Supporting Information

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General

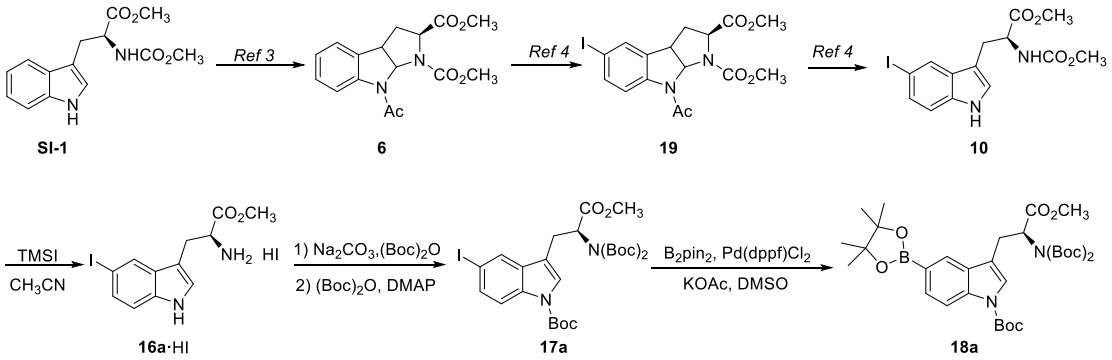
Methods:
Chemistry: Nuclear magnetic resonance spectra were obtained on a Bruker AVANCE III 600 MHz spectrometer (^{1}H NMR at 600 MHz, ^{13}C at 151 MHz, ^{19}F at 564 MHz), or a 400 MHz spectrometer (^{1}H NMR at 400 MHz and ^{13}C at 101 MHz, and ^{19}F at 376 MHz). ^{1}H NMR are reported in the following format: chemical shift, multiplicity (s = singlet, br s = broad singlet, d = doublet, dd = doublet of doublet, t = triplet, q = quartet, m = multiplet), coupling constant (Hz), and integration. All NMR spectra are calibrated relative to residual protiated solvent resonances (^{1}H NMR: $CDCl_3$ at 7.26 ppm, D_2O at 4.79 ppm; ^{13}C NMR: $CDCl_3$ at 77.0 ppm). ^{19}F NMR spectra are reported relative to $CFCl_3$ (0.0 ppm). High-resolution mass spectra were obtained on a Thermo Finnigan LTQ FT mass spectrometer in positive ion mode using flow injection electrospray ionization. Low resolution mass spectra were obtained on an Advion Expression MS. Calculated values for the monoisotopic ion masses were determined with the aid of ChemCalc.[1] Oxygen sensitive reactions were assembled under a nitrogen atmosphere in an Inert glovebox. All reactions were performed under a nitrogen atmosphere, unless otherwise noted. HPLC was carried out with either a Shimadzu Nexera XR LC-20AD equipped with a PDA detector or a Shimadzu LC-20AT Prominence equipped with UV detection.

Materials: All chemicals were used as received from their manufacturer (Sigma-Aldrich, Fisher Scientific, and Alfa Aesar) unless otherwise noted.

5-Fluoro-DL-tryptophan was purchased from Oakwood Chemical. 6-Fluoro-DL-tryptophan was purchased from Acros Organics. 4-Fluoro-DL-tryptophan was purchased from Chem-Impex Int'l Inc. Tetrahydrofuran was distilled over lithium aluminum hydride and stored under a nitrogen atmosphere. Dichloromethane and methanol were used as received. Anhydrous acetonitrile was purchased from Sigma-Aldrich. Anhydrous *N*,*N*-dimethylformamide was purchased from Acros Organics.

Compound Synthesis and Characterization Data

5-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-N_a-*tert*-butoxycarbonyl-N_b,N_b-di-*tert*-butoxycarbonyl-L-tryptophan methyl ester (18a)



N_b-Methoxycarbonyl-L-tryptophan methyl ester (**SI-1**) was synthesized based on literature report. The crude product was used without further purification. Analytical data matched literature values.[2]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.55 (d, *J* = 7.8 Hz, 1H), 7.33 (d, *J* = 8.1 Hz, 1H), 7.23 – 7.16 (m, 1H), 7.16 – 7.09 (m, 1H), 6.96 (s, 1H), 5.31 (d, *J* = 7.6 Hz, 1H), 4.71 (dd, *J* = 13.1, 5.5 Hz, 1H), 3.68 (s, 3H), 3.66 (s, 3H), 3.30 (d, *J* = 5.4 Hz, 2H).

The synthesis of dimethyl (2*S*, 3a*R*, 8a*S*)-8-acetyl-1,2,3,3a,8,8a-hexahydropyrrolo [2,3-b]indole-1,2 –dicarboxylate（**6**) was performed based on literature report and the analytical data matched literature values.[3]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.17 (t, *J* = 7.7 Hz, 1H), 7.08 (d, *J* = 7.4 Hz, 1H), 6.99 (t, *J* = 7.4 Hz, 1H), 6.18 (s, 1H), 4.54 (d, *J* = 7.6 Hz, 1H), 4.00 (t, *J* = 6.4 Hz, 1H), 3.66 (s, 3H), 3.06 (s, 3H), 2.58 (s, 3H), 2.51 (ddd, *J* = 13.2, 8.9, 6.9 Hz, 2H).

The synthesis of dimethyl (2*S*, 3a*R*, 8a*S*)-8-acetyl-5-iodo-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole-1,2-dicarboxylate （**19**) was performed based on literature report and the analytical data matched literature values.[3]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.53 (d, *J* = 8.5 Hz, 1H), 7.43 (s, 1H), 6.19 (d, *J* = 5.8 Hz, 1H), 4.60 (d, *J* = 6.8 Hz, 1H), 4.02 (t, *J* = 6.4 Hz, 1H), 3.72 (s, 3H), 3.24 (s, 3H), 2.62 (s, 3H), 2.53 (ddd, *J* = 13.3, 8.9, 6.9 Hz, 2H).

The synthesis of 5-Iodo-N_b-methoxycarbonyl-L-tryptophan methyl ester (**10**) was performed based on literature report and the analytical data matched literature values.[4] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (s, 1H), 7.84 (s, 1H), 7.46 – 7.36 (m, 1H), 7.12 (d, *J* = 8.5 Hz, 1H), 6.96 (d, *J* = 2.2 Hz, 1H), 5.23 (d, *J* = 7.7 Hz, 1H), 4.75 – 4.60 (m, 1H), 3.72 (s, 3H), 3.70 (s, 3H), 3.26 (d, *J* = 4.6 Hz, 2H).

TMSI (1.1 g, 5.22 mmol, 1.5 equiv) was added dropwise to the solution of 5-iodo-N_b-methoxycarbonyl-L-tryptophan methyl ester (1.4 g, 3.48 mmol, 1.0 equiv) in dry CH_3CN (14 mL) in a Schlenk tube. After being stirred at 110 °C for 1 h under N_2, the reaction mixture was cooled to room temperature and quenched with MeOH (1 mL). Then, the solvent was evaporated to afford desired product 5-iodo-L-tryptophanate methyl hydroiodide **16a**•HI without further purification (off-white solid, 1.6 g).

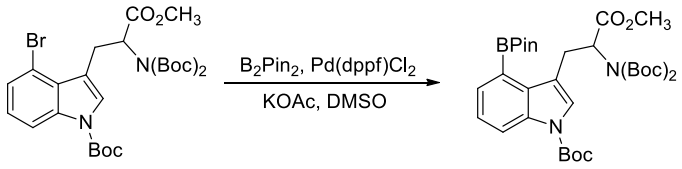
The protection procedure outlined by Crich was followed.[5] Na_2CO_3 (185 mg, 1.74 mmol, 2.0 equiv) was added slowly to a suspension of **16a**•HI (350 mg, 0.87 mmol, 1.0 equiv) in THF/H_2O (20 mL/10 mL). After $(Boc)_2O$ (380 mg, 1.74 mmol, 2.0 equiv) was added dropwise at 0 °C, the reaction mixture was stirred at room temperature for 5 h and then extracted with EtOAc (10 mL X 2). The combined organic extract was washed with saturated NH_4Cl solution, H_2O and saturated brine, dried with Na_2SO_4 and concentrated under reduced pressure. Then, DMAP (106 mg, 0.87 mmol, 1.0 equiv) and $(Boc)_2O$ (570 mg, 2.61 mmol, 3.0 equiv) were sequentially added to the above solution. After being stirred at room temperature overnight, the reaction mixture was concentrated under reduced pressure and then diluted with EtOAc. The organic phase was washed with saturated NH_4Cl solution and H_2O, dried with Na_2SO_4 and concentrated under reduced pressure. Chromatographic purification of the residue using EtOAc: Petroleum ether (1:10) afforded the target product 5-iodo-N_a-*tert*-butoxycarbonyl-N_b,N_b-di-*tert*-butoxycarbonyl-L-tryptophan methyl ester **17a** (off-white solid, 67% yield, 375 mg).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.7 Hz, 1H), 7.82 (d, *J* = 1.4 Hz, 1H), 7.56 (dd, *J* = 8.7, 1.5 Hz, 1H), 7.35 (s, 1H), 5.15 (dd, *J* = 10.2, 4.8 Hz, 1H), 3.77 (s, 3H), 3.39 (ddd, *J* = 25.2, 15.0, 7.5 Hz, 2H), 1.63 (s, 9H), 1.35 (s, 18H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.62, 151.78, 149.18, 134.74, 132.89, 132.79, 127.85, 125.07, 117.08, 115.66, 86.60, 83.92, 83.13, 58.34, 52.37, 28.11, 27.76, 25.40. IR (KBr) 2980, 2865, 1736, 1369, 1140, 1053, 1033 cm^{-1}. HRMS (APCI): Calcd. for $C_{27}H_{37}IN_2O_8$ $[M+H]^+$: 645.1667, found 645.1657.

The borylation procedure described by Miyaura was followed.[6] A flask charged with Pd(dppf)Cl_2, (18 mg, 0.025 mmol, 5 mol%), KOAc (147 mg, 1.5 mmol, 3.0 equiv), and bis(pinacolato)diboron (140 mg, 0.55 mmol, 1.1 equiv) was flushed with N_2.

DMSO (3 mL) and 5-iodo-N_a-*tert*-butoxycarbonyl-N_b,N_b-di-*tert*-butoxycarbonyl -L-tryptophan methyl ester (322 mg, 0.5 mmol, 1.0 equiv) were then added sequentially. Then, the reaction mixture was stirred at 80 °C for 12 h under N_2. Upon cooling to room temperature, chromatographic purification of the mixture using EtOAc: Petroleum ether (1: 10) afforded the product **18a** (off-white solid, 79% yield, 254 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 7.7 Hz, 1H), 7.99 (s, 1H), 7.74 (d, *J* = 8.3 Hz, 1H), 7.36 (s, 1H), 5.22 (dd, *J* = 10.4, 4.8 Hz, 1H), 3.78 (s, 3H), 3.53 (dd, *J* = 14.8, 4.6 Hz, 1H), 3.38 (dd, *J* = 14.9, 10.5 Hz, 1H), 1.63 (s, 9H), 1.35 (s, 12H), 1.31 (s, 18H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.83, 151.57, 149.42, 137.57, 130.84, 129.98, 125.98, 124.34, 116.64, 114.47, 83.61, 83.49, 82.91, 58.10, 52.30, 28.12, 27.70, 25.38, 24.88, 24.84. IR (KBr) 2981, 2865, 1735, 1370, 1254, 1142, 1054, 1033 cm^{-1} HRMS (APCI): Calcd. for $C_{33}H_{49}BN_2O_{10}$ $[M+H]^+$: 645.3553, found 645.3554.

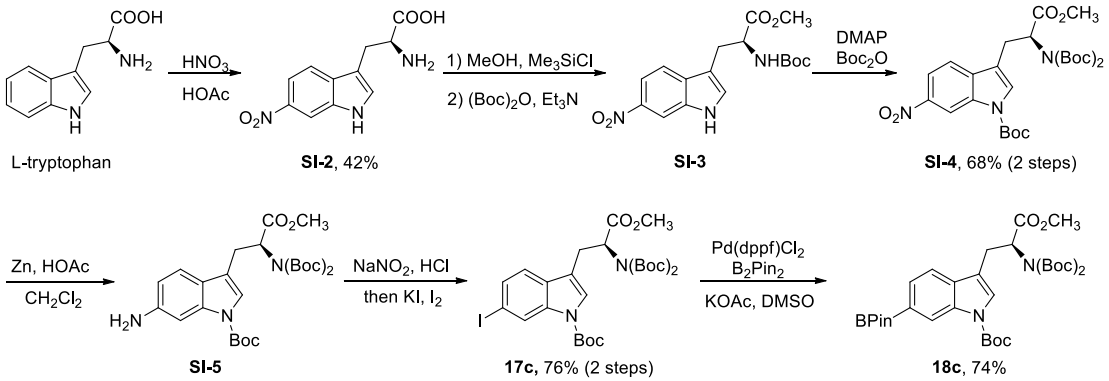
4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-N_a-*tert*-butoxycarbonyl-N_b,N_b-di-*tert*-butoxycarbonyl-DL-tryptophan methyl ester (18b)



The tryptophan core (**17'b**) was prepared utilizing the procedure outlined by Howard,[7] and borylated using the procedure described for 5-BPin-Trp (**18a**).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, *J* = 8.1 Hz, 1H), 7.77 (d, *J* = 7.3 Hz, 1H), 7.31 (s, 1H), 7.27 (s, 1H), 7.24 (d, *J* = 7.5 Hz, 1H), 5.53 (dd, *J* = 11.5, 4.2 Hz, 1H), 3.97 (dd, *J* = 14.2, 4.1 Hz, 1H), 3.75 (s, 3H), 3.24 (dd, *J* = 14.1, 11.7 Hz, 1H), 1.61 (s, 9H), 1.35 (s, 6H), 1.31 (s, 6H), 1.22 (s, 18H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.19, 151.42, 149.18, 135.83, 133.43, 131.83, 126.48, 123.20, 118.00, 117.49, 83.75, 83.24, 82.33, 58.04, 51.85, 28.03, 27.53, 24.92, 24.70, 24.38 (carbon adjacent to boron was not observed). IR (KBr) 2981, 1733, 1631, 1397, 1260, 1135, 1105 cm^{-1}. HRMS (ESI): Calcd. for $C_{33}H_{49}BN_2O_{10}$ $[M+Na]^+$: 667.3372, found 667.3362.

6-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-N_a-*tert*-butoxycarbonyl-N_b,N_b-di-*tert*-Butoxycarbonyl-L-tryptophan methyl ester (18c)



A solution of fuming nitric acid (0.75 mL) in glacial acetic acid (3 mL) was added to a solution of L-tryptophan (4.08 g, 20 mmol, 1.0 equiv) and urea (60 mg, 1 mmol, 0.05 equiv) in glacial acetic acid (50 mL). After being stirred in an ice-cold bath for 20 minutes, the above solution changed to a suspension. The additional fuming nitric acid (1.75 mL) in glacial acetic acid (7 mL) was carefully added dropwise at 15 ^{o}C. The reaction mixture was stirred at room temperature for 18 h, diluted with 30 mL H_2O, and then concentrated to approximate 30 mL solution. After the mixture was kept at 0 ^{o}C overnight, the yellow solid was precipitated and collected by filtration (3.41g). Na_2CO_3 (0.42 g) was added to the suspension of the above yellow solid (2.50 g) in hot water (20 mL). After cooling to room temperature, the precipitate was isolated by filtration to afford the 6-Nitro-L-tryptophan·H_2O (**SI-2**·H_2O) (1.62 g, 43% yield).[8]

Me_3SiCl (2.5 mL, 19.6 mmol, 7.6 equiv) was carefully added to the suspension of **SI-2**·H_2O (687 mg, 2.57 mmol, 1.0 equiv) in dry MeOH (9 mL) in an ice-cold bath. The reaction mixture was stirred at room temperature overnight. Then, Et_3N (5 mL, 3.6 mmol, 1.4 equiv) and $(Boc)_2O$ (897 mg, 4.1 mmol, 1.6 equiv) were added respectively and continued to stir at room temperature overnight. After the starting material 6-Nitro-L-tryptophan was consumed, the reation mixture was concentrated under reduced pressure and H_2O (15 mL) was added. The formed suspension was extracted with EtOAc (15mL X 2). The combined organic layers were dried over Na_2SO_4, and concentrated under reduced pressure. The desired product **SI-3** was obtained without further purification.

Then DMAP (314 mg, 2.57 mmol, 1.0 equiv) and $(Boc)_2O$ (1.68 g, 7.71 mmol, 3.0 equiv) was added to the solution of above concentrate **SI-3** in dry CH_3CN (9 mL) and the reaction mixture was stirred overnight at room temperature. The solvent was removed under reduced pressure, and silica gel chromatographic purification of the residue using EtOAc: Petroleum ether (1: 10) afforded 6-nitro-N_a-*tert*-butoxycarbonyl-N_b,N_b-di-*tert*-butoxycarbonyl- L-tryptophan methyl ester **SI-4** (yellow solid, 68% yield, 985 mg).

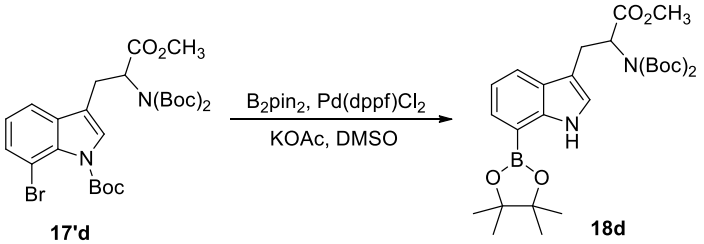
At 0 ^{o}C, HOAc (1.4 mL) was carefully added drop by drop to the suspension of **SI-4** (862 mg, 1.53 mmol) and Zn dust (5.0 g) in CH_2Cl_2 (18 mL) . The suspension was filtered after the reaction mixture was stirred at room temperature for 30 min. The obtained filtrate was washed with saturated aqueous $NaHCO_3$, dried with Na_2SO_4 and concentrated under reduced pressure. The crude product **SI-5** was obtained without further purification.

Then $NaNO_2$ (116 mg, 1.68 mmol, 1.1 equiv) was slowly added to the solution of the above concentrate **SI-5** in THF (11.2 mL), H_2O (7.9 mL) and 5% HCl (4.3 mL) at 0 ^{o}C. The mixture solution continued to be stirred at 0 ^{o}C for 5 min, then it was added to the solution of NaI (1.43 g, 9.52 mmol, 6.2 equiv) and I_2 (388 mg 1.53 mmol) in H_2O

(15 mL). After being stirred at room temperature for 1 h, the reaction mixture was adjusted to pH = 8 with saturated aqueous $NaHCO_3$. The aqueous solution was extracted with EtOAc (100 mL X 2), and the organic phases were combined and washed with saturated aqueous $Na_2S_2O_3$, H_2O and saturated brine, dried with Na_2SO_4 and concentrated under reduced pressure. The obtained concentrate was purified by flash column chromatography to afford the target product 6-iodo-N_a-*tert*-butoxycarbonyl-N_b,N_b-di-*tert*-butoxycarbonyl-L-tryptophan methyl ester **2c** using EtOAc: Petroleum ether (1: 10) (off-white solid, 76% yield, 748 mg).[9]

The borylation procedure described by Miyaura was followed.[6] A flask charged with $Pd(dppf)Cl_2$, (11 mg, 0.015 mmol, 5 mol%), KOAc (88 mg, 0.9 mmol, 3.0 equiv), bis(pinacolato)diboron (84 mg, 0.33 mmol, 1.1 equiv) was flushed with N_2. Then, DMSO (1.5 mL) and **17c** (193 mg, 0.3 mmol, 1.0 equiv) were added sequentially. The reaction mixture was stirred at 80 °C for 12 h under N_2. Upon cooling to the room temperature, chromatographic purification of the mixture afforded the product **18c** using EtOAc: Petroleum ether (1: 10) (white solid, 74% yield, 143 mg).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.51 (d, *J* = 7.8 Hz, 1H), 7.42 (s, 1H), 5.19 (dd, *J* = 10.2, 4.8 Hz, 1H), 3.76 (s, 3H), 3.51 (dd, *J* = 15.0, 4.7 Hz, 1H), 3.35 (dd, *J* = 14.9, 10.2 Hz, 1H), 1.64 (s, 9H), 1.33 (s, 12H), 1.31 (s, 18H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.75, 151.67, 149.31, 135.18, 132.86, 128.47, 125.32, 121.69, 118.10, 116.39, 83.53, 83.28, 82.92, 58.09, 52.27, 28.05, 27.67, 25.44, 24.83, 24.81 (carbon adjacent to boron was not observed). IR (KBr) 2981, 2844, 1644, 1386, 1055, 1033, 1016 cm^{-1}. HRMS (ESI): Calcd. for $C_{33}H_{49}BN_2O_{10}$ $[M+Na]^+$: 667.3372, found 667.3373.

7-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-N_b,N_b-di-*tert*-butoxycarbonyl-D L-tryptophan methyl ester (18d)

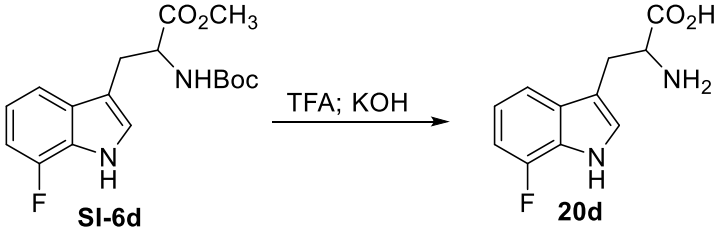


17'd 18d

The tryptophan core was prepared utilizing the procedure outlined by Howard,[7] and borylated using the procedure described for 5-BPin-Trp (**18a**). The Boc protecting group on the indole nitrogen atom was cleaved during the borylation reaction.
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.07 (s, 1H), 7.70 (d, *J* = 7.8 Hz, 1H), 7.60 (d, *J* = 6.6 Hz, 1H), 7.09 (t, *J* = 7.5 Hz, 1H), 7.05 (d, *J* = 1.9 Hz, 1H), 5.15 (dd, *J* = 10.2, 4.8 Hz, 1H), 3.74 (s, 3H), 3.59 (dd, *J* = 14.8, 4.8 Hz, 1H), 3.41 (dd, *J* = 14.8, 10.2 Hz, 1H), 1.35 (s, 12H), 1.26 (s, 18H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.90, 151.47, 141.23, 128.99, 126.35, 122.90, 122.11, 118.69, 110.87, 83.52, 82.48, 59.01, 51.95, 27.46, 25.61, 24.78, 24.67 (carbon adjacent to boron was not observed). IR (KBr) 2981,

1748, 1456, 1387, 1123, 1057, 1033, 1015 cm^{-1}. HRMS (ESI): Calcd. for $C_{28}H_{41}BN_2O_8$ $[M+Na]^+$: 567.2848, found 567.2843.

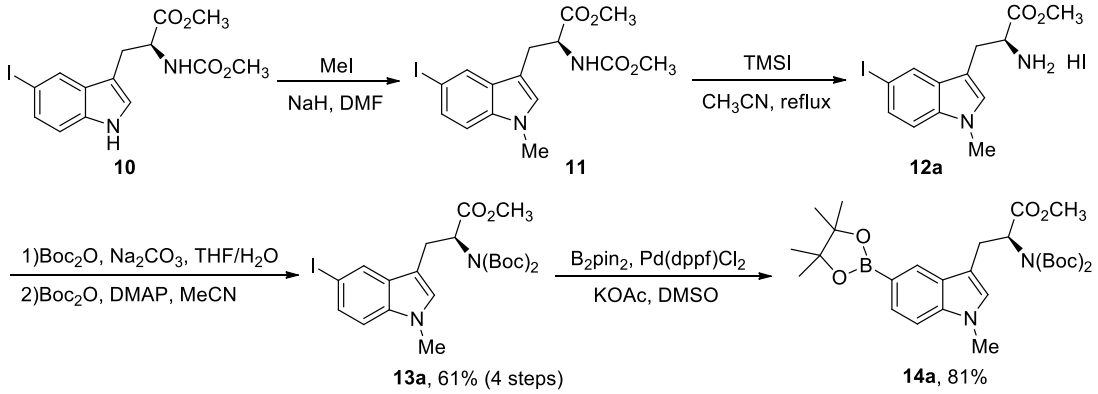
Synthesis of 7-fluoro-DL-Tryptophan (20d)



The tryptophan core was prepared utilizing the procedure outlined by Howard,[7] and protected using the procedures described above to yield **SI-6d**.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (s, 1H), 7.30 (d, *J* = 7.9 Hz, 1H), 7.06 – 6.96 (m, 2H), 6.87 (dd, *J* = 10.9, 8.1 Hz, 1H), 5.14 (s, 1H), 4.68 – 4.60 (m, 1H), 3.66 (s, 3H), 3.36 – 3.17 (m, 2H), 1.45 (m, 9H).^{13}C NMR (101 MHz, $CDCl_3$) δ 172.63, 155.83 ($J_{C\text{-}F}$ = 129.1 Hz), 150.77, 148.34, 131.34 ($J_{C\text{-}F}$ = 5.1 Hz), 124.46 ($J_{C\text{-}F}$ = 13.6 Hz), 123.57, 119.62 ($J_{C\text{-}F}$ = 5.5 Hz), 114.44, 110.87, 106.78 ($J_{C\text{-}F}$ = 16.0 Hz), 79.88, 79.63, 54.10, 52.21, 28.24, 28.17, 28.01. ^{19}F NMR (376 MHz, $CDCl_3$) δ -135.30. IR (KBr) 2980, 1646, 1386, 1033, 1016 cm^{-1}. HRMS (ESI): Calcd. for $C_{17}H_{21}FN_2O_4$ $[M+Na]^+$: 359.1378, found 359.1365.

Protected precursor **SI-6d** (5.0 mg, 0.01487 mmol) was dissolved in 0.2 mL TFA and stirred at room temperature for 15 minutes. After removing the TFA with a stream of nitrogen, the residue was suspended in 0.2 mL MeOH. Sodium hydroxide (1 N solution, 0.2 mL) was added, and the reaction was allowed to stir for 17.5 hours. The reaction was quenched with 0.2 mL of 1 N HCl. The methanol was removed in vacuo. HPLC purification afforded 3.7 mg (74 % yield) of the trifluoroacetate salt of 7-F-DL-tryptophan **20d**. Semi-prep HPLC conditions: Column: Phenomenex Luna C18 10µ 100 Å, 250 x 10 mm. Mobile phase: water (0.1% TFA) and acetonitrile (0.1% TFA). Gradient: Held at 5% acetonitrile for 2 minutes and ramped to 95% acetonitrile over 30 minutes. Flow rate: 3 mL/min.)
^{1}H NMR (600 MHz, D_2O): δ 7.42 (d, *J* = 8.3 Hz, 1 H), 7.29 (s, 1 H), 7.06 (m, 1 H), 6.96 (dd, *J* = 7.7, 11.2 Hz, 1 H), 4.23 (dd, *J* = 5.3, 7.4 Hz, 1 H), 3.45 (dd, *J* = 5.3, 15.3 Hz, 1 H), 3.35 (dd, *J* = 7.3, 15.5 Hz, 1 H). ^{13}C NMR (151 MHz, D_2O): NOTE: Additional peaks are present due to C-F coupling. δ 175.0, 152.8, 151.2, 132.9, 128.4, 128.3, 127.1, 127.0, 122.3, 119.7, 117.8, 116.6, 110.1, 109.4, 109.3, 56.2, 28.4.^{19}F{^{1}H} NMR (564 MHz, D_2O): δ -75.7, -134.5. HRMS (ESI) Calc. for $[C_{11}H_{11}FN_2O_2+H]^+$ 223.08828, Found 223.08748.

5-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-N_a-methyl-N_b,N_b-di-*tert*-butoxycarbonyl-L-tryptophan methyl ester (14a)



At 0 °C, a suspension of NaH (62 mg, 60%, 1.54 mmol, 1.1 equiv) in dry DMF (4.2 mL) was added dropwise to the solution of the 5-iodo-N_b-methoxycarbonyl-*L*-tryptophan methyl ester **10** (563 mg, 1.4 mmol, 1.0 equiv) in dry DMF (2.8 mL). Then the reaction mixture was stirred at 0 °C for 30 minutes, followed by dropwise addition of MeI (219 mg, 95 μL, 1.54 mmol, 1.1 equiv). After being stirred at room temperature for 2 h，the reaction mixture was quenched with saturated aqueous NH_4Cl solution. The aqueous solution was extracted with EtOAc (14 mL X 2). The organic phases were combined and washed with saturated brine (5 mL), dried with Na_2SO_4, filtered and concentrated under reduced pressure. The crude product **11** was obtained without further purification.

Then TMSI (422 mg, 2.1 mmol, 1.5 equiv) was added dropwise to the solution of the above residue **11** in dry CH_3CN (6 mL) in a Schlenk tube. After being stirred at 110 ^oC for 1 h under N_2, the reaction was cooled to room temperature, quenched with MeOH (1 mL) andconcentrated to afford desired product 5-iodo-N_a-methyl-L-tryptophanate methyl hydroiodide **12a** without further purification (a light-brown solid).

To the solution of **12a** in THF/H_2O (32 mL/16 mL), Na_2CO_3 (297mg, 2.8 mmol, 2.0 equiv) was added, followed by dropwise addition of $(Boc)_2O$ (611 mg, 2.8 mmol, 2.0 equiv) at 0 ^oC. After being stirred at room temperature for 5 h, the aqueous solution was extracted with EtOAc (16 mL X 2). The obtained organic extracts were combined and washed with saturated NH_4Cl solution, H_2O and saturated brine, dried with Na_2SO_4 and concentrated under reduced pressure. DMAP (172 mg, 1.4 mmol, 1.0 equiv) and $(Boc)_2O$ (917 mg, 4.2 mmol, 3.0 equiv) were sequentially added to the solution of the above concentrate in CH_3CN (32 mL). After being stirred at room temperature overnight, the reaction mixture was concentrated and the concentrate was diluted with EtOAc and washed with saturated NH_4Cl solution, H_2O and saturated brine. The EtOAc solution was dried with Na_2SO_4 and concentrated under reduced pressure. Chromatographic purification of the residue afforded 5-indo-N_a-methyl-N_b,N_b-di-*tert*- butoxycarbonyl-L-tryptophan methyl ester **13a** using EtOAc: Petroleum ether (1:10) (off-white solid, 61% yield, 477 mg).

The borylation procedure described by Miyaura was followed.[6] A flask charged with Pd(dppf)Cl_2, (8 mg, 0.01 mmol, 5 mol%), KOAc (59 mg, 0.6 mmol, 3.0 equiv), and bis(pinacolato)diboron (56 mg, 0.22 mmol, 1.1 equiv) was flushed with N_2. DMSO (1 mL) and **13a** (112 mg, 0.2 mmol, 1.0 equiv) were added sequentially. The mixture reaction was stirred at 80 °C for 12 h under N_2. Upon cooling to the room temperature, chromatographic purification of the mixture afforded the product 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) -N_a-methyl-N_b,N_b-di-*tert*-butoxycarbonyl-L-tryptophan methyl ester **14a** using EtOAc: Petroleum ether (1: 10) (off-white solid, 81% yield, 90 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.64 (d, *J* = 8.3 Hz, 1H), 7.23 (d, *J* = 8.3 Hz, 1H), 6.83 (s, 1H), 5.17 (dd, *J* = 10.3, 4.7 Hz, 1H), 3.76 (s, 3H), 3.69 (s, 3H), 3.61 (dd, *J* = 14.9, 4.7 Hz, 1H), 3.37 (dd, *J* = 14.8, 10.4 Hz, 1H), 1.35 (s, 12H), 1.27 (s, 18H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.02, 151.37, 138.85, 127.91, 127.77, 127.66, 126.54, 110.82, 108.40, 83.25, 82.66, 59.01, 52.08, 32.53, 27.59, 25.54, 24.84, 24.76 (carbon adjacent to boron was not observed). IR (KBr) 2980, 1640, 1386, 1260, 1141, cm^{-1}. HRMS (ESI): Calcd. for $C_{29}H_{43}BN_2O_8$ $[M+Na]^+$: 581.3005, found 581.3004.

4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-N_a-methyl-N_b,N_b-di-*tert*-butoxycarbonyl-DL-tryptophan methyl ester (14b)

13'b **14b**

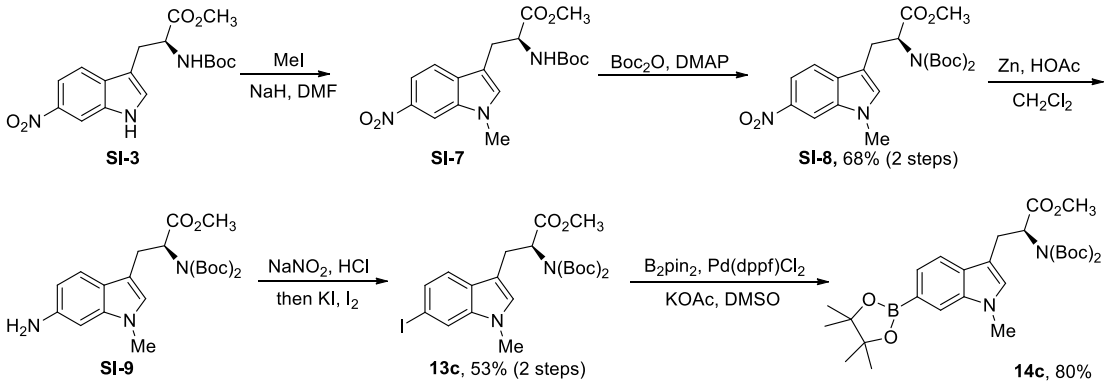
The tryptophan core of the 4-bromo-N_a-methyl-N_b,N_b-di-*tert*-butoxycarbonyl-DL-tryptophan methyl ester **13'b** was prepared utilizing the procedure outlined by Howard,[7] and protected using the procedures described above.

The borylation procedure described by Miyaura was followed.[6] A flask charged with Pd(dppf)Cl_2, (10 mg, 0.0125 mmol, 5 mol%), KOAc (74 mg, 0.75 mmol, 3.0 equiv), bis(pinacolato)diboron (70 mg, 0.275 mmol, 1.1 equiv) was flushed with N_2. Then, DMSO (1.25 mL) and 4-bromo-N_a-methyl-N_b,N_b-di-*tert*-butoxycarbonyl-DL-tryptophan methyl ester (128 mg, 0.25 mmol, 1.0 equiv) were added sequentially. The reaction mixture was stirred at 80 °C for 12 h under N_2. Upon cooling to the room temperature, chromatographic purification of the mixture afforded the product **14b** using EtOAc: Petroleum ether (1: 5) (white solid, 45% yield, 63 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 7.0 Hz, 1H), 7.34 (d, *J* = 8.2 Hz, 1H), 7.17 (t, *J* = 7.6 Hz, 1H), 6.78 (s, 1H), 5.51 (dd, *J* = 11.4, 3.8 Hz, 1H), 4.04 (dd, *J* = 14.4, 3.8 Hz, 1H), 3.75 (s, 3H), 3.68 (s, 3H), 3.29 – 3.04 (m, 1H), 1.35 (s, 6H), 1.31 (s, 6H), 1.16 (s, 18H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.37, 151.10, 137.04, 130.66, 130.04, 128.80, 120.40, 112.26, 111.11, 83.43, 82.24, 59.06, 51.67, 32.49, 27.41, 24.91, 24.64, 24.33 (carbon adjacent to boron was not observed). IR (KBr) 2980, 1640, 1382, 1252,

1123, 1057, 1033, 1014 cm^{-1}. HRMS (ESI): Calcd. for $C_{28}H_{41}BN_2O_8$ $[M+Na]^+$: 581.3005, found 581.3004.

6-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-N_a-methyl-N_b,N_b-di-*tert*-butoxycarbonyl-L-tryptophan methyl ester (14c)



At 0 °C, a suspension of NaH (101 mg, 60%, 2.53 mmol, 1.1 equiv) in dry DMF (6.9 mL) was added dropwise to the solution of the 6-Nitro-N_b-*tert*-Butoxycarbonyl-L-tryptophan methyl ester **SI-3** (836 mg, 2.30 mmol, 1.0 equiv) in dry DMF (4.6 mL). Then the reaction mixture was stirred at 0 °C for 30 minutes, followed by dropwise addition of MeI (359 mg, 156 μL, 2.53 mmol, 1.1 equiv). After being stirred at room temperature for 2 h，the reaction mixture was quenched with saturated aqueous NH_4Cl solution. The aqueous solution was extracted with EtOAc (25 mL X 2). The organic phases were combined and washed with saturated brine (5 mL), dried with Na_2SO_4, filtered and concentrated under reduced pressure. The crude product **SI-7** was obtained without further purification.

Then DMAP (281 mg, 2.3 mmol, 1.0 equiv) and $(Boc)_2O$ (1.51 g, 6.9 mmol, 3.0 equiv) were sequentially added to the solution of the above concentrate **SI-7** in CH_3CN (9 mL). After being stirred at room temperature overnight, the reaction mixture was concentrated and the concentrate was diluted with EtOAc and washed with saturated NH_4Cl solution, H_2O and saturated brine. The EtOAc solution was dried with Na_2SO_4 and concentrated under reduced pressure. Chromatographic purification of the residue afforded 6-Nitro-N_a-Methyl-N_b,N_b-di-*tert*-Butoxycarbonyl-L-tryptophan methyl ester **SI-8** using EtOAc: Petroleum ether (1: 3) (yellow solid, 68% yield, 985 mg).

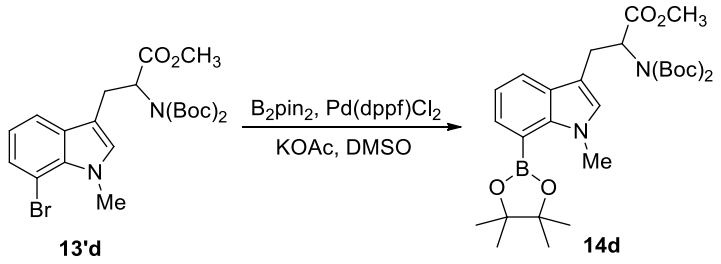
At 0 °C, HOAc (1.4 mL) was carefully added drop by drop to the suspension of **SI-8** (731 mg, 1.53 mmol) and Zn dust (5.0 g) in CH_2Cl_2 (18 mL). The suspension was filtered after the reaction mixture was stirred at room temperature for 30 min. The obtained filtrate was washed with saturated aqueous $NaHCO_3$, dried with Na_2SO_4 and concentrated under reduced pressure. The crude product **SI-9** was obtained without further purification.

Then $NaNO_2$ (116 mg, 1.68 mmol, 1.1 equiv) was slowly added to the solution of the above concentrate **SI-9** in THF (11.2 mL), H_2O (7.9 mL) and 5% HCl (4.3 mL) at 0

°C The mixture solution continued to be stirred at 0 °C for 5 min, then itwas added to the solution of NaI (1.43 g, 9.52 mmol, 6.2 equiv) and I_2 (388 mg 1.53 mmol) in H_2O (15 mL). After being stirred at room temperature for 1 h, the reaction mixture was adjusted to pH = 8 with saturated aqueous $NaHCO_3$. The aqueous solution was extracted with EtOAc (100 mL X 2), and the organic phases were combined and washed with saturated aqueous $Na_2S_2O_3$, H_2O and saturated brine, dried with Na_2SO_4 and concentrated under reduced pressure. The obtained concentrate was purified by flash column chromatography to afford the target product 6-iodo-*N*a-methyl-*N*b,*N*b-di-*tert*-butoxycarbonyl-L-tryptophan methyl ester **13c** using EtOAc: Petroleum ether (1: 4) (yellow solid, 53% yield, 450 mg).[9]

The borylation procedure described by Miyaura was followed.[6] A flask charged with Pd(dppf)Cl_2, (15 mg, 0.020 mmol, 5 mol%), KOAc (118 mg, 1.2 mmol, 3.0 equiv), bis(pinacolato)diboron (112 mg, 0.44 mmol, 1.1 equiv) was flushed with N_2. Then, DMSO (2 mL) and **13c** (223 mg, 0.4 mmol, 1.0 equiv) were added sequentially. The reaction mixture was stirred at 80 °C for 12 h under N_2. Upon cooling to the room temperature, chromatographic purification of the mixture afforded the product **14c** using EtOAc: Petroleum ether (1: 3) (white solid, 80% yield, 179 mg).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 6.92 (s, 1H), 5.13 (dd, *J* = 10.0, 4.8 Hz, 1H), 3.75 (s, 3H), 3.74 (s, 3H), 3.58 (dd, *J* = 14.9, 4.8 Hz, 1H), 3.35 (dd, *J* = 14.9, 10.1 Hz, 1H), 1.36 (s, 12H), 1.28 (s, 18H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.01, 151.55, 136.52, 130.49, 129.19, 124.79, 118.01, 116.03, 110.15, 83.41, 82.70, 59.07, 52.10, 32.68, 27.61, 25.61, 24.95, 24.80 (carbon adjacent to boron was not observed). IR (KBr) 2981, 2844, 1748, 1688, 1387, 1055, 1033, 1013 cm^{-1}. HRMS (ESI): Calcd. for $C_{29}H_{43}BN_2O_8$ $[M+Na]^+$: 581.3005, found 581.3002.

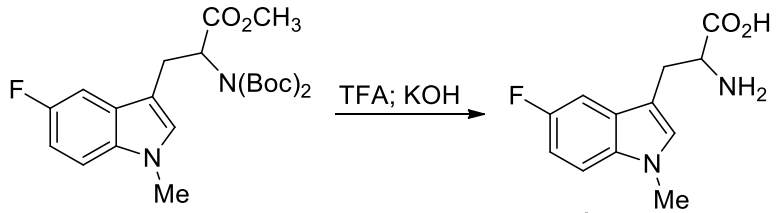
7-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-*N*a-Methyl-*N*b,*N*b-di-*tert*-butoxycarbonyl-DL-tryptophan methyl ester (14d)



The tryptophan core of the 7-bromo-*N*a-methyl-*N*b,*N*b-di-*tert*-butoxycarbonyl-DL-tryptophan methyl ester **13'd** was prepared utilizing the procedure outlined by Howard,[7] and protected using the procedures described above.
The borylation procedure described by Miyaura was followed.[6] A flask charged with Pd(dppf)Cl_2, (8 mg, 0.010 mmol, 5 mol%), KOAc (59 mg, 0.6 mmol, 3.0 equiv), bis(pinacolato)diboron (56 mg, 0.22 mmol, 1.1 equiv) was flushed with N_2. Then, DMSO (1 mL) and 7-bromo-*N*a-methyl-*N*b,*N*b-di-*tert*-butoxycarbonyl-L-tryptophan methyl ester (102 mg, 0.20 mmol, 1.0 equiv) were added sequentially. The reaction

mixture was stirred at 80 °C for 12 h under N_2. Upon cooling to the room temperature, chromatographic purification of the mixture afforded the product **14d** using EtOAc: Petroleum ether (1: 5) (off-white solid, 31% yield, 35 mg).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 7.8 Hz, 1H), 7.64 (d, *J* = 7.0 Hz, 1H), 7.08 (t, *J* = 7.5 Hz, 1H), 6.84 (s, 1H), 5.14 (dd, *J* = 10.0, 4.8 Hz, 1H), 3.88 (s, 3H), 3.75 (s, 3H), 3.58 (dd, *J* = 14.9, 4.7 Hz, 1H), 3.35 (dd, *J* = 15.0, 10.0 Hz, 1H), 1.38 (s, 12H), 1.29 (s, 18H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.09, 151.62, 139.68, 130.47, 129.29, 128.36, 121.84, 118.14, 109.95, 83.74, 82.70, 77.32, 77.00, 76.68, 59.07, 52.09, 36.03, 27.63, 25.52, 24.73, 24.66 (carbon adjacent to boron was not observed). IR (KBr) 2981, 1640, 1386, 1057, 1033, 1015 cm^{-1}. HRMS (ESI): Calcd. for $C_{29}H_{43}BN_2O_8$ $[M+Na]^+$: 581.3005, found 581.3006.

Synthesis of 5-fluoro-1-methyl-DL-tryptophan (15a)



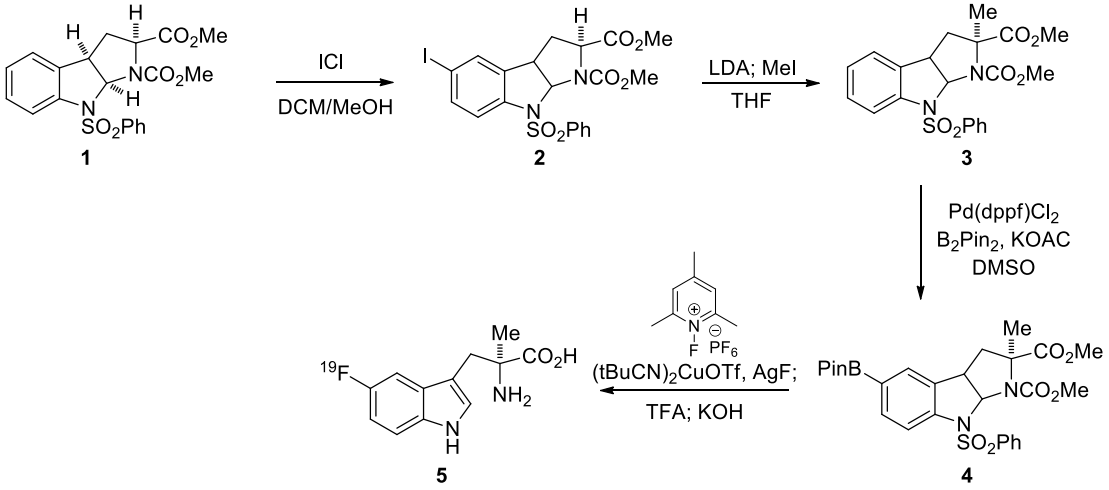
SI-10a **15a**

The tryptophan core was prepared utilizing the procedure outlined by Howard,[7] and protected using the procedures described above to yield **SI-10a**.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (dd, *J* = 9.7, 2.3 Hz, 1H), 7.14 (dd, *J* = 8.8, 4.3 Hz, 1H), 6.93 (dd, *J* = 9.1, 2.3 Hz, 1H), 6.90 (s, 1H), 5.10 (dd, *J* = 10.0, 4.9 Hz, 1H), 3.75 (s, 3H), 3.69 (s, 3H), 3.51 (dd, *J* = 14.9, 4.8 Hz, 1H), 3.33 (dd, *J* = 14.9, 10.1 Hz, 1H), 1.30 (s, 18H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.90, 157.67 (J_{C-F} = 234.0 Hz), 151.68, 133.49, 129.41, 128.34 (J_{C-F} = 9.6 Hz), 110.10 (J_{C-F} = 4.9 Hz), 109.77 (d, J_{C-F} = 15.3 Hz), 109.59 (J_{C-F} = 0.7 Hz), 103.77 (J_{C-F} = 23.4 Hz), 82.77, 59.12, 52.12, 32.78, 27.60, 25.65. ^{19}F NMR (376 MHz, $CDCl_3$) δ -125.83. IR (KBr) 2980, 1387, 1252, 1123, 1057, 1033, 1015, 956 cm^{-1}. HRMS (ESI): Calcd. for $C_{23}H_{31}FN_2O_6$ $[M+Na]^+$: 473.2058, found 473.2058.

An unprotected sample of the amino acid was prepared according to the following procedure. Protected precursor **SI-10a** (5.0 mg, 0.01110 mmol) was dissolved in 0.2 mL TFA and stirred at room temperature for 15 minutes. After removing the TFA with a stream of nitrogen, the residue was suspended in 0.2 mL MeOH. Sodium hydroxide (1 N solution, 0.2 mL) was added, and the reaction was allowed to stir for 17.5 hours. The reaction was quenched with 0.2 mL of 1 N HCl. The methanol was removed in vacuo. HPLC purification afforded 3.3 mg (85 % yield) of the trifluoroacetate salt of 5-fluoro-1-methyl-L-tryptophan **15a**. Semi-prep HPLC conditions: Column: Phenomenex Luna C18 10µ 100 Å, 250 x 10 mm. Mobile phase: water (0.1% TFA) and acetonitrile (0.1% TFA). Gradient: Held at 5% acetonitrile for 2 minutes and ramped to 95% acetonitrile over 30 minutes. Flow rate: 3 mL/min.)

^{1}H NMR (600 MHz, D_2O): δ 7.36 (dd, *J* = 4.4, 9.0 Hz, 1 H), 7.29 (dd, *J* = 2.5, 10.0 Hz, 1 H), 7.18 (s, 1 H), 4.19 (dd, *J* = 5.4, 7.2 Hz, 1 H), 3.71 (s, 3 H), 3.37 (dd, *J* = 5.1, 15.6 Hz, 1 H), 3.31 (dd, *J* = 6.9, 15.5 Hz, 1 H). ^{13}C NMR (151 MHz, D_2O): NOTE: Additional peaks are present due to C-F coupling. δ 175.00, 165.6, 165.4, 160.8, 159.3, 136.1, 133.55, 133.5, 129.6, 129.5, 119.8, 117.9, 113.5, 112.7, 112.5, 107.92, 107.9, 105.65, 105.6, 105.5, 105.4, 56.2, 56.1, 34.9, 34.8, 28.2. ^{19}F{^{1}H} NMR (564 MHz, D_2O): δ -75.7, -125.4. HRMS (ESI) Calc. for $[C_{12}H_{13}FN_2O_2+H]^+$ 237.10393, Found 237.10328

Synthesis of 5-fluoro-α-methyl-L-tryptophan (5)



Precursor **1** was synthesized using the procedure described by Movassaghi.[10]

The iodination procedure was adapted from that described by Ames.[4] Precursor **1** (0.6000 g, 1.441 mmol, 1.0 equiv) was suspended in 8.6 mL of methanol in a glass bomb covered with aluminum foil. The reaction mixture was placed under an atmosphere of nitrogen. ICl (1.0 M solution in DCM, 8.6 mL, 8.644 mmol, 6.0 equiv) was then added dropwise. The bomb was sealed and heated at 55 °C for 20 hours. The reaction was cooled to room temperature and quenched with 100 mL of a solution consisting of 50 mL of 10% $Na_2S_2O_5$ and 50 mL of 10% $NaHCO_3$. The reaction was allowed to stir for 20 minutes to fully consume the remaining ICl. The phases were separated, and the aqueous layer was further extracted three times with DCM. The combined organic phases were washed once with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (1:2 hexanes:EtOAc) to afford 0.6321 g (81% yield) of **2** as a colorless solid.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.75 (d, *J* = 8.2 Hz, 2 H), 7.54 (m, 2 H), 7.44 (t, *J* = 7.2 Hz, 2 H), 7.35 (s, 1 H), 7.21 (br. s, 1 H), 6.22 (br. s, 1 H), 4.61 (br. s, 1 H), 3.58 (br. m, 4 H), 3.26 (s, 3 H), 2.53 (br. m, 1 H), 2.45 (ddd, *J* = 7.2, 9.3, 13.3 Hz, 1 H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 171.0, 154.5, 142.5, 139.8, 137.9, 135.3, 133.2, 133.0, 129.1, 126.1, 120.0, 88.0, 79.8, 58.8, 52.7, 52.2, 45.6, 33.0. HRMS (ESI) Calc. for $[C_{20}H_{19}IN_2O_6S+Na]^+$ 564.99063, Found 564.99153.

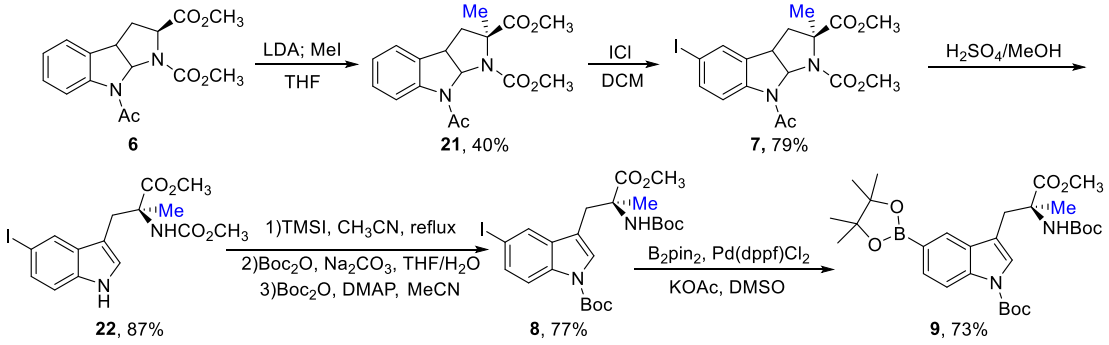
The alkylation procedure described by Crich was followed.[5] Diisopropylamine (0.10 mL, 0.7375 mmol, 1.6 equiv) was dissolved in 2 mL of THF and cooled to 0 °C. n-Butyllithium (1.6 M in hexanes, 0.43 mL, 0.6914 mmol, 1.5 equiv) was added dropwise. After stirring for 5 minutes, the reaction was cooled to -55 °C. Iodide **2** (0.2500 g, 0.4610 mmol, 1.0 equiv) was dissolved in 4.6 mL of THF and added to the LDA solution dropwise. After 2 minutes, methyl iodide (0.08 mL, 1.245 mmol, 2.7 equiv) was added dropwise. The cooling bath was then removed and the reaction was allowed to stir at room temperature for 20 minutes. The reaction was quenched with 100 mL of saturated NH_4Cl and extracted three times with EtOAc. The combined organic phases were washed once with brine, dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified via flash chromatography (1:1 hexanes:EtOAc) to afford 0.1560 g (61% yield) of **3** as a light yellow solid.
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.68 (d, *J* = 8.1 Hz, 2 H), 7.53 (m, 2 H), 7.42, (t, *J* = 7.9 Hz, 2 H), 7.30 (s, 1 H), 7.21 (d, *J* = 8.3 Hz, 1 H), 6.24 (d, *J* = 6.2 Hz, 1 H), 3.53 (br. s, 3 H), 3.42 (t, *J* = 6.6 Hz, 1 H), 3.18 (s, 3 H), 2.68 (d, *J* = 13.8 Hz, 1 H), 2.17 (dd, *J* = 7.5, 13.1 Hz, 1 H), 1.67 (br. s, 3 H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 173.1, 153.8, 142.6, 139.2, 137.6, 136.2, 133.0, 132.9, 129.1, 126.4, 120.8, 88.4, 81.6, 66.1, 52.3, 52.1, 42.8, 42.5, 24.8. LRMS (ESI) Calc. for $[C_{21}H_{21}IN_2O_6S+Na]^+$ 579.01, Found 579.10.

The borylation procedure described by Miyaura was utilized.[6] Iodide **3** (0.1500 g, 0.2696 mmol, 1.0 equiv), $Pd(dppf)Cl_2$ (9.9 mg, 0.01348 mmol, 0.05 equiv), B_2Pin_2 (0.07530 g, 0.2966 mmol, 1.1 equiv), and KOAc (0.1689 g, 1.618 mmol, 6.0 equiv) were dissolved in DMSO and degassed for 10 minutes using a gentle stream of nitrogen. The reaction mixture was heated at 80 °C for 5.5 hours. After cooling to room temperature, the reaction was quenched with water and extracted three times with ethyl acetate. The combined organic phases were washed once with brine, dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. The residue was purified via flash chromatography (1:1 hexanes:EtOAc) to afford 0.1036 g (69% yield) of **4** as a colorless solid.
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.68 (m, 3 H), 7.49 (t, *J* = 7.4 Hz, 1 H), 7.45 (2, *J* = 7.6 Hz, 1 H), 7.42, (s, 1 H), 7.38 (t, *J* = 8.0 Hz, 2 H), 6.29 (d, *J* = 6.6 Hz, 1 H), 3.54 (s, 3 H), 3.45 (t, *J* = 6.8 Hz, 1 H), 3.04 (s, 3 H), 2.79 (d, *J* = 13.3 Hz, 1 H), 2.19 (dd, *J* = 7.7, 13.4 Hz, 1 H), 1.67 (s, 3 H), 1.31 (s, 6 H), 1.30 (s, 6 H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 173.3, 154.0, 145.2, 135.6, 132.8, 132.7, 130.4, 129.0, 126.5, 83.9, 81.6, 66.1, 52.0, 42.9, 29.67, 24.8, 24.7.LRMS (ESI) Calc. for $[C_{27}H_{33}BN_2O_8S+Na]^+$ 579.19, Found 579.30.

The fluorination procedure described by Hartwig was utilized.[11] Deprotection of the crude product was accomplished using the procedure described by Chugani.[12] In a nitrogen filled glove box, 1-fluoro-2,4,6-trimethylpyridinium hexafluorophosphate (7.7 mg, 0.02696 mmol, 3.0 equiv), $Cu(^tBuCN)_2OTf$ (6.8 mg, 0.01798 mmol, 2.0 equiv), and AgF (3.0 mg, 0.02365 mmol, 2.6 equiv) were dissolved in 0.2 mL THF

and stirred for 1 hour. Pinacol boronic ester **4** (5.0 mg, 0.008987 mmol, 1.0 equiv) was dissolved in 0.1 mL THF and added to the reaction mixture, which was then taken out of the glovebox and heated at 50 °C for 24 hours. The crude product was diluted with diethyl ether and filtered through a short plug of silica. The plug was rinsed with additional diethyl ether. The residue was concentrated in vacuo, taken up in 300 uL of TFA and heated at 130 °C for 5 minutes. The reaction was then concentrated to dryness using a stream of argon and intermittent heating. The residue was suspended in 500 uL of 5N KOH and heated at 160 °C for 5 minutes. The reaction mixture was neutralized with 500 uL of 50% AcOH. HPLC purification afforded approximately 0.4 mg (14.3% yield) of the trifluoroacetate salt of 5-fluoro-α-methyl tryptophan **5**. Semi-prep HPLC conditions: Column: Phenomenex Luna C18(2) 5µ 100 Å, 250 x 10 mm. Mobile phase: water (0.1% TFA) and acetonitrile (0.1% TFA). Gradient: Held at 5% acetonitrile for 2 minutes and ramped to 95% acetonitrile over 30 minutes. Flow rate: 3 mL/min.)
^{1}H NMR (600 MHz, D_2O): δ 7.31 (dd, *J* = 4.6, 8.8 Hz, 1 H), 7.23 (dd, *J* = 2.3, 10.5 Hz, 1 H), 7.17 (s, 1 H), 6.88, (td, *J* = 3.0, 9.2 Hz, 1 H), 3.28 (d, *J* = 15.4 Hz, 1 H), 3.02 (d, *J* = 15.2 Hz, 1 H), 1.45 (s, 3 H). Carbon-13 NMR was not possible due to the low mass obtained. ^{19}F{^{1}H} NMR (564 MHz, D_2O): δ -75.7, -125.0. HRMS (ESI) Calc. for $[C_{12}H_{13}FN_2O_2+H]^+$ 237.10393, Found 237.10310.

5-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-*N*$_a$-*tert*-butoxycarbonyl-*N*$_b$-*tert*-butoxycarbonyl-*α*-methyl-L-tryptophan methyl ester (9)



The alkylation procedure outlined by Crich was followed.[5] To a solution of the dimethyl (2*S*, 3a*R*, 8a*S*)-8-acetyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole-1,2–dicarboxylate **6** (2.07 g, 6.50 mmol, 1.0 equiv) in dry THF (25 mL) was added slowly via syringe to LDA (lithium diisopropylamide) in THF (5.2 mL, 2.0 mol/L, 10.4 mmol, 1.6 equiv) at -78 °C. After complete addition, the reaction mixture was maintained at -78 °C for 90 minutes, followed by dropwise addition of methyl iodide (1.01 g, 445 µL, 2.53 mmol, 1.1 equiv). Then, the reaction mixture was stirred at room temperature for 5 h and then carefully quenched with saturated aqueous NH_4Cl solution. The aqueous solution was extracted with ethyl acetate. The combined organic phase was washed with brine (5 mL) and dried with Na_2SO_4. After filtration and evaporation of the solvents under reduced pressure, chromatographic purification of the residue afforded the product dimethyl

(2S)-8-acetyl-2-methyl-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1,2(2H)-dicarboxyla te **19** using EtOAc: Petroleum ether (1:1) (off-white solid, 40% yield, 861 mg).

Iodine monochloride (1M in CH_2Cl_2, 9.6 mL, 9.6 mmol, 4.0 equiv) and $NaHCO_3$(806 mg, 9.6 mmol, 4.0 equiv) were added to the solution of **21** (798 mg, 2.40 mmol, 1.0 equiv) in CH_2Cl_2 (12 mL), and the solution was stirred at room temperature for 2h. Then, the reaction solution was quenched with 10% $Na_2S_2O_3$ (30 mL), and continued to be stirred until the red color faded. The organic layer was collected and the aqueous layer extracted twice with $CHCl_3$. The combined organic layer was dried over Na_2SO_4, filtered and evaporated affording the crude product **7**which was purified by flash column chromatography using EtOAc: Petroleum ether (2:1) (white solid, 79% yield, 2.9 g).

Compound **7** (825 mg, 1.8 mmol, 1.0 equiv) was carefully added to the H_2SO_4/MeOH (2.2 mL/20 mL), and the solution was continued to stir at room temperature for 5h. The solution was poured into ice-water (40 mL) and extracted with EtOAc (30 mL X 2). The combined organic phase was washed with 5% $NaHCO_3$ and saturated brine, dried over Na_2SO_4 and evaporated to afford the crude product 5-iodo-N_b-methoxycarbonyl-α-methyl-L-tryptophan methyl ester **22** which was purified by flash column chromatography using EtOAc: Petroleum ether (3:1) (off-white solid, 87% yield, 362 mg).

TMSI (210 mg, 1.05 mmol, 1.5 equiv) was added dropwise to the solution of **22** (292 mg, 0.7 mmol, 1.0 equiv) in dry CH_3CN (3 mL) in a Schlenk tube. After being stirred at 110 ^oC for 2 h under N_2, the reaction was cooled to room temperature, quenched with MeOH (1 mL) and concentrated to afford desired product 5-iodo-α-methyl-L-tryptophanate methyl hydroiodide without further purification (a light-brown solid). To the solution of 5-iodo-α-methyl-L-tryptophanate methyl hydroiodide (340 mg, 0.7 mmol, 1.0 equiv) in THF/H_2O (16 mL/8 mL), Na_2CO_3 (149 mg, 1.4 mmol, 2.0 equiv) was added, followed by dropwise addition of $(Boc)_2O$ (306 mg, 1.4 mmol, 2.0 equiv) at 0 ^oC. After being stirred at room temperature for 5 h, the aqueous solution was extracted with EtOAc (8 mL X 2). The obtained organic extracts were combined and washed with saturated NH_4Cl solution, H_2O and saturated brine, dried with Na_2SO_4 and concentrated under reduced pressure. DMAP (86 mg, 0.7 mmol, 1.0 equiv) and $(Boc)_2O$ (459 mg, 2.1 mmol, 3.0 equiv) were sequentially added to the solution of the above concentrate in CH_3CN (16 mL). After being stirred at room temperature overnight, the reaction mixture was concentrated and the concentrate was diluted with EtOAc and washed with saturated NH_4Cl solution, H_2O and saturated brine. The EtOAc solution was dried with Na_2SO_4 and concentrated under reduced pressure. Chromatographic purification of the residue afforded 5-indo-N_a-*tert*-butoxycarbonyl -N_b,N_b-di-*tert*-butoxycarbonyl-α-methyl-L-tryptophan methyl ester **8** using EtOAc: Petroleum ether (1:5) (off-white solid, 77% yield, 301 mg).

The borylation procedure described by Miyaura was followed.[6] A flask charged with Pd(dppf)Cl_2, (8 mg, 0.01 mmol, 5 mol%), KOAc (59 mg, 0.6 mmol, 3.0 equiv), and Bis(pinacolato)diboron (56 mg, 0.22 mmol, 1.1 equiv) was flushed with N_2. DMSO (1 mL) and **8** (112 mg, 0.2 mmol, 1.0 equiv) were sequentially added. The mixture reaction was stirred at 80 °C for 12 h under N_2, Chromatographic purification afforded the product 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-N_a-tert-butoxycarbonyl-N_b-*tert*-butoxycarbonyl-*α*-methyl-L-tryptophan methyl ester **9** using EtOAc: Petroleum ether (1: 10) (off-white solid, 73% yield, 82 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 7.4 Hz, 1H), 7.93 (s, 1H), 7.72 (d, *J* = 8.3 Hz, 1H), 7.33 (s, 1H), 5.38 (s, 1H), 3.72 (s, 3H), 3.57 (d, *J* = 12.6 Hz, 1H), 3.34 (d, *J* = 14.4 Hz, 1H), 1.64 (s, 9H), 1.47 (s, 9H), 1.34 (d, *J* = 3.3 Hz, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.44, 154.21, 149.38, 137.25, 130.60, 130.34, 126.14, 124.89, 115.32, 114.44, 83.55, 59.80, 52.58, 28.42, 28.13, 24.93, 24.77. IR (KBr) 2981, 2889, 1748, 1457, 1381, 1252, 1151, 1072, 954 cm^{-1}. HRMS (ESI): Calcd. for $C_{29}H_{43}BN_2O_8$ $[M+Na]^+$: 581.3005, found 581.3001.

Radiochemistry

General Conditions for Radiolabeling

The ^{18}F-labeling conditions are adapted from the procedure described by Gouverneur and co-workers.[13] Pinacol boronic ester precursor (5 mg) and tetrakis(pyridine) copper (II) triflate (4 mg) were dissolved in 50 µL of DMF. The reaction vial was sealed under 1 atmosphere of air with a septum (rubber for deprotection and workup condition A and silicon/PTFE for deprotection and workup conditions B and C) and an aluminum crimp cap. ^{18}F-TBAF (in 40-50 µL MeCN) was added using a 0.5 mL insulin syringe, and the reaction mixture was heated at 110 °C for 20 minutes.

Deprotection and Workup Condition A[14]

Following radiofluorination, 300 µL of 3M H_2SO_4 was added, and the mixture was heated at 140 °C for 10 minutes. After cooling, it was neutralized with 450 µL of 2N NaOAc and passed through an alumina N Sep-Pak light (prewashed with 10 mL of water).

Deprotection and Workup Condition B[12]

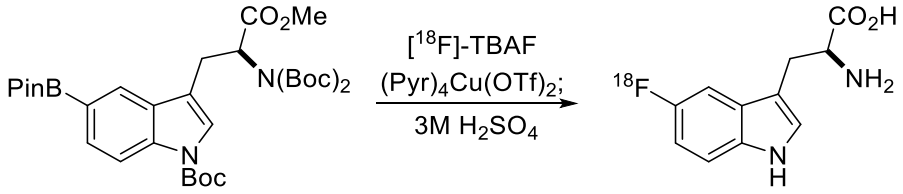
TFA (300 µl) was added to the reaction mixture, which was heated at 130 °C for 5 minutes. The reaction mixture was concentrated to approximately 50 µL using a stream of argon and intermittent heating. The residue was suspended in 500 µL of 5N KOH and heated at 160 °C for 5 minutes. The reaction mixture was neutralized with

500 µL of 50% AcOH and passed through an alumina N Sep-Pak light (prewashed with 10 mL of water).

Deprotection and Workup Condition C

To the crude product was added 200 µL of TFA. The reaction was heated at 80 °C for 5 minutes. The reaction was concentrated to approximately 50 µL using a stream of argon and heating at 80 °C. The residue was suspended in 400 µL of 4N NaOH and heated for 5 minutes at 80 °C. The reaction mixture was neutralized with 270 µL of 6N HCl and passed through an alumina N Sep-Pak light (prewashed with 10 mL of water). The cartridge was further rinsed with 400 µL of 5% acetic acid.

^{18}F-5-fluoro-L-tryptophan (^{18}F-20a)



18a **[^{18}F]-20a**

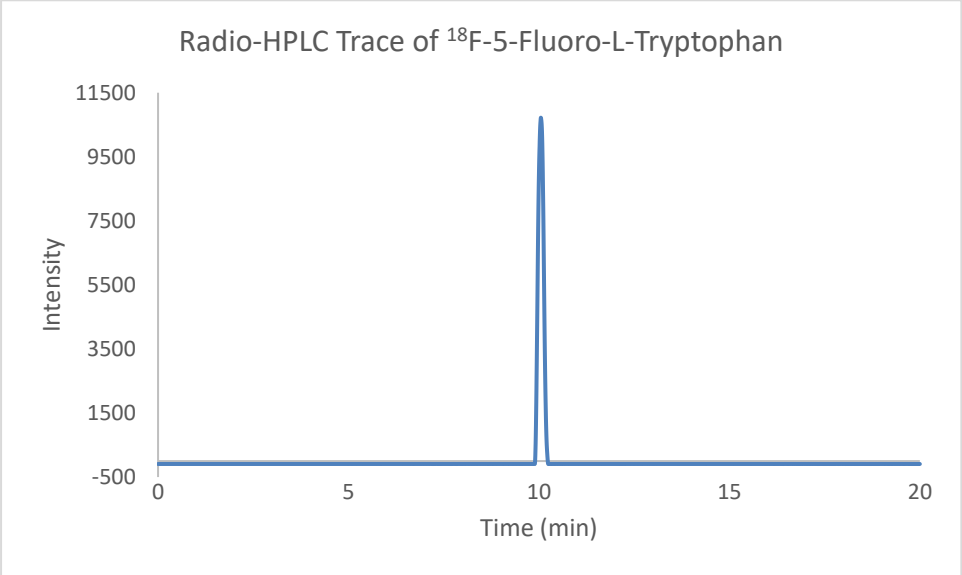
The title product was obtained using the general conditions for radiolabeling (138 mCi ^{18}F-TBAF in 50 uL MeCN) and deprotection condition A.

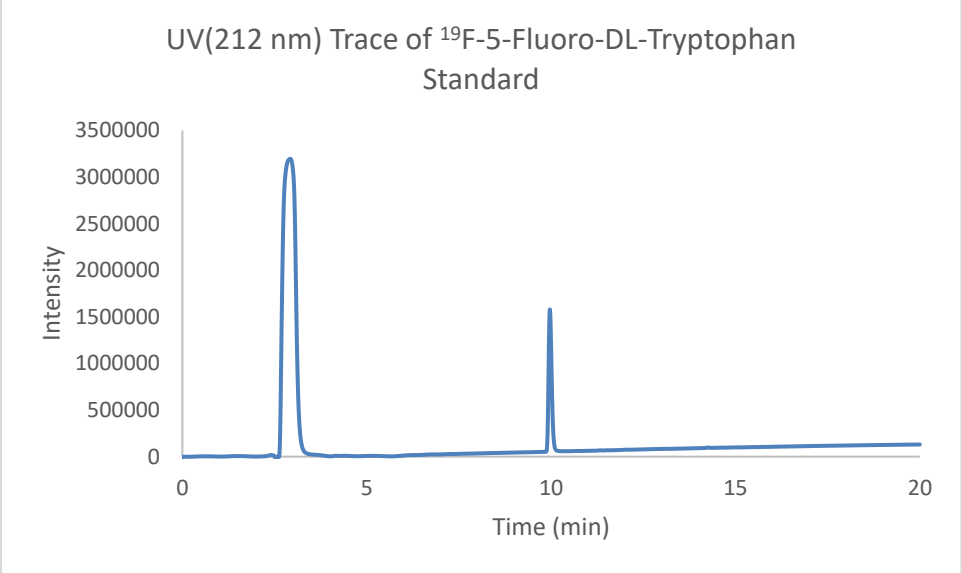
The crude reaction mixture was purified by HPLC (conditions below) to yield 11.3 mCi of the title product (8% radiochemical yield, not decay corrected; 12.0% decay corrected yield).

Column: Phenomenex Luna C18 10µ 100 Å, 250 x 10 mm. Mobile phase: water (0.1% TFA) and acetonitrile (0.1% TFA). Gradient: Held at 5% acetonitrile for 2 minutes and ramped to 95% acetonitrile over 30 minutes. Flow rate: 3 mL/min.)

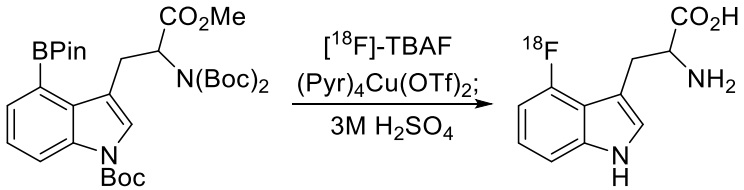
The purified product was reanalyzed by HPLC to establish radiochemical purity and identity.

Analytical conditions: Phenomenex Kinetix 5 µm EVO C18 100 Å, 250 x 4.6 mm column. Mobile phase: water (0.1% TFA) and acetonitrile (0.1% TFA). Gradient: Held at 5% acetonitrile for 2 minutes and ramped to 95% acetonitrile over 30 minutes. Flow rate: 1 mL/min.





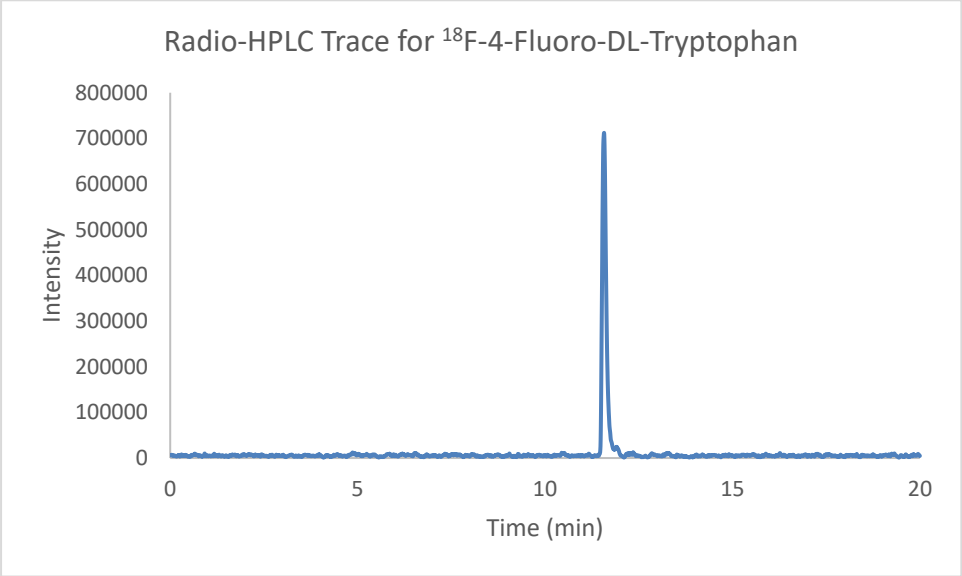
^{18}F-4-fluoro-DL-tryptophan (^{18}F-20b)

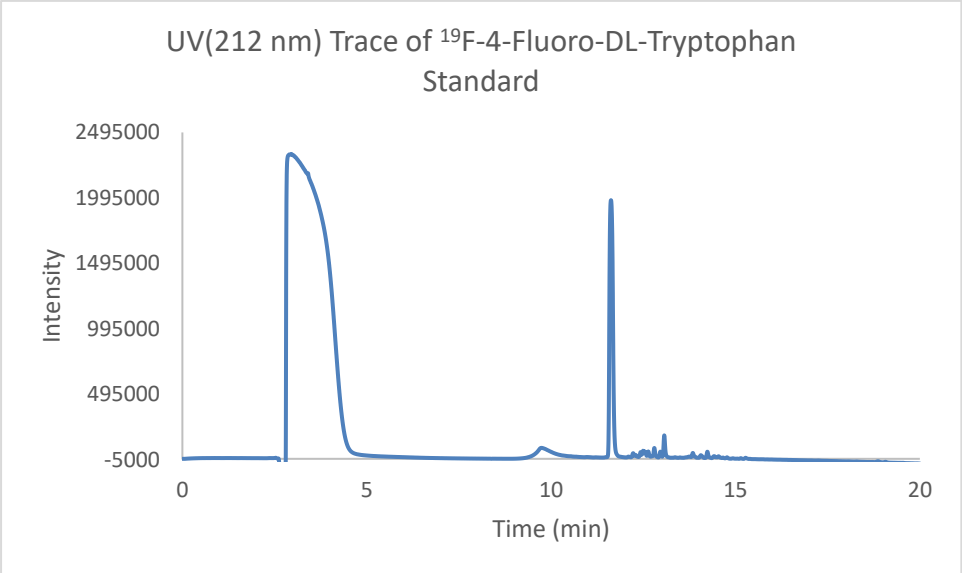


18b **[^{18}F]-20b**

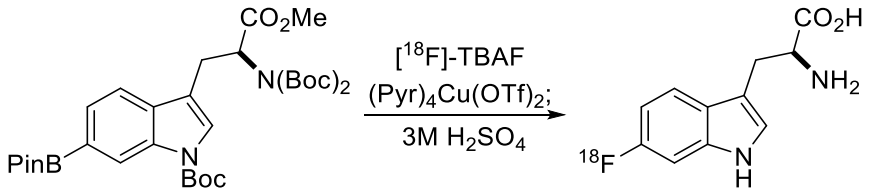
The title product was obtained using the general conditions for radiolabeling (83.6 mCi ^{18}F-TBAF in 40 uL MeCN) and deprotection condition A. After filtration through alumina, 40.5 mCi of crude residue was obtained. A 1.7 mCi aliquot was

purified using HPLC (conditions below) to yield 194 uCi of the title product (5.4% radiochemical yield, not decay corrected; 7.9% decay corrected yield).
Semi-prep conditions: Phenomenex Kinetix 5 µm EVO C18 100 Å, 250 x 4.6 mm column. Mobile phase: water (0.1% TFA) and acetonitrile (0.1% TFA). Gradient: Held at 5% acetonitrile for 2 minutes and ramped to 95% acetonitrile over 20 minutes. Flow rate: 1 mL/min.
The purified product was reanalyzed by HPLC to establish radiochemical purity and identity.
Analytical conditions: Phenomenex Kinetix 5 µm EVO C18 100 Å, 250 x 4.6 mm column. Mobile phase: water (0.1% TFA) and acetonitrile (0.1% TFA). Gradient: Held at 5% acetonitrile for 2 minutes and ramped to 95% acetonitrile over 20 minutes. Flow rate: 1 mL/min.





^{18}F-6-fluoro-L-tryptophan (^{18}F-20c)



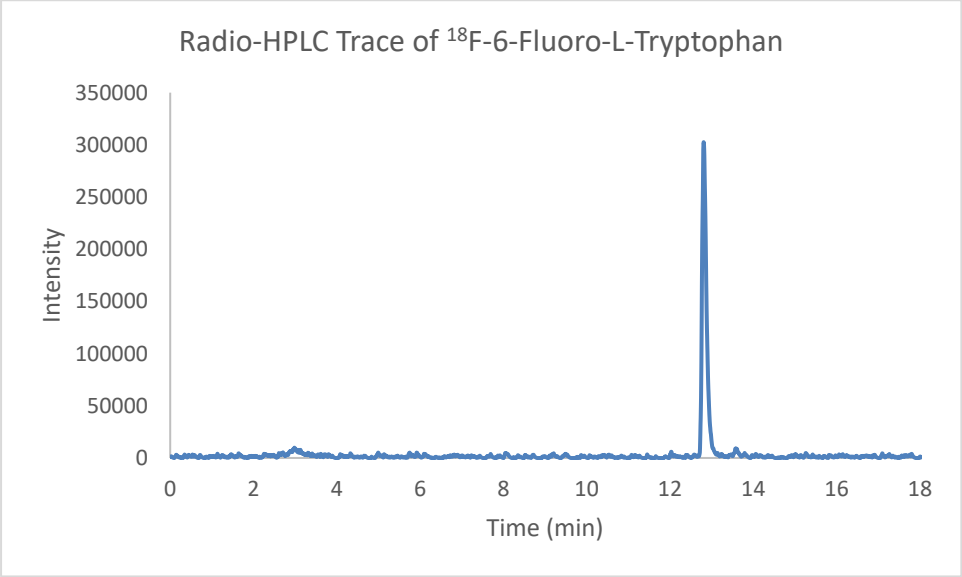
18c **[^{18}F]-20c**

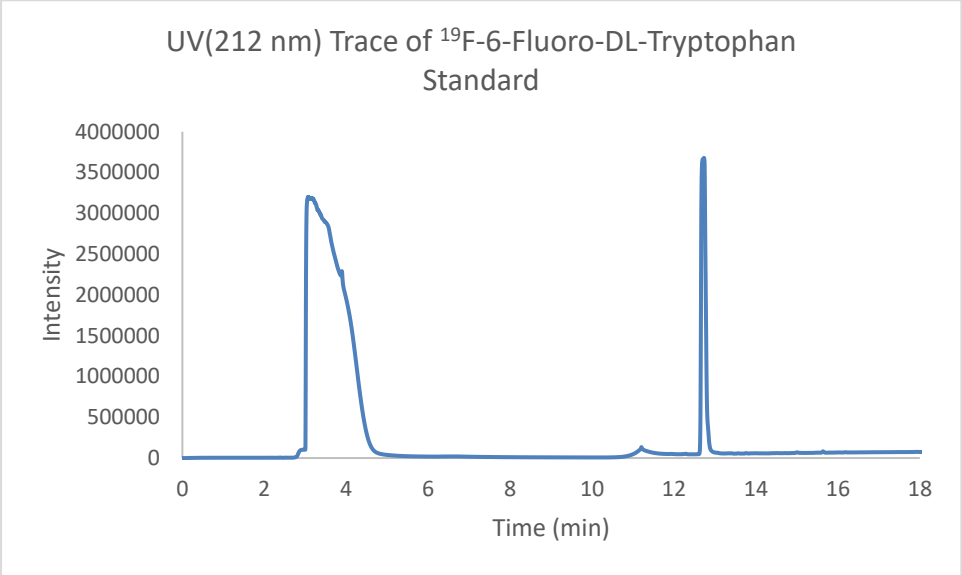
The title product was obtained using the general conditions for radiolabeling (38.6 mCi ^{18}F-TBAF in 40 uL MeCN) and deprotection condition A. After filtration through alumina, 10 mCi of crude residue was obtained. A 903 uCi aliquot was purified using HPLC (conditions below) to yield 96 uCi of the title product (2.8% radiochemical yield, not decay corrected; 4.2 % decay corrected yield).

Semi-prep conditions: Phenomenex Kinetix 5 µm EVO C18 100 Å, 250 x 4.6 mm column. Mobile phase: water (0.1% TFA) and acetonitrile (0.1% TFA). Gradient: Held at 5% acetonitrile for 2 minutes and ramped to 95% acetonitrile over 20 minutes. Flow rate: 1 mL/min.

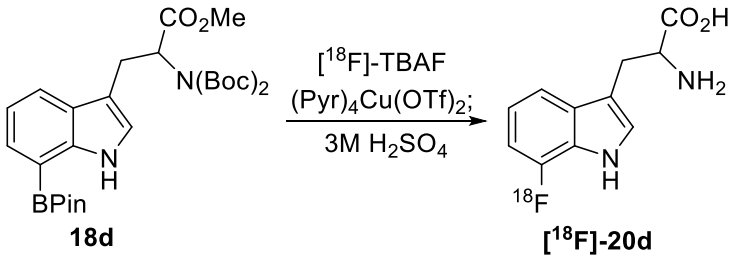
The purified product was reanalyzed by HPLC to establish radiochemical purity and identity.

Analytical conditions: Phenomenex Kinetix 5 µm EVO C18 100 Å, 250 x 4.6 mm column. Mobile phase: water (0.1% TFA) and acetonitrile (0.1% TFA). Gradient: Held at 5% acetonitrile for 2 minutes and ramped to 95% acetonitrile over 20 minutes. Flow rate: 1 mL/min.





^{18}F-7-fluoro-DL-tryptophan (^{18}F-20d)

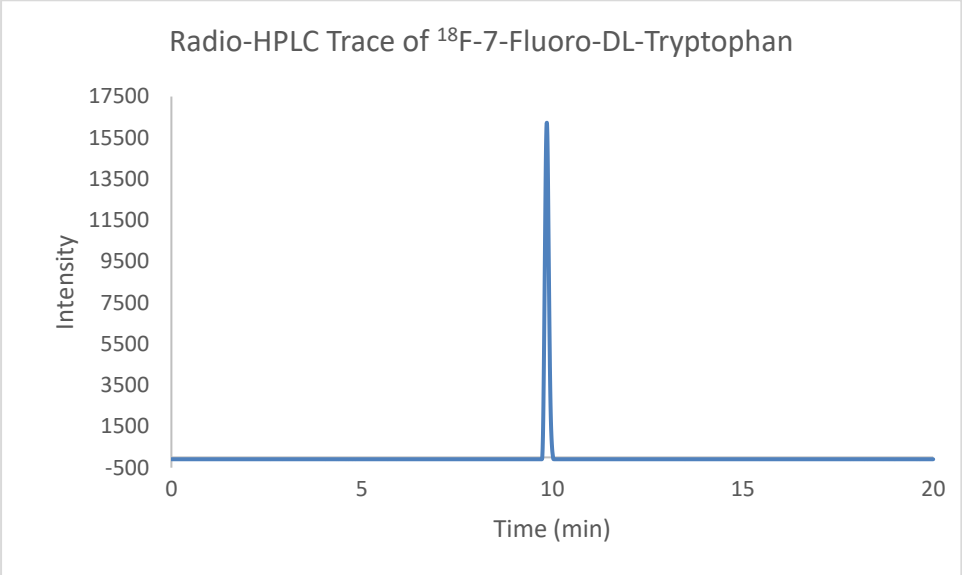


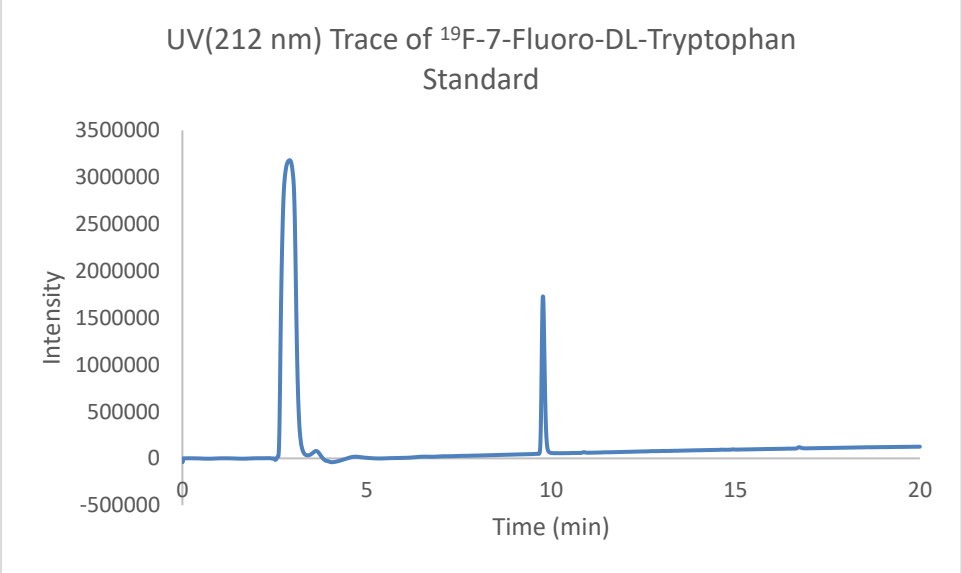
The title product was obtained using the general conditions for radiolabeling (81.4 mCi ^{18}F-TBAF in 50 uL of MeCN) and deprotection condition A. After filtration through alumina, 22 mCi of crude residue was obtained. A 2.8 mCi aliquot of the crude reaction mixture was purified using HPLC (conditions below) to yield 660 uCi of the title product (6.4% radiochemical yield, not decay corrected; 8.8% decay corrected yield).

Semi-prep conditions: Phenomenex Kinetix 5 µm EVO C18 100 Å, 250 x 4.6 mm column. Mobile phase: water (0.1% TFA) and acetonitrile (0.1% TFA). Gradient: Held at 5% acetonitrile for 2 minutes and ramped to 95% acetonitrile over 30 minutes. Flow rate: 1 mL/min.

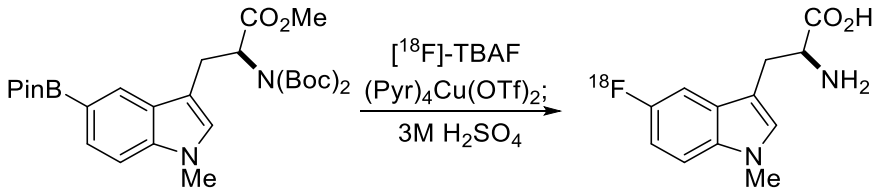
The purified product was reanalyzed by HPLC to establish radiochemical purity and identity.

Analytical conditions: Phenomenex Kinetix 5 µm EVO C18 100 Å, 250 x 4.6 mm column. Mobile phase: water (0.1% TFA) and acetonitrile (0.1% TFA). Gradient: Held at 5% acetonitrile for 2 minutes and ramped to 95% acetonitrile over 30 minutes. Flow rate: 1 mL/min.





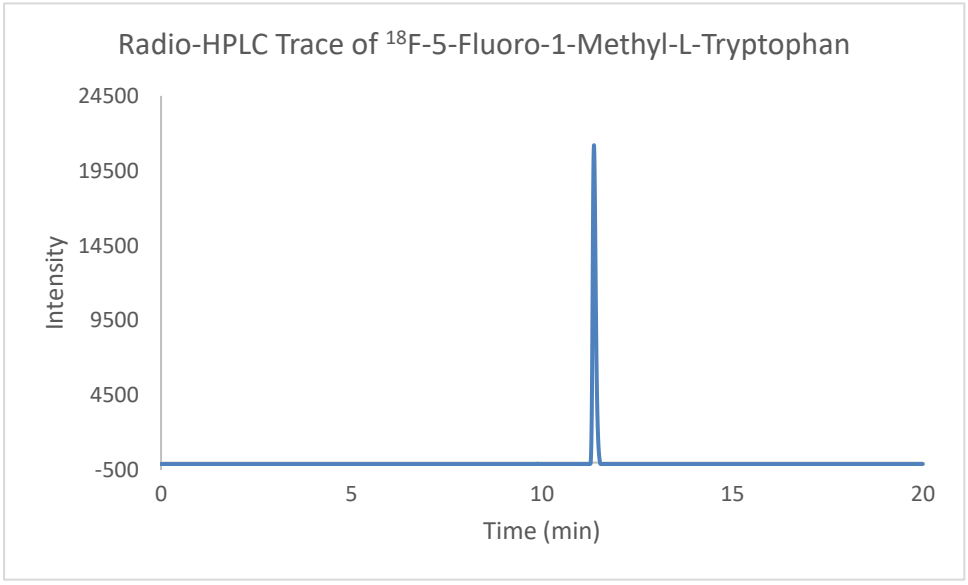
^{18}F-5-fluoro-1-methyl-L-tryptophan (^{18}F-15a)

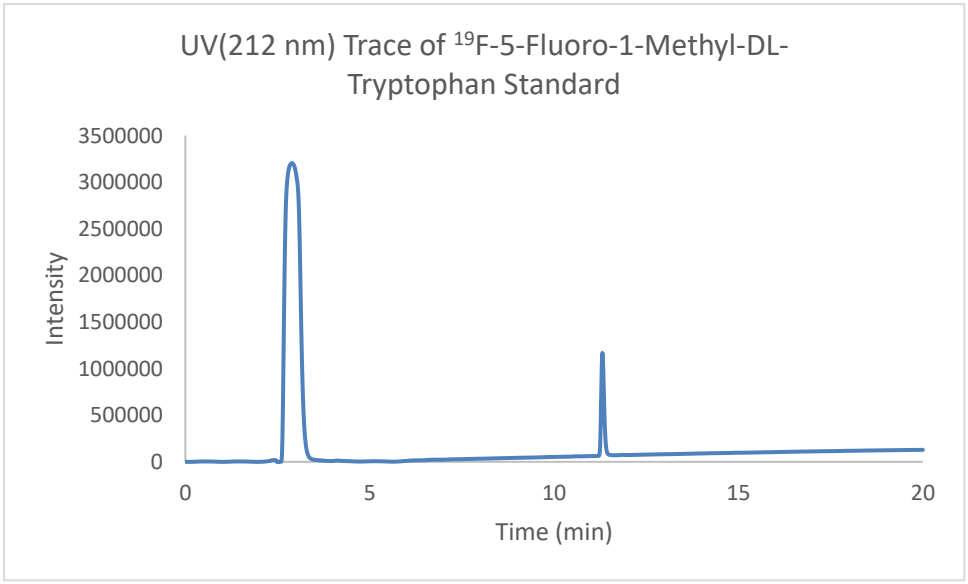


14a **15a**

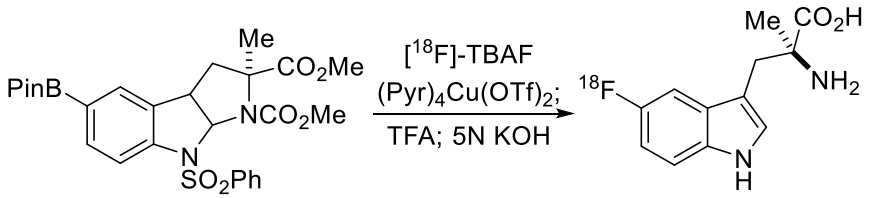
The title product was obtained using the general conditions for radiolabeling (109.7 mCi ^{18}F-TBAF in 40 uL of MeCN) and deprotection condition A. After filtration through alumina, 36 mCi of crude residue was obtained. A 3.3 mCi aliquot of the crude reaction mixture was purified using HPLC (conditions below) to yield 797 uCi

of the title product (7.9% radiochemical yield, not decay corrected; 11.2% decay corrected yield). Semi-prep HPLC conditions: Column: Phenomenex Luna C18 10µ 100 Å, 250 x 10 mm. Mobile phase: water (0.1% TFA) and acetonitrile (0.1% TFA). Gradient: Held at 5% acetonitrile for 2 minutes and ramped to 95% acetonitrile over 30 minutes. Flow rate: 3 mL/min.) The purified product was reanalyzed by HPLC to establish radiochemical purity and identity.
Analytical conditions: Phenomenex Kinetix 5 µm EVO C18 100 Å, 250 x 4.6 mm column. Mobile phase: water (0.1% TFA) and acetonitrile (0.1% TFA). Gradient: Held at 5% acetonitrile for 2 minutes and ramped to 95% acetonitrile over 30 minutes. Flow rate: 1 mL/min.



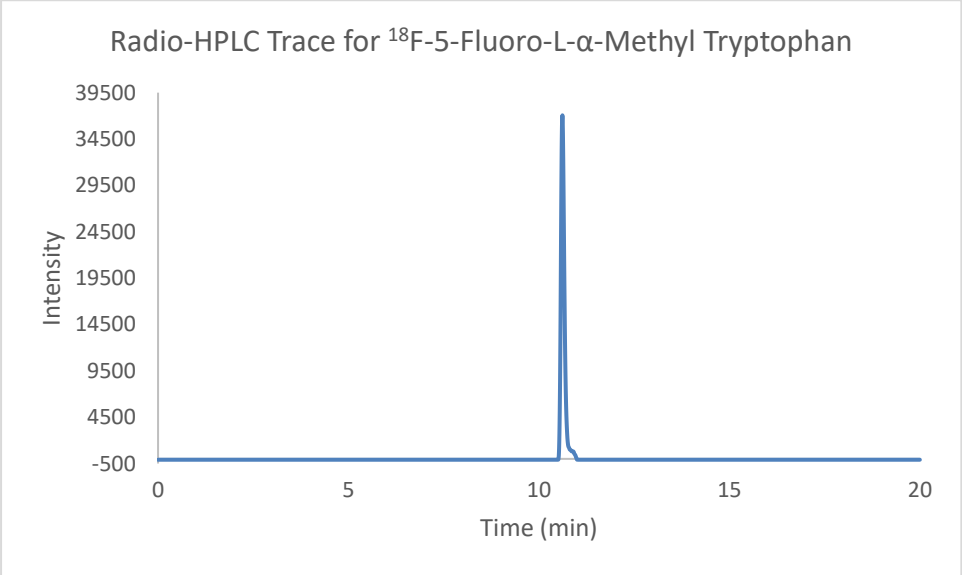


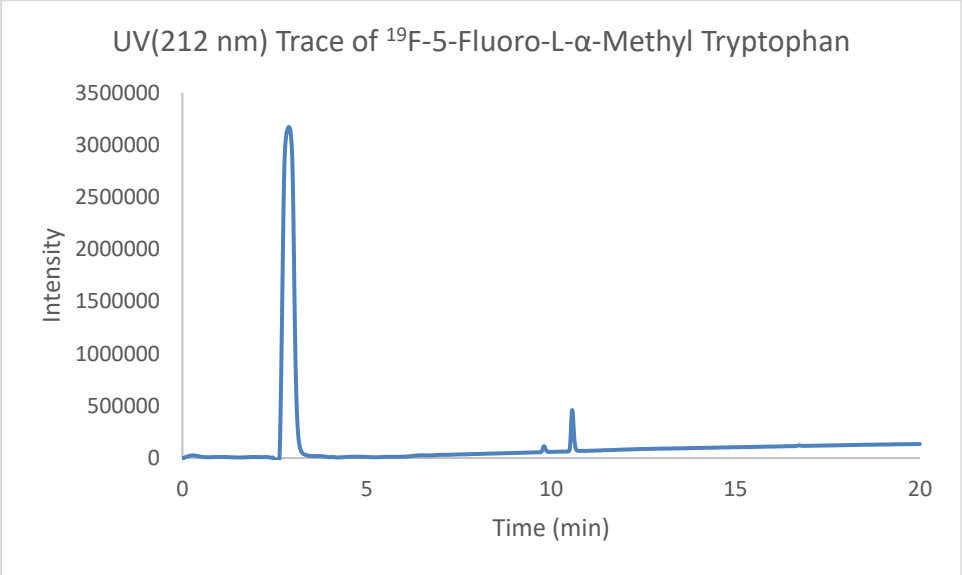
^{18}F-5-fluoro-α-methyl-L-tryptophan (^{18}F- 5)



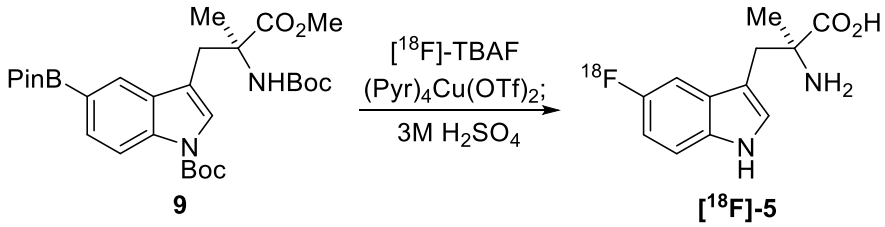
4 **[^{18}F]-5**

The title product was obtained using the general conditions for radiolabeling (55.2 mCi ^{18}F-TBAF in 50 uL MeCN) and deprotection condition B. After filtration through alumina, 8.4 mCi of crude residue was obtained. A 4.13 mCi aliquot of the crude product was purified using HPLC (conditions below) to yield 2.04 mCi of the title product (7.6% radiochemical yield, not decay corrected; 10.9% decay corrected yield). Semi-prep conditions: Phenomenex Kinetix 5 µm EVO C18 100 Å, 250 x 4.6 mm column. Mobile phase: water (0.1% TFA) and acetonitrile (0.1% TFA). Gradient: Held at 5% acetonitrile for 2 minutes and ramped to 95% acetonitrile over 30 minutes. Flow rate: 1 mL/min. The purified product was reanalyzed by HPLC to establish radiochemical purity and identity. Analytical conditions: Phenomenex Kinetix 5 µm EVO C18 100 Å, 250 x 4.6 mm column. Mobile phase: water (0.1% TFA) and acetonitrile (0.1% TFA). Gradient: Held at 5% acetonitrile for 2 minutes and ramped to 95% acetonitrile over 30 minutes. Flow rate: 1 mL/min.





^{18}F-5-fluoro-α-methyl-L-tryptophan (^{18}F- 5)



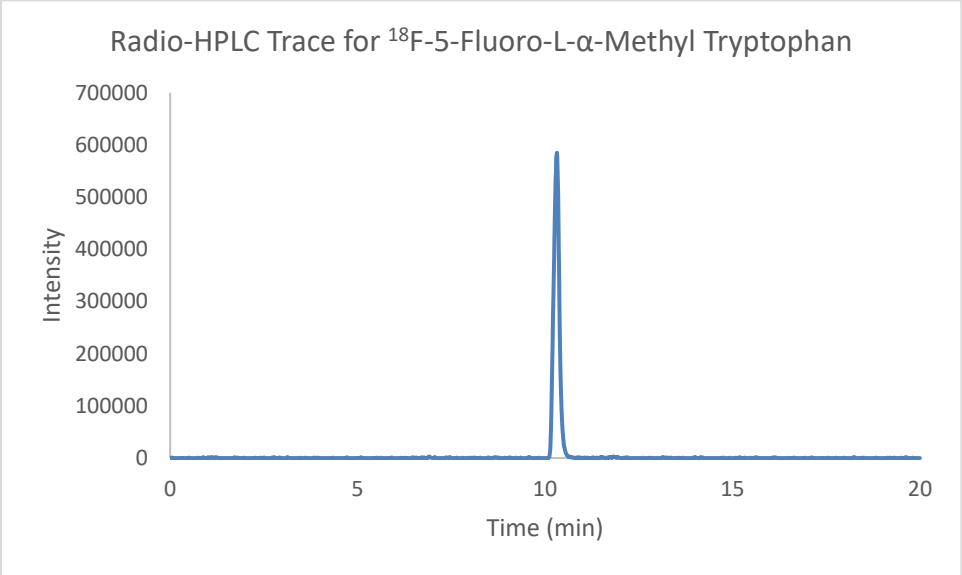
The title product was obtained using the general conditions for radiolabeling (15 mCi ^{18}F-TBAF in 50 uL MeCN) and deprotection condition C.

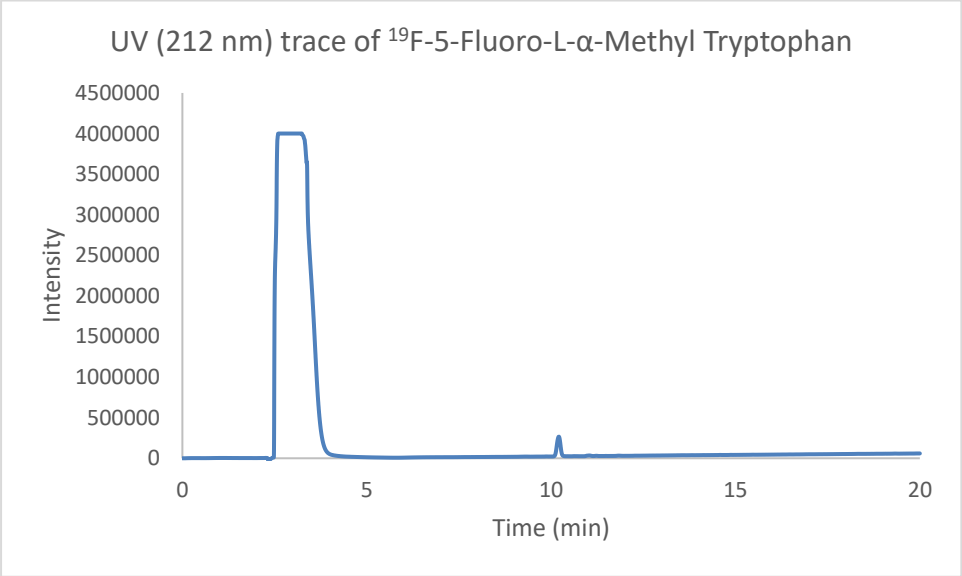
The crude reaction mixture was purified by HPLC (conditions below) to yield 1.5 mCi of the title product (10% radiochemical yield, not decay corrected; 14.9% decay corrected yield).

Column: Phenomenex Luna C18 10µ 100 Å, 250 x 10 mm. Mobile phase: water (0.1% TFA) and acetonitrile (0.1% TFA). Gradient: Held at 5% acetonitrile for 2 minutes and ramped to 95% acetonitrile over 30 minutes. Flow rate: 3 mL/min.)

The purified product was reanalyzed by HPLC to establish radiochemical purity and identity. The specific activity was estimated to be 1.1 Ci/umol, based on the UV absorption of 5-fluoro-DL-tryptophan as a cold standard.

Analytical conditions: Phenomenex Kinetix 5 µm EVO C18 100 Å, 250 x 4.6 mm column. Mobile phase: water (0.1% TFA) and acetonitrile (0.1% TFA). Gradient: Held at 5% acetonitrile for 2 minutes and ramped to 95% acetonitrile over 30 minutes. Flow rate: 1 mL/min.





Cell Biology and Enzyme Assay Procedures

Cell uptake of ^{18}F-AMT in HeLa cell in the presence of IFNγ or IDO1 inhibitor

Hela cells were cultured in Eagle's Minimum Essential Medium (EMEM) supplemented with 10% fetal bovine serum (FBS) at 37°C with 95% air and 5% CO_2. Then 1.0 million cells were seeded in 6-well plates and allowed to attach overnight. The cells were treated with 0.1 μg/ml IFNγ for 48 hours to upregulate IDO1 expression. Then about 2 uCi 5-[^{18}F]F-AMT was added into each well in the presence or absence 0.1 mM NLG919 (IDO1 inhibitor) and incubated with the cells for 60 min.

Then the medium was aspirated. The cells were washed twice with cold PBS and lysed with 2N NaOH. The intracellular radioactivity was measured using gamma counter. The ^{18}F-AMT uptake in the cells without IFNγ stimulation or inhibitors treatment were used as control. The experiment was performed in triplicate.

IDO-1 enzyme assay

The IDO-1 enzyme assay was performed in a 100 μL reaction system. In each reaction, five nM recombinant human IDO-1 (rhIDO; Sino Biological Inc) was incubated with test compounds in the assay buffer containing 50 mM K_2HPO_4 (pH 6.5), 50 mM KH_2PO_4 (pH 6.5), 20 mM l (+)-ascorbic acid (pH 7.0), 10 mM methylene blue, and 100 μg/mL catalase from bovine liver at 37 °C for 1 h. L-tryptophan (20 mM, 2μL) was added as natural substrate for IDO1 as positive control. Cl_3CCOOH (6.1 N, 100 μL) was then added, and the solution was heated at 50 °C for 15 min, and centrifuged to harvest the supernatant. Then equal volume of p-dimethylaminobenzaldehyde (DMAB; 2 g/ml) in 95% ethanol and concentrated HCl was added to the supernatant. The absorbance derived from kynurenine (Kyn) was measured at 490 nm with a VersaMaxSK microplate reader (Molecular Devices). The experiment was performed in triplicate and repeated 3 times.

Tph enzyme kinetics assay

This reaction was performed at room temperature in 100 μL reaction system. Each reaction contained 50 mM MOPS (pH 7.0), 60 μM tryptophan, 100 mM ammonium sulfate, 100 μM ferrous ammonium sulfate, 0.5 mM TCEP, 0.3 mM 6-methyl tetrahydropterin, 0.05 mg/ml catalase, 1 mM DTT and 25 ng (0.5mg/mL) Recombinant Human Tryptophan Hydroxylase protein (Tph; Abcam). Using Shimadzu Spectrofluorophotometer (RF-5301 PC) the Fluorescence signal measurement at Em360nm/Ex300nm was performed three times before the substrate was added and the values served as baseline. Then the fluorescence signal was measured after the substrate was added every 2-5 min for 60 min.

Cell culture and animal models: Animal procedures were performed according to protocol approved by the University of North Carolina Institutional Animal Care and Use Committee. Mouse melanoma cell line B16F10 was obtained from American Type Culture Collection (Manassas, VA, USA) and were cultured in Dulbecco's Modified Eagle's Medium (DMEM) (Gibco, Grand Island, NY, USA) supplemented with 10% fetal bovine serum (FBS) (Omega Scientific, Tarzana, CA, USA). The cells were maintained at 37°C in a humidified atmosphere containing 5% CO_2. Tumor models were established in 4- to 6-week old female C57BL6 mice (Charles River laboratory). The tumor cells were suspended in PBS (2×10^6 /mL) and mixed with MatriGel at 1:1 (vol:vol) ratio. Then 100 μL cell suspension was inoculated subcutaneously at the right shoulder. The mice were used for small animal PET imaging studies when the tumor size greater than 0.6 cm in diameter (8-10 days after cancer cells inoculation).

Small animal PET imaging: Small animal PET scans were performed as described previously. [15] About 100-200 μCi dose of PET probe 5-[^{18}F]F-AMT was intravenously injected into each mouse under isoflurane anesthesia (2-4% for induction and 2% for maintenance in 100% O_2). Static scans were acquired at 0.5 hour after injection. The images were reconstructed by 2-dimensional ordered-subsets expectation maximum.

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