; **^{19}F NMR** (470 MHz, acetone-*d6*): –143.6 (dd, *J* = 78.6, 39.0 Hz); **^{11}B NMR** (160 MHz, acetone-*d6*): –0.32 (q, *J* = 39.5 Hz); **IR** (v/cm^{-1}, neat): 2918, 2802, 1598, 1067, 1029, 974, 899; **HRMS** (ESI pos.): calculated for $C_{13}H_{18}BF_3N_2Na$ [M + Na]$^+$: 293.1410, found: 293.1417.



S7 was prepared from potassium 4-methoxybenzoyltrifluoroborate (0.10 g, 0.41 mmol, 1.0 equiv) by the general procedure. Purification by flash column chromatography (hexanes/acetone 2:1) gave the product as a white solid (83 mg, 0.32 mmol, 79%).

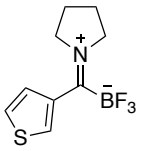
m.p.: 125 °C; **^{1}H NMR** (500 MHz, acetone-*d6*): 7.44 – 7.38 (m, 2 H), 7.06 – 7.01 (m, 2 H), 4.28 (t, *J* = 7.4 Hz, 2 H), 3.90 (t, *J* = 7.1 Hz, 2 H), 3.86 (s, 3 H), 2.20 – 2.14 (m, 2 H), 2.09 – 2.01 (m, 2 H); **^{13}C NMR** (151 MHz, acetone-*d6*): 204.6 (m), 162.2, 130.9, 129.7, 114.4, 56.6, 56.3, 55.9, 25.0, 24.9; **^{19}F NMR** (376 MHz, acetone-*d6*): –142.7 (dd, *J* = 80.1, 39.8 Hz); **^{11}B NMR** (128 MHz, acetone-*d6*): –0.26 (q, *J* = 40.1 Hz); **IR** (v/cm^{-1}, neat): 2959, 2844, 1604, 1514, 1444, 1256, 1038, 1009 971, 884, 818; **HRMS** (ESI pos.): calculated for $C_{12}H_{15}BF_3NNaO$ [M + Na]$^+$: 280.1093, found: 280.1095.



S8 was prepared from potassium 1-naphthoyltrifluoroborate (0.20 g, 0.76 mmol, 1.0 equiv) by the general procedure. Purification by flash column chromatography (hexanes/acetone 2:1) gave the product as a white solid (189 mg, 0.68 mmol, 89%).

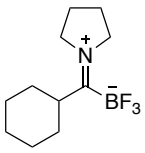
m.p.: 126 °C; **^{1}H NMR** (500 MHz, acetone-*d6*): 8.01 – 7.97 (m, 2 H), 7.71 – 7.67 (m, 1 H), 7.62 – 7.52 (m, 3 H), 7.32 (dd, *J* = 7.1, 1.1 Hz, 1 H), 4.60 – 4.39 (m, 2 H), 3.78 (dt, *J* = 14.7, 7.5 Hz, 1 H), 3.41 (dt, *J* = 14.5, 7.1 Hz, 1 H), 2.32 – 2.21 (m, 2 H), 2.11 – 2.01 (m, 2 H); **^{13}C NMR** (151 MHz, acetone-*d6*): 208.7 (m), 137.3, 134.3, 129.9, 129.4, 128.6, 127.8,

127.5, 126.1, 125.6, 121.9, 56.4, 56.3, 25.3, 24.5; **^{19}F NMR** (470 MHz, acetone-*d6*): –144.9 (dd, *J* = 77.4, 38.7 Hz); **^{11}B NMR** (160 MHz, acetone-*d6*): –0.21 (q, *J* = 38.8 Hz); **IR** (v/cm^{-1}, neat): 2956, 1624, 1082, 1036, 992, 889, 802, 778; **HRMS** (ESI pos.): calculated for $C_{15}H_{15}BF_3NNa$ [M + Na]$^+$: 300.1145, found: 300.1143.



S9 was prepared from potassium 3-thiophenoyltrifluoroborate (0.20 g, 0.92 mmol, 1.0 equiv) by the general procedure. Purification by flash column chromatography (hexanes/acetone 2:1) gave the product as a white solid (0.21 g, 0.91 mmol, 98%).

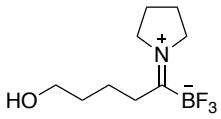
m.p.: 111 °C; **^{1}H NMR** (500 MHz, acetone-*d6*): 7.98 (dd, *J* = 3.1, 1.2 Hz, 1 H), 7.61 (dd, *J* = 5.1, 2.9 Hz, 1 H), 7.40 (ddd, *J* = 5.1, 1.3, 0.7 Hz, 1 H), 4.29 (t, *J* = 7.3 Hz, 2 H), 4.05 (t, *J* = 7.1 Hz, 2 H), 2.20 – 2.14 (m, 2 H), 2.13 – 2.07 (m, 2 H); **^{13}C NMR** (151 MHz, acetone-*d6*): 198.4 (m), 138.4, 131.3, 128.6, 126.5, 56.9, 56.5, 25.0, 24.9; **^{19}F NMR** (470 MHz, acetone-*d6*): –162.6 (dd, *J* = 79.2, 39.5 Hz); **^{11}B NMR** (160 MHz, acetone-*d6*): –0.24 (q, *J* = 39.8 Hz); **IR** (v/cm^{-1}, neat): 3118, 1593, 1014, 974, 945; **HRMS** (ESI pos.): calculated for $C_9H_{11}BF_3NNaS$ [M + Na]$^+$: 256.0551, found: 256.0554.



S10 was prepared from potassium 3-cyclohexoyltrifluoroborate (0.10 g, 0.46 mmol, 1.0 equiv) by the general procedure. Purification by flash column chromatography (hexanes/acetone 1:1) gave the product as a white solid (59 mg, 0.25 mmol, 55%).

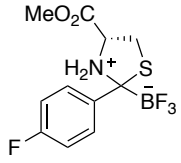
m.p.: 181 °C; **^{1}H NMR** (500 MHz, acetone-*d6*): 4.10 – 4.01 (m, 4 H), 2.69 (br, 1 H), 2.15 – 2.09 (m, 2 H), 2.08 – 2.04 (m, 2 H), 2.03 – 1.95 (m, 2 H), 1.80 – 1.76 (m, 2 H), 1.70 – 1.67 (m, 1 H), 1.56 – 1.52 (m, 2 H), 1.34 – 1.24 (m, 3 H); **^{13}C NMR** (151 MHz, acetone-*d6*): 211.5 (m), 56.8, 53.4, 49.1, 27.2, 26.3, 26.1, 25.2, 24.4; **^{19}F NMR** (470 MHz, acetone-*d6*): –141.8 (dd, *J* = 85.3, 42.5 Hz); **^{11}B NMR** (160 MHz, acetone-*d6*): –0.39 (q, *J* = 43.0

Hz); **IR** (v/cm^{-1}, neat): 2922, 2849, 1616, 1454, 1016, 997, 950; **HRMS** (ESI pos.): calculated for $C_{11}H_{19}BF_3NNa$ [M + Na]$^+$: calculated: 256.1457, found: 256.1460.



S11 was prepared from potassium 5-hydroxypentoyltrifluoroborate (0.20 g, 0.96 mmol, 1.0 equiv) by the general procedure. Purification by flash column chromatography (hexanes/acetone 1:1) gave the product as a colorless oil (0.17 g, 0.78 mmol, 81%).

^{1}H NMR (500 MHz, acetone-*d6*): 4.08 (t, *J* = 7.0 Hz, 2 H), 3.99 (t, *J* = 7.1 Hz, 2 H), 3.61 – 3.55 (m, 2 H), 3.52 – 3.46 (m, 1 H), 2.68 – 2.60 (m, 2 H), 2.19 – 2.07 (m, 4 H), 1.68 – 1.56 (m, 4 H); **^{13}C NMR** (151 MHz, acetone-*d6*): 210.3 (m), 61.9, 56.2, 52.9, 36.9, 33.8, 25.2, 24.5, 21.8; **^{19}F NMR** (470 MHz, acetone-*d6*): –147.0 (dd, *J* = 82.4, 41.0 Hz); **^{11}B NMR** (160 MHz, acetone-*d6*): –0.54 (q, *J* = 41.2 Hz); **IR** (v/cm^{-1}, neat): 3396, 2941, 2877, 1029, 998, 967; **HRMS** (ESI pos.): calculated for $C_9H_{17}BF_3NNaO$ [M + Na]$^+$: 246.1249, found: 246.1249.



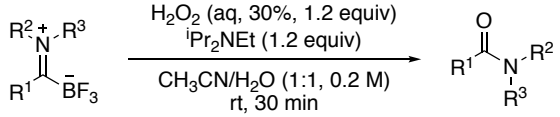
S12 was prepared from potassium 4-fluorobenzoyltrifluoroborate (0.20 g, 0.96 mmol, 1.0 equiv) by the general procedure with a slight modification. As the amine hydrochloride salt was used, no additional AcOH was added. Purification by flash column chromatography (hexanes/acetone 2:1 to 1:1) gave the product as a colorless oil (0.26 g, 0.83 mmol, 95%).

^{1}H NMR (600 MHz, methanol-d_4): 7.55 – 7.45 (m, 2 H), 6.88 – 6.81 (m, 2 H), 3.76 (s, 3 H), 3.72 (t, *J* = 8.0 Hz, 1 H), 3.01 (dd, *J* = 10.3, 8.1, 1 H), 2.77 (dd, *J* = 10.3, 7.9 Hz, 1 H); **^{13}C NMR** (151 MHz, methanol-d_4): 174.6, 162.7 (d, *J* = 240.6 Hz), 145.3, 129.5 (d, *J* = 7.6 Hz), 114.2 (d, *J* = 21.0 Hz), 81.1 (br), 65.7, 52.7, 38.4; **^{19}F NMR** (470 MHz, methanol-d_4): –122.4, –151.1 (br); **^{11}B NMR** (160 MHz, methanol-d_4): 2.85 (br); **IR** (neat): 1741, 1705, 1597, 1501, 1440, 1338, 1247, 1217, 1217, 1247, 1567, 1132, 1088, 1064, 1012 cm^{-1};

HRMS (ESI neg): calculated for $C_{11}H_{11}BF_4NO_2S$ $[M - H]^-$: 308.0547, found: 308.0553; $\mathbf{[\alpha]_D^{28}}$ (c = 0.05, CH_3OH)= –212.7.

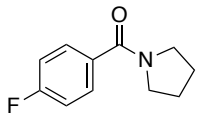
4. Oxidation of trifluoroborate iminiums (TIMs) to amides

4.1. General procedure



The trifluoroborate iminium (TIM, 0.2 mmol, 1.0 equiv) was dissolved in CH_3CN/H_2O (1.0 mL, 0.2 M), H_2O_2 (30% aq, 27 μL, 0.24 mmol, 1.2 equiv) and *N,N*-diisopropylethylamine (41 μL, 0.24 mmol, 1.2 equiv) were added and the reaction was stirred for 30 min. The reaction was diluted with H_2O (10 mL) and EtOAc (10 mL) and the aqueous layer was extracted three times with EtOAc (3 x 10 mL). The combined organic layers were washed with brine (30 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. If necessary, the crude product was purified by flash column chromatography.

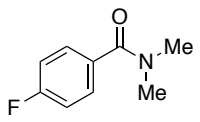
4.2. Synthesis of amides



2a was prepared from the corresponding TIM (49 mg, 0.20 mmol, 1.0 equiv) by the general procedure, no purification by flash column chromatography was necessary. The product was isolated as a pale yellow oil (37 mg, 0.19 mmol, 96%).

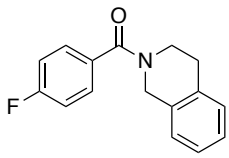
^{1}H NMR (400 MHz, chloroform-*d*): 7.57 – 7.48 (m, 2 H), 7.11 – 7.01 (m, 2 H), 3.62 (t, *J* = 6.9 Hz, 2 H), 3.41 (t, *J* = 6.6 Hz, 2 H), 2.00 – 1.82 (m, 4 H); **^{13}C NMR** (101 MHz, chloroform-*d*): 168.8, 163.6 (d, *J* = 249.6 Hz), 133.4 (d, *J* = 3.4 Hz), 129.6 (d, *J* = 8.6 Hz), 115.4 (d, *J* = 21.7 Hz), 49.8, 46.5, 26.6, 24.6; **^{19}F NMR** (376 MHz, chloroform-*d*): –110.4 (m). The spectral characteristics are in agreement with spectral data previously reported.[7]

[7] D. Leow, *Org. Lett.*, 2014, **16**, 5812–5815.



2b was prepared from the corresponding TIM (44 mg, 0.20 mmol, 1.0 equiv) by the general procedure, no purification by flash column chromatography was necessary. The product was isolated as a white solid (31 mg, 0.18 mmol, 92%).

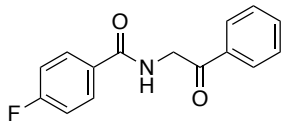
^{1}H NMR (400 MHz, chloroform-*d*): 7.54 – 7.36 (m, 2 H), 7.16 – 7.02 (m, 2 H), 3.04 (br, 6 H); **^{13}C NMR** (101 MHz, chloroform-*d*): 170.8, 163.4 (d, *J* = 249.4 Hz), 132.4 (d, *J* = 3.5 Hz), 129.5 (d, *J* = 8.4 Hz), 115.5 (d, *J* = 21.8 Hz), 39.7, 35.6; **^{19}F NMR** (376 MHz, chloroform-*d*): –110.7. The spectral characteristics are in agreement with spectral data previously reported.[8]



2c was prepared from the corresponding TIM (61 mg, 0.20 mmol, 1.0 equiv) by the general procedure and the crude product was purified by flash column chromatography using hexanes/EtOAc (5:1 to 3:1). The product was isolated as a colorless oil (49 mg, 0.19 mmol, 95%).

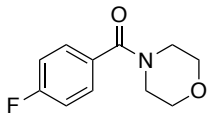
^{1}H NMR (500 MHz, chloroform-*d*): 7.55 – 7.42 (m, 2 H), 7.29 – 7.02 (m, 6 H), 5.02 – 4.51 (m, 2 H), 4.07 – 3.53 (m, 2 H), 3.07 – 2.82 (m, 2 H); **^{13}C NMR** (126 MHz, chloroform-*d*): 170.1, 169.8, 163.6 (d, *J* = 249.9 Hz), 134.8, 133.8, 129.4, 128.8, 126.8, 126.0, 132.2 (d, *J* = 3.5 Hz), 115.7 (d, *J* = 21.8 Hz), 50.0, 45.5, 45.1, 40.8, 29.7, 28.3; **^{19}F NMR** (470 MHz, chloroform-*d*): –110.2. The spectral characteristics are in agreement with spectral data previously reported.[9]

[8] L. Gao, H. Tang and Z. Wang, *Chem. Commun.*, 2014, **50**, 4085–4088.
[9] F. K. Leung, J. Cui, T. Hui, K. K. Kung and M. Wong, *Asian J. Org. Chem.*, 2015, **4**, 533–536.



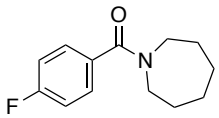
2d was prepared from the corresponding TIM (62 mg, 0.20 mmol, 1.0 equiv) by the general procedure, no purification by flash column chromatography was necessary. The product was isolated as a white solid (48 mg, 0.19 mmol, 94%).

^{1}H NMR (400 MHz, chloroform-*d*): 8.07 – 8.00 (m, 2 H), 7.94 – 7.86 (m, 2 H), 7.68 – 7.61 (m, 1 H), 7.56 – 7.49 (m, 2 H), 7.29 (s, 1 H), 7.18 – 7.11 (m, 2 H), 4.95 (d, *J* = 4.2 Hz, 2 H); **^{13}C NMR** (101 MHz, chloroform-*d*): 194.3, 166.5, 165.0 (d, *J* = 252.2 Hz), 134.5, 134.4, 130.1 (d, *J* = 3.2 Hz), 129.6 (d, *J* = 9.0 Hz), 129.1, 128.1, 115.8 (d, *J* = 21.9 Hz), 47.1; **^{19}F NMR** (376 MHz, chloroform-*d*): –107.7 (tt, *J* = 8.4, 5.3 Hz). The spectral characteristics are in agreement with spectral data previously reported.[10]



2e was prepared from the corresponding TIM (52 mg, 0.20 mmol, 1.0 equiv) by the general procedure, no purification by flash column chromatography was necessary. The product was isolated as a pale yellow oil (42 mg, 0.20 mmol, 99%).

^{1}H NMR (500 MHz, chloroform-*d*): 7.46 – 7.40 (m, 2 H), 7.14 – 7.08 (m 2 H), 3.95 – 3.30 (m, 8 H); **^{13}C NMR** (126 MHz, chloroform-*d*): 169.6, 163.6 (d, *J* = 250.2 Hz), 131.4 (d, *J* = 3.5 Hz), 129.5 (d, *J* = 8.5 Hz), 115.8 (d, *J* = 21.8 Hz), 66.9, 48.4, 42.9; **^{19}F NMR** (470 MHz, chloroform-*d*): –109.9 (m). The spectral characteristics are in agreement with spectral data previously reported.[11]

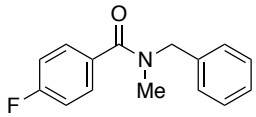


2f was prepared from the corresponding TIM (55 mg, 0.20 mmol, 1.0 equiv) by the general procedure, no purification by flash column

[10] A. Osuna Gálvez, C. P. Schaack, H. Noda and J. W. Bode, *J. Am. Chem. Soc.*, 2017, **139**, 1826–1829.
[11] J. Melomedov, A. Wünsche von Leupoldt, M. Meister, F. Laquai and K. Heinze, *Dalton Trans.*, 2013, **42**, 9727–9739.

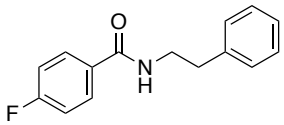
chromatography was necessary. The product was isolated as a pale yellow oil (42 mg, 0.19 mmol, 94%).

^{1}H NMR (500 MHz, chloroform-*d*): 7.43 – 7.36 (m, 2 H), 7.12 – 7.05 (m, 2 H), 3.72 – 3.64 (m, 2 H), 3.38 (t, *J* = 5.8 Hz, 2 H), 1.89 – 1.80 (m, 2 H), 1.69 – 1.56 (m, 6 H); **^{13}C NMR** (126 MHz, chloroform-*d*): 170.8, 163.1 (d, *J* = 248.7 Hz), 133.4 (d, *J* = 3.6 Hz), 128.8 (d, *J* = 8.3 Hz), 115.5 (d, *J* = 21.7 Hz), 49.9, 46.6, 29.6, 27.9, 27.3, 26.5; **^{19}F NMR** (470 MHz, chloroform-*d*): –111.4 (tt, *J* = 8.5, 5.3 Hz). The spectral characteristics are in agreement with spectral data previously reported.[12]



2g was prepared from the corresponding TIM (59 mg, 0.20 mmol, 1.0 equiv) by the general procedure and the crude product was purified by flash column chromatography using hexanes/EtOAc (5:1 to 4:1). The product was isolated as a colorless oil (45 mg, 0.18 mmol, 92%).

^{1}H NMR (500 MHz, chloroform-*d*): 7.49 – 7.44 (m, 2 H), 7.40 – 7.27 (m, 4 H), 7.22 – 7.00 (m, 3 H), 4.81 – 4.45 (m, 2 H), 3.11 – 2.79 (m, 3 H); **^{13}C NMR** (126 MHz, chloroform-*d*): 171.4, 170.7, 163.4 (d, *J* = 249.6 Hz), 137.0, 136.6, 132.2, 129.3 (d, *J* = 16.2 Hz), 128.8, 128.3, 127.7, 126.7, 115.6 (d, *J* = 21.7 Hz), 55.3, 51.0, 37.2, 33.5; **^{19}F NMR** (470 MHz, chloroform-*d*): –110.4 (d, *J* = 49.6 Hz). The spectral characteristics are in agreement with spectral data previously reported.[13]

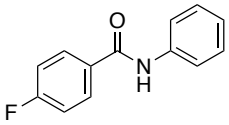


2h was prepared from the corresponding TIM (59 mg, 0.20 mmol, 1.0 equiv) by the general procedure, no purification by flash column chromatography was necessary. The product was isolated as a white solid (45 mg,

[12] V. Kubyshkin, Y. Kheylik and P. K. Mykhailiuk, *J. Fluorine Chem.*, 2015, **175**, 73–83.
[13] J. Wang, J. Li, F. Xu and Q. Shen, *Adv. Synth. Catal.*, 2009, **351**, 1363–1370.

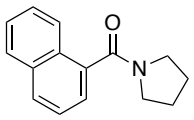
0.18 mmol, 92%).

^{1}H NMR (500 MHz, chloroform-*d*): 7.79 – 7.69 (m, 2 H), 7.37 – 7.32 (m, 2 H), 7.29 – 7.23 (m, 3 H), 7.12 – 7.04 (m, 2 H), 6.33 (br, 1 H), 3.72 (td, *J* = 7.0, 5.8 Hz, 2 H), 2.95 (t, *J* = 7.0 Hz, 2 H); **^{13}C NMR** (126 MHz, chloroform-*d*): 166.7, 164.7 (d, *J* = 251.8 Hz), 138.9, 130.9 (d, *J* = 3.1 Hz), 129.3 (d, *J* = 8.9 Hz), 128.9, 128.8, 126.7, 115.7 (d, *J* = 21.8 Hz), 41.3, 35.8; **^{19}F NMR** (470 MHz, chloroform-*d*): –108.4 (tt, *J* = 8.1, 5.4 Hz). The spectral characteristics are in agreement with spectral data previously reported.[14]



2i was prepared from the corresponding TIM (53 mg, 0.20 mmol, 1.0 equiv) by the general procedure and the crude product was purified by flash column chromatography using hexanes/EtOAc (2:1). The product was isolated as a white solid (35 mg, 0.16 mmol, 81%).

^{1}H NMR (400 MHz, chloroform-*d*): 7.94 – 7.84 (m, 2 H), 7.76 (s, 1 H), 7.66 – 7.59 (m, 2 H), 7.42 – 7.34 (m, 2 H), 7.22 – 7.11 (m, 3 H); **^{13}C NMR** (101 MHz, chloroform-*d*): 165.1 (d, *J* = 253.7 Hz), 164.8, 137.9, 131.3 (d, *J* = 3.1 Hz), 129.5 (d, *J* = 9.0 Hz), 129.3, 124.9, 120.4, 116.0 (d, *J* = 22.0 Hz); **^{19}F NMR** (376 MHz, chloroform-*d*): –107.4. The spectral characteristics are in agreement with spectral data previously reported.[15]

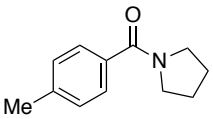


2j was prepared from the corresponding TIM (55 mg, 0.20 mmol, 1.0 equiv) by the general procedure with a slight modification. The reaction was stirred for 2 h to reach full conversion. No purification by flash column chromatography was necessary. The product was isolated as a pale yellow oil (43 mg,

[14] A. Osuna Gálvez, C. P. Schaack, H. Noda and J. W. Bode, *J. Am. Chem. Soc.*, 2017, **139**, 1826–1829.
[15] S. K. Jain, K. A. A. Kumar, S. B. Bharate and R. A. Vishwakarma, *Org. Biomol. Chem.*, 2014, **12**, 6465–6469.

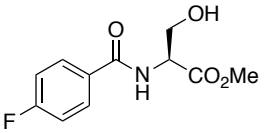
0.19 mmol, 96%).

^{1}H NMR (500 MHz, chloroform-*d*): 7.92 – 7.84 (m, 3 H), 7.54 – 7.43 (m, 4 H), 3.80 (t, *J* = 7.0 Hz, 2 H), 3.13 (t, *J* = 6.8 Hz, 2 H), 2.04 – 1.96 (m, 2 H), 1.87 – 1.78 (m, 2 H); **^{13}C NMR** (126 MHz, chloroform-*d*): 169.4, 136.0, 133.7, 129.3, 129.2, 128.5, 127.1, 126.5, 125.3, 125.0, 123.9, 48.7, 45.8, 26.2, 24.8. The spectral characteristics are in agreement with spectral data previously reported.[16]



2k was prepared from the corresponding TIM (48 mg, 0.20 mmol, 1.0 equiv) by the general procedure, no purification by flash column chromatography was necessary. The product was isolated as a colorless oil (38 mg, 0.20 mmol, 99%).

^{1}H NMR (500 MHz, chloroform-*d*): 7.44 – 7.38 (m, 2 H), 7.20 – 7.15 (m, 2 H), 3.62 (t, *J* = 7.0 Hz, 2 H), 3.42 (t, *J* = 6.6 Hz, 2 H), 2.35 (s, 3 H), 1.98 – 1.89 (m, 2 H), 1.88 – 1.80 (m, 2 H); **^{13}C NMR** (126 MHz, chloroform-*d*): 169.9, 140.0, 134.4, 128.9, 127.3, 49.7, 46.3, 26.5, 24.6, 21.5. The spectral characteristics are in agreement with spectral data previously reported.[13]

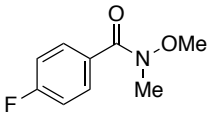


2l was prepared from the corresponding TIM (59 mg, 0.20 mmol, 1.0 equiv) by the general procedure and the crude product was purified by flash column chromatography using CH_2Cl_2/CH_3OH (20:1). The product was isolated as a white solid (44 mg, 0.18 mmol, 92%).

^{1}H NMR (400 MHz, chloroform-*d*): 7.88 – 7.76 (m, 2 H), 7.18 – 7.03 (m, 3 H), 4.83 (dt, *J* = 7.2, 3.6 Hz, 1 H), 4.10 – 3.98 (m, 2 H), 3.80 (s, 3 H), 2.78 (br, 1 H); **^{13}C NMR** (101 MHz, chloroform-*d*): 171.2, 166.8, 165.2 (d, *J* = 252.8 Hz), 129.8 (d, *J* = 3.1 Hz), 129.7 (d, *J* =

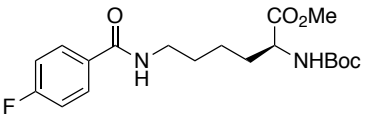
[16] D. Leow, *Org. Lett.*, 2014, **16**, 5812–5815.

9.0 Hz), 115.8 (d, *J* = 22.0 Hz), 63.5, 55.3, 53.0; **^{19}F NMR** (376 MHz, chloroform-*d*): –107.2. The spectral characteristics are in agreement with spectral data previously reported.[17]



2m was prepared from the corresponding TIM (47 mg, 0.20 mmol, 1.0 equiv) by the general procedure and the crude product was purified by flash column chromatography using CH_2Cl_2/CH_3OH (30:1). The product was isolated as a colorless oil (29 mg, 0.16 mmol, 78%).

^{1}H NMR (400 MHz, chloroform-*d*): 7.80 – 7.67 (m, 2 H), 7.14 – 7.03 (m, 2 H), 3.54 (s, 3 H), 3.36 (s, 3 H); **^{13}C NMR** (101 MHz, chloroform-*d*): 168.8, 164.2 (d, *J* = 251 Hz), 131.0 (d, *J* = 8.7 Hz), 130.1 (d, *J* = 3.3 Hz), 115.2 (d, *J* = 21.7 Hz), 61.2, 33.7; **^{19}F NMR** (376 MHz, chloroform-*d*): –109.0. The spectral characteristics are in agreement with spectral data previously reported.[18]

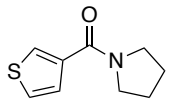


2n was prepared from the corresponding TIM (87 mg, 0.20 mmol, 1.0 equiv) by the general procedure, no purification by flash column chromatography was necessary. The product was isolated as a pale yellow oil (69 mg, 0.18 mmol, 90%).

^{1}H NMR (500 MHz, chloroform-*d*): 7.81 – 7.74 (m, 2 H), 7.09 – 7.00 (m, 2 H), 6.57 (br, 1 H), 5.19 (d, *J* = 7.9 Hz, 1 H), 4.24 (q, *J* = 7.6 Hz, 1 H), 3.69 (s, 3 H), 3.39 (q, *J* = 6.8 Hz, 2 H), 1.84 – 1.75 (m, 1 H), 1.68 – 1.56 (m, 3 H), 1.46 – 1.33 (m, 11 H); **^{13}C NMR** (126 MHz, chloroform-*d*): 173.3, 166.8, 164.7 (d, *J* = 251.5 Hz), 155.7, 130.9 (d, *J* = 3.1 Hz), 129.4 (d, *J* = 8.9 Hz), 115.5 (d, *J* = 21.8 Hz), 79.9, 53.2, 52.3, 39.7, 32.4, 29.0, 28.3, 22.7; **^{19}F**

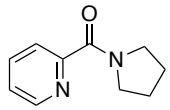
[17] A. Osuna Gálvez, C. P. Schaack, H. Noda and J. W. Bode, *J. Am. Chem. Soc.*, 2017, **139**, 1826–1829.
[18] C. W. Muir, A. R. Kennedy, J. M. Redmond and A. J. B. Watson, *Org. Biomol. Chem.*, 2013, **11**, 3337–3340.

NMR (470 MHz, chloroform-*d*): –108.6; **IR** (v/cm^{-1}, neat): 2935, 1697, 1642, 1501, 1227, 1160; **HRMS** (ESI pos.): calculated for $C_{19}H_{28}FN_2O_5$ [M + H]$^+$: 383.1977, found: 383.1978, **[α]$_D^{27}$** (c = 0.1, $CHCl_3$) = +0.42.



2o was prepared from the corresponding TIM (47 mg, 0.20 mmol, 1.0 equiv) by the general procedure, no purification by flash column chromatography was necessary. The product was isolated as a pale yellow oil (34 mg, 0.19 mmol, 95%).

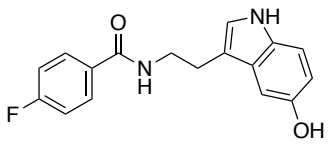
^{1}H NMR (500 MHz, chloroform-*d*): 7.63 (dd, *J* = 2.9, 1.3 Hz, 1 H), 7.34 (dd, *J* = 5.0, 1.3 Hz, 1 H), 7.27 (dd, *J* = 5.1, 2.9 Hz, 1 H), 3.65 – 3.53 (dt, *J* = 20.7, 6.4 Hz, 4 H), 1.94 – 1.86 (m, 4 H); **^{13}C NMR** (126 MHz, chloroform-*d*): 164.5, 138.0, 127.7, 127.4, 125.4, 49.3, 46.6, 26.6, 24.3. The spectral characteristics are in agreement with spectral data previously reported.[19]



2p was prepared from the corresponding TIM (46 mg, 0.20 mmol, 1.0 equiv) by the general procedure, no purification by flash column chromatography was necessary. The product was isolated as a pale yellow oil (31 mg, 0.18 mmol, 89%).

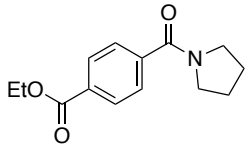
^{1}H NMR (400 MHz, chloroform-*d*): 8.80 – 8.74 (m, 1 H), 8.63 (dd, *J* = 4.9, 1.7 Hz, 1 H), 7.85 (dt, *J* = 7.8, 2.0 Hz, 1 H), 7.37 – 7.31 (m, 1 H), 3.64 (t, J = 6.9 Hz, 2 H), 3.44 (t, J = 6.5 Hz, 2 H), 2.00 – 1.87 (m, 4 H); **^{13}C NMR** (101 MHz, chloroform-*d*): 167.2, 150.8, 148.1, 135.2, 133.0, 123.4, 49.7, 46.5, 26.5, 24.5. The spectral characteristics are in agreement with spectral data previously reported.[20]

[19] D. Leow, *Org. Lett.*, 2014, **16**, 5812–5815.
[20] X. Wang, S. Yu, C. Wang, D. Xue and J. Xiao, *Org. Biomol. Chem.*, 2016, **14**, 7028–7037.



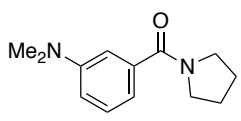
2q was prepared from the corresponding TIM (70 mg, 0.20 mmol, 1.0 equiv) by the general procedure, no purification by flash column chromatography was necessary. The product was isolated as a pale yellow oil (57 mg, 0.19 mmol, 95%).

^{1}H NMR (500 MHz, acetone-*d6*): 9.74 (br, 1 H), 7.98 – 7.93 (m, 2 H), 7.86 (br, 1 H), 7.68 (s, 1 H), 7.22 – 7.16 (m, 3 H), 7.11 (d, *J* = 2.4 Hz, 1 H), 7.04 (d, *J* = 2.4 Hz, 1 H), 6.71 (dd, *J* = 8.6, 2.4 Hz, 1 H), 3.70 – 3.64 (m, 2 H), 3.01 – 2.95 (m, 2 H); **^{13}C NMR** (126 MHz, acetone-*d6*): 166.3, 165.2 (d, *J* = 248.5 Hz), 151.6, 132.6 (d, *J* = 3.1 Hz), 132.,5, 130.5 (d, *J* = 8.9 Hz), 129.4, 124.0, 115.9 (d, *J* = 21.9 Hz), 112.6, 112.5, 112.3, 103.5, 41.3, 26.4; **^{19}F NMR** (470 MHz, acetone-*d6*): –111.4 (tt, *J* = 8.7, 5.4 Hz); **IR** (v/cm^{-1}, neat): 3310, 2929, 2853, 1703, 1634, 1498, 1225, 1185, 1158, 849; **HRMS** (ESI pos.): calculated for $C_{17}H_{15}FN_2NaNO_2$ $[M + Na]^+$: 321.1010, found: 321.1008.



2r was prepared from the corresponding TIM (60 mg, 0.20 mmol, 1.0 equiv) by the general procedure, no purification by flash column chromatography was necessary. The product was isolated as a colorless oil (48 mg, 0.20 mmol, 98%).

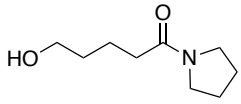
^{1}H NMR (500 MHz, chloroform-*d*): 8.10 – 7.99 (m, 2 H), 7.60 –7.48 (m, 2 H), 4.36 (q, *J* = 7.1 Hz, 2 H), 3.62 (t, *J* = 7.0 Hz, 2 H), 3.35 (t, *J* = 6.7 Hz, 2 H), 1.97 – 1.90 (m, 2 H), 1.89 – 1.82 (m, 2 H), 1.37 (t, *J* = 7.1 Hz, 3 H),; **^{13}C NMR** (126 MHz, chloroform-*d*): 168.0, 166.0, 141.4, 131.6, 129.6, 127.1, 61.3, 49.5, 46.3, 26.4, 24.5, 14.4; **IR** (v/cm^{-1}, neat): 2975, 2877, 1713, 1624, 1420, 1269, 1099, 1019, 729; **HRMS** (ESI pos.): calculated for $C_{14}H_{17}NNaO_3$ $[M + Na]^+$: 270.1101, found: 270.1095.



2s was prepared from the corresponding TIM (54 mg, 0.20 mmol, 1.0 equiv) by the general procedure and the crude product was

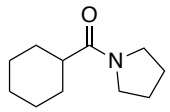
purified by flash column chromatography using hexanes/EtOAc (1:1 to 1:2). The product was isolated as a pale yellow oil (39 mg, 0.18 mmol, 90%).

^{1}H NMR (500 MHz, chloroform-*d*): 7.24 – 7.17 (m, 1 H), 6.86 – 6.70 (m, 3 H), 3.62 (t, *J* = 7.0 Hz, 2 H), 3.41 (t, *J* = 6.7 Hz, 2 H), 2.94 (s, 6 H), 1.96 – 1.89 (m, 2 H), 1.87 – 1.79 (m, 2 H); **^{13}C NMR** (126 MHz, chloroform-*d*): 170.6, 150.5, 138.2, 128.9, 114.9, 113.7, 111.1, 49.7, 46.1, 40.6, 26.4, 24.6; **IR** (v/cm^{-1}, neat): 2951, 2874, 2804, 1620, 1596, 1572, 1434, 1403, 999, 746; **HRMS** (ESI pos.): calculated for $C_{13}H_{18}N_2NaO$ [M + Na]$^+$: 241.1311, found: 241.1315.



2t was prepared from the corresponding TIM (45 mg, 0.20 mmol, 1.0 equiv) by the general procedure, no purification by flash column chromatography was necessary. The product was isolated as a yellow oil (24 mg, 0.14 mmol, 70%).

^{1}H NMR (500 MHz, chloroform-*d*): 3.62 (t, *J* = 6.2 Hz, 2 H), 3.46 (t, *J* = 6.9 Hz, 2 H), 3.40 (t, *J* = 6.8 Hz, 2 H), 2.30 (t, *J* = 7.0 Hz, 2 H), 1.99 – 1.91 (m, 2 H), 1.90 – 1.80 (m, 2 H), 1.81 – 1.72 (m, 2 H), 1.64 – 1.57 (m, 2 H); **^{13}C NMR** (126 MHz, chloroform-*d*): 172.0, 62.0, 46.8, 45.9, 34.2, 32.5, 26.2, 24.5, 20.5. The spectral characteristics are in agreement with spectral data previously reported.[21]

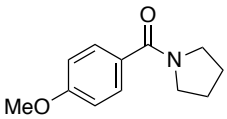


2u was prepared from the corresponding TIM (47 mg, 0.20 mmol, 1.0 equiv) by the general procedure, no purification by flash column chromatography was necessary. The product was isolated as a white solid (34 mg, 0.19 mmol, 93%).

m.p.: 61 °C; **^{1}H NMR** (500 MHz, chloroform-*d*): 3.42 (dt, *J* = 10.1, 6.9 Hz, 4 Hz), 2.30 (tt,

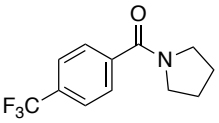
[21] C. Madelaine, V. Valerio and N. Maulide, *Angew. Chem. Int. Ed.*, 2010, **49**, 1583–1586.

J = 11.7, 3.5 Hz, 1 H), 1.95 – 1.86 (m, 2 H), 1.84 – 1.58 (m, 7 H), 1.49 (qd, *J* = 12.5, 3.6 Hz, 2 H), 1.27 – 1.15 (m, 3 H); **^{13}C NMR** (126 MHz, chloroform-*d*): 174.9, 46.4, 45.7, 43.0, 29.0, 26.3, 26.0, 25.9, 24.4; **IR** (v/cm^{-1}, neat): 2972, 2926, 2871, 2850, 1620, 1434, 1362; **HRMS** (ESI pos.): calculated for $C_{11}H_{19}NNaO$ [M + Na]$^{+}$: 204.1359, found: 204.1361.



2v was prepared from the corresponding TIM (51 mg, 0.20 mmol, 1.0 equiv) by the general procedure, no purification by flash column chromatography was necessary. The product was isolated as a colorless oil (36 mg, 0.17 mmol, 87%).

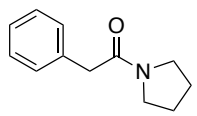
^{1}H NMR (500 MHz, chloroform-*d*): 7.53 – 7.45 (m, 2 H), 6.90 – 6.82 (m, 2 H), 3.79 (s, 3 H), 3.64 – 3.57 (m, 2 H), 3.49 – 3.40 (m, 2 H), 1.95 – 1.87 (m, 2 H), 1.87 – 1.78 (m, 2 H); **^{13}C NMR** (126 MHz, chloroform-*d*): 169.5, 160.8, 129.5, 129.2, 113.4, 55.4, 49.8, 46.4, 26.6, 24.5. The spectral characteristics are in agreement with spectral data previously reported.[22]



2w was prepared from the corresponding TIM (59 mg, 0.20 mmol, 1.0 equiv) by the general, no purification by flash column chromatography was necessary. The product was isolated as a yellow oil (46 mg, 0.19 mmol, 95%).

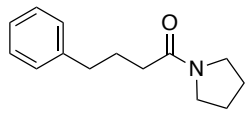
^{1}H NMR (500 MHz, chloroform-*d*): 7.72 – 7.54 (m, 4 H), 3.64 (t, *J* = 7.0 Hz, 2 H), 3.37 (t, *J* = 6.7 Hz, 2 H), 2.00 – 1.84 (m, 4 H); **^{13}C NMR** (126 MHz, chloroform-*d*): 168.4, 140.7 (br), 131.7 (q, *J* = 32.6 Hz), 127.6, 125.5 (q, *J* = 3.8 Hz), 123.9 (q, *J* = 272.4 Hz), 49.6, 46.4, 26.5, 24.5; **^{19}F NMR** (470 MHz, chloroform-*d*): –62.9. The spectral characteristics are in agreement with spectral data previously reported.[19]

[22] D. Leow, *Org. Lett.*, 2014, **16**, 5812–5815.



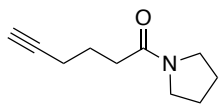
2x was prepared from the corresponding TIM (48 mg, 0.20 mmol, 1.0 equiv) by the general procedure, no purification by flash column chromatography was necessary. The product was isolated as a colorless oil (36 mg, 0.19 mmol, 96%).

^{1}H NMR (500 MHz, chloroform-*d*): 7.37– 7.30 (m, 1 H), 7.30– 7.23 (m, 3 H), 7.23– 7.17 (m, 1 H), 3.66 (s, 2 H), 3.50 (t, *J* = 6.9 Hz, 2 H), 3.41 (t, *J* = 6.8 Hz, 2 H), 1.92 – 1.85 (m, 2 H), 1.85 – 1.77 (m, 2 H); **^{13}C NMR** (126 MHz, chloroform-*d*): 169.9, 134.9, 129.0, 128.7, 126.8, 47.0, 46.1, 42.3, 26.2, 24.4. The spectral characteristics are in agreement with spectral data previously reported.[23]



2y was prepared from the corresponding TIM (54 mg, 0.20 mmol, 1.0 equiv) by the general procedure and the crude product was purified by flash column chromatography using hexanes/EtOAc (1:1). The product was isolated as a colorless oil (39 mg, 0.18 mmol, 89%).

^{1}H NMR (500 MHz, chloroform-*d*): 7.30 – 7.23 (m, 2 H), 7.22 – 7.13 (m, 3 H), 3.44 (t, *J* = 6.9 Hz, 2 H), 3.31 (t, *J* = 6.8 Hz, 2 H), 2.68 (t, *J* = 7.6 Hz, 2 H), 2.25 (t, *J* = 7.5 Hz, 2 H), 2.03 – 1.95 (m, 2 H), 1.94 – 1.87 (m, 2 H), 1.85 – 1.78 (m, 2 H); **^{13}C NMR** (126 MHz, chloroform-*d*): 171.4, 141.9, 128.6, 128.4, 125.9, 46.6, 45.6, 35.4, 33.9, 26.3, 26.2, 24.5. The spectral characteristics are in agreement with spectral data previously reported.[24]

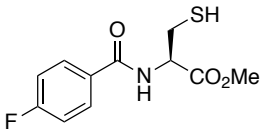


2z was prepared from the corresponding TIM (43 mg, 0.20 mmol, 1.0 equiv) by the general procedure and the crude product was purified by flash column chromatography using hexanes/EtOAc (2:1 to 1:1). The product was

[23] D. G. Pintori and M. F. Greaney, *Org. Lett.*, 2011, **13**, 5713–5715.
[24] B. Peng, D. Geerdink, C Farès and N. Maulide, *Angew. Chem. Int. Ed.*, 2014, **53**, 5462–5466.

isolated as a colorless oil (31 mg, 0.19 mmol, 93%).

^{1}H NMR (500 MHz, chloroform-*d*): 3.44 (dt, *J* = 13.6, 6.9 Hz, 4 H), 2.40 (t, *J* = 7.3 Hz, 2 H), 2.29 (td, *J* = 6.8, 2.6 Hz, 2 H), 1.98 – 1.91 (m, 3 H), 1.91 – 1.81 (m, 4 H); **^{13}C NMR** (126 MHz, chloroform-*d*): 170.9, 84.2, 68.9, 46.7, 45.7, 33.2, 26.2, 24.6, 23.7, 18.1. The spectral characteristics are in agreement with spectral data previously reported.[25]



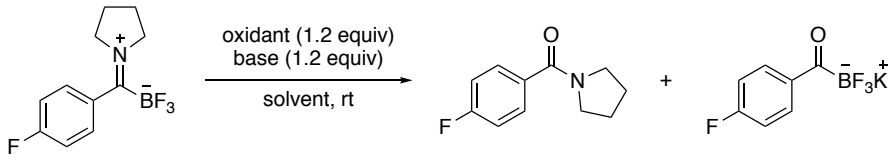
2aa was prepared from the corresponding TIM (62 mg, 0.20 mmol, 1.0 equiv) by the general procedure with a slight modification. 2 equiv of H_2O_2 and 2 equiv of ^{i}PrNEt$_2$ were used. Since the disulfide was formed, TCEP•HCl (171 mg, 0.60 mmol, 3.0 equiv) was added after 30 min of stirring, the reaction was stirred for 2 min longer before the work-up. The crude product was purified by flash column chromatography using CH_2Cl_2/CH_3OH (30:1) and the product was isolated as a white solid (46 mg, 0.18 mmol, 89%).

m.p.: 133 °C; **^{1}H NMR** (400 MHz, chloroform-*d*): 7.89 – 7.82 (m, 2 H), 7.17 – 7.10 (m, 2 H), 7.00 (br, 1 H), 5.10 – 5.03 (m, 1 H), 3.84 (s, 3 H), 3.14 (dd, *J* = 9.0, 4.0 Hz, 2 H), 1.39 (t, *J* = 9.0 Hz, 1 H); **^{13}C NMR** (101 MHz, chloroform-*d*): 170.8, 166.0, 165.2 (d, *J* = 252.7 Hz), 129.7 (d, *J* = 9.0 Hz), 115.9 (d, *J* = 21.9 Hz), 54.1, 53.1, 27.1; **^{19}F NMR** (376 MHz, chloroform-*d*): –107.2; **IR** (v/cm^{-1}, neat): 3308, 1743, 1645, 1604, 1540, 1502, 1230, 1160; **HRMS** (ESI pos.): calculated for $C_{11}H_{12}FNNaO_3S$ [M + Na]$^+$: 280.0414, found: 383.0420; **$[\alpha]_D^{27}$** (c = 0.1, $CHCl_3$) = + 27.4.

[25] A. de la Torre, D. Kaiser and N. Maulide, *J. Am. Chem. Soc.*, 2017, **139**, 6578–6581.

4.3. Condition optimization and mechanistic experiments

Condition optimization:



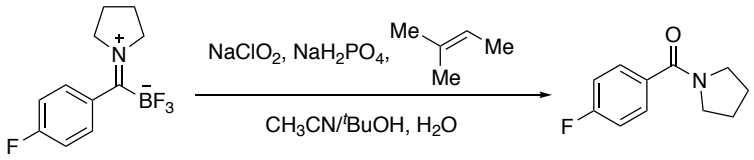
1a **2a** **3**

1a was subjected to the conditions shown in the table below. The ratio between the compounds **1a**, **2a**, and **3** was determined using LC-MS analysis of the reaction mixture.

Entry	Oxidant	Base	Solvent	Time	Results[a]
1	H_2O_2 (aq, 30%)	K_2HPO_4	CH_3CN / H_2O (1:1, 0.2 M)	2 h	**2a**, 100%
2	H_2O_2 (aq, 30%)	K_2CO_3	CH_3CN / H_2O (1:1, 0.2 M)	30 min	**2a**, 100%
3	H_2O_2 (aq, 30%)	–	CH_3CN / *k*-phos (pH 7.4, 0.1 M)[b] (1:1, 0.2 M)	24 h	**1a**, 50%; **2a**, 50%
4	H_2O_2 (aq, 30%)	$^iPr_2NEt$	CH_3CN / H_2O (1:1, 0.2 M)	30 min	**2a**, 100%
5	H_2O_2 (aq, 30%)	$^iPr_2NEt$	CH_3CN / H_2O (1:1, 0.01 M)	30 min	**2a**, 100%
6	H_2O_2 (aq, 30%)	–	CH_3CN / H_2O (1:1, 0.2 M)	24 h	**1a**, 70%; **2a**, 30%
7	H_2O_2 (aq, 30%)	–	CH_3CN / *k*-ac (pH 3.8, 0.1 M)[c] (1:1, 0.2 M)	24 h	**1a**, 95%; **2a**, 5%
8	–	$^iPr_2NEt$	CH_3CN / H_2O (1:1, 0.2 M)	24 h	**3**, 100%
9	H_2O_2 (aq, 30%)	$^iPr_2NEt$	THF / H_2O (1:1, 0.2 M)	30 min	**2a**, 100%
10	H_2O_2 (aq, 30%)	$^iPr_2NEt$	CH_3CN (0.2 M)	30 min	**2a**, 100%
11	H_2O_2–urea	$^iPr_2NEt$	DMF (0.2 M)	30 min	**2a**, 100%
12	H_2O_2–urea	$^iPr_2NEt$	CH_3CN / H_2O (1:1, 0.2 M)	30 min	**2a**, 100%
13	mCPBA	$^iPr_2NEt$	CH_3CN / H_2O (1:1, 0.2 M)	30 min	**2a**, 100%
14	*t*BuOOH	$^iPr_2NEt$	CH_3CN / H_2O (1:1, 0.2 M)	30 min	**2a**, 100%

Table 1: Evaluation of different oxidation conditions to form the amide from the trifluoroborate iminium (TIM).
a Analyses performed using LC-MS. Conversions were determined integrating peaks in the 220 nm UV trace;
b *k*-phos: aqueous buffer prepared with KH_2PO_4 and K_2HPO_4; *k*-ac: aqueous buffer prepared with KOAc and HOAc.

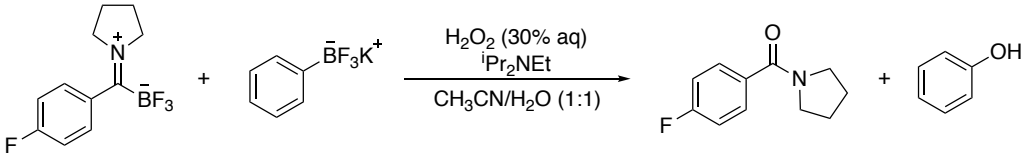
Pinnick reaction:



1a **2a**

1a (10 mg, 0.041 mmol, 1.0 equiv) was dissolved in $CH_3CN/^tBuOH$ (1:1, 0.27 mL, 0.15 M) and cooled to 0 °C. H_2O (0.13 mL), 2-methylbut-2-ene (27 μL), NaH_2PO_4 (45 mg, 0.29 mmol, 7.0 equiv), and $NaClO_2$ (37 mg, 0.41 mmol, 10 equiv) were added and the reaction mixture was stirred for 3 h. After 3 h, clean and full conversion to **2a** was observed by LC-MS and NMR.

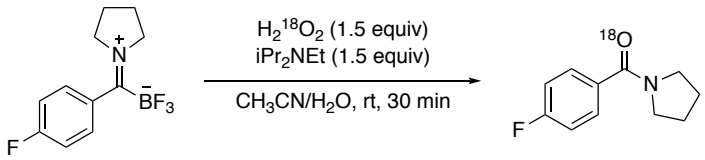
Competition experiment:



1a **S13** **2a** **S14**

1a (12 mg, 0.050 mmol, 1.0 equiv) and **S13** (9.2 mg, 0.050 mmol, 1.0 equiv) were dissolved in CH_3CN/H_2O (0.5 mL, 0.1 M). H_2O_2 (30% aq, 5.7 μL, 0.045 mmol, 0.9 equiv) and *N,N*-diisopropylethylamine (8.7 μL, 0.045 mmol, 0.9 equiv) were added and the mixture was stirred for 3 h. After 3 h, analysis was performed using LC-MS and NMR. **1a**, **2a**, and **S13** were detected, **S14** was not detected. The different molecules were detected with the ratio: **1a** / **S13** / **2a** 0.1 : 1.0 : 0.9.

Isotope labelling with ^{18}O-labelled hydrogen peroxide experiment:



1a **2a**

1a (4.1 mg, 17 μmol, 1.0 equiv) was dissolved in CH_3CN/H_2O (1:1, 33 μL, 0.50 M). $H_2{}^{18}O_2$ (2.2% aq, ≥90% ^{18}O-enriched, 43 mg, 25 μmol, 1.5 equiv) and *N,N*-diisopropylethylamine (5.0 μL, 25 μmol, 1.5 equiv) were added and the mixture was stirred for 30 min. The reaction was diluted with H_2O and EtOAc and the aqueous layer was extracted three times with EtOAc (3 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered and

concentrated under reduced pressure. Analysis by HR-MS showed labelling with ^{18}O for ≥ 95% **2a**.

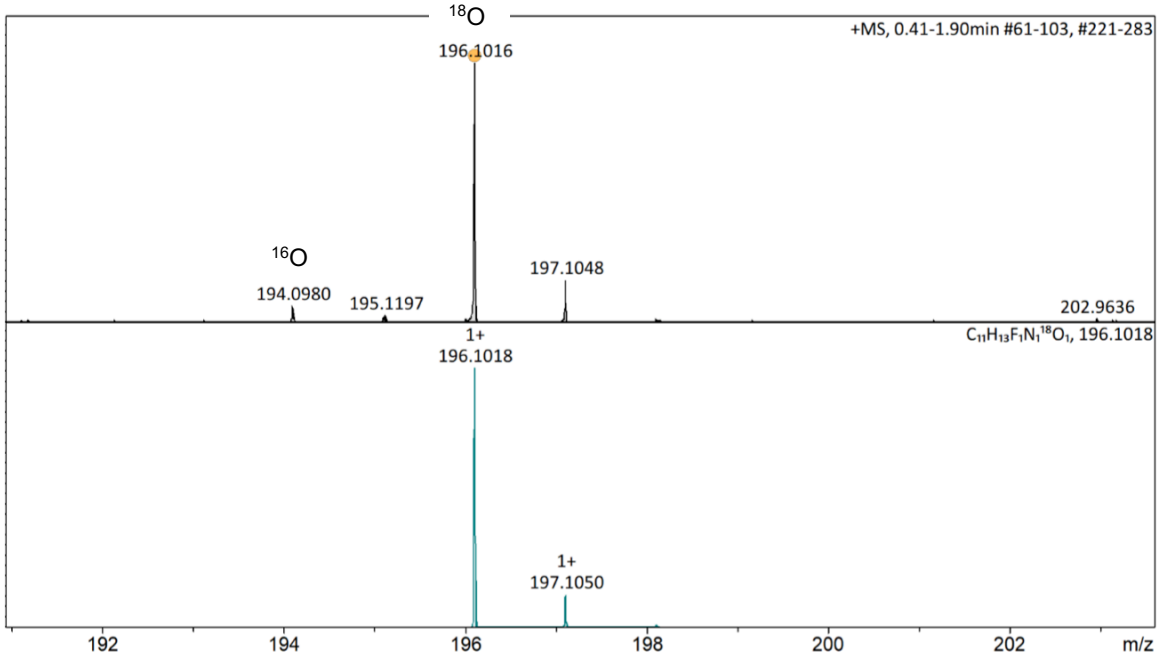
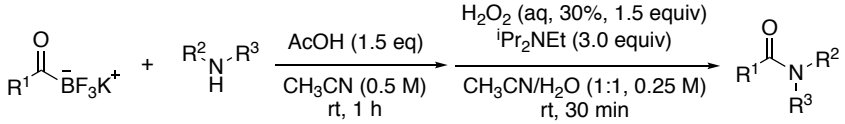


Figure 1. ESI-HR-MS for ^{18}O-labelling experiment. Top: measured spectrum; bottom: calculated spectrum for ^{18}O-labelled product.

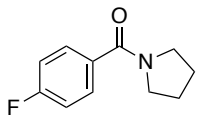
5. One-pot synthesis of amides from KATs

5.1. General procedure

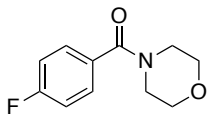


The potassium acyltrifluoroborate (KAT, 0.2 mmol, 1.0 equiv) was dissolved in CH_3CN (0.4 mL, 0.5 M), AcOH (17 μL, 0.3 mmol, 1.5 equiv) and the amine (0.3 mmol, 1.5 equiv) were added and the reaction was stirred for 1 hour. H_2O (0.4 mL, 0.5 M), H_2O_2 (30% aq, 34 μl, 0.3 mmol, 1.5 equiv), and *N,N*-diisopropylethylamine (105 μL, 0.6 mmol, 3.0 equiv) were added and the reaction was stirred for additional 30 min. The reaction mixture was diluted with H_2O (10 mL) and EtOAc (10 mL) and the aqueous layer was extracted three times with EtOAc (3 x 10 mL). The combined organic layers were washed with brine (30 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. If necessary, the crude product was purified by flash column chromatography.

5.2. Synthesis of amides

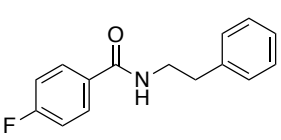


2a was prepared from potassium 4-fluorobenzoyltrifluoroborate (46 mg, 0.20 mmol, 1.0 equiv) and pyrrolidine (25 μL, 0.30 mmol, 1.5 equiv) by the general procedure and the crude product was purified by flash column chromatography using hexanes/EtOAc (2:1 to 1:1). The product was isolated as a colorless oil (37 mg, 0.19 mmol, 95%). The characterization data were identical with the ones obtained for the oxidation from the TIM and are not duplicated here.

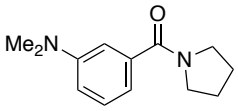


2e was prepared from potassium 4-fluorobenzoyltrifluoroborate (46 mg, 0.20 mmol, 1.0 equiv) and morpholine (26 μL, 0.30 mmol, 1.5 equiv) by the general procedure and the crude product was purified by flash column

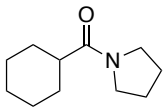
chromatography using hexanes/EtOAc (2:1 to 1:1). The product was isolated as a colorless oil (39 mg, 0.19 mmol, 93%). The characterization data were identical with the ones obtained for the oxidation from the TIM and are not duplicated here.



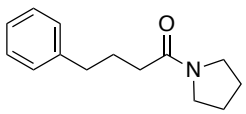
2h was prepared from potassium 4-fluorobenzoyltrifluoroborate (46 mg, 0.20 mmol, 1.0 equiv) and 2-phenylethylamine (38 μL, 0.30 mmol, 1.5 equiv) by the general procedure. Purification by flash column chromatography was not necessary and the product was isolated as a colorless oil (43 mg, 0.18 mmol, 88%). The characterization data were identical with the ones obtained for the oxidation from the TIM and are not duplicated here.



2s was prepared from potassium 3-(dimethylamino)-benzoyltrifluoroborate (51 mg, 0.20 mmol, 1.0 equiv) and pyrrolidine (25 μL, 0.30 mmol, 1.5 equiv) by the general procedure. Purification by flash column chromatography was not necessary and the product was isolated as a colorless oil (39 mg, 0.18 mmol, 89%). The characterization data were identical with the ones obtained for the oxidation from the TIM and are not duplicated here.



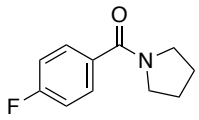
2u was prepared from potassium 3-cyclohexoyltrifluoroborate (44 mg, 0.20 mmol, 1.0 equiv) and pyrrolidine (25 μL, 0.30 mmol, 1.5 equiv) by the general procedure and the crude product was purified by flash column chromatography using hexanes/EtOAc (2:1 to 1:1). The product was isolated as a colorless oil (33 mg, 0.18 mmol, 91%). The characterization data were identical with the ones obtained for the oxidation from the TIM and are not duplicated here.



2y was prepared from potassium 3-phenylpropanoyltrifluoroborate (51 mg, 0.20 mmol, 1.0 equiv) and pyrrolidine (25 μL, 0.30 mmol,

1.5 equiv) by the general procedure and the crude product was purified by flash column chromatography using hexanes/EtOAc (3:1 to 1:1). The product was isolated as a colorless oil (37 mg, 0.17 mmol, 87%). The characterization data were identical with the ones obtained for the oxidation from the TIM and are not duplicated here.

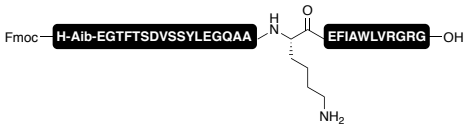
5.3. Large-scale synthesis of amide 2a



2a was prepared from potassium 4-fluorobenzoyltrifluoroborate (690 mg, 3.00 mmol, 1.00 equiv) and pyrrolidine (376 μL, 4.50 mmol, 1.50 equiv) by the general procedure. Purification by flash column chromatography was not necessary and the product was isolated as a colorless oil (539 mg, 2.79 mmol, 93%). The characterization data were identical with the ones obtained for the oxidation from the TIM and are not duplicated here.

6. Modification of peptides with KATs

6.1. Preparation of the peptides



The peptide **6** was prepared on HMPB ChemMatrix® resin with a loading capacity of 0.44 mmol/g. Fmoc-Gly-OH (2.62 g, 8.80 mmol, 10 equiv) was suspended in CH_2Cl_2 and cooled to 0 °C. *N,N'*-diisopropylcarbodiimide (0.68 mL, 4.4 mmol, 5.0 equiv) was added and it was stirred at 0 °C for 20 min. The solvent was removed under reduced pressure, the residue was resuspended in DMF and 4-dimethylaminopyridine (11 mg, 0.088 mmol, 0.10 equiv) was added. The resin was treated with this solution for 60 min. The resin was treated with 20% piperidine in DMF (2 x 10 min). Fmoc-Arg(Pbf)-OH (0.34 g, 0.56 mmol, 1.0 equiv) and HATU (0.21 g, 0.54 mmol, 0.90 equiv) were dissolved in DMF, *N,N*-diisopropylethylamine (0.19 mL, 1.1 mmol, 2.0 equiv) was added, and the solution was vortexed for 3 min. The resin was treated with this solution for 90 min. The resin loading was determined to be 0.25 mmol/g. The resin was treated with 20% Ac_2O in DMF (2 x 15 min). The synthesis was performed on 0.5 mmol scale (2 g of resin) using automated Fmoc SPPS up to Glu_{29} using the procedure described in the general methods. The resin was treated with 20% piperidine in DMF (2 x 10 min). Fmoc-Aib-OH (0.81 g, 2.5 mmol, 5.0 equiv) and HATU (0.93 g, 2.4 mmol, 4.9 equiv) were dissolved in DMF, *N,N*-diisopropylethylamine (0.87 mL, 5.0 mmol, 10 equiv) was added, and the solution was vortexed for 3 min. The resin was treated with this solution for 60 min. The resin was treated with 20% Ac_2O in DMF (2 x 15 min). The resin was treated with 20% piperidine in DMF (2 x 10 min). Fmoc-His(1-Trt)-OH (1.5 g, 2.5 mmol, 5.0 equiv) and HATU (0.93 g, 2.5 mmol, 4.9 equiv) were dissolved in DMF, *N,N*-diisopropylethylamine (0.87 mL, 5.0 mmol, 10 equiv) was added, and the solution was vortexed for 3 minutes. The resin was treated with this solution for 60 min. The resin was treated with 20% Ac_2O in DMF (2

x 15 min). The resin-supported peptide was treated with TFA/H_2O/TIPS (95:2.5:2.5) for 2 h, filtered to remove the solid support, and the volatiles were removed under reduced pressure. The residue was triturated with Et_2O, centrifuged, and decanted (three repeated cycles) to obtain the crude peptide. The crude peptide was purified by preparative HPLC using a Shiseido Capcell pak C18 UG80 column (5 µm, 50 mm I.D. x 250 mm) at 60 °C with a gradient of 15% to 85% CH_3CN in H_2O (with 0.1% TFA) in 25 min affording peptide **6** as a white solid (0.67 g, 0.19 mmol, 37%) after lyophilization.

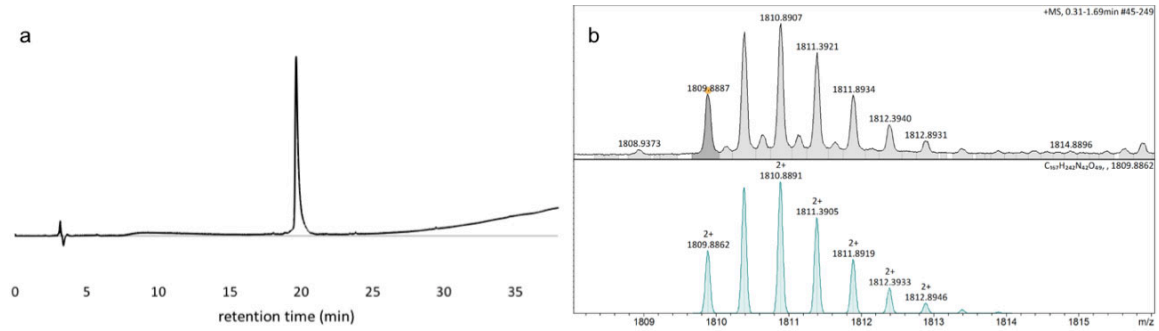
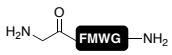


Figure 2. HPLC trace and HR-MS for peptide **6**: a) HPLC trace (220 nm, gradient: 20-95% CH_3CN in H_2O in 30 min) of the purified peptide; b) ESI HR-MS measured (top) and calculated (bottom).



The peptide **9** was prepared on MBHA Rink amide resin with a loading capacity of 0.56 mmol/g. The resin was treated with 20% piperidine in DMF (2 x 10 min). Fmoc-Gly-OH (0.13 g, 0.43 mmol, 1.0 equiv) and HATU (0.16 g, 0.41 mmol, 0.95 equiv) were dissolved in DMF, *N,N*-diisopropylethylamine (0.15 mL, 0.86 mmol, 2.0 equiv) was added, and the solution was vortexed for 3 min. The resin was treated with this solution for 90 min. The resin was treated with 20% Ac_2O in DMF (2 x 15 min). The resin loading was determined to be 0.39 mmol/g. The synthesis was performed on 0.39 mmol scale (1.0 g of resin). The resin was treated with 20% piperidine in DMF (2 x 10 min). Fmoc-Trp(Boc)-OH (0.57 g, 1.5 mmol, 4.0 equiv) and HATU (0.57 g, 1.5 mmol, 3.9 equiv) were dissolved in DMF, *N,N*-diisopropylethylamine (0.54 mL, 3.1 mmol, 8.0 equiv) was added, and the solution was vortexed for 3 min. The resin was treated with this solution for 2 x 45 min. The resin was treated with 20% Ac_2O in DMF (2 x 15 min). The resin was treated with

20% piperidine in DMF (2 x 10 min). Fmoc-Met-OH (0.58 g, 1.5 mmol, 4.0 equiv) and HATU (0.57 g, 1.5 mmol, 3.9 equiv) were dissolved in DMF, *N,N*-diisopropylethylamine (0.54 mL, 3.1 mmol, 8.0 equiv) was added, and the solution was vortexed for 3 min. The resin was treated with this solution for 2 x 45 min. The resin was treated with 20% Ac_2O in DMF (2 x 15 min). The resin was treated with 20% piperidine in DMF (2 x 10 min). Fmoc-Phe-OH (0.60 g, 1.5 mmol, 4.0 equiv) and HATU (0.57 g, 1.5 mmol, 3.9 equiv) were dissolved in DMF, *N,N*-diisopropylethylamine (0.54 mL, 3.1 mmol, 8.0 equiv) was added, and the solution was vortexed for 3 min. The resin was treated with this solution for 2 x 45 min. The resin was treated with 20% Ac_2O in DMF (2 x 15 min). The resin was treated with 20% piperidine in DMF (2 x 10 min). Fmoc-Gly-OH (0.46 g, 1.5 mmol, 4.0 equiv) and HATU (0.57 g, 1.5 mmol, 3.9 equiv) were dissolved in DMF, *N,N*-diisopropylethylamine (0.54 mL, 3.1 mmol, 8.0 equiv) was added, and the solution was vortexed for 3 min. The resin was treated with this solution for 2 x 45 min. The resin was treated with 20% Ac_2O in DMF (2 x 15 min). The resin was treated with 20% piperidine in DMF (2 x 10 min). The resin-supported peptide was treated with TFA/H_2O/TIPS (95:2.5:2.5) for 2 h, filtered to remove the solid support, and the volatiles were removed under reduced pressure. The residue was triturated with Et_2O, centrifuged, and decanted (three repeated cycles) to obtain the crude peptide. The crude peptide was purified by preparative HPLC using a Shiseido Capcell pak C18 UG80 column (5 μm, 50 mm I.D. x 250 mm) at 60 °C with a gradient of 20% to 85% CH_3CN in H_2O (with 0.1% TFA) in 25 min affording peptide **9** as a white solid (0.19 g, 0.31 mmol, 81%) after lyophilization.

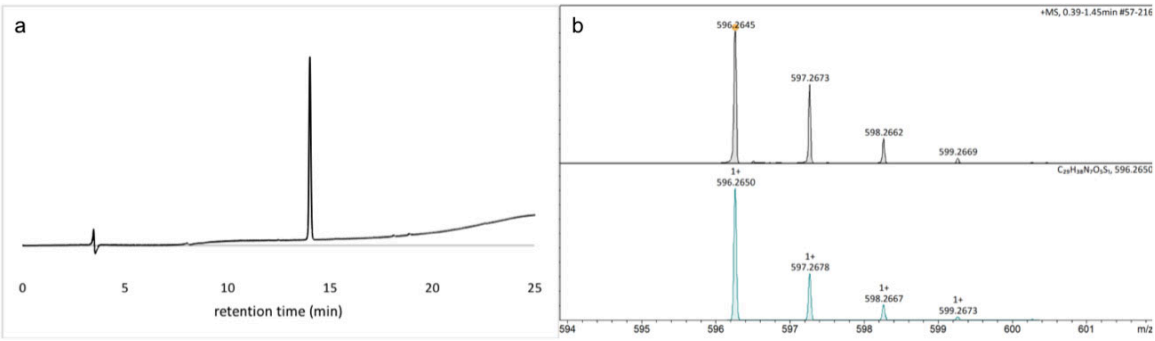
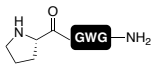


Figure 3. HPLC trace and HR-MS for peptide **9**: a) HPLC trace (220 nm, gradient: 20-95% CH_3CN in H_2O in 30 min) of the purified peptide; b) ESI HR-MS measured (top) and calculated (bottom).



The peptide **11** was prepared on MBHA Rink amide resin with a loading capacity of 0.56 mmol/g. The resin was treated with 20% piperidine in DMF (2 x 10 min). Fmoc-Gly-OH (0.13 g, 0.43 mmol, 1.0 equiv) and HATU (0.16 g, 0.41 mmol, 0.95 equiv) were dissolved in DMF, *N,N*-diisopropylethylamine (0.15 mL, 0.86 mmol, 2.0 equiv) was added, and the solution was vortexed for 3 min. The resin was treated with this solution for 90 min. The resin was treated with 20% Ac_2O in DMF (2 x 15 min). The resin loading was determined to be 0.43 mmol/g. The synthesis was performed on 0.43 mmol scale (1.0 g of resin). The resin was treated with 20% piperidine in DMF (2 x 10 min). Fmoc-Trp(Boc)-OH (0.91 g, 1.7 mmol, 4.0 equiv) and HATU (0.64 g, 1.7 mmol, 3.9 equiv) were dissolved in DMF, *N,N*-diisopropylethylamine (0.60 mL, 3.5 mmol, 8.0 equiv) was added, and the solution was vortexed for 3 min. The resin was treated with this solution for 2 x 45 min. The resin was treated with 20% Ac_2O in DMF (2 x 15 min). The resin was treated with 20% piperidine in DMF (2 x 10 min). Fmoc-Gly-OH (0.51 g, 1.5 mmol, 4.0 equiv) and HATU (0.64 g, 1.7 mmol, 3.9 equiv) were dissolved in DMF, *N,N*-diisopropylethylamine (0.60 mL, 3.5 mmol, 8.0 equiv) was added, and the solution was vortexed for 3 min. The resin was treated with this solution for 2 x 45 min. The resin was treated with 20% Ac_2O in DMF (2 x 15 min). The resin was treated with 20% piperidine in DMF (2 x 10 min). Fmoc-Pro-OH (0.60 g, 1.5 mmol, 4.0 equiv) and HATU (0.64 g, 1.7 mmol, 3.9 equiv) were dissolved in DMF, *N,N*-diisopropylethylamine (0.60 mL, 3.5 mmol, 8.0 equiv) was added,

and the solution was vortexed for 3 min. The resin was treated with this solution for 2 x 45 min. The resin was treated with 20% Ac_2O in DMF (2 x 15 min). The resin was treated with 20% piperidine in DMF (2 x 10 min). The resin-supported peptide was treated with TFA/H_2O/TIPS (95:2.5:2.5) for 2 h, filtered to remove the solid support, and the volatiles were removed under reduced pressure. The residue was triturated with Et_2O, centrifuged, and decanted (three repeated cycles) to obtain the crude peptide. The crude peptide was purified by preparative HPLC using a Shiseido Capcell pak C18 UG80 column (5 μm, 50 mm I.D. x 250 mm) at 60 °C with a gradient of 20% to 85% CH_3CN in H_2O (with 0.1% TFA) in 25 min affording peptide **11** as a white solid (0.19 g, 0.31 mmol, 81%) after lyophilization.

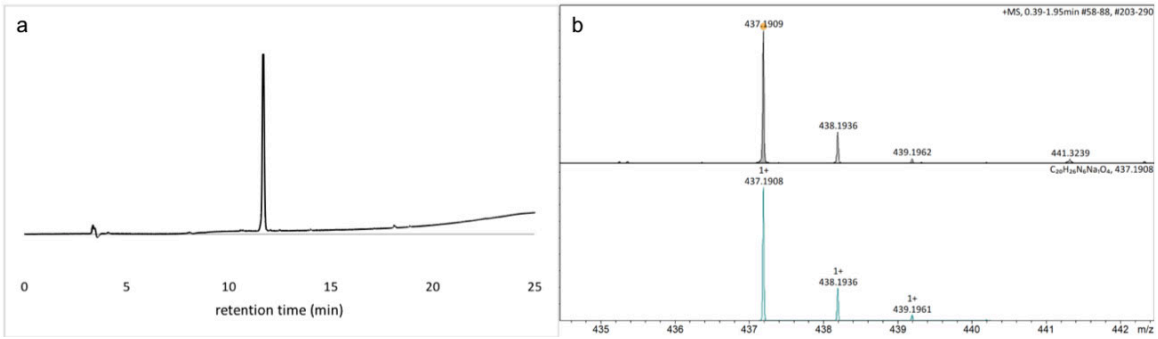
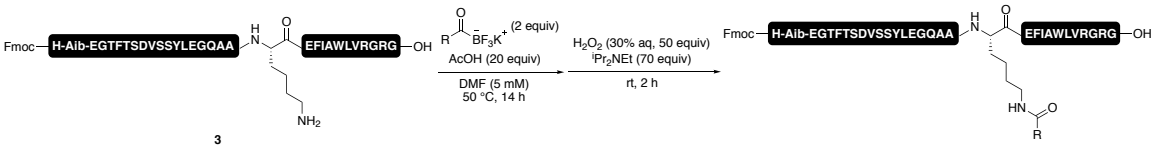


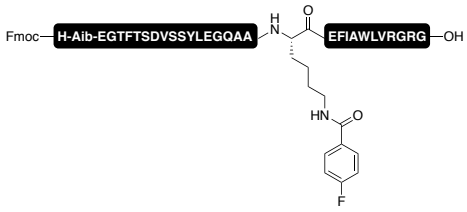
Figure 4. HPLC trace and HR-MS for peptide **11**: a) HPLC trace (220 nm, gradient: 5-95% CH_3CN in H_2O in 17 min) of the purified peptide; b) ESI HR-MS measured (top) and calculated (bottom).

6.2. Modification of peptide 6



Peptide **6** (10 mg, 2.8 μmol, 1.0 equiv) and KAT (5.5 μmol, 2.0 equiv) were dissolved in DMF (0.55 mL, 5.0 mM) and AcOH (3.2 μL, 55 μmol, 20 equiv) was added. The reaction was placed in a shaker at 50 °C for 14 h. H_2O_2 (aq, 30%, 16 μl, 0.14 mmol, 50 equiv) and *N,N*-diisopropylethylamine (34 μL, 0.19 mmol, 70 equiv) were added and the reaction was

placed in a shaker at room temperature for 2 h. The reaction was acidified with TFA, diluted with 1:1 CH_3CN/H_2O + 0.1% TFA and purified by preparative HPLC using a Shiseido Capcell Pak C18 column (20 x 250 mm) with a gradient of 15% to 95% CH_3CN in H_2O (with 0.1% TFA) in 25 min affording the product after lyophilization.



S15 was prepared with potassium 4-fluorobenzoyltrifluoroborate [26] (1.3 mg, 5.5 μmol, 2.0 equiv) according to the general procedure. The product was isolated as a white solid (8.5 mg, 2.3 μmol, 82%).

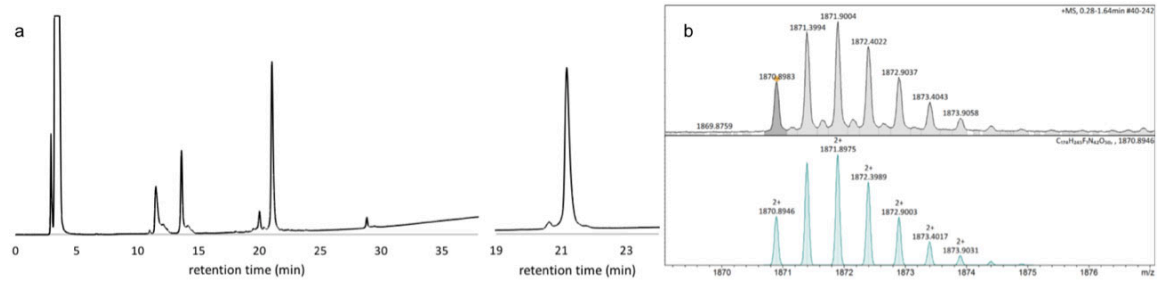
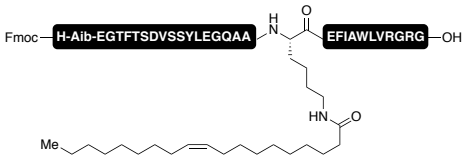


Figure 5. HPLC traces and HR-MS for peptide **S15**: a) HPLC trace (220 nm, gradient: 20-95% CH_3CN in H_2O in 30 min) of the crude reaction mixture (left) and the purified peptide (middle); b) ESI HR-MS measured (top) and calculated (bottom).



7a was prepared with potassium (*Z*)-nonadec-10-enoyltrifluoroborate [27] (1.27 mg, 5.5 mmol, 2.0 equiv) according to the general procedure. The product was isolated as a white solid (6.1 mg, 1.6 μmol, 57%).

[26] H. Noda, G. Erős and J. W. Bode, *J. Am. Chem. Soc.*, 2014, **136**, 5611–5614.
[27] S. Oriana, A. Fracassi, C. Archer and Y. Yamakoshi, *Langmuir*, 2018, **34**, 13244–13251.

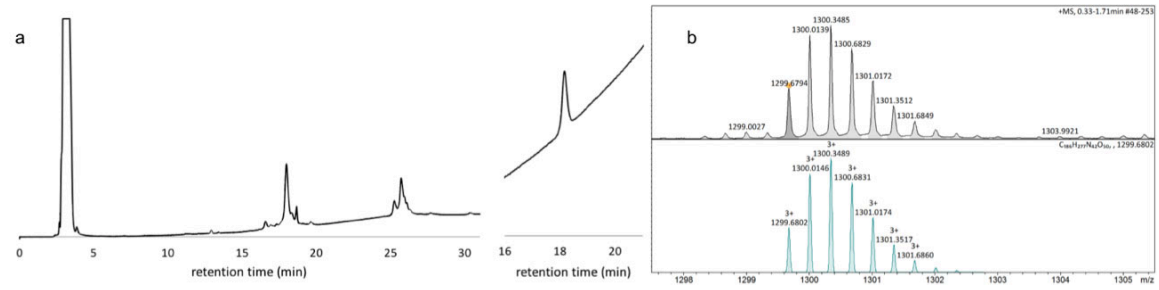
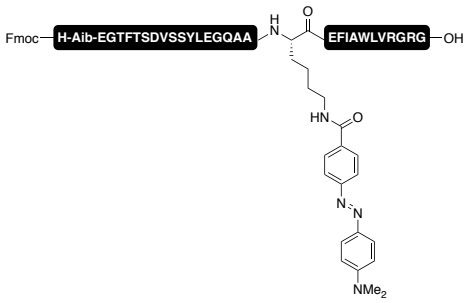


Figure 6. HPLC traces and HR-MS for peptide **7a**: a) HPLC trace (220 nm, gradient: 40-95% CH_3CN in H_2O in 17 min) of the crude reaction mixture (left) and the purified peptide (middle); b) ESI HR-MS measured (top) and calculated (bottom).



7b was prepared with potassium (*E*)-(4-((dimethylamino)phenyl)diazenyl)benzoyltrifluoroborate [28] (2.0 mg, 5.5 μmol, 2.0 equiv) according to the general procedure. The product was isolated as an orange solid (7.0 mg, 1.8 μmol, 65%).

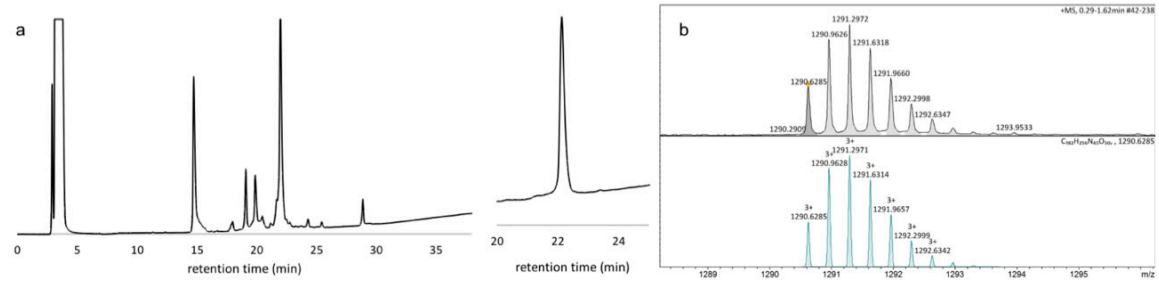
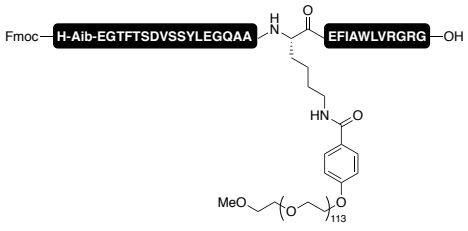


Figure 7. HPLC traces and HR-MS for peptide **7b**: a) HPLC trace (220 nm, gradient: 20-95% CH_3CN in H_2O in 30 min) of the crude reaction mixture (left) and the purified peptide (middle); b) MALDI HR-MS measured (top) and calculated (bottom).



7c was prepared with potassium *O*-(4-benzoyltrifluoroborate)-*O*'-methylpolyethylene glycol 5,000[29] (1.3 mg, 5.5 μmol, 2.0 equiv) according to the general procedure. The product was isolated as a white solid (15 mg, 1.7 μmol, 62%).

[28] D. Wu, N. A. Fohn and J. W. Bode, *Angew. Chem. Int. Ed.*, 2019, **58**, 11058–11062.
[29] H. Noda, G. Erős and J. W. Bode, *J. Am. Chem. Soc.*, 2014, **136**, 5611–5614.

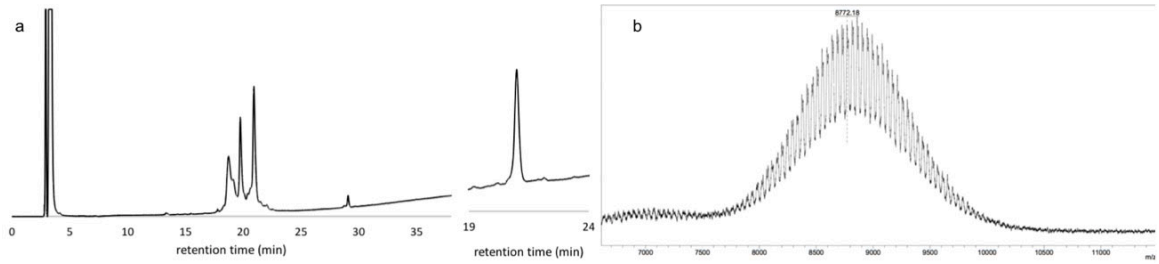
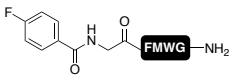


Figure 8. HPLC traces and MS for peptide **7c**: a) HPLC trace (220 nm, gradient: 20-95% CH_3CN in H_2O in 30 min) of the crude reaction mixture (left) and the purified peptide (middle); b) measured MALDI MS.

6.3. Modification of peptides 9 and 11



Peptide **9** (10 mg, 17 μmol, 1.0 equiv) and potassium 4-fluorobenzoyltrifluoroborate (7.7 mg, 34 μmol, 2.0 equiv) were dissolved in DMF (0.34 mL, 50 mM) and AcOH (19 μL, 0.34 mmol, 20 equiv) was added. The reaction was placed in a shaker at 50 °C for 14 h. H_2O_2 (aq, 30%, 95 μl, 0.84 mmol, 50 equiv) and *N,N*-diisopropylethylamine (0.21 mL, 1.2 mmol, 70 equiv) were added and the reaction was placed in a shaker at room temperature for 2 h. The reaction was acidified with TFA, diluted with 1:1 CH_3CN/H_2O + 0.1% TFA and purified by preparative HPLC using a Shiseido Capcell Pak C18 column (20 x 250 mm) with a gradient of 15% to 95% CH_3CN in H_2O (with 0.1% TFA) in 25 min affording the product **10** as a white solid (8.3 mg, 12 μmol, 69%) after lyophilization.

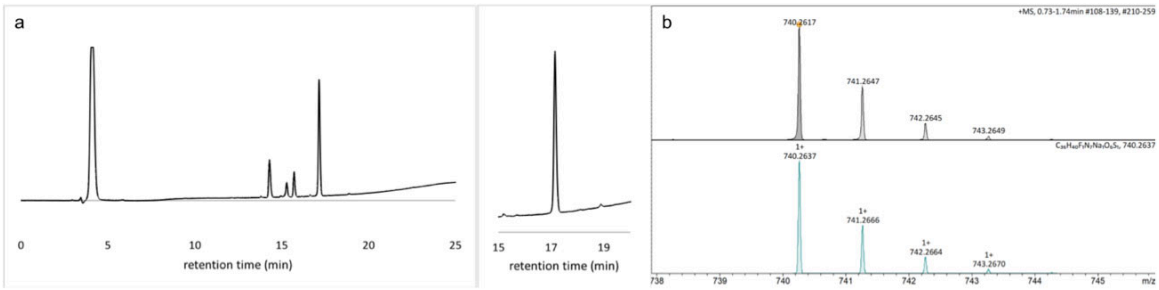
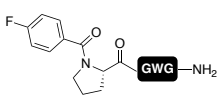


Figure 9. HPLC traces and HR-MS for peptide **10**: a) HPLC trace (220 nm, gradient: 5-95% CH_3CN in H_2O in 17 min) of the crude reaction mixture (left) and the purified peptide (middle); b) ESI HR-MS measured (top) and calculated (bottom).



Peptide **11** (10 mg, 24 μmol, 1.0 equiv) and potassium 4-fluorobenzoyltrifluoroborate (11 mg, 48 μmol, 2.0 equiv) were

dissolved in DMF (0.48 mL, 50 mM) and AcOH (28 μL, 0.48 mmol, 20 equiv) was added. The reaction was placed in a shaker at 50 °C for 14 h. H_2O_2 (aq, 30%, 0.14 mL, 1.2 mmol, 50 equiv) and *N,N*-diisopropylethylamine (0.29 mL, 1.7 mmol, 70 equiv) were added and the reaction was placed in a shaker at room temperature for 2 h. The reaction was acidified with TFA, diluted with 1:1 CH_3CN/H_2O + 0.1% TFA and purified by preparative HPLC using a Shiseido Capcell Pak C18 column (20 x 250 mm) with a gradient of 15% to 95% CH_3CN in H_2O (with 0.1% TFA) in 25 min affording the product **12** as a white solid (11 mg, 20 μmol, 82%) after lyophilization.

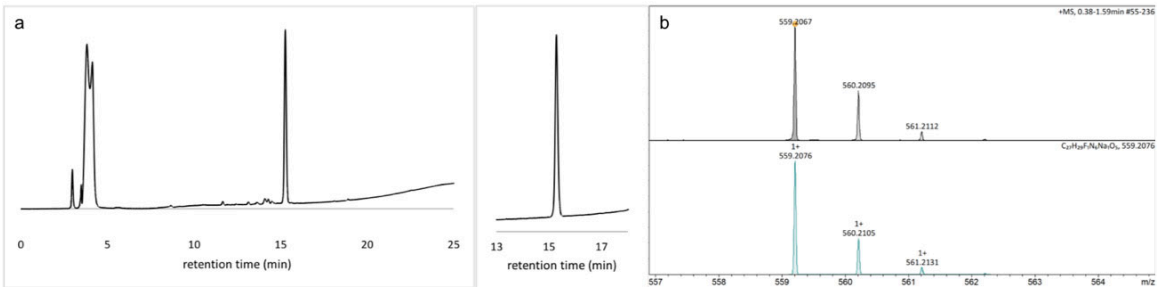
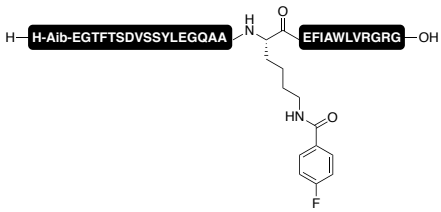


Figure 10. HPLC traces and HR-MS for peptide **12**: a) HPLC trace (220 nm, gradient: 5-95% CH_3CN in H_2O in 17 min) of the crude reaction mixture (left) and the purified peptide (middle); b) ESI HR-MS measured (top) and calculated (bottom).

6.4. Fmoc removal from the modified peptide



S15 (5.0 mg, 1.3 μmol, 1.0 equiv) was dissolved in DMSO (0.65 mL, 2 mM) and *N,N*-diethylamine (41 μL, 6 vol%) was added. The reaction was placed in a shaker at room temperature for 20 min. The mixture was cooled over ice, TFA (54 μL, 8 vol%) was added and the mixture was diluted with 1:1 CH_3CN/H_2O + 0.1% TFA. The reaction was purified by preparative HPLC using a Shiseido Capcell Pak C18 column (20 x 250 mm) with a gradient of 15% to 95% CH_3CN in H_2O (with 0.1% TFA) in 25 min affording **5** (3.9 mg, 1.1 μmol, 81%) after lyophilization as a white solid.

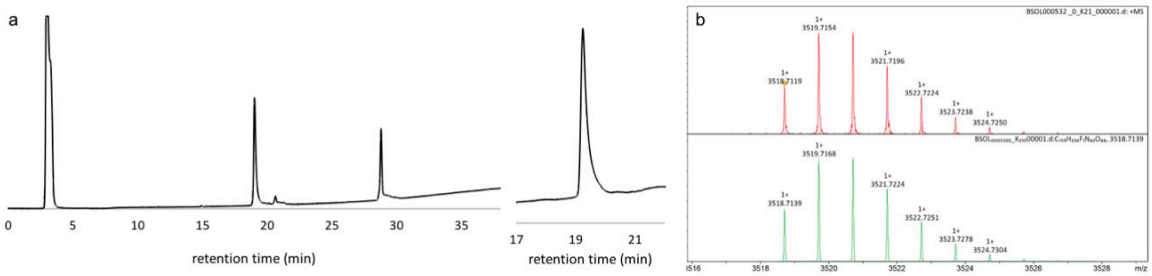
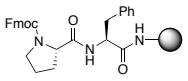


Figure 11. HPLC traces and HR-MS for peptide **5**: a) HPLC trace (220 nm, gradient: 20-95% CH_3CN in H_2O in 30 min) of the crude reaction mixture (left) and the purified peptide (middle); b) MALDI HR-MS measured (top) and calculated (bottom).

7. Solid-phase peptide synthesis using KAT amino acid analogues

7.1. Preparation of the dipeptide (11)



MBHA Rink amide resin loaded with peptide **4** was prepared on MBHA Rink amide resin with a loading capacity of 0.56 mmol/g. The resin was treated with 20% piperidine in DMF (2 x 10 min). Fmoc-Phe-OH (0.11 g, 0.27 mmol, 1.0 equiv) and HATU (99 mg, 0.26 mmol, 0.90 equiv) were dissolved in DMF, *N,N*-diisopropylethylamine (92 μL, 0.54 mmol, 2.0 equiv) was added, and the solution was vortexed for 3 min. The resin was treated with this solution for 90 min. The resin was treated with 20% Ac_2O in DMF (2 x 15 min). The resin loading was determined to be 0.20 mmol/g. The synthesis was performed on 0.20 mmol scale (1.0 g of resin). The resin was treated with 20% piperidine in DMF (2 x 10 min). Fmoc-Pro-OH (0.17 g, 0.49 mmol, 4.0 equiv) and HATU (0.18 g, 0.45 mmol, 3.9 equiv) were dissolved in DMF, *N,N*-diisopropylethylamine (0.17 mL, 0.93 mmol, 8.0 equiv) was added, and the solution was vortexed for 3 min. The resin was treated with this solution for 2 x 45 min. The resin was treated with 20% Ac_2O in DMF (2 x 15 min). Cleavage was performed with 50 mg of resin. The resin-supported peptide was treated with TFA/H_2O/TIPS (95:2.5:2.5) for 2 h, filtered to remove the solid support, and the volatiles were removed under reduced pressure. The residue was triturated with Et_2O, centrifuged, and decanted (three repeated cycles) to obtain the crude peptide. HPLC analyses of the peptide shows that the crude peptide **4** contains no impurities.

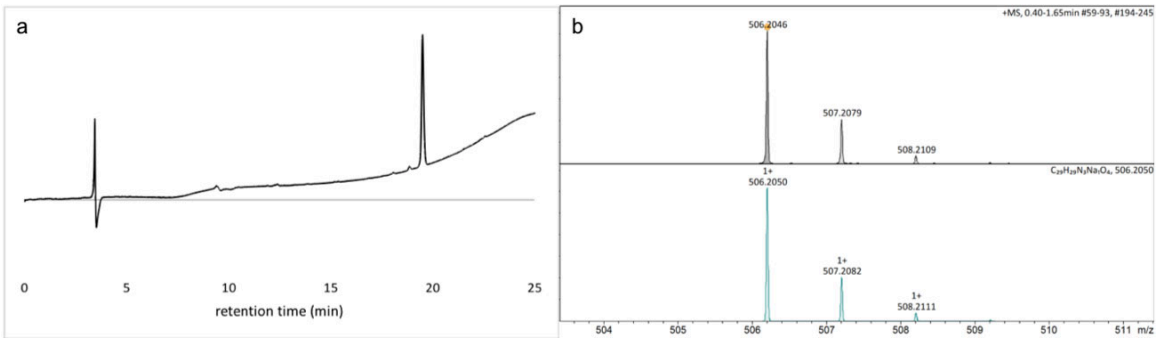
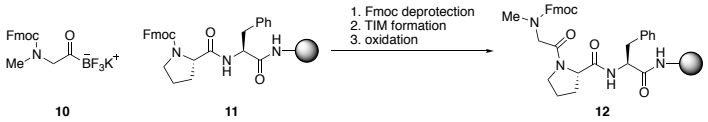


Figure 12. HPLC trace and HR-MS for peptide **4**: a) HPLC trace (220 nm, gradient: 5-95% CH_3CN in H_2O in 17 min) of the crude peptide; b) ESI HR-MS measured (top) and calculated (bottom).

7.2. SPPS coupling of Fmoc-protected *N*-methylglycine KAT analogue (10)



Resin **4** (30.0 mg, 7.11 μmol, 1.00 equiv) was treated with 20% piperidine in DMF (2 x 10 min). **3** (285 mg, 0.711 mmol, 100 equiv) was dissolved in DMF and AcOH (20.4 μL, 0.356 mmol, 50.0 equiv) was added. The resin was treated with this solution for 60 min. H_2O_2–urea (67.7 mg, 0.711 mmol, 100 equiv) was dissolved in DMF, *N,N*-diisopropylethylamine (123 μL, 0.711 mmol, 100 equiv) was added, and the solution was quickly vortexed. The resin was treated with this solution for 10 min. Both steps were repeated (the recovered solution of **3** was used again). The loading of the resin was determined to be 0.20 mmol/g The resin-supported peptide was treated with TFA/H_2O/TIPS (95:2.5:2.5) for 2 h, filtered to remove the solid support, and the volatiles were removed under reduced pressure. The residue was triturated with Et_2O, centrifuged, and decanted (three repeated cycles) to obtain the crude peptide. Loading determination and HPLC analyses of the peptide shows that the crude peptide **5** contains no impurities and the coupling proceeds cleanly with complete conversion.

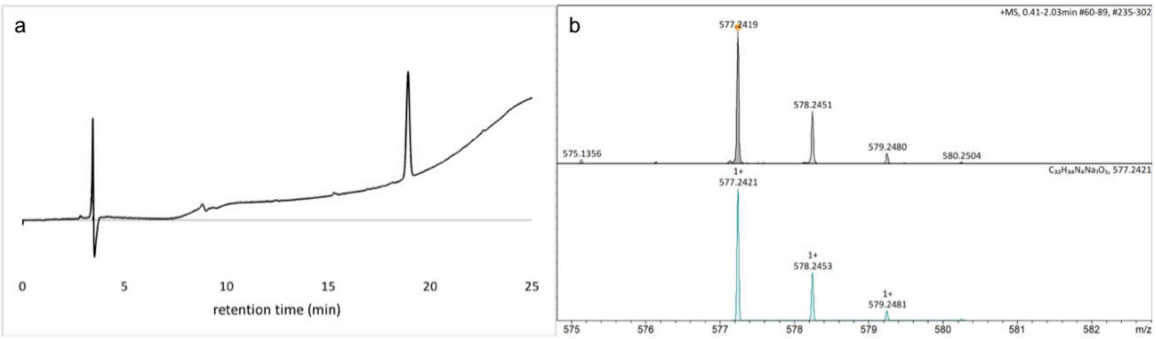
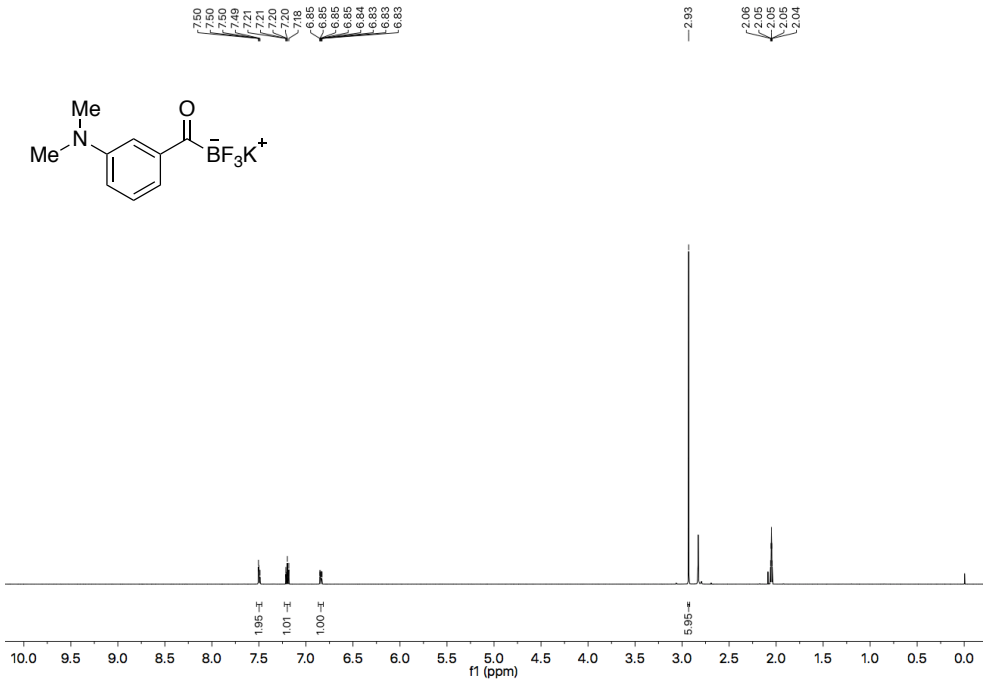


Figure 13. HPLC trace and HR-MS for peptide **5**: a) HPLC trace (220 nm, gradient: 5-95% CH_3CN in H_2O in 17 min) of the crude peptide; b) ESI HR-MS measured (top) and calculated (bottom).

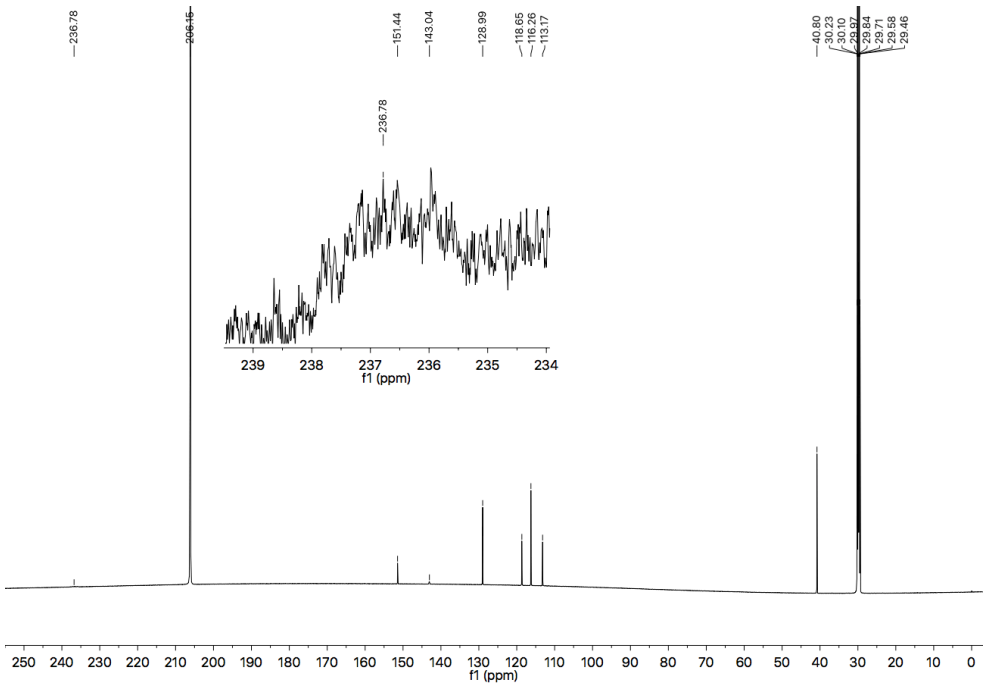
8. NMR spectra

8.1. Potassium acyltrifluoroborates (KATs)

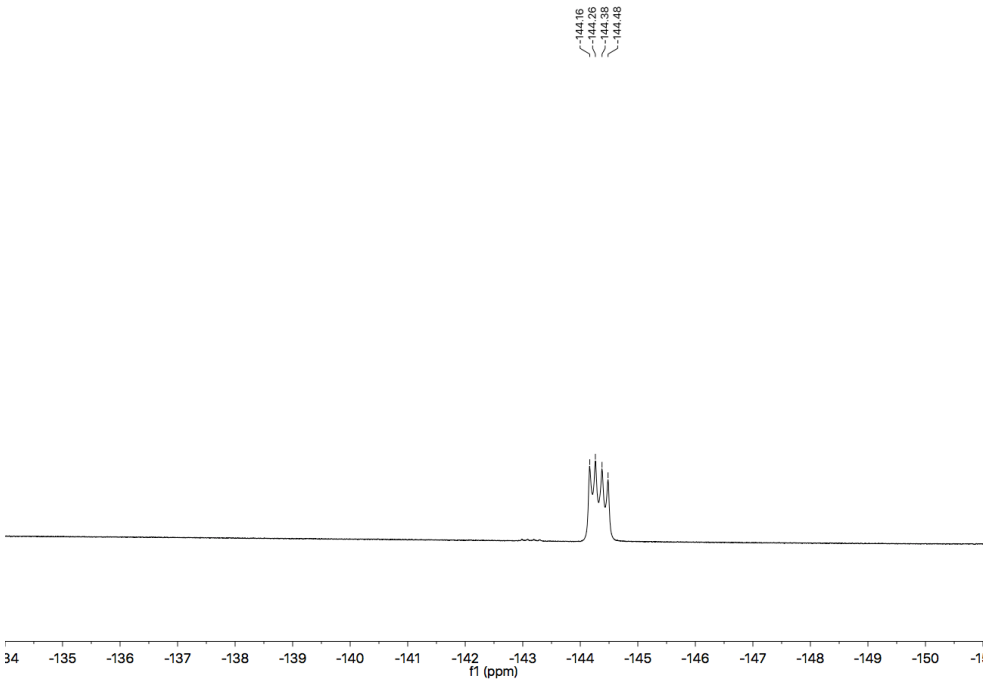
^{1}H NMR spectrum (500 MHz, acetone-*d6*)



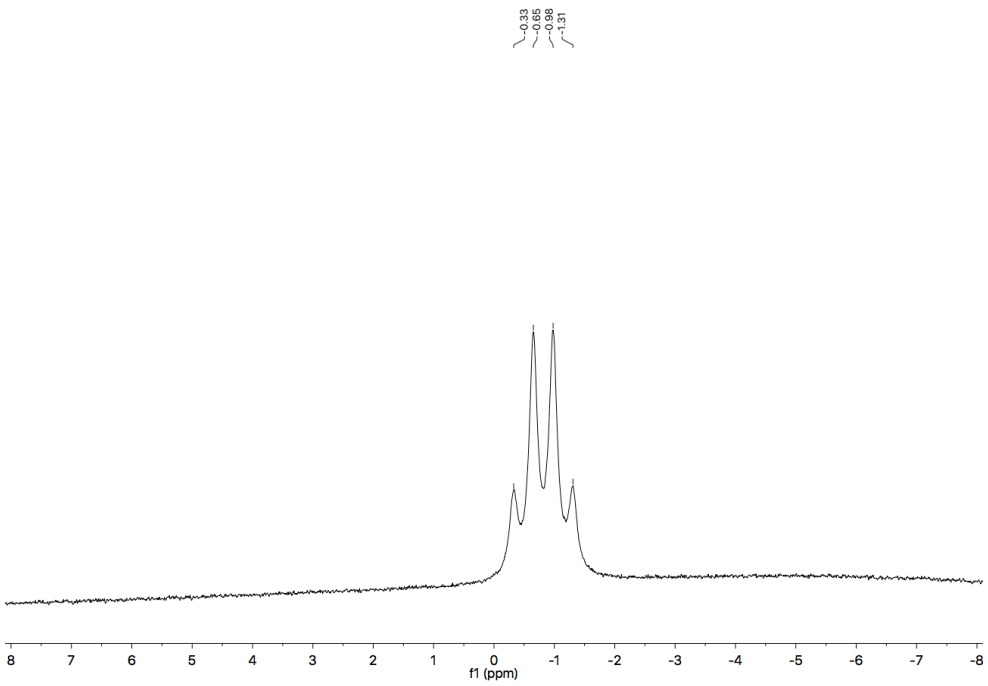
^{13}C NMR spectrum (151 MHz, acetone-*d6*)



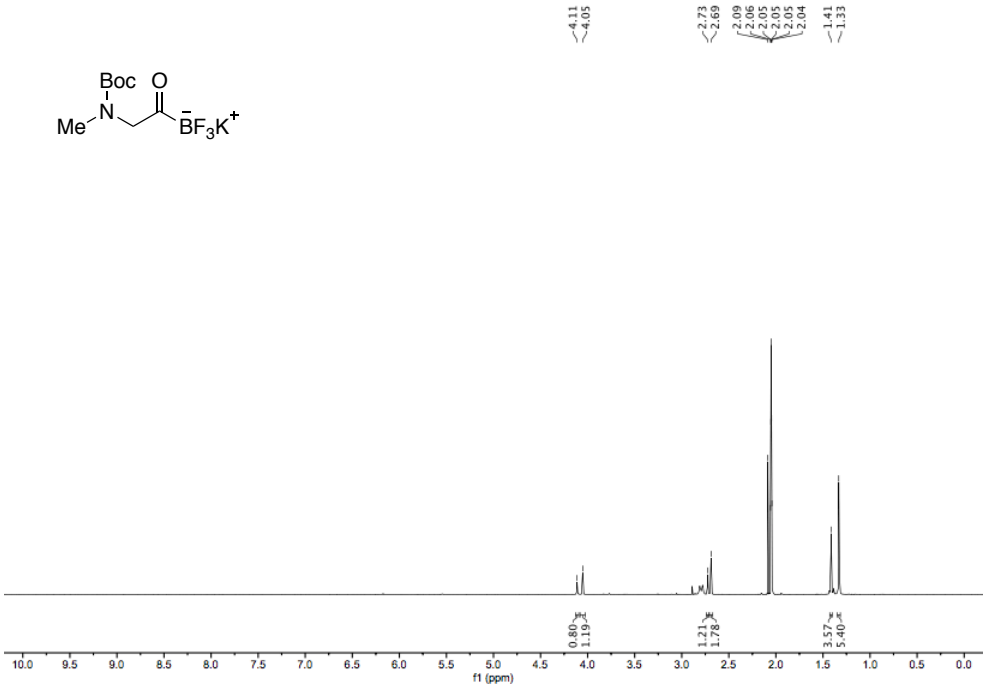
^{19}F NMR spectrum (470 MHz, acetone-*d6*)



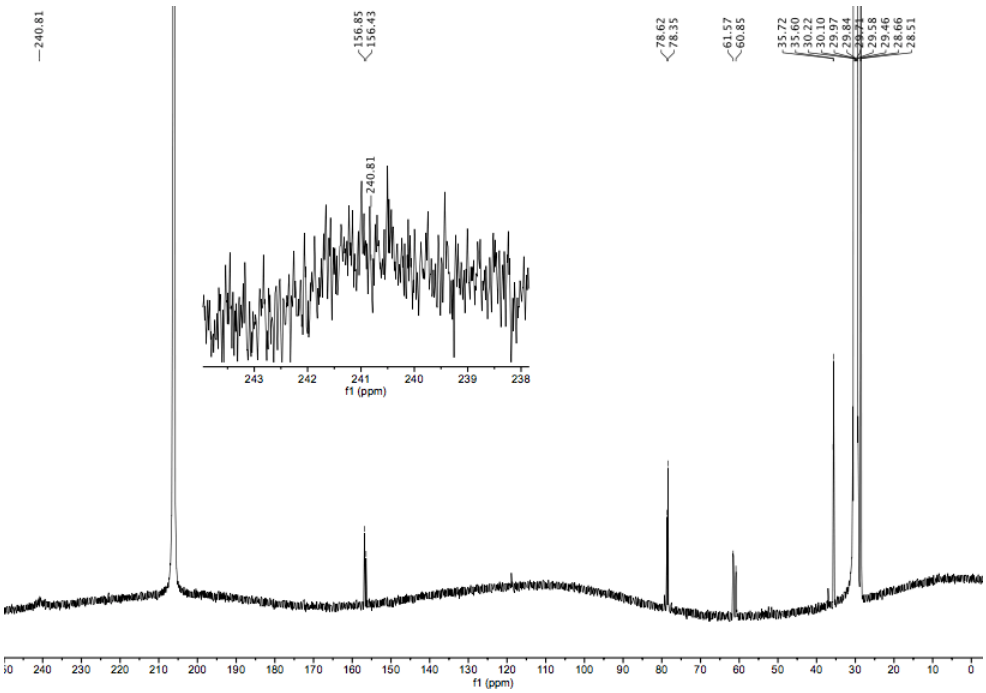
^{11}B NMR spectrum (160 MHz, acetone-*d6*)



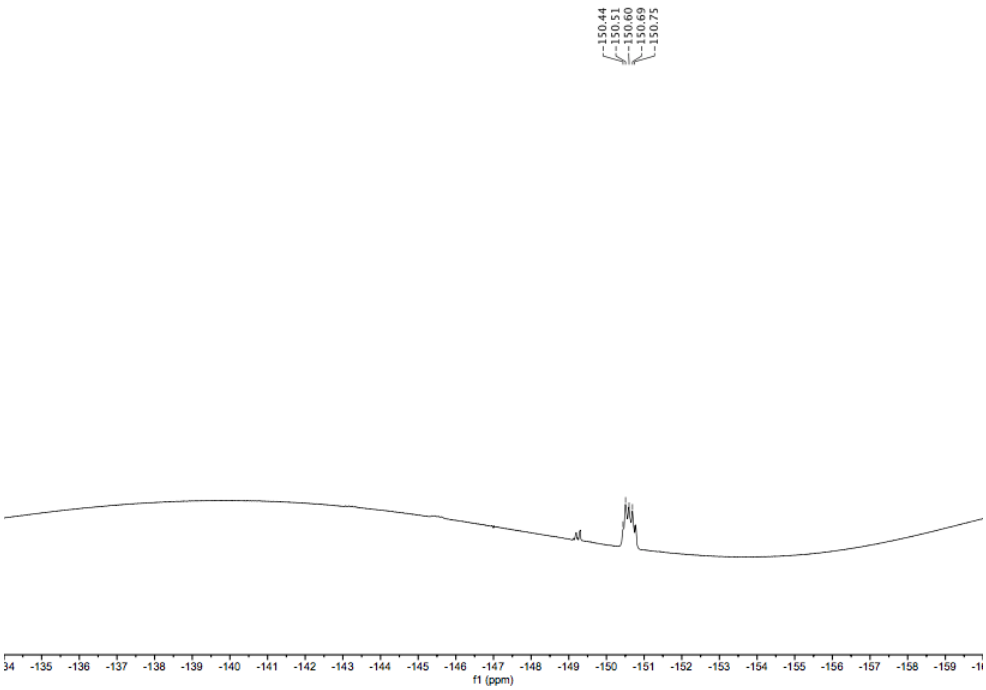
^{1}H NMR spectrum (600 MHz, acetone-*d6*)



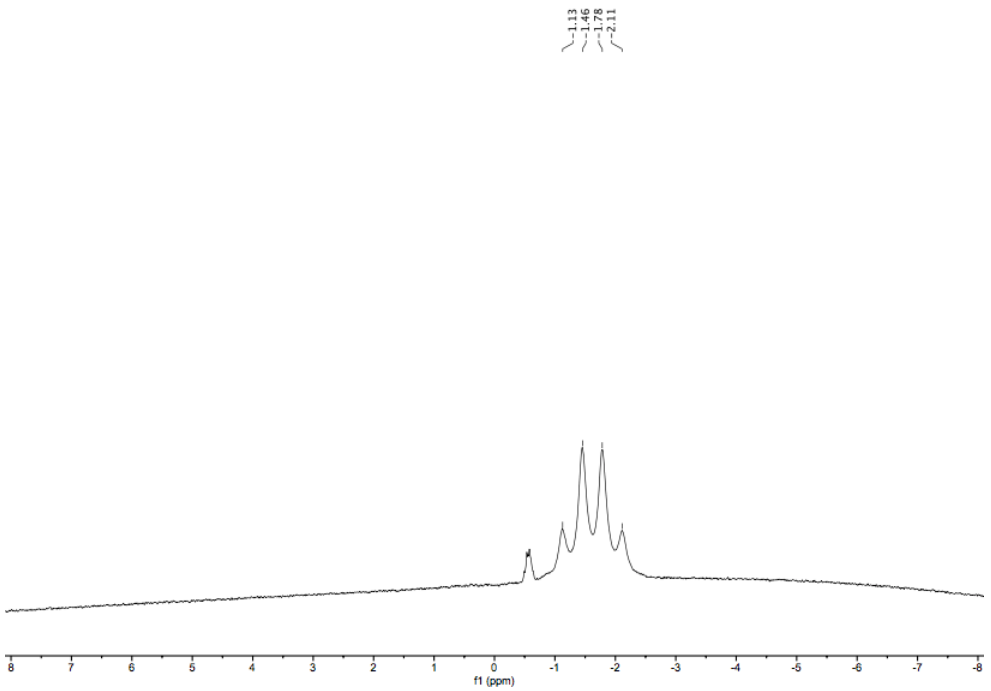
^{13}C NMR spectrum (151 MHz, acetone-*d6*)



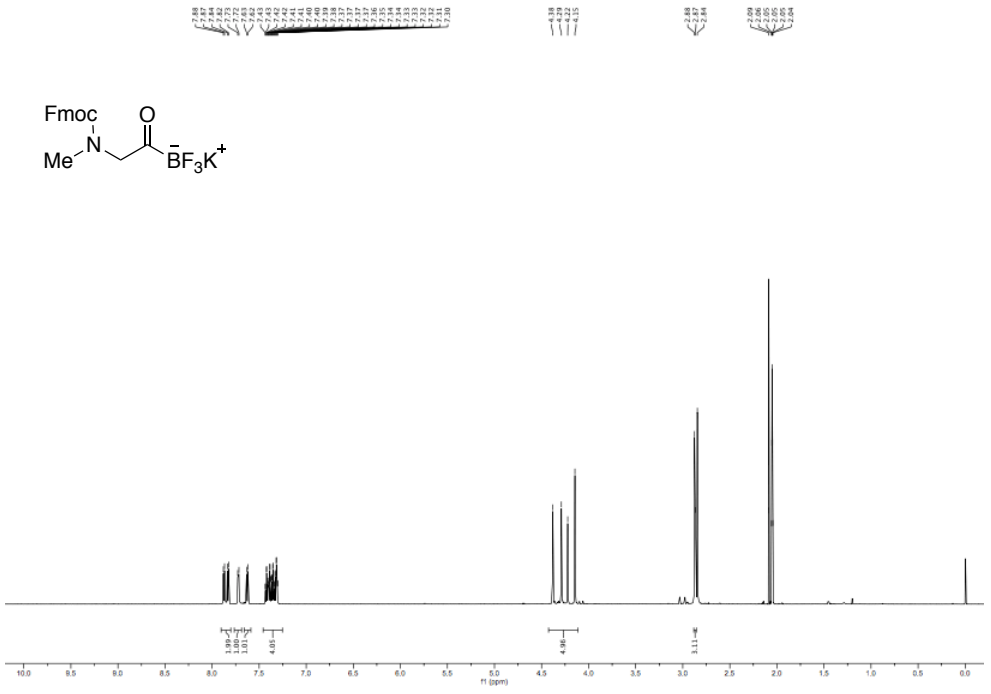
^{19}F NMR spectrum (470 MHz, acetone-*d6*)



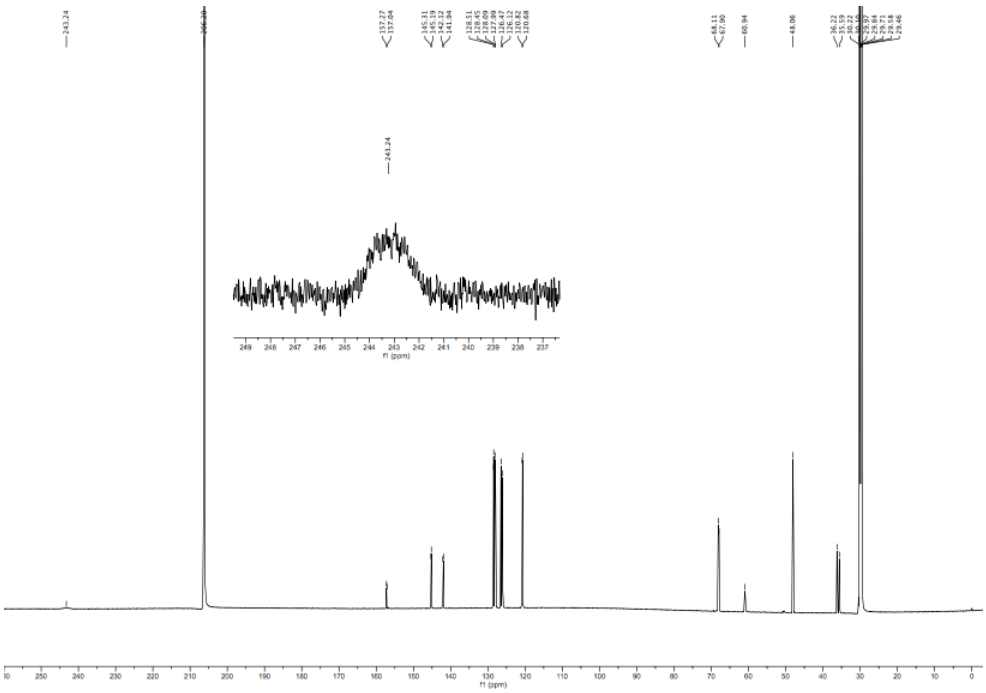
^{11}B NMR spectrum (160 MHz, acetone-*d6*)



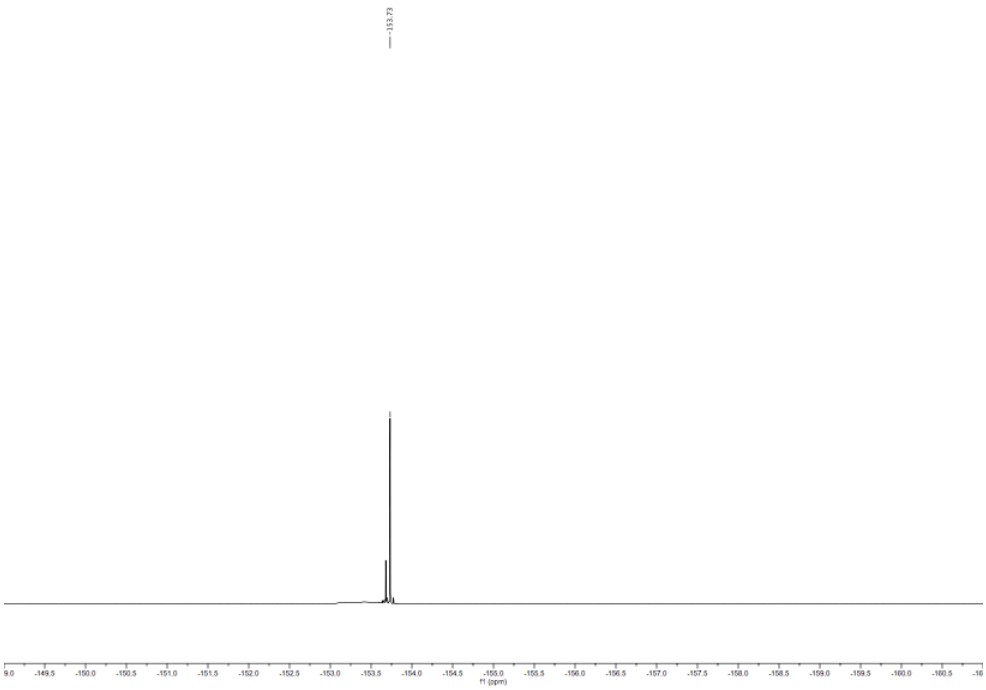
^{1}H NMR spectrum (600 MHz, acetone-*d6*)



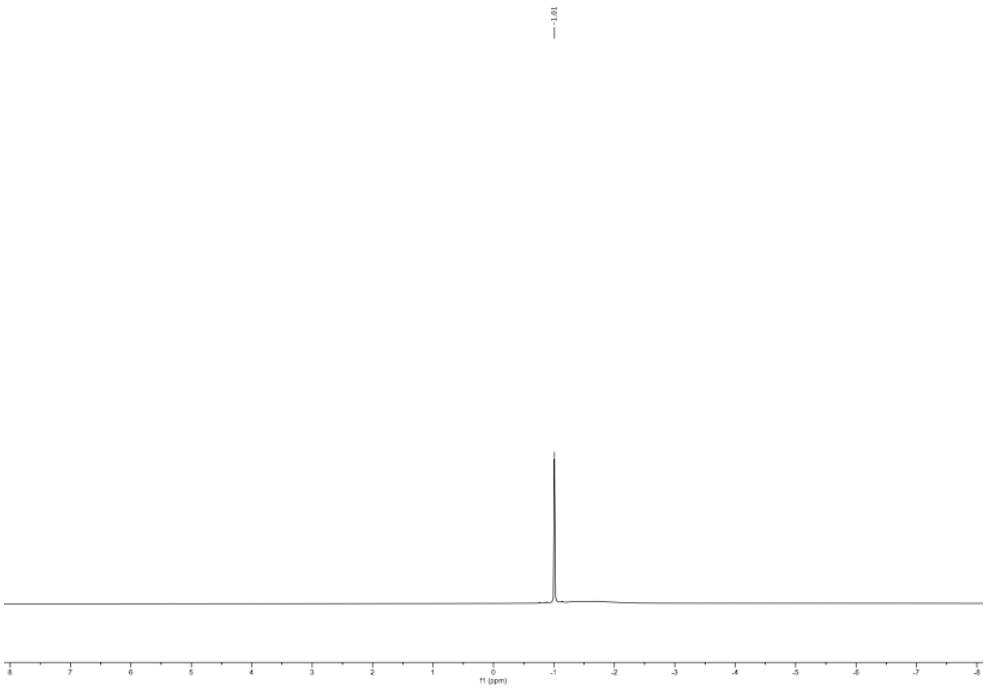
^{13}C NMR spectrum (151 MHz, acetone-*d6*)



^{19}F NMR spectrum (470 MHz, acetone-*d6*)

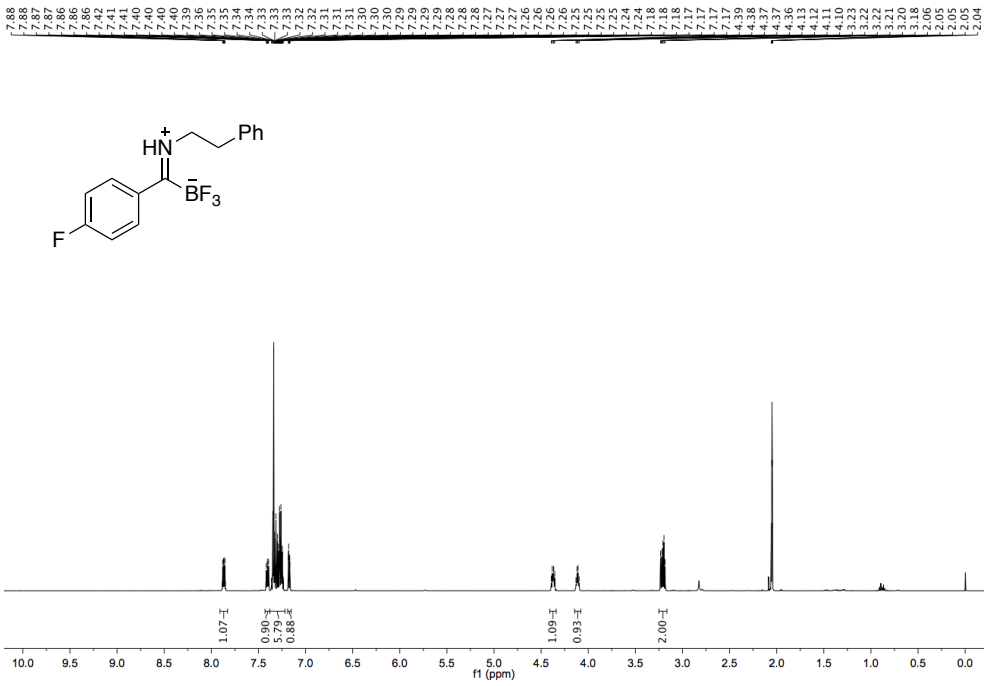


^{11}B NMR spectrum (160 MHz, acetone-*d6*)

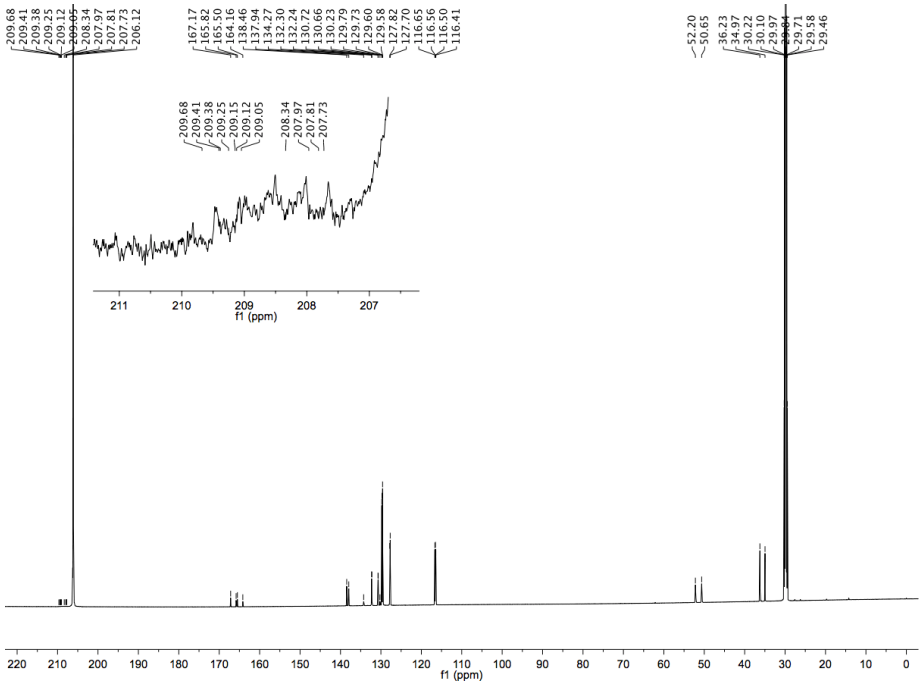


8.2. Trifluoroborate iminiums (TIMs)

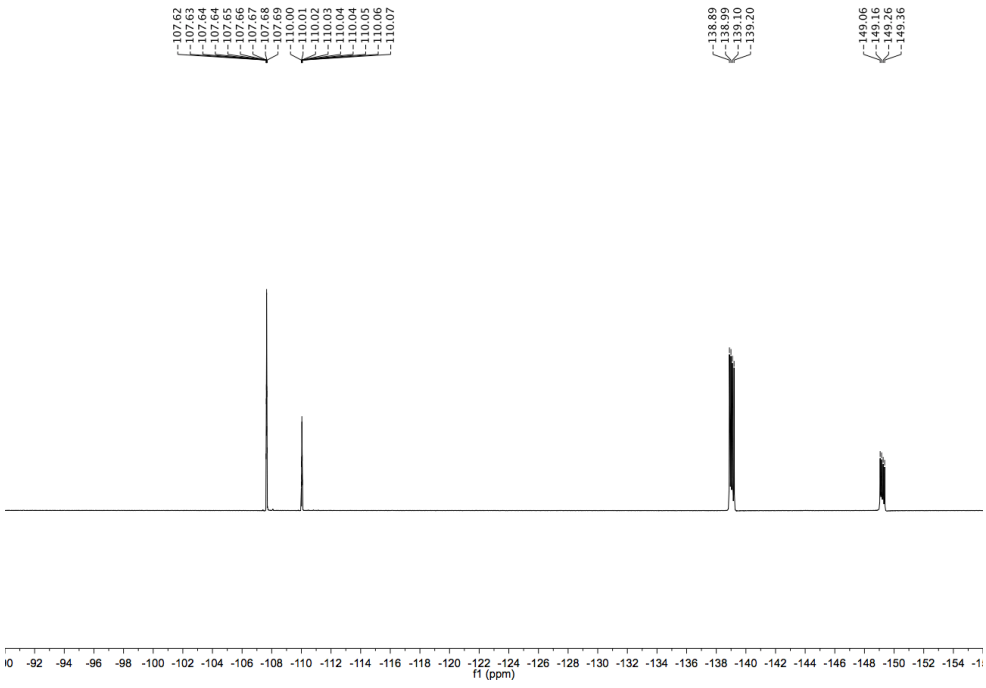
^{1}H NMR spectrum (600 MHz, acetone-*d6*)



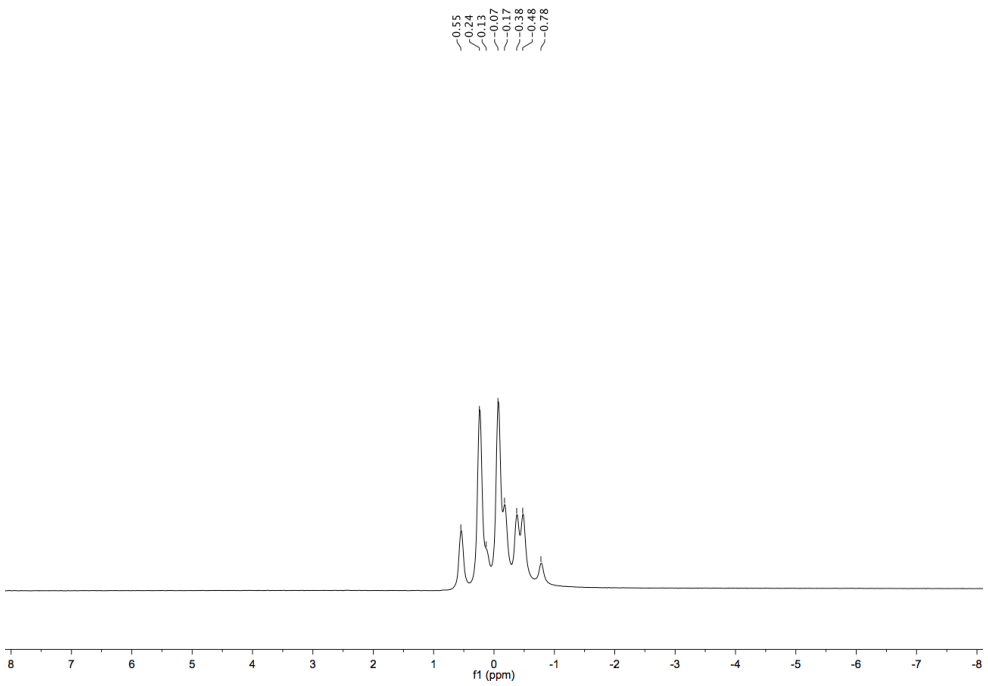
^{13}C NMR spectrum (151 MHz, acetone-*d6*)



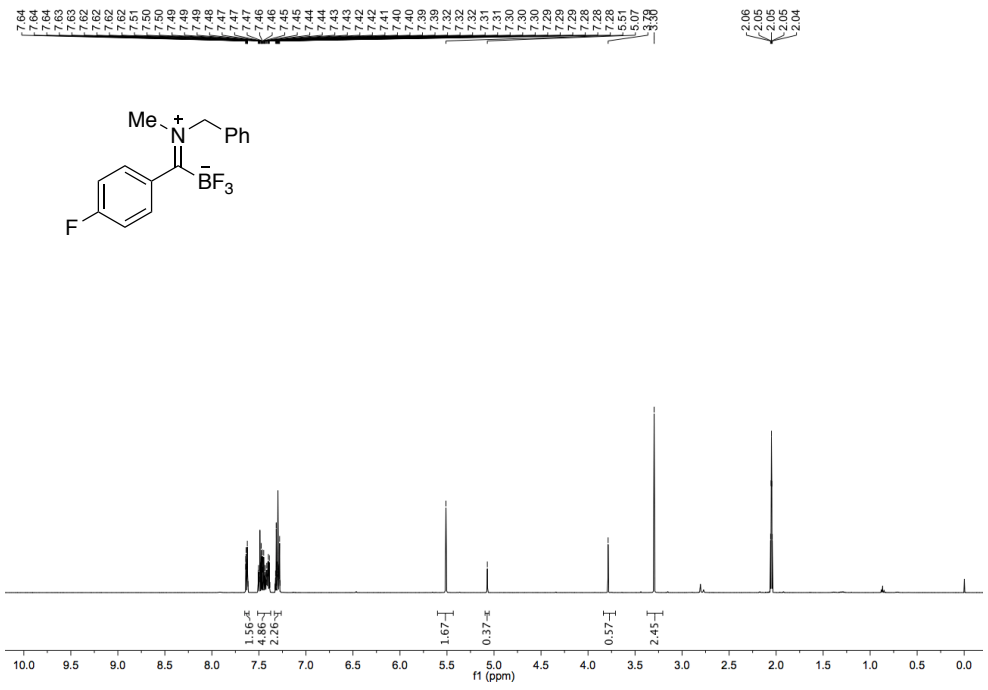
^{19}F NMR spectrum (376 MHz, acetone-*d6*)



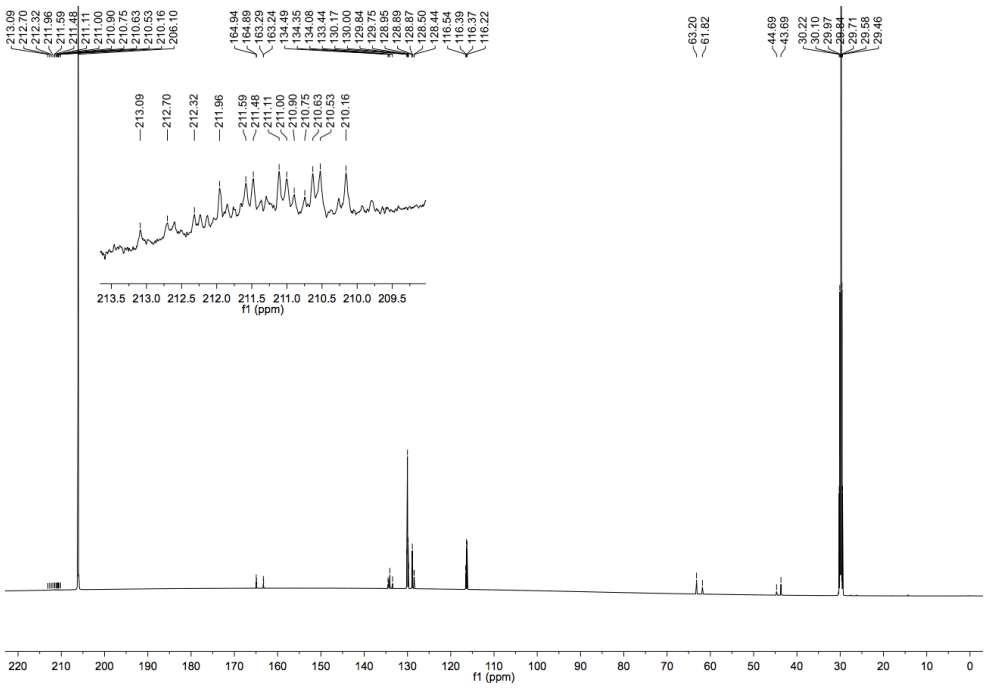
^{11}B NMR spectrum (128 MHz, acetone-*d6*)



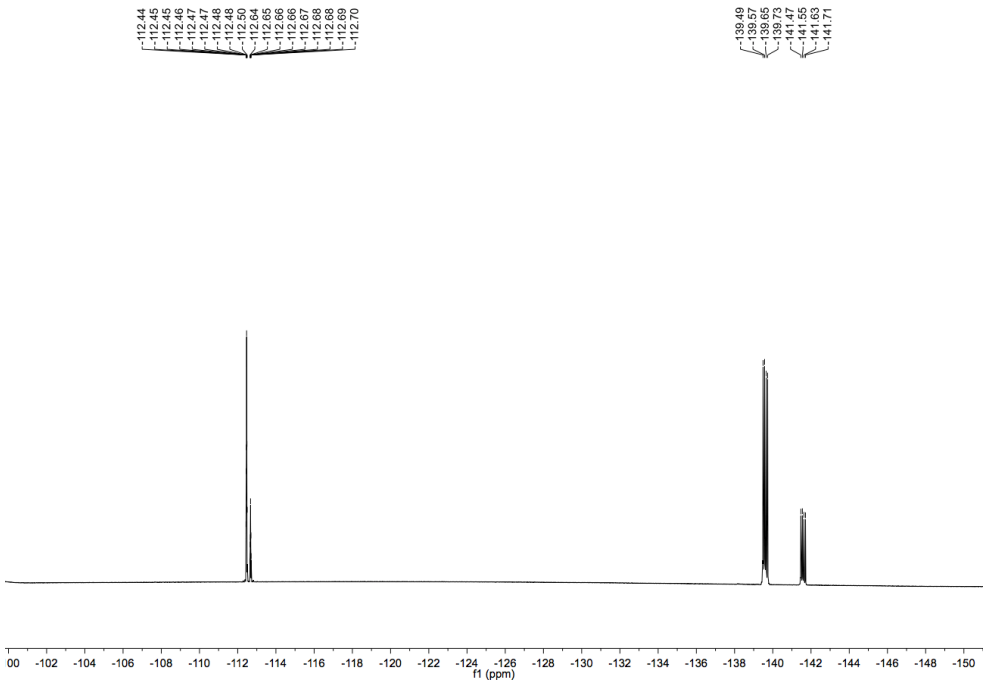
^{1}H NMR spectrum (500 MHz, acetone-*d6*)



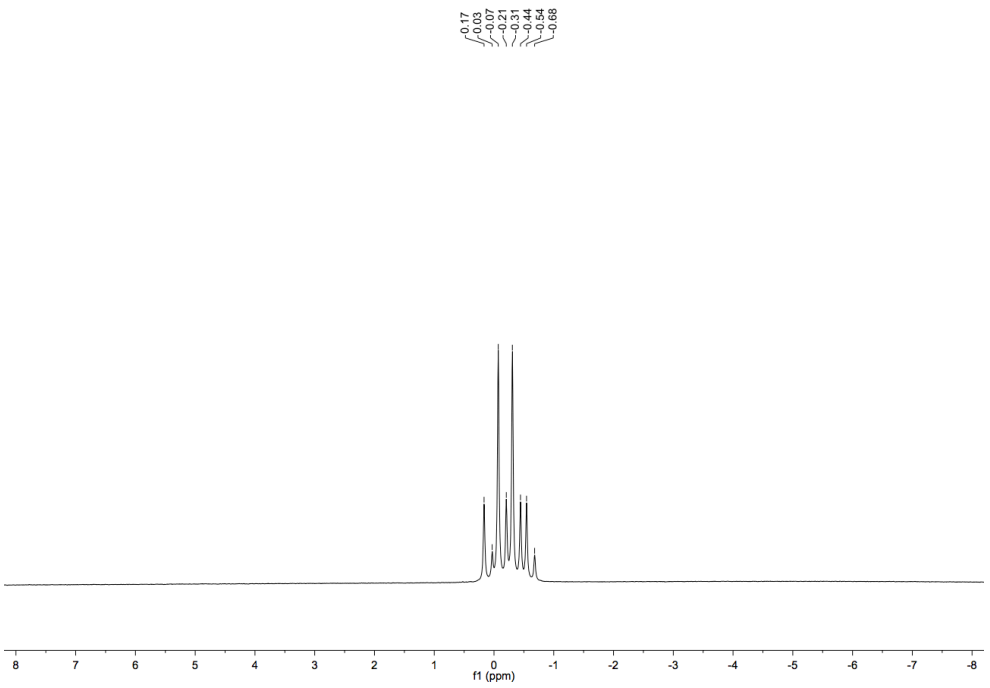
^{13}C NMR spectrum (151 MHz, acetone-*d6*)



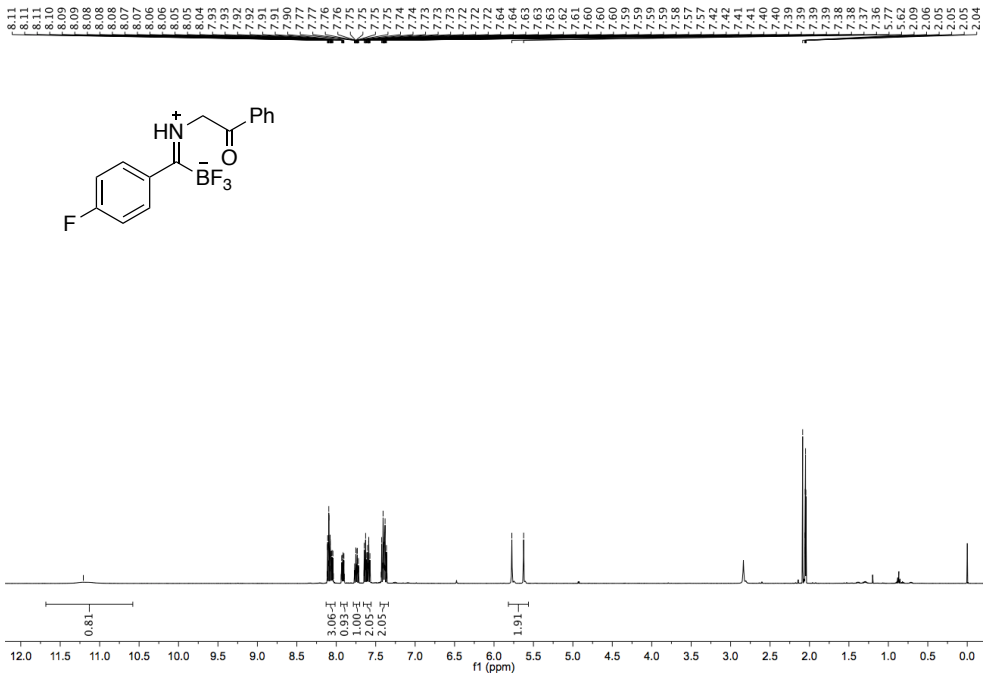
^{19}F NMR spectrum (470 MHz, acetone-*d6*)



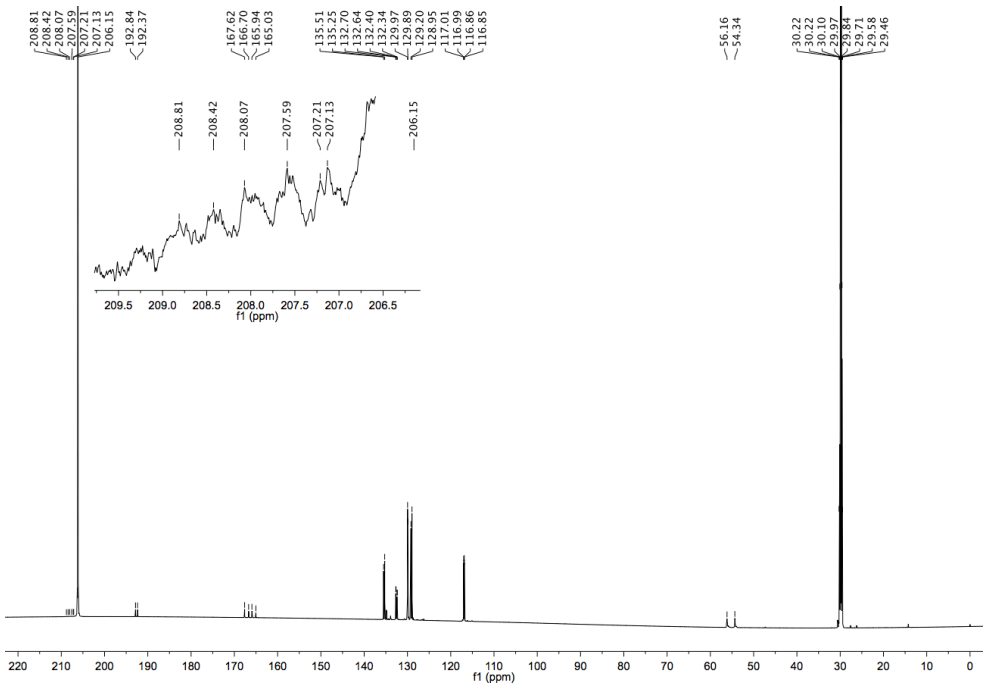
^{11}B NMR spectrum (160 MHz, acetone-*d6*)



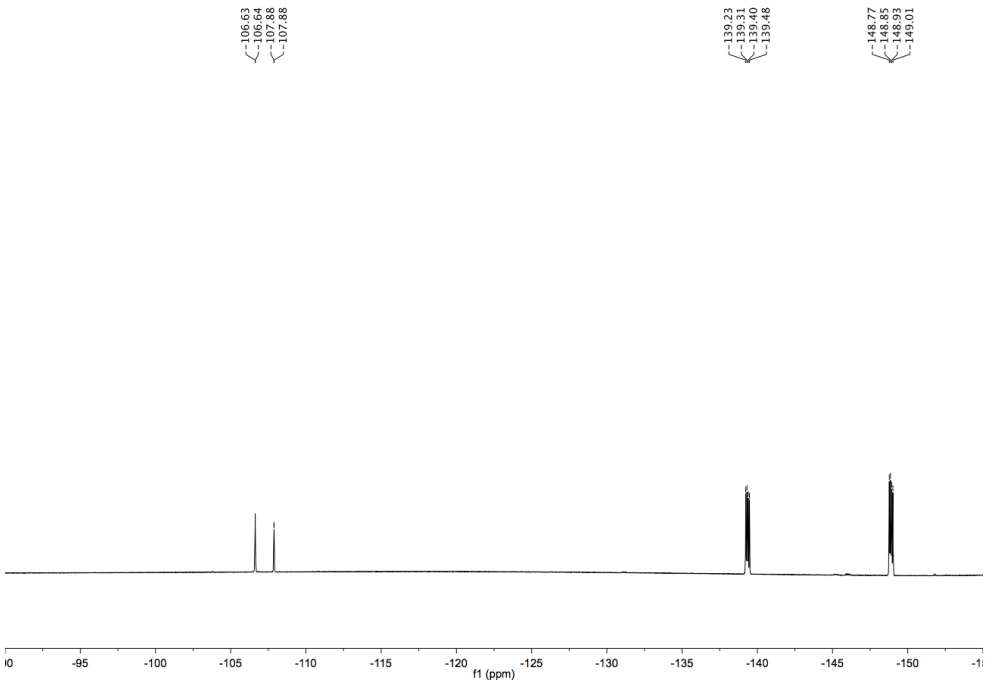
^{1}H NMR spectrum (500 MHz, acetone-*d6*)



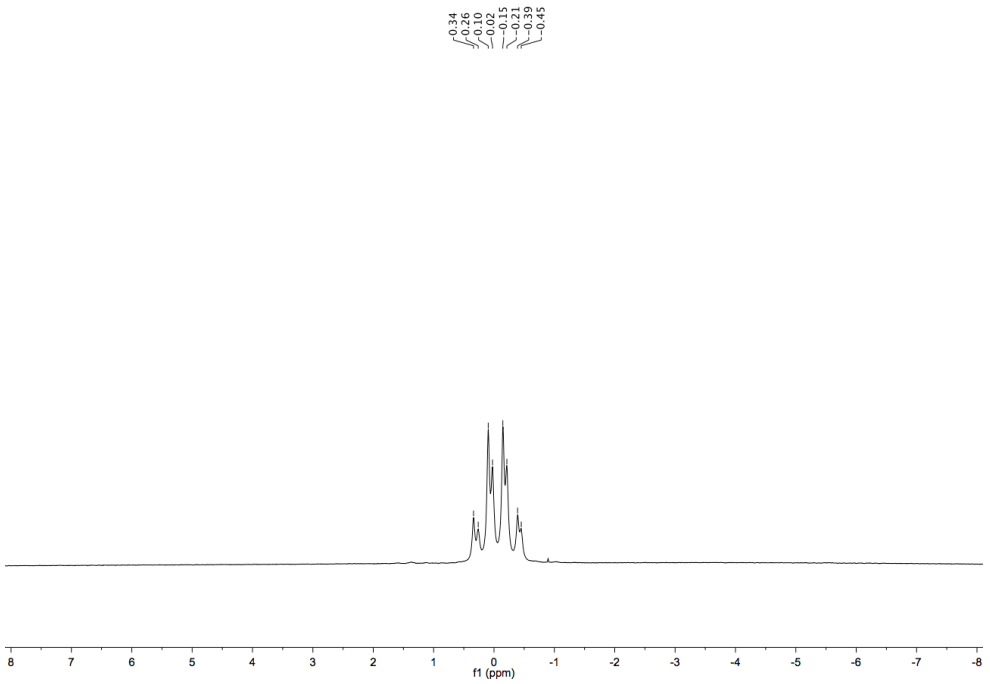
^{13}C NMR spectrum (151 MHz, acetone-*d6*)



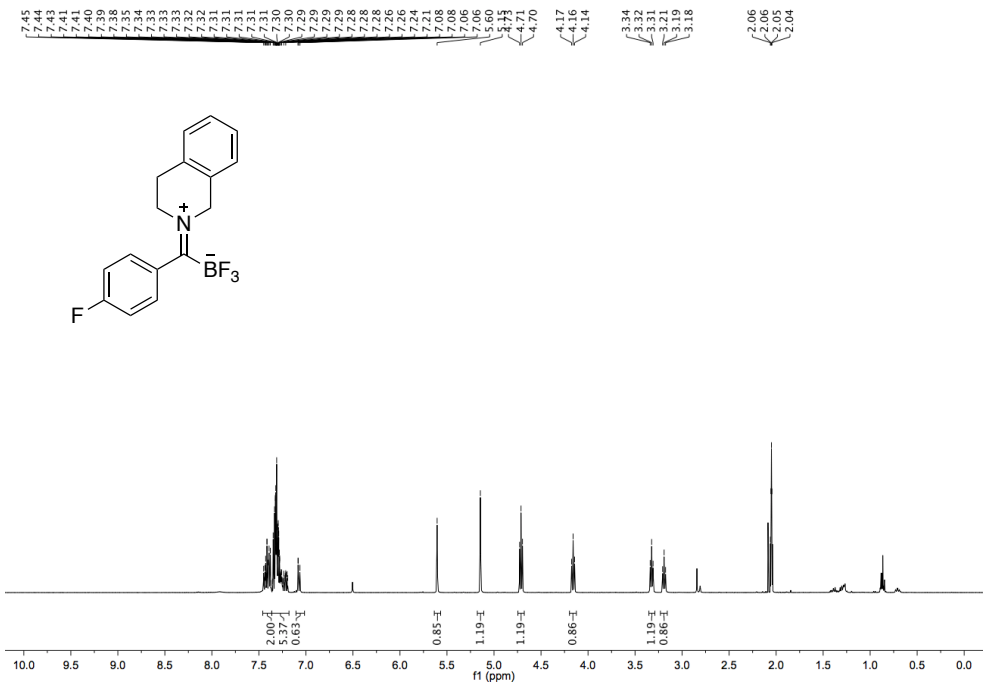
^{19}F NMR spectrum (470 MHz, acetone-*d6*)



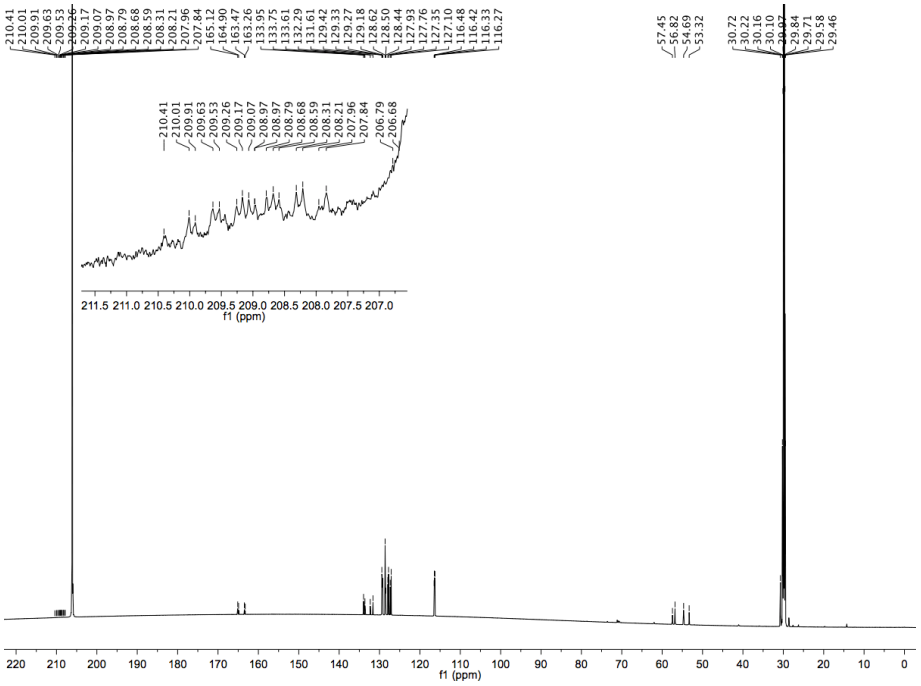
^{11}B NMR spectrum (160 MHz, acetone-*d6*)



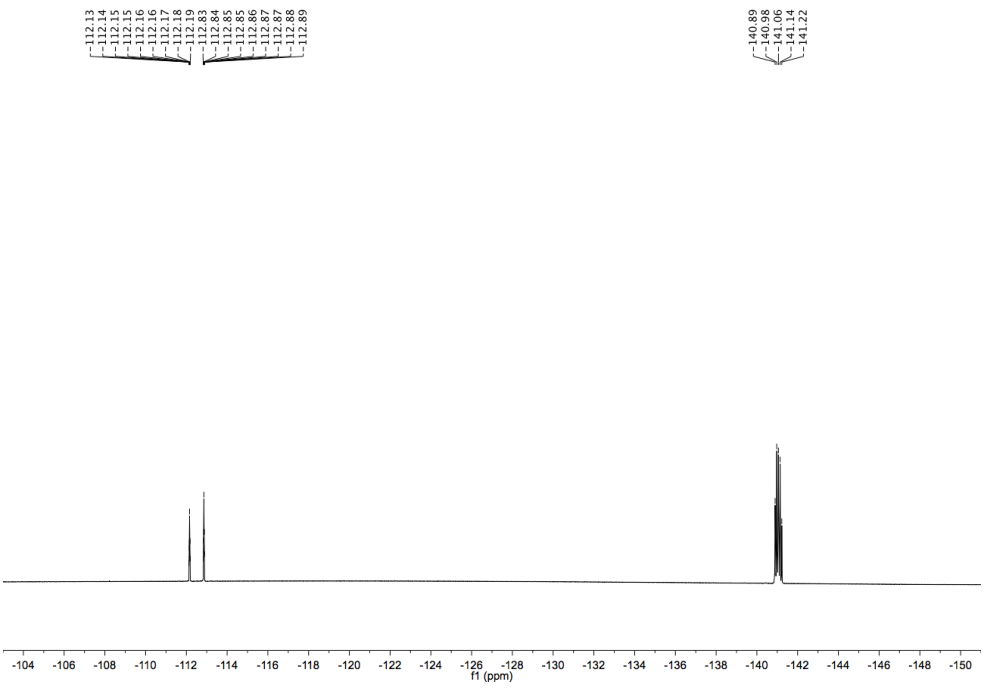
^{1}H NMR spectrum (400 MHz, acetone-*d6*)



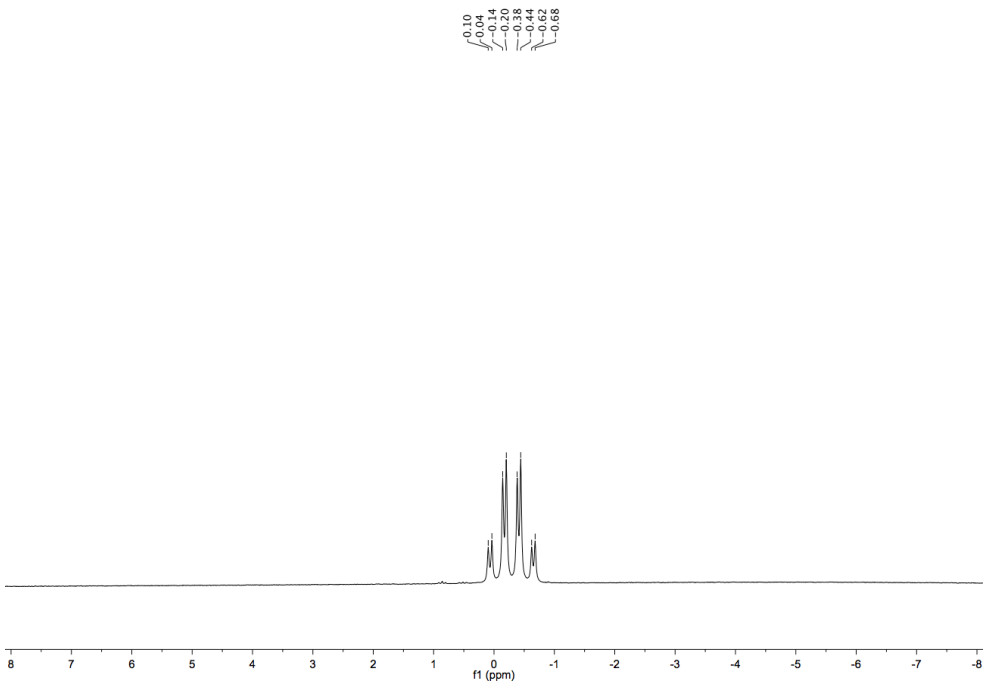
^{13}C NMR spectrum (151 MHz, acetone-*d6*)



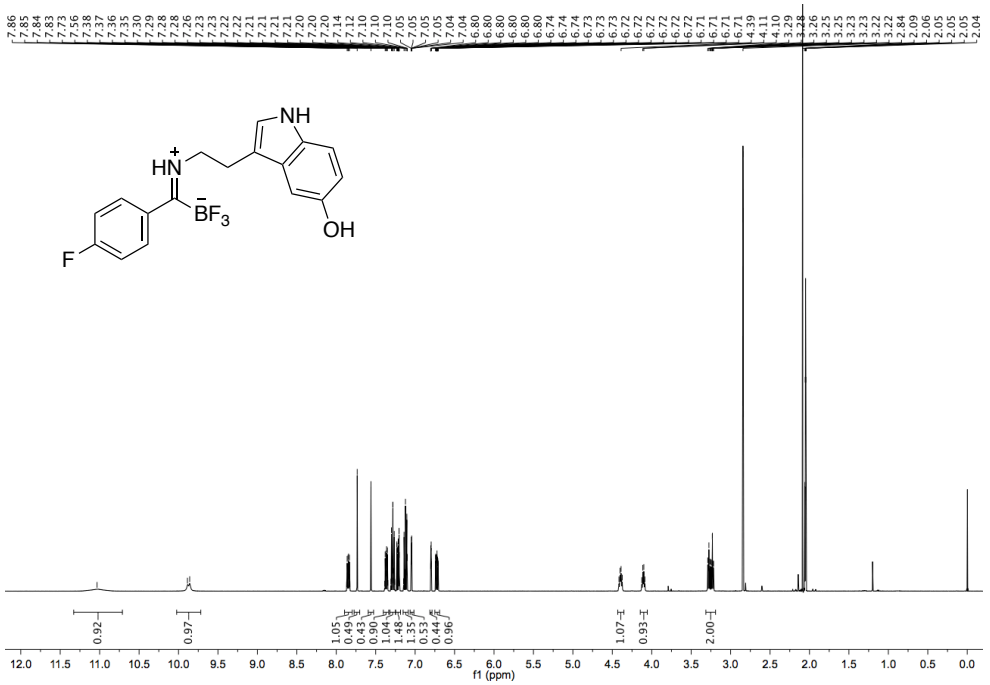
^{19}F NMR spectrum (470 MHz, acetone-*d6*)



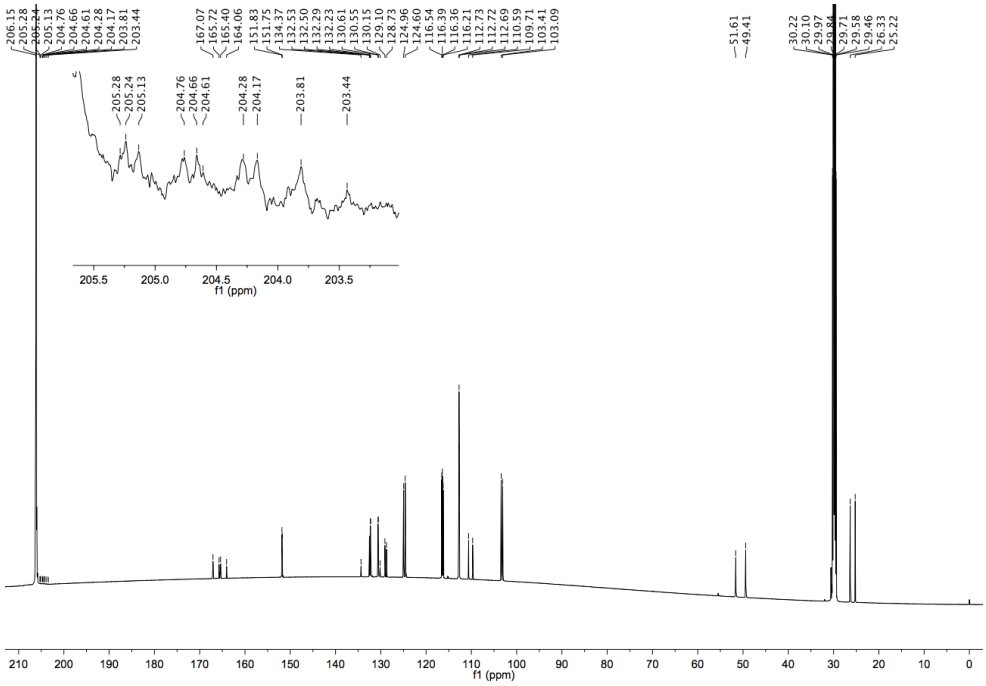
^{11}B NMR spectrum (160 MHz, acetone-*d6*)



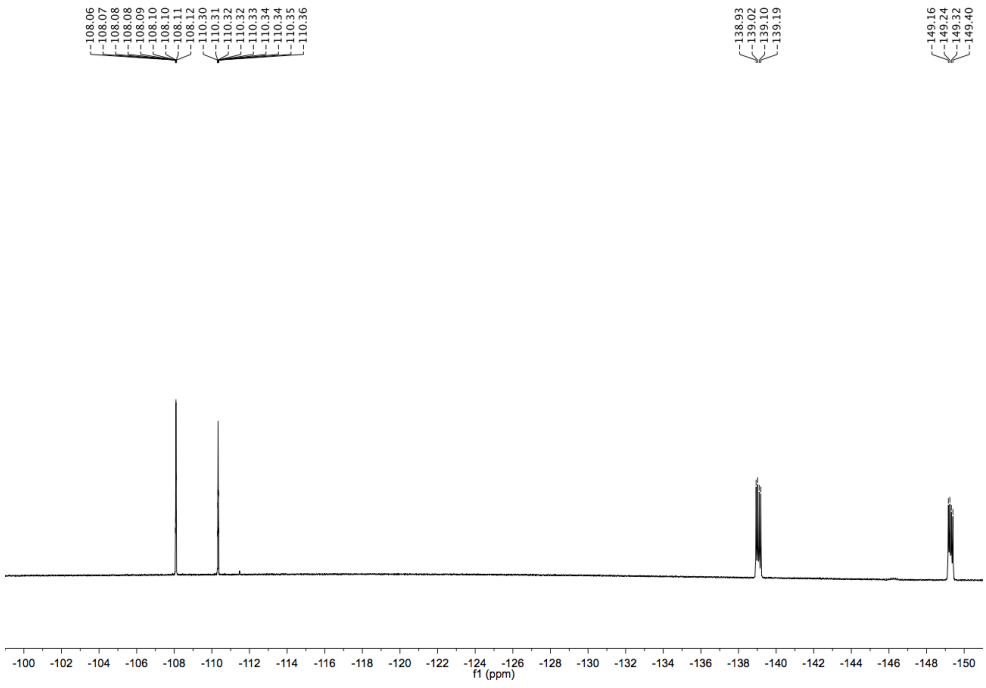
^{1}H NMR spectrum (500 MHz, acetone-*d6*)



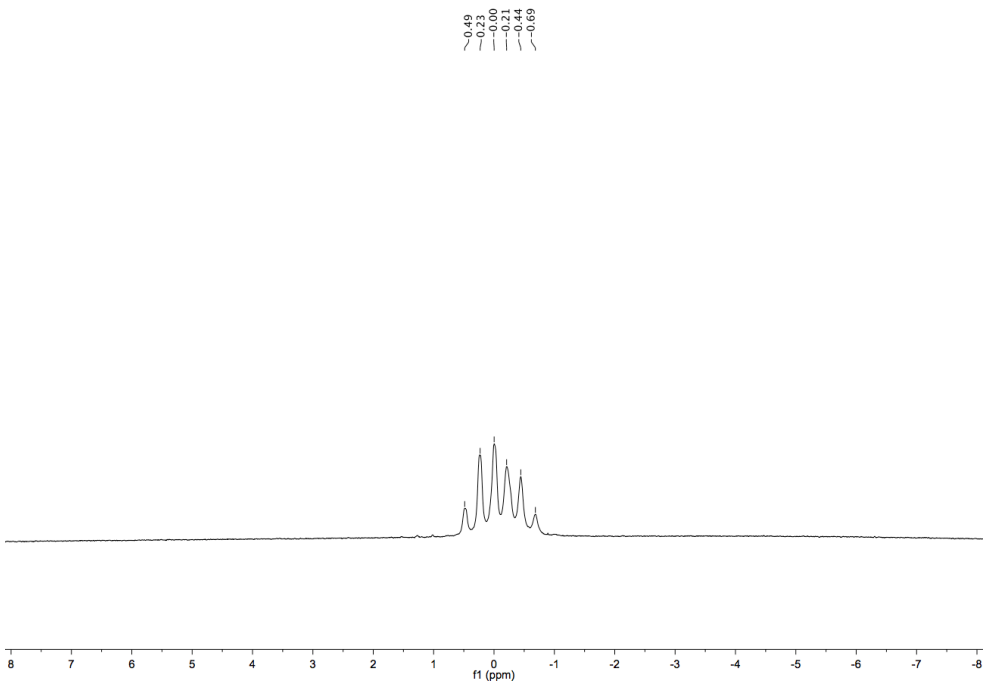
^{13}C NMR spectrum (151 MHz, acetone-*d6*)



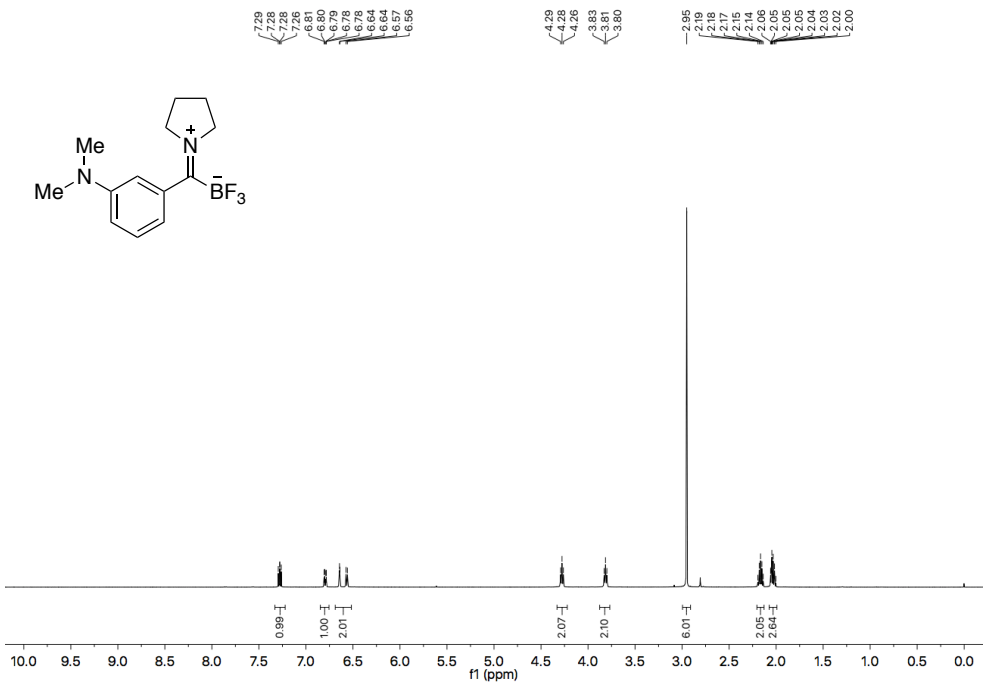
^{19}F NMR spectrum (470 MHz, acetone-*d6*)



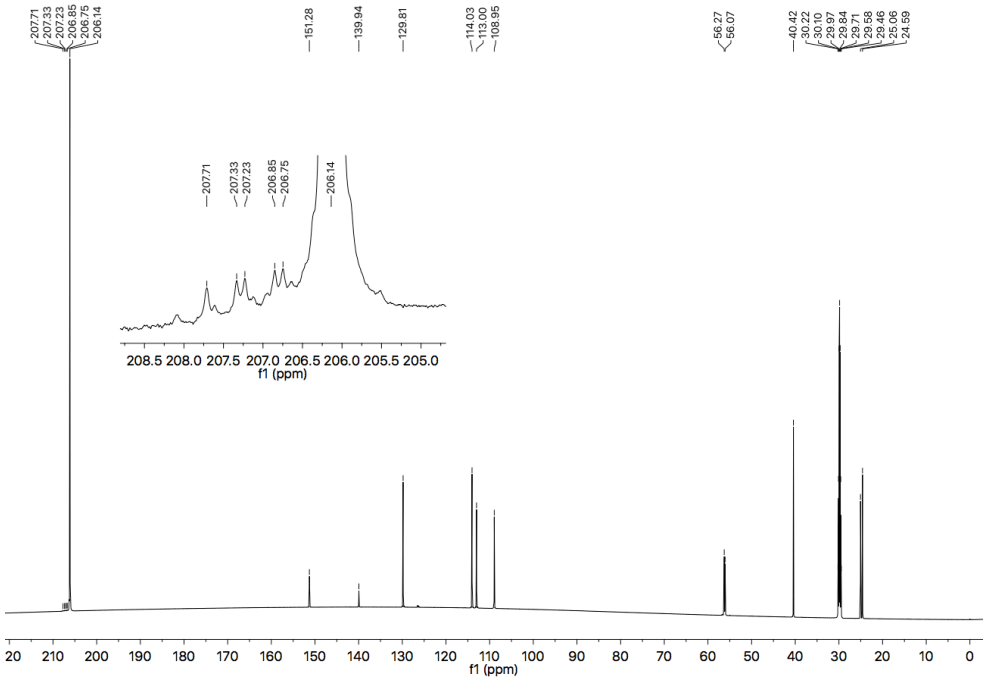
^{11}B NMR spectrum (160 MHz, acetone-*d6*)



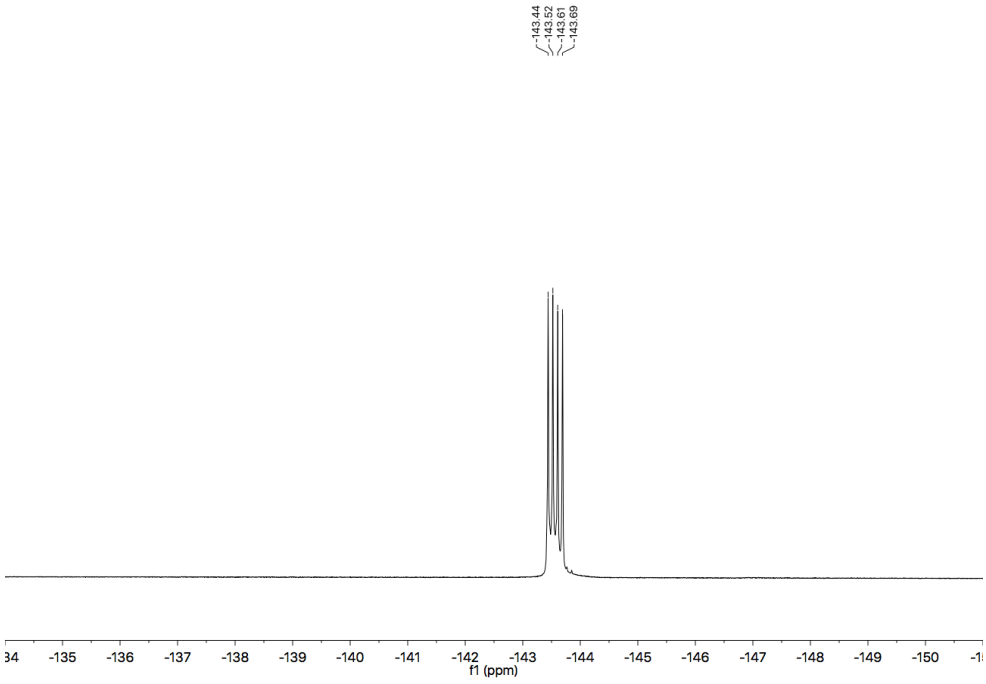
^{1}H NMR spectrum (500 MHz, acetone-*d6*)



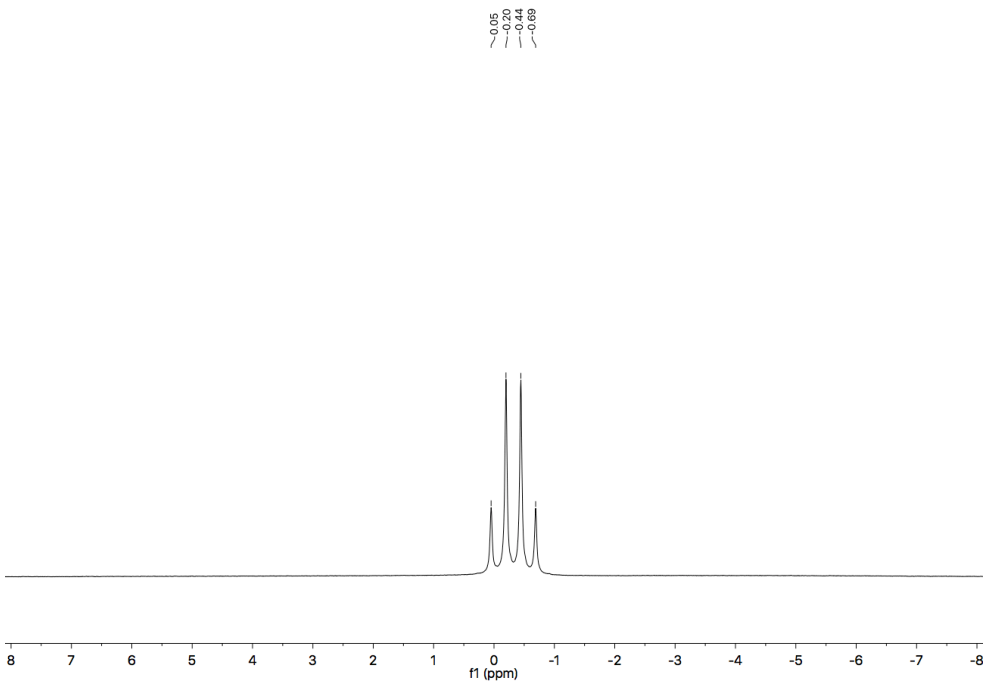
^{13}C NMR spectrum (151 MHz, acetone-*d6*)



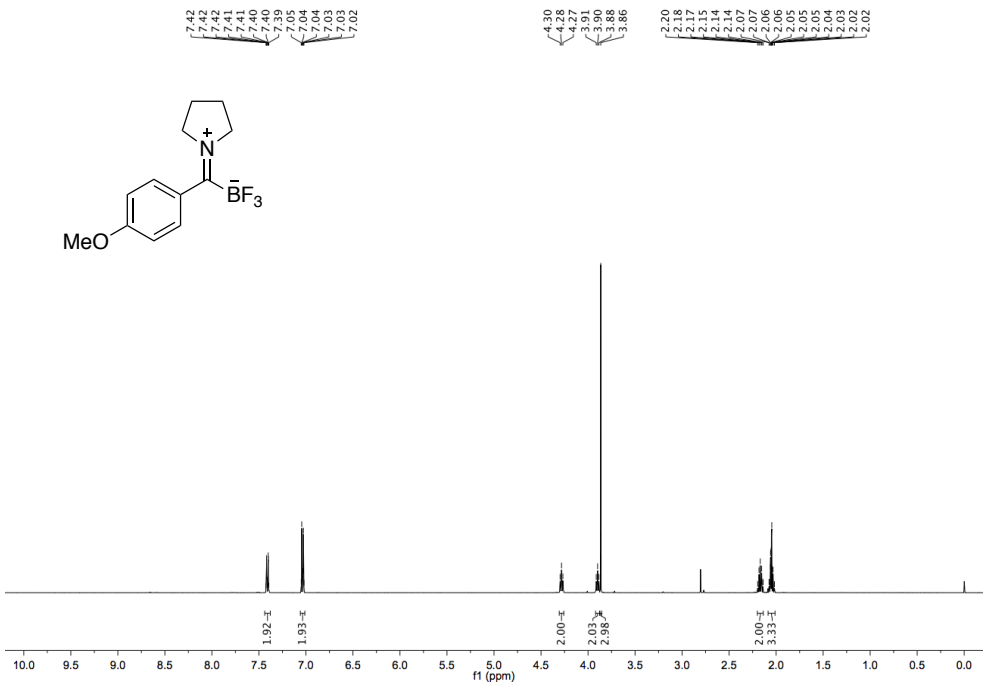
^{19}F NMR spectrum (470 MHz, acetone-*d6*)



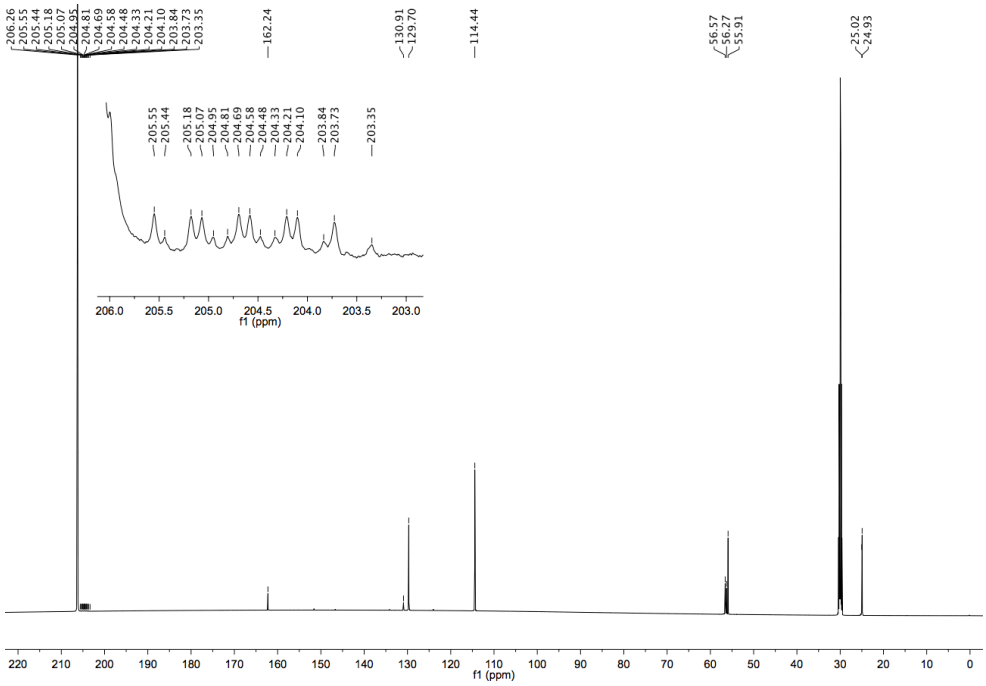
^{11}B NMR spectrum (160 MHz, acetone-*d6*)



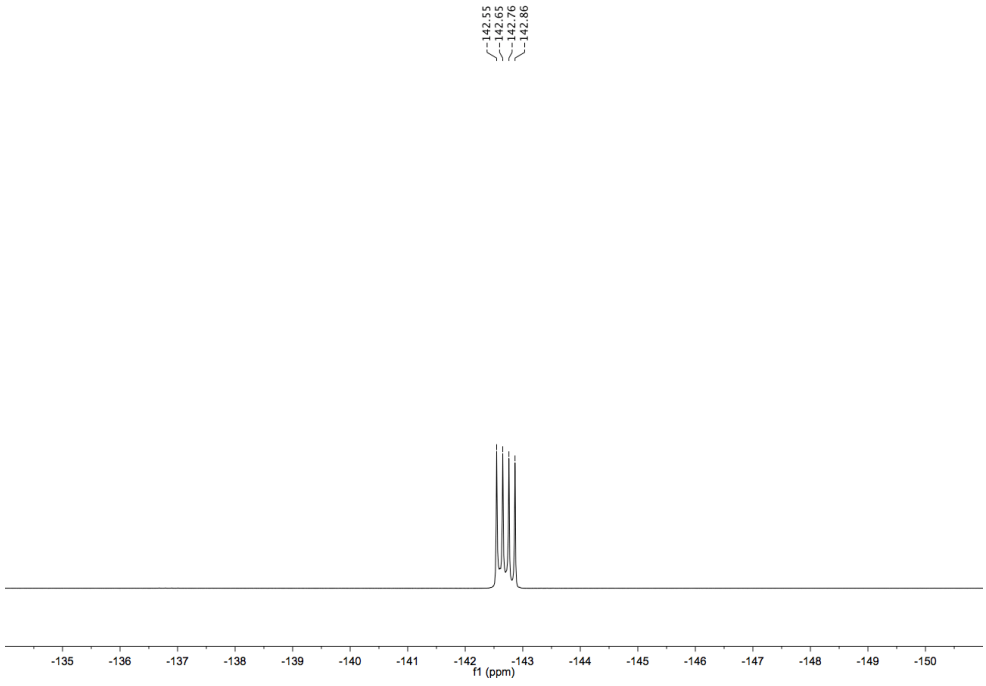
^{1}H NMR spectrum (500 MHz, acetone-*d6*)



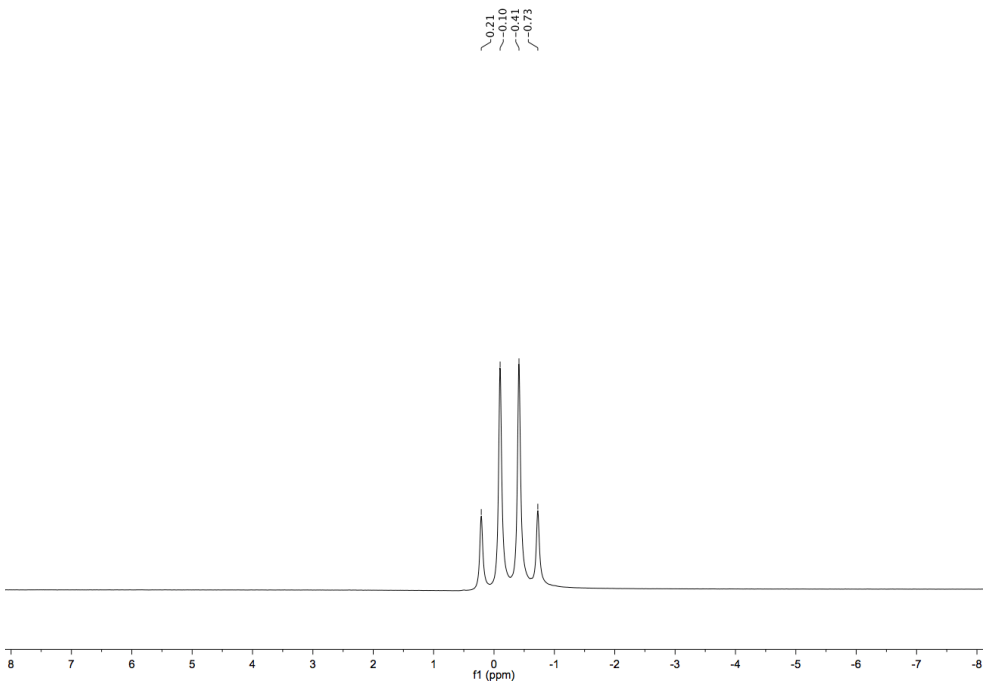
^{13}C NMR spectrum (151 MHz, acetone-*d6*)



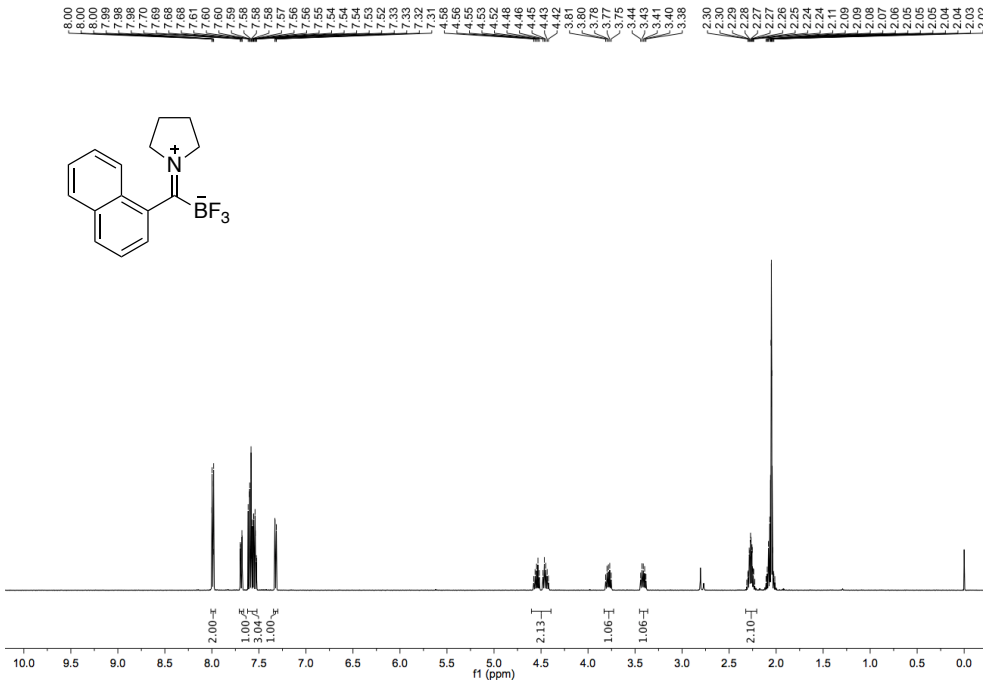
^{19}F NMR spectrum (376 MHz, acetone-*d6*)



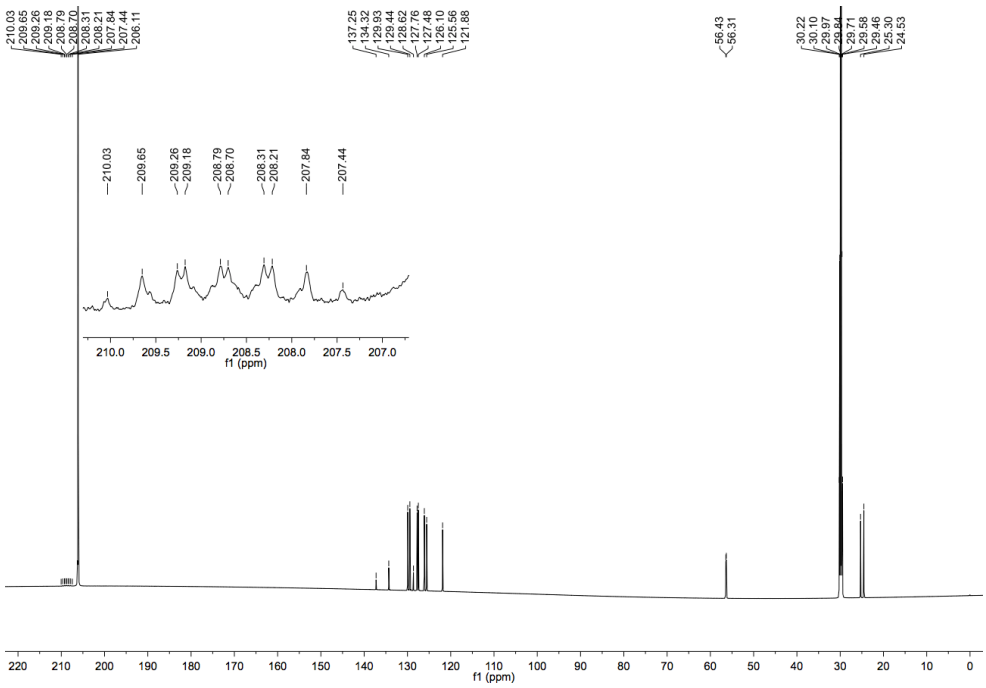
^{11}B NMR spectrum (128 MHz, acetone-*d6*)



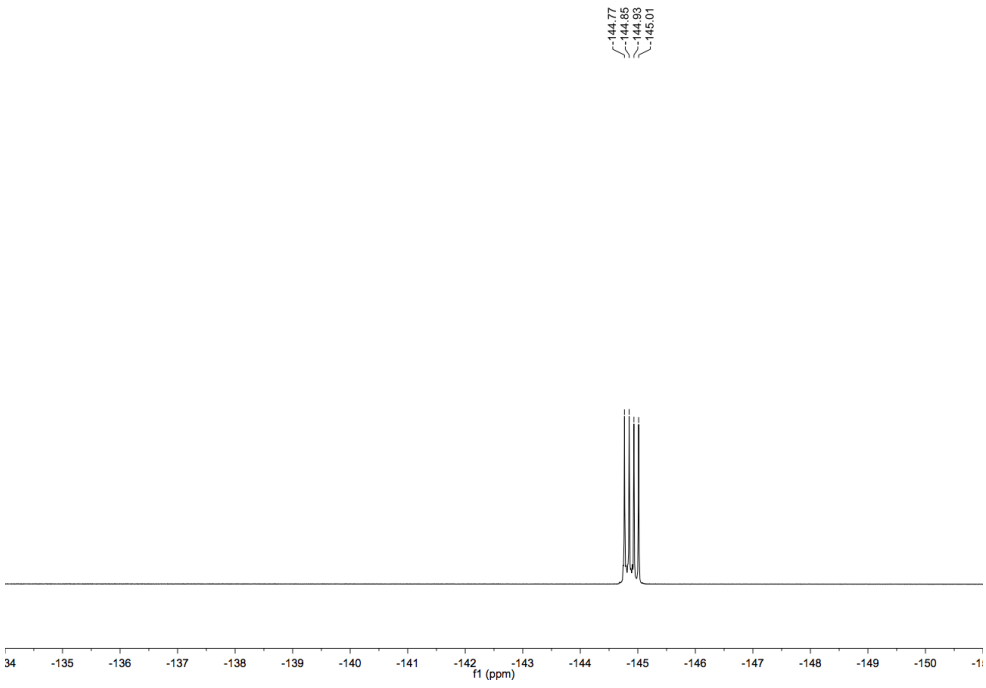
^{1}H NMR spectrum (500 MHz, acetone-*d6*)



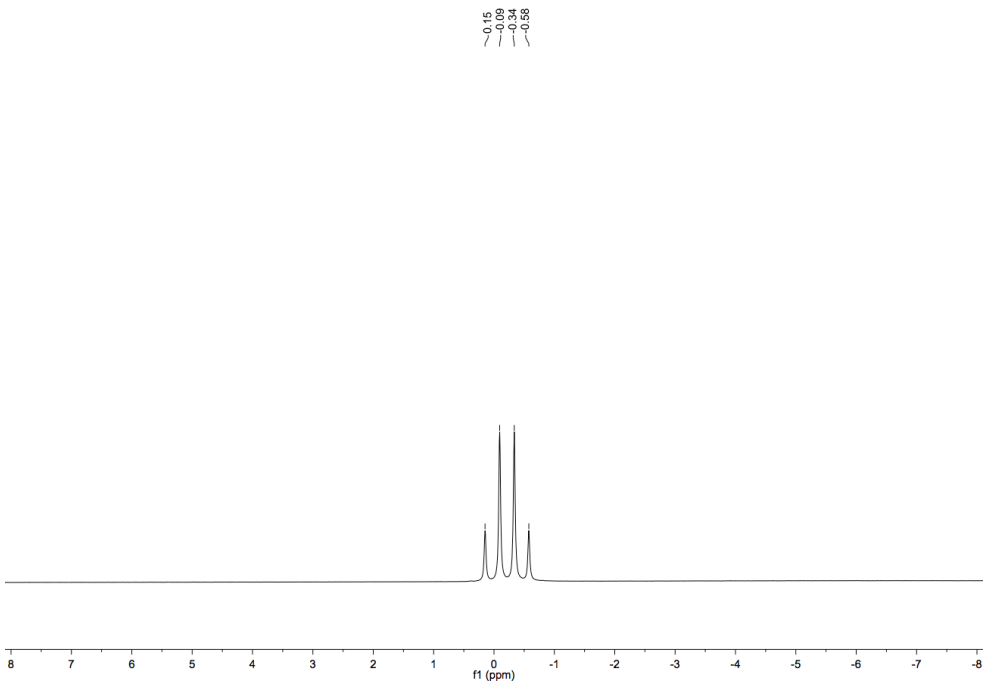
^{13}C NMR spectrum (151 MHz, acetone-*d6*)



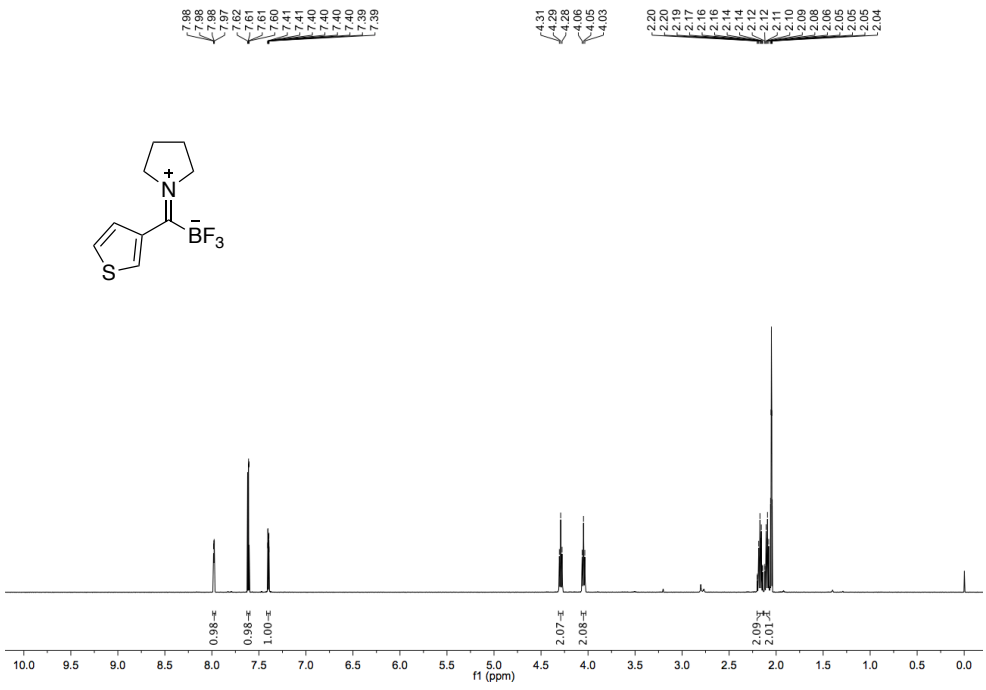
^{19}F NMR spectrum (470 MHz, acetone-*d6*)



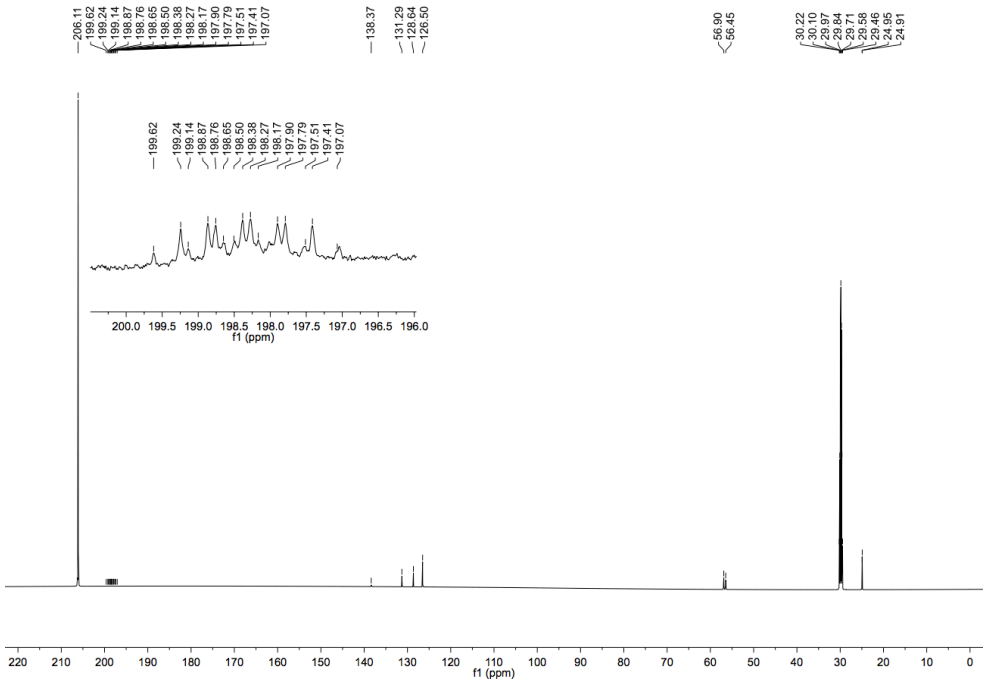
^{11}B NMR spectrum (160 MHz, acetone-*d6*)



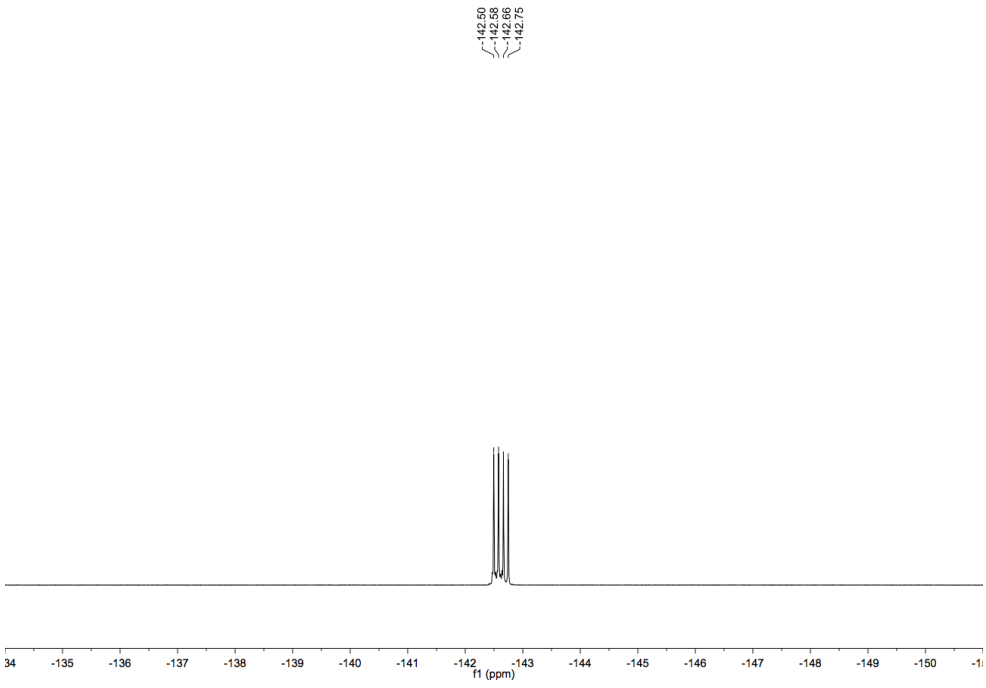
^{1}H NMR spectrum (500 MHz, acetone-*d6*)



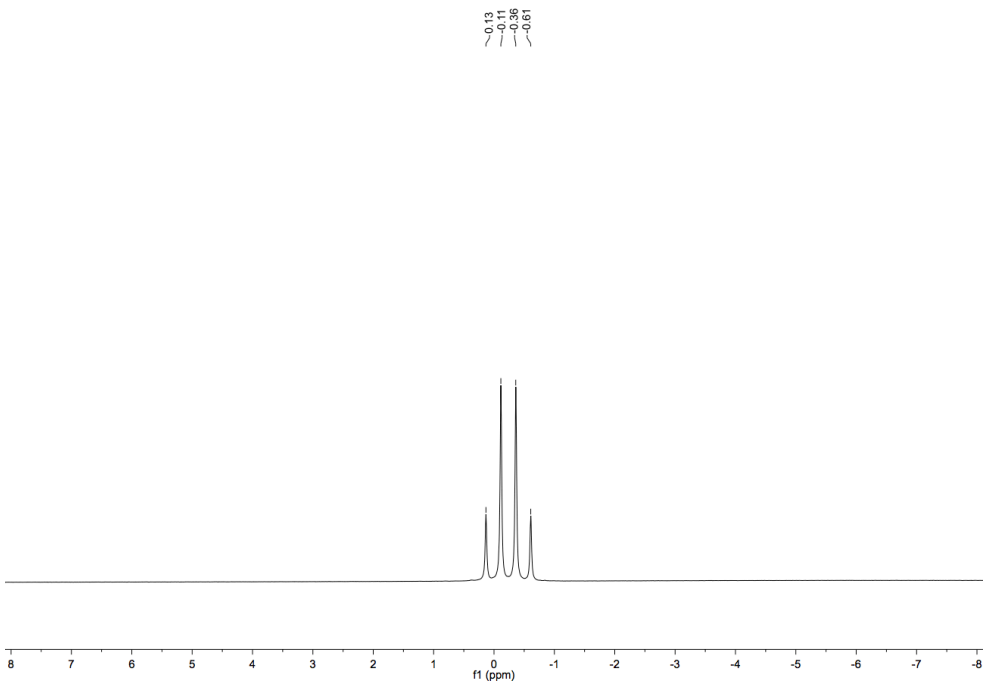
^{13}C NMR spectrum (151 MHz, acetone-*d6*)



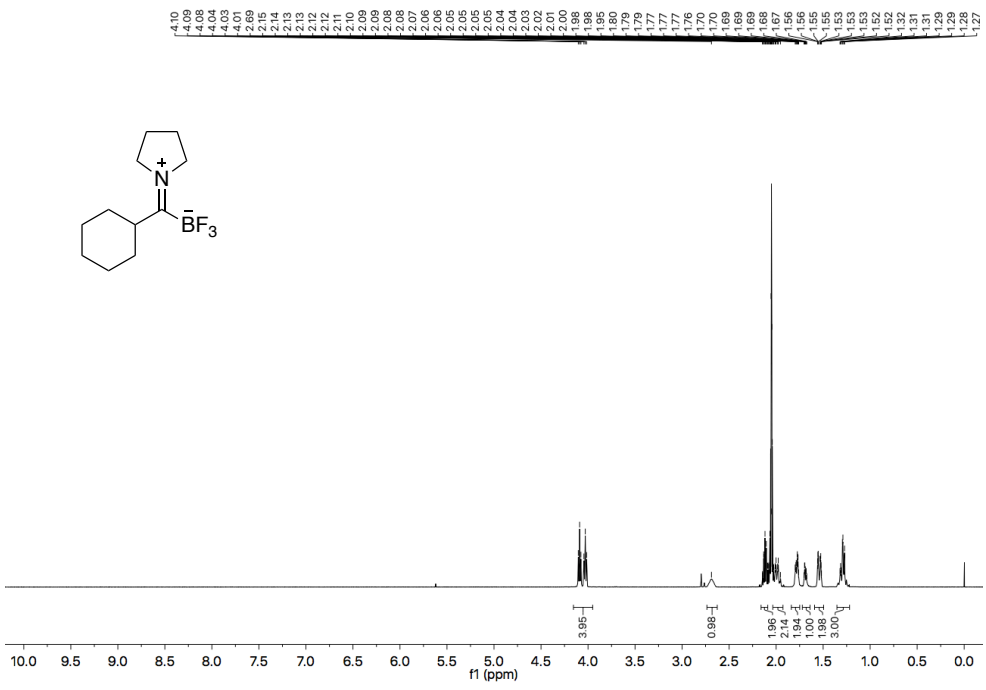
^{19}F NMR spectrum (470 MHz, acetone-*d6*)



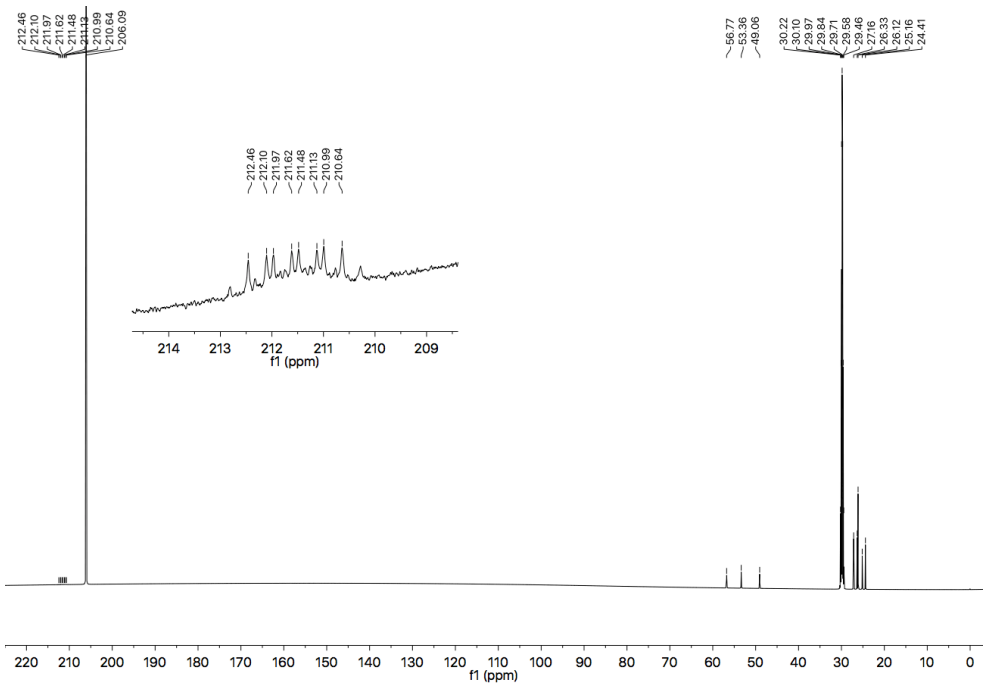
^{11}B NMR spectrum (160 MHz, acetone-*d6*)



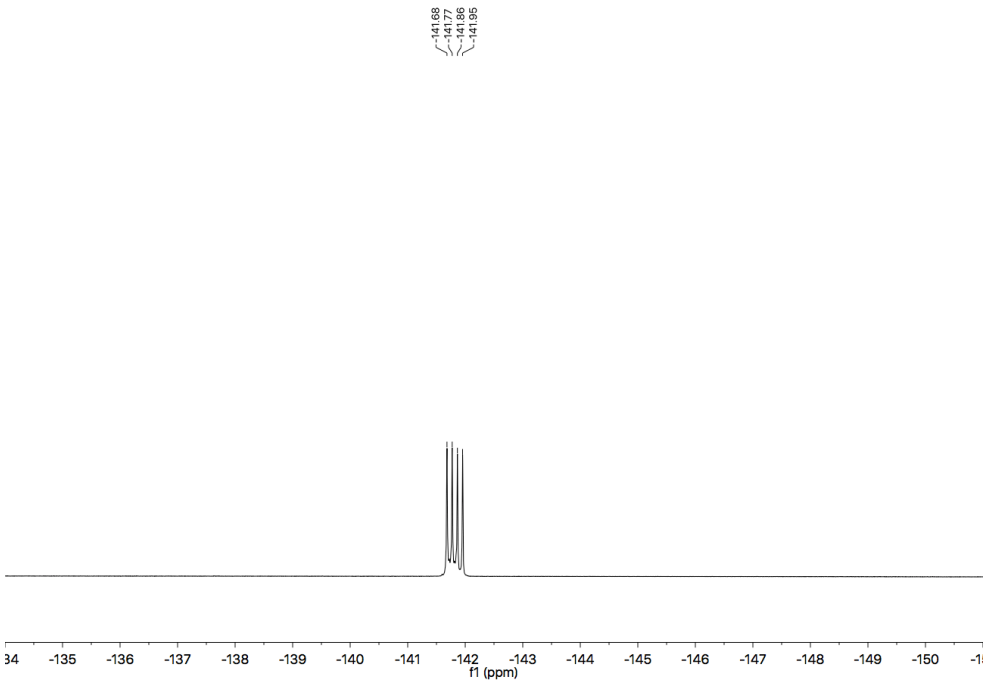
^{1}H NMR spectrum (500 MHz, acetone-*d6*)



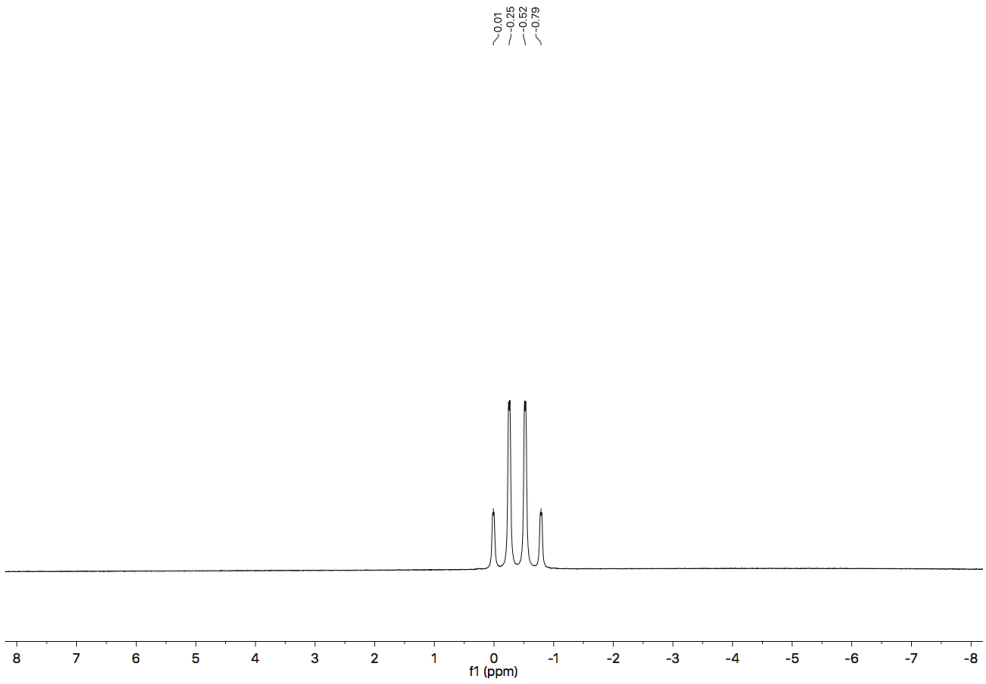
^{13}C NMR spectrum (151 MHz, acetone-*d6*)



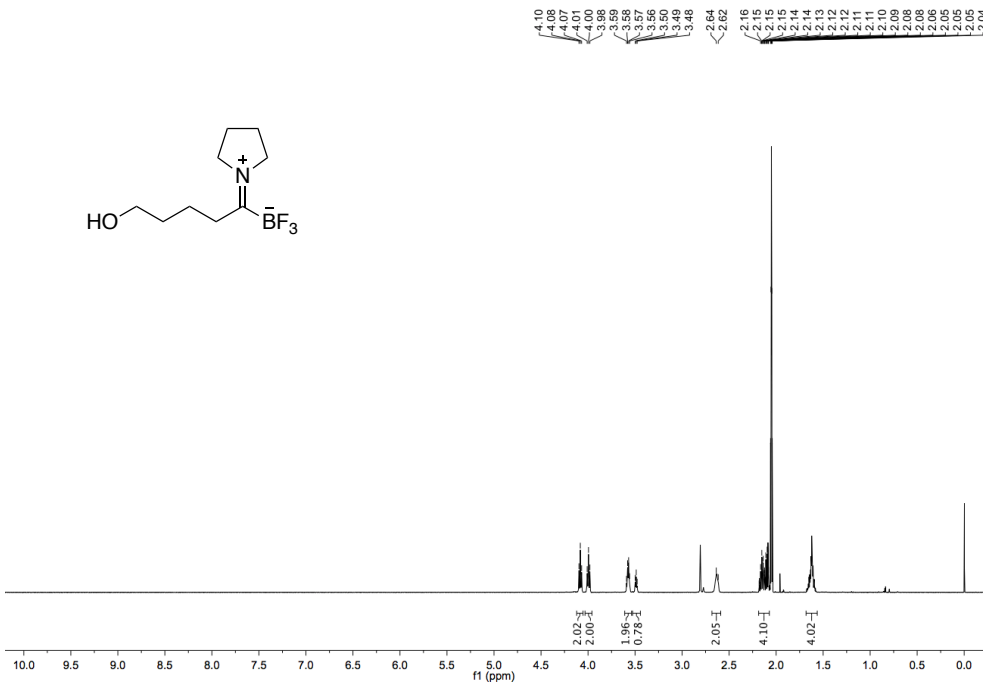
^{19}F NMR spectrum (470 MHz, acetone-*d6*)



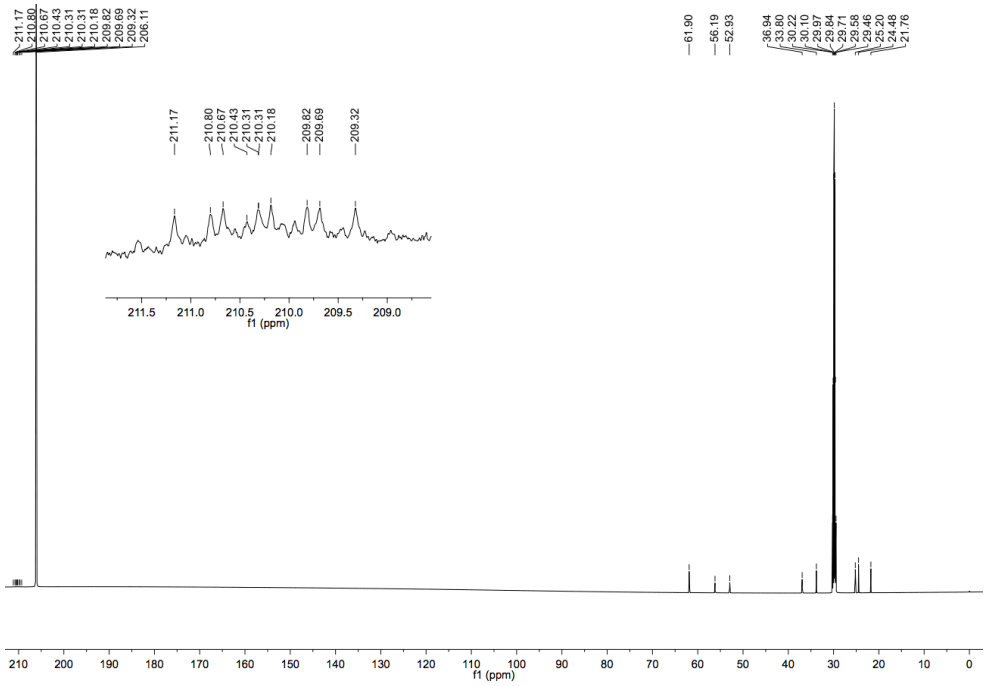
^{11}B NMR spectrum (160 MHz, acetone-*d6*)



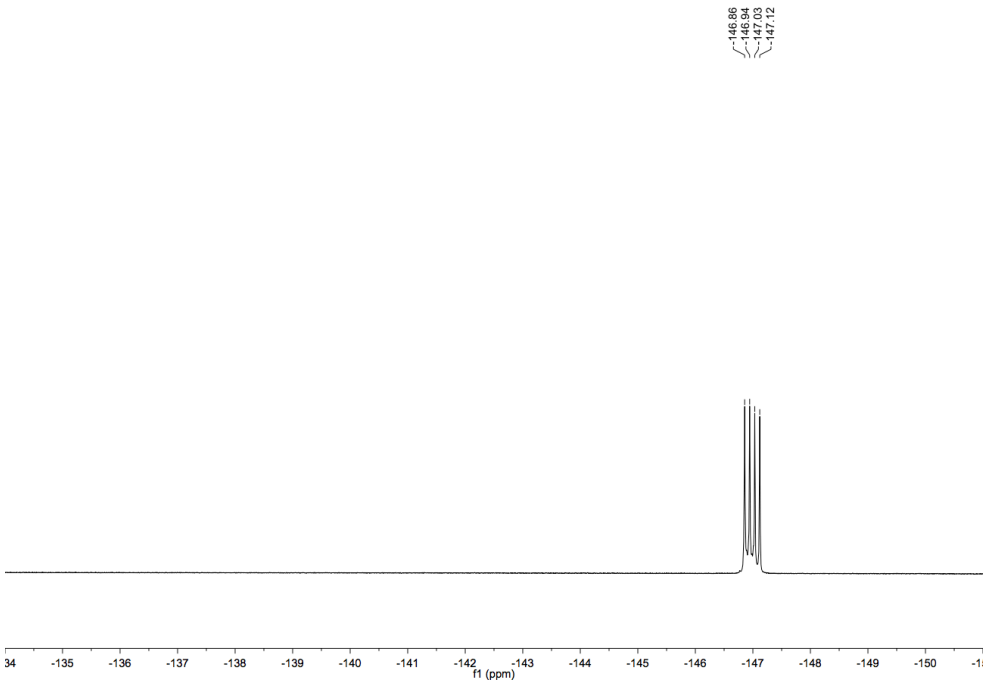
^{1}H NMR spectrum (500 MHz, acetone-*d6*)



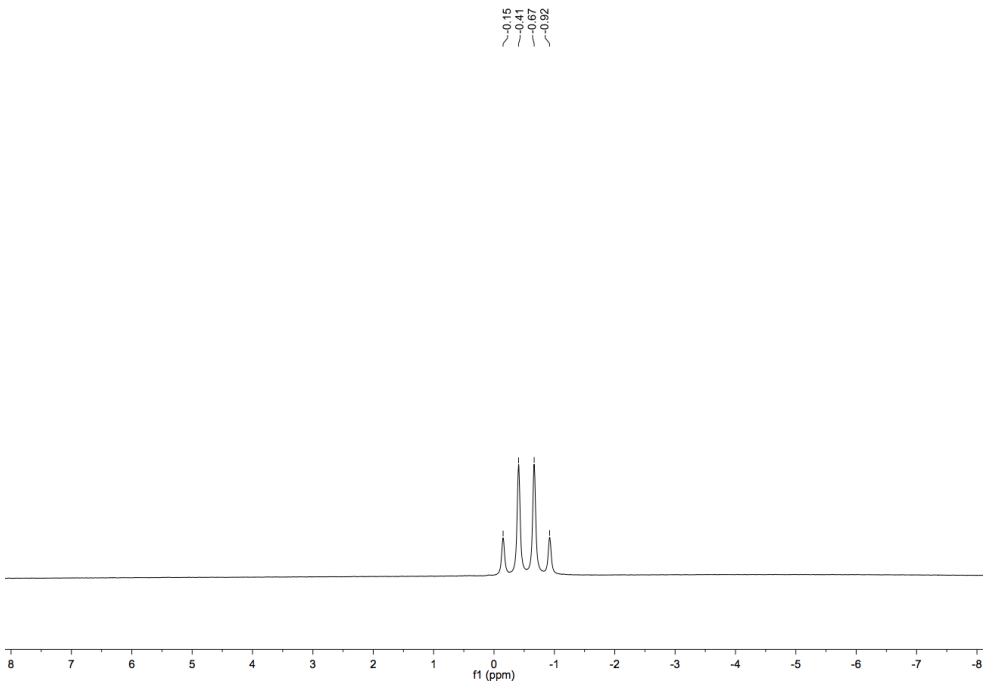
^{13}C NMR spectrum (151 MHz, acetone-*d6*)



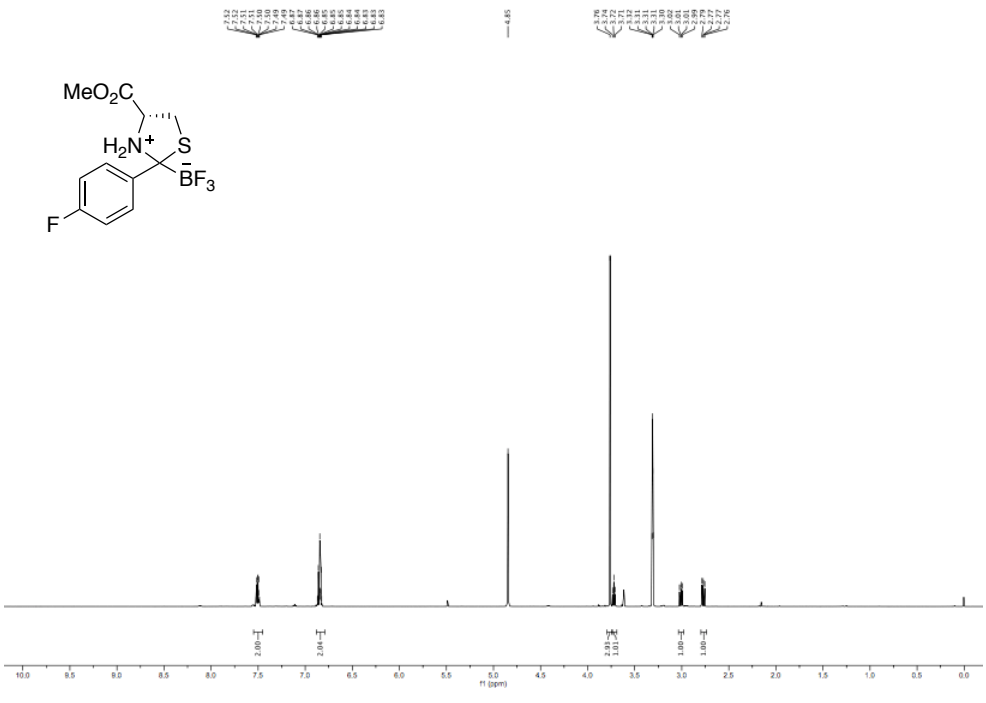
^{19}F NMR spectrum (470 MHz, acetone-*d6*)



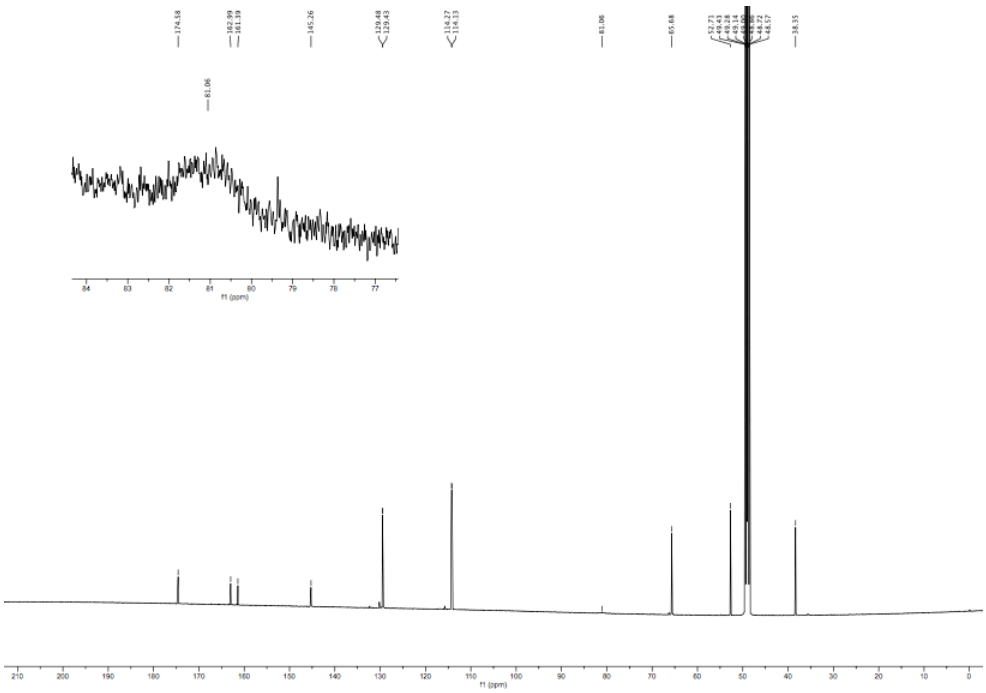
^{11}B NMR spectrum (160 MHz, acetone-*d6*)



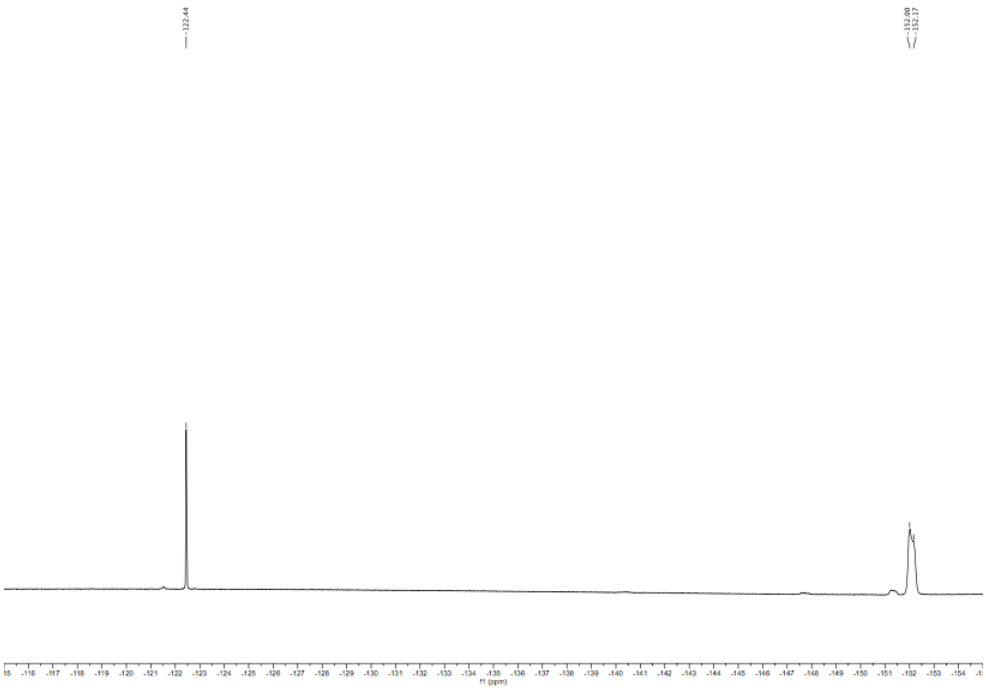
^{1}H NMR spectrum (600 MHz, methanol-*d4*)



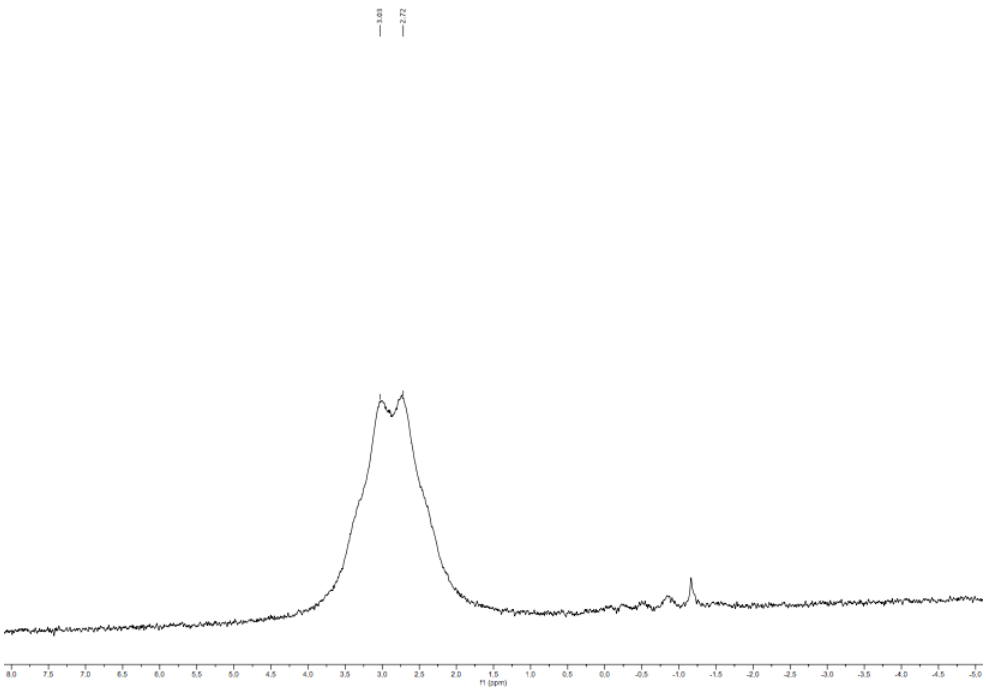
^{13}C NMR spectrum (151 MHz, methanol-*d4*)



^{19}F NMR spectrum (470 MHz, methanol-*d4*)

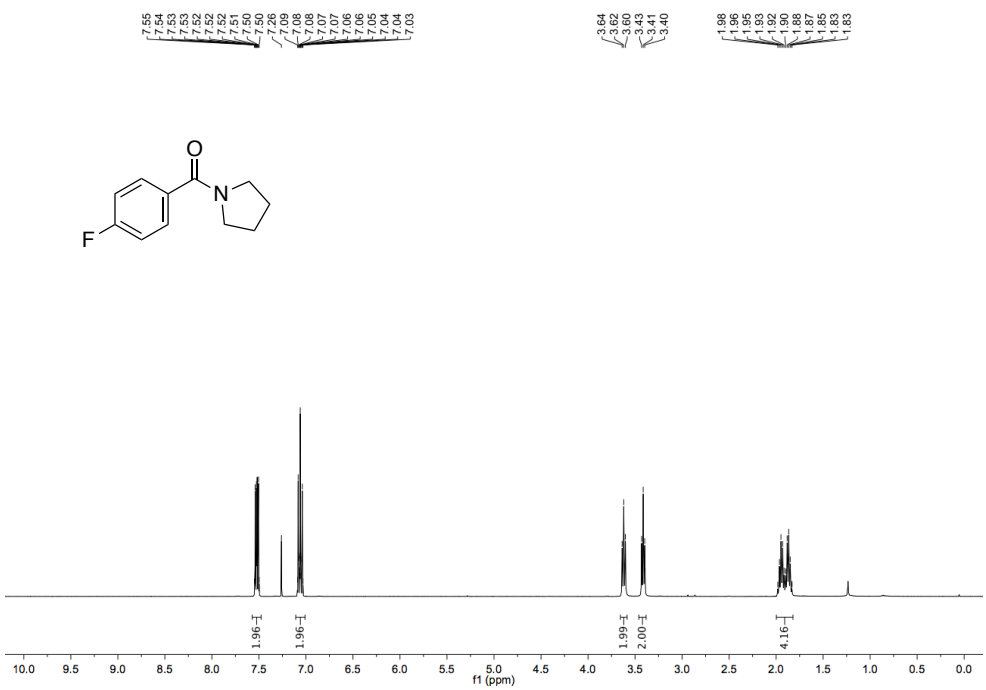


^{11}B NMR spectrum (160 MHz, methanol-*d4*)

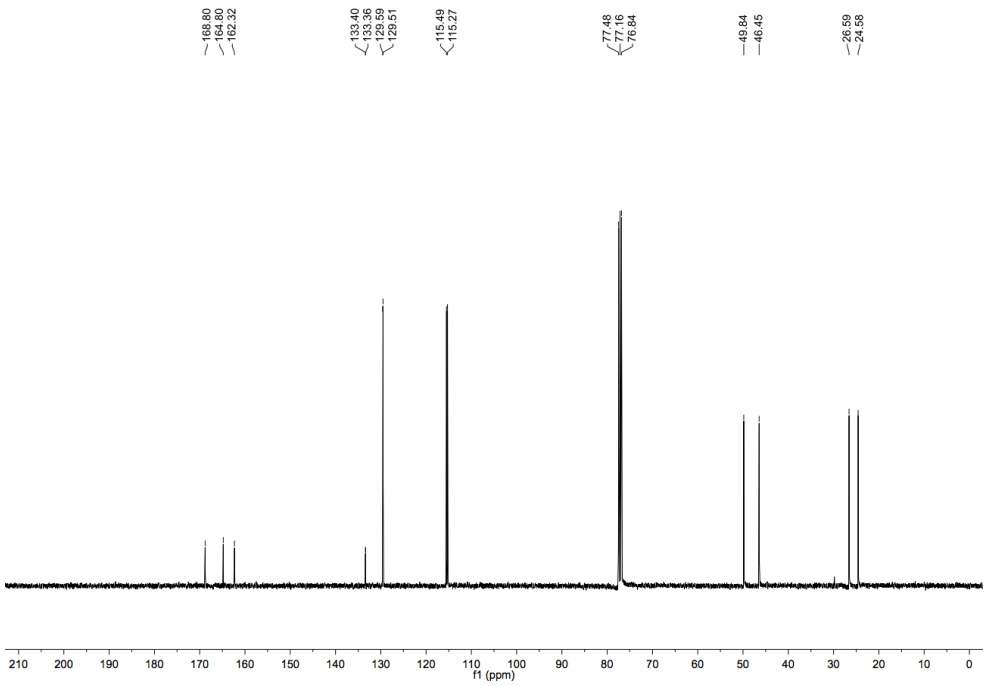


8.3. Amides

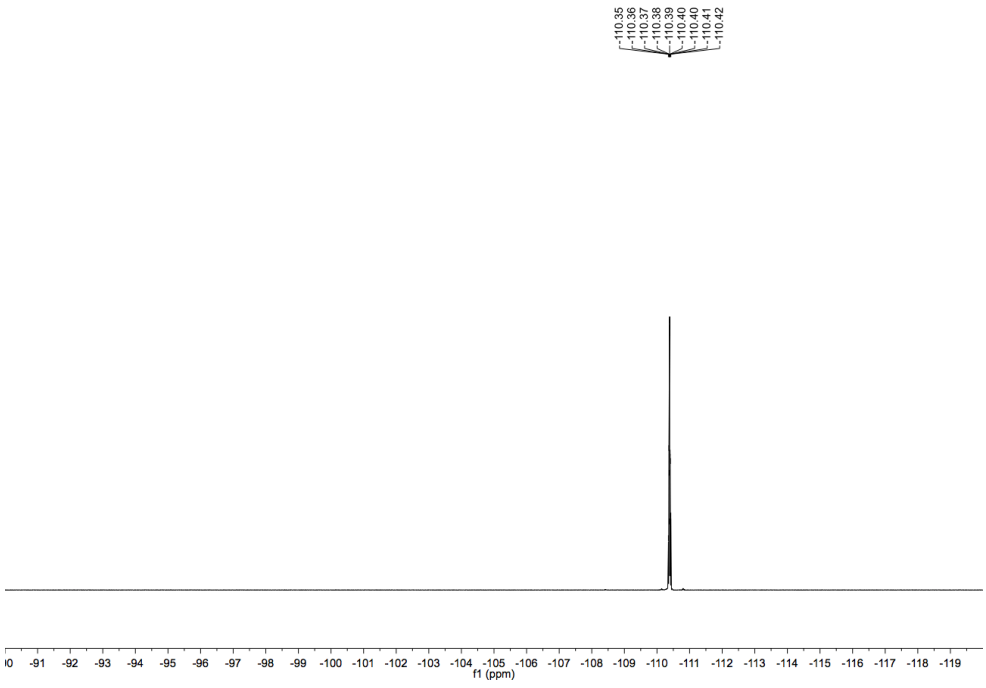
^{1}H NMR spectrum (400 MHz, chloroform-*d*)



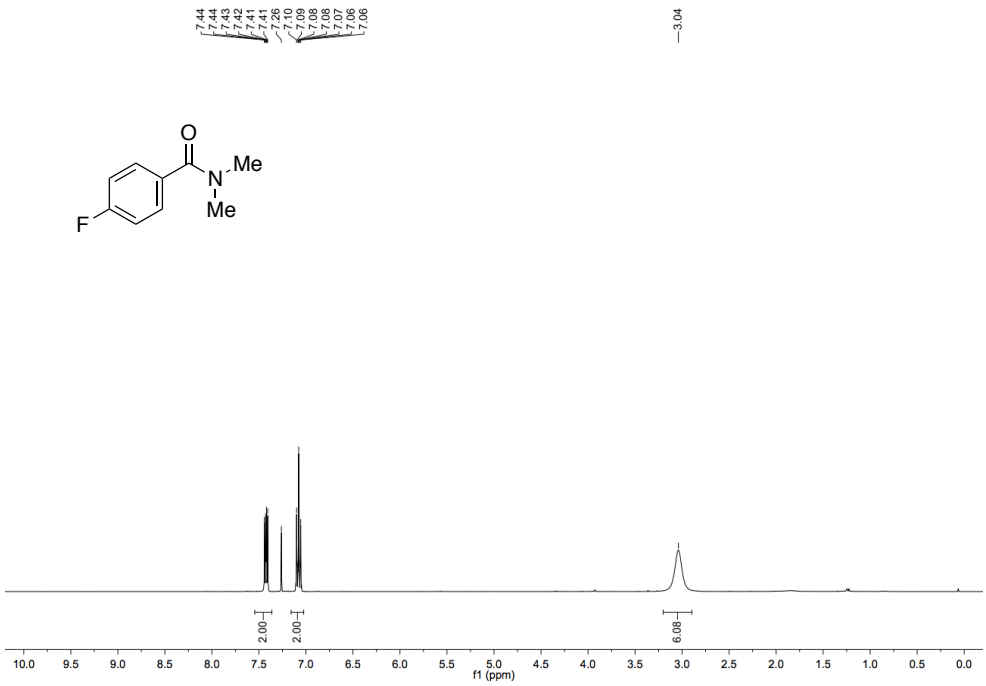
^{13}C NMR spectrum (101 MHz, chloroform-*d*)



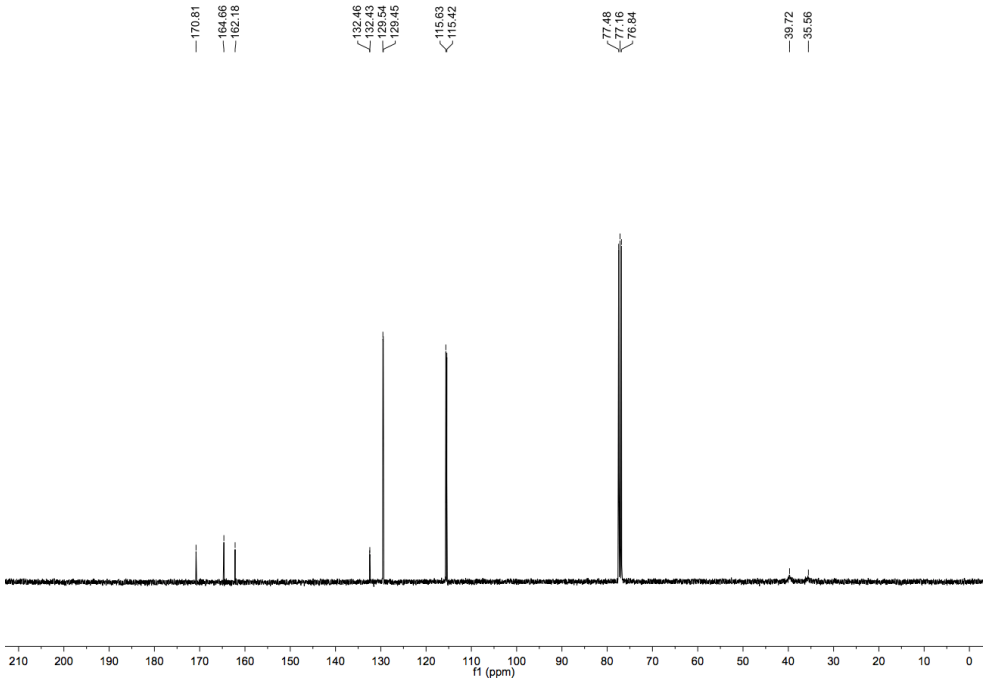
^{19}F NMR spectrum (376 MHz, chloroform-*d*)



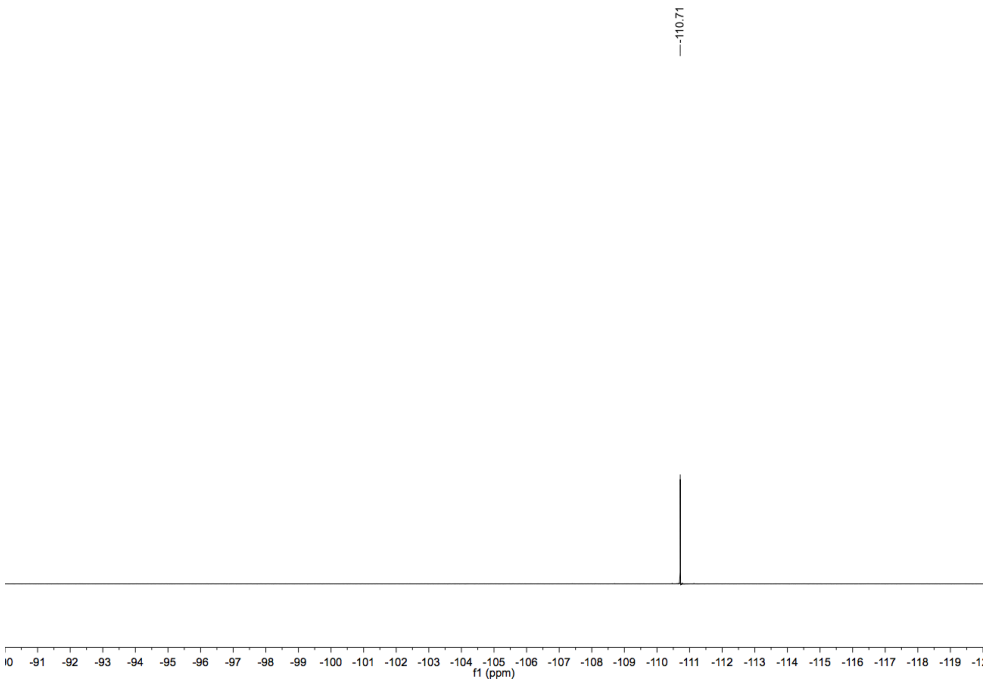
^{1}H NMR spectrum (400 MHz, chloroform-*d*)



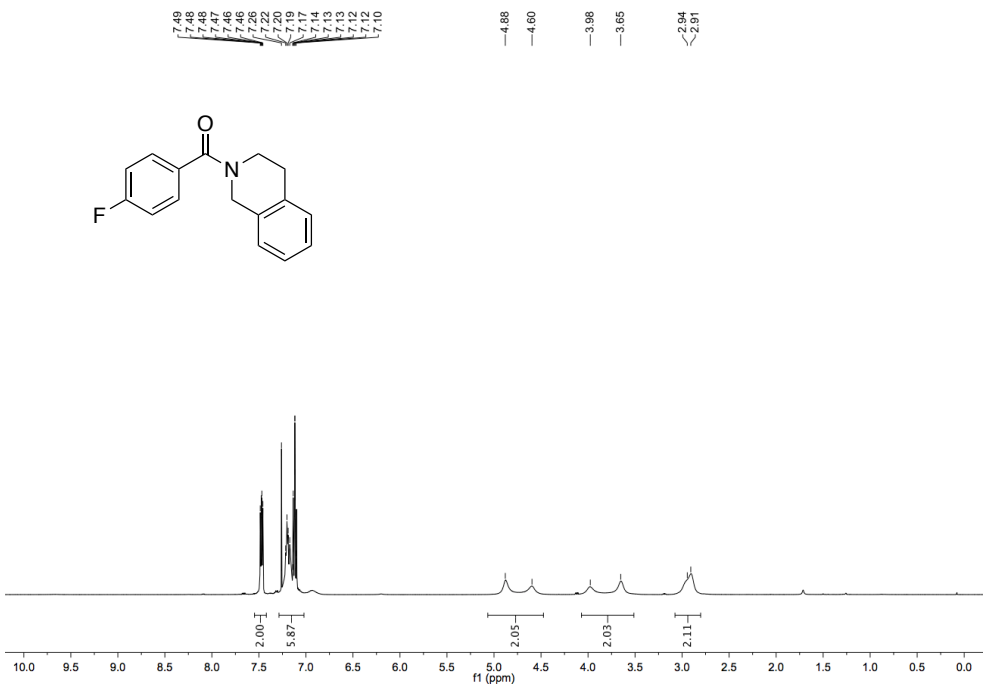
^{13}C NMR spectrum (101 MHz, chloroform-*d*)



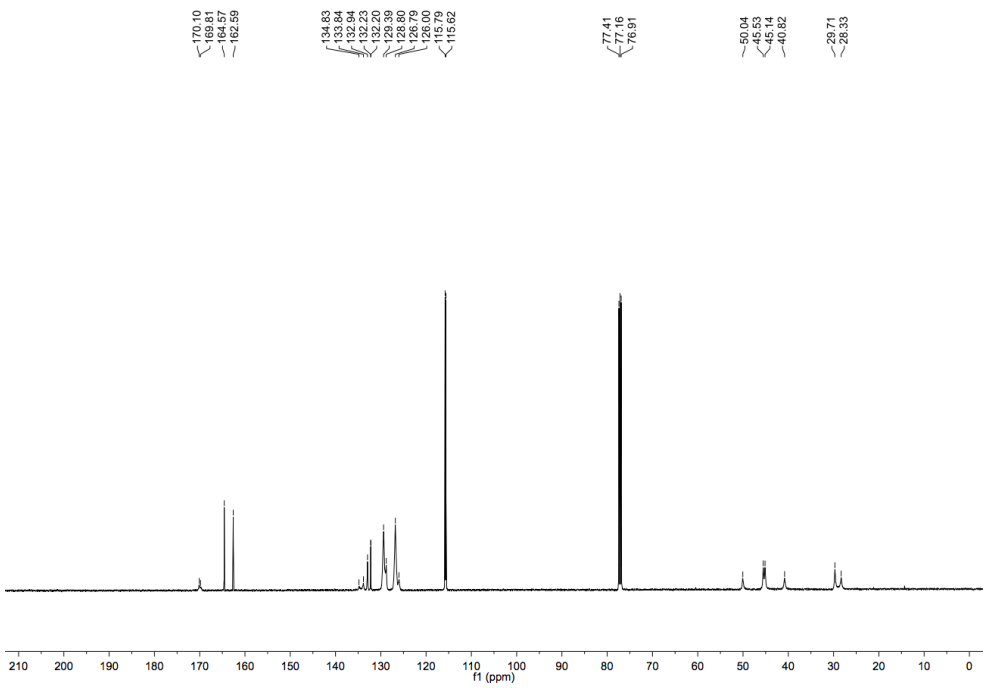
^{19}F NMR spectrum (376 MHz, chloroform-*d*)



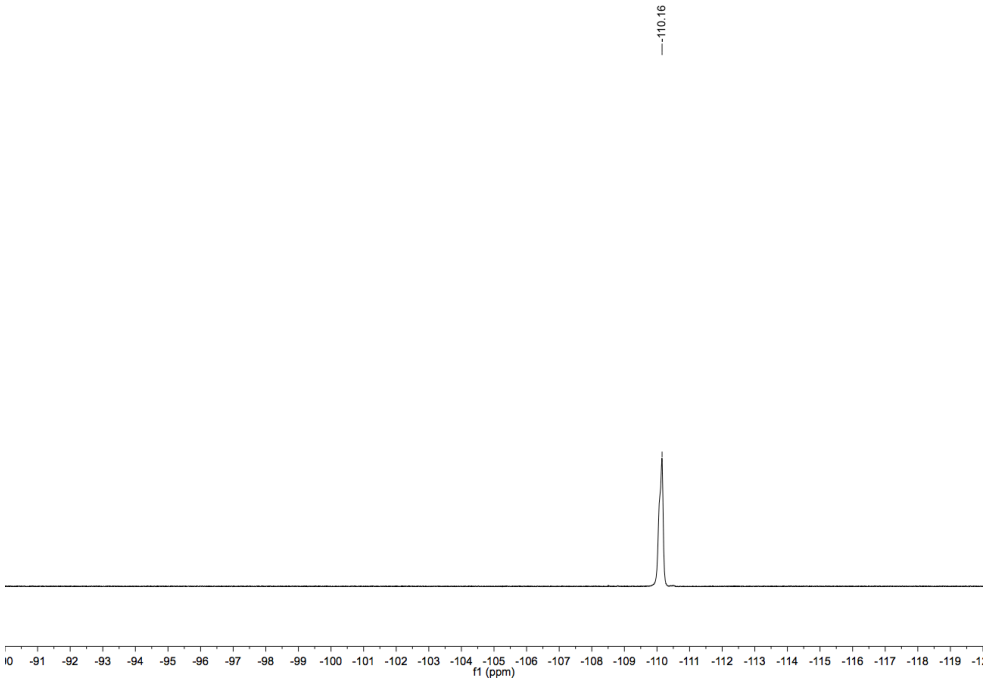
^{1}H NMR spectrum (500 MHz, chloroform-*d*)



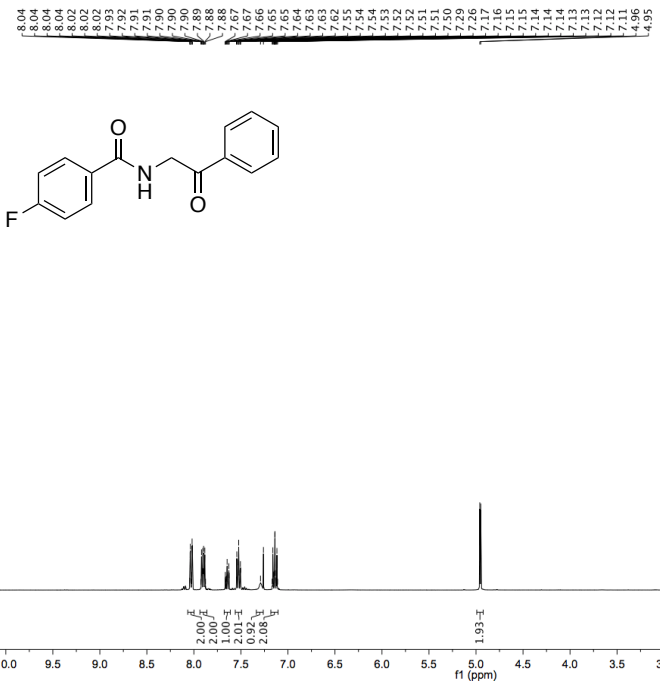
^{13}C NMR spectrum (126 MHz, chloroform-*d*)



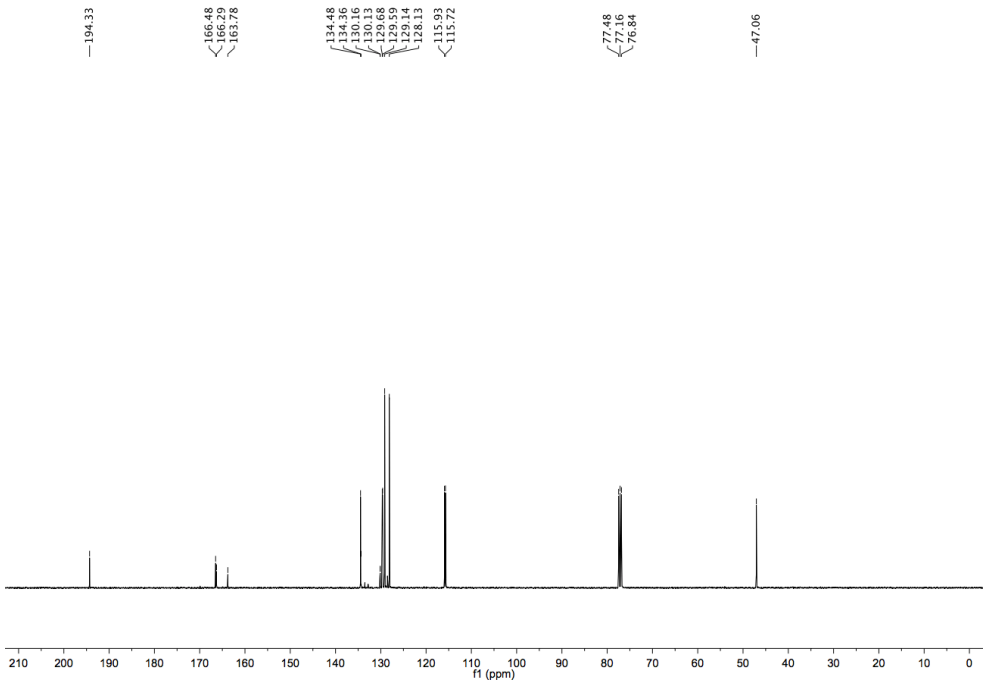
^{19}F NMR spectrum (470 MHz, chloroform-*d*)



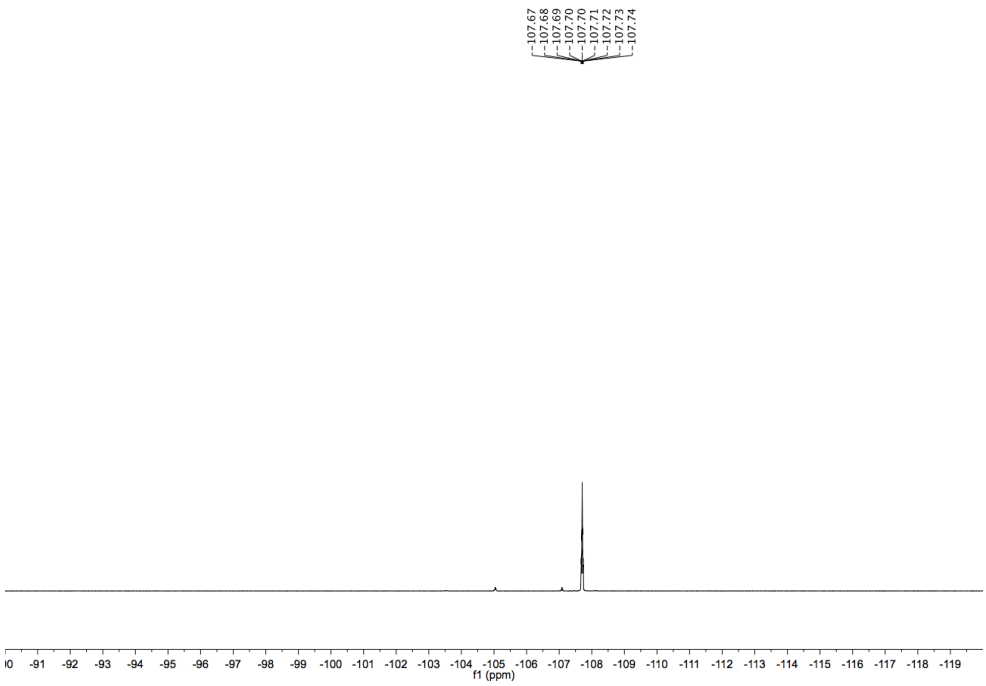
^{1}H NMR spectrum (400 MHz, chloroform-*d*)



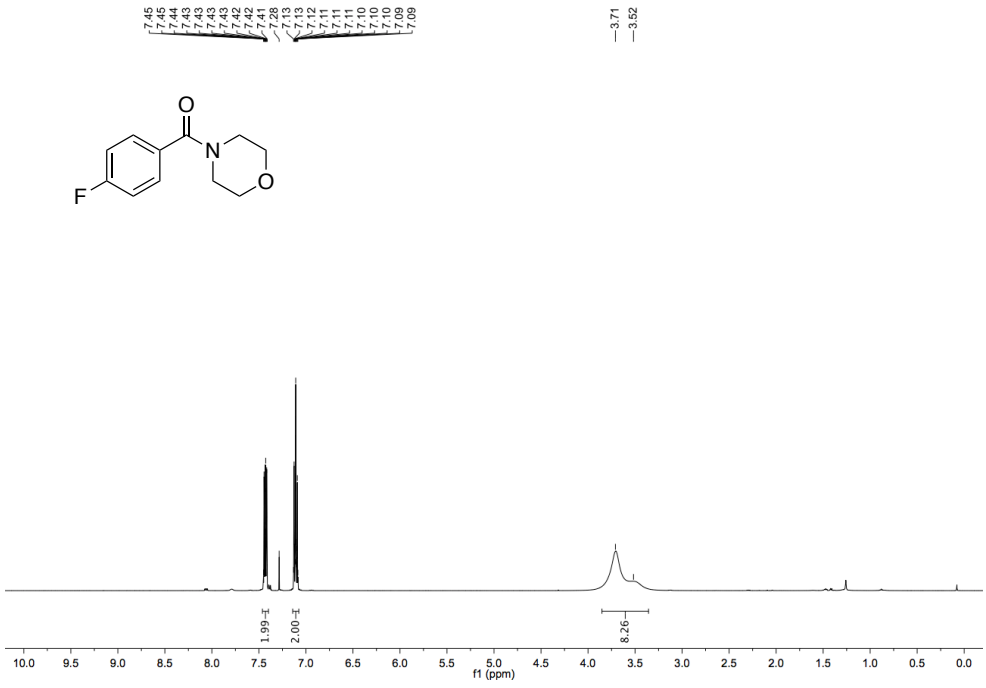
^{13}C NMR spectrum (101 MHz, chloroform-*d*)



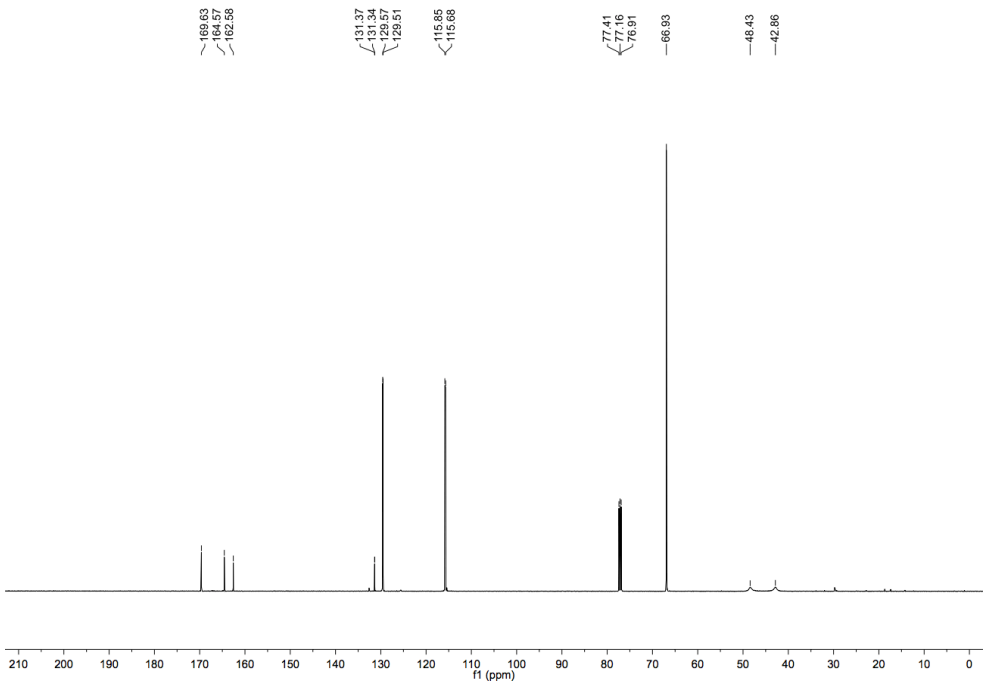
^{19}F NMR spectrum (376 MHz, chloroform-*d*)



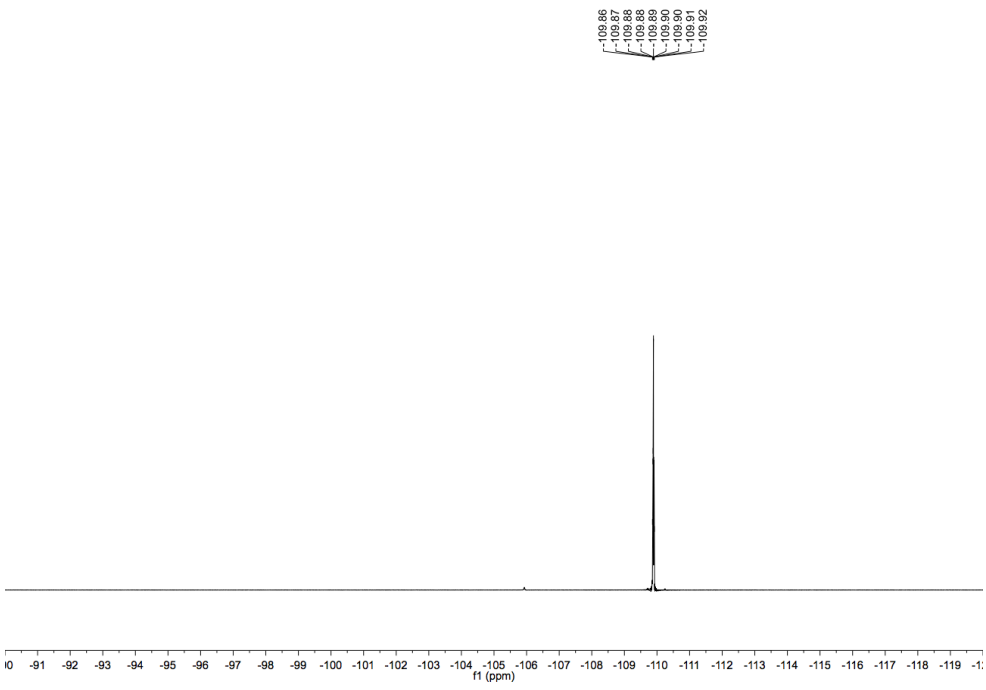
^{1}H NMR spectrum (500 MHz, chloroform-*d*)



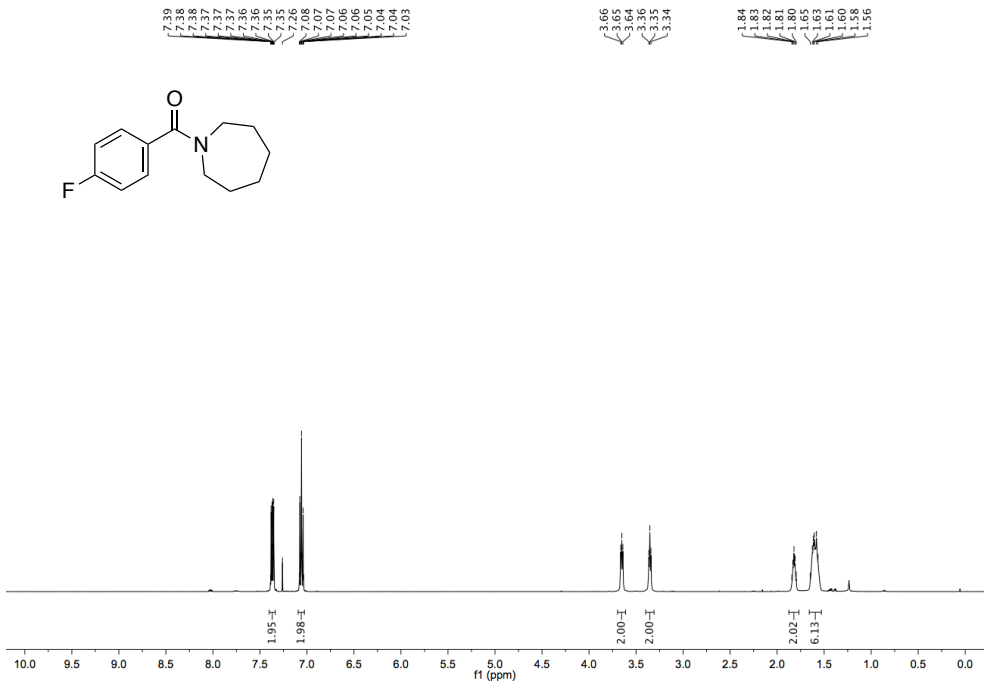
^{13}C NMR spectrum (126 MHz, chloroform-*d*)



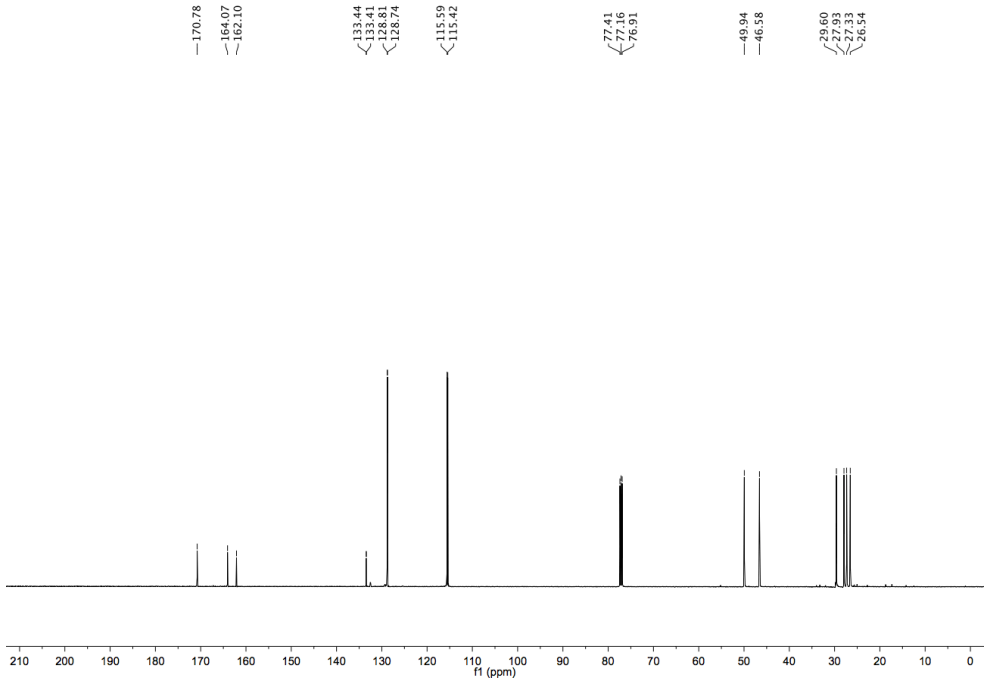
^{19}F NMR spectrum (470 MHz, chloroform-*d*)



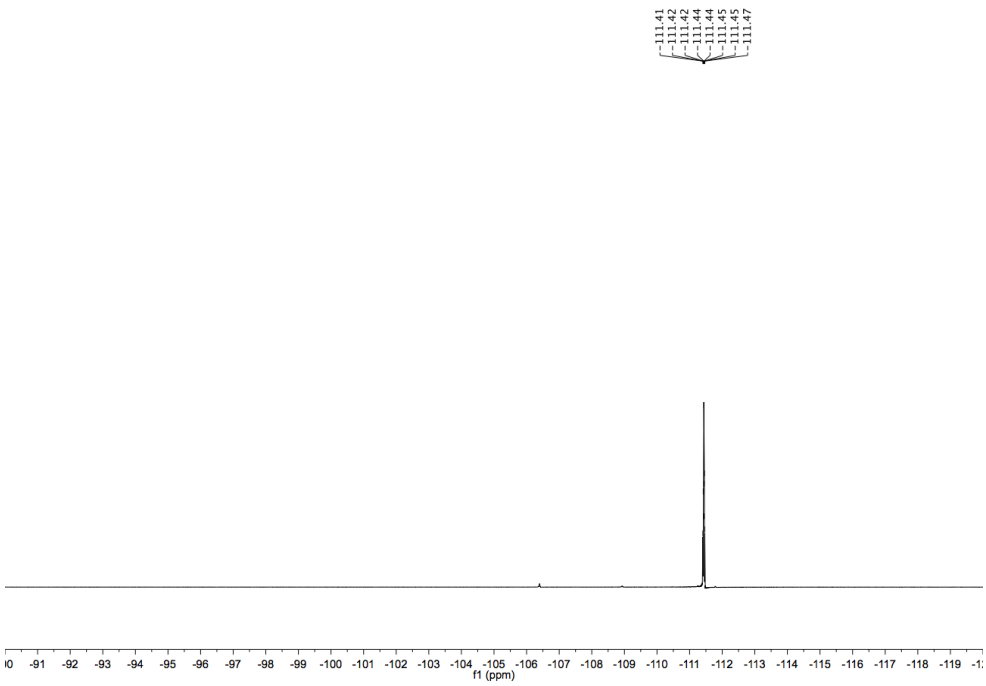
^{1}H NMR spectrum (500 MHz, chloroform-*d*)



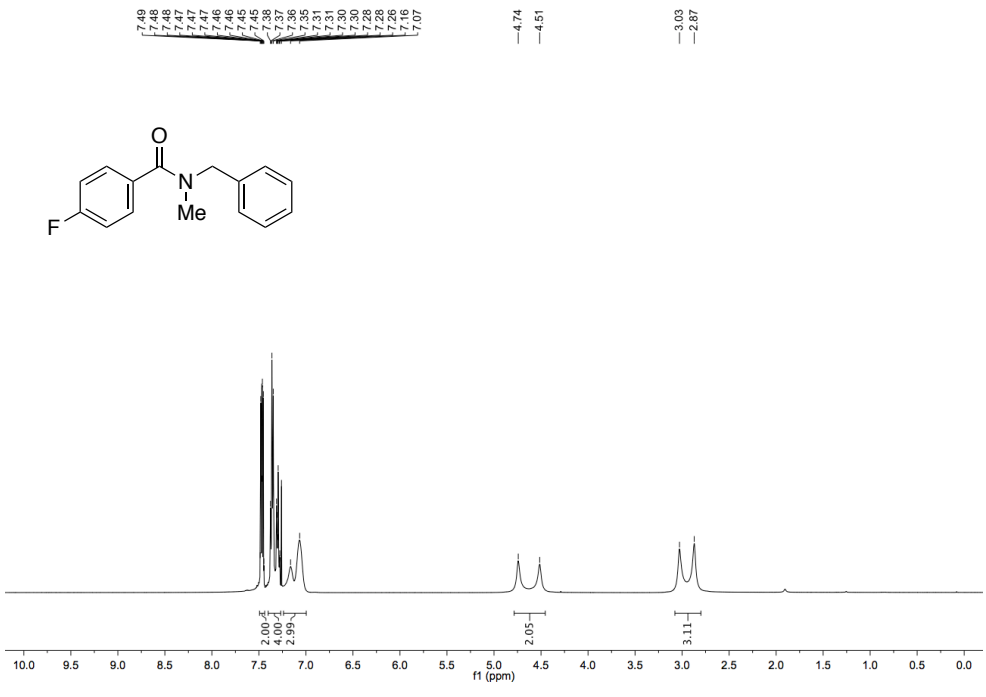
^{13}C NMR spectrum (126 MHz, chloroform-*d*)



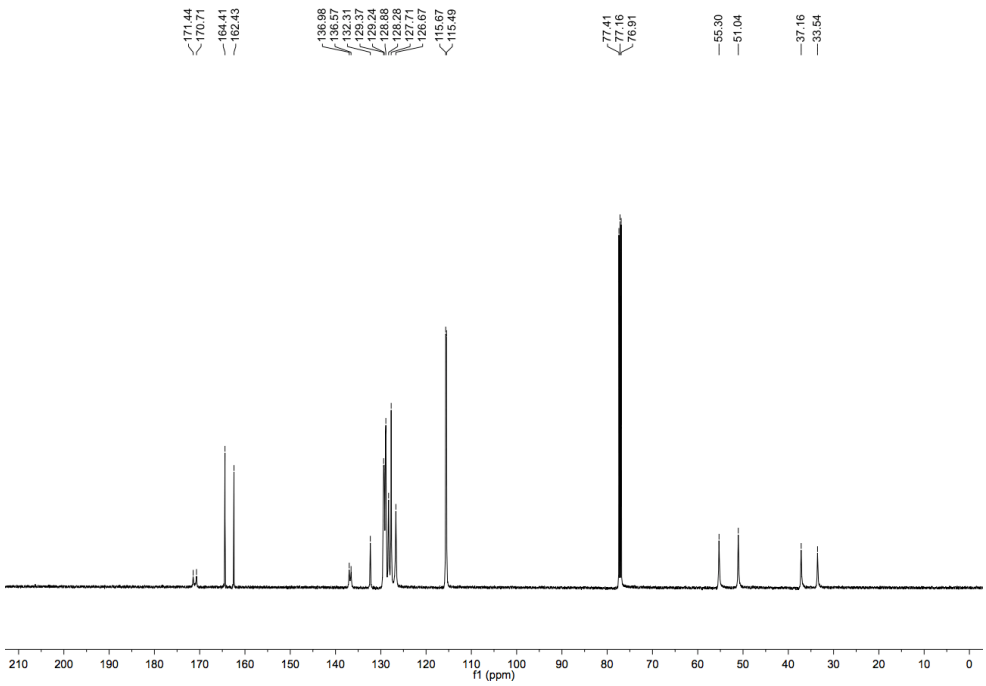
^{19}F NMR spectrum (470 MHz, chloroform-*d*)



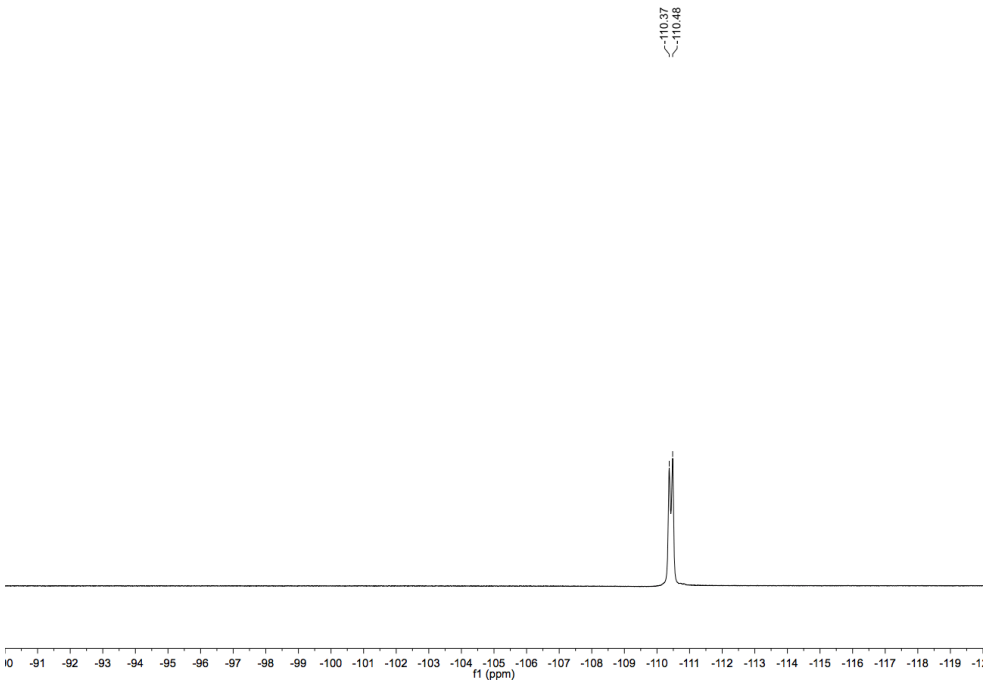
^{1}H NMR spectrum (500 MHz, chloroform-*d*)



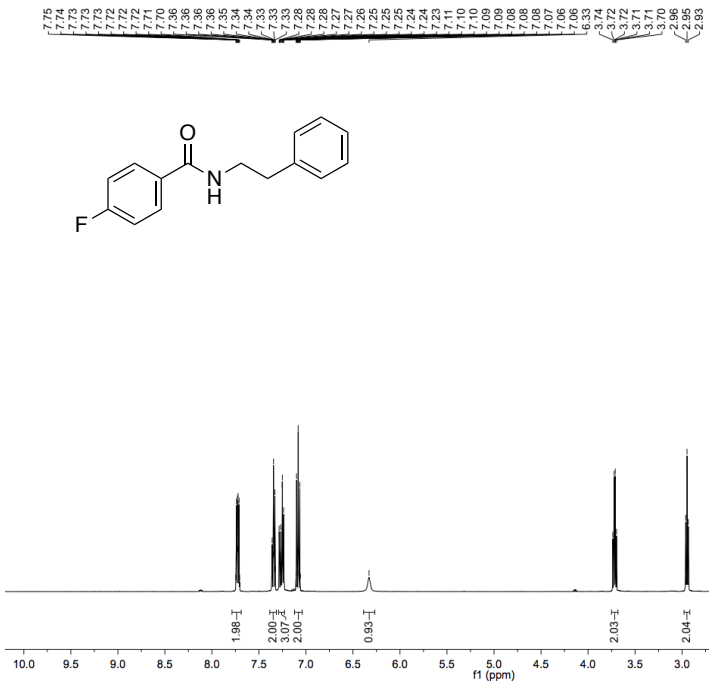
^{13}C NMR spectrum (126 MHz, chloroform-*d*)



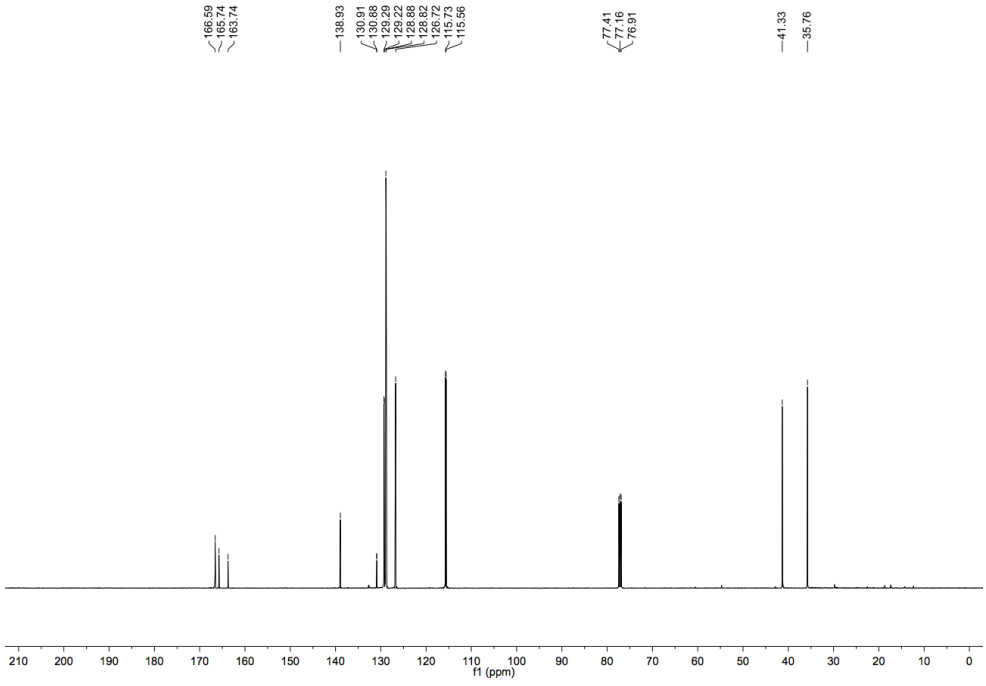
^{19}F NMR spectrum (470 MHz, chloroform-*d*)



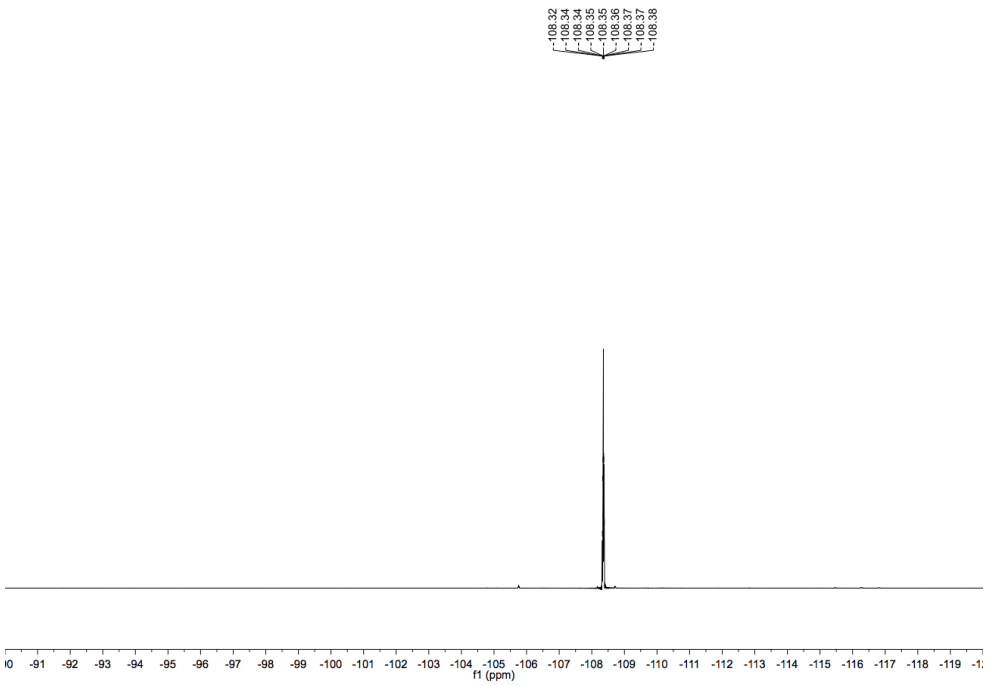
^{1}H NMR spectrum (500 MHz, chloroform-*d*)



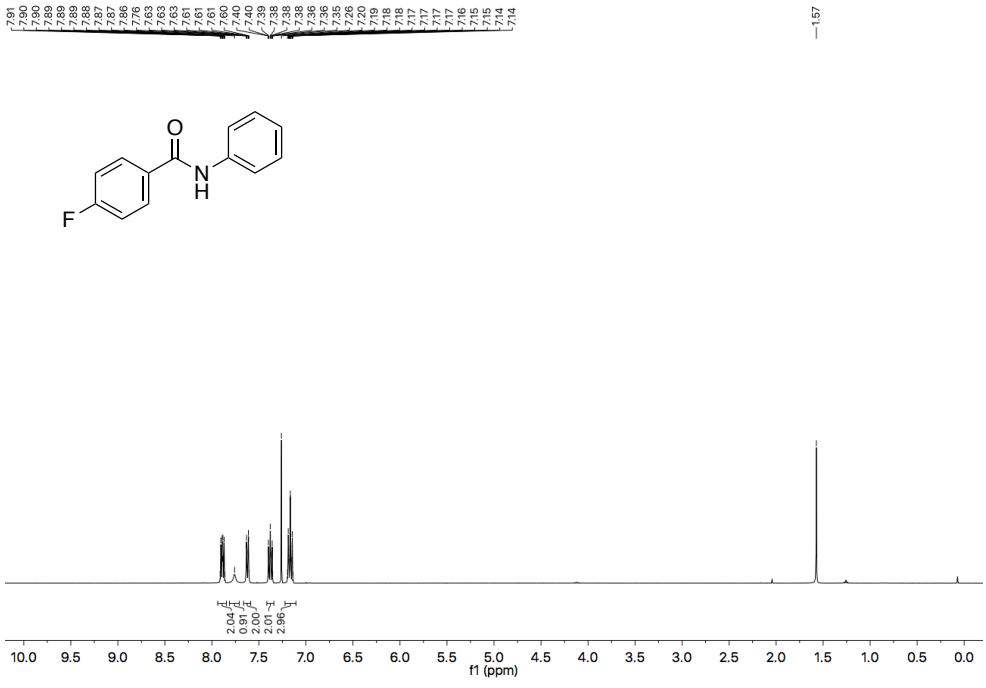
^{13}C NMR spectrum (126 MHz, chloroform-*d*)



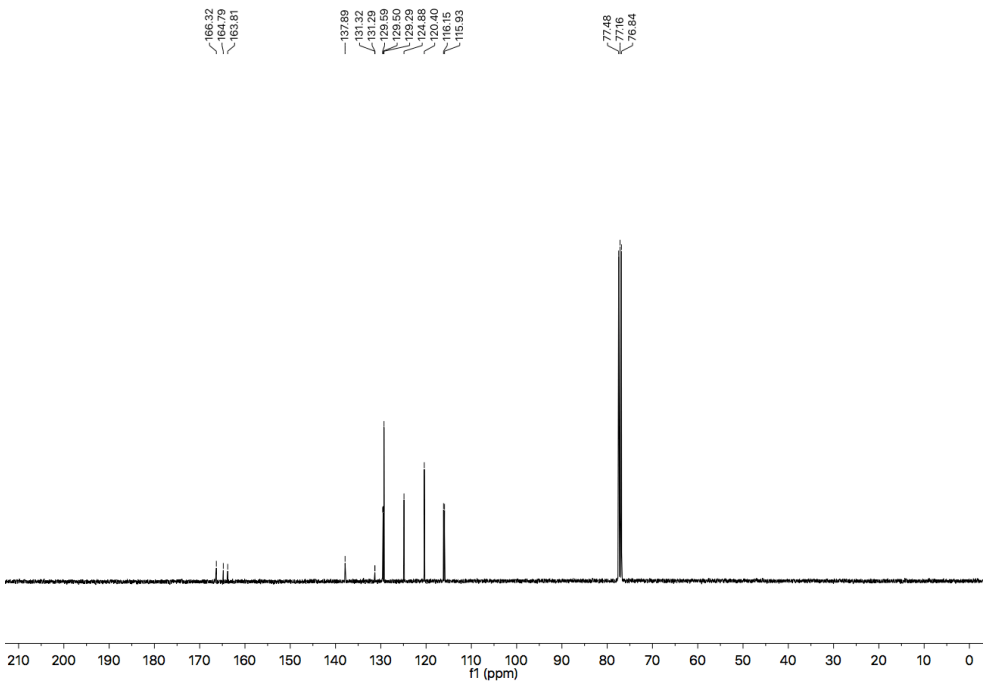
^{19}F NMR spectrum (470 MHz, chloroform-*d*)



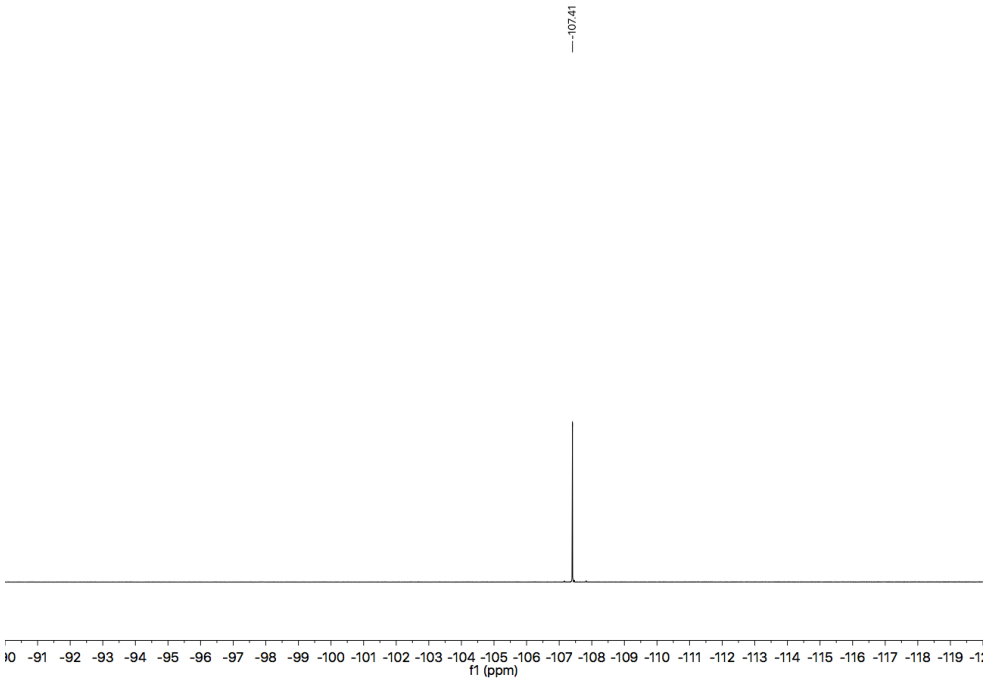
^{1}H NMR spectrum (400 MHz, chloroform-*d*)



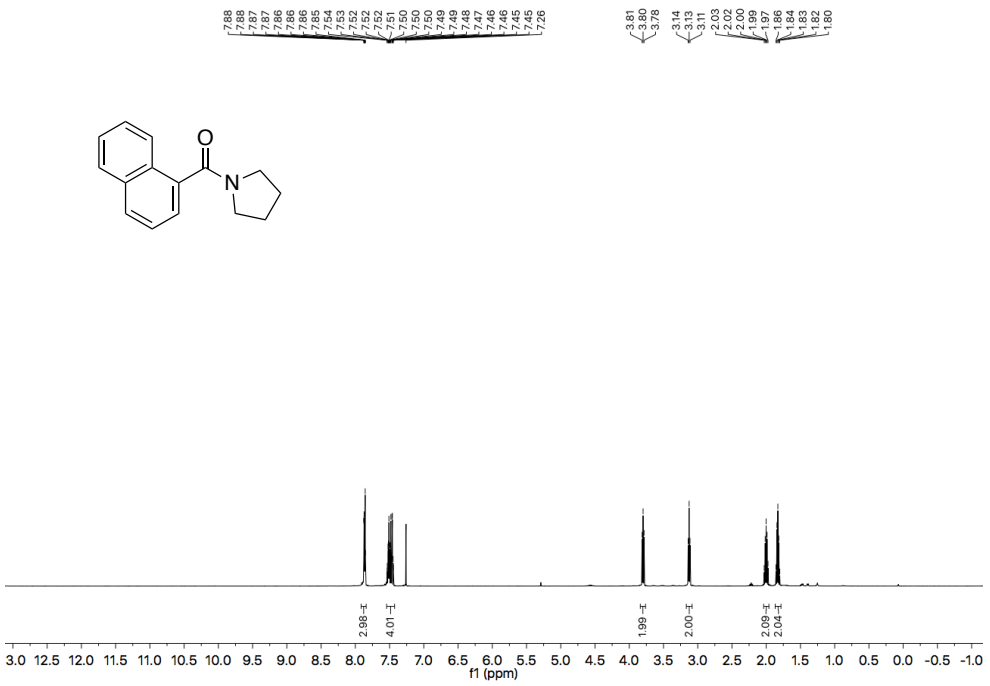
^{13}C NMR spectrum (101 MHz, chloroform-*d*)



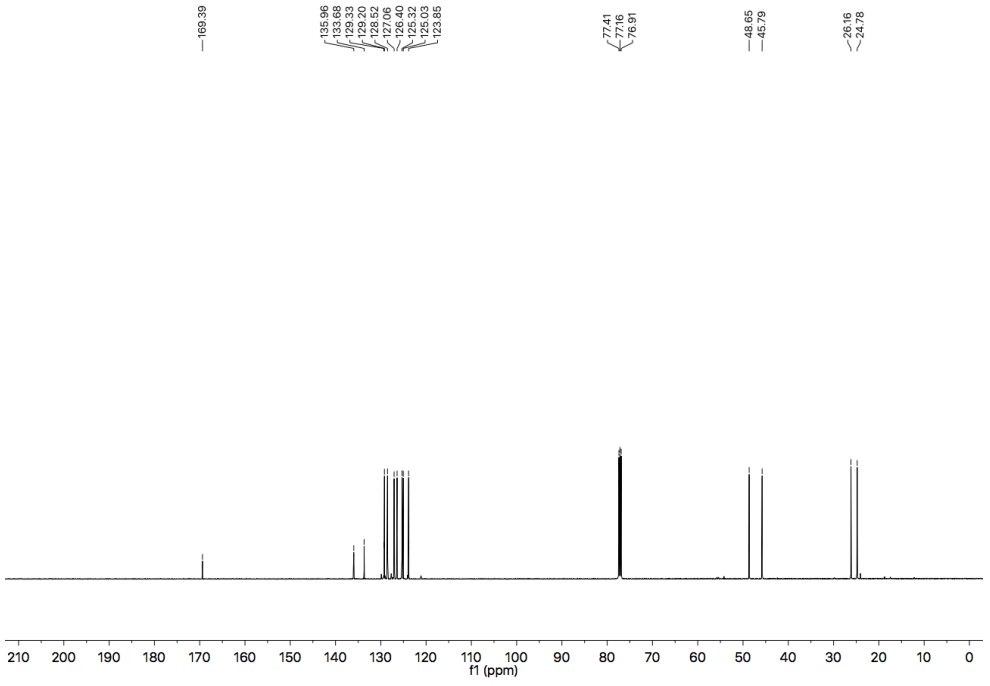
^{19}F NMR spectrum (376 MHz, chloroform-*d*)



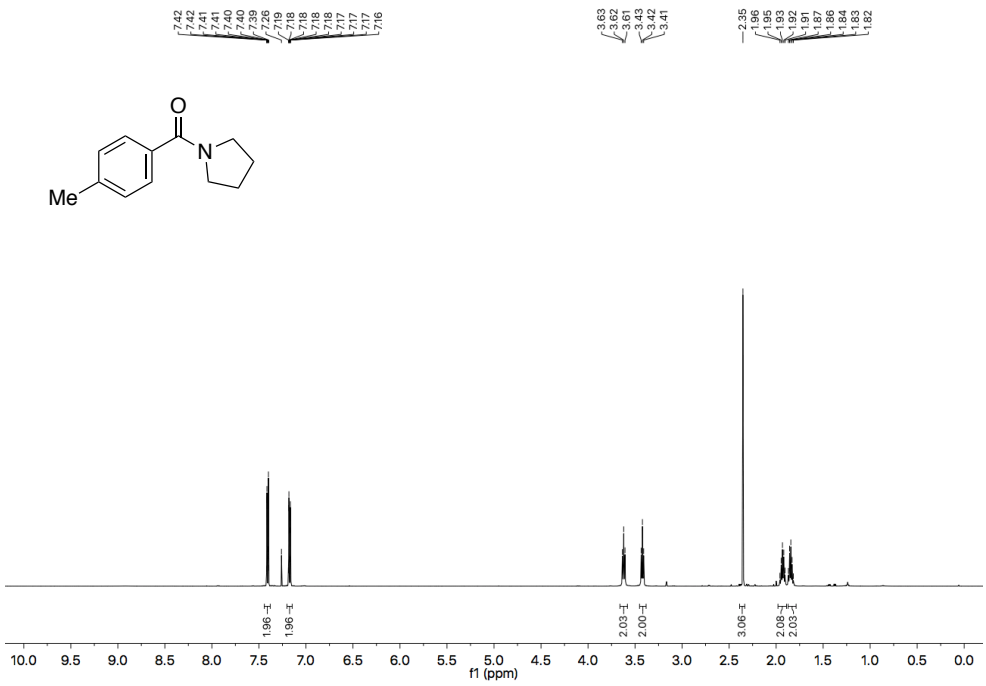
^{1}H NMR spectrum (500 MHz, chloroform-*d*)



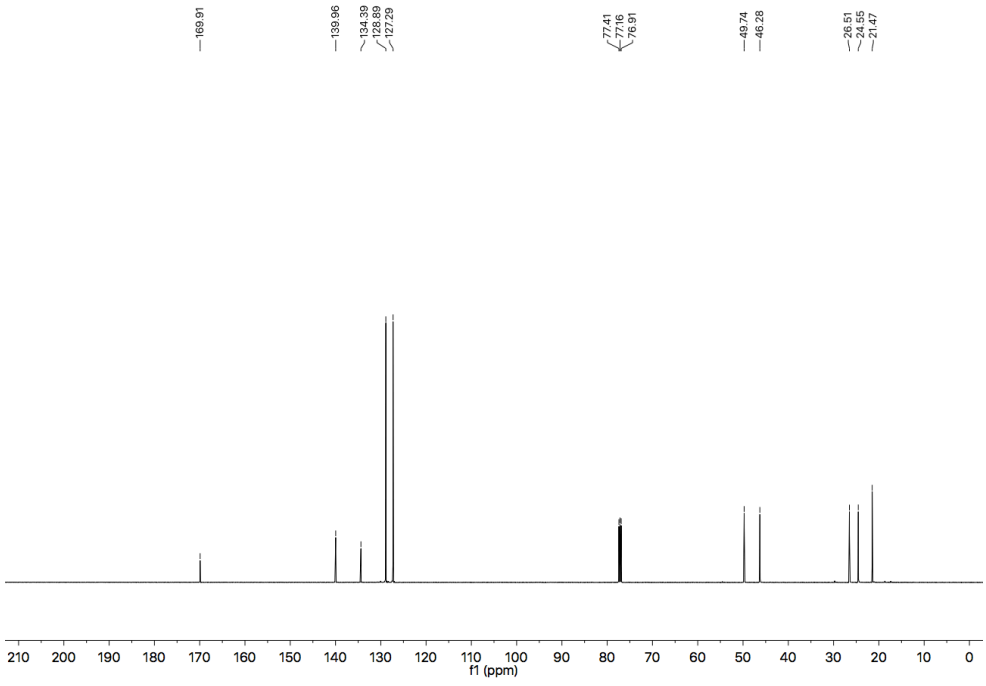
^{13}C NMR spectrum (126 MHz, chloroform-*d*)



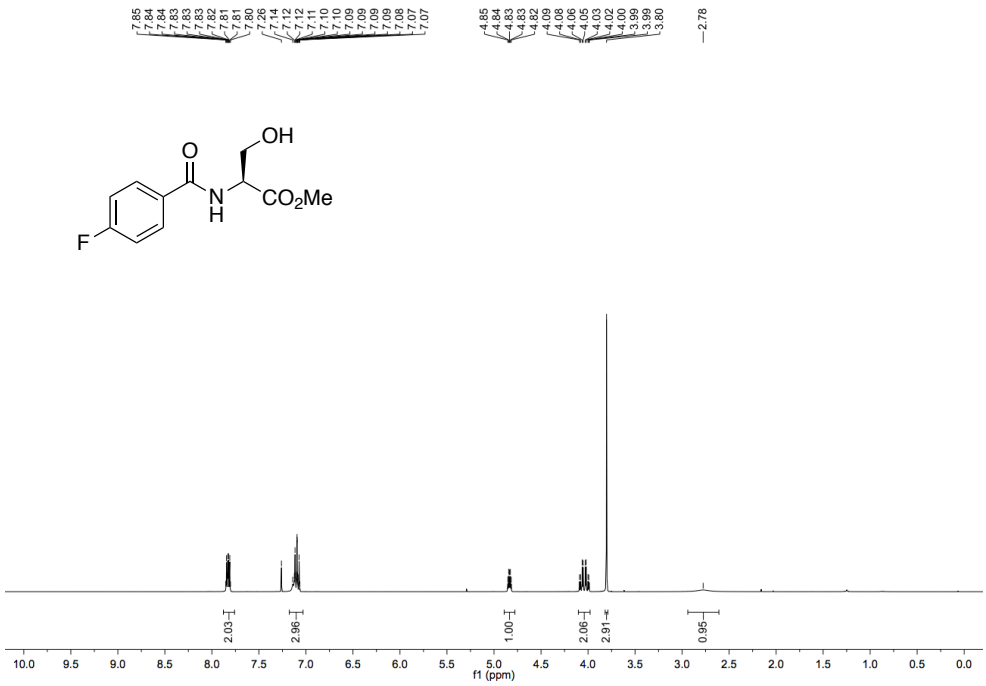
^{1}H NMR spectrum (500 MHz, chloroform-*d*)



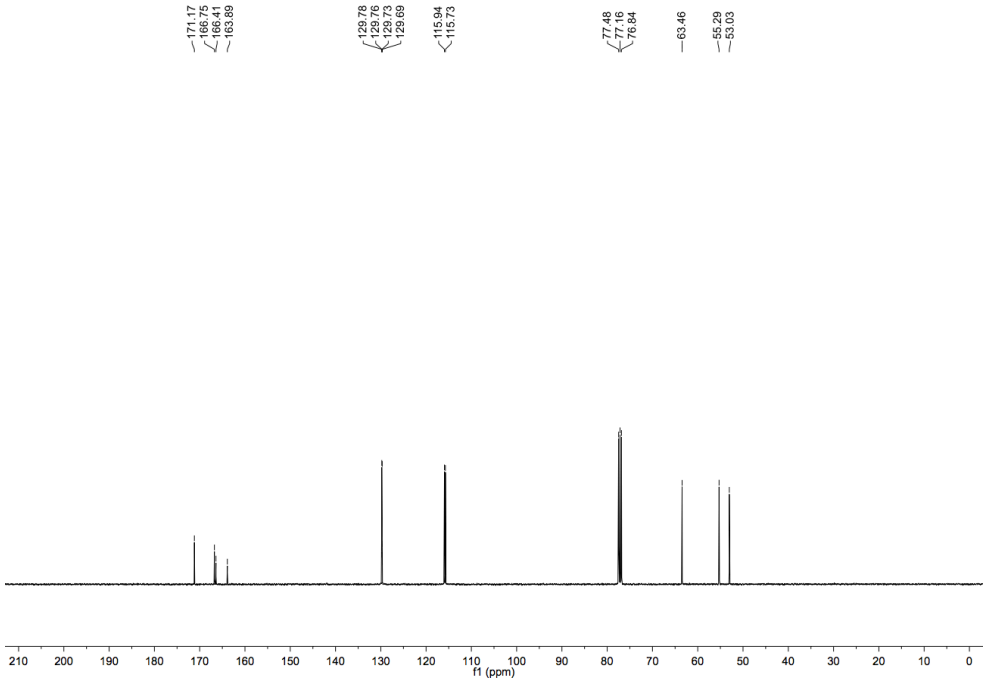
^{13}C NMR spectrum (126 MHz, chloroform-*d*)



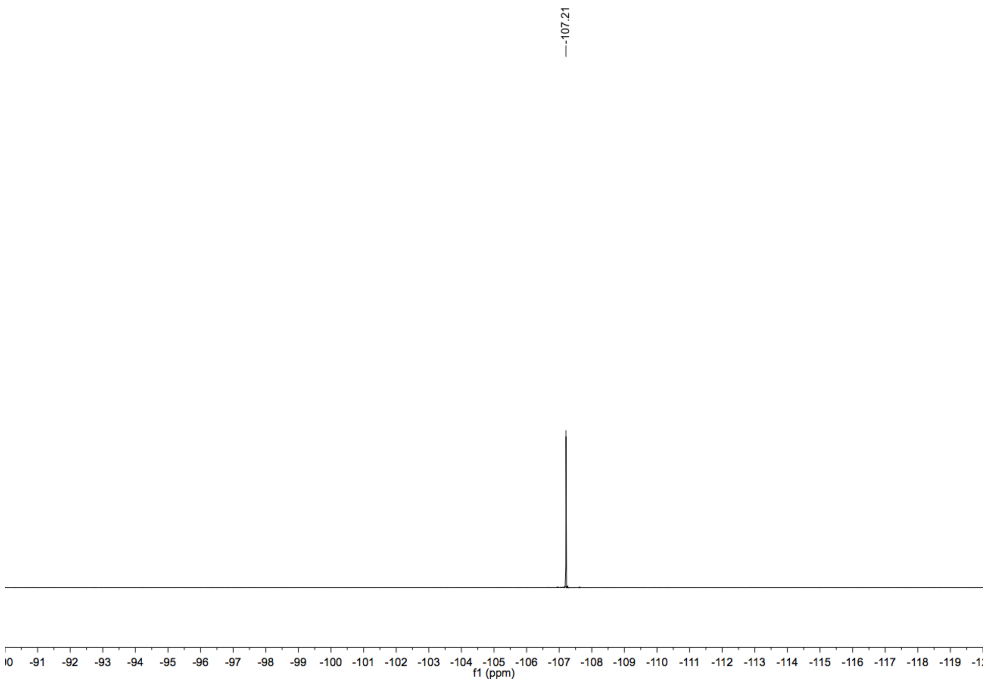
^{1}H NMR spectrum (400 MHz, chloroform-*d*)



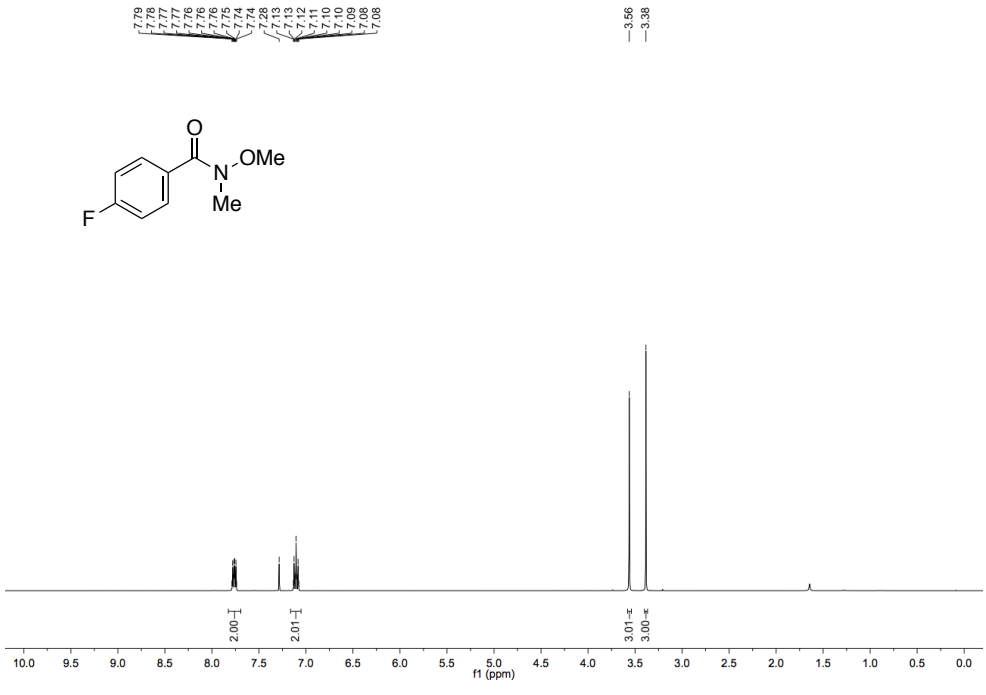
^{13}C NMR spectrum (101 MHz, chloroform-*d*)



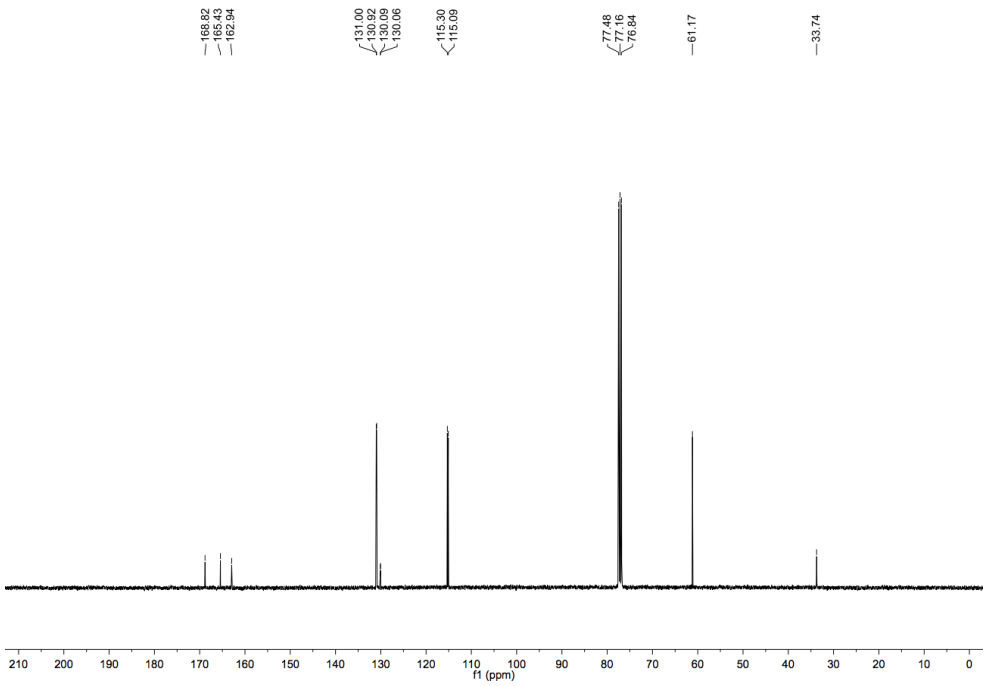
^{19}F NMR spectrum (376 MHz, chloroform-*d*)



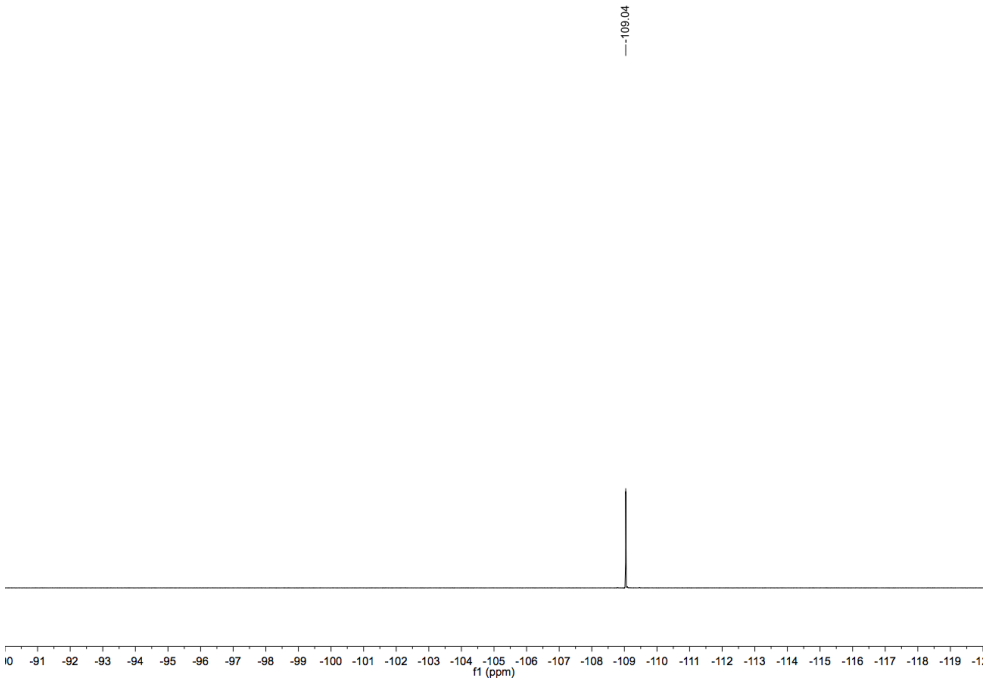
^{1}H NMR spectrum (400 MHz, chloroform-*d*)



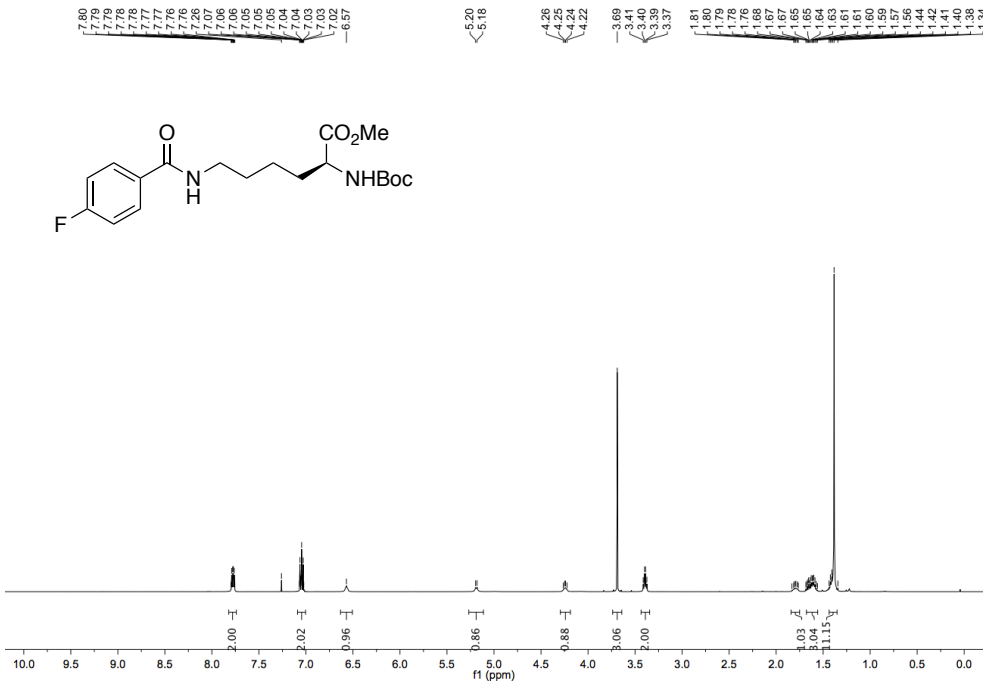
^{13}C NMR spectrum (101 MHz, chloroform-*d*)



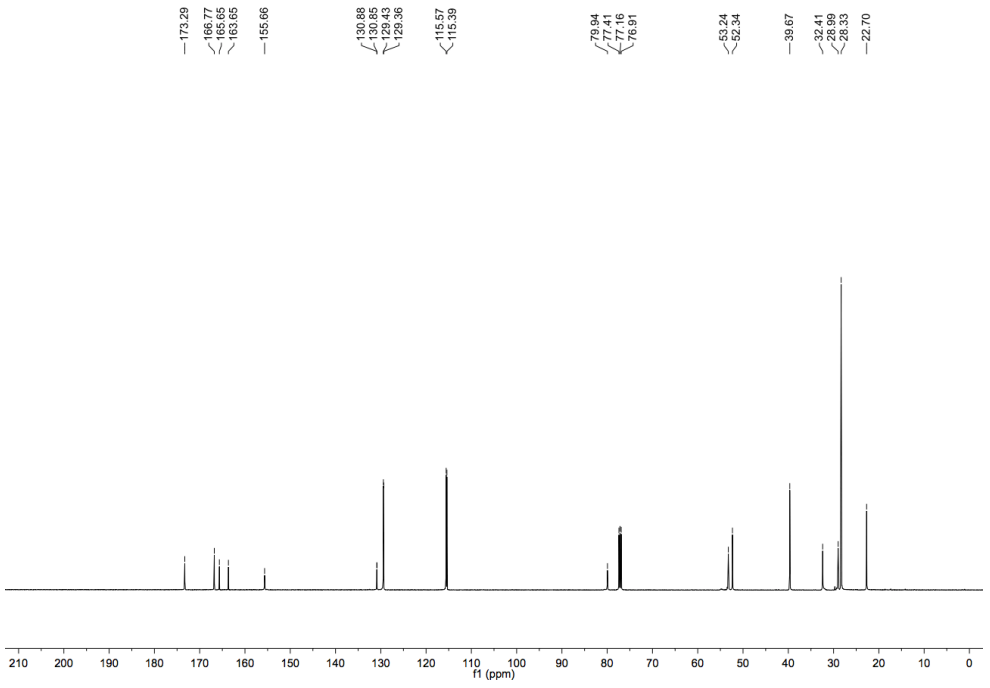
^{19}F NMR spectrum (376 MHz, chloroform-*d*)



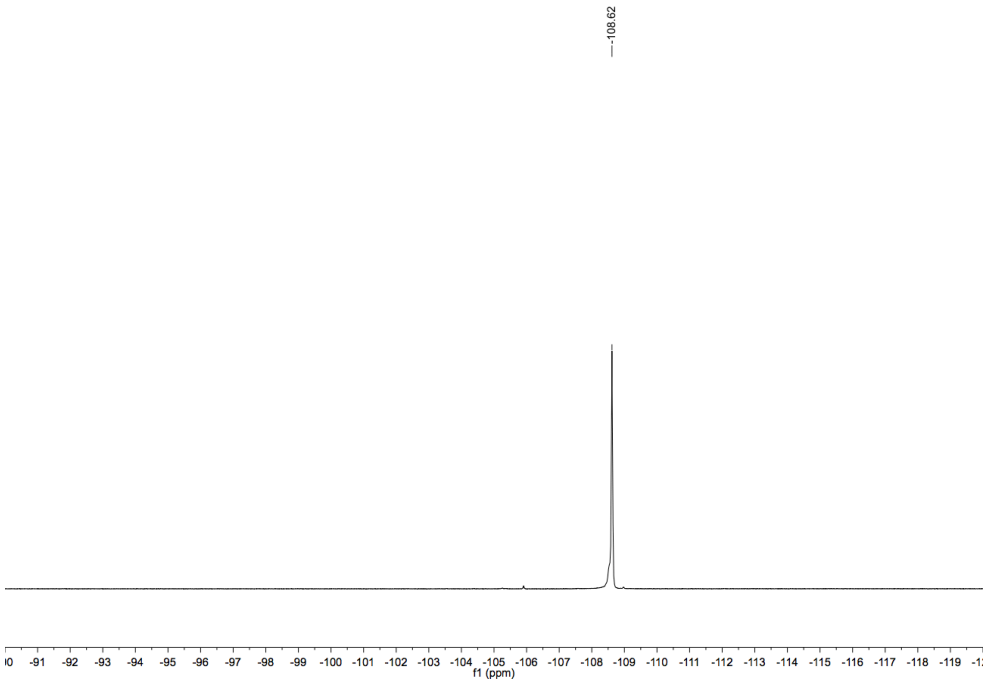
^{1}H NMR spectrum (500 MHz, chloroform-*d*)



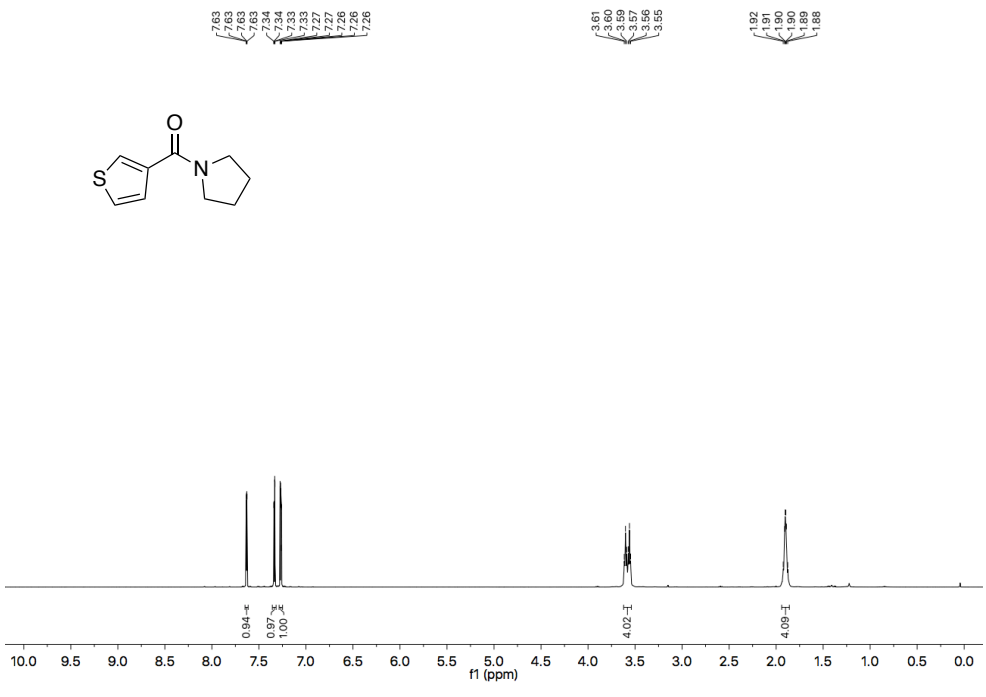
^{13}C NMR spectrum (126 MHz, chloroform-*d*)



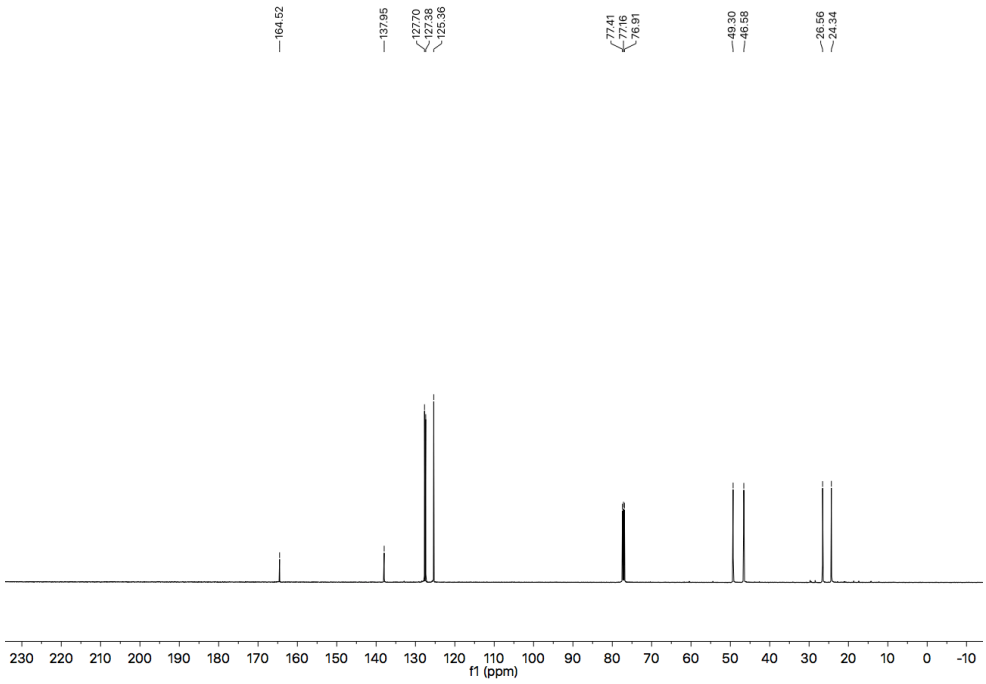
^{19}F NMR spectrum (470 MHz, chloroform-*d*)



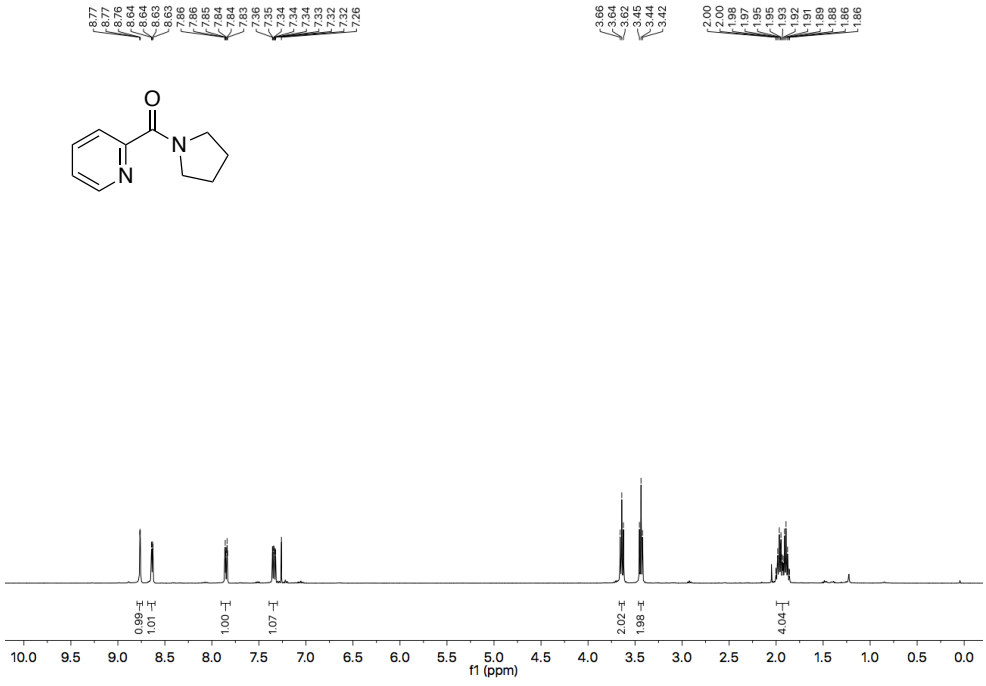
^{1}H NMR spectrum (500 MHz, chloroform-*d*)



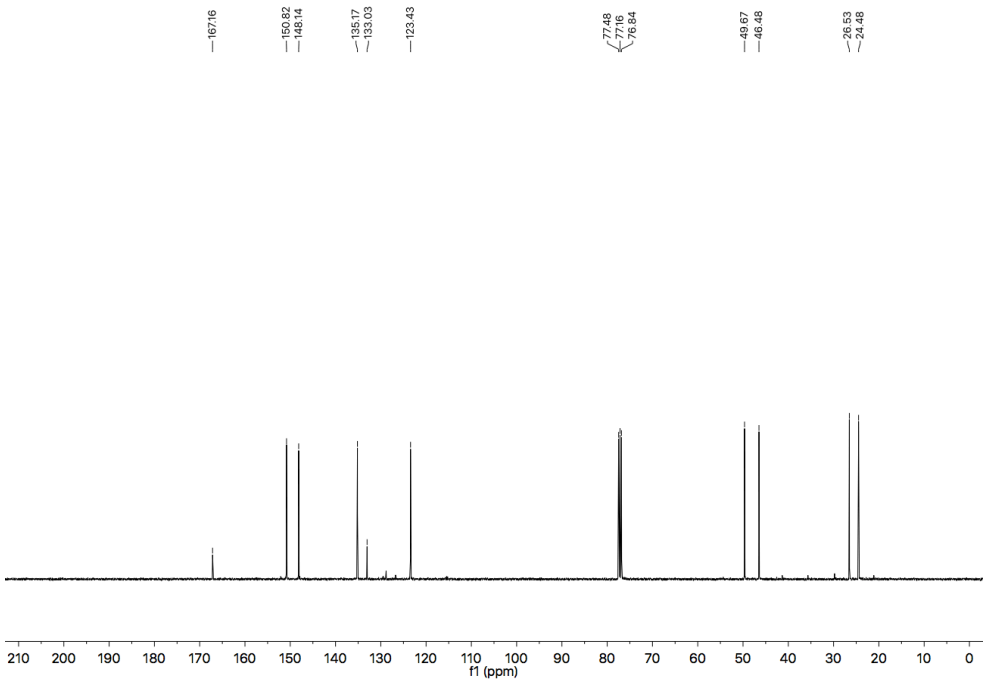
^{13}C NMR spectrum (126 MHz, chloroform-*d*)



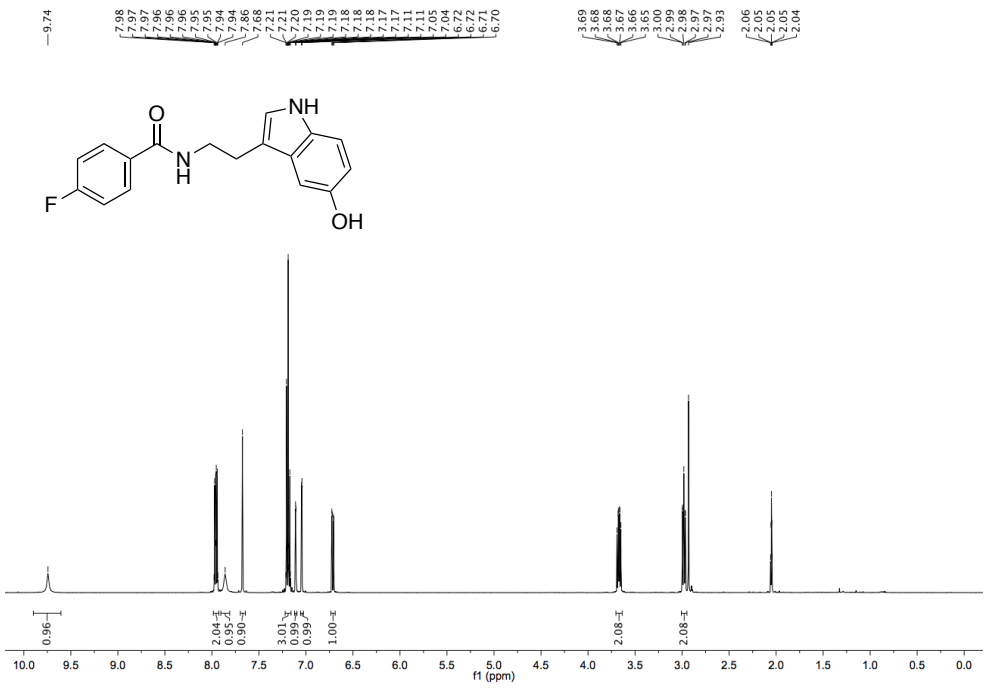
^{1}H NMR spectrum (400 MHz, chloroform-*d*)



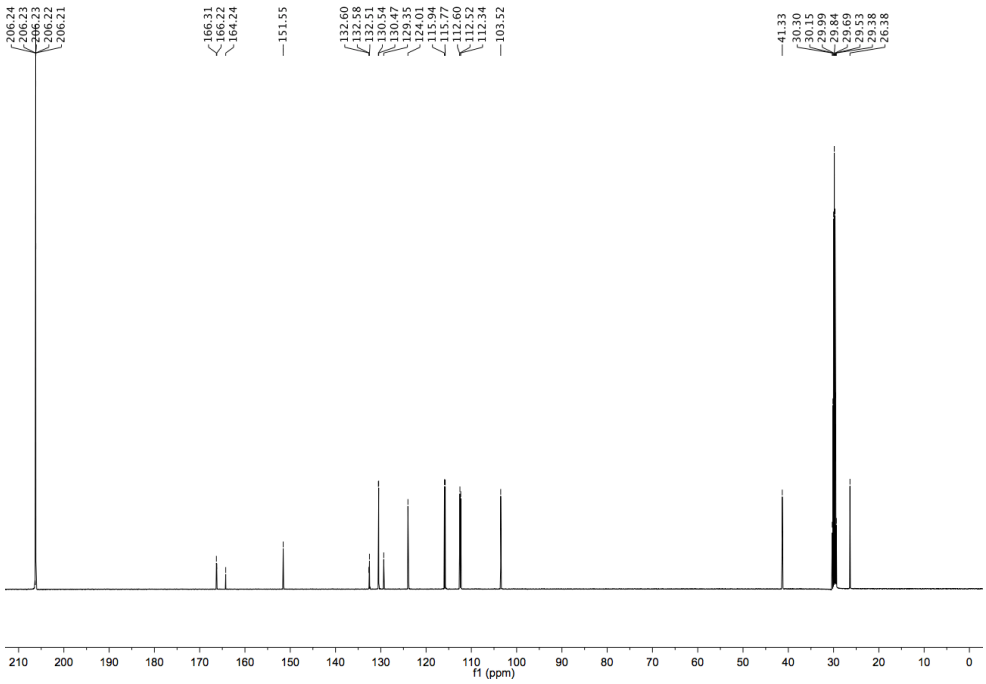
^{13}C NMR spectrum (101 MHz, chloroform-*d*)



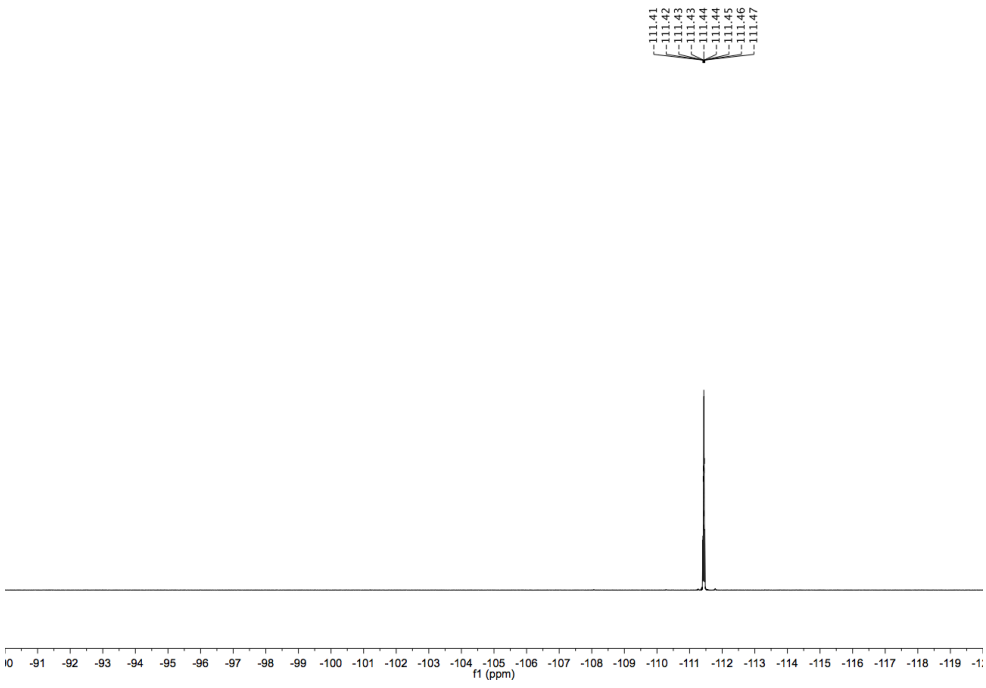
^{1}H NMR spectrum (500 MHz, acetone-*d6*)



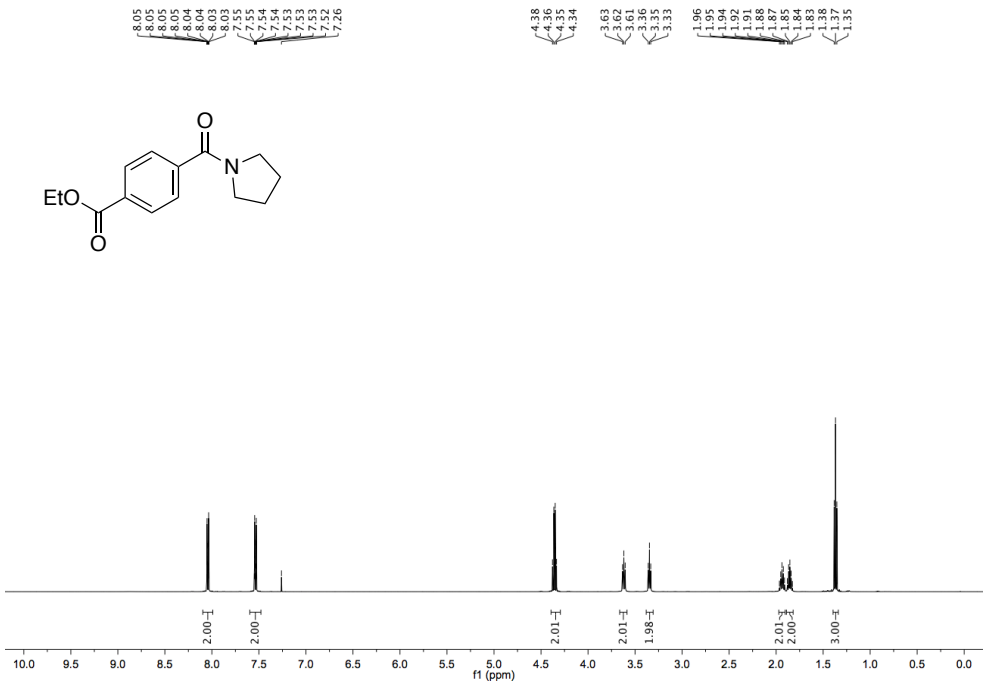
^{13}C NMR spectrum (126 MHz, acetone-*d6*)



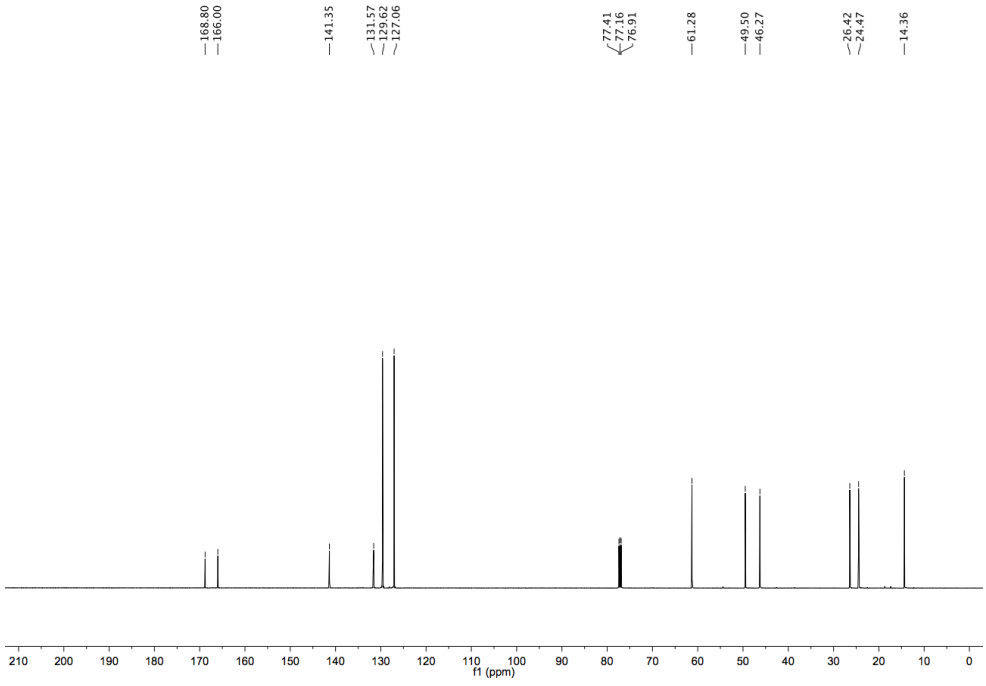
^{19}F NMR spectrum (470 MHz, acetone-*d6*)



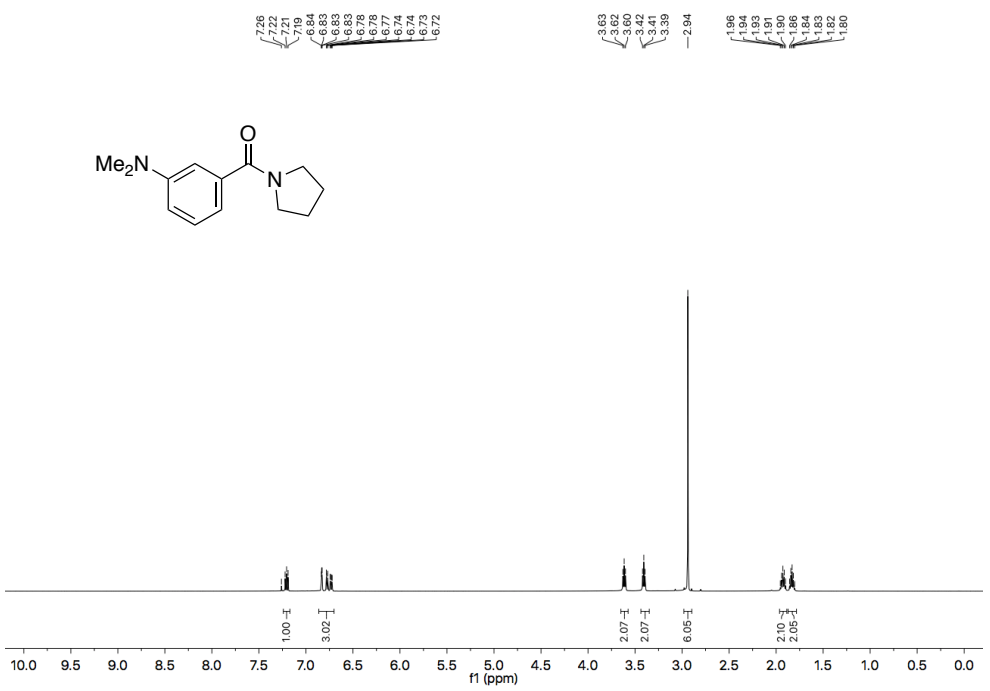
^{1}H NMR spectrum (500 MHz, chloroform-*d*)



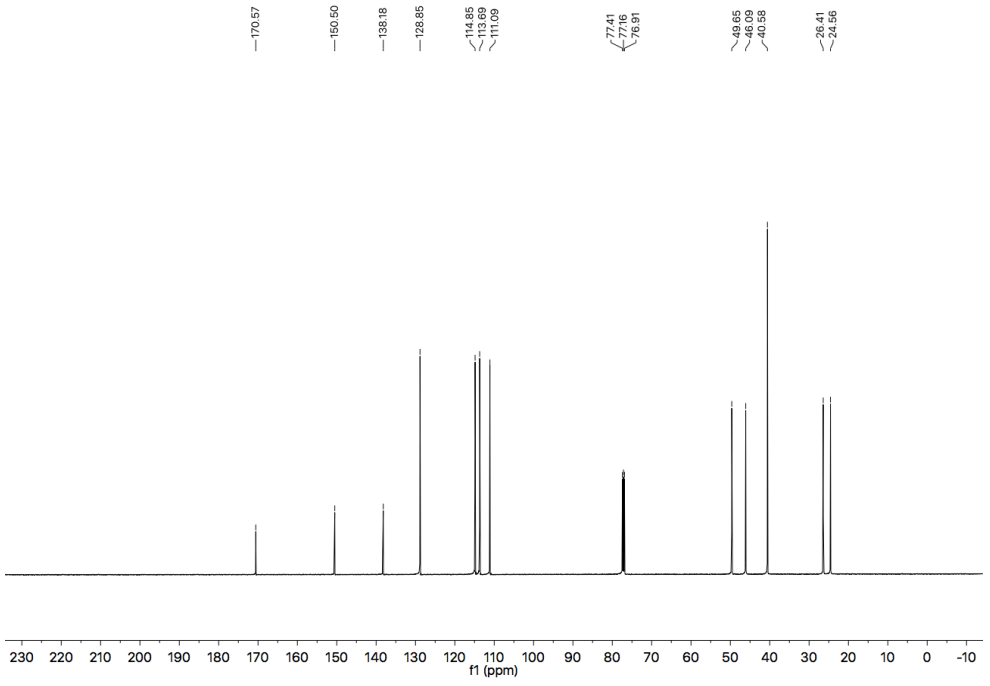
^{13}C NMR spectrum (126 MHz, chloroform-*d*)



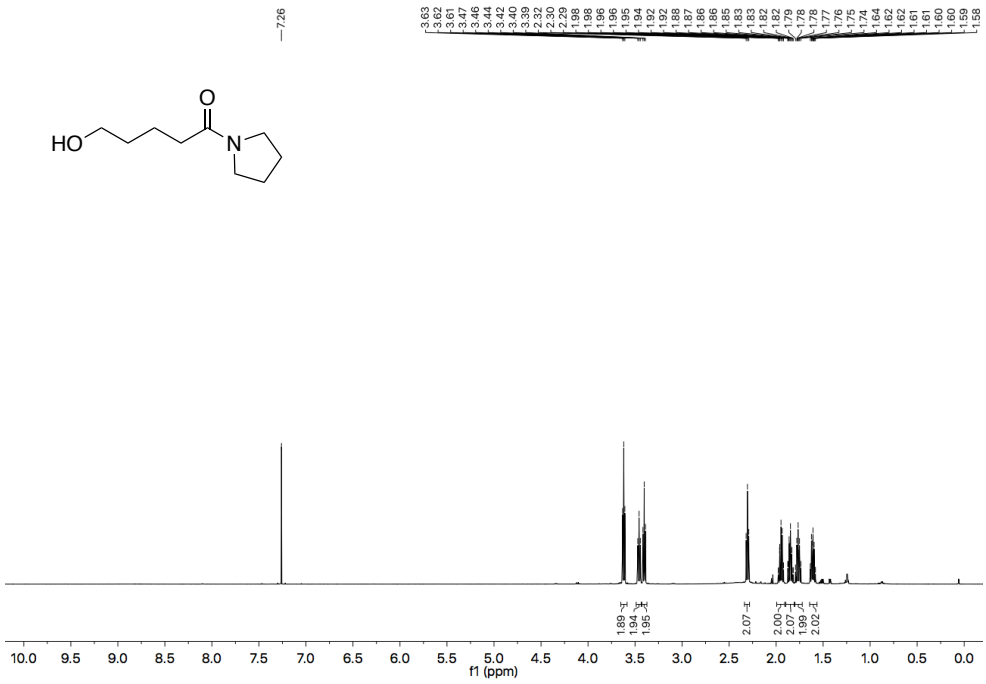
^{1}H NMR spectrum (500 MHz, chloroform-*d*)



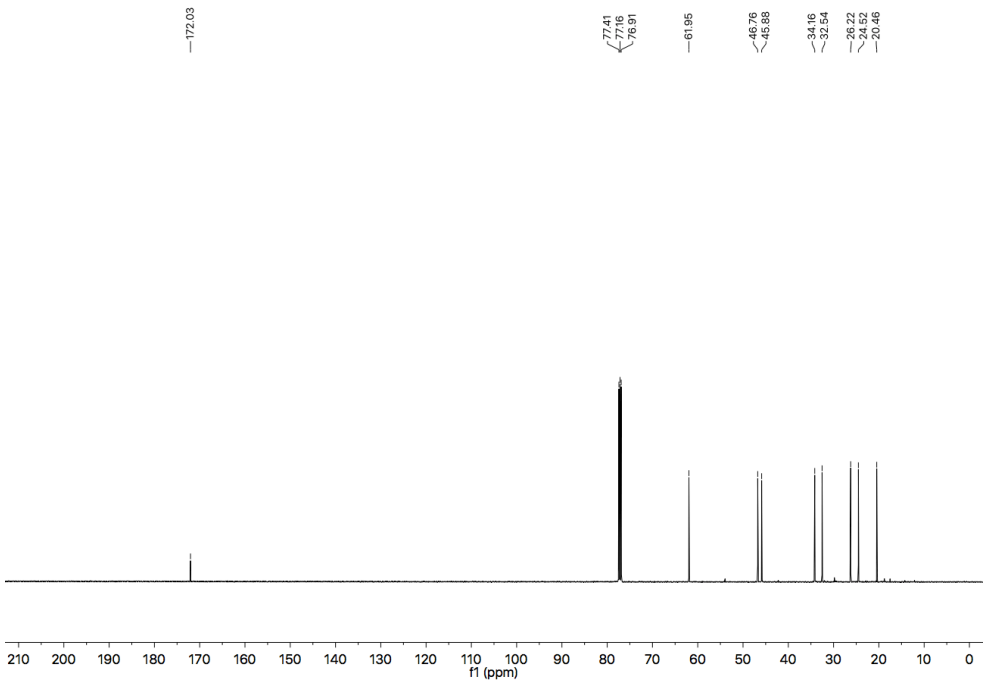
^{13}C NMR spectrum (126 MHz, chloroform-*d*)



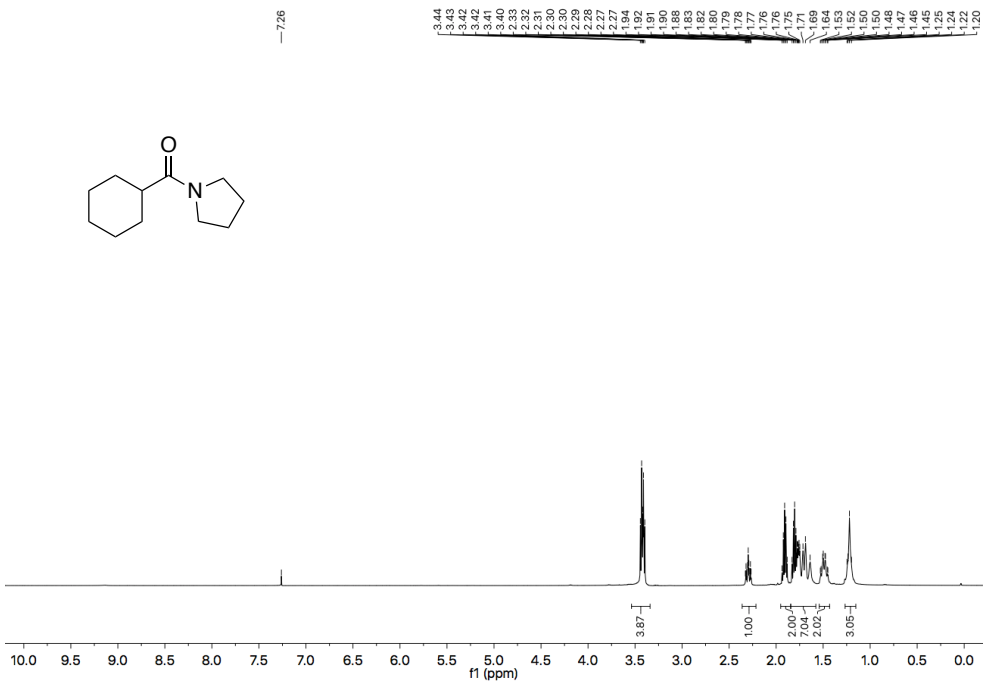
^{1}H NMR spectrum (500 MHz, chloroform-*d*)



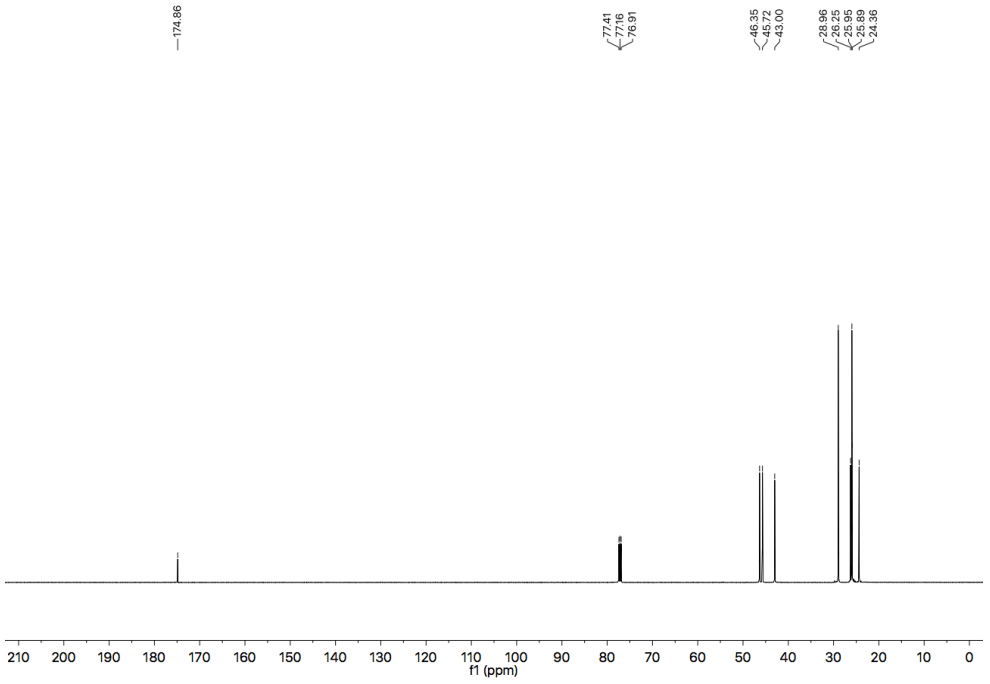
^{13}C NMR spectrum (126 MHz, chloroform-*d*)



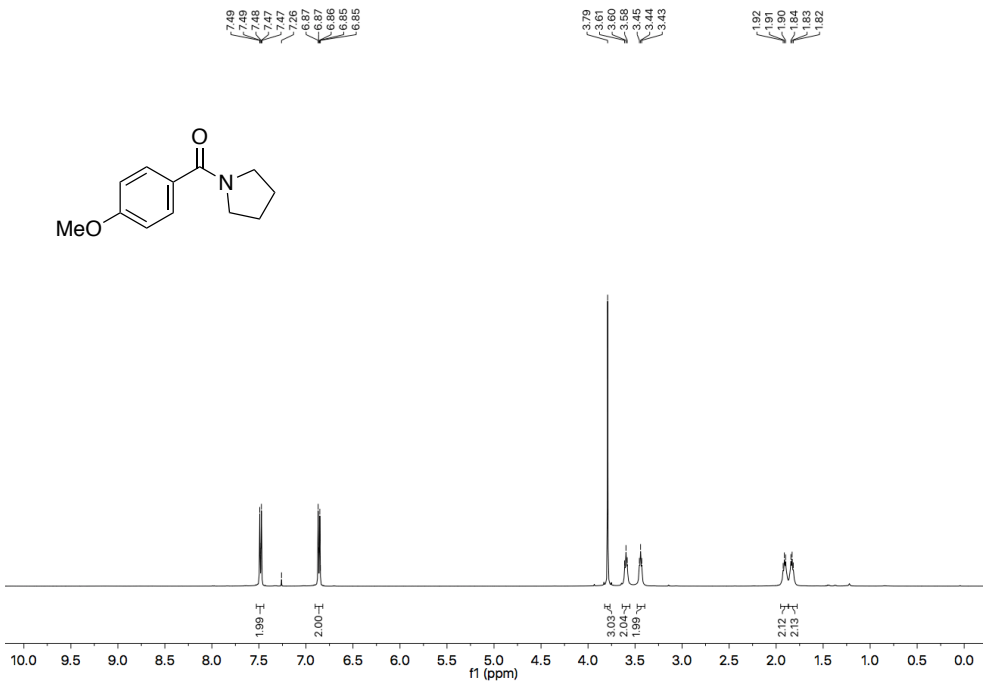
^{1}H NMR spectrum (500 MHz, chloroform-*d*)



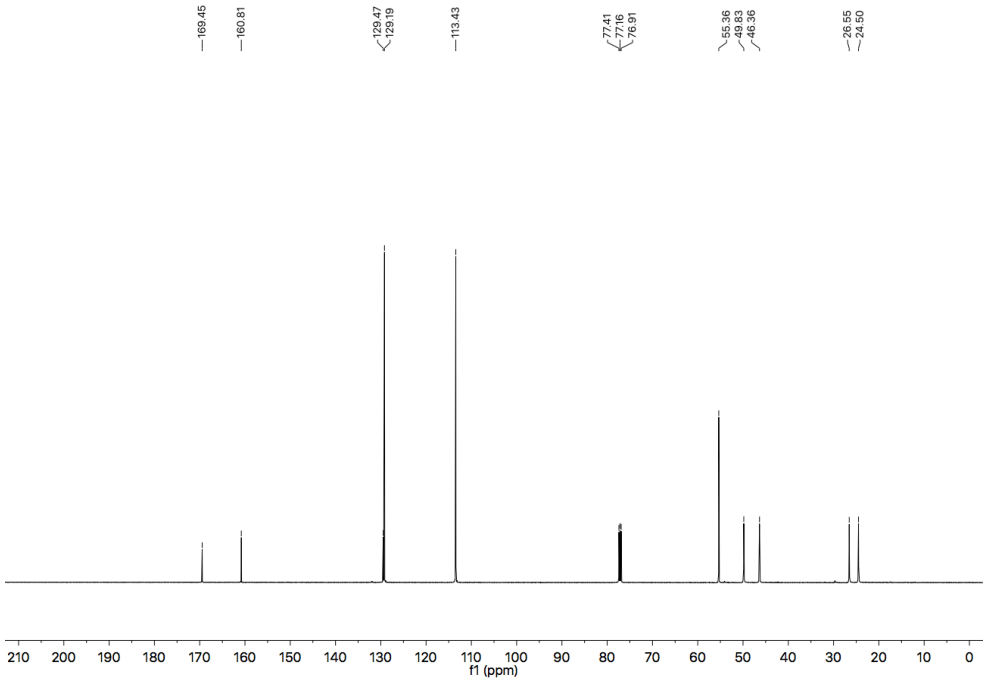
^{13}C NMR spectrum (126 MHz, chloroform-*d*)



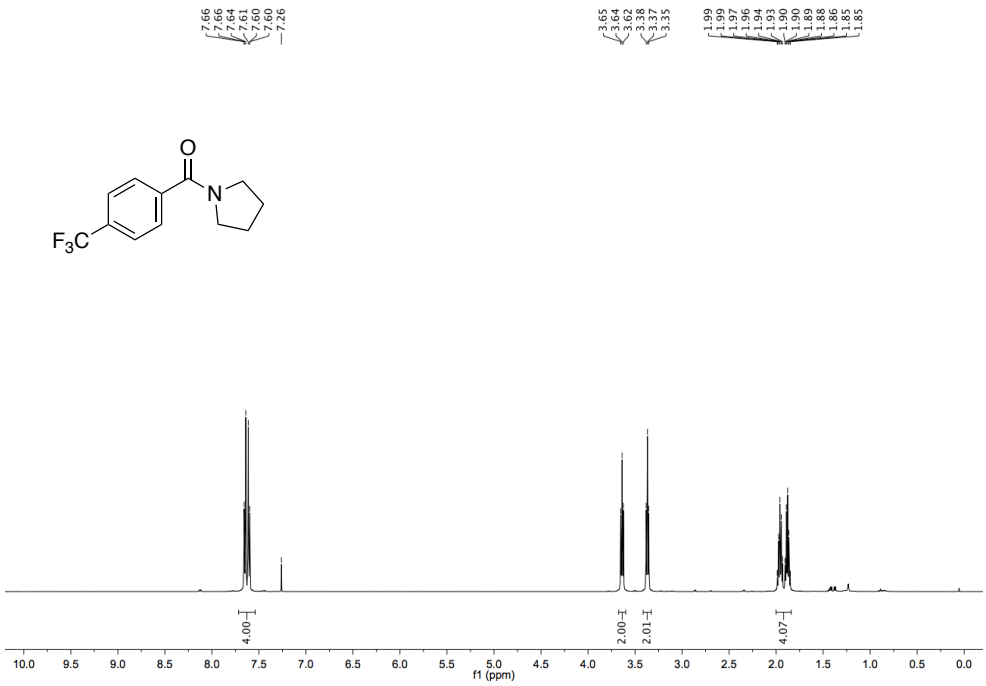
^{1}H NMR spectrum (500 MHz, chloroform-*d*)



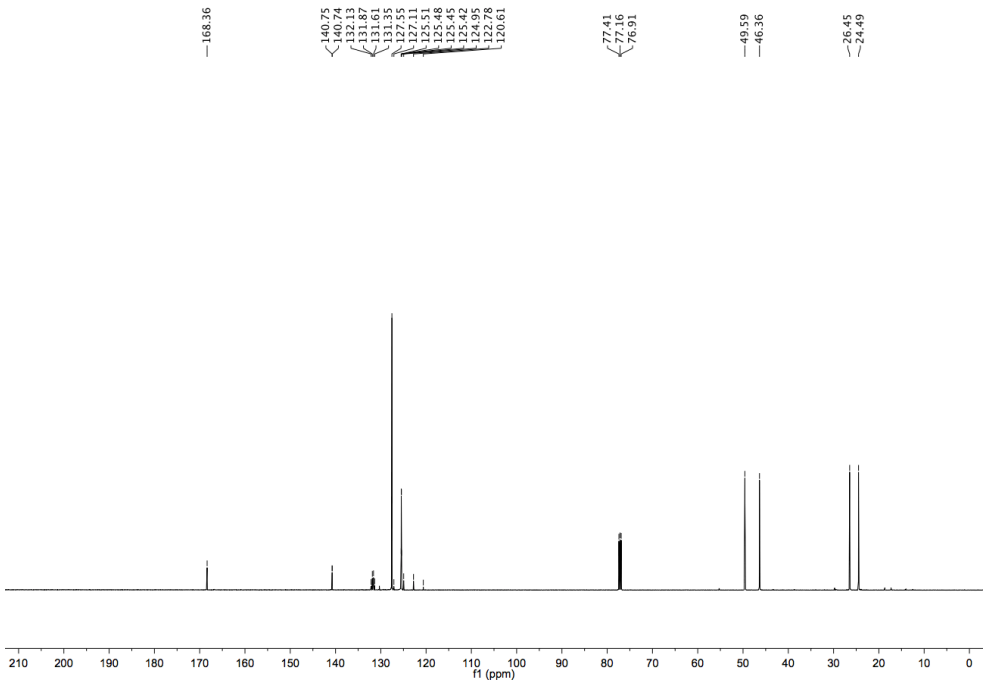
^{13}C NMR spectrum (126 MHz, chloroform-*d*)



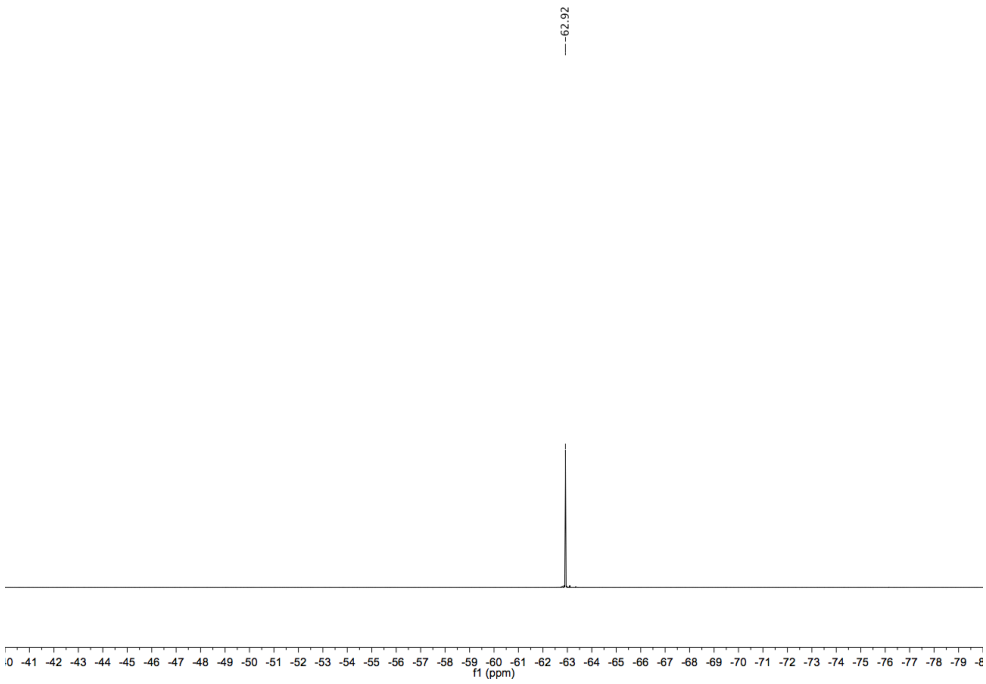
^{1}H NMR spectrum (500 MHz, chloroform-*d*)



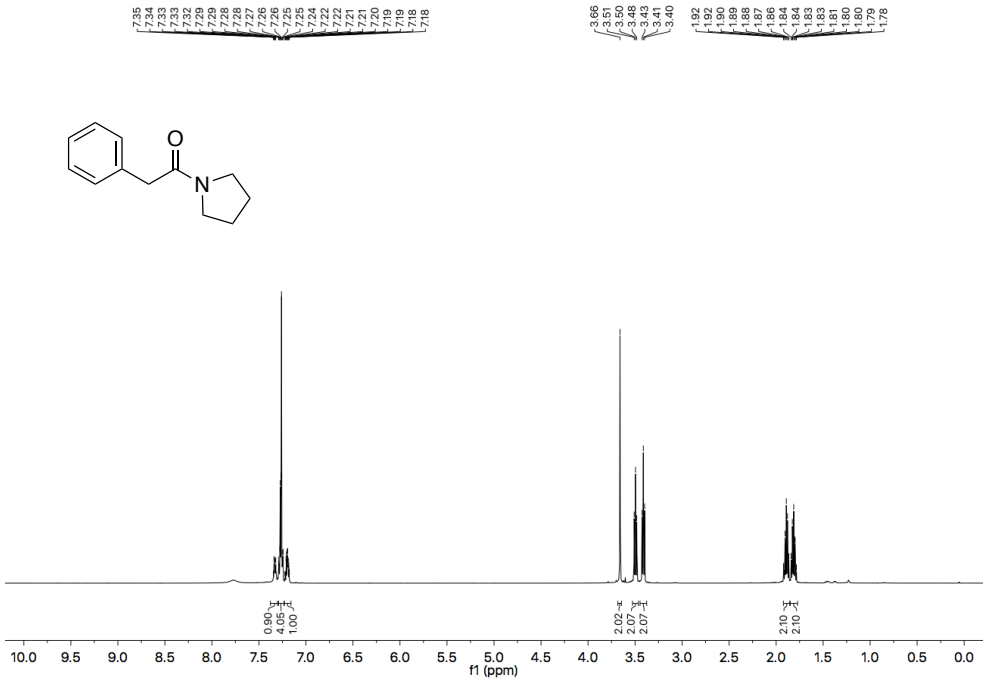
^{13}C NMR spectrum (126 MHz, chloroform-*d*)



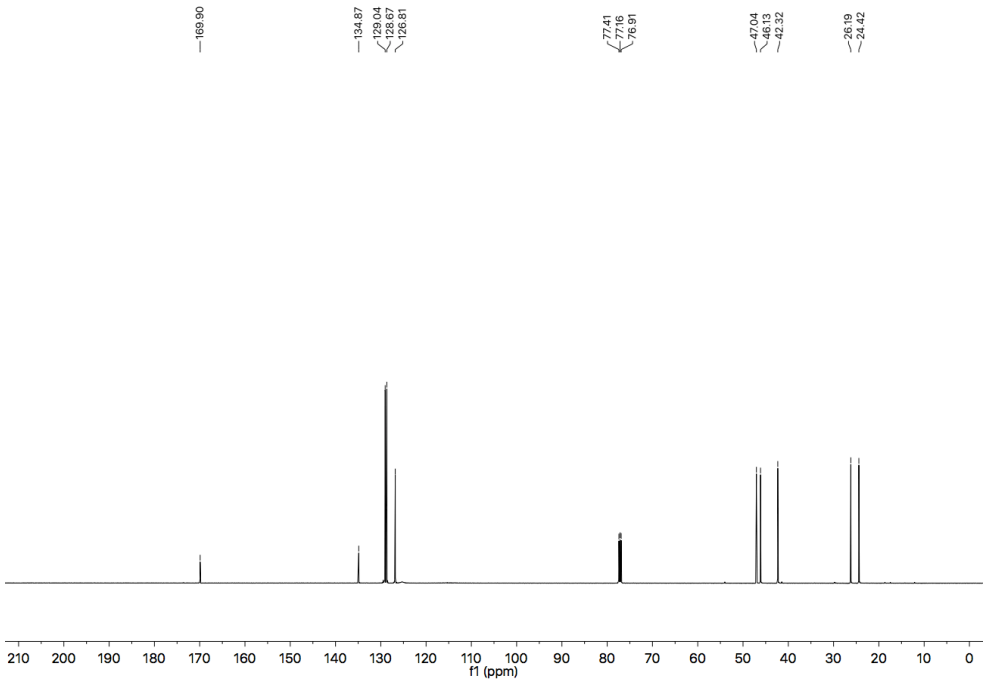
^{19}F NMR spectrum (470 MHz, chloroform-*d*)



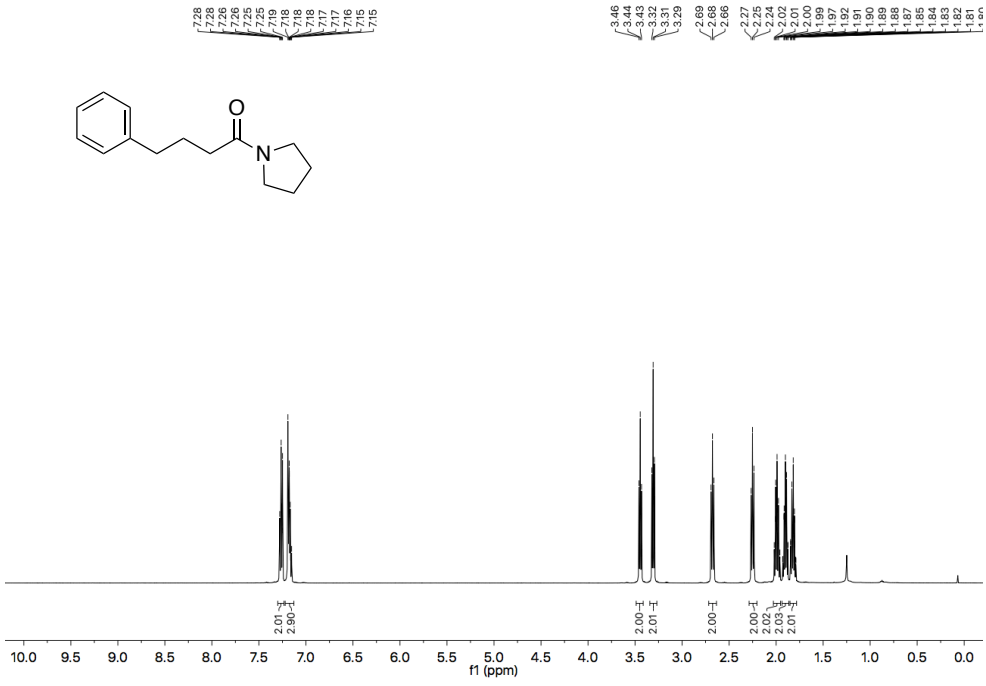
^{1}H NMR spectrum (500 MHz, chloroform-*d*)



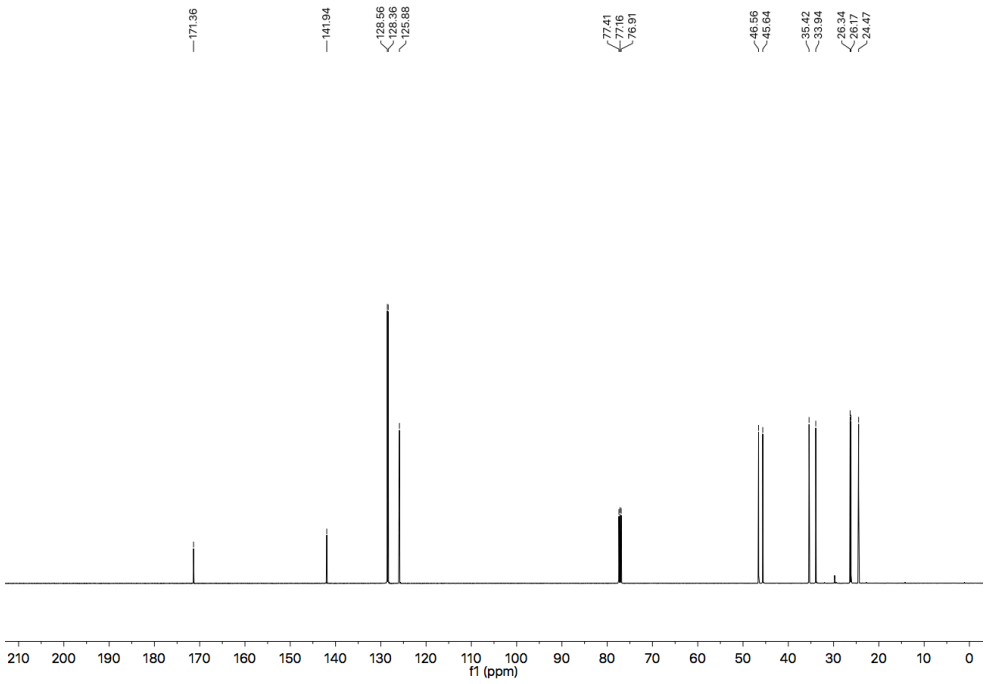
^{13}C NMR spectrum (126 MHz, chloroform-*d*)



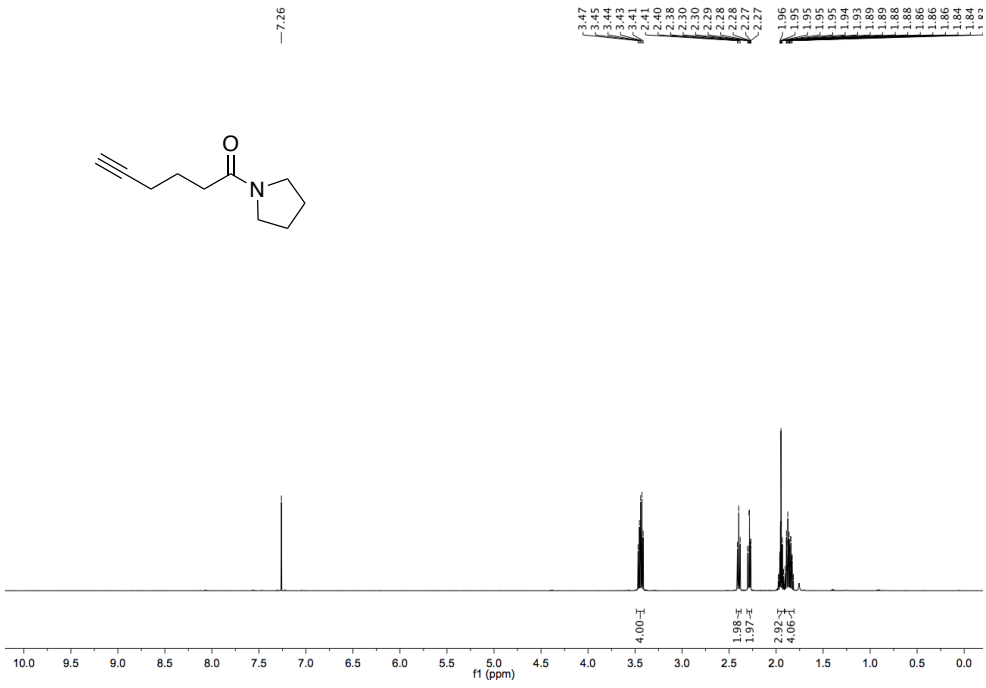
^{1}H NMR spectrum (500 MHz, chloroform-*d*)



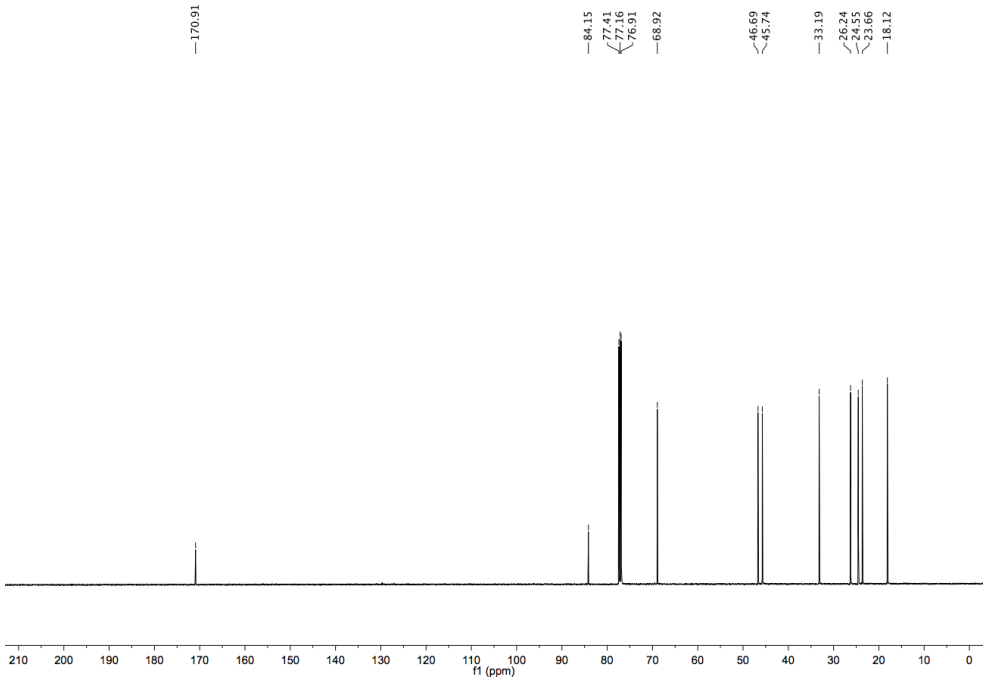
^{13}C NMR spectrum (126 MHz, chloroform-*d*)



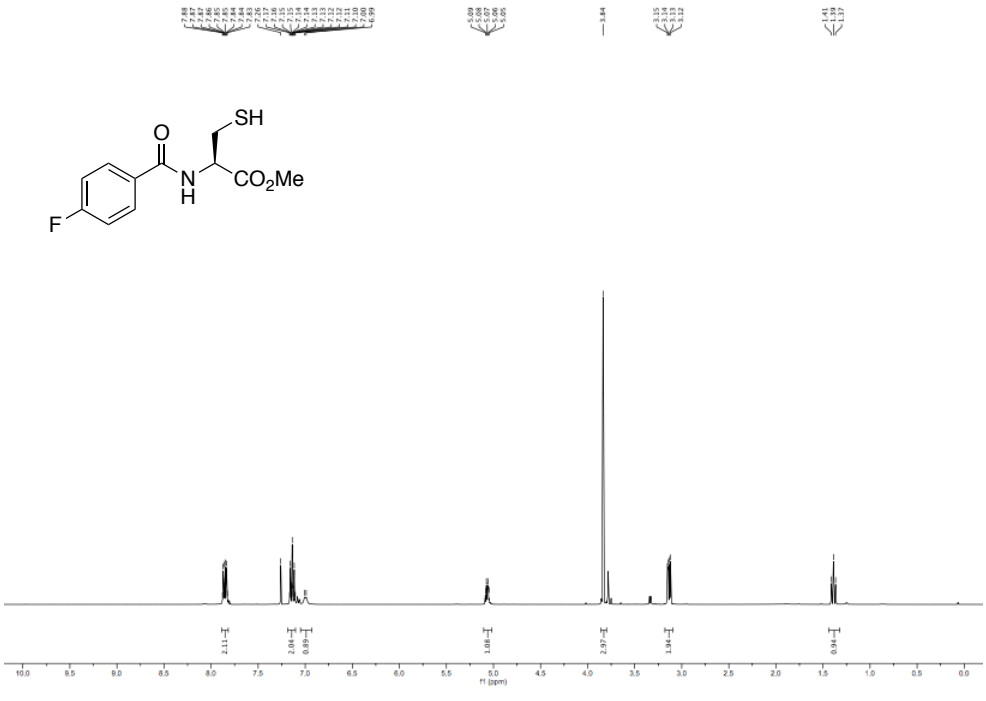
^{1}H NMR spectrum (500 MHz, chloroform-*d*)



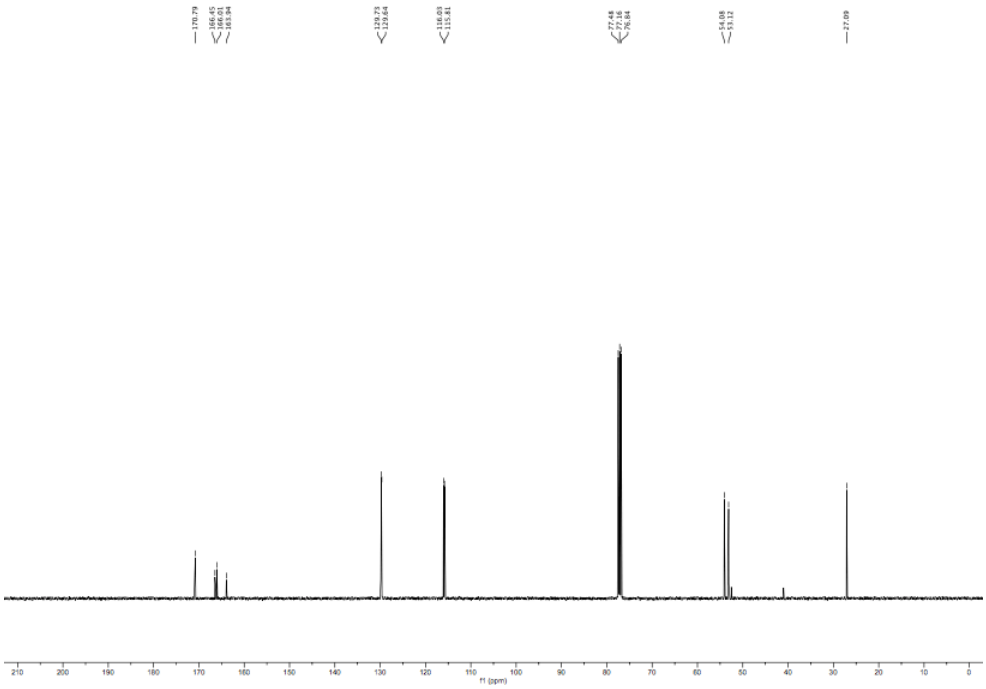
^{13}C NMR spectrum (126 MHz, chloroform-*d*)



^{1}H NMR spectrum (400 MHz, chloroform-*d*)



^{13}C NMR spectrum (101 MHz, chloroform-*d*)



^{19}F NMR spectrum (376 MHz, chloroform-*d*)