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
Table of Contents

1. General Procedures, Materials, and Methods S4
2. Synthesis and Characterization of Arylstannanes S4
   2.1 General Procedures
   2.2 Arylstannane Substrates
      2.2.1 4-Trimethylstannylanisole (2-SnMe₃)
      2.2.2 4-Tributylstannyl-1,1'-biphenyl (3-SnBu₃)
      2.2.3 4-Trimethylstannyl-1,1'-biphenyl (3-SnMe₃)
      2.2.4 4-Tributylstannylacetophenone (4-SnBu₃)
      2.2.5 4-Trimethylstannylacetophenone (4-SnMe₃)
      2.2.6 2-Tributylstannylanisole (6-SnBu₃)
      2.2.7 (3,4-dimethoxyphenyl)tributylstannane (7-SnBu₃)
      2.2.8 Tributyl(3,4,5-trimethoxy)stannane (8-SnBu₃)
      2.2.9 NHBoc-Phe(4-SnMe₃) ethyl ester (14-SnMe₃)
      2.2.10 NBoc₂-Phe(4-SnMe₃) ethyl ester (15-SnMe₃)
      2.2.11 Boc₄DOPA(2-F) methyl ester (16-SnMe₃)
      2.2.12 MPP-SnMe₃ (17-SnMe₃)
      2.2.13 PEB-SnBu₃ (18-SnBu₃)
3. Synthesis and Characterization of Fluorinated Standards S16
   3.1 Fluorinated Products
      3.1.1 (E)-Fluorostyrene (S8)
      3.1.2 NHBoc-Phe(4-F) ethyl ester (S9)
      3.1.3 NBoc₂-Phe(4-F) ethyl ester (S10)
      3.1.4 Boc₄DOPA(2-F) methyl ester (S11)
      3.1.5 F-PEB (S12)
4. Experimental Details (Optimization) S19
   4.1 Copper Screen
   4.2 Fluoride Screen
   4.3 Copper Loading Screen
   4.4 Fluoride Loading Screen
   4.5 Solvent Screen
   4.6 Temperature Screen
   4.7 Time Study
   4.8 Additives
   4.9 18-crown-6 Loading Screen
   4.10 Control Reactions
5. Radiochemistry S30
   5.1 Materials and Methods
   5.2 Synthesis of [¹⁸F]KF
   5.3 Synthesis of ¹⁸F-Labeled Molecules (Manual Synthesis)
   5.4 General HPLC Conditions
   5.5 Additional Optimization Results
      5.5.1 Acetonitrile Addition Screen
      5.5.2 Temperature Study in DMF
5.5.3 Temperature Study in DMA
5.5.4 Addition of DMF in DMA
5.5.5 Cu(OTf)$_2$ Loading Study
5.5.6 Pyridine Concentration Screen
5.5.7 Cu(OTf)$_2$:Pyridine Loading Study
5.5.8 Water Addition Study
5.5.9 Time Study
5.5.10 Control Reactions
5.5.11 Substrate Optimization
5.5.12 Comparison to Other Metal-Mediated Methods
5.5.13 Protected $[^{18}\text{F}]$F-DOPA Comparison

5.6 Automated Synthesis of $[^{18}\text{F}]$MPPF ($[^{18}\text{F}]$17)
  5.6.1 Specific Activity Calculations
  5.6.2 QC Validation

6. References
    S50

7. Spectra Data
    S51
    7.1 $^1$H, $^{13}$C, $^{19}$F NMR Spectra
    S51
    7.2 Radio-HPLC/Radio-TLC Analysis for $^{18}$F-Labeled Compounds
    S93
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.
4-Trimethylstannylanisole (2-SnMe₃)
The published procedure was followed with small modifications.³ Under nitrogen atmosphere, 4-methoxyaniline (491.7 mg, 4.0 mmol, 1 equiv) and TsOH•H₂O (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 Sn₂Me₆ (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-SnMe₃ as a colorless oil (59.3 mg, 22% yield, Rᵣ = 0.8 in 10% ethyl acetate in hexanes). The ¹H and ¹³C NMR spectra matched those reported previously in the literature.³ HRMS (EI) [M – CH₃⁺] Calculated for C₉H₁₃OSn: 256.9989; Found 256.9979.

4-Tributylstannyl-1,1'-biphenyl (3-SnBu₃)
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-SnBu₃ as a colorless oil (191.0 mg, 43% yield, Rᵣ = 0.6 in 100% hexanes). The ¹H and ¹³C NMR spectra matched those reported previously in the literature.⁴ HRMS (EI) [M – C₄H₉⁺] Calculated for C₂₀H₂₇Sn: 387.1135; Found 387.1135.

4-Trimethylstannyl-1,1'-biphenyl (3-SnMe₃)
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-SnMe₃ as a colorless oil (275.0 mg, 87% yield, Rᵣ = 0.5 in 100% hexanes). The ¹H and ¹³C NMR spectra matched those reported previously in the literature.⁵ HRMS (EI) [M⁺] Calculated for C₁₅H₁₈Sn: 318.0430; Found 318.0415.
4-Tributylstannylacetophenone (4-SnBu₃)
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-SnBu₃ as a colorless oil (284.3 mg, 69 %, Rᵢ = 0.56 in 5% ethyl acetate in hexanes). The ¹H and ¹³C NMR spectra matched those reported previously in the literature. HRMS (ESI⁺) [M + K⁺] Calculated for C₂₀H₃₄KO: 449.1263; Found 449.1263.

4-Trimethylstannylacetophenone (4-SnMe₃)
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-SnMe₃ as a colorless oil (147.0 mg, 52% yield, Rᵢ = 0.7 in 10% ethyl acetate in hexanes). The ¹H and ¹³C NMR spectra matched those reported previously in the literature. HRMS (EI) [M – CH₃⁺] Calculated for C₁₀H₁₃O: 268.9988; Found 268.9984.

2-Tributylstannylanisole (6-SnBu₃)
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-SnBu₃ as a colorless oil (604.2 mg, 62% yield, Rᵢ = 0.6 in 100% hexanes). The ¹H and ¹³C NMR spectra matched those reported previously in the literature. HRMS (EI) [M – C₄H₉⁺] Calculated for C₁₅H₂₅O: 341.0927; Found 341.0934.
(3,4-dimethoxyphenyl)tributylstannane (7-SnBu₃)
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-SnBu₃ as a colorless oil (171.7 mg, 40% yield, R_f = 0.5 in 10% ethyl acetate in hexanes). The ¹H NMR spectra matched that reported previously in the literature.⁶ HRMS (ESI) [M + Na⁺] Calculated for C₂₀H₃₆NaO₂Sn: 451.1629; Found 451.1629.

¹H NMR (CDCl₃): 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)

¹³C NMR (CDCl₃): 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

Tributyl(3,4,5-trimethoxy)stannane (8-SnBu₃)
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-SnBu₃ as a colorless oil (326.7 mg, 71% yield, R_f = 0.7 in 20% ethyl acetate in hexanes). The ¹H and ¹³C NMR spectra matched those reported previously in the literature.⁷ HRMS (ESI) [M + H⁺] Calculated for C₂₁H₃₉O₃Sn: 459.1916; Found 459.1915.
NHBoc-Phe(4-SnMe₃) ethyl ester (14-SnMe₃) was prepared by the following 2 step procedure.

**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 hexanes) affording the product (S1) as a white solid (1.01 g, 93% yield, Rf = 0.2 in 20% ethyl acetate in hexanes, mp = 91 – 92 °C).

¹H NMR (CDCl₃): 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)
¹³C NMR (CDCl₃): 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 C₁₆H₂₂INaO₄: 442.0486; Found 442.0489.

**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-SnBu₃ as a colorless oil (73.4 mg, 17% yield, Rf = 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, 2H), 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$_4$Sn: 458.1348; Found 458.1352.
NBoc$_2$-Phe(4-SnMe$_3$) ethyl ester (15-SnMe$_3$) was prepared by the following 3 step procedure.

**Step 1:** See above procedure

**Step 2:** Iodide S2 was prepared via a modified literature procedure. 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$_{30}$INaO$_6$: 542.0101; Found 542.0102.
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-SnBu3 as a yellow oil (230.4 mg, 53% yield, Rf = 0.6 in 20% ethyl acetate in hexanes).

1H NMR (CDCl3): 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)

13C NMR (CDCl3): 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 C24H40NO6Sn: 558.1883; Found 558.1883.

Boc3DOPA(2-SnMe3) methyl ester (16-SnMe3)
Arylstannane 16-SnMe3 was prepared via a modified literature procedure. To a solution of Boc3DOPA-SnMe3 (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-SnMe3 as a yellow oil (407.6 mg, 80% yield, Rf = 0.46 in 20% ethyl acetate in hexanes).

1H NMR (CDCl3): 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)

13C NMR (CDCl3): δ 170.59, 151.79, 150.72, 150.59, 142.95, 142.44, 141.28, 140.50, 140.00, 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 C33H53NNaO12Sn: 798.2482; Found 798.2491.
MPP-SnMe₃ (17-SnMe₃) was prepared by the following 5-step procedure.

1. **Step 1:**
   - **Reagents:** Pyridine, Et₃N, DCM
   - **Reaction:** H₂N₆C₆H₅ + ClCOCl → ClCO₆C₆H₅N₆H₃
   - **Yield:** 75-91%

2. **Step 2:**
   - **Reagents:** DMF, K₂CO₃
   - **Reaction:** ClCO₆C₆H₅N₆H₃ + 2-N,N,N-Trimethylaniline → OMe₆C₆H₅N₆H₃N₆H₃
   - **Yield:** 40-80%

3. **Step 3:**
   - **Reagents:** LAH, THF
   - **Reaction:** OMe₆C₆H₅N₆H₃N₆H₃ + LAH → OMe₆C₆H₅N₆H₃N₆H₃
   - **Yield:** 70-94%

4. **Step 4:**
   - **Reagents:** Et₃N, DCM
   - **Reaction:** OMe₆C₆H₅N₆H₃N₆H₃ + 2-N,N,N-Trimethylaniline → OMe₆C₆H₅N₆H₃N₆H₃
   - **Yield:** 77-85%
Step 1: Intermediate S3 was prepared according to a literature procedure.\textsuperscript{10} Purification afforded S3 as a white solid (0.734 g, 91\% yield, mp = 120 – 121 °C). The 1\textsuperscript{H} NMR spectra matched that reported previously in the literature.\textsuperscript{10} HRMS [M + H\textsuperscript{+}] Calculated for C\textsubscript{7}H\textsubscript{8}ClN\textsubscript{2}O: 171.0320; Found 171.0318.

Step 2: Intermediate S4 was prepared according to a literature procedure.\textsuperscript{10} Purification afforded S4 as a yellow oil (1.01 g, 80\% yield). The 1\textsuperscript{H} NMR spectra matched that reported previously in the literature.\textsuperscript{10} HRMS [M + H\textsuperscript{+}] Calculated for C\textsubscript{18}H\textsubscript{23}N\textsubscript{4}O\textsubscript{2}: 327.1816; Found 327.1915.

Step 3: Precursor S5 was prepared according to a literature procedure.\textsuperscript{10} Purification afforded S5 as a tan solid (0.903 g, 94\% yield, mp = 87 – 89 °C). The 1\textsuperscript{H} NMR spectra matched that reported previously in the literature.\textsuperscript{10} HRMS [M + H\textsuperscript{+}] Calculated for C\textsubscript{18}H\textsubscript{25}N\textsubscript{4}O: 313.2023; Found 313.2022.

Step 4: Precursor S6 was prepared according to the procedure in the literature.\textsuperscript{10} Purification afforded S6 as a white solid (0.670 g, 77\% yield, mp = 104 – 105 °C). The 1\textsuperscript{H} NMR
spectra matched that reported previously in the literature.10 HRMS [M + H⁺] Calculated for C_{25}H_{29}N_{4}O_{2}: 543.1251; Found 543.1247.

**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-SnMe₃ 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 (CDCl₃): \(\delta\) 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, 2H), 3.82 (s, 3H), 2.90 (broad peak, 4H), 2.73 (t, \(J = 7.0\) Hz, 2H), 2.61 (broad peak, 4H), 0.22 (s, 9H)

\(^{13}\)C NMR (CDCl₃): \(\delta\) 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_{4}O_{2}Sn: 581.1933; Found 581.1950.
PEB-SnBu₃ (18-SnBu₃) was prepared by the following 2 step procedure.

**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, Rᵢ = 0.32 in 30% ethyl acetate in hexanes, mp = 108 – 109 °C). The ¹H and ¹³C NMR spectra matched those reported previously in the literature.¹²,¹³ HRMS (ESI+) [M + H⁺] Calculated for C₁₄H₈BrN₂: 282.9865; Found 282.9865.

**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-SnBu₃ as a yellow oil (245.8 mg, 54% yield, Rᵢ = 0.43 in 20% ethyl acetate in hexanes). The ¹H and ¹³C NMR spectra matched those reported previously in the literature.¹³ HRMS (EI) [M + H⁺] Calculated for C₂₆H₃₅N₂Sn: 495.1817; Found 495.1820.
3. Synthesis and Characterization of Fluorinated Standards

(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 °C 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 \(^{19}\text{F}\) NMR spectroscopic data was identical to that reported.\(^\text{14}\)

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

Authentic standard S9 was prepared by the following procedure via a modification of a literature procedure.\(^\text{9}\) 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 \(^1\text{H}\) and \(^{13}\text{C}\) NMR spectra matched those reported previously in the literature.\(^\text{15}\) HRMS (ESI) [M + H\(^+\)] Calculated for C\(_{16}\)H\(_{23}\)FNO\(_4\): 312.1606; Found 312.1611.

\(^{19}\text{F}\) NMR (CDCl\(_3\)): \(\delta -116.01\)
NBOc<sub>2</sub>-Phe(4-F) ethyl ester (S10)

Authentic standard S10 was prepared via a modification of a literature procedure. 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<sub>f</sub> = 0.5 in 20% ethyl acetate in hexanes).

<sup>1</sup>H NMR (CDCl<sub>3</sub>): 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)

<sup>13</sup>C NMR (CDCl<sub>3</sub>): 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

<sup>19</sup>F NMR (CDCl<sub>3</sub>): δ –116.93

HRMS (ESI) [M + H<sup>+</sup>] Calculated for C<sub>21</sub>H<sub>31</sub>FNO<sub>6</sub>: 412.2130; Found 412.2136.

Boc<sub>4</sub>DOPA(2-F) methyl ester (S11)

In a nitrogen atmosphere glovebox, 16-SnMe<sub>3</sub> (311.0 mg, 0.4 mmol, 1 equiv), Cu(OTf)<sub>2</sub> (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<sub>f</sub> = 0.6 in 40% ethyl acetate in hexanes).

<sup>1</sup>H NMR (CDCl<sub>3</sub>): 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\textsubscript{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\textsubscript{3}): δ –117.64
HRMS (ESI) [M + NH\textsubscript{4}^+] Calculated for C\textsubscript{30}H\textsubscript{48}FN\textsubscript{2}O\textsubscript{12}: 647.3186; Found 647.3184.

**F-PEB (S12)**

Aryl fluoride S12 was prepared via a literature procedure\textsuperscript{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\textsubscript{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\textsuperscript{12,16}.

^19^F NMR (CDCl\textsubscript{3}): δ –108.9
HRMS (ESI+) [M + H\textsuperscript{+}] Calculated for C\textsubscript{14}H\textsubscript{8}FN\textsubscript{2}: 223.0666; Found 223.0664.
4. Experimental Details

Copper Screen for Cu-Mediated Fluorination of **1-SnBu₃** with KF

![Chemical structure](image)

In a nitrogen atmosphere glovebox, substrate **1-SnBu₃** (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-SnBu₃** 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)$_4$Cu(OTf) | nd        |
| 6     | (py)$_4$Cu(OTf)$_2$ | nd     |

$^a$nd = not detected
Fluoride Screen for Cu-Mediated Fluorination of 1-SnBu₃ with KF

\[
\begin{align*}
\text{(1-SnBu₃)} & \quad \text{Cu(OTf)₂, MF} & \quad \text{MeCN, 60 °C, 18 h} & \quad \text{F} \\
\end{align*}
\]

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 °C 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·3H₂O| 25%           |

\(^{a}\) nd = not detected
Copper Loading for Cu-Mediated Fluorination of 1-SnBu$_3$ with KF

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-SnBu3 with KF

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 °C 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 19F NMR spectroscopy. The yields of 1 are listed in Table S4.

| entry | KF (equiv) | Yielda |
|-------|------------|--------|
| 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
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 °C 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$_3$CN | 47%       |
| 2     | tBuCN   | 25%       |
| 3     | dioxane | nd        |
| 4     | DMF     | nd        |
| 5     | DMSO    | nd        |
| 6     | THF     | nd        |


$^a$ nd = not detected
**Temperature Screen for Cu-Mediated Fluorination of 1-SnBu$_3$ with KF**

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-SnBu₂ versus 1-BF₃K

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 ¹⁹F 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] = SnBu₂ | Yield (%) [M] = BF₃K |
|-------|----------|-----------------------|----------------------|
| 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 $\text{1-SnBu}_3$ with KF

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 °C 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$_4$OTf       | 49%       |
| 6     | NBu$_4$BF$_4$    | 45%       |
| 7     | NBu$_4$PF$_6$    | 42%       |
| 8     | NBu$_4$Cl        | nd        |
| 9     | NBu$_4$CN        | nd        |
| 10    | NBu$_4$I         | nd        |

$^a$nd = not detected
18-Crown-6 Loading for Cu-Mediated Fluorination of \(1-\text{SnBu}_3\) with KF

![Chemical Reaction Diagram]

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 °C 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 \(^{19}\text{F} \) 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

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

| 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 the fluorination of substrate 1-SnBu₃ 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 $^{[18}\text{F}]\text{KF}$
All loading operations were conducted under an ambient atmosphere. Argon was used as a pressurizing gas during automated sample transfers. Potassium $^{[18}\text{F}]$fluoride was prepared using a TRACERLab FXFN automated radiochemistry synthesis module (General Electric, GE). $^{[18}\text{F}]$Fluoride was produced via the $^{18}\text{O}(p,n)^{18}\text{F}$ nuclear reaction using a GE PETTrace cyclotron (40 μA beam for 2-5 min generated ca. 150-375 mCi of $^{[18}\text{F}]$fluoride). The $^{[18}\text{F}]$fluoride was delivered to the synthesis module in a 1.5 mL bolus of $^{18}\text{O}$water and trapped on a QMA-light Sep-Pak to remove $^{18}\text{O}$water and other impurities. $^{[18}\text{F}]$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 $^{[18}\text{F}]\text{KF}$. 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 $^{[18}\text{F}]\text{KF}$ 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 $^{18}\text{F}$-Labeled Molecules (Manual Synthesis)
Unless otherwise noted, this procedure was used for the synthesis of the $^{[18}\text{F}]$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 $^{[18}\text{F}]$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 $^{[18}\text{F}]\text{KF}$ (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 °C 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\(_3\)CN + 0.05% TFA) in (H\(_2\)O + 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\(_2\)O + 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$_2$CO$_3$. All RCC are n = 2 or greater.

**Acetonitrile Addition Screen**

![Reaction scheme for Acetonitrile Addition Screen]

**Table S11. Acetonitrile Addition Screen$^a$**

| entry | DMF:CH$_3$CN (% | 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$_3$CN (0.1 mL, 300-700 μCi). Total reaction volume = 1.0 mL. $^b$nd = desired product was not detected

**Figure S1: Acetonitrile Addition Screen**

![Graph showing yield vs. percentage of DMF in CH$_3$CN]
Temperature Study in DMF

\[
\begin{align*}
&\text{3-SnBu}_3 + \text{Cu(OTf)}_2, \text{pyridine}, [^{18}\text{F}]\text{KF} \\
&\text{DMF, temp, 30 min}
\end{align*}
\]

**Table S12:** Temperature Study in DMF<sup>a</sup>

| entry | temperature (°C) | RCC of \([^{18}\text{F}]3\) (%)<sup>b</sup> |
|-------|------------------|---------------------------------|
| 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                          |

<sup>a</sup>Reaction conditions: 3-SnBu<sub>3</sub> (0.01 mmol), Cu(OTf)<sub>2</sub> (2 equiv), pyridine (15 equiv), [<sup>18</sup>F]KF in DMF (0.1 mL, 300-700 μCi). Total reaction volume = 1.0 mL. <sup>b</sup>nd = desired product was not detected

**Figure S2:** Temperature Study in DMF
**Table S13: Temperature Study in DMA\textsuperscript{a}**

| entry | temperature (°C) | RCC of [\textsuperscript{18}F]3 (%) |
|-------|------------------|-------------------------------------|
| 1     | 80 °C            | 36 ± 1                              |
| 2     | 100 °C           | 51 ± 2                              |
| 3     | 120 °C           | 59 ± 1                              |
| 4     | 140 °C           | 58 ± 9                              |

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

**Figure S3: Temperature Study in DMA**

Yield (% RCC) vs. Temperature (°C)
DMF versus DMA

Table S14: Addition of DMA

| Entry | DMF:DMA | RCC of $[^{18}\text{F}]3$ (%) |
|-------|--------|-------------------------------|
| 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), $[^{18}\text{F}]$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

![Cu(OTf)$_2$, pyridine, $[^{18}\text{F}]\text{KF}$](image)

DMA, 140 °C, 30 min

**Table S15: Cu(OTf)$_2$ Loading$^a$**

| Entry | Cu(OTf)$_2$ (equiv) | RCC of $[^{18}\text{F}]\text{3}$ (%)$^b$ |
|-------|---------------------|-------------------------------------|
| 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), $[^{18}\text{F}]\text{KF}$ 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**

![Graph showing yield vs. Cu(OTf)$_2$ equiv](image)
Pyridine Concentration Screen

\[
\begin{align*}
\text{3-SnBu}_3 \quad &\xrightarrow{\text{Cu(OTf)}_2, \text{pyridine}, [^{18}\text{F}]K^+} \quad \text{[^{18}\text{F}]}3 \\
\end{align*}
\]

DMA, 140 °C, 30 min

**Table S16: Pyridine Concentration Screen**

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

aReaction conditions: 3-SnBu\(_3\) (0.01 mmol), Cu(OTf)\(_2\) (2 equiv), pyridine (varied), [\(^{18}\text{F}\)]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**

![Graph showing yield (% RCC) vs. pyridine concentration (equiv)](attachment:graph.png)
Cu(OTf)$_2$-Pyridine Loading Study

\[ \text{Ph} \text{-SnBu}_3 \xrightarrow{\text{Cu(OTf)$_2$:pyridine (XX:XX), [^{18}\text{F}]KF}} \text{Ph}^{^{18}\text{F}} \]

DMA, 140 °C, 30 min

### 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

![Graph showing yield vs Cu(OTf)$_2$:pyridine ratio (equiv)](image)
**Water Addition Study**

![Chemical Structure]

**Table S18: Water Addition Study**

| Entry | $\text{H}_2\text{O}$ (equiv) | RCC of $^{18}\text{F}$3 (%) |
|-------|-----------------------------|---------------------------|
| 1     | 0                           | 66 ± 1                    |
| 2     | 0.1                         | 68 ± 1                    |
| 3     | 0.5                         | 66 ± 1                    |
| 4     | 1                           | 67 ± 1                    |
| 5     | 5                           | 59 ± 1                    |

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

**Figure S8: Water Addition Study**

![Bar Chart]
Time Study

![Chemical diagram](image)

**Table S19: Time Study**

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

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

**Figure S9: Time Study**

![Graph showing yield (%) vs. time (min)](image)
Control reactions for the radiofluorination of substrate 3-SnBu₃ were conducted without copper salt and without pyridine. In both cases, the fluorinated product [¹⁸F]3 was not observed.
Substrate Optimization

Optimization Conditions:

\[
\text{CuOTf}_2 \text{ (2 equiv), Py (15 equiv)} \xrightarrow{K^{18}F \text{ in DMA}} \text{R-}^{18}\text{F}
\]

DMA (0.01 M), temp, 30 mins

0.01 mmol

Substrates from Figure 1:

1. \(\text{(9-SnBu}_3\)\)
   - 32 ± 3 \((n=4)\)
   - 30 equiv py: 29 ± 1 \((n=2)\)

2. \(\text{(10-SnBu}_3\)\)
   - 72 ± 1 \((n=2)\)
   - 30 equiv py: 67 ± 1 \((n=2)\)

3. \(\text{(11-SnBu}_3\)\)
   - 30 equiv py: 55 ± 6 \((n=6)\)
   - 15 equiv py: 37 ± 1 \((n=2)\)

Substrates from Figure 2:

1. \(\text{(13-SnBu}_3\)\)
   - 100 °C: 34 ± 11 \((n=6)\)
   - 140 °C: 9 ± 1 \((n=2)\)
   - 18-crown-6 (0.5 equiv): 31 ± 1 \((n=2)\)

2. \(\text{(14-SnBu}_3\)\)
   - 100 °C, 18-crown-6 (0.5 equiv): 7 ± 1 \((n=4)\)
   - 140 °C: 2 ± 1 \((n=2)\)
   - 100 °C: 4 ± 3 \((n=2)\)

3. \(\text{(18-SnMe}_3\)\}
   - 40 ± 5\% \((n=4)\)
   - 30 equiv py: 24 ± 1\% \((n=2)\)

4. \(\text{(19-SnMe}_3\)\}
   - 41 ± 1\% \((n=2)\)

5. \(\text{(20-SnMe}_3\)\}
   - 30 equiv py: 57 ± 14\% \((n=6)\)
   - 15 equiv py: 25 ± 6\% \((n=2)\)

6. \(\text{(21-SnMe}_3\)\}
   - 33 ± 4\% \((n=4)\)
   - 30 equiv py: 24 ± 1\% \((n=2)\)
   - 4 Cu, 30 py: 18 ± 3\% \((n=2)\)

7. \(\text{(22-SnBu}_3\)\}
   - 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):

\[
\begin{align*}
\text{SnBu}_3 & \quad \text{Cu(OTf)}_2 \text{ (2 equiv), pyridine (15 equiv), } [^{18}\text{F}]\text{KF} \\
\text{DMA, 140 °C, 30 min}
\end{align*}
\]

**condition B** (Sanford/Scott):

\[
\begin{align*}
\text{IMesBF}_4 & \quad (\text{CH}_3\text{CN})_4\text{CuOTf} \text{ (1 equiv), } [^{18}\text{F}]\text{KF}\cdot18\text{-crown-6}+\text{K}_2\text{CO}_3 \\
\text{DMF, 85 °C, 20 min}
\end{align*}
\]

**condition C** (Sanford/Scott):

\[
\begin{align*}
\text{B(OH)}_2 & \quad \text{Cu(OTf)}_2 \text{ (5 equiv), pyridine (125 equiv), } [^{18}\text{F}]\text{KF} \\
\text{DMF, 110 °C, 20 min}
\end{align*}
\]

**condition D** (Gouverneur):

\[
\begin{align*}
\text{Bpin} & \quad \text{Cu(OTf)}_2\text{(py)}_4 \text{ (0.1 equiv), } [^{18}\text{F}]\text{KF/K}_{222} \\
\text{DMF, 110 °C, 20 min}
\end{align*}
\]

**condition E** (Ritter):

\[
\begin{align*}
[\text{Ni}] & \quad \text{oxidant, 18-crown-6, } [^{18}\text{F}]\text{KF} \\
\text{CH}_3\text{CN, 23 °C, <1 min}
\end{align*}
\]

References: condition A (this work), condition B (Cu-mediated method),\textsuperscript{12} condition C (Cu-mediated method),\textsuperscript{1} condition D (Cu-catalyzed method, note: decay corrected “RCY”),\textsuperscript{17} and condition E (Ni-mediated method).\textsuperscript{16}
### Table S20: Comparison of Substrates by Other Metal-Mediated Methods

| Substrate | R'            | Conditions | Yield (RCC) |
|-----------|---------------|------------|-------------|
| MeO       | -SnBu₃        | A          | 56 ± 4%     |
|           | -IMesBF₄      | B          | 79 ± 8%     |
|           | -B(OH)₂       | C          | 19 ± 3%     |
| Ph        | -SnBu₃        | A          | 55 ± 10%    |
|           | -IMesBF₄      | B          | 51 ± 8%     |
|           | -B(OH)₂       | C          | 46 ± 6%     |
|           | -Bpin         | D          | 74 ± 5%     |
|           | -[Ni]         | E          | 42 ± 8%     |
| BnO       | -SnBu₃        | A          | 50 ± 3%     |
|           | -Bpin         | D          | 43 ± 5%     |
| OMe       | -SnBu₃        | A          | 48 ± 4%     |
|           | -IMesBF₄      | B          | 30 ± 8%     |
|           | -Bpin         | D          | 11 ± 2%     |
| MeO       | -SnBu₃        | A          | 54 ± 8%     |
|           | -IMesBF₄      | B          | 51 ± 6%     |
|           | -Bpin         | D          | 54 ± 3%     |
| MeO       | -SnBu₃        | A          | 59 ± 3%     |
|           | -IMesBF₄      | B          | 14 ± 1%     |
|           | -B(OH)₂       | C          | 36 ± 11%    |
Protected $[^{18}\text{F}]\text{F-DOPA}$ Comparison

**Figure S10:** Protected $[^{18}\text{F}]\text{F-DOPA}$ Comparison

**conditions A:** *This work*

![Chemical structure and reaction conditions for conditions A.]

**conditions B** (Ritter):

![Chemical structure and reaction conditions for conditions B.]

**conditions C** (Sanford/Scott)

![Chemical structure and reaction conditions for conditions C.]

**conditions D** (Gouverneur):

![Chemical structure and reaction conditions for conditions D.]

References: condition A (this work), condition B (Ni-mediated method), condition C (Cu-mediated method), and condition D (Cu-catalyzed method).
5.6 Automated Synthesis of $^{18}$F-MPPF ($^{18}$F$^{17}$F)

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. $^{18}$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 $^{18}$FKF 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$_4$OAc, 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$_2$O. 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% HNO₃ 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

1. Ichiishi, N.; Brooks, A. F.; Topczewski, J. J.; Rodnick, M. E.; Sanford, M. S.; Scott, P. J. H. *Org. Lett.* 2014, 16, 3224-3227.
2. Arai, T. *Nucl. Med. Biol.* 2012, 39, 702-708.
3. Qiu, D.; Meng, H.; Jin, L.; Wang, S.; Tang, S.; Wang, X.; Mo, F.; Zhang, Y.; Wang, J. *Angew. Chem., Int. Ed.* 2013, 52, 11581-11584.
4. Komeyama, K.; Asakura, R.; Takaki, K. *Org. Biomol. Chem.* 2015, 13, 8713-8716.
5. Luo, P.; Dinnocenzo, J. P. *J. Org. Chem.* 2015, 80, 9240-9246.
6. Kozyrod, R. P.; Morgan, J.; Pinhey, J. T. *Aust. J. Chem.* 1985, 38, 1147-1153.
7. Huang, C.; Liang, T.; Harada, S.; Lee, E.; Ritter, T. *J. Am. Chem. Soc.* 2011, 133, 13083-13310.
8. Hupp, C. D.; Tepe, J. J. *J. Org. Chem.* 2009, 74, 3406-3413.
9. Edwards, R.; Westwell, A. D.; Daniels, S.; Wirth, T. *Eur. J. Org. Chem.* 2015, 2015, 625-630.
10. Zhuang, Z.-P.; Kung, M.-P.; Kung, H. F. *J. Med. Chem.* 1994, 37, 1406-1407.
11. Telu, S.; Chun, J.-H.; Simeon, F. G.; Lu, S.; Pike, V. W. *Org. Biomol. Chem.* 2011, 9, 6629-6638.
12. Mossine, A. V.; Brooks, A. F.; Makaravage, K. J.; Miller, J. M.; Ichiiishi, N.; Sanford, M. S.; Scott, P. J. H. *Org. Lett.* 2015, 17, 5780-5783.
13. Kil, K.-E.; Zhu, A.; Zhang, Z.; Choi, J.-K.; Kura, S.; Gong, C.; Brownell, A.-L. *ACS Med. Chem. Lett.* 2014, 5, 652-656.
14. Wang, Q.; Wei, H.-X.; Schlosser, M. *Eur. J. Org. Chem.* 1999, 3263-3268.
15. Chang, M.-Y.; Lin, C.-Y.; Sun, P.-P. *J. Chin. Chem. Soc.* 2005, 52, 1061-1067.
16. Alegille, D.; DaCosta, H.; Chen, Y.; Hemstapat, K.; Rodriguez, A.; Baldwin, R. M.; Conn, P. J.; Tamagnan, G. D. *Bioorg. Med. Chem. Lett.* 2011, 21, 3243-3247.
17. Tredwell, M.; Preshlock, S. M.; Taylor, N. J.; Gruber, S.; Huihan, M.; Passchier, J.; Mercier, J.; Genicot, C.; Gouverneur, V. *Angew. Chem., Int. Ed.* 2014, 53, 7751-7755.
18. Lee, E.; Hooker, J. M.; Ritter, T. *J. Am. Chem. Soc.* 2012, 134, 17456-17458.
19. Stenhagen, I. S. R.; Kirjavainen, A. K.; Forsback, S. J.; Jorgensen, C. G.; Robins, E. G.; Luthra, S. K.; Solin, O.; Gouverneur, V., *Chem. Commun.* 2013, 49, 1386-1388.
7 Spectral Data

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

![Chemical structure](image)

$^1$H NMR

- 7.415 ppm
- 7.403 ppm
- 6.929 ppm
- 3.898 ppm
- 2.100 ppm
- 2.094 ppm
- 3.179 ppm
- 1.781 ppm
- 0.268 ppm

f1 (ppm)
(3-SnBu$_3$)

$^1$H NMR
$^{13}$C NMR
$^{1}H$ NMR

\[
\text{Ph} \begin{array}{c}
\text{SnMe}_3 \\
(3-\text{SnMe}_3)
\end{array}
\]
$^1$H NMR

(4-SnBu$_3$)

$^{13}$C NMR
$^1$H NMR
\(^{13}\text{C NMR}\)
\[
\text{SnBu}_3
\]

\text{OMe}

\((6\text{-SnBu}_3)\)

\(^1\text{H NMR}\)
$^{13}$C NMR
$^{13}$C NMR
$^{1}H$ NMR
(S2)

\( ^1H \text{ NMR} \)

\[ \text{ peaks at: } 7.572, 5.075, 4.197, 3.117, 2.000 \]
\[ \text{OMe} \]
\[ \text{H NMR} \]

\[ \begin{align*}
\text{1H NMR} \\
8.419 & \quad 8.412 \\
8.410 & \quad 7.810 \\
8.333 & \quad 7.777 \\
8.333 & \quad 7.213 \\
8.333 & \quad 7.263 \\
8.333 & \quad 7.202 \\
8.333 & \quad 7.000 \\
8.333 & \quad 6.996 \\
8.333 & \quad 6.992 \\
8.333 & \quad 6.985 \\
8.333 & \quad 6.990 \\
8.333 & \quad 6.941 \\
8.333 & \quad 6.875 \\
8.333 & \quad 6.859 \\
8.333 & \quad 6.840 \\
8.333 & \quad 6.821 \\
8.333 & \quad 6.820 \\
8.333 & \quad 6.748 \\
8.333 & \quad 4.294 \\
8.333 & \quad 4.274 \\
8.333 & \quad 3.826 \\
8.333 & \quad 3.373 \\
8.333 & \quad 2.728 \\
8.333 & \quad 2.128 \\
8.333 & \quad 0.222
\end{align*} \]

\[ \text{H NMR} \]
(S7)

$^1$H NMR

S79
$^{1}H$ NMR
$\text{(S8)}$

$^{19}\text{F NMR}$

$\delta = -129.754$
S9

$^1$H NMR

[Chemical structure and NMR spectrum diagram]
$^{19}$F NMR

[Graph of $^{19}$F NMR spectrum]
(S10)

$^1$H NMR

\[
\begin{array}{c}
\text{S87}
\end{array}
\]
$^{19}$F NMR
\[ \text{S11} \]

$^{1}H$ NMR

\[ 7.059, 6.983, 5.202, 5.192, 5.181, 5.171, 3.725, 3.458, 3.440, 3.420, 3.375, 3.222, 2.244, 1.914, 1.383 \]
$^{19}$F NMR
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.

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

**HPLC Conditions: A**
4-[\(^{18}\text{F}\)]fluoro-1,1'-biphenyl (\([^{18}\text{F}]3\)) RAD trace overlaid with UV trace (256 nm) spiked with 4-fluoro-1,1'-biphenyl

HPLC Conditions: A
4-$^{18}\text{F}]$fluoroacetophenone ($[^{18}\text{F}]4$) RAD trace overlaid with UV trace (256 nm) spiked with 4-fluoroacetophenone

HPLC Conditions: A
4-[¹⁸F]fluoro-1-(benzyloxy)benzene ([¹⁸F]5) RAD trace overlaid with UV trace (256 nm) spiked with 1-(benzyloxy)-4-fluorobenzene

HPLC Conditions: A
2-[\textsuperscript{18}F]fluoroanisole ([\textsuperscript{18}F]6) RAD trace overlaid with UV trace (256 nm) spiked with 2-fluoroanisole

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

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

HPLC Conditions: A
3-[\(^{18}\text{F}\)]fluoro-N,N-dimethylaniline \(([^{18}\text{F}9]\)\) RAD trace overlaid with UV trace (256 nm) spiked with 3-fluoro-N,N-dimethylaniline

HPLC Conditions: B
4-$^{18}$Ffluoro-N,N-dimethylaniline ($^{18}$F10) RAD trace overlaid with UV trace (256 nm) spiked with 4-fluoro-N,N-dimethylaniline

HPLC Conditions: B
8-[18F]fluoroquinoline ([18F]11) RAD trace overlaid with UV trace (256 nm) spiked with 8-fluoroquinoline

HPLC Conditions: B
(E)-(2-[\textsuperscript{18}F]fluorovinyl)benzene ([\textsuperscript{18}F]12) RAD trace overlaid with UV trace (256 nm) spiked with (E)-(2-fluorovinyl)benzene

HPLC Conditions: A

![Graph](image-url)
4-[^18]Ffluoro-1-chlorobenzene ([^18]F13) RAD trace overlaid with UV trace (256 nm) spiked with 1-chloro-4-fluorobenzene

HPLC Conditions: A
NHBoc-Phe(4-[\(^{18}\text{F}\)]F) ethyl ester ([\(^{18}\text{F}\)]14) RAD trace overlaid with UV trace (256 nm) spiked with NHBoc-Phe(4-[\(^{18}\text{F}\)]F) ethyl ester

HPLC Conditions: A
NBoc₂-Phe(4-[¹⁸F]F) ethyl ester ([¹⁸F]15) RAD trace overlaid with UV trace (256 nm) spiked with NBoc₂-Phe(4-[¹⁸F]F) ethyl ester

HPLC Conditions: A
Boc₄DOPA(4-[¹⁸F]F) methyl ester ([¹⁸F]¹⁶) RAD trace overlaid with UV trace (256 nm) spiked with 4-F-Boc₄DOPA

HPLC Conditions: A
4-[^18F]MPPF ([^18F]17) RAD trace overlaid with UV trace (256 nm) spiked with 4-MPPF

HPLC Conditions: A
4-$^{18}$F-F-PEB ($^{18}$F18) RAD trace overlaid with UV trace (256 nm) spiked with 4-F-PEB

HPLC Conditions: A