Supporting Information

Copper-Mediated Radiofluorination of Arylstannanes with [^{18}F]KF

Katarina J. Makaravage,[†] Allen F. Brooks,[‡] Andrew V. Mossine,[‡]
Melanie S. Sanford,[†] and Peter J. H. Scott[‡,#]

[†]Department of Chemistry, University of Michigan, 930 North University Avenue, Ann Arbor, Michigan 48109, United States
[‡]Department of Radiology, University of Michigan Medical School, 1301 Catherine Street, Ann Arbor, Michigan 48109, United States
[#]The Interdepartmental Program in Medicinal Chemistry, University of Michigan, Ann Arbor, Michigan 48109, USA

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1. General Procedures and Materials and Methods

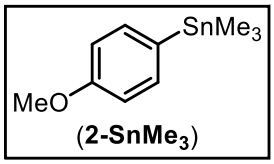
Instrumental Information. NMR spectra were obtained on a Varian MR400 (400 MHz for ^{1}H; 377 MHz for ^{19}F; 100 MHz for ^{13}C), a Varian vnmrs 500 (500 MHz for ^{1}H), or a Varian vnmrs 700 (700 MHz for ^{1}H; 175 MHz for ^{13}C) spectrometer. ^{1}H and ^{13}C NMR chemical shifts are reported in parts per million (ppm) relative to TMS, with the residual solvent peak used as an internal reference. ^{19}F NMR spectra are referenced based on the internal standard 1,2-difluorobenzene, which appears at –140.53 ppm. ^{1}H and ^{19}F NMR multiplicities are reported as follows: singlet (s), doublet (d), triplet (t), quartet (q), and multiplet (m). ICP-OES data was obtained from Cerium Laboratories, LLC in Austin, TX. Melting point data (mp) were collected on an OptiMelt Automated Melting Point System. High performance liquid chromatography (HPLC) was performed using a Shimadzu LC-2010A HT system equipped with a Bioscan B-FC-1000 radiation detector. Radio-TLC analysis was performed using a Bioscan AR 2000 Radio-TLC scanner with EMD Millipore TLC silica gel 60 plates (3.0 cm wide x 6.5 cm long).

Materials and Methods. All commercial products were used as received unless otherwise stated. Arylstannane precursors were purchased from Frontier Scientific, Oakwood Products and Sigma Aldrich. Fluorine-19 reference standards were sourced commercially. Boc-Phe(4-I)-OH (CAS 62129-44-6) was purchased from Fisher. TriBoc-L-DOPA methyl ester (CAS: 857502-21-7) was obtained from ABX.

2. Synthesis and Characterization of Arylstannanes

General Procedure: Preparation of Trialkylarylstannanes

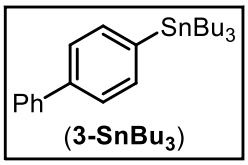
The general procedure is adapted from the literature.[1,2] In a nitrogen atmosphere glovebox, a 20 mL vial was charged with aryl iodide (1 mmol), $Pd(PPh_3)_4$ (224.6 mg, 0.19 mmol), and lithium chloride (202.9 mg, 4.8 mmol). The combined solids were dissolved in toluene (12.5 mL, 0.08 M) at room temperature. Hexabutylditin (2.6 mL, 5.2 mmol) or hexamethylditin (1.1 mL, 5.2 mmol) was added via syringe, and the vial was sealed and removed from the glovebox. The sealed vial was heated to 100 °C using an aluminum block. Once the reaction mixture turned black (generally 2-4 h), it was cooled to room temperature. Aqueous potassium fluoride (5.0 mL, 2 M solution) was added, and the mixture was stirred vigorously. After 30 min, the mixture was filtered through a plug of Celite (eluting with hexanes or toluene). The filtrate was washed with brine (25 mL), dried over magnesium sulfate, filtered, and concentrated under vacuum. The crude product was purified via flash column chromatography.



(**2-SnMe$_3$**)

4-Trimethylstannylanisole (2-SnMe$_3$)

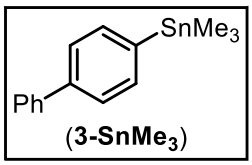
The published procedure was followed with small modifications.[3] Under nitrogen atmosphere, 4-methoxyaniline (491.7 mg, 4.0 mmol, 1 equiv) and TsOH•H_2O (929.0 mg, 4.9 mmol, 1.2 equiv) were weighed into an oven-dried round bottom flask. 1,2-Dichloroethane (DCE) (20 mL, 0.2 M) was added, and the flask was cooled to 0 °C. *t*-BuONO (0.4 mL, 8.2 mmol, 2.0 equiv) and Sn_2Me_6 (0.9 mL, 4.3 mmol, 1.1 equiv) were added in succession. The resulting reaction solution was stirred for 4 h at 0 °C under nitrogen. The solution was then filtered through a silica plug and concentrated under reduced pressure. Purification by flash column chromatography eluting with 20% diethyl ether in pentanes afforded **2-SnMe$_3$** as a colorless oil (59.3 mg, 22% yield, R_f = 0.8 in 10% ethyl acetate in hexanes). The ^{1}H and ^{13}C NMR spectra matched those reported previously in the literature.[3] HRMS (EI) [M – CH_3^+] Calculated for $C_9H_{13}OSn$: 256.9989; Found 256.9979.



(**3-SnBu$_3$**)

4-Tributylstannyl-1,1'-biphenyl (3-SnBu$_3$)

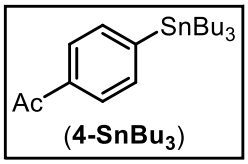
The general procedure was followed using 4-iodo-1,1'-biphenyl (279.5 mg, 1.0 mmol) and heating for 3 h. Purification by flash column chromatography eluting with hexanes afforded **3-SnBu$_3$** as a colorless oil (191.0 mg, 43% yield, R_f = 0.6 in 100% hexanes). The ^{1}H and ^{13}C NMR spectra matched those reported previously in the literature.[4] HRMS (EI) [M – $C_4H_9^+$] Calculated for $C_{20}H_{27}Sn$: 387.1135; Found 387.1135.



(**3-SnMe$_3$**)

4-Trimethylstannyl-1,1'-biphenyl (3-SnMe$_3$)

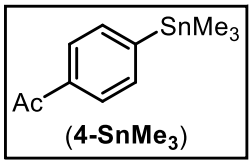
The general procedure was followed using 4-iodo-1,1'-biphenyl (280.1 mg, 1.0 mmol) and heating for 2 h. Purification by flash column chromatography eluting with hexanes afforded **3-SnBu$_3$** as a colorless oil (275.0 mg, 87% yield, R_f = 0.5 in 100% hexanes). The ^{1}H and ^{13}C NMR spectra matched those reported previously in the literature.[5] HRMS (EI) [M^+] Calculated for $C_{15}H_{18}Sn$: 318.0430; Found 318.0415.



(**4-SnBu$_3$**)

4-Tributylstannylacetophenone (4-SnBu$_3$)

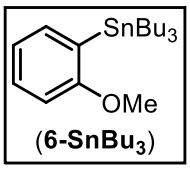
The general procedure was followed using 4-iodoacetophenone (246.3 mg, 1.0 mmol) and heating for 4 h. Purification by flash column chromatography eluting with hexanes afforded **4-SnBu$_3$** as a colorless oil (284.3 mg, 69 %, R_f = 0.56 in 5% ethyl acetate in hexanes). The ^{1}H and ^{13}C NMR spectra matched those reported previously in the literature.[4] HRMS (ESI$^+$) [M + K$^+$] Calculated for $C_{20}H_{34}KOSn$: 449.1263; Found 449.1263.



(**4-SnMe$_3$**)

4-Trimethylstannylacetophenone (4-SnMe$_3$)

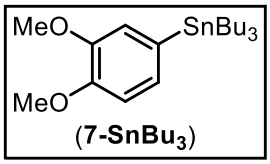
The general procedure was followed using 4-iodoacetophenone (245.9 mg, 1.0 mmol) and heating for 4 h. Purification by flash column chromatography eluting with 20% ethyl acetate in hexanes afforded **4-SnMe$_3$** as a colorless oil (147.0 mg, 52% yield, R_f = 0.7 in 10% ethyl acetate in hexanes). The ^{1}H and ^{13}C NMR spectra matched those reported previously in the literature.[3] HRMS (EI) [M – CH$_3^+$] Calculated for $C_{10}H_{13}OSn$: 268.9988; Found 268.9984.



(**6-SnBu$_3$**)

2-Tributylstannylanisole (6-SnBu$_3$)

The general procedure was followed using 2-iodoanisole (0.32 mL, 2.5 mmol) and heating for 6 h. Purification by flash column chromatography eluting with hexanes afforded **6-SnBu$_3$** as a colorless oil (604.2 mg, 62% yield, R_f = 0.6 in 100% hexanes). The ^{1}H and ^{13}C NMR spectra matched those reported previously in the literature.[4] HRMS (EI) [M – C$_4$H$_9^+$] Calculated for $C_{15}H_{25}OSn$: 341.0927; Found 341.0934.

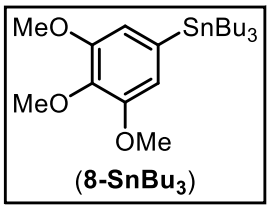


(**7-SnBu$_3$**)

(3,4-dimethoxyphenyl)tributylstannane (7-SnBu$_3$)

The general procedure was followed using 1-iodo-3,4-dimethoxybenzene (265.2 mg, 1.0 mmol) and heating for 2.5 h. Purification by flash column chromatography eluting with 20% ethyl acetate in hexanes afforded **7-SnBu$_3$** as a colorless oil (171.7 mg, 40% yield, R_f = 0.5 in 10% ethyl acetate in hexanes). The ^{1}H NMR spectra matched that reported previously in the literature.[6] HRMS (ESI) [M + Na^+] Calculated for $C_{20}H_{36}NaO_2Sn$: 451.1629; Found 451.1629.

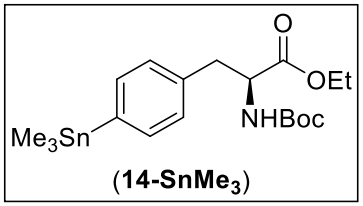
^{1}H NMR ($CDCl_3$): δ 6.99 (d, *J* = 7.7 Hz, 1H), 6.94 (s, 1H), 6.89 (d, *J* = 7.7 Hz, 1H), 3.89 (s, 3H), 2.87 (s, 3H), 1.56-1.52 (multiple peaks, 6H), 1.36-1.30 (multiple peaks, 6H), 1.05-1.03 (multiple peaks, 6H), 0.89 (t, *J* = 7 Hz, 9H)
^{13}C NMR ($CDCl_3$): δ 149.12, 148.65, 132.52, 129.17, 118.63, 111.20, 55.83, 55.62, 29.10, 27.37, 13.90, 9.67



(**8-SnBu$_3$**)

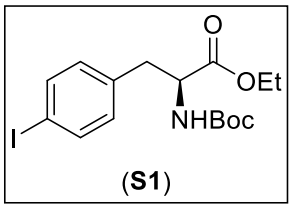
Tributyl(3,4,5-trimethoxy)stannane (8-SnBu$_3$)

The general procedure was followed using 5-iodo-1,2,3-trimethoxybenzene (294.5 mg, 1.0 mmol) and heating for 2 h. Purification by flash column chromatography eluting with 20% ethyl acetate in hexanes afforded **8-SnBu$_3$** as a colorless oil (326.7 mg, 71% yield, R_f = 0.7 in 20% ethyl acetate in hexanes). The ^{1}H and ^{13}C NMR spectra matched those reported previously in the literature.[7] HRMS (ESI) [M + H^+] Calculated for $C_{21}H_{39}O_3Sn$: 459.1916; Found 459.1915.



(**14-SnMe$_3$**)

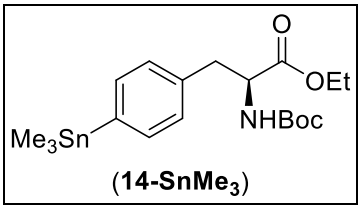
NHBoc-Phe(4-SnMe$_3$) ethyl ester (14-SnMe$_3$) was prepared by the following 2 step procedure.



(**S1**)

Step 1:
Iodide **S1** was prepared via a modification of a literature procedure.[8] To an oven-dried flask, Boc-Phe(4-I)-OH (1016.6 mg, 2.6 mmol, 1.0 equiv) was dissolved in dichloromethane (22 mL) at room temperature. DMAP (34.3 mg, 0.3 mmol, 0.1 equiv) and ethanol (0.3 mL, 5.1 mmol, 2.0 equiv) were added to the solution, and the reaction was placed under nitrogen and cooled to 0 °C. DCC (862.5 mg, 4.2 mmol, 1.6 equiv) was added slowly. The mixture was allowed to warm up to room temperature and react overnight at room temperature under nitrogen. The white precipitate formed was filtered off and the organic filtrate was washed with brine (1 x 20 mL), dried using magnesium sulfate, and concentrated. The crude residue was purified by column chromatography (silica gel, 20% ethyl acetate in hexane) affording the product (**S1**) as a white solid (1.01 g, 93% yield, R_f = 0.2 in 20% ethyl acetate in hexanes, mp = 91 – 92 °C).

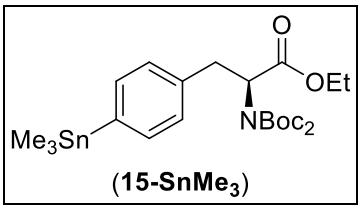
^{1}H NMR ($CDCl_3$): δ 7.57 (d, *J* = 7.7 Hz, 2H), 6.85 (d, *J* = 7.7 Hz, 2H), 5.00 (d, *J* = 7.0 Hz, 2H), 4.49 (d, *J* = 7.0 Hz, 2H), 4.11 (q, *J* = 7.0 Hz, 2H), 3.03 (m, 2H), 1.37 (s, 9H), 1.19 (t, *J* = 7.0 Hz, 3H)
^{13}C NMR ($CDCl_3$): δ 171.45, 154.90, 137.40, 135.76, 131.30, 92.32, 79.86, 61.38, 54.14, 37.82, 28.21, 14.06
HRMS (ESI+) [M + Na^+] Calculated for $C_{16}H_{22}INNaO_4$: 442.0486; Found 442.0489.



(**14-SnMe$_3$**)

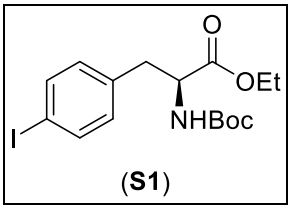
Step 2:
The general procedure for stannane synthesis was followed using **S1** (404.8 mg, 1.0 mmol) and heating for 2 h. Purification by flash column chromatography eluting with 20% ethyl acetate in hexanes afforded **14-SnBu$_3$** as a colorless oil (73.4 mg, 17% yield, R_f = 0.5 in 20% ethyl acetate in hexanes).

^{1}H NMR ($CDCl_3$): δ 7.39 (d, *J* = 10.5 Hz, 2H), 7.09 (d, *J* = 10.5 Hz, 2H), 4.96 (d, *J* = 10.5 Hz, 1H), 4.53 (d, *J* = 10.5 Hz, 1H), 4.14 (q, *J* = 9.8 Hz, 2 H), 3.03 (m, 2H), 1.39 (s, 9H), 1.22 (t, *J* = 9.8 Hz, 3H), 0.25 (s, 9H)
^{13}C NMR ($CDCl_3$): δ 171.59, 155.00, 135.95, 134.63, 130.70, 128.58, 61.47, 54.31, 37.79, 28.29, 14.13, –0.97, –9.61
HRMS (ESI) [M + H^+] Calculated for $C_{19}H_{32}NO_4Sn$: 458.1348; Found 458.1352.



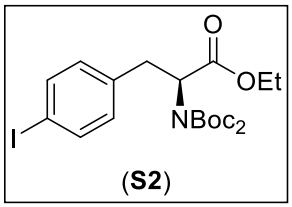
(**15-SnMe$_3$**)

NBoc$_2$-Phe(4-SnMe$_3$) ethyl ester (15-SnMe$_3$) was prepared by the following 3 step procedure.



(**S1**)

Step 1: see above procedure



(**S2**)

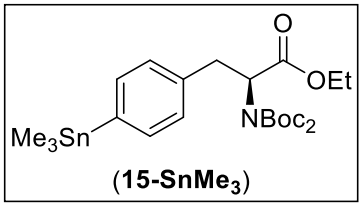
Step 2:

Iodide **S2** was prepared via a modified literature porcedure.[9] To a solution of **S1** (546.0 mg, 1.3 mmol) in dry acetonitrile (25 mL) under nitrogen was added 4-dimethylaminopyridine (DMAP) (75.3 mg, 0.6 mmol) in dry acetonitrile (10 mL) and then di-*tert*-butyl dicarbonate (0.7 mL, 3.1 mmol) in dry acetonitrile (10 mL). The mixture was stirred at room temperature overnight and then concentrated under vacuum. Purification by flash column chromatography eluting with 20% ethyl acetate in hexanes afforded **S2** as a colorless oil (407.9 mg, 60% yield, R_f = 0.54 in 20% ethyl acetate in hexanes).

^{1}H NMR ($CDCl_3$): δ 7.56 (d, *J* = 11.9 Hz, 2H), 6.91 (d, *J* = 11.9 Hz, 2H), 5.05 (dd, *J* = 7.3, 14.2 Hz, 1H), 4.18 (m, 2H), 3.35 (dd, *J* = 7.3, 19.6 Hz, 1H), 3.13 (dd, *J* = 14.2, 19.6 Hz, 1H), 1.38 (s, 18H), 1.25 (t, *J* = 9.8 Hz, 3H)

^{13}C NMR ($CDCl_3$): δ 170.08, 151.79, 137.42, 137.32, 131.62, 91.82, 83.04, 61.40, 59.11, 35.63, 27.84, 14.11

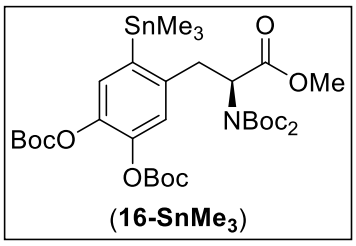
HRMS (ESI+) [M + Na^+] Calculated for $C_{21}H_{30}INNaO_6$: 542.0101; Found 542.0102.



(**15-SnMe$_3$**)

Step 3:
The general procedure for stannane synthesis was followed using **S2** (407.9 mg, 0.8 mmol) and heating for 2 h. Purification by flash column chromatography eluting with 20% ethyl acetate in hexanes afforded **15-SnBu$_3$** as a yellow oil (230.4 mg, 53% yield, R_f = 0.6 in 20% ethyl acetate in hexanes).

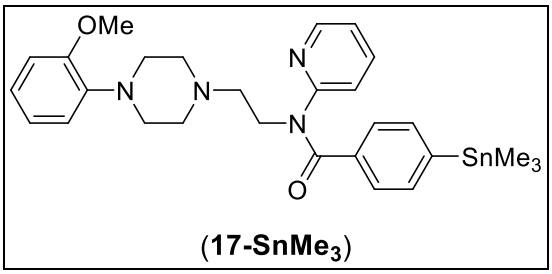
^{1}H NMR ($CDCl_3$): δ 7.36 (d, *J* = 7.7 Hz, 2H), 7.14 (d, *J* = 7.7 Hz, 2H), 5.08 (dd, *J* = 10.5, 4.9 Hz, 1H), 4.18 (m, 2H), 3.38 (dd, *J* = 14.0, 4.9 Hz, 1H), 3.18 (dd, *J* = 14.0, 10.5 Hz, 1H) 1.36 (s, 18H), 1.25 (t, *J* = 7 Hz, 3H), 0.22 (s, 9H)
^{13}C NMR ($CDCl_3$): δ 170.38, 151.66, 139.78, 137.71, 135.82, 129.35, 82.83, 61.34, 59.60, 36.07, 27.86, 14.15, –9.71
HRMS (ESI) [M + H$^+$] Calculated for $C_{24}H_{40}NO_6Sn$: 558.1883; Found 558.1883.



(**16-SnMe$_3$**)

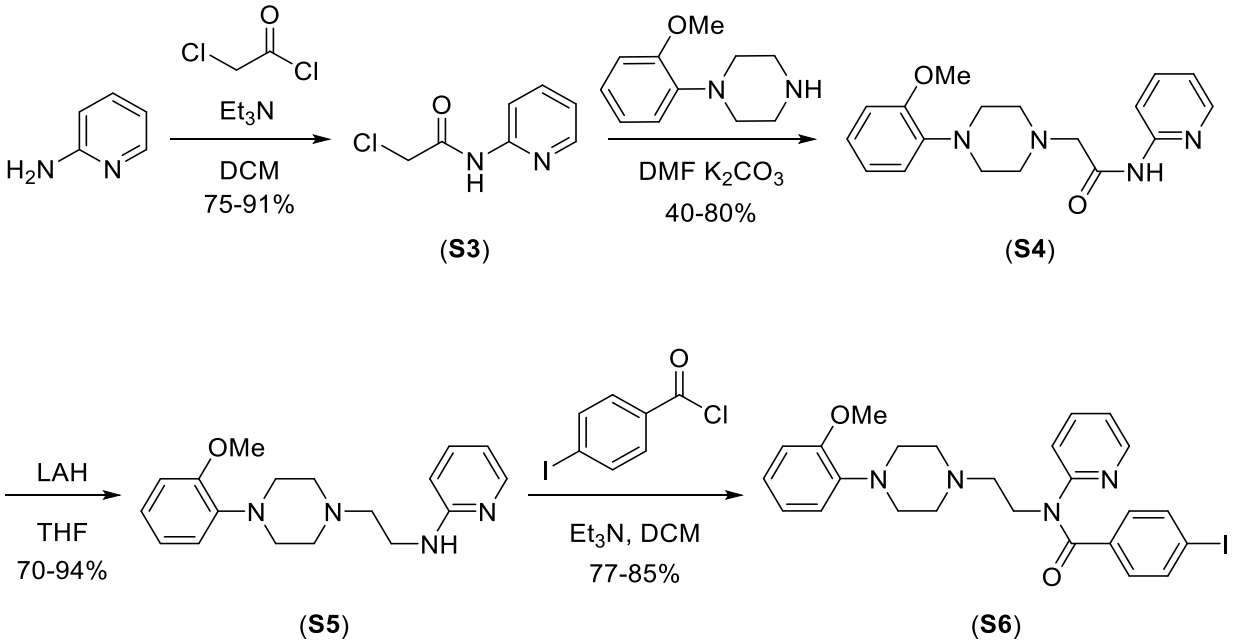
Boc$_4$DOPA(2-SnMe$_3$) methyl ester (16-SnMe$_3$)
Arylstannane **16-SnMe$_3$** was prepared via a modified literature porcedure.[9] To a solution of Boc_3DOPA-$SnMe_3$ (445.1 mg, 0.7 mmol) in dry acetonitrile (10 mL) under nitrogen was added 4-dimethylaminopyridine (DMAP) (32.3.0 mg, 0.28 mmol, 0.4 equiv) in dry acetonitrile (4.6 mL) and di-*tert*-butyl dicarbonate (0.3 mL, 1.3 mmol, 2 equiv) in dry acetonitrile (4.4 mL). The reaction was stirred at room temperature overnight and then concentrated under vacuum. Purification by flash column chromatography eluting with 20% ethyl acetate in hexanes afforded **16-SnMe$_3$** as a yellow oil (407.6 mg, 80% yield, R_f = 0.46 in 20% ethyl acetate in hexanes).

^{1}H NMR ($CDCl_3$): δ 7.22 (s, 1H), 7.01, (s, 1H), 5.03 (dd, *J* = 10.5, 4.2 Hz, 1H), 3.73 (s, 3H), 3.38 (dd, *J* = 14.7, 4.2 Hz, 1H), 3.29 (dd, *J* = 14.7, 10.5 Hz, 1H) 1.52 (s, 9H), 1.50 (s, 9H), 1.37 (s, 18H), 0.31 (s, 9H)
^{13}C NMR ($CDCl_3$): δ 170.59, 151.79, 150.72, 150.59, 142.95, 142.44, 141.28, 140.50, 130.00, 123.82, 83.44, 83.36, 83.19, 59.24, 52.36, 37.98, 27.84, 27.62, 27.61, –8.13
HRMS (ESI) [M + Na$^+$] Calculated for $C_{33}H_{53}NNaO_{12}Sn$: 798.2482; Found 798.2491.

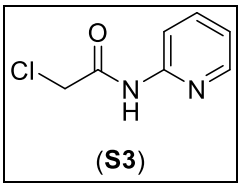


(**17-SnMe$_3$**)

MPP-SnMe$_3$ (17-SnMe$_3$) was prepared by the following 5-step procedure.



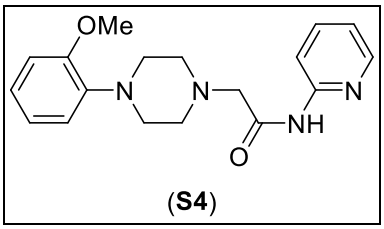
(**S3**) (**S4**) (**S5**) (**S6**)



(**S3**)

Step 1:

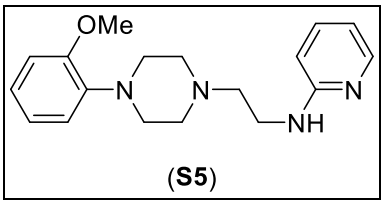
Intermediate **S3** was prepared according to a literature procedure.[10] Purification afforded **S3** as a white solid (0.734 g, 91% yield, mp = 120 – 121 °C). The ^{1}H NMR spectra matched that reported previously in the literature.[10] HRMS [M + H$^+$] Calculated for $C_7H_8ClN_2O$: 171.0320; Found 171.0318.



(**S4**)

Step 2:

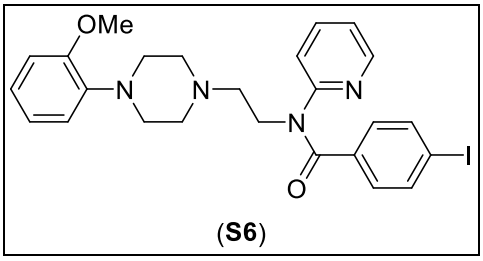
Intermediate **S4** was prepared according to a literature procedure.[10] Purification afforded **S4** as a yellow oil (1.01 g, 80% yield). The ^{1}H NMR spectra matched that reported previously in the literature.[10] HRMS [M + H$^+$] Calculated for $C_{18}H_{23}N_4O_2$: 327.1816; Found 327.1915.



(**S5**)

Step 3:

Precursor **S5** was prepared according to a literature procedure.[10] Purification afforded **S5** as a tan solid (0.903 g, 94% yield, mp = 87 – 89 °C). The ^{1}H NMR spectra matched that reported previously in the literature.[10] HRMS [M + H$^+$] Calculated for $C_{18}H_{25}N_4O$: 313.2023; Found 313.2022.

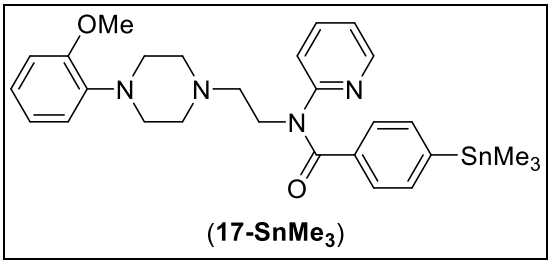


(**S6**)

Step 4:

Precursor **S6** was prepared according to the procedure in the literature.[10] Purification afforded **S6** as a white solid (0.670 g, 77% yield, mp = 104 – 105 °C). The ^{1}H NMR

spectra matched that reported previously in the literature.[10] HRMS [M + H^+] Calculated for $C_{25}H_{28}IN_4O_2$: 543.1251; Found 543.1247.

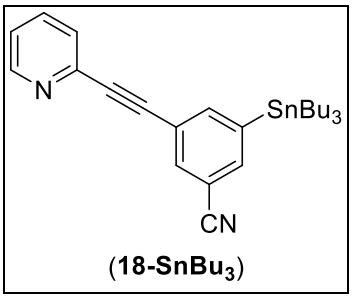


(**17-SnMe$_3$**)

Step 5:

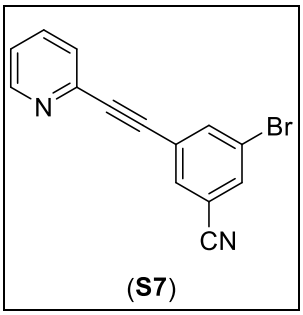
The general procedure was followed using **S6** (200.0 mg, 0.37 mmol) and heating for 2 h. Purification by flash column chromatography eluting with 50% ethyl acetate in hexanes afforded **17-SnMe$_3$** as a white solid (132.8 mg, 62% yield, R_f = 0.16 in 50% ethyl acetate in hexanes, mp = 140 – 141 °C).

^{1}H NMR ($CDCl_3$): δ 8.41 (dd, *J* = 4.9, 1.4 Hz, 1H), 7.37 (td, *J* = 7.7, 2.1 Hz, 1H), 7.30 (d, *J* = 7.7 Hz, 2H), 7.25 (d, *J* = 7.7 Hz, 2H), 6.84-7.00 (multiple peaks, 5H), 6.82 (dd, *J* = 8.4, 1.4 Hz, 1H), 6.75 (d, *J* = 8.4 Hz, 1H), 4.27 (t, *J* = 7.0 Hz, 2 H), 3.82 (s, 3H), 2.90 (broad peak, 4H), 2.73 (t, *J* = 7.0 Hz, 2 H), 2.61 (broad peak, 4H), 0.22 (s, 9H)
^{13}C NMR ($CDCl_3$): δ 170.72, 156.59, 152.22, 148.52, 145.70, 141.39, 136.94, 135.97, 135.30, 127.93, 122.91, 122.73, 120.90, 120.70, 118.05, 111.17, 56.41, 55.32, 53.32, 50.62, 45.49, –9.56
HRMS (ESI+) [M + H^+] Calculated for $C_{28}H_{37}N_4O_2Sn$: 581.1933; Found 581.1950.



(**18-SnBu$_3$**)

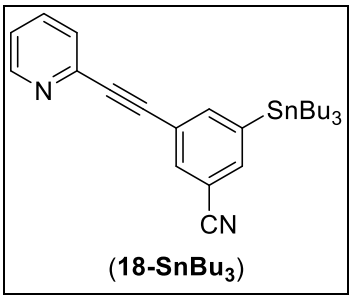
PEB-SnBu$_3$ (18-SnBu$_3$) was prepared by the following 2 step procedure.



(**S7**)

Step 1:

Aryl bromide **S7** was prepared via a literature procedure.[11,12] The product was purified by flash column chromatography on silica gel (15% ethyl acetate in hexanes), which afforded **S7** as a yellow solid (687.0 mg, 49% yield, R_f = 0.32 in 30% ethyl acetate in hexanes, mp = 108 – 109 °C). The ^{1}H and ^{13}C NMR spectra matched those reported previously in the literature.[12,13] HRMS (ESI+) [M + H$^+$] Calculated for $C_{14}H_8BrN_2$: 282.9865; Found 282.9865.

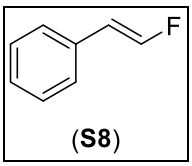


(**18-SnBu$_3$**)

Step 2:

The general procedure was followed using **S7** (263.9 mg, 0.93 mmol) and heating for 7 h. Purification by flash column chromatography eluting with 30% ethyl acetate in hexanes afforded **18-SnBu$_3$** as a yellow oil (245.8 mg, 54% yield, R_f = 0.43 in 20% ethyl acetate in hexanes). The ^{1}H and ^{13}C NMR spectra matched those reported previously in the literature.[13] HRMS (EI) [M + H$^+$] Calculated for $C_{26}H_{35}N_2Sn$: 495.1817; Found 495.1820.

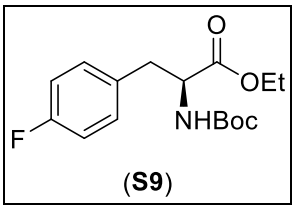
3. Synthesis and Characterization of Fluorinated Standards



(**S8**)

(*E*)-Fluorostyrene (S8)

In a nitrogen atmosphere glovebox, tributyl(phenylethenyl)tin (415.9 mg, 1.1 mmol, 1 equiv), $Cu(OTf)_2$ (766.2 mg, 2.1 mmol, 2 equiv), KF (245.3 mg, 4.2 mmol, 4 equiv), and pyridine (1.3 mL, 16.1 mmol, 15 equiv) were weighed into a flask equipped with a magnetic stir bar. DMA (100 mL) was added. The reaction mixture was allowed to stir at 140 ºC for 4 h. The resulting solution was cooled to room temperature, diluted with diethyl ether and washed with water (2 x 200 mL), and brine (200 mL). The organic extracts were dried and concentrated. Purification by flash column chromatography eluting with 20% diethyl ether in pentane afforded **S8** as a colorless oil. The ^{19}F NMR spectroscopic data was identical to that reported.[14]

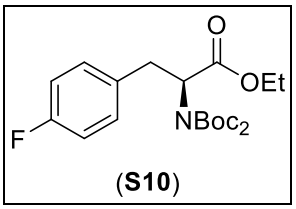


(**S9**)

NHBoc-Phe(4-F) ethyl ester (S9)

Authentic standard **S9** was prepared by the following procedure via a modification of a literature procedure.[8] To an oven-dried flask, NHBoc-Phe(4-F)-OH (509.4 mg, 1.8 mmol, 1.0 equiv) was dissolved in dichloromethane (15 mL, 0.12 M) at room temperature. DMAP (22.2 mg, 0.18 mmol, 0.1 equiv) and ethanol (0.21 mL, 3.6 mmol, 2.0 equiv) were added to the solution and the reaction was placed under nitrogen and cooled to 0 °C. DCC (595.0 mg, 2.9 mmol, 1.6 equiv) was added slowly. The mixture was allowed to warm to room temperature and was then stirred overnight at room temperature under nitrogen. Over this time, a white precipitate formed and was removed by filtration. The filtrate was washed with brine (1 x 20 mL), dried over magnesium sulfate, and concentrated. The crude residue was purified by column chromatography (silica gel, 20% ethyl acetate in hexane) affording the product (**S9**) as a colorless oil (453.1 mg, 81% yield, R_f = 0.44 in 20% ethyl acetate in hexanes). The ^1H and ^{13}C NMR spectra matched those reported previously in the literature.[15] HRMS (ESI) [M + H^+] Calculated for $C_{16}H_{23}FNO_4$: 312.1606; Found 312.1611.

^{19}F NMR ($CDCl_3$): δ –116.01

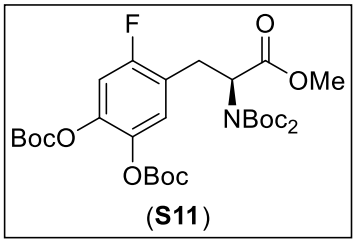


(**S10**)

NBoc$_2$-Phe(4-F) ethyl ester (S10)

Authentic standard **S10** was prepared via a modification of a literature procedure.[9] To a solution of **S9** (334.5 mg, 1.07 mmol, 1 equiv) in dry acetonitrile (20 mL) under nitrogen was added 4-dimethylaminopyridine (DMAP) (54.0 mg, 0.44 mmol, 0.4 equiv) in dry acetonitrile (5 mL) and di-*tert*-butyl dicarbonate (0.5 mL, 2.2 mmol, 2.0 equiv) in dry acetonitrile (5 mL). The mixture was stirred at room temperature overnight and then concentrated under nitrogen. Purification by flash column chromatography eluting with 20% ethyl acetate in hexanes afforded **S10** as a colorless oil (81.5 mg, 18% yield, R_f = 0.5 in 20% ethyl acetate in hexanes).

^{1}H NMR ($CDCl_3$): δ 7.12 (dd, *J* = 8.4, 4.9 Hz, 2H), 6.93 (t, *J* = 8.4 Hz, 2H, 5.06 (dd, *J* = 9.8, 4.9 Hz, 1H), 4.18 (m, 2H), 3.37 (dd, *J* = 14.0, 4.9 1H), 3.16 (dd, *J* = 14.0, 9.8 Hz, 1H), 1.38 (s, 18H), 1.25 (t, *J* = 7.0 Hz, 3H)
^{13}C NMR ($CDCl_3$): δ 170.24, 162.42, 161.03, 151.83, 133.46, 133.44, 131.00, 130.96, 115.14, 115.02, 82.98, 61.39, 59.39, 35.27, 27.88, 14.14
^{19}F NMR ($CDCl_3$): δ –116.93
HRMS (ESI) [M + H$^+$] Calculated for $C_{21}H_{31}FNO_6$: 412.2130; Found 412.2136.



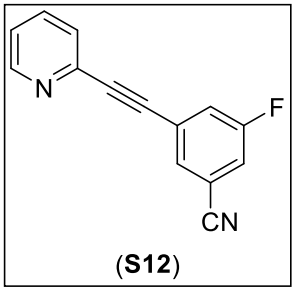
(**S11**)

Boc$_4$DOPA(2-F) methyl ester (S11)

In a nitrogen atmosphere glovebox, **16-SnMe$_3$** (311.0 mg, 0.4 mmol, 1 equiv), $Cu(OTf)_2$ (290.0 mg, 0.8 mmol, 2 equiv), KF (93.3 mg, 1.6 mmol, 4 equiv), and pyridine (0.5 mL, 6.2 mmol, 15 equiv) were weighed into a flask equipped with a magnetic stir bar. DMA (40 mL, 0.01M) was added. The reaction mixture was allowed to stir at 100 ºC for 2 h. The resulting solution was cooled to room temperature, diluted with diethyl ether, and washed with water (2 x 200 mL) and brine (200 mL). The organic extracts were dried over magnesium sulfate and concentrated. Purification by flash column chromatography eluting with 20% ethyl acetate in hexanes afforded **S11** as a colorless oil (19.1 mg, 8% yield, R_f = 0.6 in 40% ethyl acetate in hexanes).

^{1}H NMR ($CDCl_3$): δ 7.05 (d, *J* = 9.8 Hz, 1H), 6.97 (d, *J* = 13.3 Hz, 1H), 5.18 (dd, *J* = 14.0, 7.0 Hz, 1H), 3.73 (s, 3H), 3.43 (dd, *J* = 19.6, 7.0 Hz, 1H), 3.21 (dd, *J* = 19.6, 14.0 Hz, 1H), 1.51 (s, 18H), 1.38 (s, 18H)

^{13}C NMR ($CDCl_3$): δ 170.45, 158.88, 157.46 151.55, 150.57, 150.09, 141.80, 138.39, 125.37, 122.66, 110.43, 84.05, 83.76, 83.29, 57.73, 52.34, 29.45, 27.81, 27.57
^{19}F NMR ($CDCl_3$): δ –117.64
HRMS (ESI) [M + NH_4^+] Calculated for $C_{30}H_{48}FN_2O_{12}$: 647.3186; Found 647.3184.

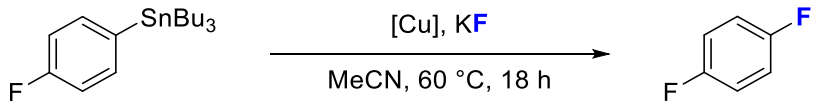


(**S12**)

F-PEB (S12)
Aryl fluoride **S12** was prepared via a literature procedure.[12] The product was purified by flash chromatography on silica gel (15% ethyl acetate in hexanes), which afforded **S12** as a brown solid (142.9 mg, 63% yield R_f = 0.15 in 20% ethyl acetate in hexanes, mp = 75 – 77 °C). The ^{1}H and ^{13}C NMR spectra matched those reported previously in the literature.[12,16]
^{19}F NMR ($CDCl_3$): δ –108.9
HRMS (ESI+) [M + H^+] Calculated for $C_{14}H_8FN_2$: 223.0666; Found 223.0664.

4. Experimental Details

Copper Screen for Cu-Mediated Fluorination of **1-SnBu$_3$** with KF



(**1-SnBu$_3$**) (**1**)

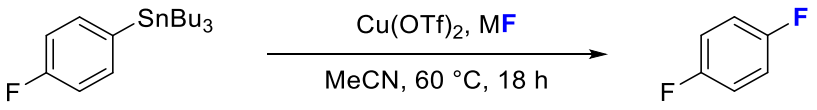
In a nitrogen atmosphere glovebox, substrate **1-SnBu$_3$** (0.1 mL, 0.25 M, 0.025 mmol, 1 equiv), copper salt (0.1 mmol, 4 equiv) and KF (5.8 mg, 0.1 mmol, 4 equiv) were weighed into a 4 mL vial. MeCN (0.3 mL total volume) was added, and the vial was sealed with a Teflon-lined cap. The reaction mixture was allowed to stir at 60 ºC for 18 h. The resulting solution was diluted with MeCN (1 mL). 1,2-Difluorobenzene was added as an internal standard, and the crude reaction was analyzed by ^{19}F NMR spectroscopy. The yields of **1** are listed in **Table S1**.

Table S1. Copper Screen for Cu-Mediated Fluorination of **1-SnBu$_3$** with KF

entry	[Cu]	Yield[a]
1	$Cu(OTf)_2$	35%
2	$Cu(OAc)_2$	nd
3	Cu(OAc)	nd
4	CuF_2	nd
5	$(MeCN)_4Cu(OTf)$	nd
6	$(py)_4Cu(OTf)_2$	nd

[a]nd = not detected

Fluoride Screen for Cu-Mediated Fluorination of **1-SnBu$_3$** with KF



(**1-SnBu$_3$**) (**1**)

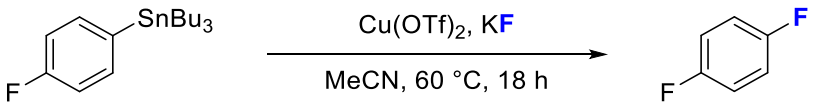
In a nitrogen atmosphere glovebox, substrate **1** (0.1 mL, 0.25 M, 0.025 mmol, 1 equiv), $Cu(OTf)_2$ (36 mg, 0.1 mmol, 4 equiv), and the appropriate metal fluoride(0.1 mmol, 4 equiv) were weighed into a 4 mL vial. MeCN (0.3 mL total volume) was added, and the vial was sealed with a Teflon-lined cap. The reaction mixture was allowed to stir at 60 ºC for 18 h. The resulting solution was diluted with MeCN (1 mL). 1,2-Difluorobenzene was added as an internal standard, and the crude reaction was analyzed by ^{19}F NMR spectroscopy. The yields of **1** are listed in **Table S2**.

Table S2. Fluoride Evaluation for Cu-Mediated Fluorination of **1**

entry	M[F]	Yield[a]
1	KF	35%
2	NaF	nd
3	LiF	nd
4	CsF	trace
5	AgF	trace
6	TBAF•3H_2O	25%

[a]nd = not detected

Copper Loading for Cu-Mediated Fluorination of **1-SnBu$_3$** with KF



(**1-SnBu$_3$**) (**1**)

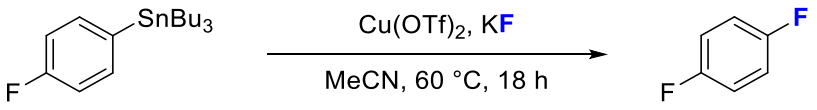
In a nitrogen atmosphere glovebox, substrate **1** (0.1 mL, 0.25 M, 0.025 mmol, 1 equiv), $Cu(OTf)_2$, and KF (5.8 mg, 0.1 mmol, 4 equiv) were weighed into a 4 mL vial. MeCN (0.3 mL total volume) was added, and the vial was sealed with a Teflon-lined cap. The reaction mixture was allowed to stir at 60 ºC for 18 h. The resulting solution was diluted with MeCN (1 mL). 1,2-Difluorobenzene was added as an internal standard, and the crude reaction was analyzed by ^{19}F NMR spectroscopy. The yields of **1** are listed in **Table S3**.

Table S3. Copper Loading for Cu-Mediated Fluorination of **1**

entry	$Cu(OTf)_2$ (equiv)	Yield[a]
1	0	nd
2	1	14%
3	2	42%
4	3	40%
5	4	32%
6	8	22%
7	10	17%
8	15	20%

[a]nd = not detected

Fluoride Loading for Cu-Mediated Fluorination of **1-SnBu$_3$** with KF



(**1-SnBu$_3$**) (**1**)

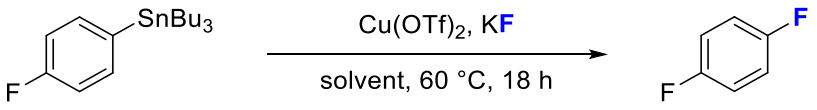
In a nitrogen atmosphere glovebox, substrate **1** (0.1 mL, 0.25 M, 0.025 mmol, 1 equiv), $Cu(OTf)_2$ (36 mg, 0.1 mmol, 4 equiv), and KF were weighed into a 4 mL vial. MeCN (0.3 mL total volume) was added, and the vial was sealed with a Teflon-lined cap. The reaction mixture was allowed to stir at 60 ºC for 18 h. The resulting solution was diluted with MeCN (1 mL). 1,2-Difluorobenzene was added as an internal standard, and the crude reaction was analyzed by ^{19}F NMR spectroscopy. The yields of **1** are listed in **Table S4**.

Table S4. Fluoride Loading for Cu-Mediated Fluorination of **1**

entry	KF (equiv)	Yield[a]
1	0	nd
2	1	18%
3	2	37%
4	3	34%
5	4	48%
6	5	30%
7	8	46%
8	10	48%

[a]nd = not detected

Solvent Screen for Cu-Mediated Fluorination of **1-SnBu$_3$** with KF



(**1-SnBu$_3$**) (**1**)

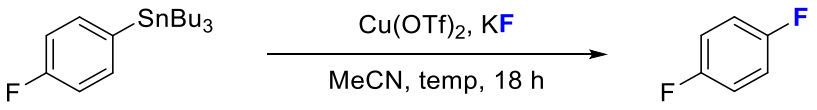
In a nitrogen atmosphere glovebox, substrate **1** (0.1 mL, 0.25 M, 0.025 mmol, 1 equiv), $Cu(OTf)_2$ (36 mg, 0.1 mmol, 4 equiv), and KF (5.8 mg, 0.1 mmol, 4 equiv) were weighed into a 4 mL vial. Solvent (0.3 mL total volume) was added, and the vial was sealed with a Teflon-lined cap. The reaction mixture was allowed to stir at 60 ºC for 18 h. The resulting solution was diluted with MeCN (1 mL). 1,2-Difluorobenzene was added as an internal standard, and the crude reaction was analyzed by ^{19}F NMR spectroscopy. The yields of **1** are listed in **Table S5**.

Table S5. Solvent Screen for Cu-Mediated Fluorination of **1**

Entry	Solvent	Yield[a]
1	CH_3CN	47%
2	^{t}BuCN	25%
3	dioxane	nd
4	DMF	nd
5	DMSO	nd
6	THF	nd

nd = not detected

Temperature Screen for Cu-Mediated Fluorination of **1-SnBu$_3$** with KF



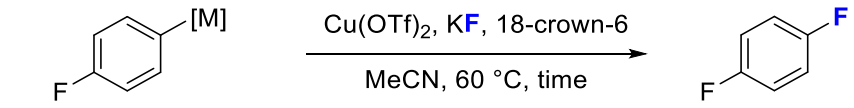
(**1-SnBu$_3$**) (**1**)

In a nitrogen atmosphere glovebox, substrate **1** (0.1 mL, 0.25 M, 0.025 mmol, 1 equiv), $Cu(OTf)_2$ (36 mg, 0.1 mmol, 4 equiv), and KF (5.8 mg, 0.1 mmol, 4 equiv) were weighed into a 4 mL vial. MeCN (0.3 mL total volume) was added, and the vial was sealed with a Teflon-lined cap. The reaction mixture was allowed to stir for 18 h at the appropriate temperature. The resulting solution was diluted with MeCN (1 mL). 1,2-Difluorobenzene was added as an internal standard, and the crude reaction was analyzed by ^{19}F NMR spectroscopy. The yields of **1** are listed in **Table S6**.

Table S6. Temperature Screen for Cu-Mediated Fluorination of **1**

entry	Temperature	Yield
1	rt	48%
2	60 °C	47%
3	80 °C	51%
4	110 °C	32%
5	140 °C	13%

Time Study for Cu-Mediated Fluorination of **1-SnBu$_3$** versus **1-BF$_3$K**



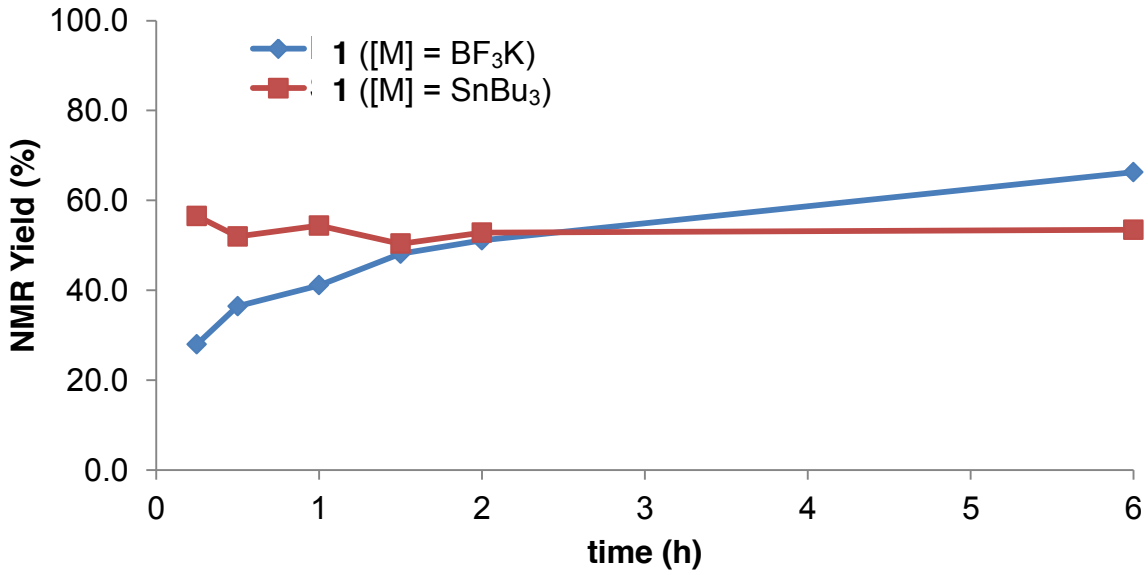
[M] = SnBu$_3$ (**1-SnBu$_3$**)
[M] = BF$_3$K (**1-BF$_3$K**)

(**1**)

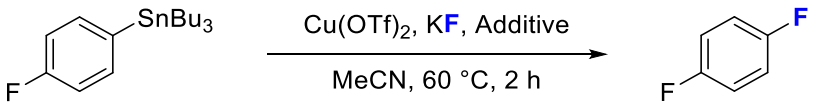
In a nitrogen atmosphere glovebox, substrate **1** (0.025 mmol, 1 equiv), Cu(OTf)$_2$ (36 mg, 0.1 mmol, 4 equiv), KF (5.8 mg, 0.1 mmol, 4 equiv), and 18-crown-6 (26 mg, 0.1 mmol, 4 equiv) were weighed into a 4 mL vial. MeCN (0.3 mL total volume) was added, and the vial was sealed with a Teflon-lined cap. The reaction mixture was allowed to stir at 60 ºC for the appropriate time. The resulting solution was diluted with MeCN (1 mL). 1,2-Difluorobenzene was added as an internal standard, and the crude reaction was analyzed by ^{19}F NMR spectroscopy. The yields of **1** are listed in **Table S7**.

Table S7. Solvent Screen for Cu-Mediated Fluorination of **1**

entry	Time (h)	Yield (%) [M] = SnBu$_3$	Yield (%) [M] = BF$_3$K
1	0.25	56	28
2	0.5	52	37
3	1	54	41
4	1.5	50	48
5	2	53	51
6	6	54	66



Effects of Additives for Cu-Mediated Fluorination of **1-SnBu$_3$** with KF



(**1-SnBu$_3$**) (**1**)

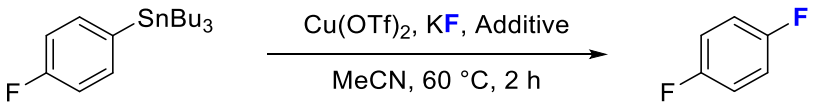
In a nitrogen atmosphere glovebox, substrate **1** (0.1 mL, 0.25 M, 0.025 mmol, 1 equiv), $Cu(OTf)_2$ (36 mg, 0.1 mmol, 4 equiv), KF (5.8 mg, 0.1 mmol, 4 equiv), and the appropriate additive (0.1 mmol, 4 equiv) were weighed into a 4 mL vial. MeCN (0.3 mL total volume) was added, and the vial was sealed with a Teflon-lined cap. The reaction mixture was allowed to stir at 60 ºC for 2 h. The resulting solution was diluted with MeCN (1 mL). 1,2-Difluorobenzene was added as an internal standard, and the crude reaction was analyzed by ^{19}F NMR spectroscopy. The yields of **1** are listed in **Table S8**.

Table S8. Effects of Additives for Cu-Mediated Fluorination of **1**

entry	additive	Yield[a]
1	--	42%
2	18-crown-6	56%
3	dibenzo-24-crown-8	28%
4	12-crown-4 (2.5)	42%
5	NBu_4OTf	49%
6	NBu_4BF_4	45%
7	NBu_4PF_6	42%
8	NBu_4Cl	nd
9	NBu_4CN	nd
10	NBu_4I	nd

[a]nd = not detected

18-Crown-6 Loading for Cu-Mediated Fluorination of **1-SnBu$_3$** with KF



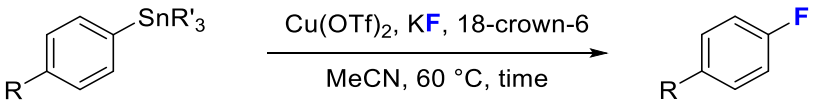
(**1-SnBu$_3$**) (**1**)

In a nitrogen atmosphere glovebox, substrate **1** (0.1 mL, 0.25 M, 0.025 mmol, 1 equiv), $Cu(OTf)_2$ (36 mg, 0.1 mmol, 4 equiv), KF (5.8 mg, 0.1 mmol, 4 equiv), and 18-crown-6 were weighed into a 4 mL vial. MeCN (0.3 mL total volume) was added, and the vial was sealed with a Teflon-lined cap. The reaction mixture was allowed to stir at 60 ºC for 2 h. The resulting solution was diluted with MeCN (1 mL). 1,2-Difluorobenzene was added as an internal standard, and the crude reaction was analyzed by ^{19}F NMR spectroscopy. The yields of **1** are listed in **Table S9**.

Table S9. 18-crown-6 Loading for Cu-Mediated Fluorination of **1**

entry	18-crown-6 (equiv)	Yield
1	0	46%
2	0.5	47%
3	1	49%
4	2	50%
5	4	63%

Trimethyltin versus Tributyltin Substrates

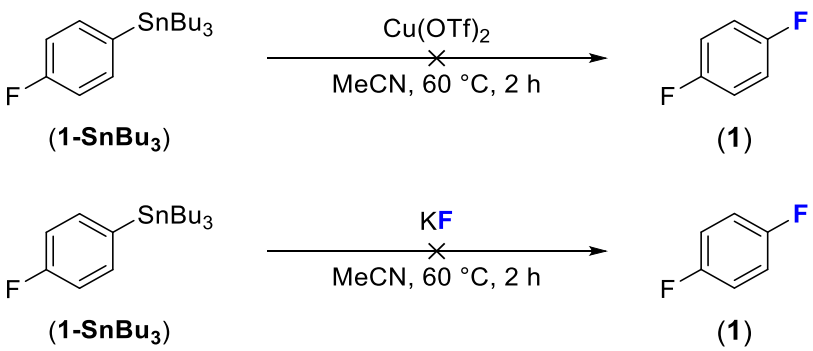


In a nitrogen atmosphere glovebox, arylstannane substrate (0.1 mL, 0.25 M, 0.025 mmol, 1 equiv), $Cu(OTf)_2$ (36 mg, 0.1 mmol, 4 equiv), KF (5.8 mg, 0.1 mmol, 4 equiv), and 18-crown-6 (26 mg, 0.1 mmol, 4 equiv) were weighed into a 4 mL vial. MeCN (0.3 mL total volume) was added, and the vial was sealed with a Teflon-lined cap. The reaction mixture was allowed to stir at 60 ºC for 2 h. The resulting solution was diluted with MeCN (1 mL). 1,2-Difluorobenzene was added as an internal standard, and the crude reaction was analyzed by ^{19}F NMR spectroscopy. The yields of aryl fluoride product are listed in **Table S10**.

Table S10. Trimethyltin versus Tributyltin Substrates

entry	R	R'	Yield (%) (15 min)	Yield (%) (2 h)
1	F	Bu	52	53
2	MeO	Bu	23	21
3	MeO	Me	24	25
4	Ph	Bu	34	30
5	Ph	Me	64	52
6	Ac	Bu	57	69
7	Ac	Me	65	75

Control Reactions for Fluorination of **1-SnBu$_3$**



Control reactions for the fluorination of substrate **1-SnBu$_3$** were conducted without copper salt and without KF. In both cases, the fluorinated product **1** was not observed. The reactions were conducted using to the general procedure (*vida infra*), on a 0.025 mmol scale.

5. Radiochemistry

5.1 Materials and Methods

Unless otherwise stated, reagents and solvents were commercially available and used without further purification. HPLC grade acetonitrile, anhydrous *N,N*-dimethylformamide, anhydrous *N,N*-dimethylacetamide, potassium trifluoromethanesulfonate, and potassium carbonate were purchased from Fisher Scientific. Sterile product vials were purchased from Hollister-Stier. QMA-light Sep-Paks were purchased from Waters Corporation. QMA-light Sep-Paks were flushed with 10 mL of ethanol, followed by 10 mL of 90 mg/mL potassium trifluoromethanesulfonate solution, and finally 10 mL of sterile water prior to use.

5.2 Synthesis of [^{18}F]KF

All loading operations were conducted under an ambient atmosphere. Argon was used as a pressurizing gas during automated sample transfers. Potassium [^{18}F]fluoride was prepared using a TRACERLab FXFN automated radiochemistry synthesis module (General Electric, GE). [^{18}F]Fluoride was produced via the ^{18}O(p,n)^{18}F nuclear reaction using a GE PETTrace cyclotron (40 μA beam for 2-5 min generated ca. 150-375 mCi of [^{18}F]fluoride). The [^{18}F]fluoride was delivered to the synthesis module in a 1.5 mL bolus of [^{18}O]water and trapped on a QMA-light Sep-Pak to remove [^{18}O]water and other impurities. [^{18}F]Fluoride was eluted into the reaction vessel using 550 μL of an aqueous solution containing 10 mg potassium trifluoromethanesulfonate and 50 μg of potassium carbonate. One milliliter of acetonitrile was added to the reaction vessel, and the resulting solution was dried by azeotropic distillation to provide anhydrous [^{18}F]KF. Azeotropic drying/evaporation was achieved by heating the reaction vessel to 100 ºC and drawing vacuum for 6 min. The reaction vessel was then subjected to an argon stream and simultaneous vacuum draw for an additional 6 min. *N,N*-Dimethylacetamide (8 mL) was added to the dried reagent, and the sample was cooled to 40 ºC and was transferred to a S10 sterile vial for subsequent use in reactions. As an example, approximately 80 mCi of prepared [^{18}F]KF in 8 mL DMA is isolated with a 5 min cyclotron beam. It should be noted that percent recovery data is only relevant for manual reactions, not automated one-pot syntheses.

5.3 Synthesis of ^{18}F-Labeled Molecules (Manual Synthesis)

Unless otherwise noted, this procedure was used for the synthesis of the [^{18}F]fluorinated substrates described in main text. Stock solutions of arylstannane precursor (0.1 M), copper (II) trifluoromethanesulfonate (0.2 M), and pyridine (1M) in DMA were prepared immediately prior to the start of the reaction. Aliquots of these solutions were used to carry out subsequent [^{18}F]fluorination reactions. In a typical reaction, a 0.1 mL (0.020 mmol, 2 equiv) aliquot of copper(II) trifluoromethanesulfonate was mixed with a 0.15 mL (0.15 mmol, 15 equiv) aliquot of pyridine in a 4 mL vial. Next, a 0.1 mL (0.01 mmol, 1 equiv) aliquot of arylstannane precursor was added along with the remaining solvent volume (0.55 mL DMA, total volume 1 mL). The reaction vial was sealed under an atmosphere of ambient air with a PTFE/Silicone septum cap, and a 0.1 mL aliquot of [^{18}F]KF (150-3000 μCi, depending on the time required for HPLC analysis) was added to the reaction vial through the septum via a syringe. The vial was then heated in an

aluminum block without stirring at 140 ºC for 30 min. After 30 min, the reaction was allowed to cool to room temperature. Radio-TLC analysis was conducted to determine radiochemical conversion (% RCC). The crude reaction mixture was spotted onto a standard silica-coated glass plate and run using 1:1 hexane/ethyl acetate in a glass TLC chamber. The RCC was then determined by dividing the integrated area under the fluorinated product spot by the total integrated area of the fluorine-18 on the TLC plate. To prepare samples for HPLC analysis: 0.1 mL of the reaction mixture or for the co-injection analysis 0.1 mL of the reaction mixture spiked with 0.1 mL of 1 mg/mL fluorinated standard solution were transferred to an HPLC autosampler vial. Eluent systems and columns used for HPLC analysis are described below.

RCC = integration of ^{18}F product peak / sum of integration of all ^{18}F peaks

5.4 General HPLC Conditions

Two general sets of HPLC conditions were used. A gradient method (Conditions A) or an isocratic method (Conditions B) was used for all manual reactions.

HPLC Conditions A

Condition: 5-95% gradient of (CH_3CN + 0.05%TFA) in (H_2O + 0.05%TFA)
Flow rate: 2 mL/min
Column: Luna C-18 Column 150 x 4.6 mm. 5µm.

0-3 min	5% MeCN	isocratic
3-20 min	5% to 95% MeCN	linear increase
20-30 min	5% MeCN	isocratic

HPLC Conditions B

Condition: 20% (MeCN + 0.05%TFA) in (H_2O + 0.05%TFA)
Flow Rate: 2 mL/min
Column: Luna C-18 Column 150 x 4.6 mm. 5µm

5.5 Additional Optimization Results (manual synthesis conditions)

Unless otherwise stated, 4-(tributylstannane)-1,1'-biphenyl (**3-SnBu$_3$**) was used for all optimization screens. The reaction scheme and accompanying tables in each subsection describe the reaction conditions employed, with **bold** typeface in the reaction scheme denoting the variable tested in each case. All reactant values are expressed in equivalents relative to arylstannane for brevity and simplicity. Red typeface denotes the ^{18}F source used, typically 0.1 mL of a 8 mL DMA solution containing [^{18}F]KF, 10 mg KOTf and 50 µg K_2CO_3. All RCC are n = 2 or greater.

Acetonitrile Addition Screen

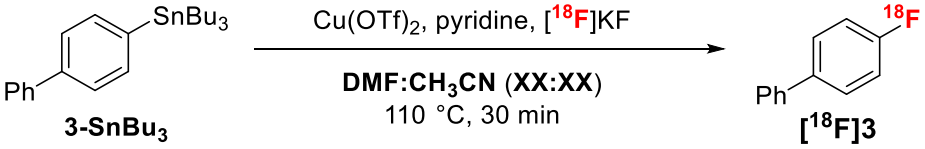
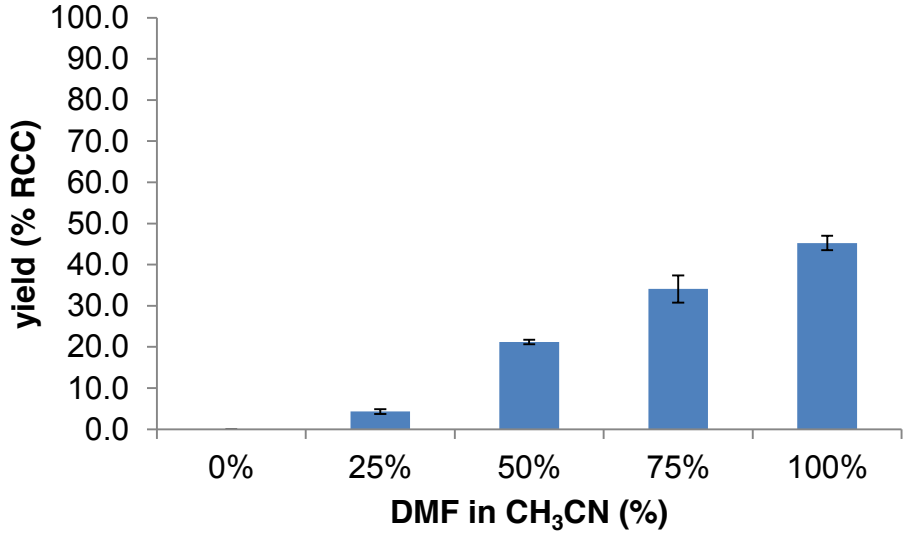


Table S11. Acetonitrile Addition Screen[a]

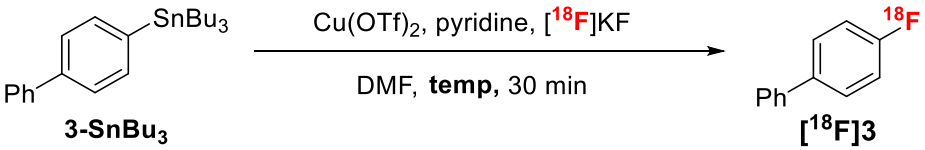
entry	DMF:CH_3CN	RCC of [^{18}F]3 (%)[b]
1	0:100	nd
2	25:75	4 ± 1
3	50:50	21 ± 1
4	75:25	34 ± 3
5	100:0	45 ± 2

[a]Reaction conditions: **3-SnBu$_3$** (0.01 mmol), $Cu(OTf)_2$ (2 equiv), pyridine (15 equiv), [^{18}F]KF in DMF or CH_3CN (0.1 mL, 300-700 µCi). Total reaction volume = 1.0 mL. [b]nd = desired product was not detected

Figure S1: Acetonitrile Addition Screen



Temperature Study in DMF



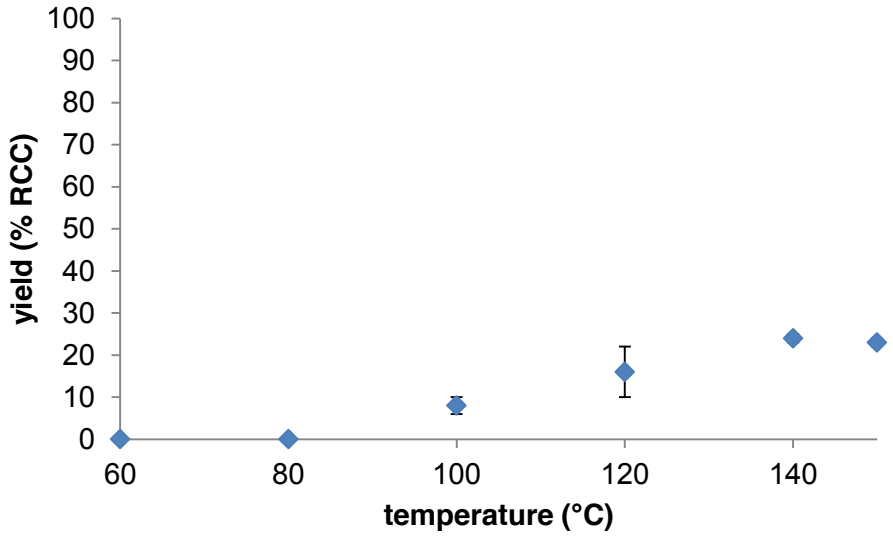
3-SnBu$_3$ **[^{18}F]3**

Table S12: Temperature Study in DMF[a]

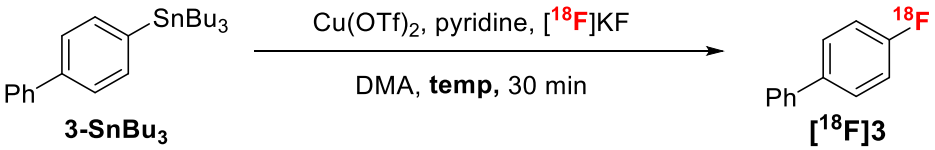
entry	temperature	RCC of [^{18}F]3 (%)[b]
1	60 °C	nd
2	80 °C	nd
3	100 °C	8 ± 2
4	120 °C	16 ± 6
5	140 °C	24 ± 1
6	150 °C	23 ± 1

[a]Reaction conditions: **3-SnBu$_3$** (0.01 mmol), Cu(OTf)$_2$ (2 equiv), pyridine (15 equiv), [^{18}F]KF in DMF (0.1 mL, 300-700 µCi). Total reaction volume = 1.0 mL. [b]nd = desired product was not detected

Figure S2: Temperature Study in DMF



Temperature Study in DMA



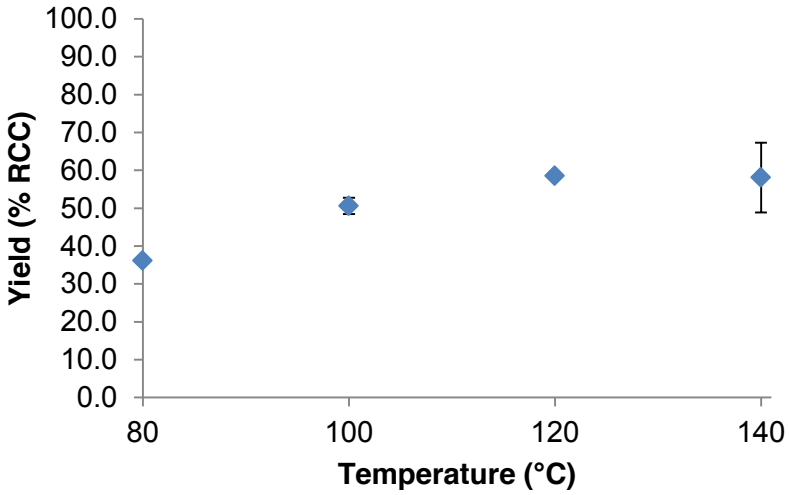
3-SnBu$_3$ **[^{18}F]3**

Table S13: Temperature Study in DMA[a]

entry	temperature	RCC of [^{18}F]3 (%)
1	80 ºC	36 ± 1
2	100 ºC	51 ± 2
3	120 ºC	59 ± 1
4	140 ºC	58 ± 9

[a]Reaction conditions: **3-SnBu$_3$** (0.01 mmol), Cu(OTf)$_2$ (2 equiv), pyridine (15 equiv), [^{18}F]KF in DMA (0.1 mL, 300-700 µCi). Total reaction volume = 1.0 mL.

Figure S3: Temperature Study in DMA



DMF versus DMA

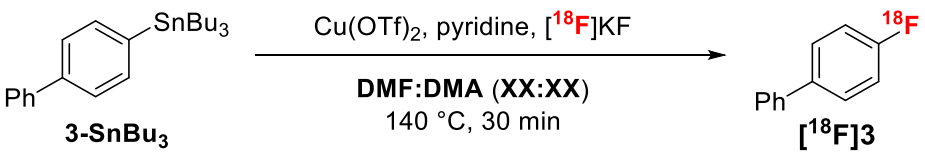
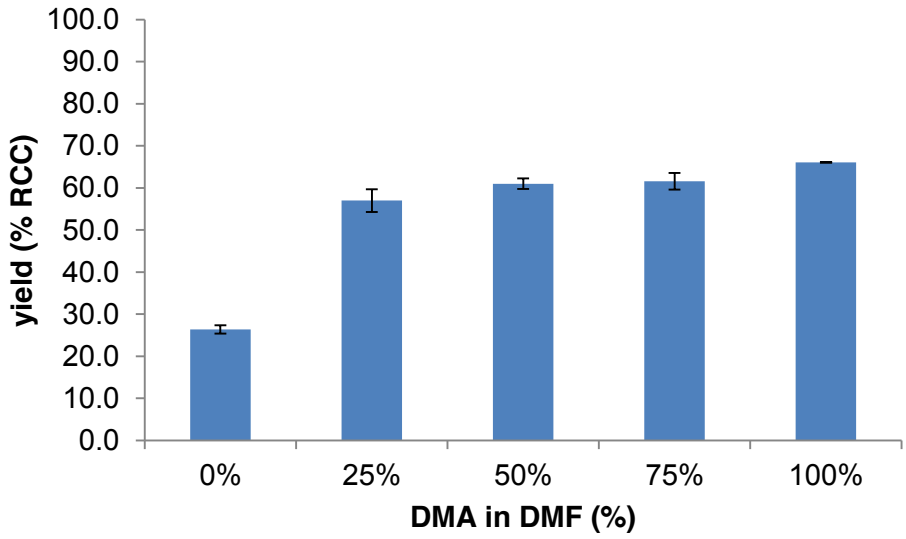


Table S14: Addition of DMA[a]

Entry	DMF:DMA	RCC of [^{18}F]3 (%)
1	100:0	26 ± 1
2	75:25	57 ± 3
3	50:50	61 ± 1
4	25:75	62 ± 2
5	0:100	66 ± 1

[a]Reaction conditions: **3-SnBu$_3$** (0.01 mmol), Cu(OTf)$_2$ (2 equiv), pyridine (15 equiv), [^{18}F]KF in DMF or DMA (0.1 mL, 300-700 µCi). Total reaction volume = 1.0 mL.

Figure S4: Addition of DMA



$Cu(OTf)_2$ Loading Study

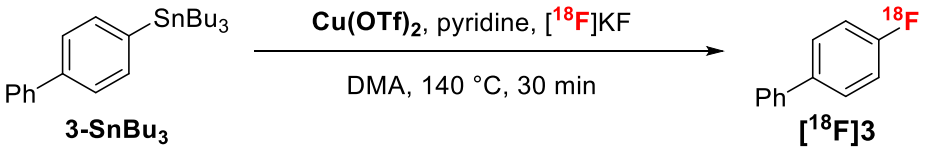
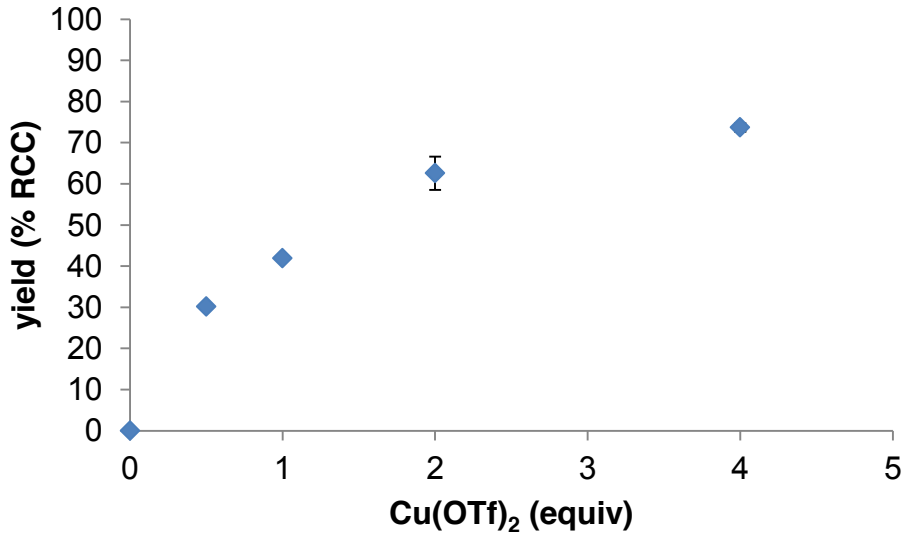


Table S15: $Cu(OTf)_2$ Loading[a]

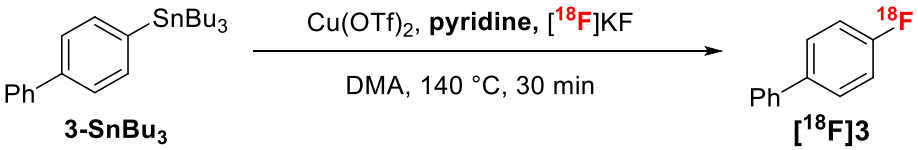
Entry	$Cu(OTf)_2$ (equiv)	RCC of [^{18}F]3 (%)[b]
1	0	nd
2	0.5	30 ± 1
3	1	42 ± 1
4	2	63 ± 4
5	4	74 ± 1

[a]Reaction conditions: **3-SnBu$_3$** (0.01 mmol), $Cu(OTf)_2$ (varied), pyridine (15 equiv), [^{18}F]KF in DMA (0.1 mL, 300-700 µCi). Total reaction volume = 1.0 mL. [b]nd = desired product was not detected.

Figure S5: $Cu(OTf)_2$ Loading



Pyridine Concentration Screen



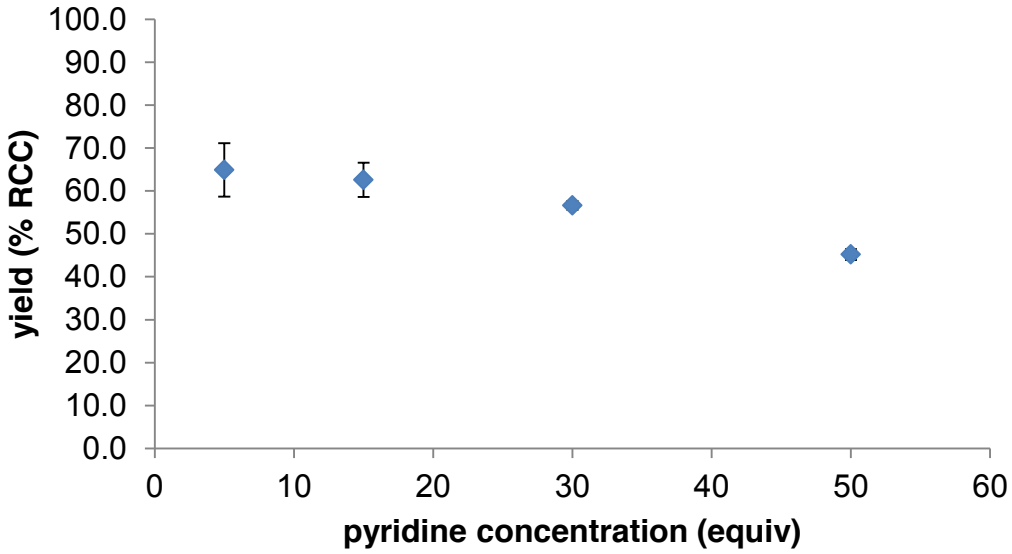
3-SnBu$_3$ **[^{18}F]3**

Table S16: Pyridine Concentration Screen[a]

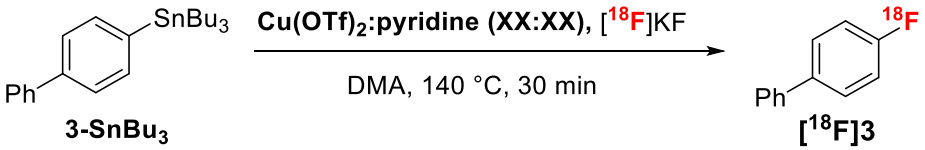
Entry	pyridine (equiv)	RCC of [^{18}F]3 (%)[b]
1	0	nd
3	5	65 ± 6
4	15	63 ± 4
5	30	57 ± 1
6	50	45 ± 1

[a]Reaction conditions: **3-SnBu$_3$** (0.01 mmol), Cu(OTf)$_2$ (2 equiv), pyridine (varied), [^{18}F]KF in DMA (0.1 mL, 300-700 µCi). Total reaction volume = 1.0 mL. [b]nd = desired product was not detected

Figure S6: Pyridine Concentration Screen



$Cu(OTf)_2$:Pyridine Loading Study



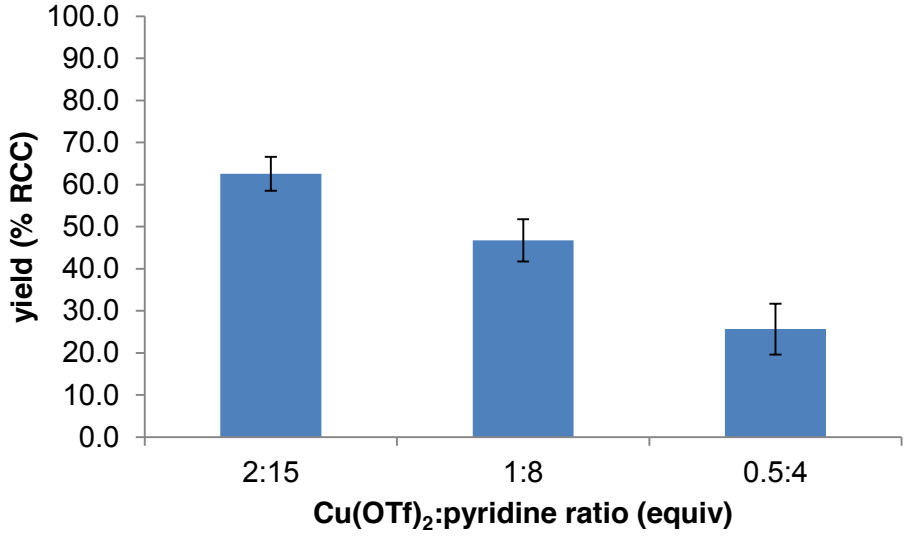
3-SnBu$_3$ **[^{18}F]3**

Table S17: $Cu(OTf)_2$:Pyridine Loading Study[a]

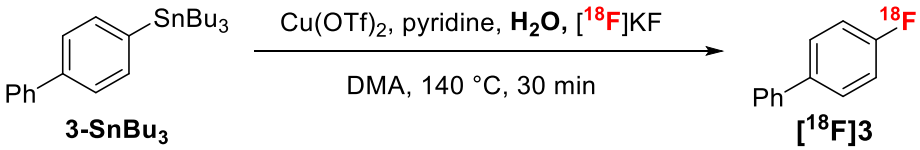
entry	$Cu(OTf)_2$	pyridine	RCC of [^{18}F]3 (%)
1	2	15	63 ± 4
2	1	8	47 ± 5
3	0.5	4	26 ± 6

[a]Reaction conditions: **3-SnBu$_3$** (0.01 mmol), $Cu(OTf)_2$ (varied), pyridine (varied), [^{18}F]KF in DMA (0.1 mL, 300-700 µCi). Total reaction volume = 1.0 mL.

Figure S7: $Cu(OTf)_2$:Pyridine Loading Study



Water Addition Study



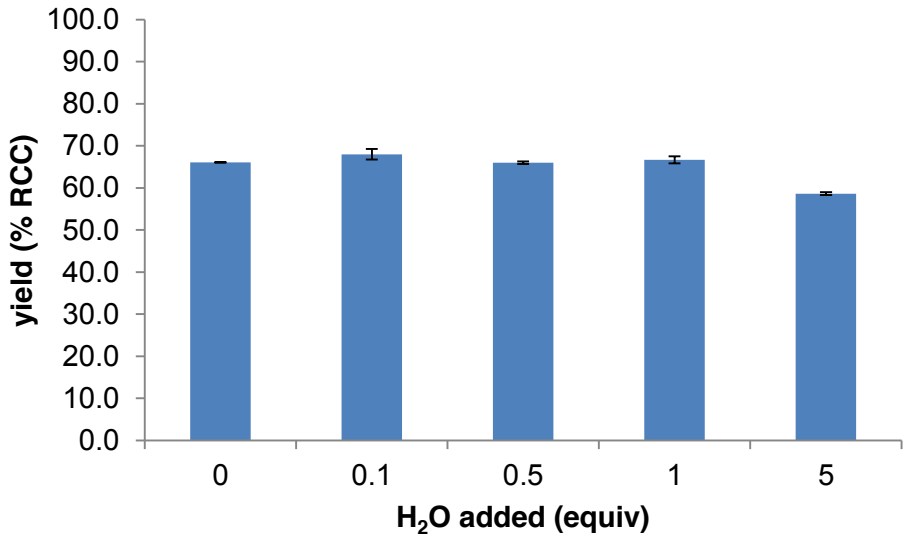
3-SnBu$_3$ **[^{18}F]3**

Table S18: Water Addition Study[a]

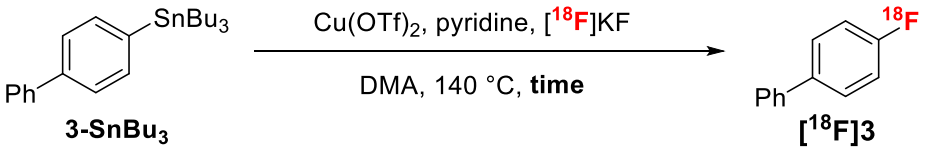
Entry	H_2O (equiv)	RCC of [^{18}F]3 (%)
1	0	66 ± 1
2	0.1	68 ± 1
3	0.5	66 ± 1
4	1	67 ± 1
5	5	59 ± 1

[a]Reaction conditions: **3-SnBu$_3$** (0.01 mmol), $Cu(OTf)_2$ (2 equiv), pyridine (15 equiv), H_2O (various), [^{18}F]KF in DMA (0.1 mL, 300-700 µCi). Total reaction volume = 1.0 mL.

Figure S8: Water Addition Study



Time Study



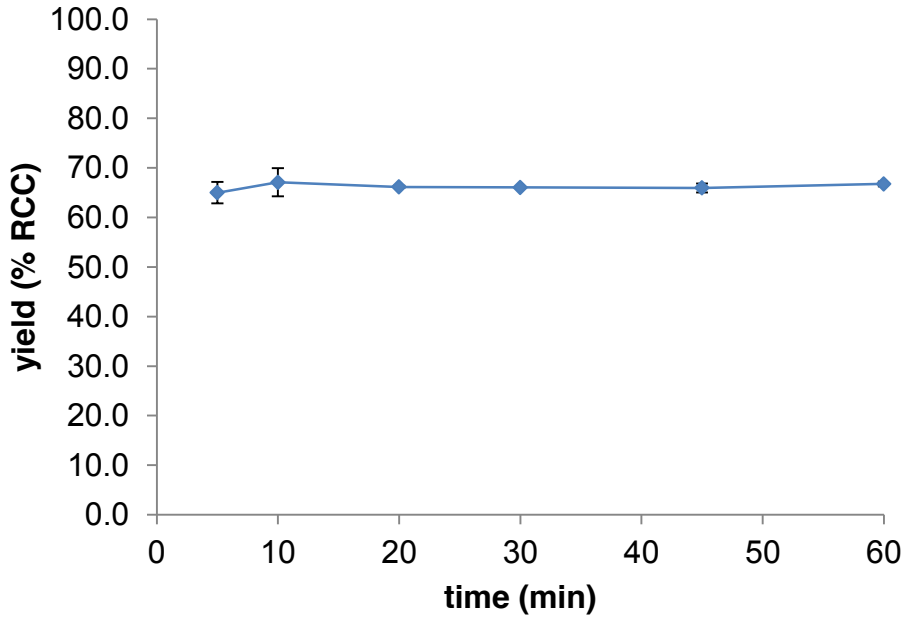
3-SnBu$_3$ **[^{18}F]3**

Table S19: Time Study[a]

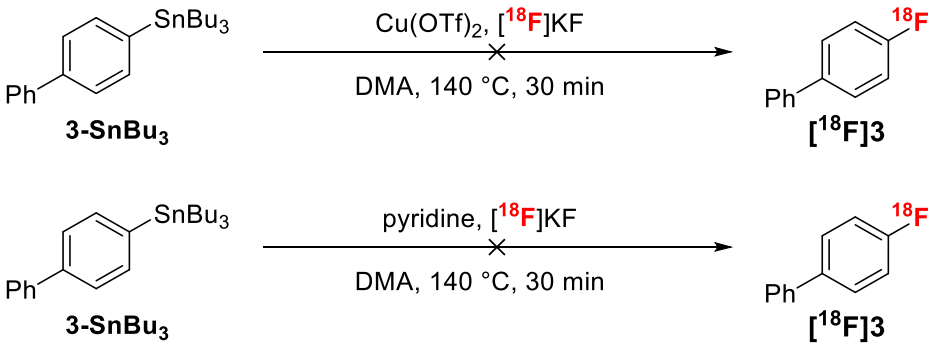
Entry	time (min)	RCC of [^{18}F]3 (%)
1	5	66 ± 2
2	10	67 ± 3
3	20	66 ± 1
4	30	66 ± 1
5	45	66 ± 1
6	60	67 ± 1

[a]Reaction conditions: **3-SnBu$_3$** (0.01 mmol), Cu(OTf)$_2$ (2 equiv), pyridine (varied), [^{18}F]KF in DMA (0.1 mL, 300-700 µCi). Total reaction volume = 1.0 mL.

Figure S9: Time Study



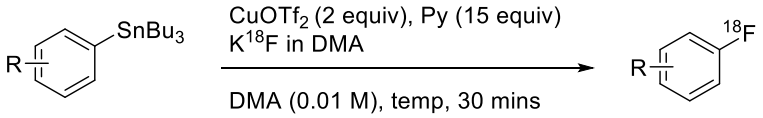
Control Reactions



Control reactions for the radiofluorination of substrate **3-SnBu$_3$** were conducted without copper salt and without pyridine. In both cases, the fluorinated product **[^{18}F]3** was not observed.

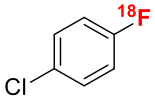
Substrate Optimization

Optimization Conditions:

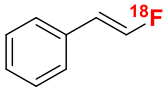


0.01 mmol

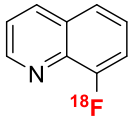
Substrates from Figure 1:



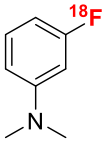
(**9-SnBu$_3$**)
32 ± 3 (n=4)
30 equiv py: 29 ± 1 (n=2)



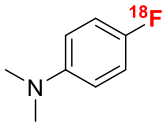
(**10-SnBu$_3$**)
72 ± 1 (n=2)
30 equiv py: 67 ± 1 (n=2)



(**11-SnBu$_3$**)
30 equiv py: 55 ± 6 (n=6)
15 equiv py: 37 ± 1 (n=2)

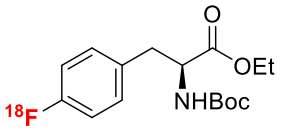


(**13-SnBu$_3$**)
100 °C: 34 ± 11 (n=6)
140 °C: 9 ± 1 (n=2)
18-crown-6 (0.5 equiv): 31 ± 1 (n=2)

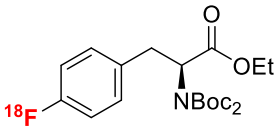


(**14-SnBu$_3$**)
100 °C, 18-crown-6 (0.5 equiv): 7 ± 1 (n=4)
140 °C: 2 ± 1 (n=2)
100 °C: 4 ± 3 (n=2)

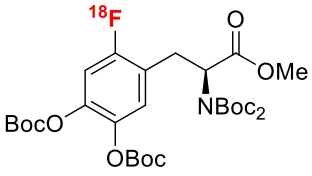
Substrates from Figure 2:



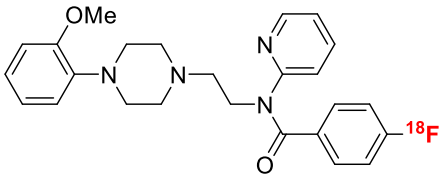
(**18-SnMe$_3$**)
40 ± 5% (n=4)
30 equiv py: 24 ± 1% (n=2)



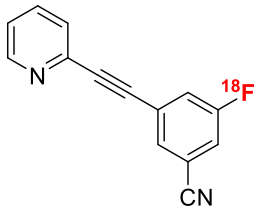
(**19-SnMe$_3$**)
41 ± 1% (n=2)



(**20-SnMe$_3$**)
30 equiv py: 57 ± 14% (n=6)
15 equiv py: 25 ± 6% (n=2)



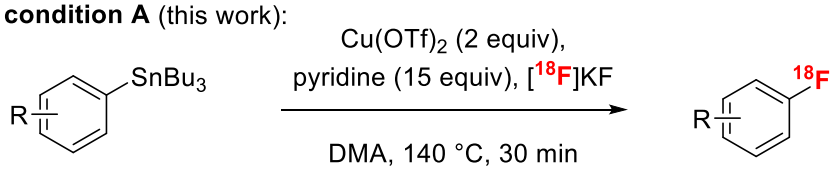
(**21-SnMe$_3$**)
33 ± 4% (n=4)
30 equiv py: 24 ± 1% (n=2)
4 Cu, 30 py: 18 ± 3% (n=2)



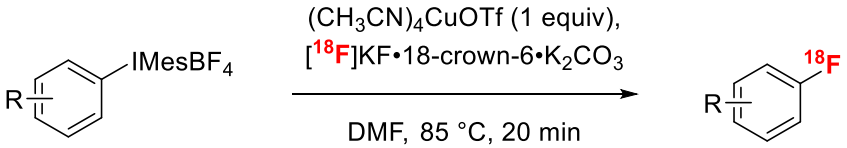
(**22-SnBu$_3$**)
30 equiv py: 11 ± 2% (n=4)
opt: nd
4 Cu, 30 py:6 ± 1% (n=2)

Comparison to Other Metal-Mediated Methods

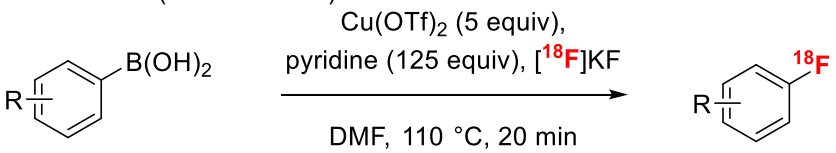
condition A (this work):



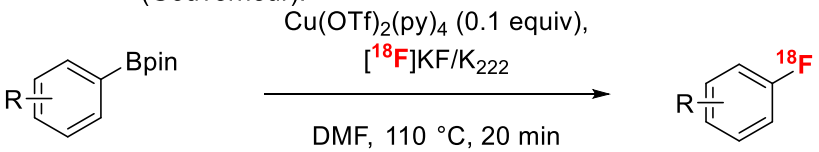
condition B (Sanford/Scott):



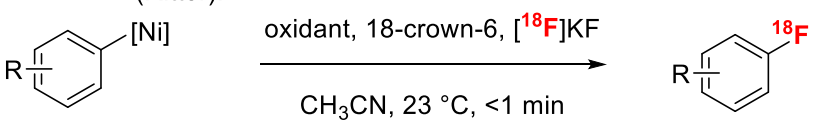
condition C (Sanford/Scott):



condition D (Gouverneur):

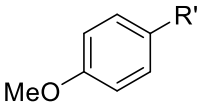
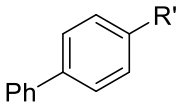
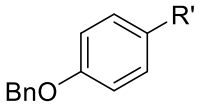
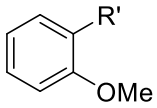
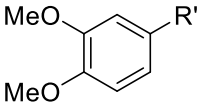
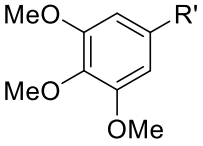


condition E (Ritter):



References: condition A (this work), condition B (Cu-mediated method),[12] condition C (Cu-mediated method),[1] condition D (Cu-catalyzed method, note: decay corrected "RCY"),[17] and condition E (Ni-mediated method).[18]

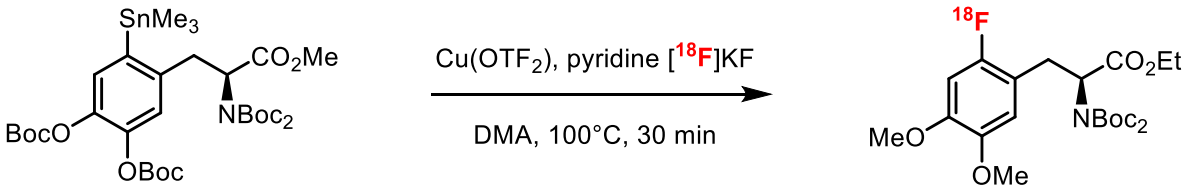
Table S20: Comparison of Substrates by Other Metal-Mediated Methods

substrate	R'	conditions	yield (RCC)
	-$SnBu_3$	A	56 ± 4%
	-$IMesBF_4$	B	79 ± 8%
	-$B(OH)_2$	C	19 ± 3%
	-$SnBu_3$	A	55 ± 10%
	-$IMesBF_4$	B	51 ± 8%
	-$B(OH)_2$	C	46 ± 6%
	-Bpin	D	74 ± 5%
	-[Ni]	E	42 ± 8%
	-$SnBu_3$	A	50 ± 3%
	-Bpin	D	43 ± 5%
	-$SnBu_3$	A	48 ± 4%
	-$IMesBF_4$	B	30 ± 8%
	-Bpin	D	11 ± 2%
	-$SnBu_3$	A	54 ± 8%
	-$IMesBF_4$	B	51 ± 6%
	-Bpin	D	54 ± 3%
	-$SnBu_3$	A	59 ± 3%
	-$IMesBF_4$	B	14 ± 1%
	-$B(OH)_2$	C	36 ± 11%

Protected [^{18}F]F-DOPA Comparison

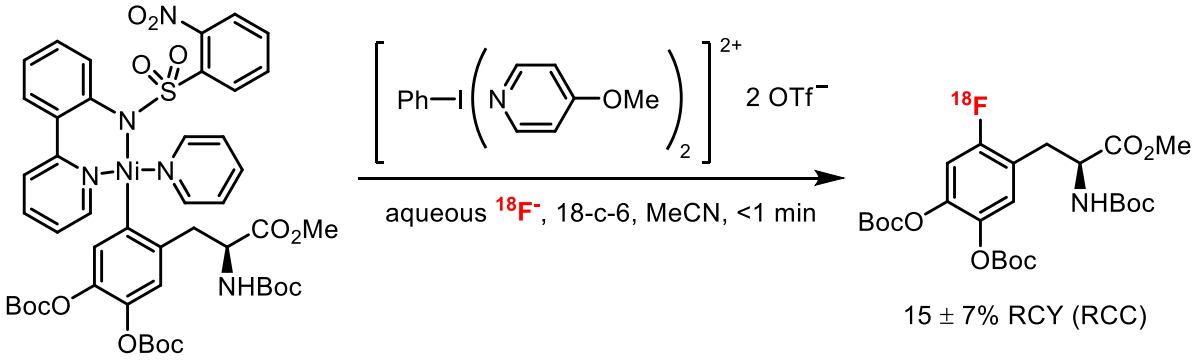
Figure S10: Protected [^{18}F]F-DOPA Comparison

conditions A: *This work*



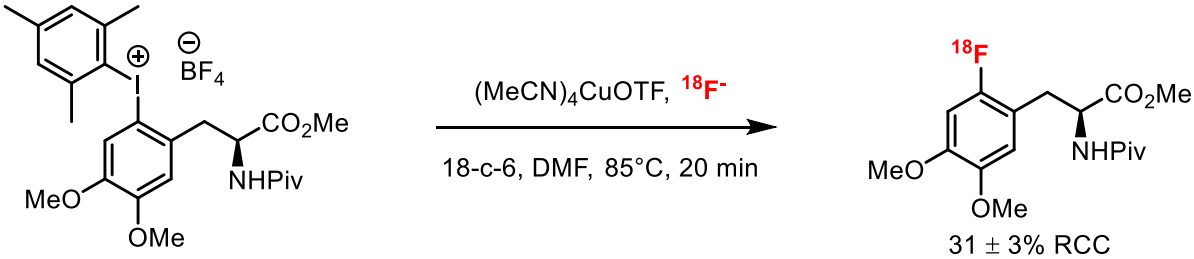
56 ± 8% RCC

conditions B (Ritter):



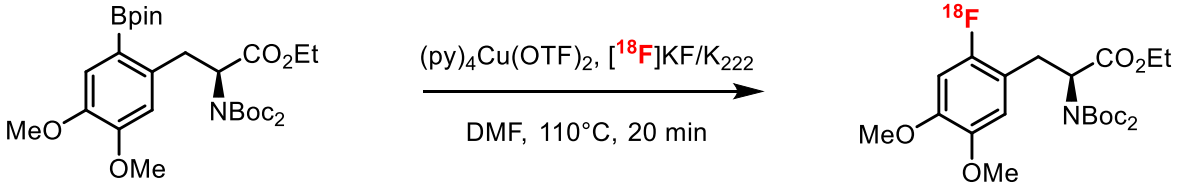
15 ± 7% RCY (RCC)

conditions C (Sanford/Scott)



31 ± 3% RCC

conditions D (Gouverneur):



55 ± 23% RCY (RCC)
(12% RCY)

References: condition A (this work), condition B (Ni-mediated method),[18] condition C (Cu-mediated method),[1] and condition D (Cu-catalyzed method).[19]

5.6 Automated Synthesis of [^{18}F]MPPF ([^{18}F]17)

All loading operations were conducted under an ambient atmosphere. Argon was used as a pressurizing gas during automated sample transfers. Potassium [^{18}F]fluoride was prepared using a TRACERLab FX_{FN} automated radiochemistry synthesis module (General Electric, GE). [^{18}F]Fluoride was produced via the $^{18}O(p,n)^{18}F$ nuclear reaction using a GE PETTrace cyclotron. [^{18}F]KF was produced as indicated above. A solution containing arylstannane precursor (0.01 mmol, 1 equiv, 0.1M stock) in 0.4 mL of anhydrous DMA in vial 3 and copper(II)trifluoromethanesulfonate (0.02 mmol, 2 equiv, 0.2 M stock), pyridine (0.015 mmol, 15 equiv, 1 M stock), in 0.25 mL of DMA from vial 4 (prepared from separate stock solutions of the three reagents) were added to a reactor containing dry [^{18}F]KF by applying Argon (Ar) gas through the valve containing the reagent solution for a final reaction volume of 1 mL of DMA. Open valves leading out of the reactor were closed, and the mixture was stirred for 15 min at 100 ºC. The mixture was then cooled to 50 ºC with compressed air cooling, and 2 mL of HPLC buffer (50% MeCN, 10 mM NH_4OAc, pH 6.0) was added to the reactor. This mixture was allowed to stir for approximately 1 min and was then transferred to an HPLC loop for injection and purification by semi-preparative chromatography (250 x 10 mm, 10µ, 4 mL/min). The product peak (retention time ~12 min) was collected and diluted into 50 mL of MQ H_2O. The product was trapped on a C18 extraction disk, washed with 10 mL of sterile water, eluted with 1 mL of EtOH, and then rinsed with 9 mL of saline solution. The resulting 10 mL solution was passed through a sterile filter and submitted to standard quality control tests (tests and results are described in detail below). [^{18}F]MPPF was produced in a 13 ± 1% (n=4) yield (200 mCi ± 20, n=4).

5.6.1 Specific Activity Calculation

An aliquot of the sample was injected onto an analytical HPLC using Conditions A. The UV peak corresponding to the radiofluorinated product was determined by overlaying the UV and RAD traces (with a 0.2 min offset as described in the HPLC section). The UV area was then used to calculate the concentration of the product based on linear regression analysis of appropriate fluoroarene standards. A standard curve was generated from the standard solutions, each run in duplicate (0.0001 mg/mL to 1.0 mg/mL). This provided the concentration of the product in mmol/mL. Dividing the activity concentration (Ci/mL) by the HPLC-derived concentration of product (mmol/mL) provided the specific activity in Ci/mmol. This reflects an end of synthesis (EoS) specific activity.

[^{18}F]MPPF was produced with a specific activity 2,400 ± 900 Ci/mmol (n=4).

5.6.2 QC Validation

Radiochemical Purity (> or = to 95%): 98.4%
Total Chemical Content (< or = to 10 µg/mL): Pass
MPPF Concentration (N/A (µg/mL)): 4.26 µg/mL
Specific Activity (N/A (Ci/mmol)): 1915 Ci/mmol
pH (4.5-7.5): 5.0

Visual Inspection (clear, colorless, no ppt): Pass
Kryptofix Analysis (< or = to 50 µg/mL): < 50 µg/mL
Residual Solvent Analysis for Acetone, 5000 µg/mL: Pass
Methanol < 3000 µg/mL: Pass
THF < 5000 µg/mL: Pass
MeCN < 410 µg/mL: Pass
DMSO < 5000 µg/mL: Pass

Radionuclide Identity (105-115 min half-life): 108.30 min
Endotoxin Analysis (<17.5 EU/mL): <2.00 EU/mL
Filter Bubble Point Test (>40 psi): >40 psi
Radiochemical Identity (0.9-1.10): 1.001

Analysis for Residual Copper and Tin: conformed to ICH guidelines
Detection limits were 0.019 ppm for Cu and 0.395 ppm for Sn
Both Sn and Cu were below the limit of detection
See “Analytical Report” below for more information

Analytical Report

Title:

Cu & Sn in Buffered Catalyst Solution

Date:

August 18, 2016

Prepared For:

Katarina Makaravage
University of Michigan

Prepared By:

Chemistry Team
Cerium Laboratories
Austin, TX

Sample Description:

Sample #	Sample ID
MPPF	MPPF, 8ml product solution <1mM substrate

Samples as received:

Only the yellow labeled sample was analyzed. The other two bottles are extra solvent and buffer just in case more analysis is needed.

Analytical Equipment:

- *Varian* Liberty Series II Inductively Coupled Plasma Optical Emission Spectrometer (ICP-OES).

Instrument Conditions:

- ICP-OES:
    1. Inlet: HF resistant torch with V-groove type pneumatic nebulizer.
    2. Plasma Flow: 15.0L/min.
    3. Aux Flow: 1.50L/min.
    4. Nebulizer Pressure: 260kPa.
    5. PMT Voltage: 660V.
    6. Method: Custom just for Cu and Sn lines.

Test Method:

1. Sample was diluted 10 times in 10% HNO_3 then analyzed by ICPOES.
2. Tool sensitivity and calibrations performed using NIST traceable standards.

Data:

"nd" implies the analyte was not detected.

Technique	Analyte	Units	MPP	Detection Limits
ICPOES-HFI	Cu	ppm	nd	0.019
ICPOES-HFI	Sn	ppm	nd	0.395

6. References

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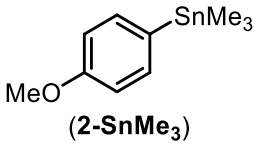
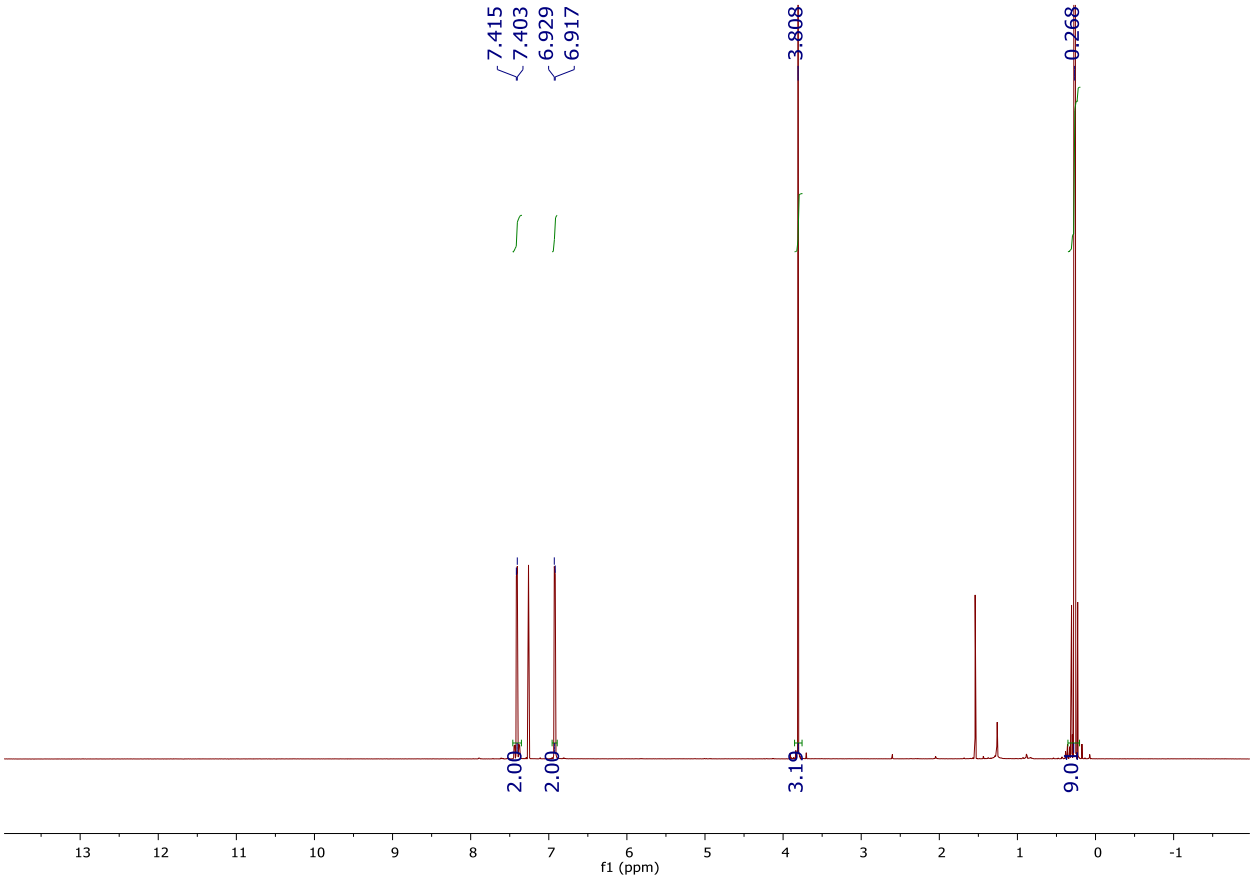
7 Spectral Data

7.1 ^{1}H, ^{13}C, ^{19}F NMR Spectra

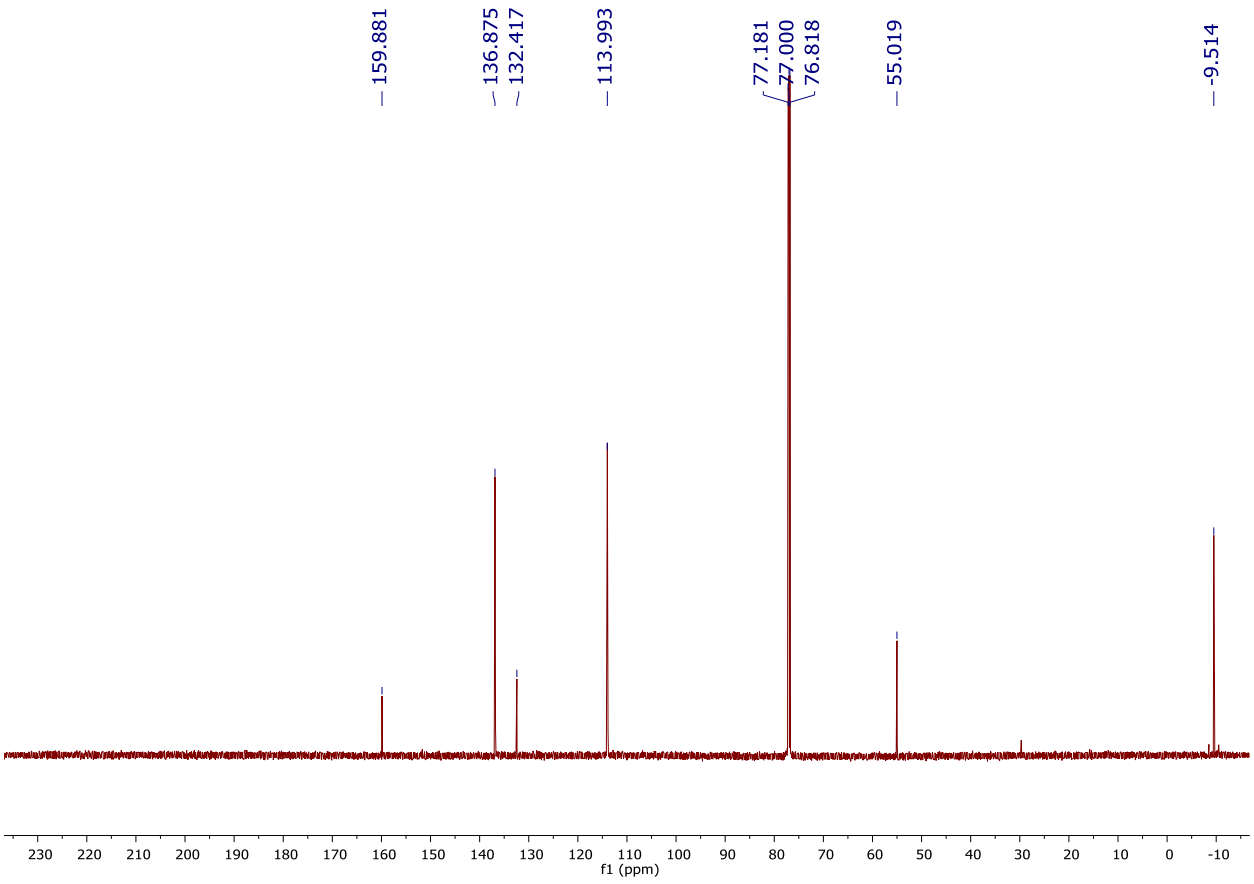


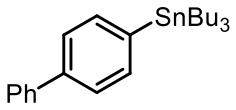
(**2-SnMe$_3$**)

^{1}H NMR



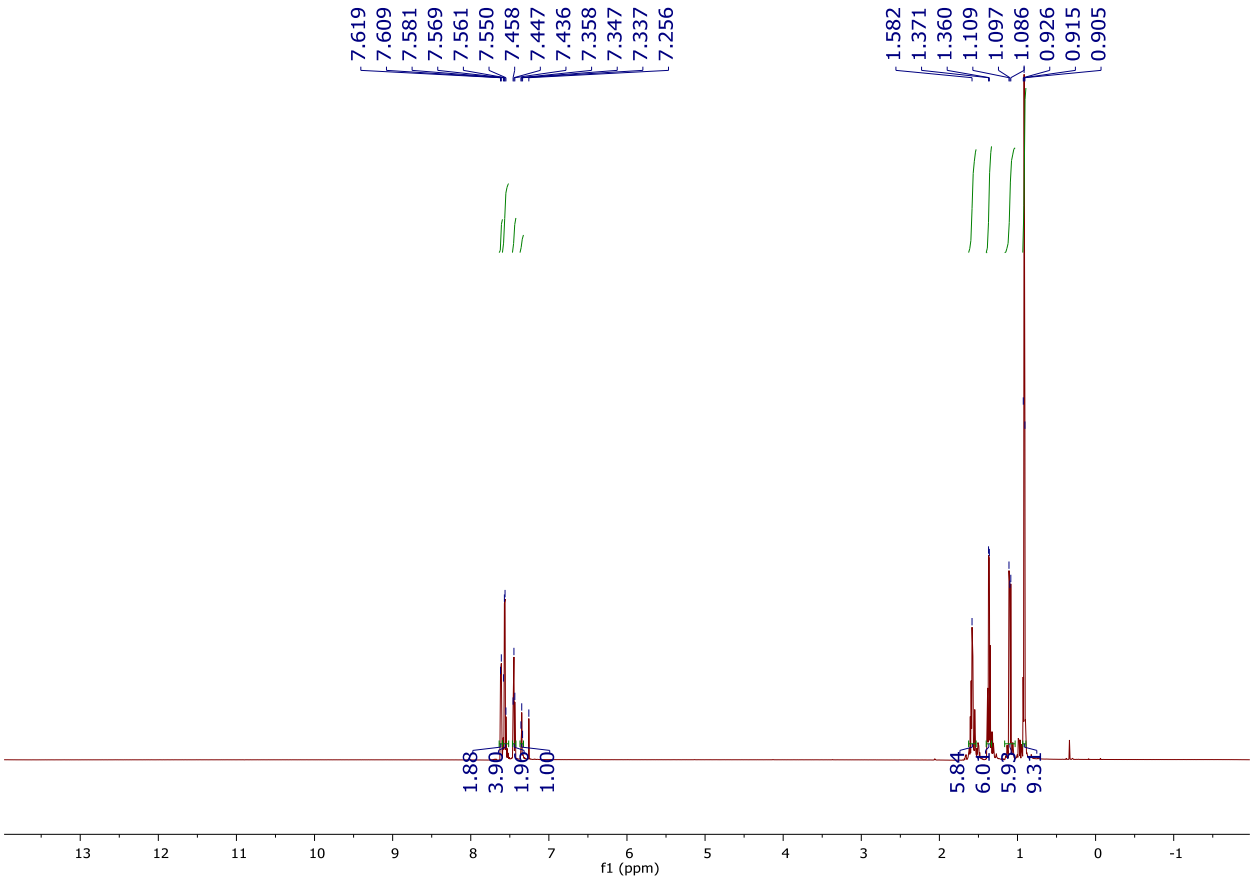
^{13}C NMR


159.881
136.875
132.417
113.993
77.181
77.000
76.818
55.019
-9.514
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

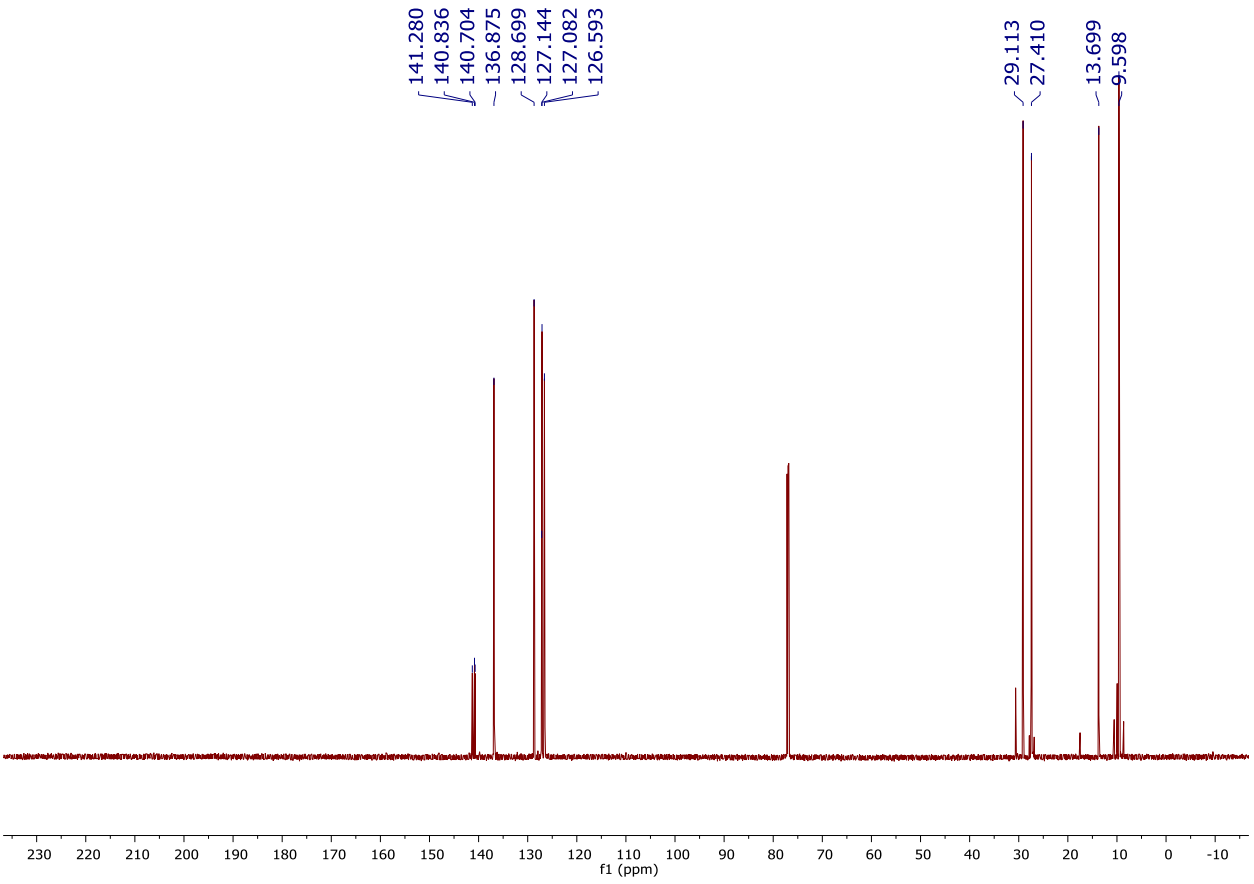


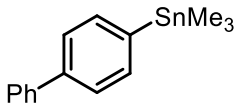
(**3-SnBu$_3$**)

^{1}H NMR



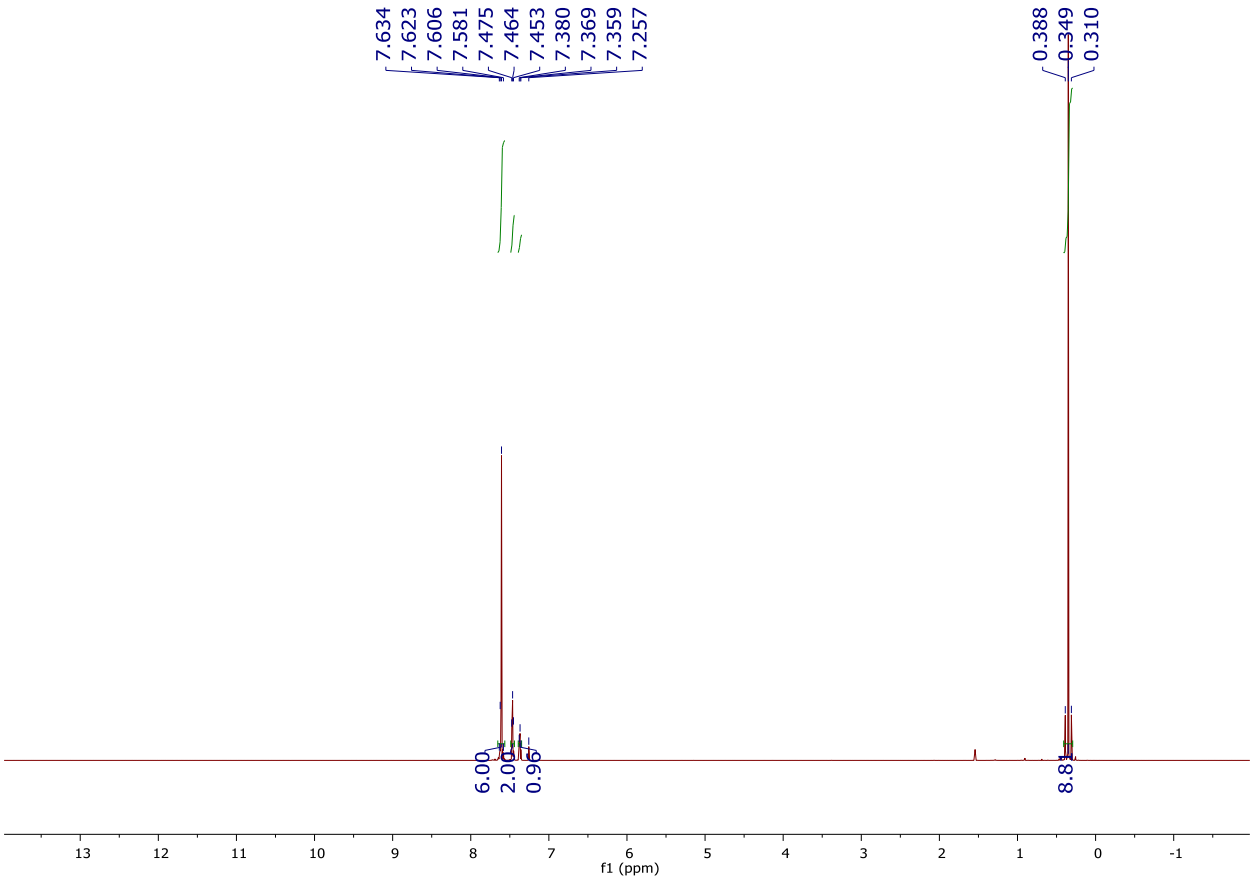
^{13}C NMR


141.280
140.836
140.704
136.875
128.699
127.144
127.082
126.593
29.113
27.410
13.699
9.598
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

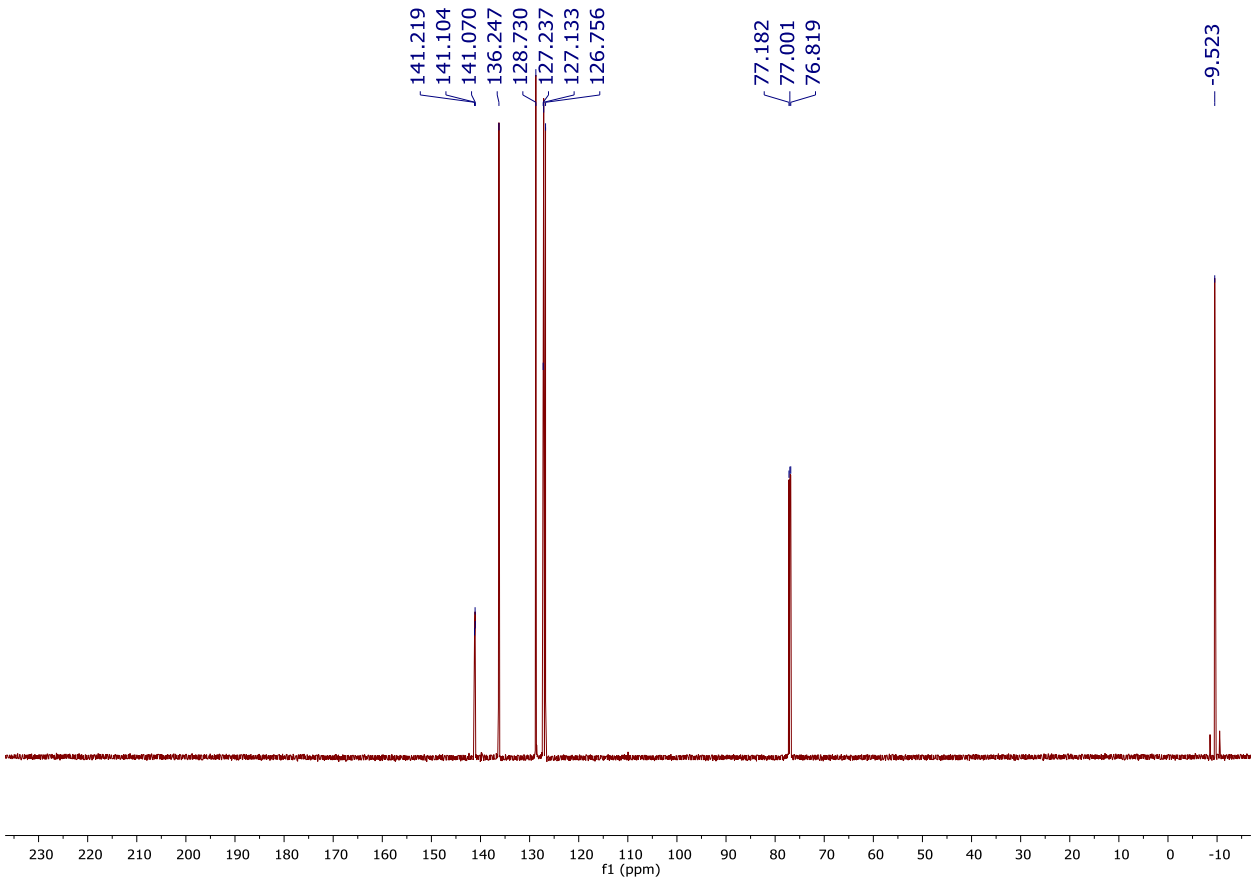


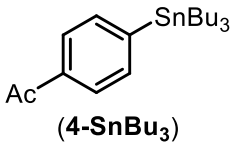
(**3-SnMe$_3$**)

^{1}H NMR



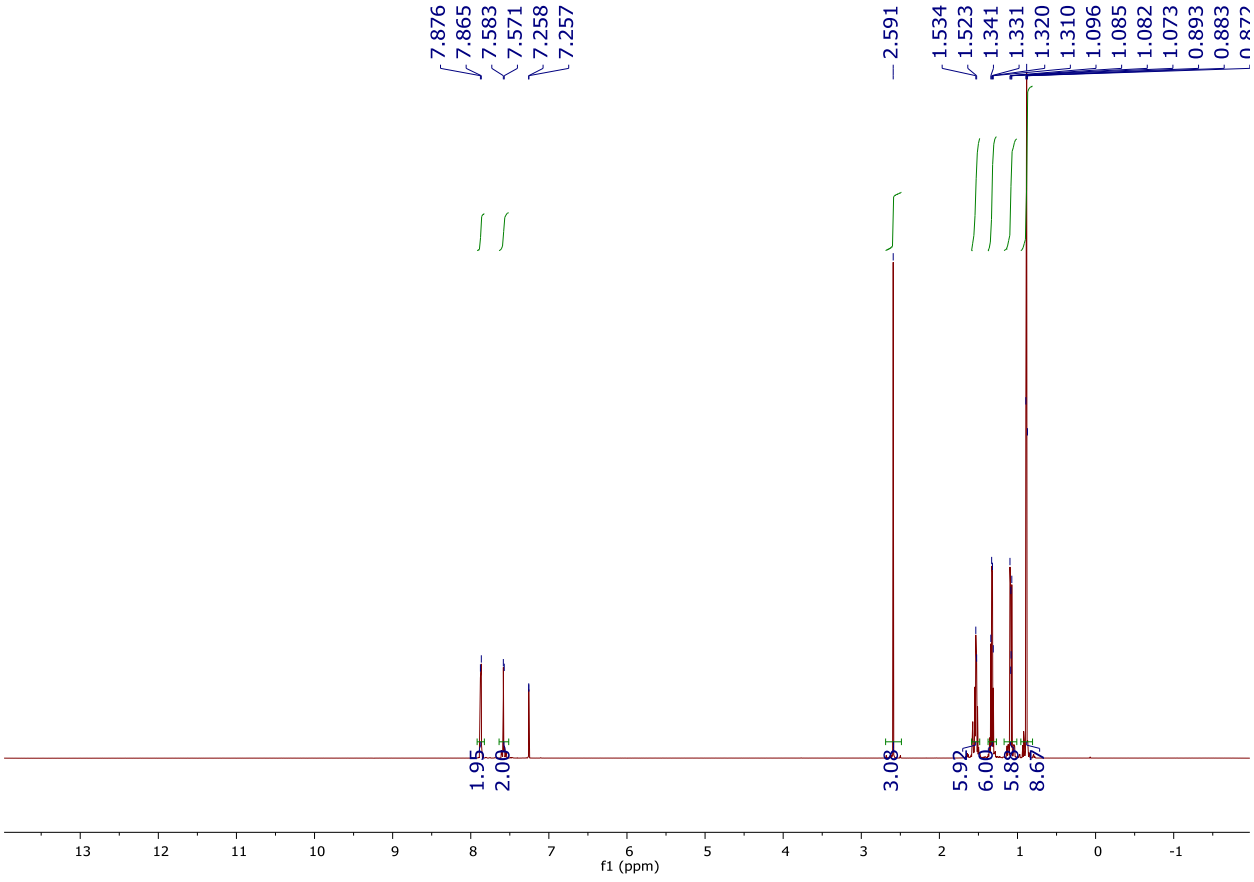
^{13}C NMR


141.219
141.104
141.070
136.247
128.730
127.237
127.133
126.756
77.182
77.001
76.819
-9.523
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

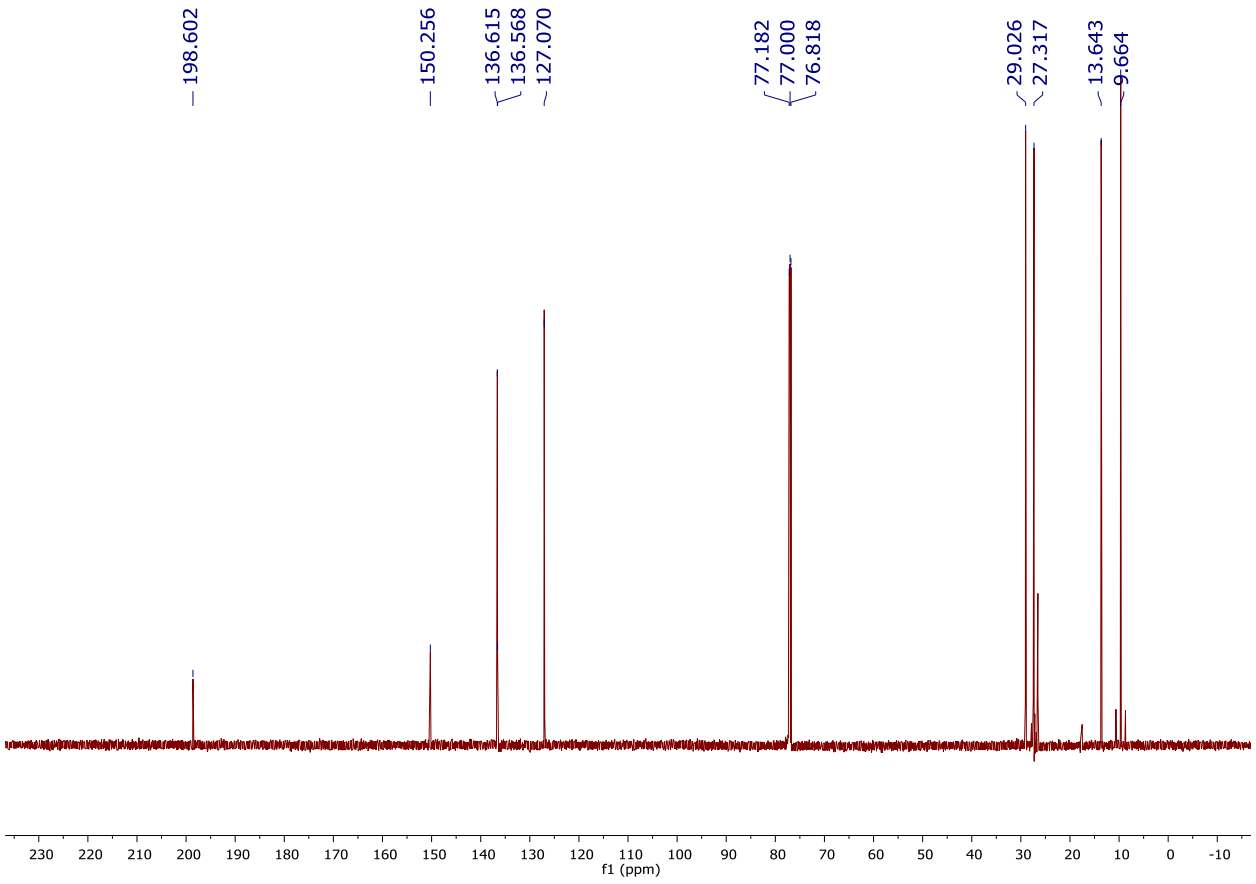


(**4-SnBu$_3$**)

^{1}H NMR



^{13}C NMR


198.602
150.256
136.615
136.568
127.070
77.182
77.000
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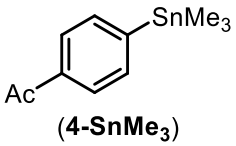
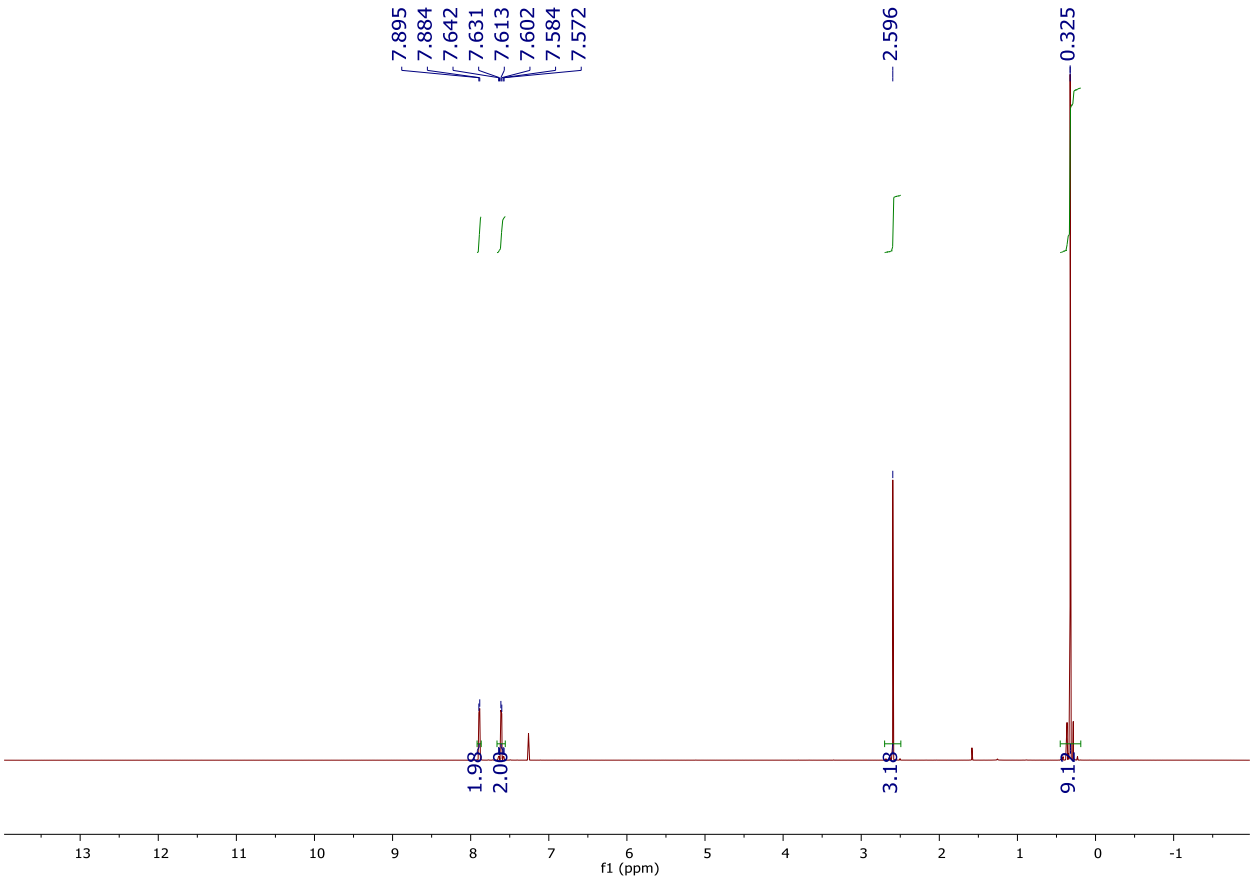
29.026
27.317
13.643
9.664
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

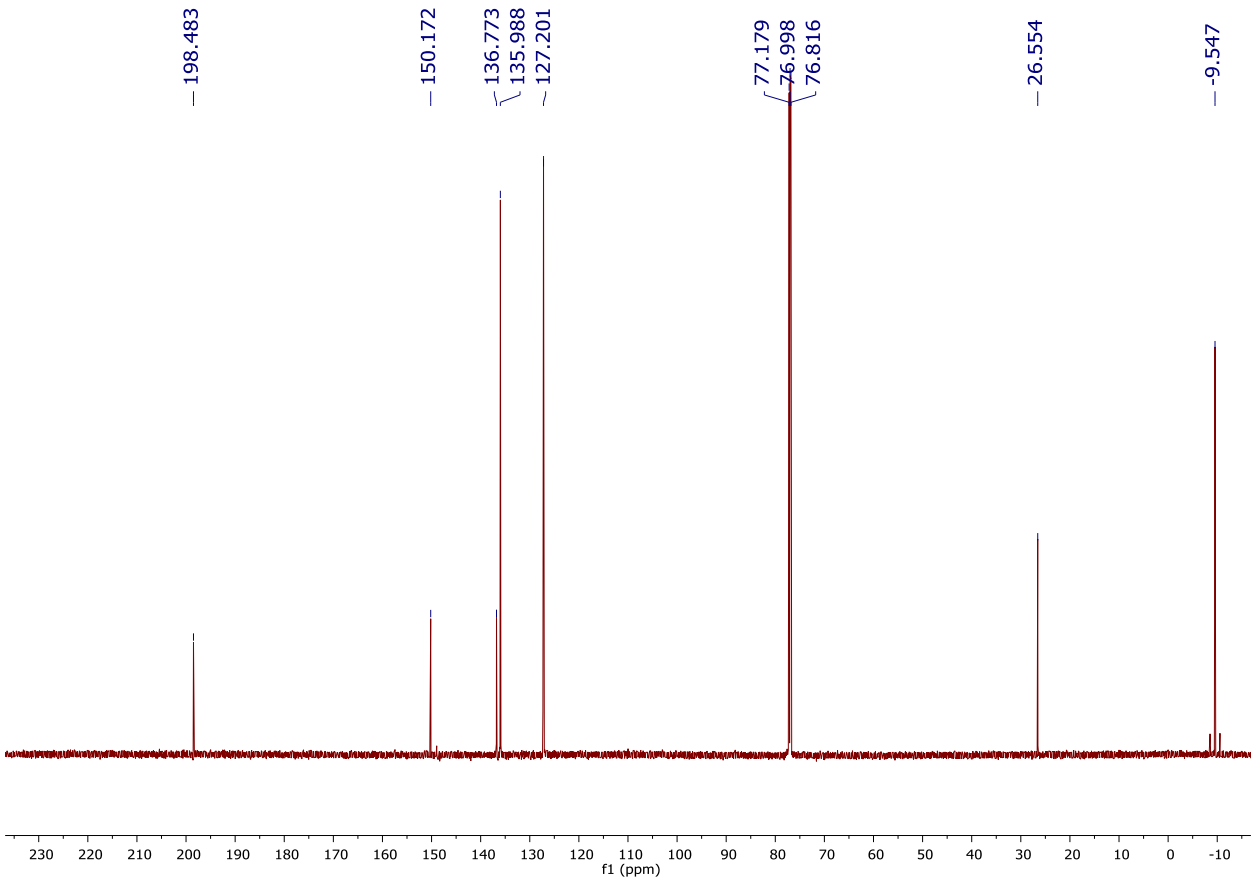


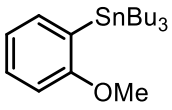
(**4-SnMe$_3$**)

^{1}H NMR



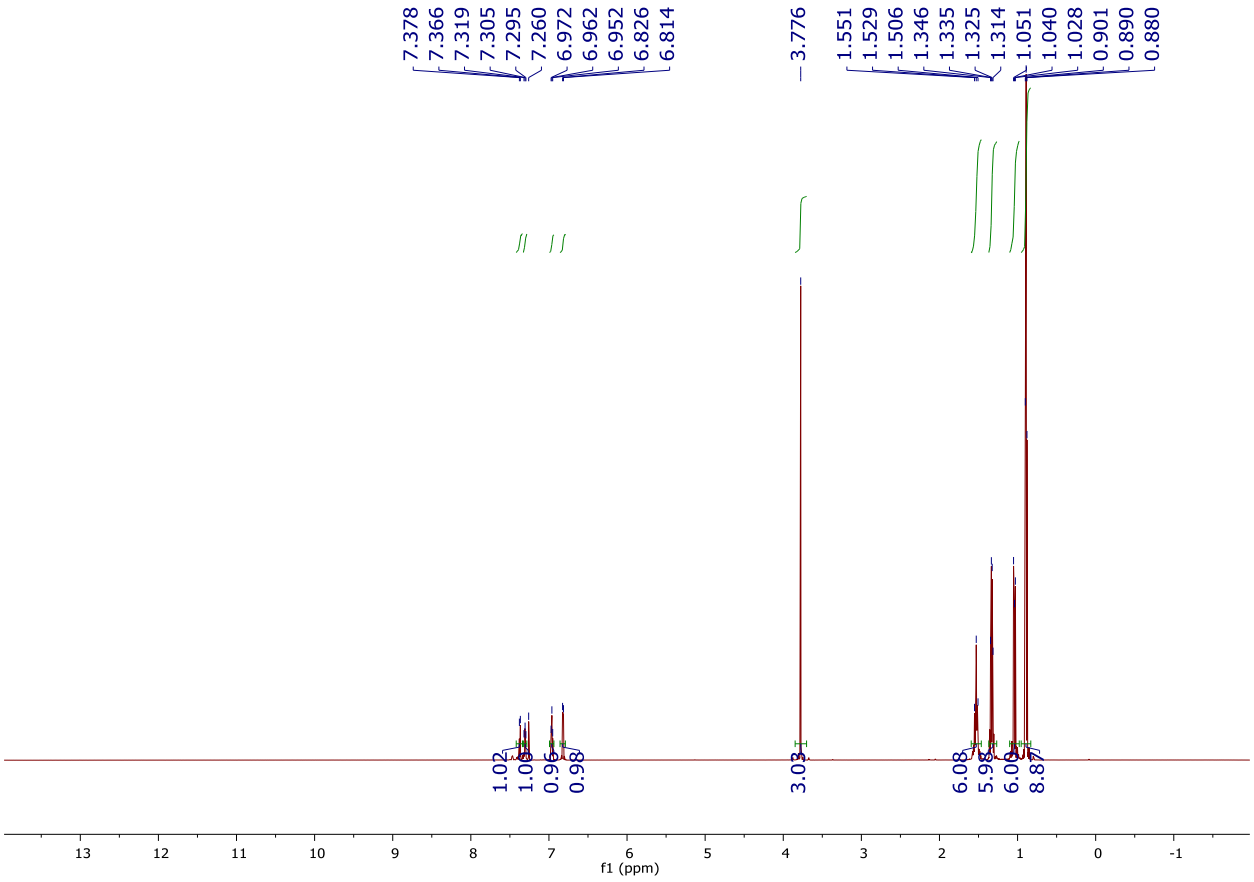
^{13}C NMR


198.483
150.172
136.773
135.988
127.201
77.179
76.998
76.816
26.554
-9.547
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

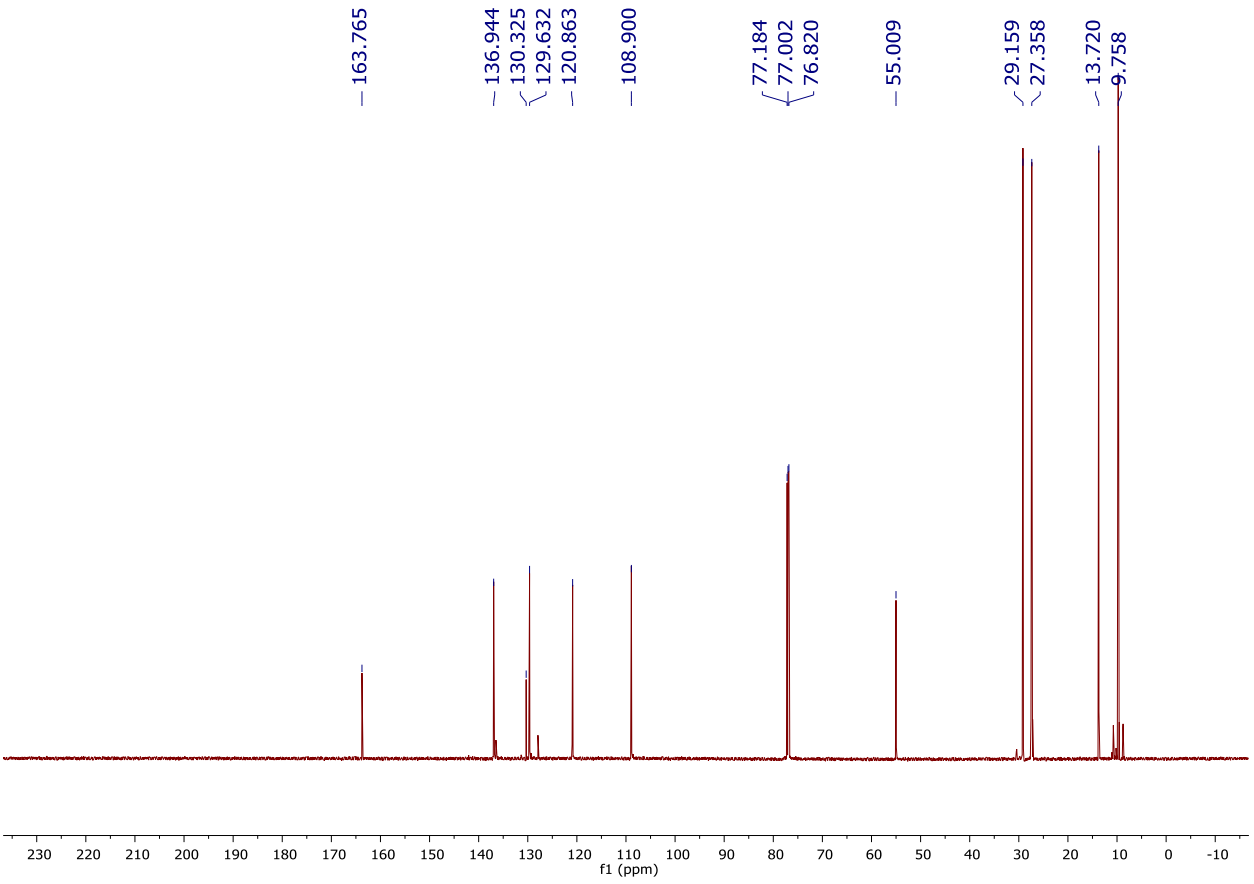


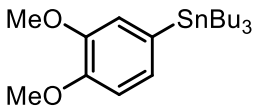
(**6-SnBu$_3$**)

^{1}H NMR



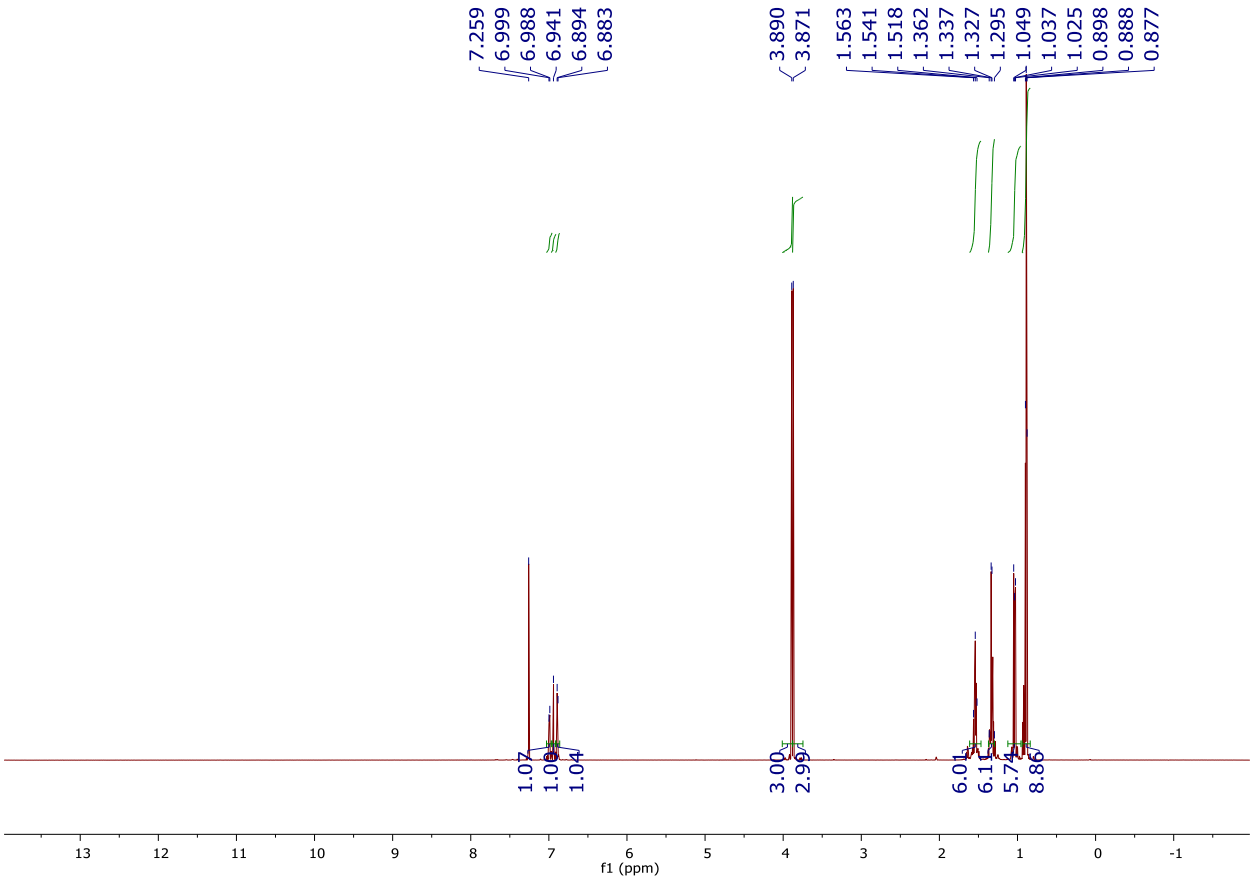
^{13}C NMR


163.765
136.944
130.325
129.632
120.863
108.900
77.184
77.002
76.820
55.009
29.159
27.358
13.720
9.758
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

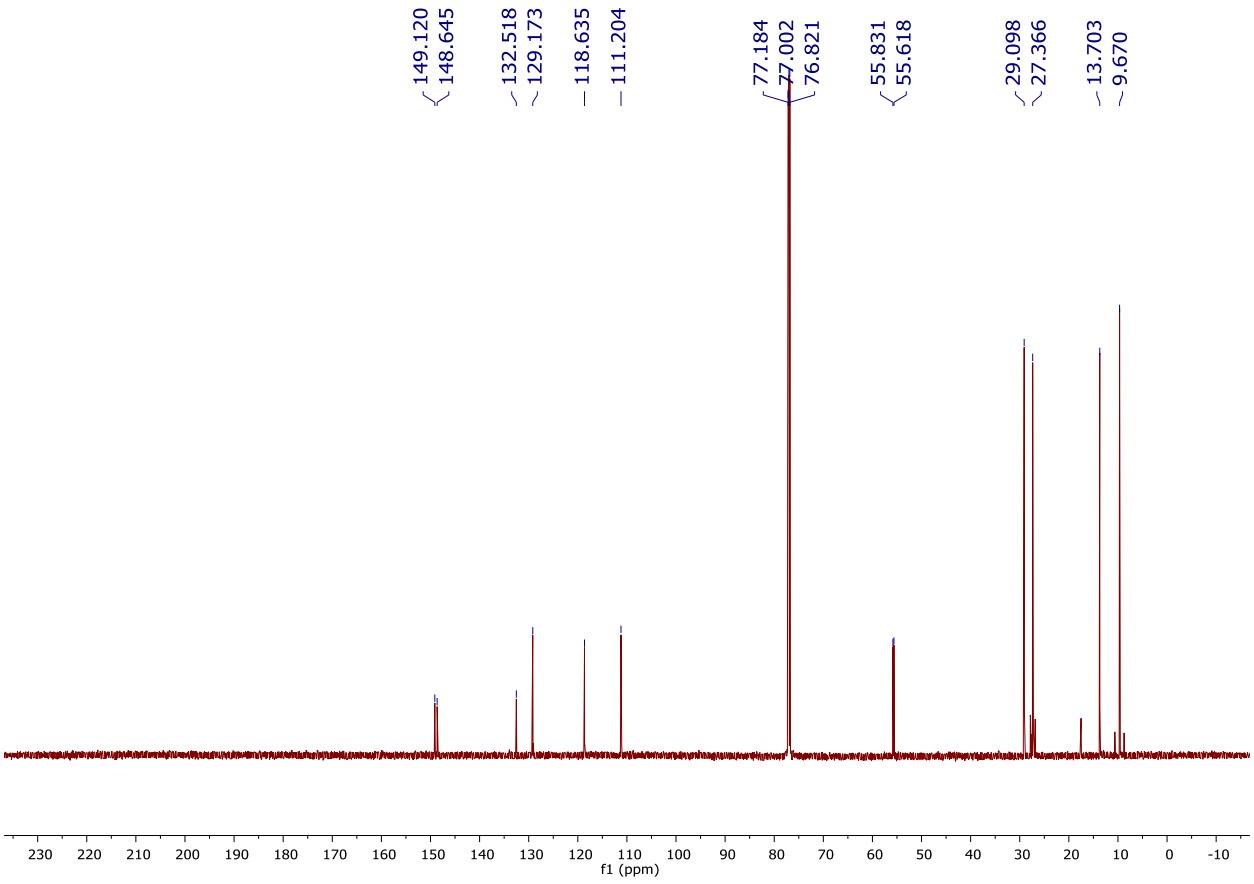


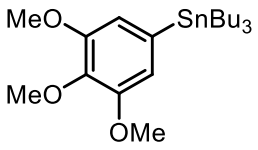
(**7-SnBu$_3$**)

^{1}H NMR



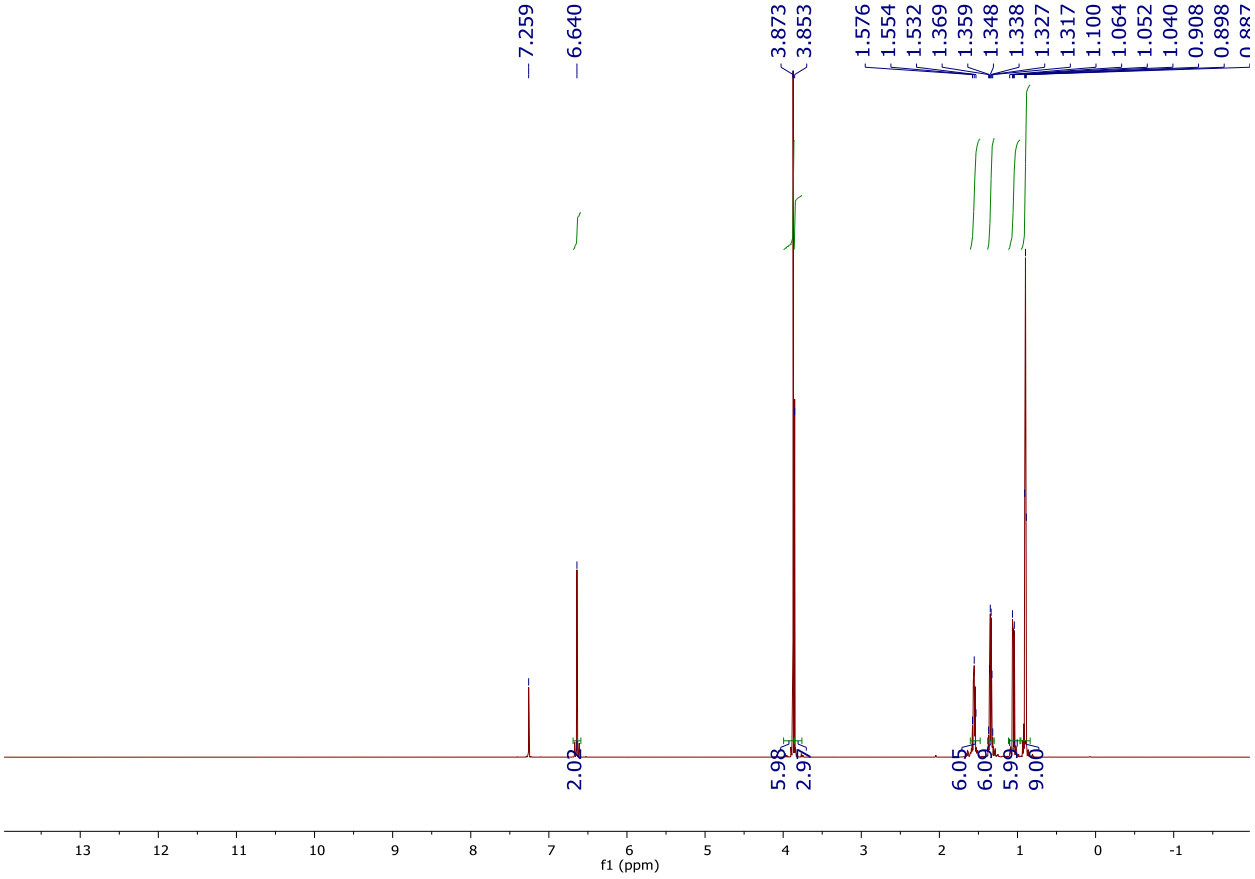
^{13}C NMR


149.120
148.645
132.518
129.173
118.635
111.204
77.184
77.002
76.821
55.831
55.618
29.098
27.366
13.703
9.670
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

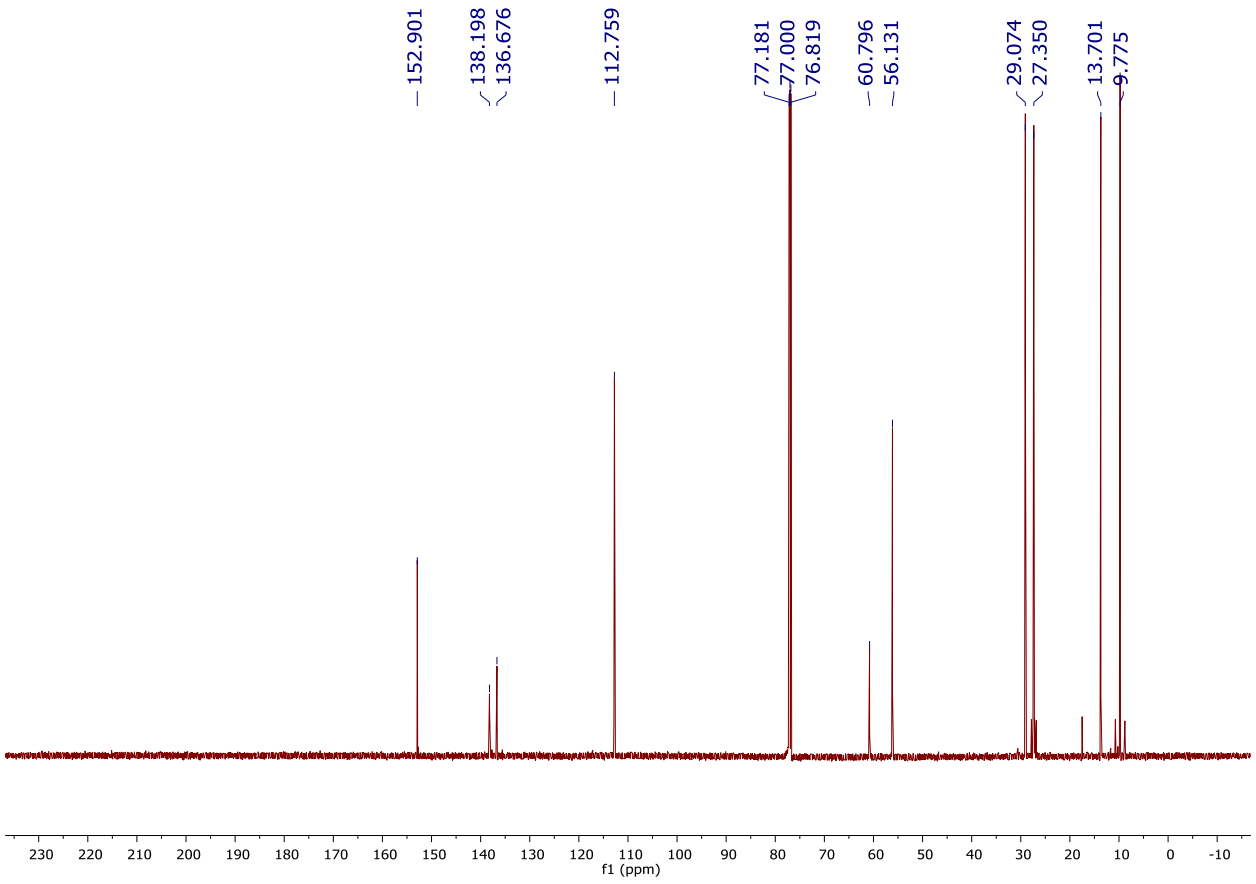


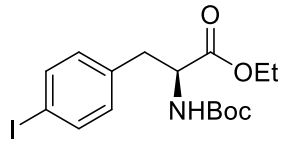
(**8-SnBu$_3$**)

^{1}H NMR



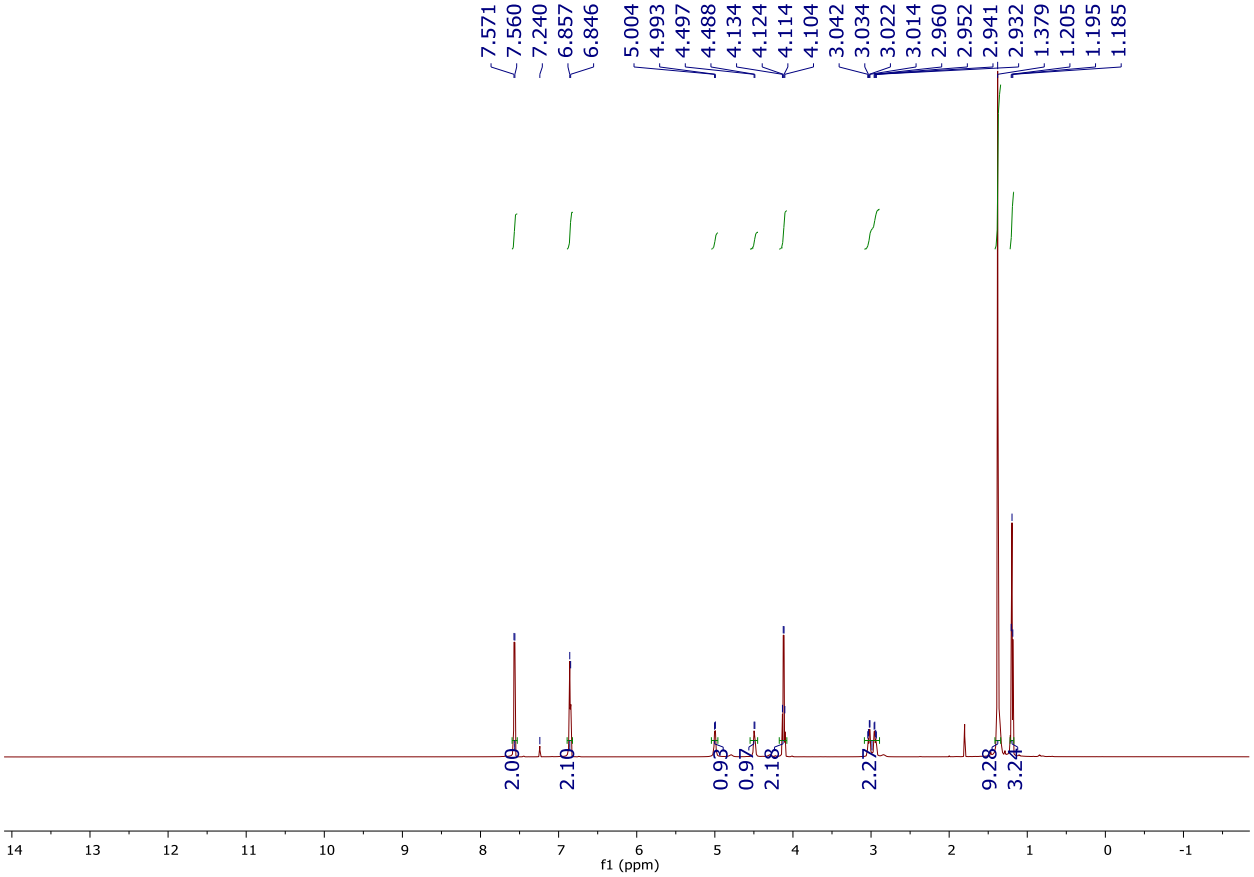
^{13}C NMR


152.901
138.198
136.676
112.759
77.181
77.000
76.819
60.796
56.131
29.074
27.350
13.701
9.775
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

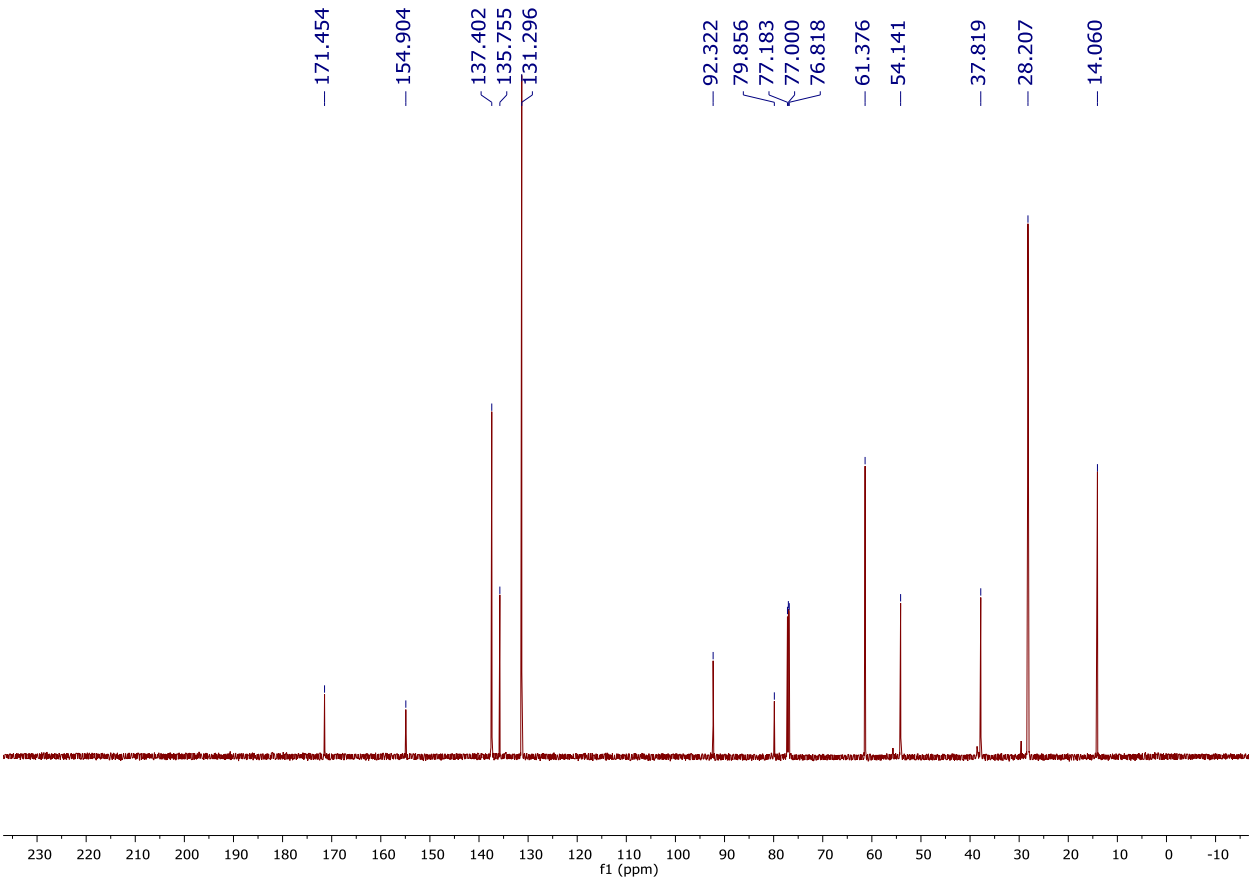

O
OEt
NHBoc
I

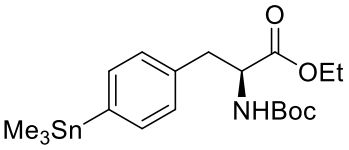
(**S1**)

^{1}H NMR


7.571
7.560
7.240
6.857
6.846
5.004
4.993
4.497
4.488
4.134
4.124
4.114
4.104
3.042
3.034
3.022
3.014
2.960
2.952
2.941
2.932
1.379
1.205
1.195
1.185
2.00
2.10
0.93
0.97
2.18
2.27
9.28
3.24
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

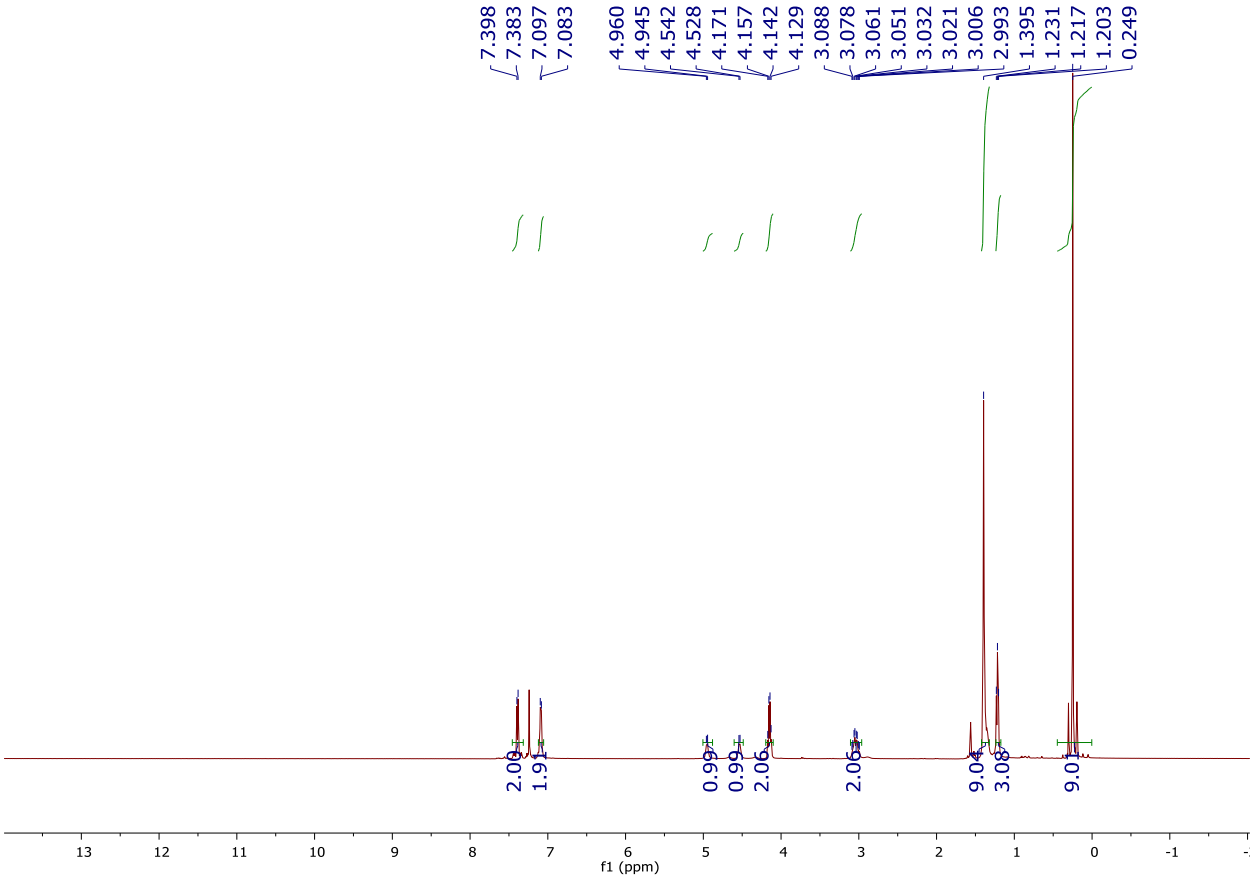
^{13}C NMR


171.454
154.904
137.402
135.755
131.296
92.322
79.856
77.183
77.000
76.818
61.376
54.141
37.819
28.207
14.060
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

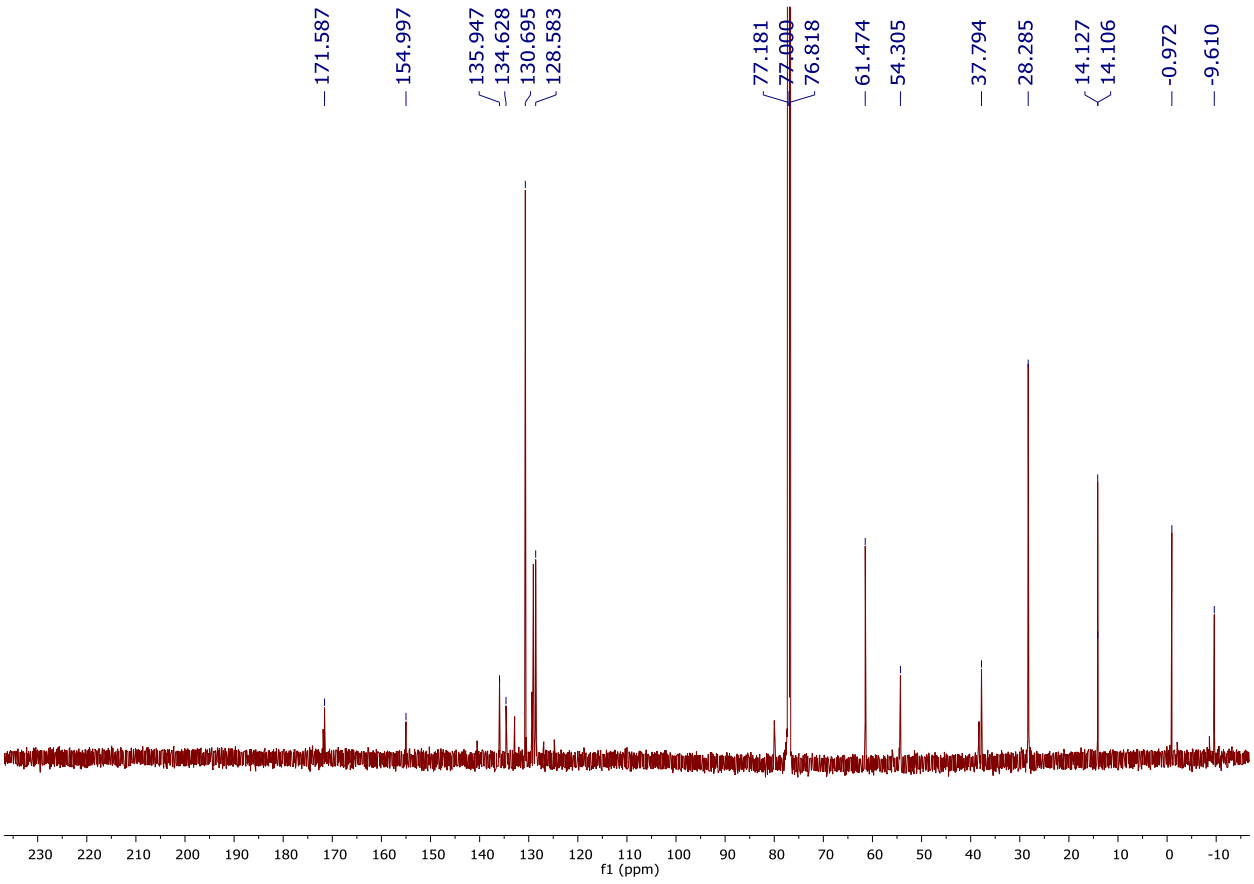


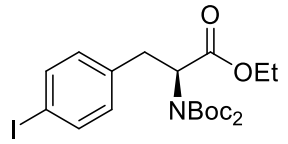
(**14-SnMe$_3$**)

^{1}H NMR



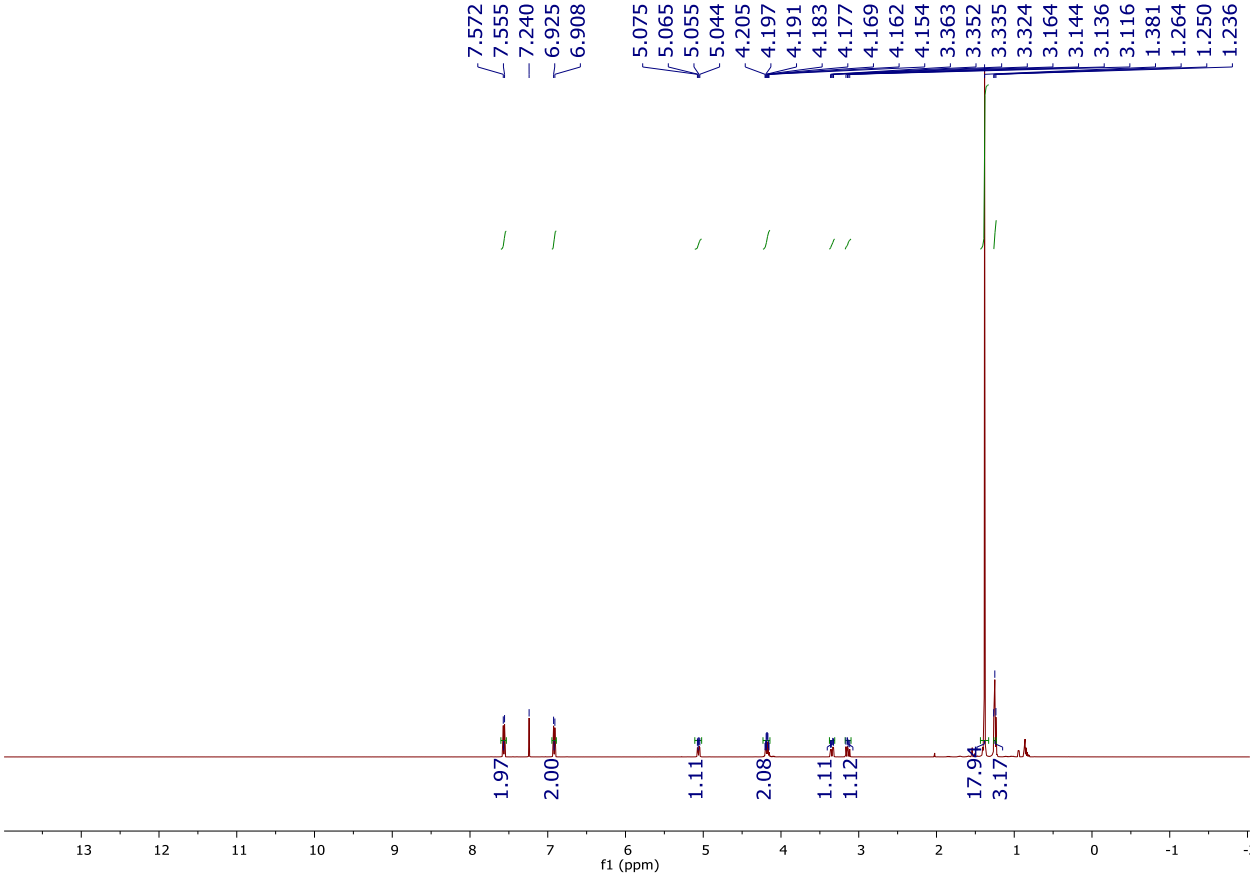
^{13}C NMR


171.587
154.997
135.947
134.628
130.695
128.583
77.181
77.000
76.818
61.474
54.305
37.794
28.285
14.127
14.106
-0.972
-9.610
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

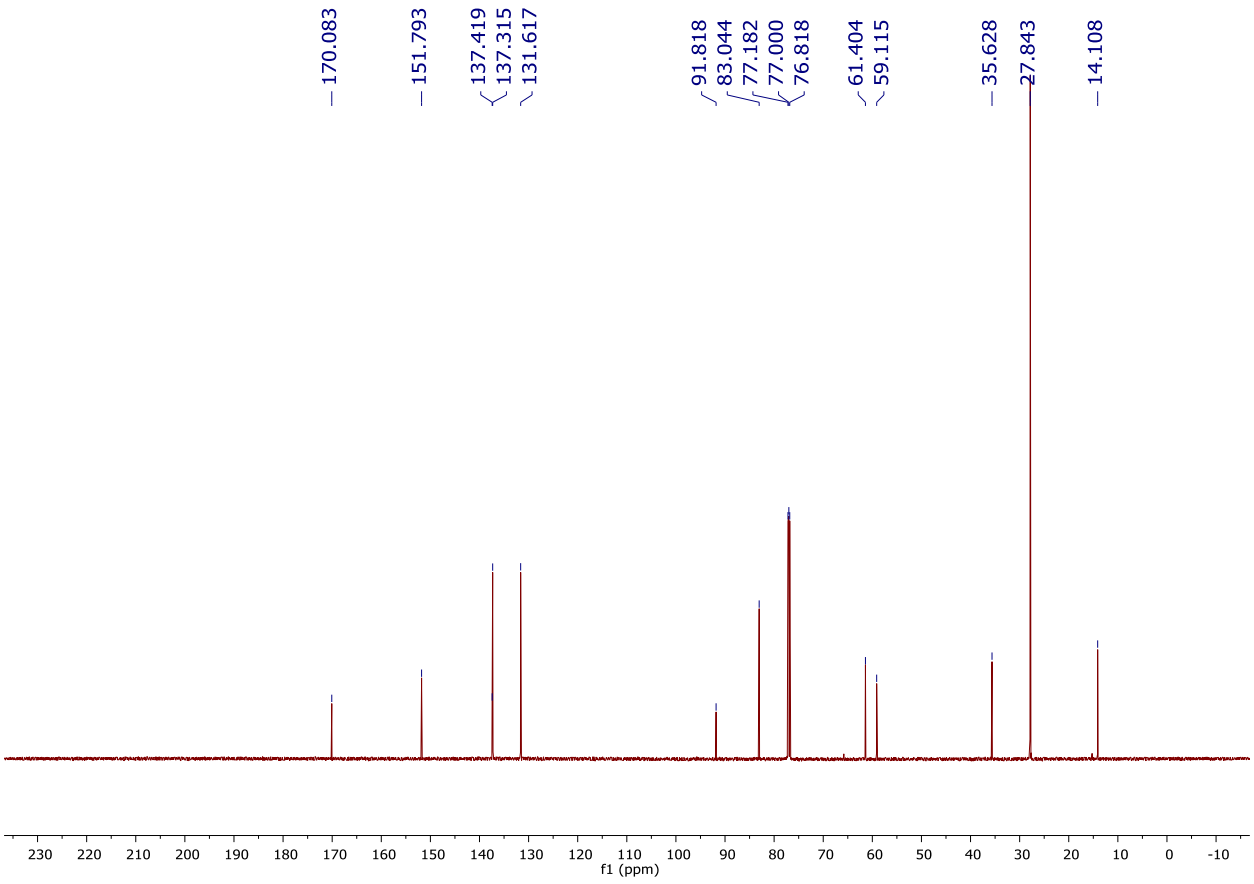

O
OEt
NBoc2
I

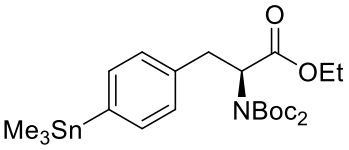
(**S2**)

^{1}H NMR


7.572
7.555
7.240
6.925
6.908
5.075
5.065
5.055
5.044
4.205
4.197
4.191
4.183
4.177
4.169
4.162
4.154
3.363
3.352
3.335
3.324
3.164
3.144
3.136
3.116
1.381
1.264
1.250
1.236
1.97
2.00
1.11
2.08
1.11
1.12
17.94
3.17
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

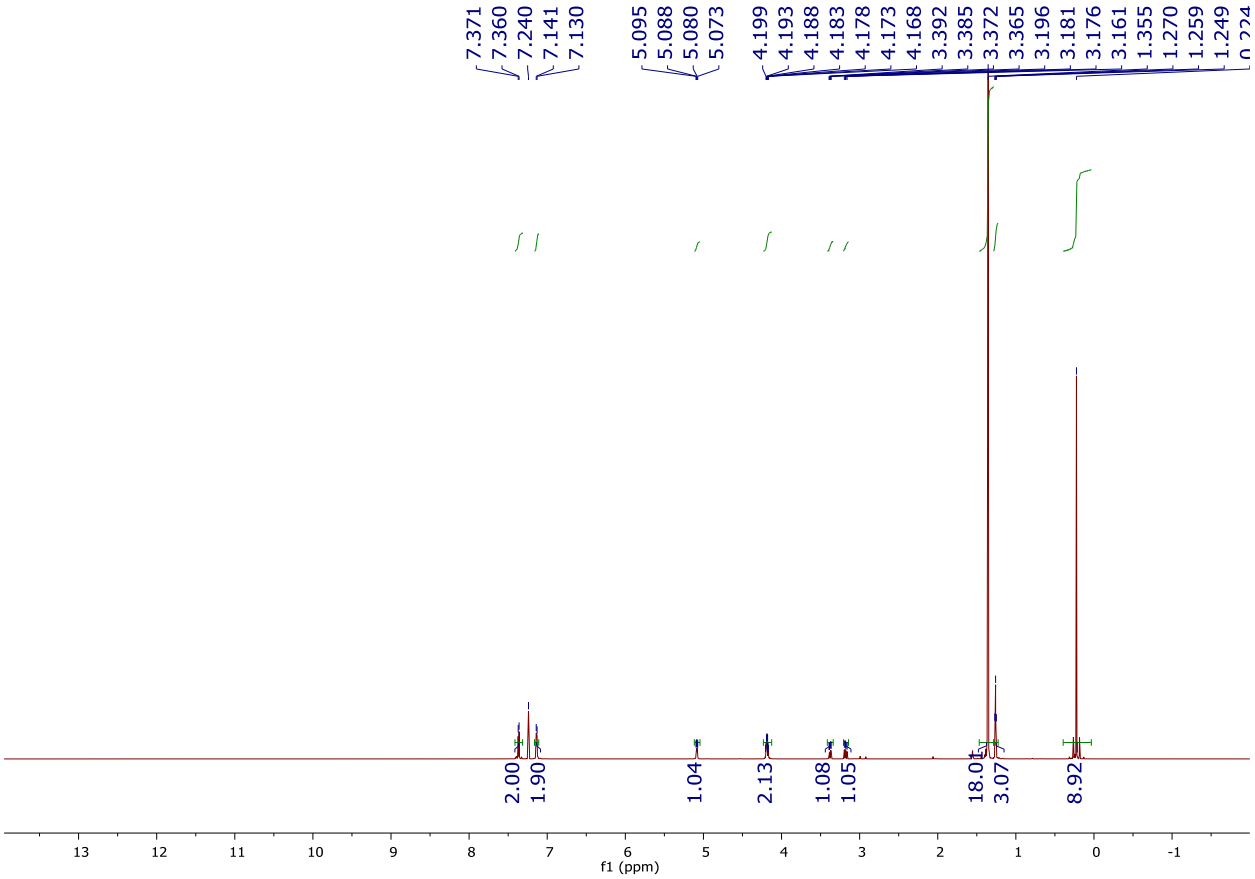
^{13}C NMR


170.083
151.793
137.419
137.315
131.617
91.818
83.044
77.182
77.000
76.818
61.404
59.115
35.628
27.843
14.108
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

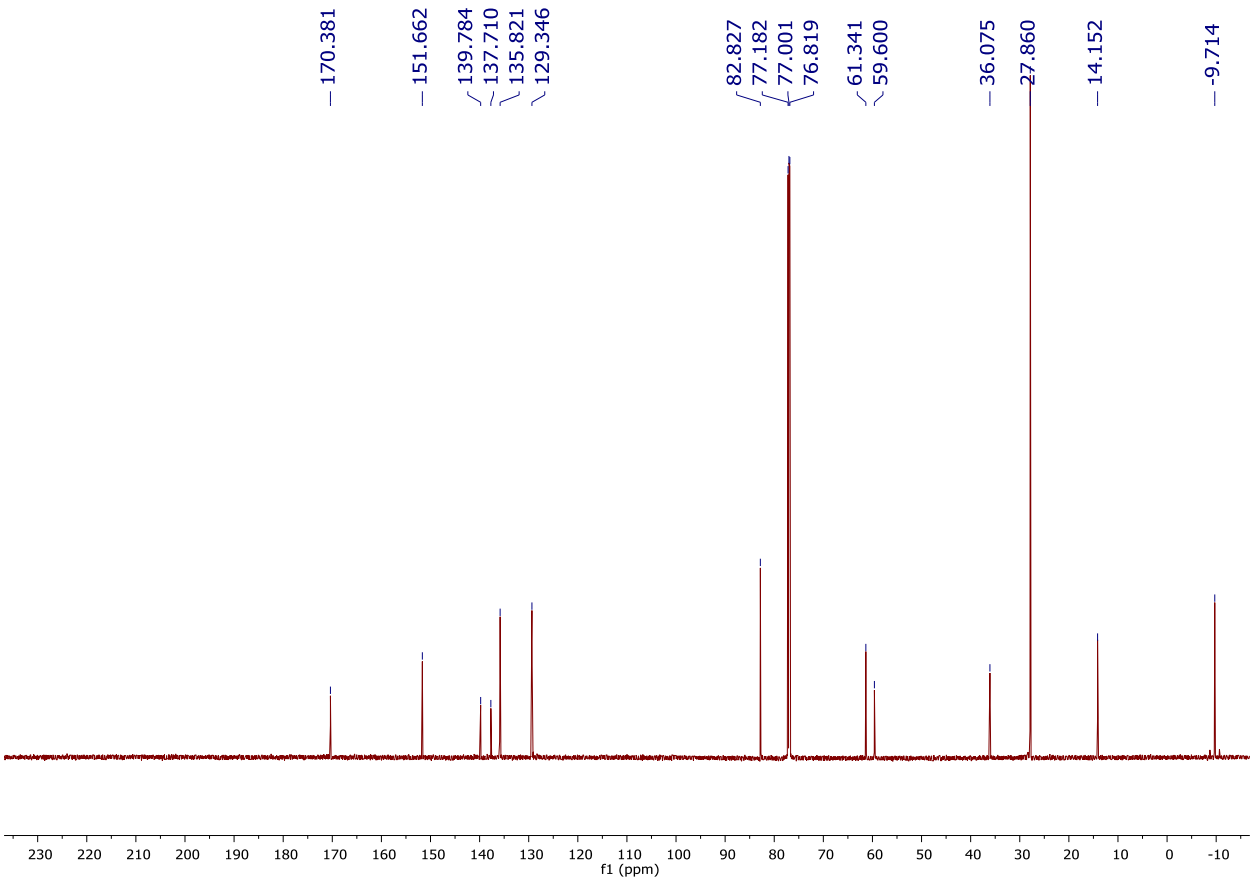


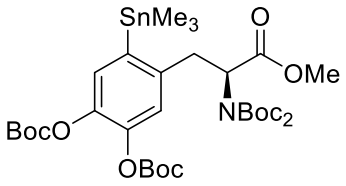
(**15-SnMe$_3$**)

^{1}H NMR



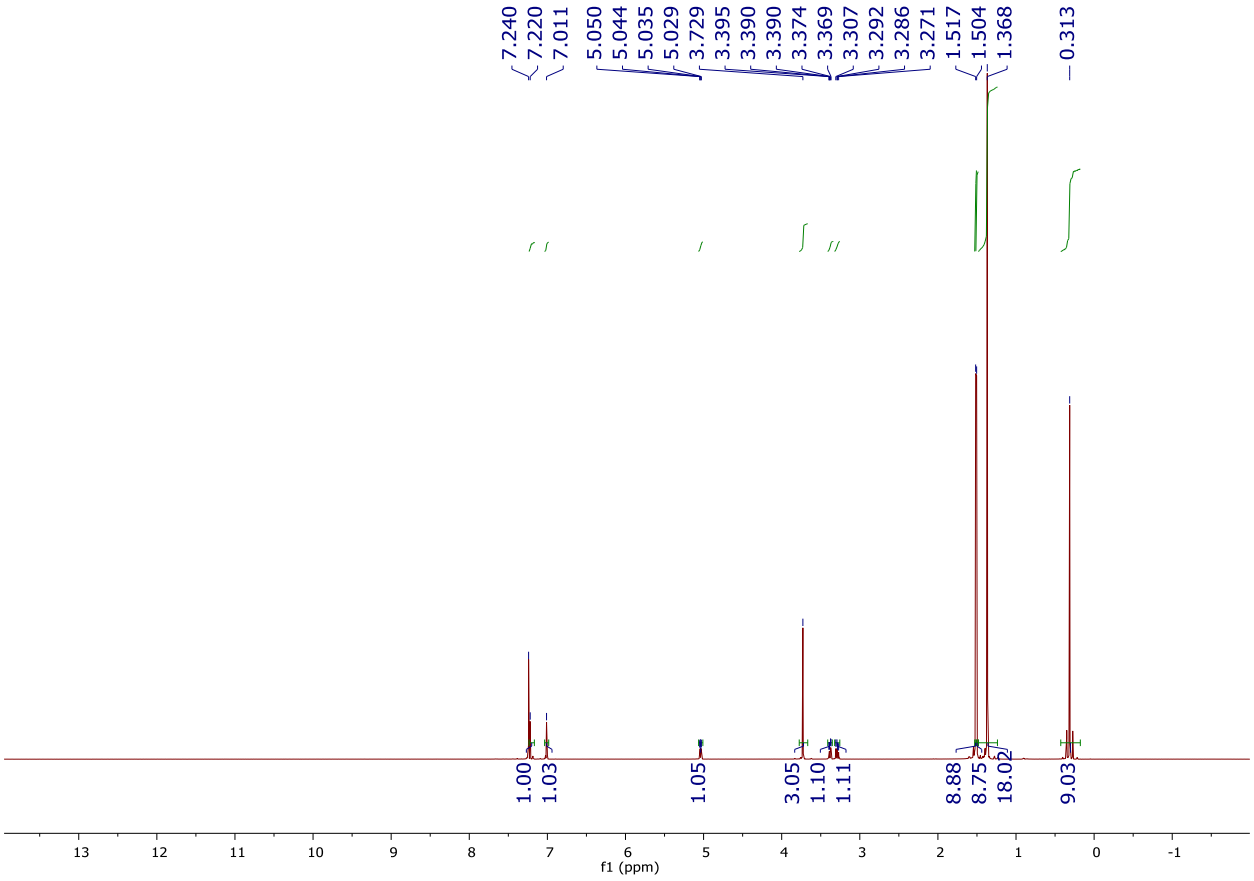
^{13}C NMR


170.381
151.662
139.784
137.710
135.821
129.346
82.827
77.182
77.001
76.819
61.341
59.600
36.075
27.860
14.152
-9.714
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

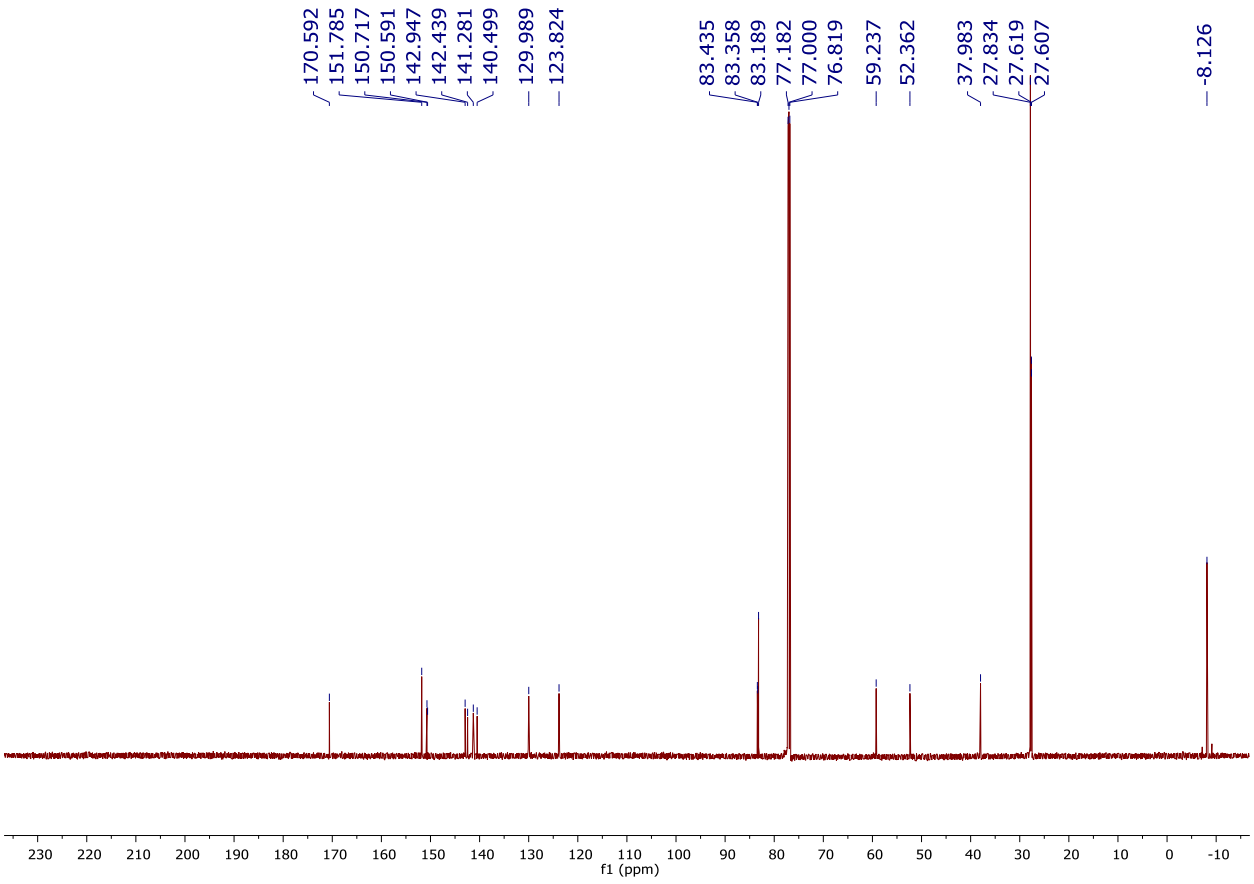


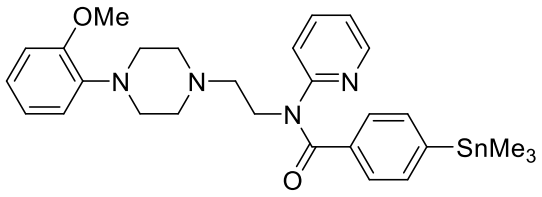
(**16-SnMe$_3$**)

^{1}H NMR



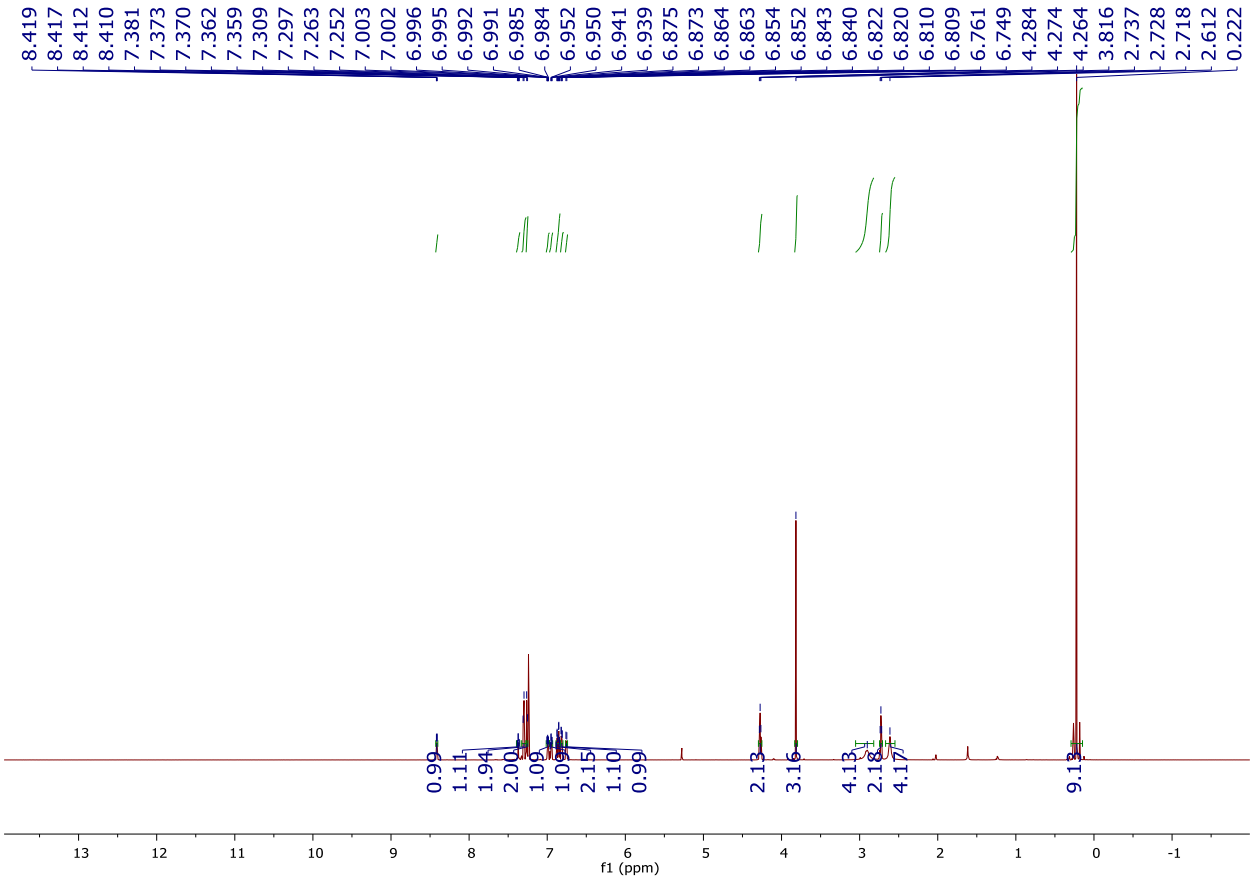
^{13}C NMR


170.592
151.785
150.717
150.591
142.947
142.439
141.281
140.499
129.989
123.824
83.435
83.358
83.189
77.182
77.000
76.819
59.237
52.362
37.983
27.834
27.619
27.607
-8.126
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

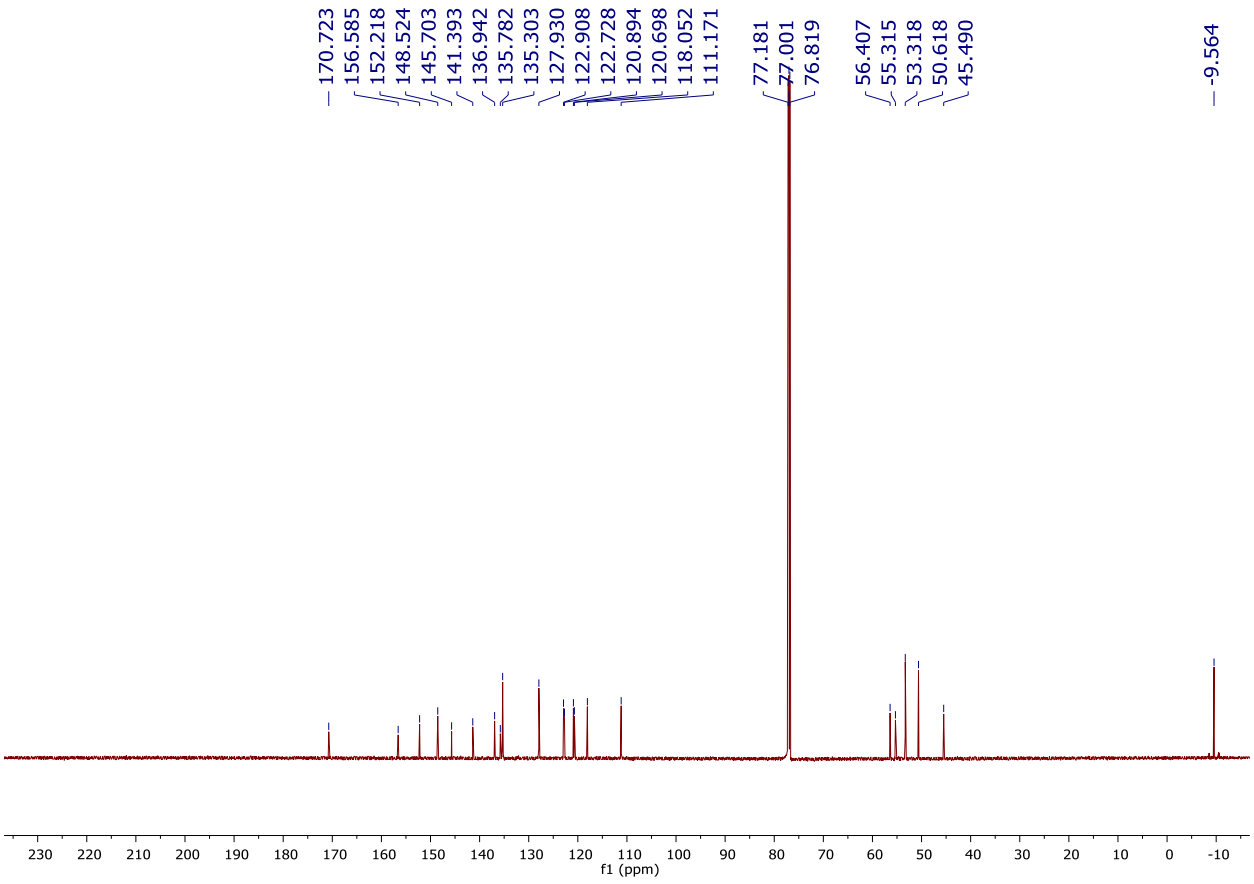


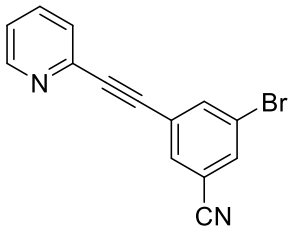
(**17-SnMe$_3$**)

^{1}H NMR



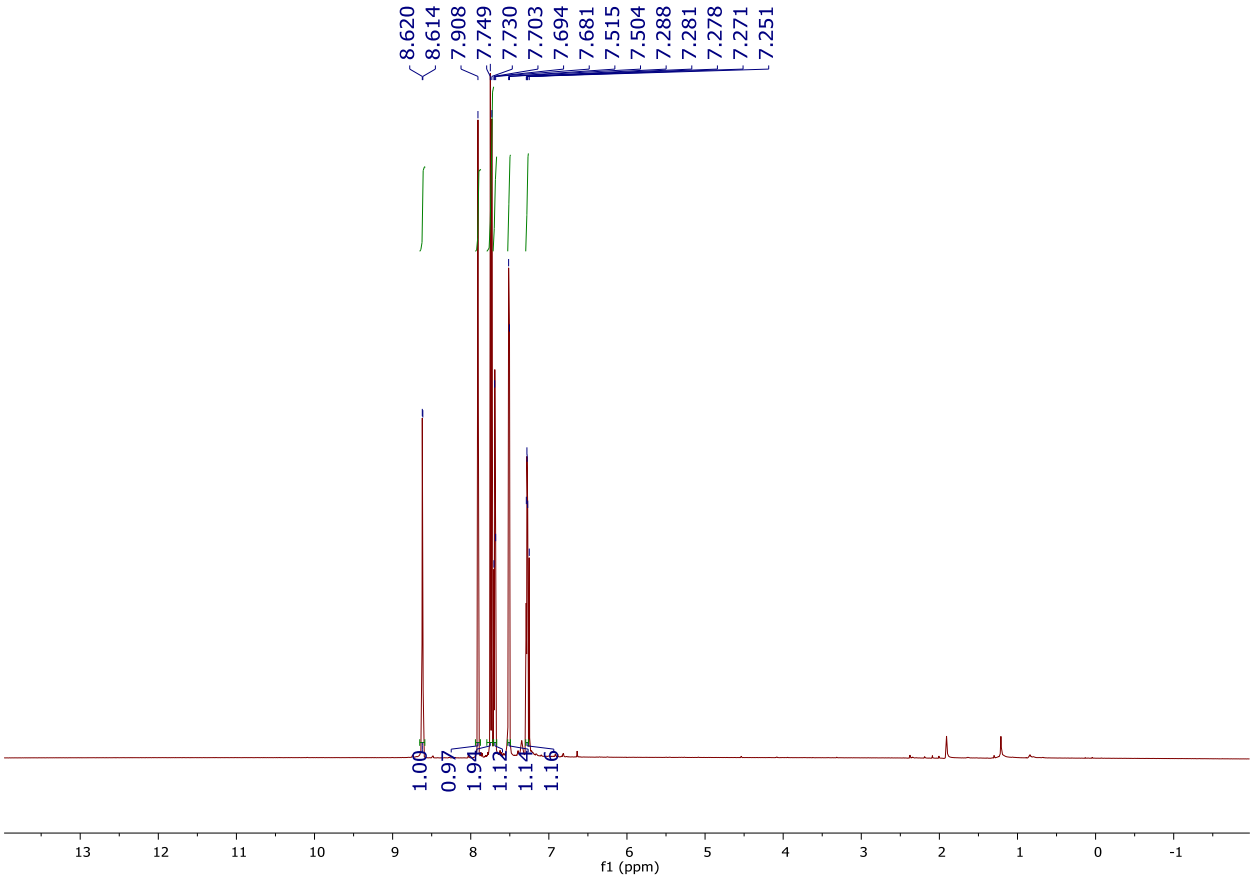
^{13}C NMR


170.723
156.585
152.218
148.524
145.703
141.393
136.942
135.782
135.303
127.930
122.908
122.728
120.894
120.698
118.052
111.171
77.181
77.001
76.819
56.407
55.315
53.318
50.618
45.490
-9.564
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

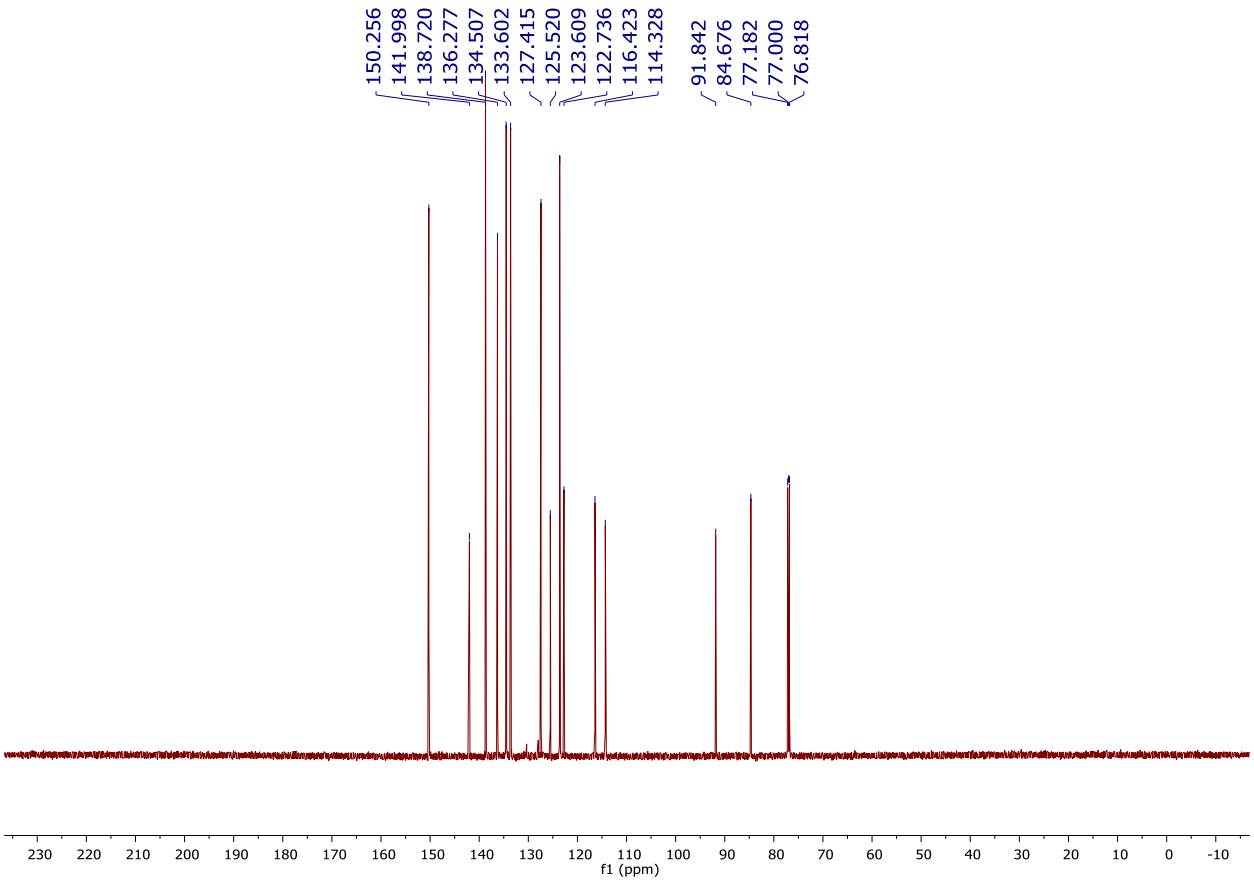

N
Br
CN

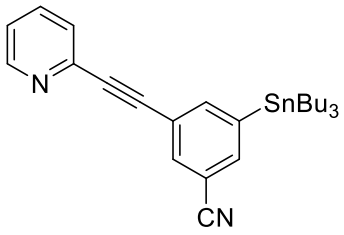
(**S7**)

^{1}H NMR


8.620
8.614
7.908
7.749
7.730
7.703
7.694
7.681
7.515
7.504
7.288
7.281
7.278
7.271
7.251
1.00
0.97
1.94
1.12
1.14
1.16
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

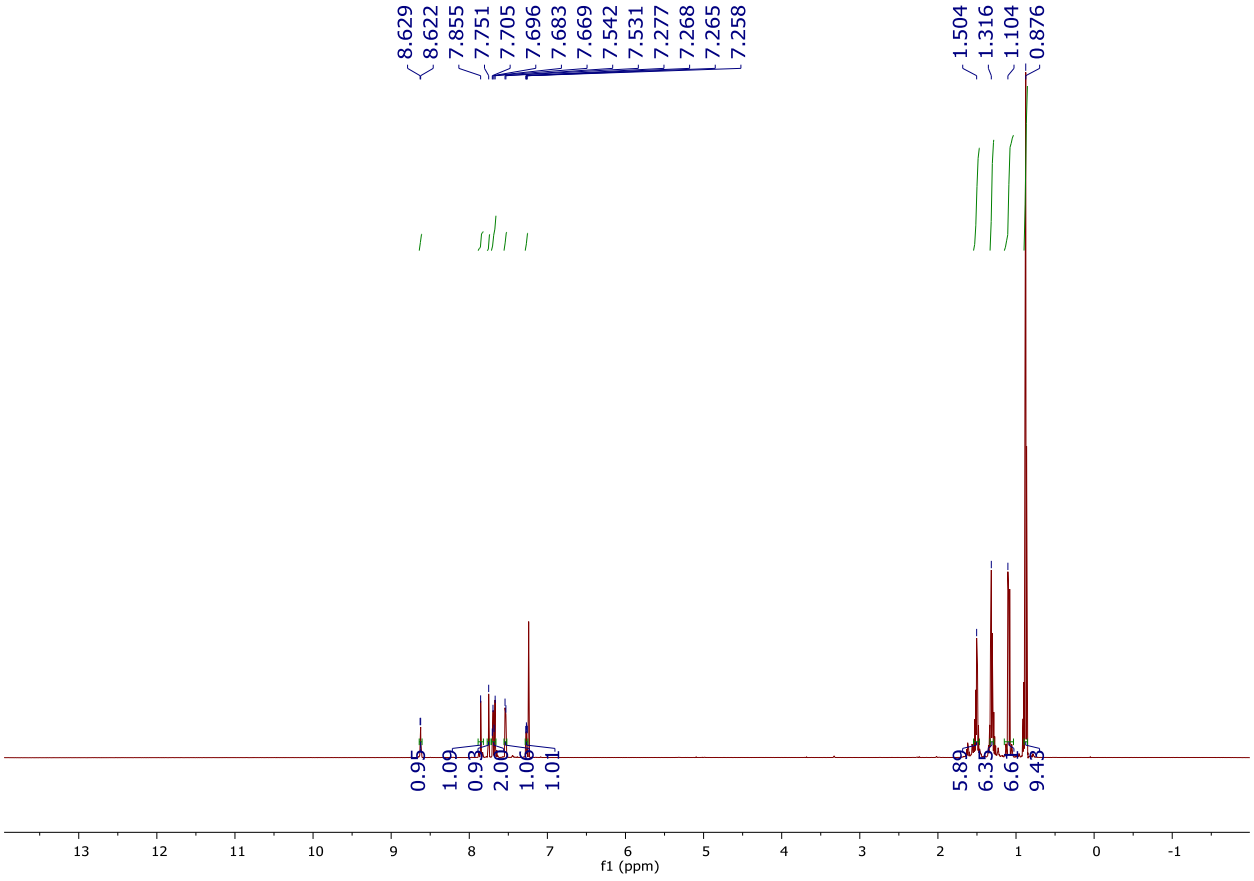
^{13}C NMR


150.256
141.998
138.720
136.277
134.507
133.602
127.415
125.520
123.609
122.736
116.423
114.328
91.842
84.676
77.182
77.000
76.818
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

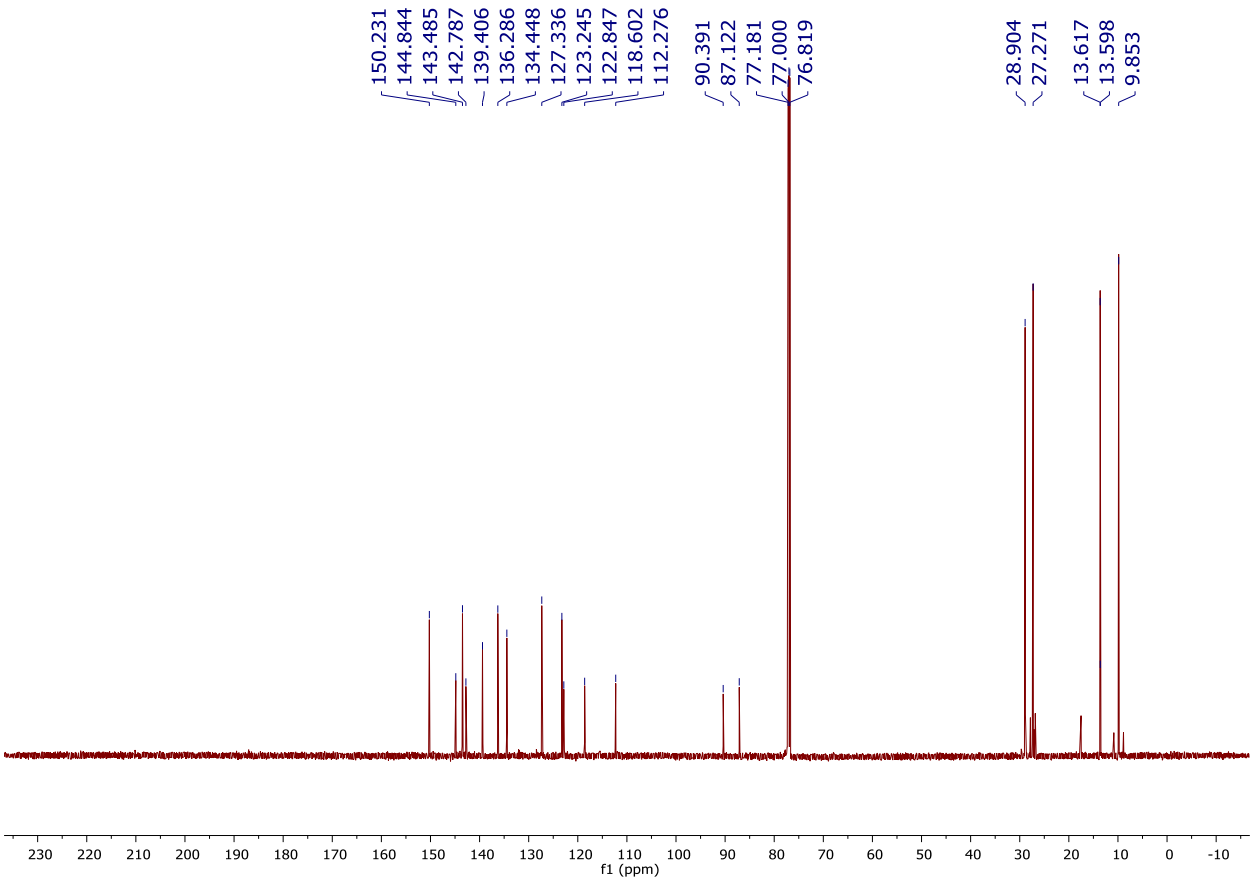


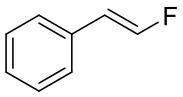
(**18-SnBu$_3$**)

^{1}H NMR



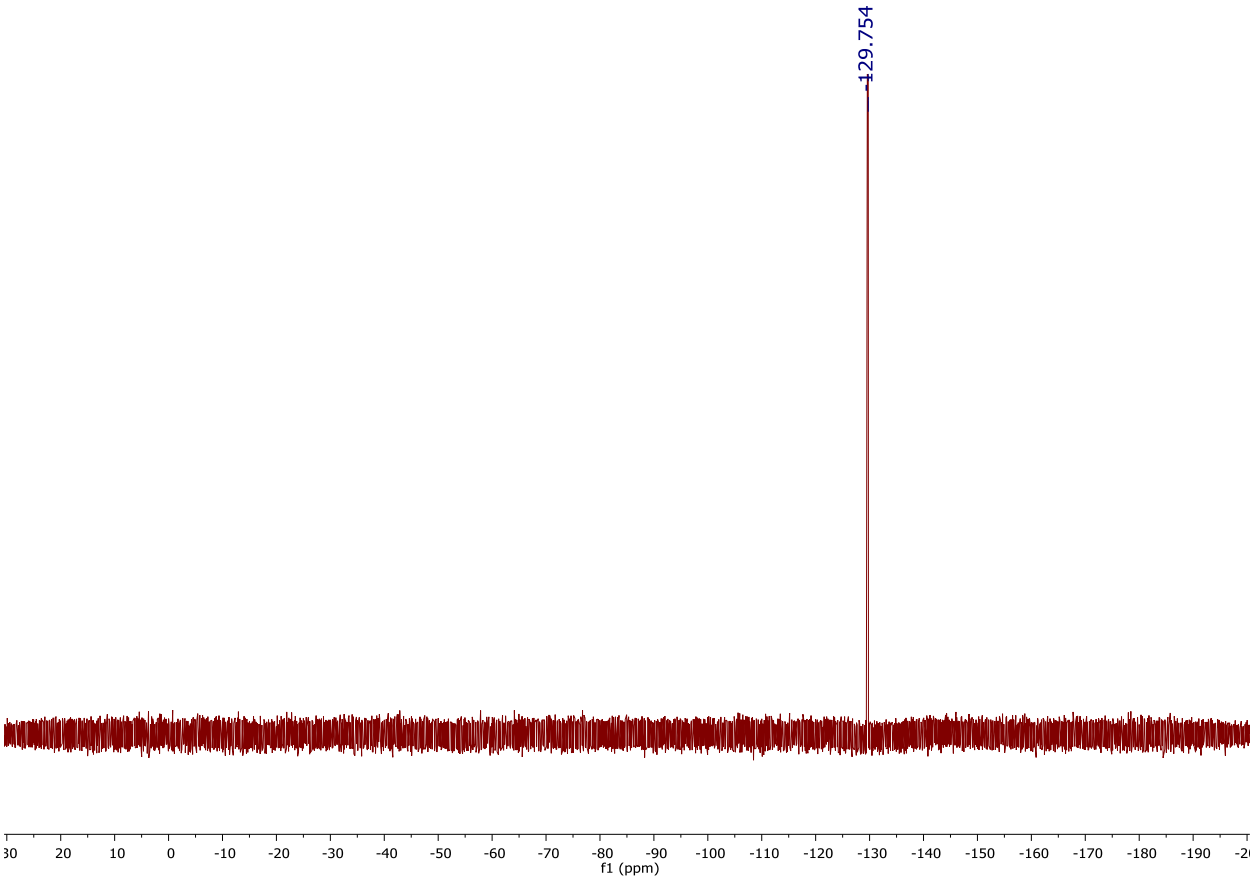
^{13}C NMR

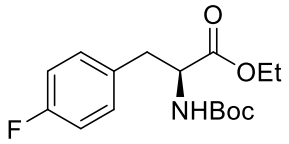

150.231
144.844
143.485
142.787
139.406
136.286
134.448
127.336
123.245
122.847
118.602
112.276
90.391
87.122
77.181
77.000
76.819
28.904
27.271
13.617
13.598
9.853
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


F

(**S8**)

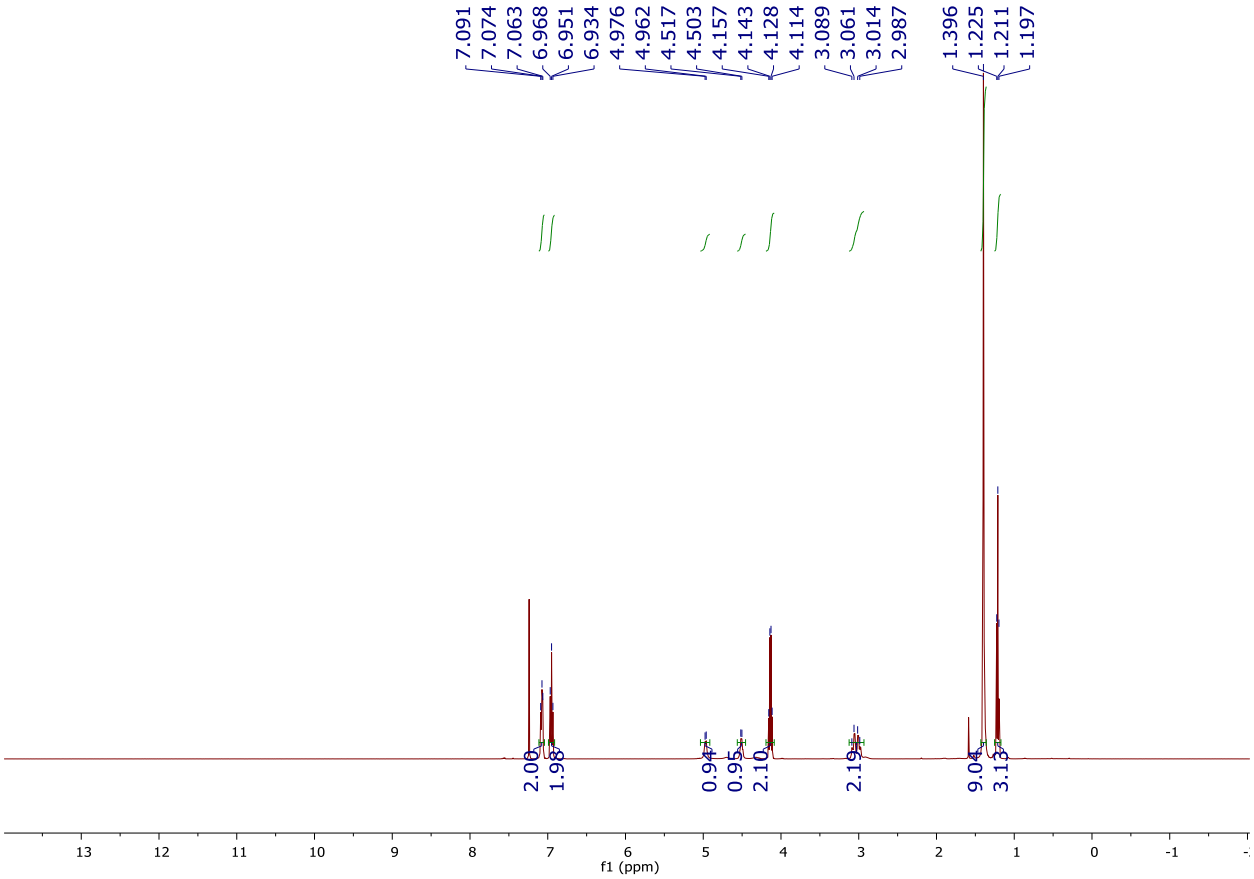
^{19}F NMR


-129.754
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

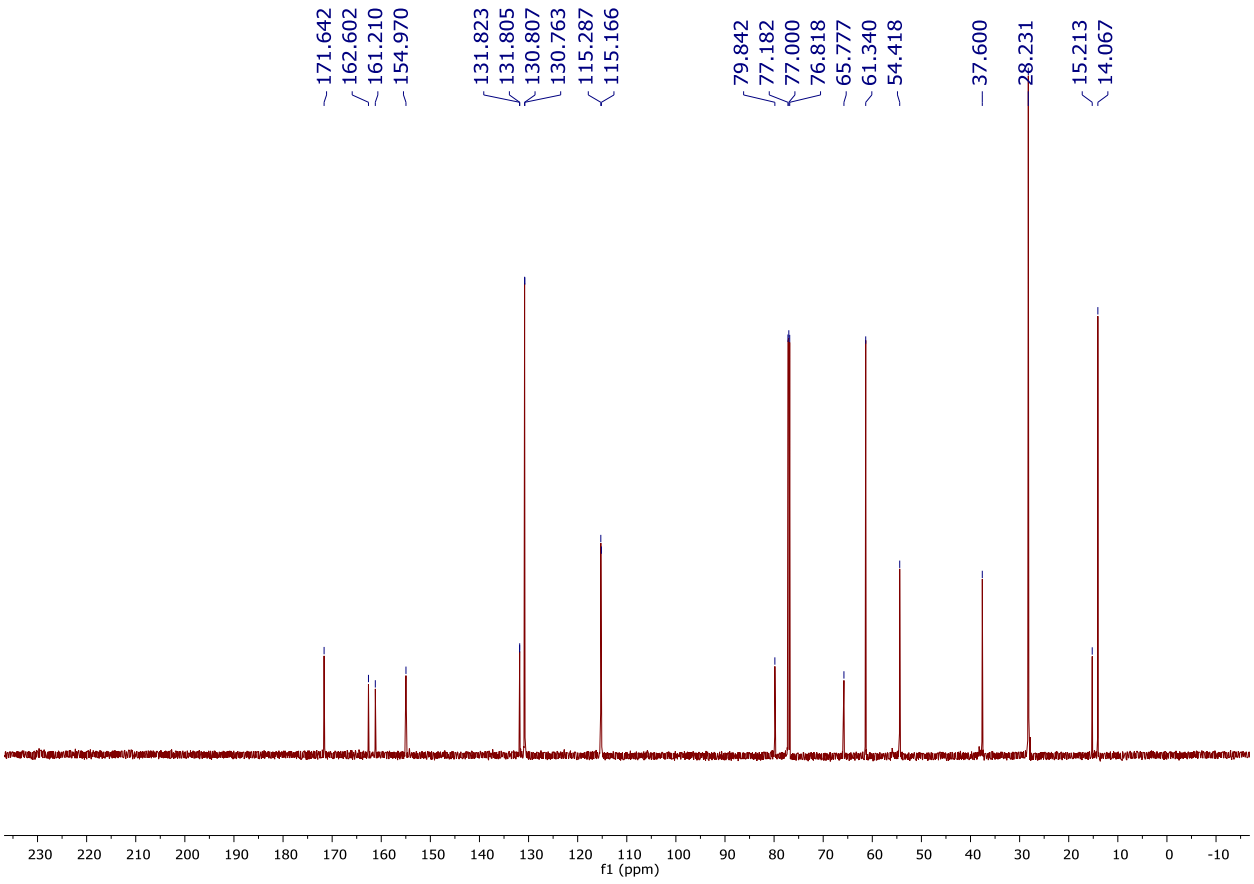

O
OEt
NHBoc
F

(**S9**)

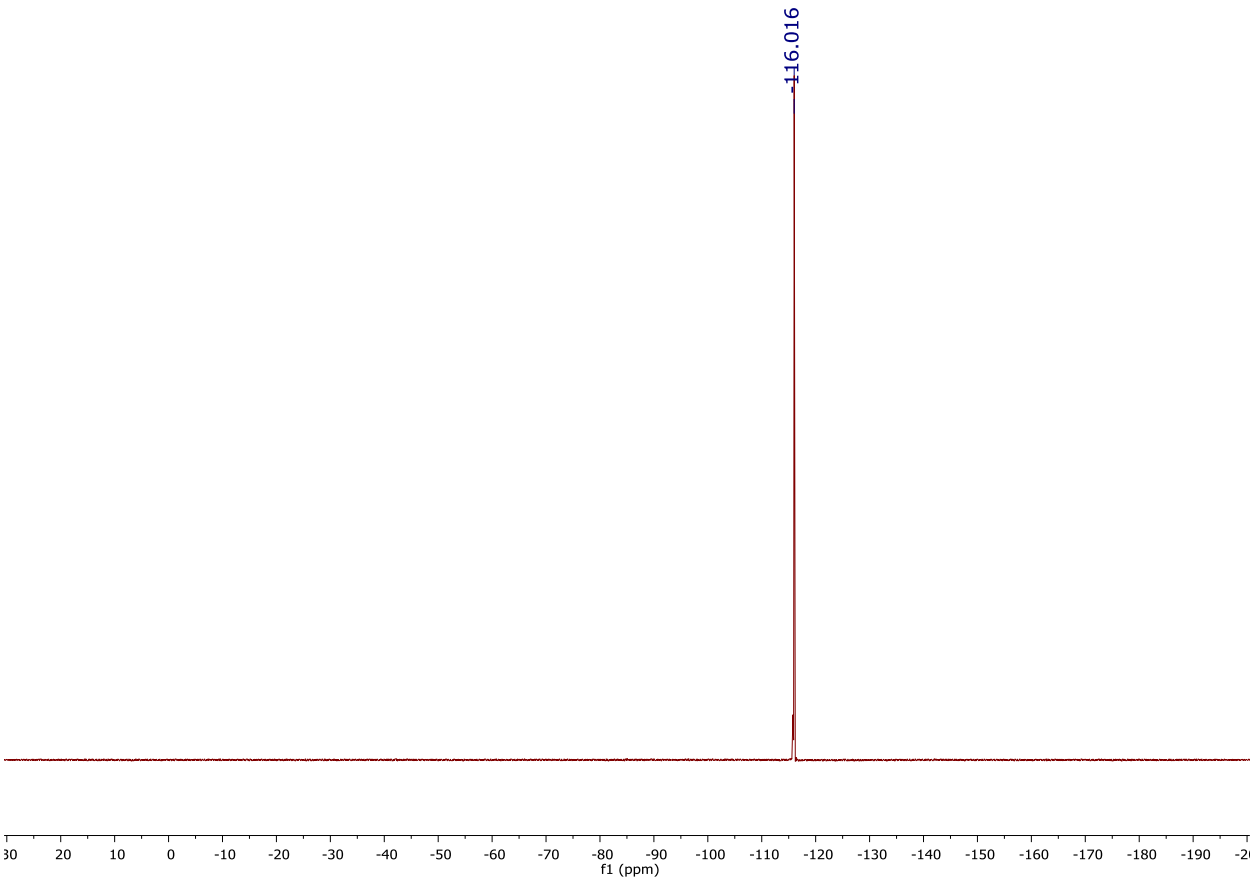
^{1}H NMR

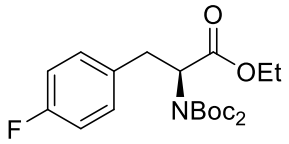

7.091
7.074
7.063
6.968
6.951
6.934
4.976
4.962
4.517
4.503
4.157
4.143
4.128
4.114
3.089
3.061
3.014
2.987
1.396
1.225
1.211
1.197
2.00
1.98
0.94
0.95
2.10
2.19
9.04
3.13
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

^{13}C NMR


171.642
162.602
161.210
154.970
131.823
131.805
130.807
130.763
115.287
115.166
79.842
77.182
77.000
76.818
65.777
61.340
54.418
37.600
28.231
15.213
14.067
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

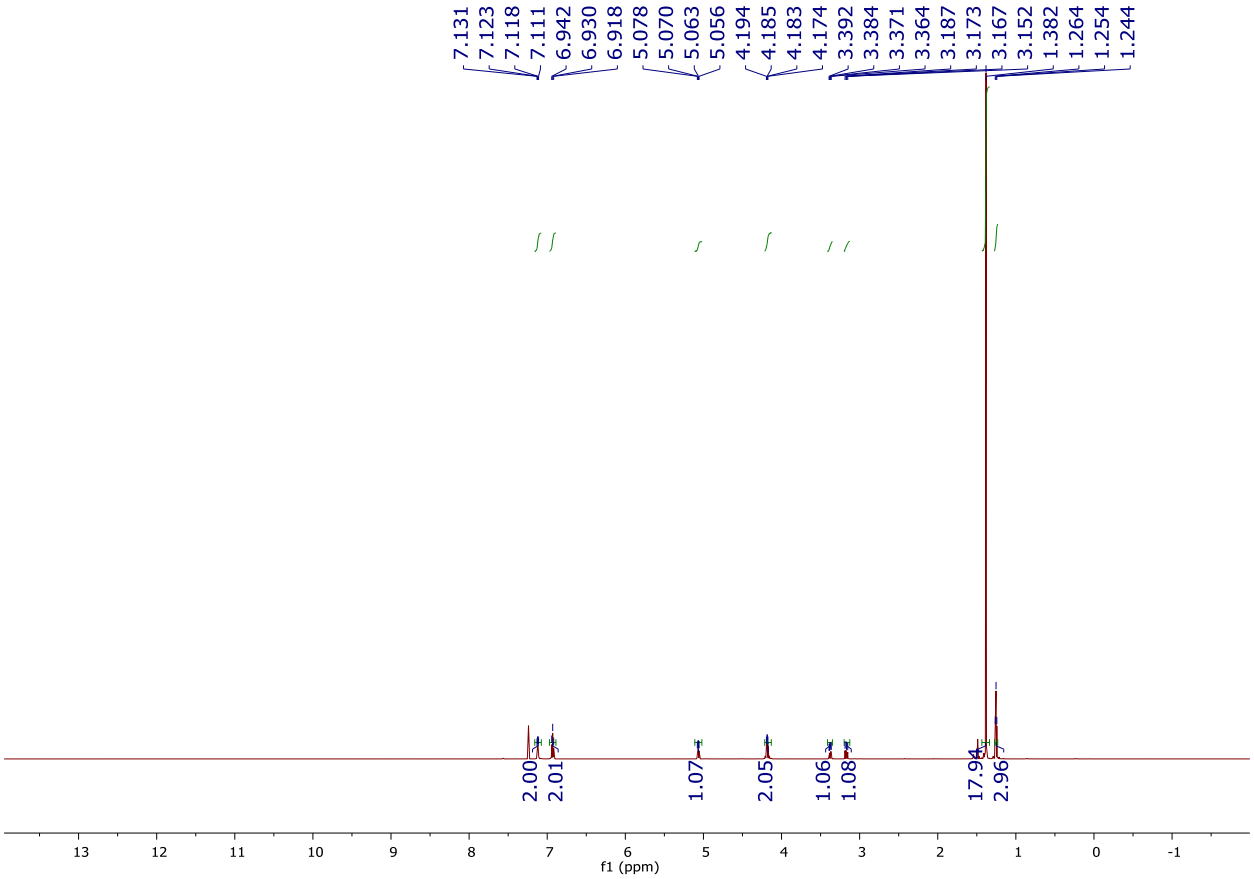
^{19}F NMR


-116.016
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

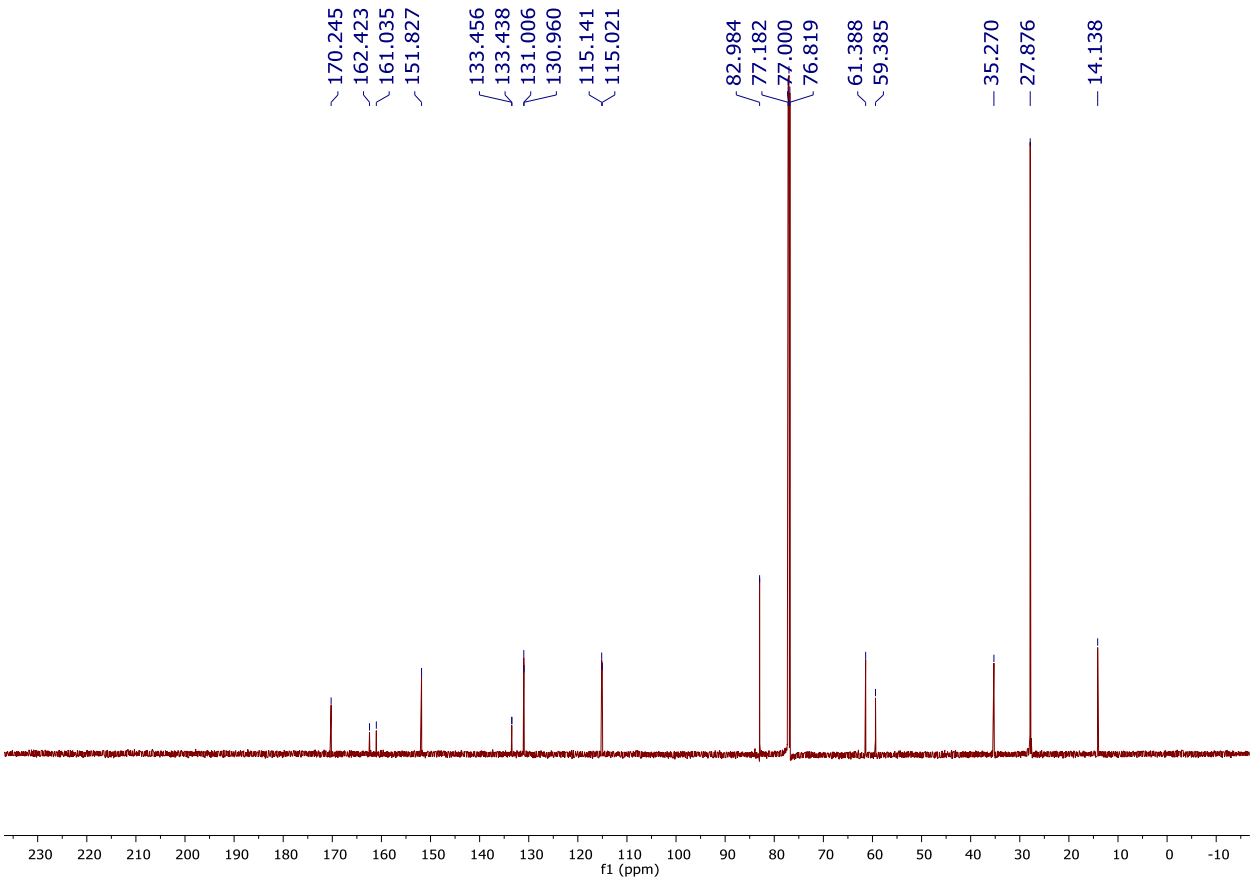

O
OEt
NBoc2
F

(**S10**)

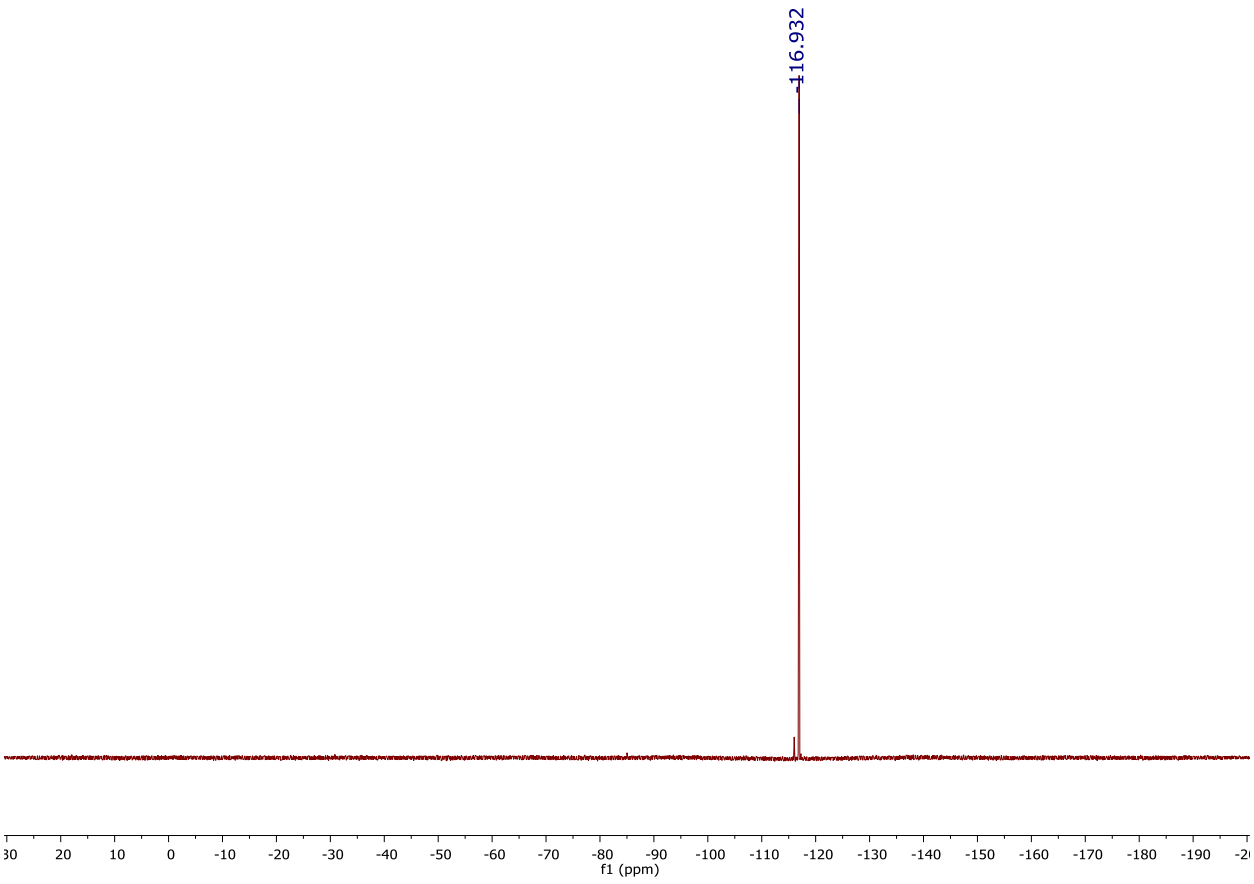
^{1}H NMR

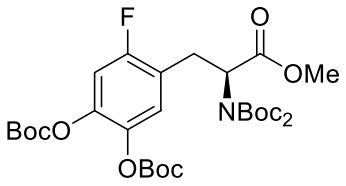

7.131
7.123
7.118
7.111
6.942
6.930
6.918
5.078
5.070
5.063
5.056
4.194
4.185
4.183
4.174
3.392
3.384
3.371
3.364
3.187
3.173
3.167
3.152
1.382
1.264
1.254
1.244
2.00
2.01
1.07
2.05
1.06
1.08
17.94
2.96
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

^{13}C NMR


170.245
162.423
161.035
151.827
133.456
133.438
131.006
130.960
115.141
115.021
82.984
77.182
77.000
76.819
61.388
59.385
35.270
27.876
14.138
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

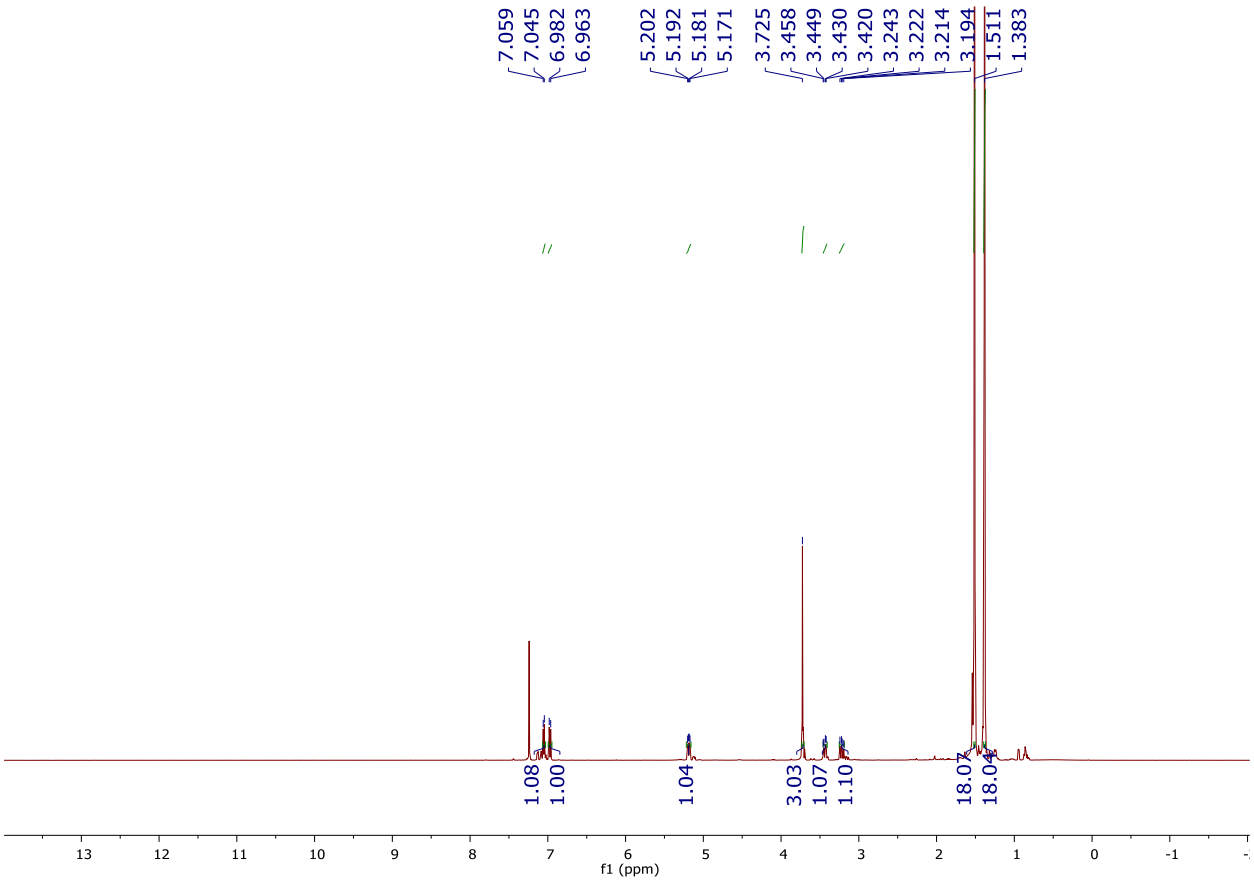
^{19}F NMR


-116.932
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

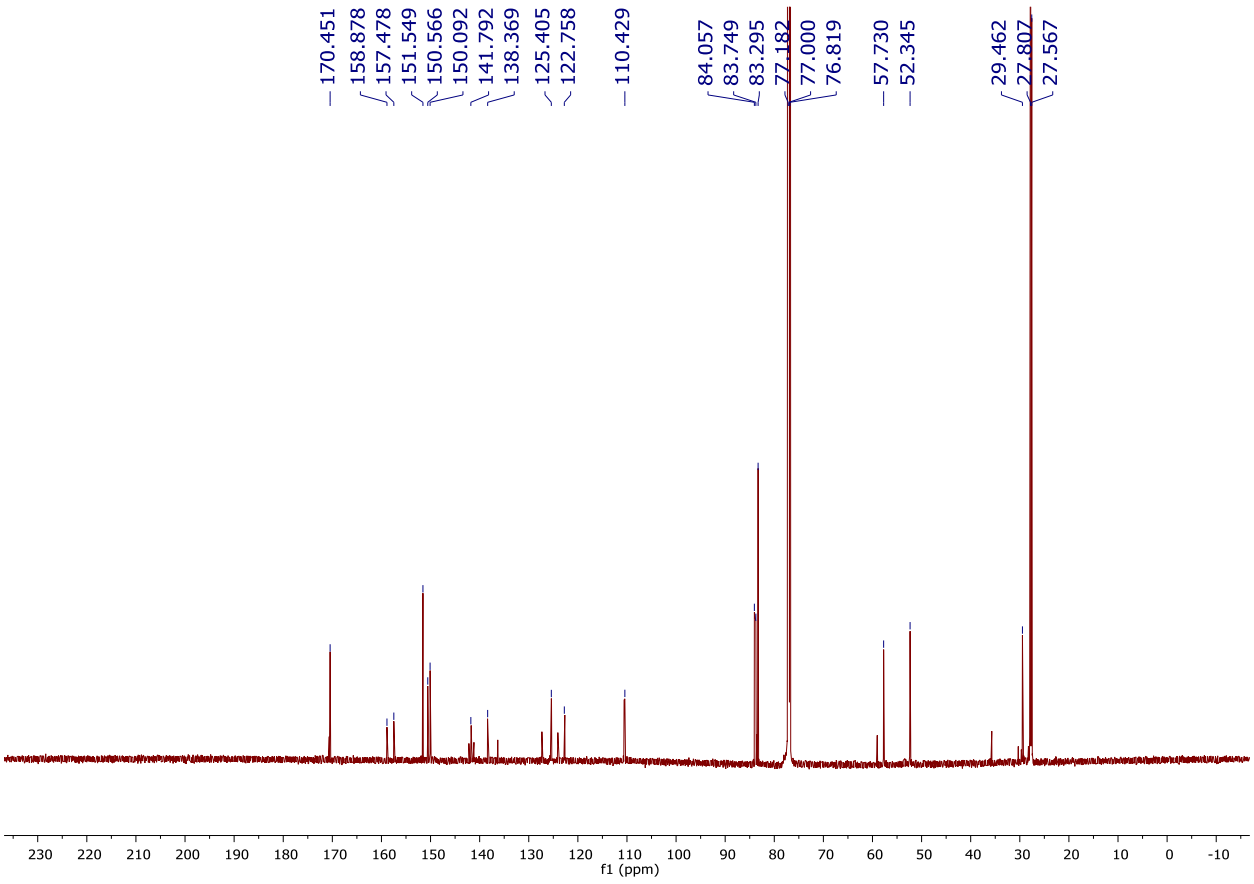

F
O
OMe
NBoc2
BocO
OBoc

(**S11**)

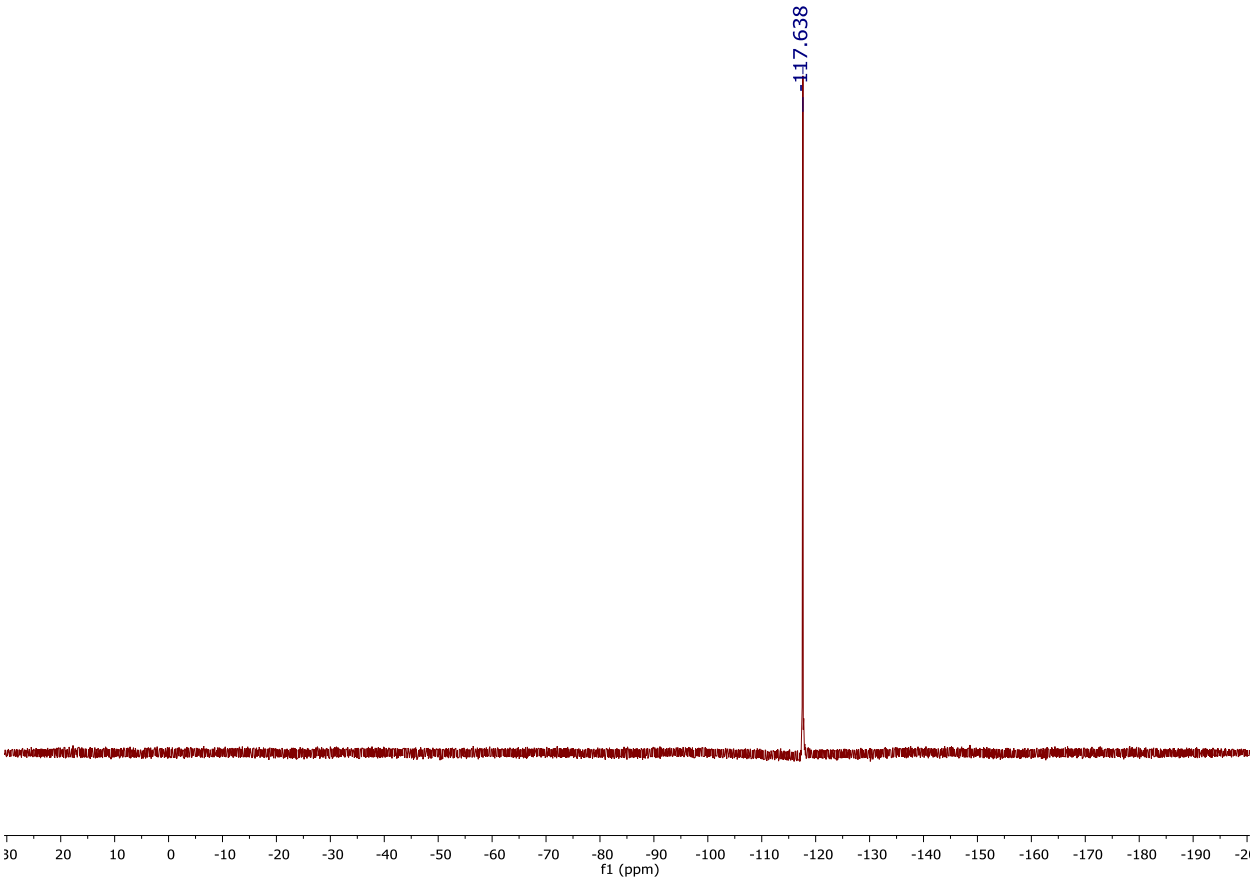
^{1}H NMR


7.059
7.045
6.982
6.963
5.202
5.192
5.181
5.171
3.725
3.458
3.449
3.430
3.420
3.243
3.222
3.214
3.194
1.511
1.383
1.08
1.00
1.04
3.03
1.07
1.10
18.07
18.04
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

^{13}C NMR

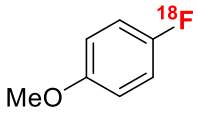

170.451
158.878
157.478
151.549
150.566
150.092
141.792
138.369
125.405
122.758
110.429
84.057
83.749
83.295
77.182
77.000
76.819
57.730
52.345
29.462
27.807
27.567
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

^{19}F NMR


-117.638
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

6.2 Radio-HPLC/Radio-TLC Analysis for ^{18}F-Labeled Compounds

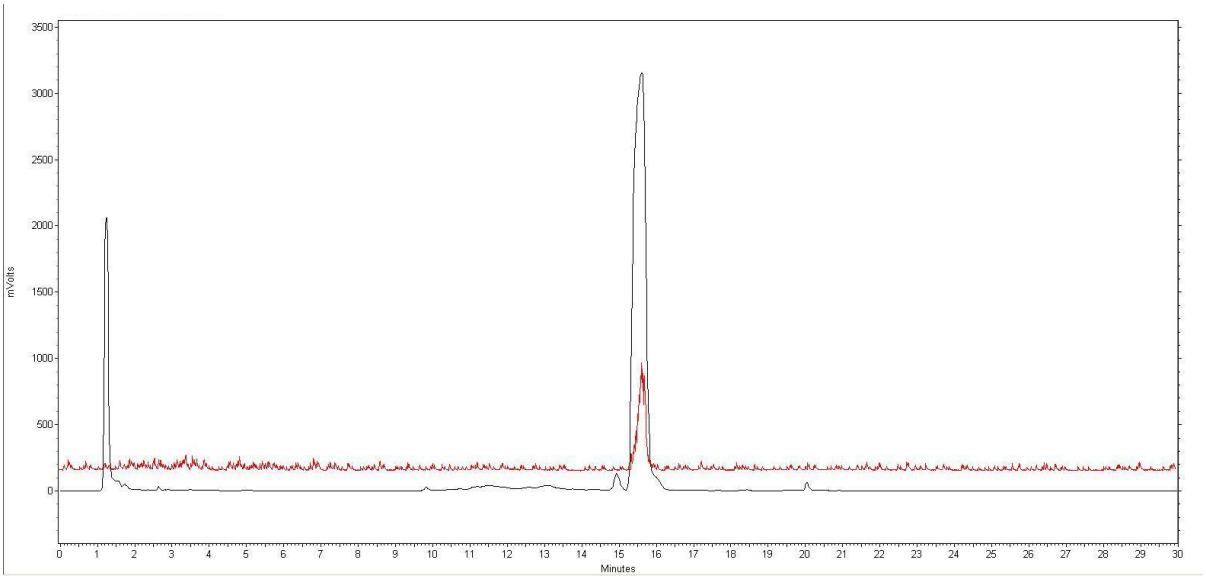
In the section below, two HPLC traces are presented for each substrate contained in Figure 2 and Figure 3. The trace shows the RAD and UV trace (254 nm or 280 nm) from the crude reaction mixture spiked with an authentic standard of the fluorinated product. This was used to confirm the identity of the radiofluorinated product. The wavelength shown is the wavelength where the analyte compound exhibited greatest absorptivity. Because of the physical separation of the two detectors, a horizontal offset of 0.2 min was applied to the UV trace to account for the line volume between detectors. This offset was applied to all traces displayed below. HPLC conditions are from 5.4.
For all HPLC traces, black trace is the UV trace and the red trace is the radiochemical trace.

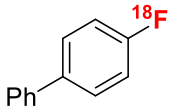


(**[^{18}F]2**)

4-[^{18}F]fluoroanisole (**[^{18}F]2**) RAD trace overlaid with UV trace (256 nm) spiked with 4-fluoroanisole

HPLC Conditions: A

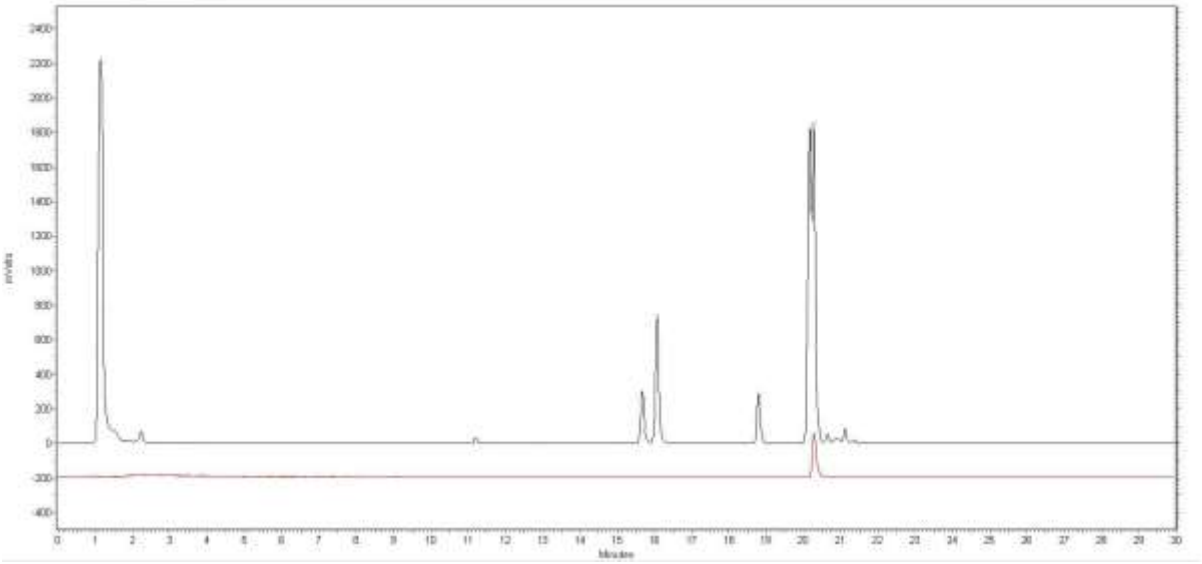


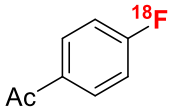


([18F]3)

4-[18F]fluoro-1,1'-biphenyl (**[18F]3)** RAD trace overlaid with UV trace (256 nm) spiked with 4-fluoro-1,1'-biphenyl

HPLC Conditions: A

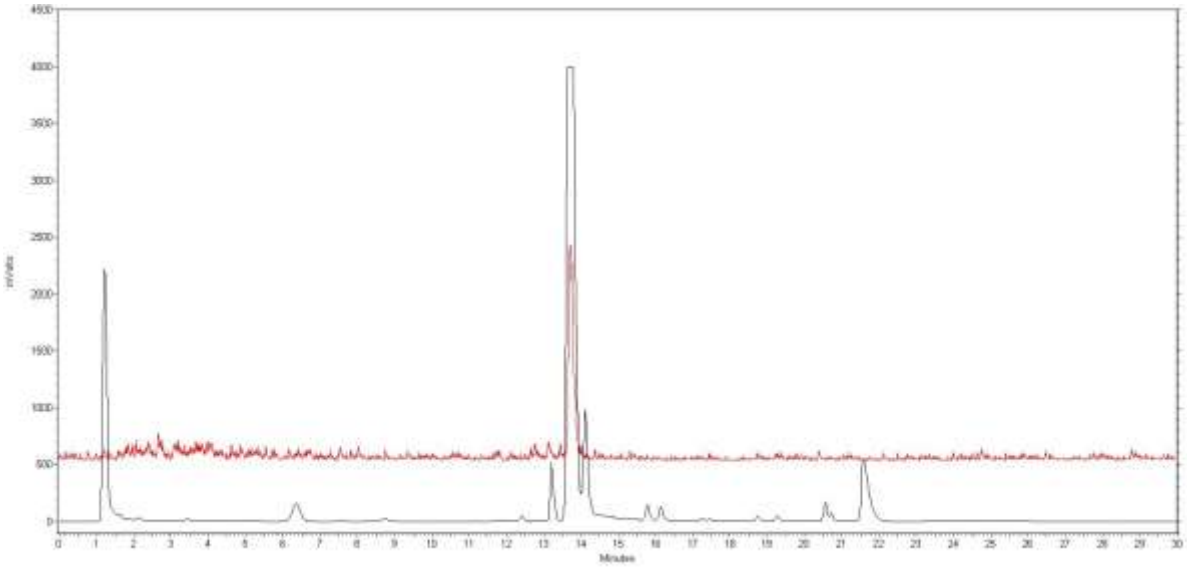


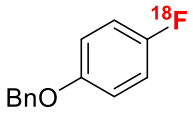


([18F]4)

4-[18F]fluoroacetophenone (**[18F]4**) RAD trace overlaid with UV trace (256 nm) spiked with 4-fluoroacetophenone

HPLC Conditions: A

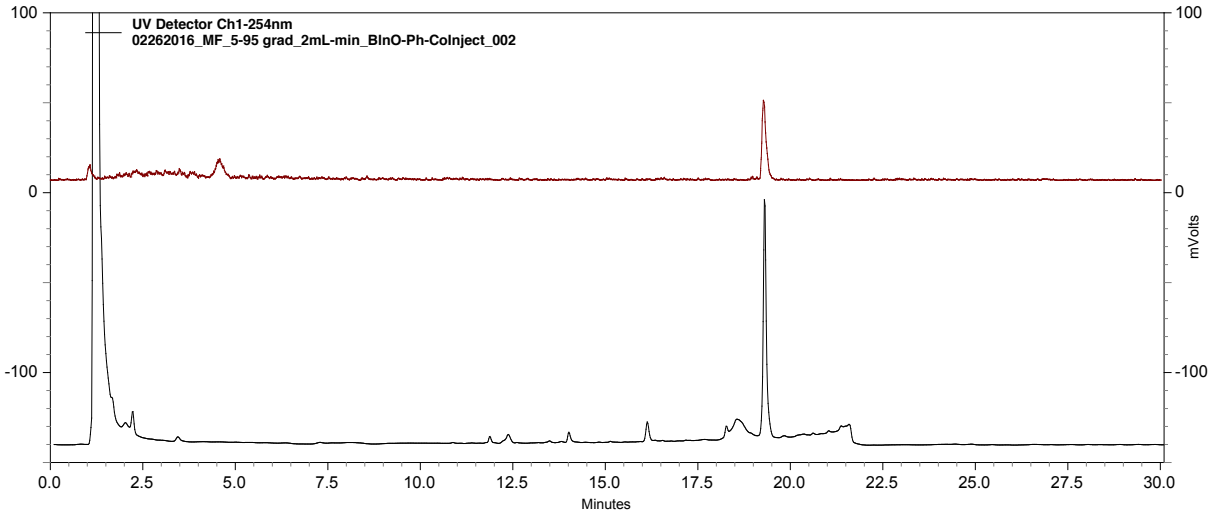




([**18F]5**)

4-[^{18}F]fluoro-1-(benzyloxy)benzene (**[^{18}F]5**) RAD trace overlaid with UV trace (256 nm) spiked with 1-(benzyloxy)-4-fluorobenzene

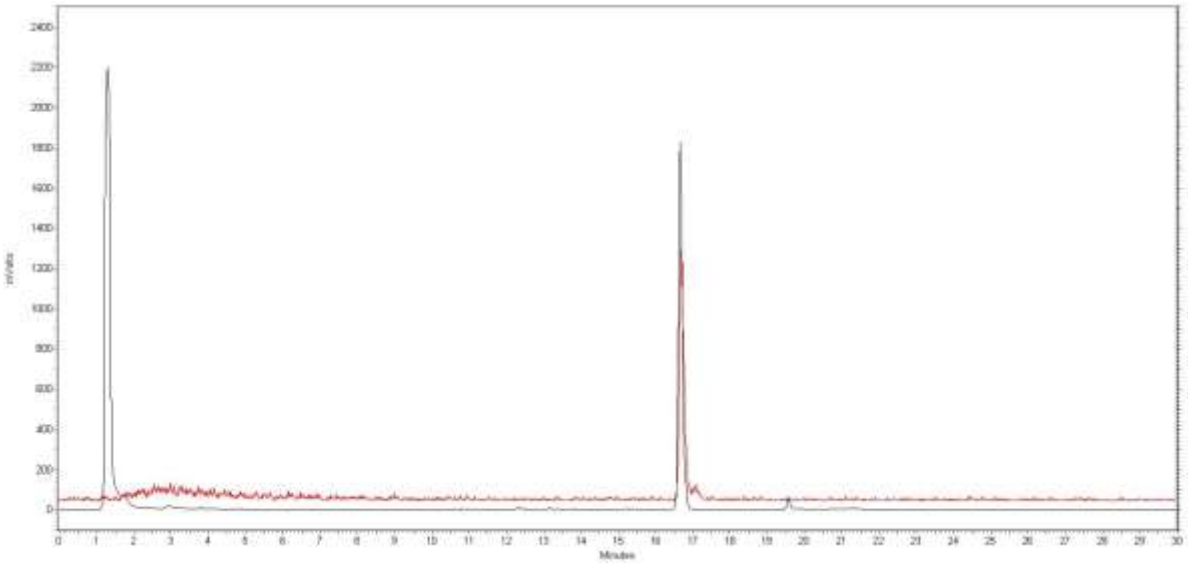
HPLC Conditions: A

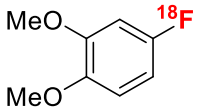


([18F]6)

2-[18F]fluoroanisole ([18F]6) RAD trace overlaid with UV trace (256 nm) spiked with 2-fluoroanisole

HPLC Conditions: A

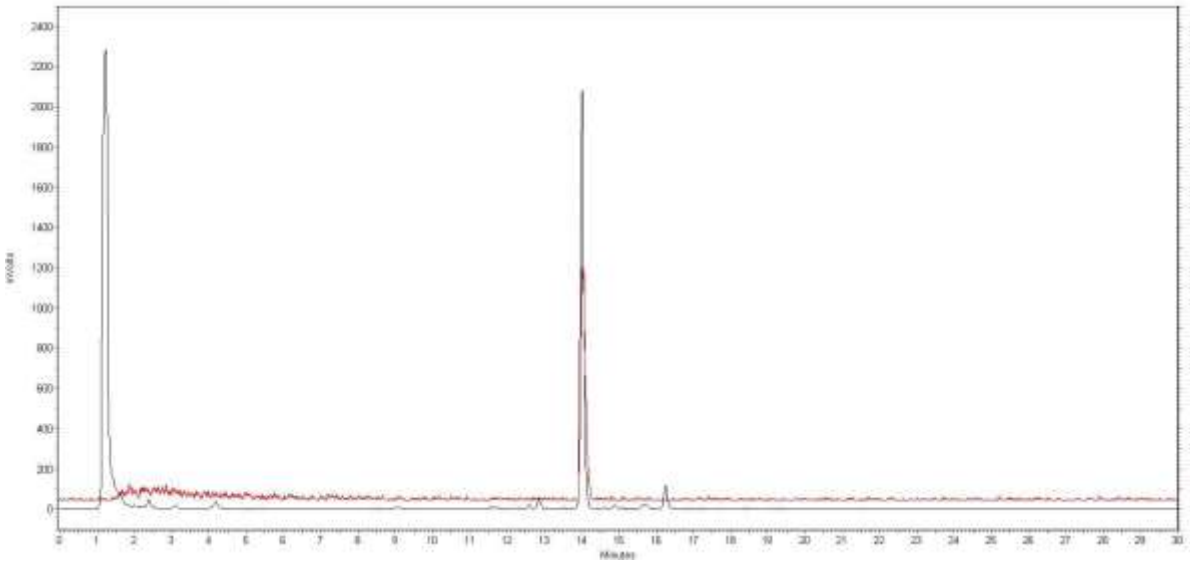


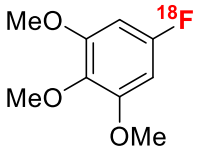


([**[^{18}F]7**])

4-[^{18}F]fluoro-1,2-dimethoxybenzene (**[^{18}F]7**) RAD trace overlaid with UV trace (256 nm) spiked with 4-fluoro-1,2-dimethyoxybenzene

HPLC Conditions: A

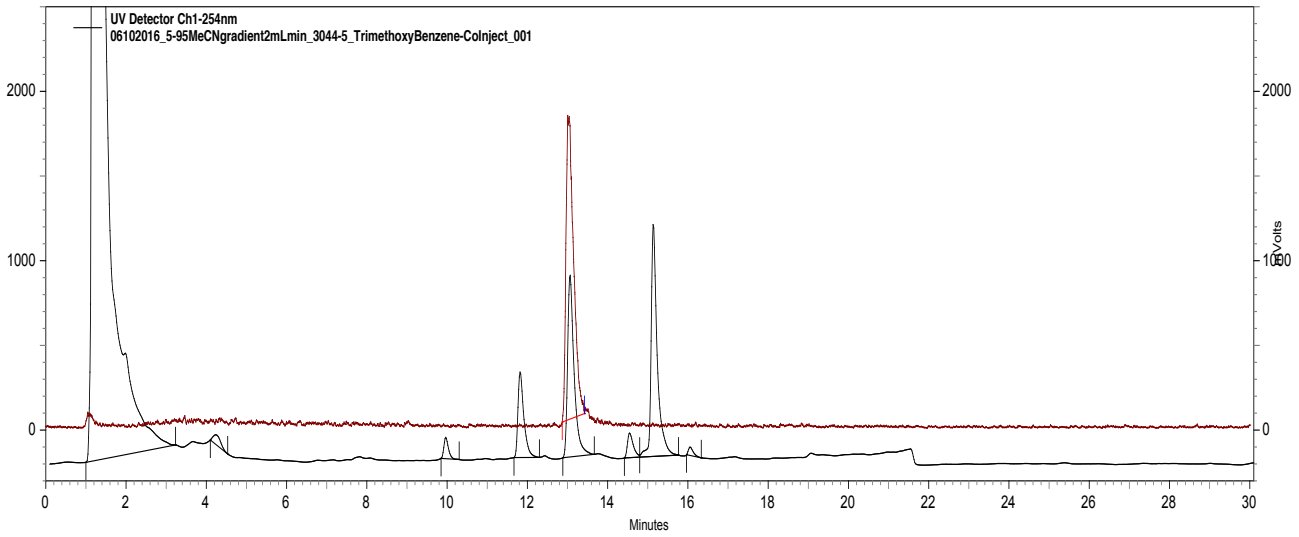


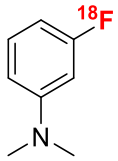


([**18F]8**)

5-[^{18}F]fluoro-1,2,3-trimethoxybenzene (**[18F]8**) RAD trace overlaid with UV trace (256 nm) spiked with 5-fluoro-1,2,3-trimethoxybenzene

HPLC Conditions: A

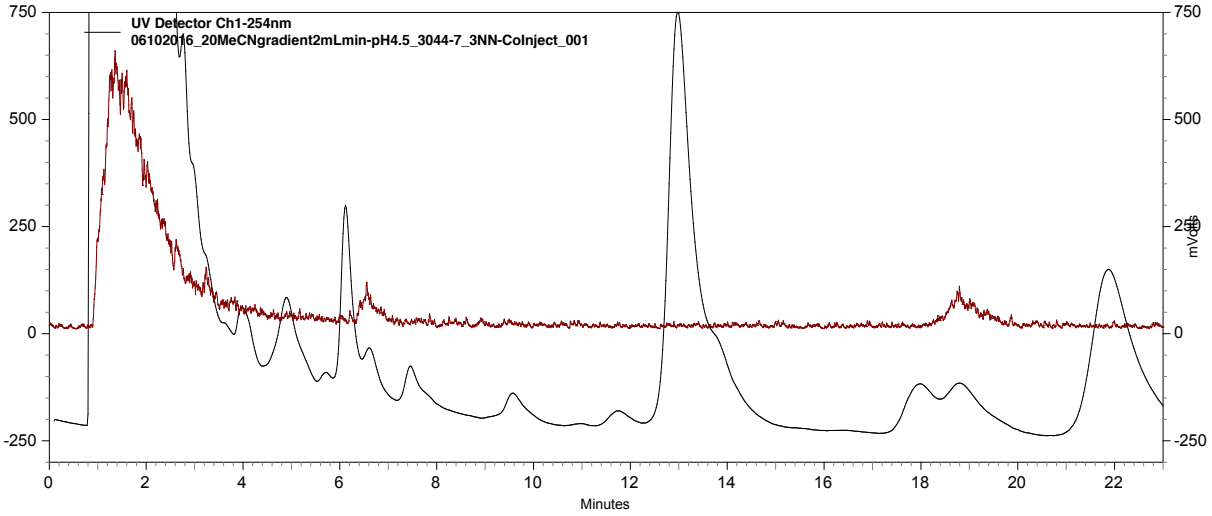


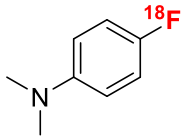


([**18F]9**)

3-[18F]fluoro-N,N-dimethylaniline (**[18F]9**) RAD trace overlaid with UV trace (256 nm) spiked with 3-fluoro-N,N-dimethylaniline

HPLC Conditions: B

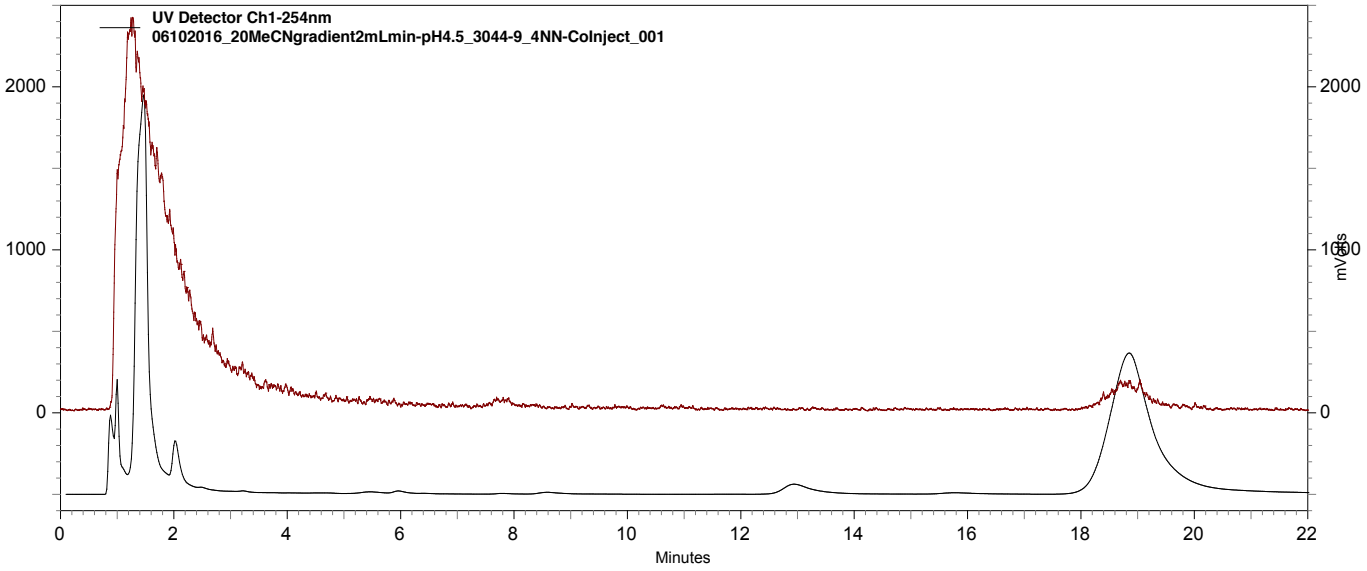


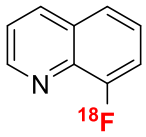


([^{18}F]**10**)

4-[^{18}F]fluoro-N,N-dimethylaniline ([^{18}F]**10**) RAD trace overlaid with UV trace (256 nm) spiked with 4-fluoro-N,N-dimethylaniline

HPLC Conditions: B

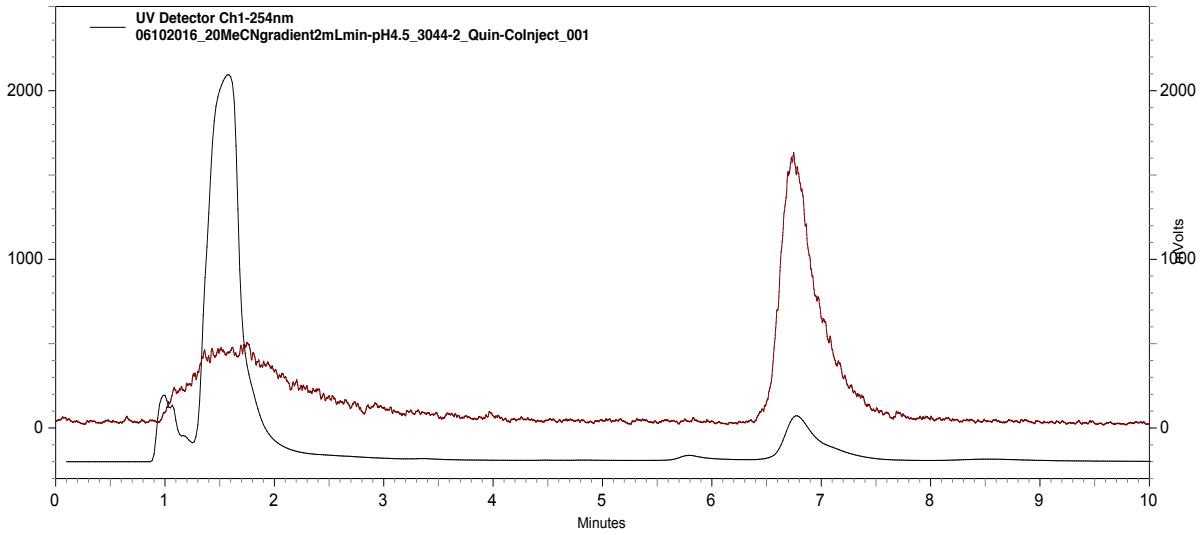


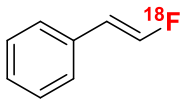


([**[^{18}F]11**])

8-[^{18}F]fluoroquinoline (**[^{18}F]11**) RAD trace overlaid with UV trace (256 nm) spiked with 8-fluoroquinoline

HPLC Conditions: B

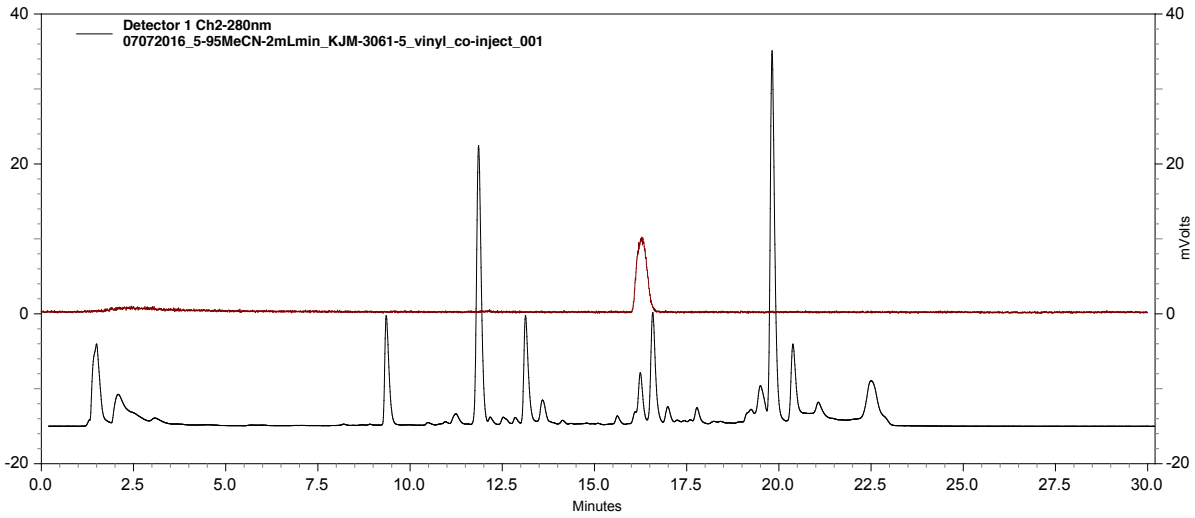


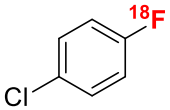


([**18F]12**)

(*E*)-(2-[^{18}F]fluorovinyl)benzene (**[^{18}F]12**) RAD trace overlaid with UV trace (256 nm) spiked with (*E*)-(2-fluorovinyl)benzene

HPLC Conditions: A

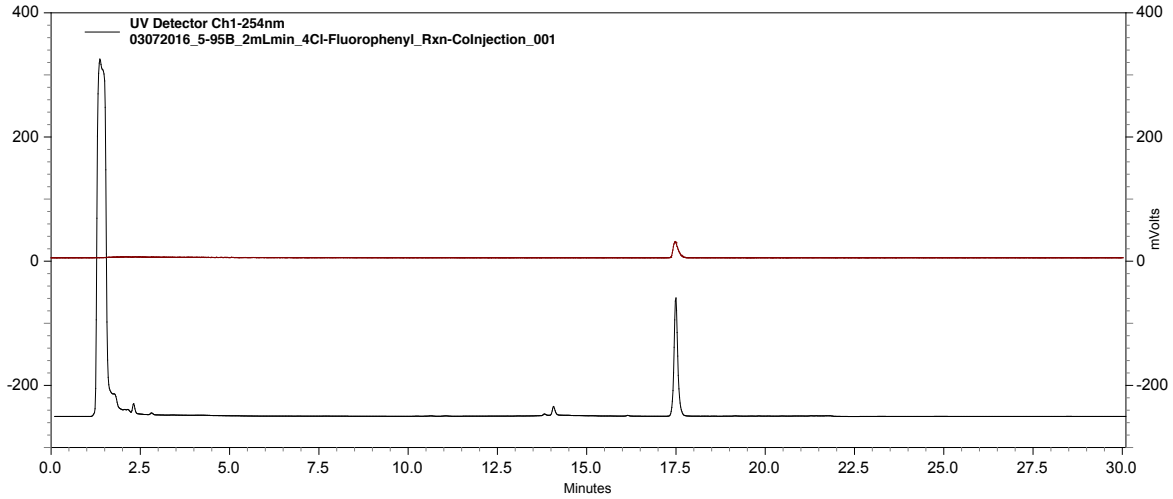




([^{18}F]**13**)

4-[^{18}F]fluoro-1-chlorobenzene (**[^{18}F]13**) RAD trace overlaid with UV trace (256 nm) spiked with 1-chloro-4-fluorobenzene

HPLC Conditions: A



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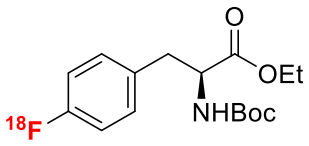
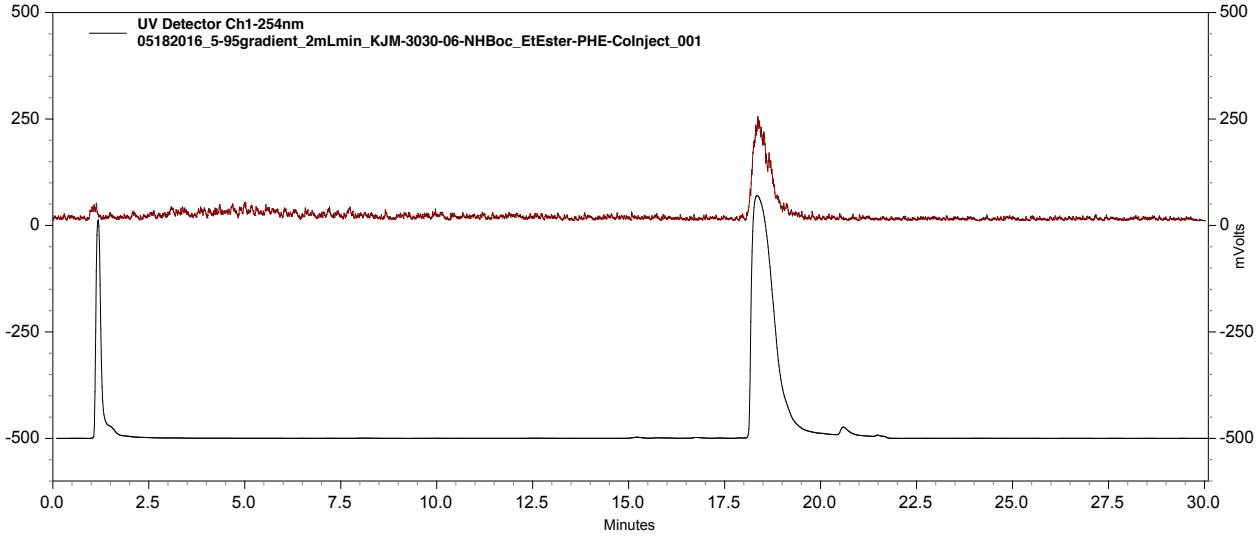
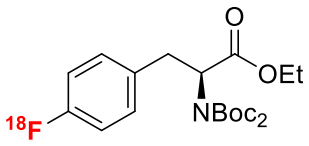


(**[^{18}F]14**)

NHBoc-Phe(4-[^{18}F]F) ethyl ester (**[^{18}F]14**) RAD trace overlaid with UV trace (256 nm) spiked with NHBoc-Phe(4-[^{18}F]F) ethyl ester

HPLC Conditions: A

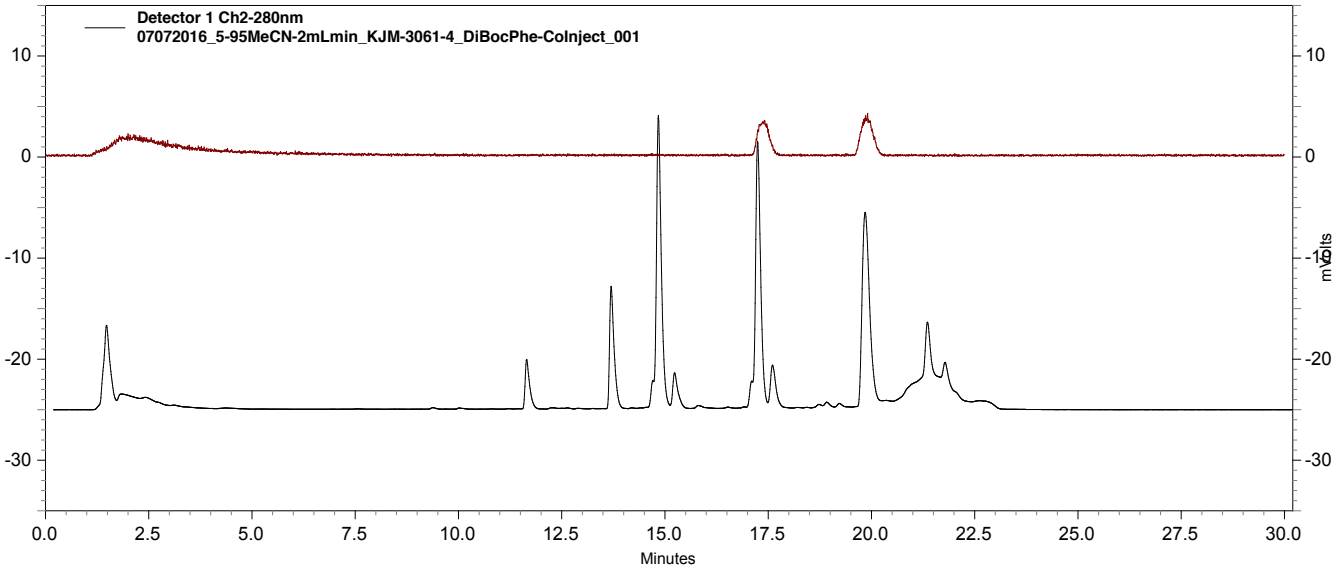


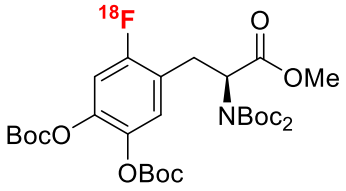


([**18F]15**)

$NBoc_2$-Phe(4-[^{18}F]F) ethyl ester (**[^{18}F]15**) RAD trace overlaid with UV trace (256 nm) spiked with $NBoc_2$-Phe(4-[^{18}F]F) ethyl ester

HPLC Conditions: A

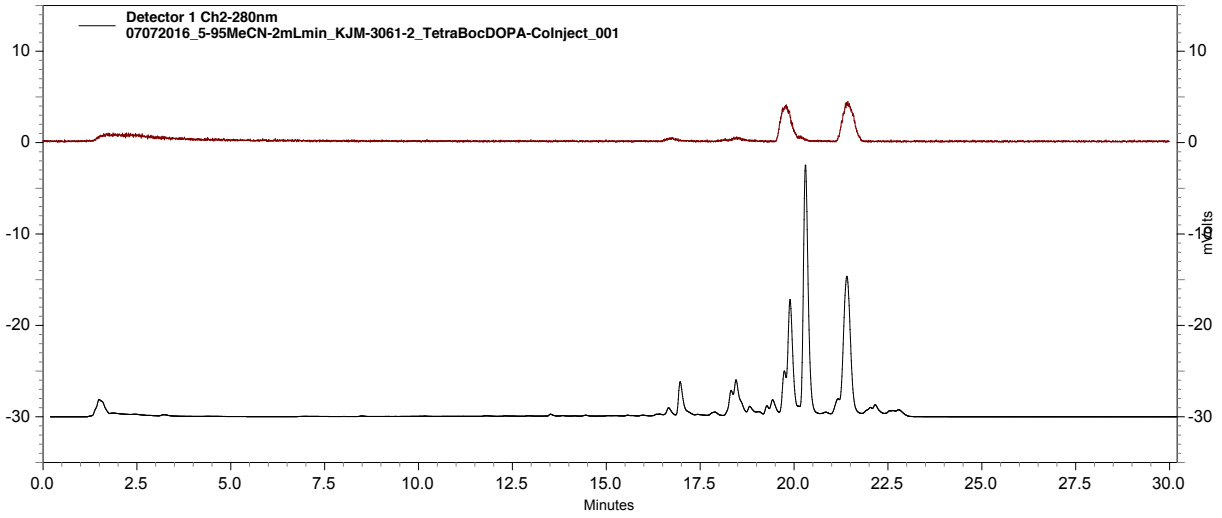


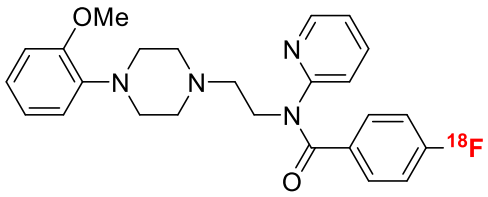


([**18F]16**)

Boc$_4$DOPA(4-[^{18}F]F) methyl ester (**[^{18}F]16**) RAD trace overlaid with UV trace (256 nm) spiked with 4-F-Boc$_4$DOPA

HPLC Conditions: A

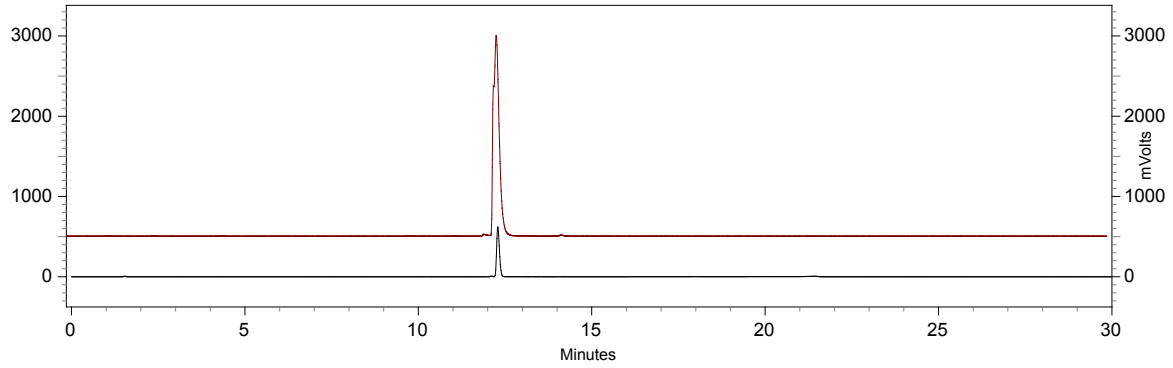


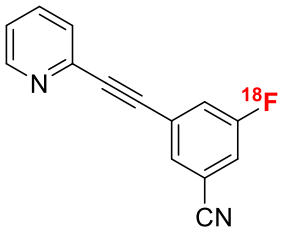


([**18F]17**)

4-[18F]MPPF (**[18F]17**) RAD trace overlaid with UV trace (256 nm) spiked with 4-MPPF

HPLC Conditions: A





([18F]18)

4-[18F]F-PEB ([18F]18) RAD trace overlaid with UV trace (256 nm) spiked with 4-F-PEB

HPLC Conditions: A