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Radiosynthesis of SPECT Tracers *via* a Copper Mediated ^{123}I-Iodination of (Hetero)Aryl Boron Reagents

Thomas. C. Wilson,[‡a] Greg McSweeney,[‡a] Sean Preshlock,[a] Stefan Verhoog,[a] Matthew Tredwell,[a,b] Thomas Cailly[a,c] and Véronique Gouverneur[a]*

[a.] *Chemistry Research Laboratory, Department of Chemistry, Oxford University, OX1 3TA, UK. E-mail: veronique.gouverneur@chem.ox.ac.uk; Fax: +44 (0)1865 285002*
[b.] *Max-Planck-Institut für Kohlenforschung, Kaiser-Wilhelm-Platz 1, D-45470 Mülheim an der Ruhr, Germany.*
[c.] *Normandie University, UNICAEN, CERMN, F-14032 Caen, France*
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‡These authors contributed equally to this study

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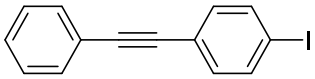
1. Precursor and Reference Synthesis

1.1 General Experimental Information

All NMR spectra were recorded on Bruker DPX200, AV400, AVB400, AVC500, AVB500 and DRX500 spectrometers. Proton and carbon-13 NMR spectra are reported as chemical shifts (δ) in parts per million (ppm) relative to the solvent peak using the Bruker internal referencing procedure (edlock). Fluorine-19 NMR spectra are referenced relative to $CFCl_3$ in $CDCl_3$. Coupling constants (J) are reported in units of hertz (Hz). The following abbreviations are used to describe multiplicities – s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), brs (broad singlet). High resolution mass spectra (HRMS, m/z) were recorded on a Bruker MicroTOF spectrometer using positive electrospray ionization (ESI+) or on a Micromass GCT spectrometer using filed ionization (FI+) or chemical ionization (CI+). Infrared spectra were recorded either as the neat compound or in a solution using a Bruker Tensor 27 FT-IR spectrometer. Absorptions are reported in wavenumbers (cm^{-1}) and only peaks of interest are reported. Optical rotations were measured on a PerkinElmer Polarimeter model 341 Specific rotations are reported in 10^{-1} deg cm^2 g^{-1} and concentrations in g/100 mL. Melting points of solids were measured on a Griffin apparatus and are uncorrected. IUPAC names were obtained using the ACD/I-Lab service. Solvents were purchased from Fisher, Rathburn or Sigma-Aldrich. When anhydrous solvents were required they were purified by expression through an activated alumina column built according to the procedures described by Pangborn and Grubbs.[1] Chemicals were purchased from Acros, Alfa Aesar, Fisher, Fluorochem, Sigma-Aldrich and used as received. Reactions were monitored by thin-layer chromatography (TLC) carried out on Merck Kiesegel 60 F254 plates, silica gel column chromatography was performed over Merck silica gel C60 (40-60 µm).

1.2 Experimental Procedures and Characterisation

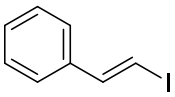
1-Iodo-4-(2-phenylethynyl)benzene (5c):



In a round bottom flask were introduced 4,4,5,5-tetramethyl-2-[4-(2-phenylethynyl)phenyl]-1,3,2-dioxaborolane (100 mg, 0.33 mmol), NaI (108 mg, 0.72 mmol), Cu_2O (2.3 mg, 1.65 µmol), 1,10-phenanthroline (11.8 mg, 0.066 mmol), MeOH (3.6 mL) and H_2O (0.8 mL). The mixture was heated for 1h at 80°C and, after cooling down to room temperature, water (20 mL) was added and extraction was performed with DCM (3 x 20mL). The organic layers were dried with MgSO4 and evaporated. Purification by silica gel chromatography using cyclohexane as eluent afforded 1-iodo-4-(2-phenylethynyl)benzene as a white powder (68 mg, 68%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71 – 7.67 (m, 2H), 7.55 – 7.50 (m, 2H), 7.38 – 7.33 (m, 3H), 7.26 (d, *J* = 8.4 Hz 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 137.6, 133.2, 131.7, 128.7, 128.5, 123.1, 122.9, 94.2, 90.9, 88.6. Data consistent with literature values.[2]

(*E*)-2-Iodoethenylbenzene (5k)

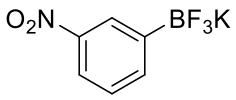


In a round bottom flask were introduced at room temperature 4,4,5,5-tetramethyl-2-[(*E*)-2-phenylethenyl]-1,3,2-dioxaborolane (104 mg, 0.45 mmol), NaI (149 mg, 0.99 mmol), Chloramine-T (140 mg, 0.49 mmol), THF (2 mL)and NaOH (1M solution in H_2O, 2 mL). The solution was allowed to

stir at room temperature for 24 h, $Na_2S_2O_3$ saturated solution was added (20 mL) and extraction was performed with DCM (3 x 20 mL). The organic layers were dried with $MgSO_4$ and evaporated. Purification by silica gel chromatography using cyclohexane as eluent afforded (*E*)-2-iodoethenylbenzene as a colourless oil (64 mg, 62%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.44 (d, *J* = 14.9 Hz, 1H), 7.38 – 7.27 (m, 5H), 6.84 (d, *J* = 14.9 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 145.1, 137.8, 128.8, 128.5, 126.1, 76.8. Data consistent with literature values.[3]

Potassium-3-nitrophenyltrifluoroborate (3b):



In a round bottom flask were introduced at room temperature 3-nitrophenyl boronic acid (400 mg, 2.40 mmol), potassium hydrogen difluoride (742 mg, 9.50 mmol) and a 1:1 mixture of H_2O:MeOH (15 mL). The solution was allowed to stir at room temperature for 2h before the solvent was removed *in vacuo.* To the crude mixture was added H_2O (20 mL) before extraction was performed with $CHCl_3$ (3 x 20 mL). The organic layers were then combined, dried with $MgSO_4$ and excess solvent removed *in vacuo* affording the title compound as a white solid (522 mg, 95%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15 – 8.08 (m, 1H), 7.93 (ddd, *J* = 8.1, 2.6, 1.2 Hz, 1H), 7.74 (d, *J* = 7.2 Hz, 1H), 7.41 (t, *J* = 7.1 Hz, 1H); **^{19}F NMR** (376 MHz, $CDCl_3$): δ = - 140.0 – - 140.6 (m, 3F). Data consistent with literature values.[4]

***N*,*N*-diethyl-2-(2-(3-iodo-4-methoxyphenyl)-5,7-dimethylpyrazolo[1,5-*a*]pyrimidin-3-yl) acetamide: DPA-713**

General procedure A:

Under argon, to a 5 mL solution of THF at – 78 °C and *n*-butyllithium (12 mmol, 2.5 M in *n*-hexane), a solution of acetonitrile (18 mmol in 10 mL THF) was added drop-wise over a period of 20 minutes. The solution was left to stir at -78 °C for one hour before the chosen benzoate (6 mmol in 10 mL THF) was added over a period of 15 minutes. After one hour the reaction was warmed to – 45 °C and the stirring continued until complete consumption of starting material was observed *via* TLC. The reaction was quenched using 2M HCl (50 mL), diluted with EtOAc (50 mL) and the layers were separated. The organic layer was washed with brine (4 x 40 mL), dried with $MgSO_4$ and concentrated to afford the expected 3-oxo-3-phenylpropanenitrile derivatives.

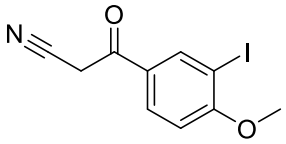
General Procedure B:

Potassium carbonate (8 mmol) was added to a reaction vessel charged with, the chosen 3-oxo-3-phenylpropanenitrile derivative (4 mmol) in THF (30 mL). Subsequently, 2-bromodiethylacetamide (6 mmol) was added dropwise and the reaction was left to stir overnight. The reaction was quenched using 1 M HCl (50 mL), followed by dilution with ethyl acetate (60 mL) and the layers were separated. The mixture was washed with brine (3 x 50 mL), dried and concentrated *in vacuo*. The crude sample was flushed through a short plug of silica using EtOAc:cyclohexane (2:8 to 4:6) as the eluent to give an oil. This oil was dissolved in ethanol (30 mL), treated with hydrazine monohydrate (8 mmol), glacial acetic acid (8 mmol) and was heated to reflux for 18 hours. The solvent was evaporated under reduced pressure and diluted with ethyl acetate before being washed with saturated sodium carbonate (3 x 50 mL). The organic layer was dried with $MgSO_4$ and concentrated i*n vacuo* prior to purification via flash column chromatography Methanol:DCM (3:97) as the eluent to afford the expected pyrazolo[1,5-*a*]pyrimidin-3-yl]acetamide derivatives.

General Procedure C:

2,4-Pentanedione (4 mmol) was added to a solution of the chosen pyrazolo[1,5-*a*]pyrimidin-3-yl]acetamide derivative (2 mmol in 10 mL of EtOH). The reaction mixture was heated at reflux for 20 h. Upon cooling to ambient temperature, the solvent was removed in *vacuo*. The crude material was purified by column chromatography using dichloromethane/methanol (9:1) as the eluent to give the expected DPA-713 analogues.

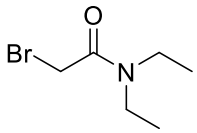
3-(3-Iodo-4-methoxyphenyl)-3-oxopropanenitrile



Synthesized following general procedure A, yielding 3-(3-iodo-4-methoxyphenyl)-3-oxopropanenitrile (1.80 g, 95% yield) as a white powder.

Mp: 128 – 130 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.32 (d, *J* = 2.2 Hz, 1H), 7.92 (dd, *J* = 8.7, 2.2 Hz, 1H), 6.89 (d, *J* = 8.7 Hz, 1H), 4.02 (s, 2H), 3.98 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 184.4, 163.0, 140.2, 130.9, 128.8, 113.7, 110.4, 86.5, 56.9, 29.1; **IR** (*ν,* cm^{-1}): 2941, 2269, 1707, 1583, 1256, 1203, 935, 818, 662; **HRMS** (ESI) for $C_{10}H_8O_2N^{127}I$ $[M + Na]^+$ requires m/z 323.9492, found 323.9490.

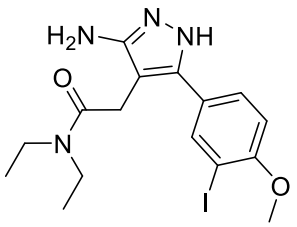
2-Bromo-*N*,*N*-diethylacetamide



Freshly distilled diethylamine (2 mL, 19.8 mmol) was slowly added to a solution of bromoacetyl bromide (860 µl, 9.9 mmol) in 50 mL dichloromethane at -78 °C. The mixture was allowed to warm to room temperature and left to stir for one hour. 25 mL of H_2O was added and the reaction mixture was extracted with dichloromethane (3 x 40 mL). The combined organic layers were dried with $MgSO_4$ and concentrated, yielding the title compound as a white solid (98%, 1.9 g, 9.8 mmol). The spectroscopic data matched that of the literature.[5]

^{1}H NMR (400 MHz; $CDCl_3$): δ = 3.86 (s, 2H), 3.41 (qd, *J* = 7.2, 2.6 Hz, 4H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.16 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 101 MHz): δ = 165.9, 42.9, 40.5, 26.4, 14.4, 12.5.

2-(3-Amino-5-(3-iodo-4-methoxyphenyl)-1*H*-pyrazol-4-yl)-*N*,*N*-diethylacetamide

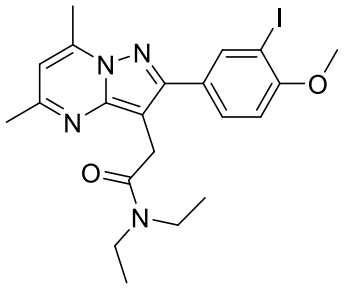


Synthesized following general procedure B, yielding 2-[5-amino-3-(3-iodo-4-methoxyphenyl)-*1H*-pyrazol-4-yl]-*N*,*N*-diethylacetamide (0.94 g, 55%) as a yellow powder.

Mp: 87 – 89°C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.78 (d, *J* = 2.1 Hz, 1H), 7.34 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.81 (d, *J* = 8.5 Hz, 1H), 5.97 (bs, 2H), 3.89 (s, 3H), 3.46 (s, 2H), 3.33 (q, *J* = 7.1 Hz, 2H), 3.12 (q, *J* = 7.1 Hz, 2H), 1.09 (t, *J* = 7.1 Hz, 3H), 0.98 (t, *J* = 7.1 Hz, 3H). (Signal due to pyrazole NH is not observed); **^{13}C**

NMR (101 MHz, $CDCl_3$): δ = 170.3, 158.2, 153.8, 141.7, 138.6, 129.2, 125.2, 111.9, 97.7, 86.2, 56.5, 42.5, 40.7, 28.3, 14.3, 13.1; **IR** (*v,* cm^{-1}): 3210, 2968, 1610, 1506, 1432, 1251, 1046, 814; **HRMS** (ESI) for $C_{16}H_{22}O_2N_4{}^{127}I$ $[M+H]^+$ requires m/z = 429.0782, found 429.0779.

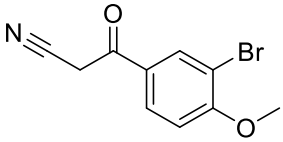
***N*,*N*-Diethyl-2-(2-(3-iodo-4-methoxyphenyl)-5,7-dimethylpyrazolo[1,5-*a*]pyrimidin-3-yl)acetamide**



Synthesised following general procedure C, yielding *N*,*N*-diethyl-2-[2-(3-iodo-4-methoxyphenyl)-5,7-dimethylpyrazolo[1,5-*a*]pyrimidin-3-yl]acetamide (836 mg, 85% Yield) as a yellow powder. The data matched that of the literature.[6]

Mp: 151 – 152 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.19 (d, *J* = 2.1 Hz, 1H), 7.87 (dd, *J* = 8.5, 2.1 Hz, 1H), 6.90 (d, *J* = 8.5 Hz, 1H), 6.52 (d, *J* = 0.6 Hz, 1H), 3.92 (s, 2H), 3.91 (s, 3H), 3.52 (q, *J* = 7.1 Hz, 2H), 3.42 (q, *J* = 7.1 Hz, 2H), 2.74 (d, *J* = 0.6 Hz, 3H), 2.55 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.13 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 169.8, 158.2, 157.7, 153.5, 139.3, 130.1, 128.3, 110.7, 108.4, 101.0, 100.0, 86.1, 56.5, 42.4, 40.7, 28.1, 24.6, 17.0, 14.5, 13.2. The data is consistent with that of the literature.[6]

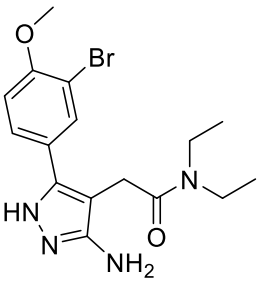
3-(3-Bromo-4-methoxyphenyl)-3-oxopropanenitrile



Synthesized following general procedure A, yielding 3-(3-bromo-4-methoxyphenyl)-3-oxopropanenitrile (1.42 g, 93%) as yellow powder.

Mp: 110 – 112°C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.11 (s, 1H), 7.88 (d, *J* = 8.7 Hz, 1H), 6.98 (d, *J* = 8.7 Hz, 1H), 4.05 (s, 2H), 3.99 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 184.7, 160.9, 133.9, 129.9, 128.2, 113.8, 112.6, 111.5, 56.8, 29.2; **IR** (*v,* cm^{-1}): 980, 2915, 2255, 1687, 1589, 1285, 1202, 966, 828, 818, 774, 676; **HRMS** (ESI) for $C_{10}H_7O_2N^{79}Br$ $[M+H]^+$ requires m/z = 251.9665 found 251.9674.

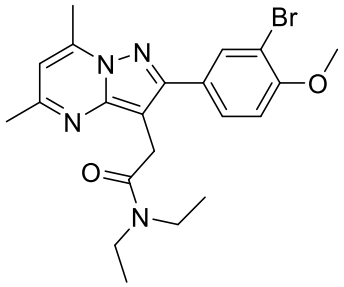
2-(3-Amino-5-(3-bromo-4-methoxyphenyl)-1*H*-pyrazol-4-yl)-*N*,*N*-diethylacetamide



Synthesized following general procedure B, yielding 2-[5-amino-3-(3-bromo-4-methoxyphenyl)-*1H*-pyrazol-4-yl]-*N*,*N*-diethylacetamide (0.81 g, 53%) as a yellow powder.

Mp: 84 – 86 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.53 (d, *J* = 2.1 Hz, 1H), 7.27 (dd, *J* = 8.5, 2.1 Hz, 1H), 6.83 (d, *J* = 8.5 Hz, 1H), 3.89 (s, 3H), 3.45 (s, 2H), 3.32 (q, *J* = 7.1 Hz, 2H), 3.10 (q, *J* = 7.1 Hz, 2H), 1.07 (t, *J* = 7.1 Hz, 3H), 0.96 (t, *J* = 7.1 Hz, 3H) (Signal due to pyrrazole NH and NH_2 are not observed); **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 170.4, 155.7, 153.3, 142.3, 132.5, 128.2, 125.1, 111.9, 111.7, 97.2, 56.3, 42.4, 40.7, 28.0, 24.7, 16.9, 14.4, 13.2; **IR** (*ν,* cm^{-1}): 3542, 2915, 1615, 1595, 1469, 1428, 1229, 1107, 971, 832, 747; **HRMS** (ESI) for $C_{16}H_{21}{}^{79}BrN_4O_2$ $[M+H]^+$ requires m/z 379.0775, found 379.0770.

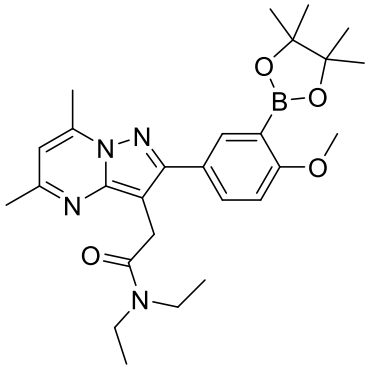
2-(2-(3-Bromo-4-methoxyphenyl)-5,7-dimethylpyrazolo[1,5-*a*]pyrimidin-3-yl)-*N*,*N*-diethyl acetamide



Synthesised following general procedure C, yielding *N*,*N*-diethyl-2-[2-(3-bromo-4-methoxyphenyl)-5,7-dimethylpyrazolo[1,5-*a*]pyrimidin-3-yl]acetamide (0.80 g, 90%) as a yellow powder.

Mp: 145 – 146 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.99 (d, *J* = 2.1 Hz, 1H), 7.84 (dd, *J* = 8.5, 2.1 Hz, 1H), 6.97 (d, *J* = 8.5Hz, 1H), 6.51 (d, *J* = 0.9 Hz, 1H), 3.93 (s, 3H), 3.91 (s, 2H), 3.52 (q, *J* = 7.1 Hz, 2H), 3.41 (q, *J* = 7.1 Hz, 2H), 2.73 (d, *J* = 0.8 Hz, 4H), 2.53 (s, 3H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.12 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 169.9, 157.8, 156.0, 153.6, 147.9, 144.9, 133.3, 129.1, 127.9, 111.9, 111.8, 108.5, 101.1, 56.4, 42.5, 40.8, 28.1, 24.8, 17.0, 14.5, 13.2; **IR** (*ν,* cm^{-1}): 2980, 1638, 1554, 1225, 1052, 945, 907, 845, 787, 763; **HRMS** (ESI) for $C_{21}H_{24}BrN_4O_2$ $[M+H]^+$ requires m/z 443.1088, found 443.1081.

***N*,*N*-Diethyl-2-(2-(4-methoxy-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-5,7-dimethylpyrazolo[1,5-*a*]pyrimidin-3-yl)acetamide**

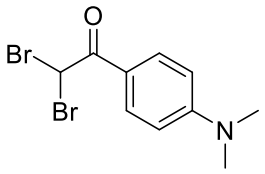


To a 10 mL round bottom under argon, flask charged with 2 mL of Toluene was added *N*,*N*-diethyl-2-[2-(3-bromo-4-methoxyphenyl)-5,7-dimethylpyrazolo[1,5-*a*]pyrimidin-3-yl]acetamide (177 mg, 0.4 mmol), $Pd(dppf)Cl_2.CH_2Cl_2$ (32 mg, 0.04 mmol), potassium acetate (157 mg, 1.6 mmol) and bis(pinacolato)diboron (305 mg, 1.2 mmol). The reaction was left to stir at 85 °C for 18 hours. The reaction was allowed to cool and the solvent removed in *vacuo* before addition of ethyl acetate (5 mL). The mixture was filtered through a short plug of celite, evaporated and subjected to column chromatography using acetone/DCM (1/9 to 2/8) as the eluent. Crystallization followed by filtration from petroleum ether and diethylether afforded *N,N*-diethyl-2-{2-[4-methoxy-3-(tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]-5,7-dimethylpyrazolo[1,5-*a*]pyrimidin-3-yl}acetamide as a white powder (118 mg, 60%).

Mp: 120 - 122 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.03 (d, *J* = 2.3 Hz, 1H), 7.89 (dd, *J* = 8.6, 2.3 Hz, 1H), 6.94 (d, *J* = 8.6 Hz, 1H), 6.49 (d, *J* = 0.7 Hz,1H), 3.90 (s, 2H), 3.87 (s, 3H), 3.46 (q, *J* = 7.2 Hz, 2H), 3.39 (q, *J* = 7.1 Hz, 2H), 2.75 (d, *J* = 0.7 Hz, 3H), 2.52 (s, 3H), 1.36 (s, 12H), 1.18 (t, *J* = 7.2 Hz, 3H), 1.10 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 170.0, 164.4, 157.3, 155.1, 147.7, 144.7, 136.9, 133.2, 125.8, 110.5, 108.1, 100.9, 83.4, 56.0, 42.3, 40.7, 28.1, 24.9, 24.7, 17.0, 14.4, 13.1 (Signal due to carbon bearing the boron is not observed); **IR** (*ν,* cm^{-1}): 2974, 1649, 1585, 1398, 1249, 1140, 1067, 1024, 859, 759. **HRMS** (ESI) for $C_{27}H_{38}{}^{11}BN_4O_4$ $[M+H]^+$ requires m/z 493.2978, found 493.2978.

(6-Iodo-2-(4'-dimethylamino-)phenyl-imidazo[1,2-*a*]pyridine): IMPY

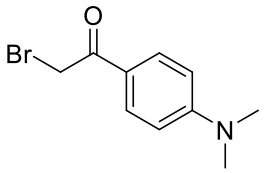
2,2-Dibromo-1-(4-(dimethylamino)phenyl)ethan-1-one



Prepared according to literature procedure.[6] Bromine (1.1 mL, 9.0 mmol) was added dropwise to a solution of 1-(5-(dimethylamino)phenyl-2-yl)ethanone (2.9 g, 18 mmol) in concentrated H_2SO_4 (95%, 18 mL) at 0 °C. The reaction mixture was stirred overnight at room temperature and subsequently poured into ice water and neutralized with 3% NaOH. The aqueous phase was extracted with EtOAc (3 x 70 mL). The organic layers were combined, washed with brine (3 x 70 mL), dried and concentrated in vacuo. Purification of the crude product by column chromatography using EtOAc/hexanes (1/9) afforded 2,2-dibromo-1-(5- (dimethylamino)pyridin-2-yl)ethanone as a yellow-green solid (5 g, 15.6 mmol, 87%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96 – 7.92 (m, 2H), 6.67 (s, 1H), 6.65 – 6.61 (m, 2H), 3.07 (s, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 184.3, 154.3, 132.4, 117.7, 110.9, 77.5, 77.2, 76.8, 40.7, 40.2. Data consistent with literature values.[7]

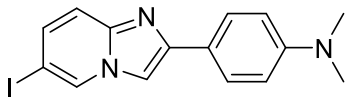
2-Bromo-1-(4-(dimethylamino)phenyl)ethan-1-one



Prepared according to literature procedure.[7] To a solution of 2,2-dibromo-1-(5-(dimethylamino)pyridin- 2-yl)ethanone (3.0 g, 9.3 mmol) in 50 mL of anhydrous THF was added triethylamine (1.4 mL, 10 mmol) and diethyl phosphite (1.3 mL, 10 mmol) at 0 °C. The reaction was stirred overnight at room temperature. The mixture was diluted with ethyl acetate and the aqueous phase further extracted with ethyl acetate (3 x 70 mL). The combined organic layers were washed with brine (3 x 50 mL), dried and concentrated in vacuo. Purification of the crude product via column chromatography using EtOAc/hexanes (1:9) afforded 2-bromo-1-(4-(dimethylamino)phenyl)ethan-1-one as a green solid (1.8 g, 7.5 mmol, 80%). Data matched that of the literature.[7]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.07 (d, *J* = 1.5 Hz, 1H), 7.98 (d, *J* = 4.4 Hz, 1H), 6.97 (dd, = 4.4, 1.5 Hz, 1H), 4.80 (s, 2H), 3.10 (s, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 189.6, 154.2, 132.0, 121.6, 110.9, 40.3, 31.3. Data consistent with literature values.[7]

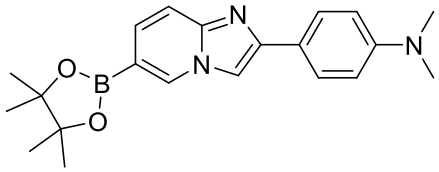
4-(6-Iodoimidazo[1,2-*a*]pyridin-2-yl)-*N*,*N*-dimethylaniline



Prepared according to literature procedure.[7] A mixture of 2-bromo-1-(4-(dimethylamino)phenyl)ethan-1-one (484 mg, 2 mmol) and 2-amino-5-iodopyridine (440 mg, 2 mmol) in EtOH (25 mL) was stirred at reflux for 2 hours. The mixture was allowed to cool and $NaHCO_3$ (250 mg) was then added. Subsequently the mixture was stirred at reflux for 4 hours before being cooled and the precipitate was filtered and washed with cold EtOH giving 4-(6-iodoimidazo[1,2-*a*]pyridin-2-yl)-*N*,*N*-dimethylaniline as a green solid (280 mg, 0.7 mmol, 39% yield).

Mp 230 – 232 °C.**^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.90 (s, 1H), 7.39 – 7.37 (m, 2H), 6.96 (d, *J* = 9.3 Hz, 1H), 6.85 (dd, *J* = 9.3, 1.4 Hz, 1H), 6.36 – 6.34 (m, 2H), 2.58 (s, 6H).**^{13}C NMR** (126 MHz, $CDCl_3$): δ = 150.5, 147.0, 144.1, 131.8, 130.0, 127.0, 121.2, 118.0, 112.4, 106.2, 74.4, 40.4; **IR** (*v,* cm^{-1}): 2981, 2360, 1615, 1512, 1383, 1196, 950, 820, 671; **HRMS** (ESI) for $C_{15}H_{14}IN_3$ $[M+H]^+$ requires m/z 364.0305, found 364.0312. Data consistent with literature values.[8]

***N*,*N*-Dimethyl-4-(6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)imidazo[1,2-*a*]pyridin-2-yl)aniline**

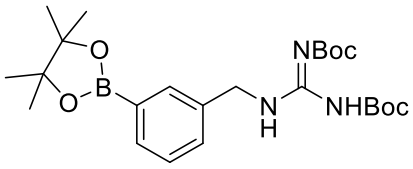


To a solution of 4-(6-iodoimidazo[1,2-*a*]pyridin-2-yl)-*N*,*N*-dimethylaniline (73 mg, 0.2 mmol) in THF (2 mL) at - 78 °C was added 2.5 M nBuLi (96 µL, 0.24 mmol). After 10 minutes 2-Isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (53 µL, 0.26 mmol) was added dropwise. The reaction was left to stir for 30 minutes before addition of NH_4Cl (10 mL). The aqueous layer was extracted with dichloromethane (3 x 20 mL), washed with brine (3 x 20 mL), dried and concentrated in vacuo. The reaction was subjected to column chromatography using MeOH:DCM (2:8) as the eluent affording *N*,*N*-dimethyl-4-(6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)imidazo[1,2-*a*]pyridin-2-yl)aniline as an off white solid (58 mg, 1.6mmol, 80% yield).

Mp: 219 – 222 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.51 (s, 1H), 7.85 (d, *J* = 8.7 Hz, 2H), 7.70 (s, 1H), 7.57 (d, *J* = 9.0 Hz, 1H), 7.43 (d, *J* = 9.0 Hz, 1H), 6.79 (d, *J* = 8.7 Hz, 2H), 3.00 (s, 6H), 1.37 (s, 12H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 149.4, 145.7, 145.2, 131.5, 127.6, 126.0, 120.6, 115.0, 111.4, 105.2, 83.2, 39.5, 23.9 (Signal due to carbon bearing the boron is not observed); **IR** (*v,* cm^{-1}): 2980, 2360, 1614, 1538, 1493, 1383, 1271, 965, 948, 820; **HRMS** (ESI) for $C_{21}H_{26}BN_3O_2$ $[M+H]^+$ requires m/z 364.2191, found 364.2183.

***meta*-Iodobenzylguanidine: mIBG**

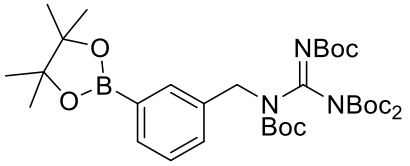
***tert*-Butyl-*N*-[(1*E*)-{[(*tert*-butoxy)carbonyl]imino}({[3-(tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]methyl}amino)methyl]carbamate.**



To a stirred solution of (3-(3,3,4,4-tetramethylborolan-1-yl)phenyl)methanaminium chloride (1.00 g, 3.8 mmol) in DCM (10 mL) was added triethylamine (1.00 mL, 7.6 mmol). After 5 minutes stirring, *N,N*'-bis(*tert*-butoxycarboyl)-*N*''-triflylguanidine (1.45 g, 3.8 mmol) was added before leaving the reaction mixture to stir for 30 min. Upon completion, the excess solvent was removed *in vacuo* before adding water (50 mL) and extracting the organic layer with DCM (3 × 30 mL). The organic layers were combined, washed with water (2 × 50 mL) and brine (50 mL), dried with $MgSO_4$, filtered and the solvent removed *in vacuo* affording *tert*-butyl-*N*-[(1*E*)-{[(*tert*-butoxy)carbonyl]imino}({[3-(tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]methyl}amino)methyl]carbamate as a white solid (1.75 g, 99%).

Mp: 100 – 101°C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 11.54 (bs, 1H), 8.52 (t, 1H), 7.76 – 7.71 (m, 2H), 7.43 (dt, 1H, *J* = 7.6, 1.4 Hz), 7.35 (t, 1H, *J* = 7.6 Hz), 4.62 (d, 2H, *J* = 5.1 Hz), 1.52 (s, 9H), 1.46 (s, 9H), 1.34 (s, 12H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 163.8, 156.2, 153.3, 136.7, 134.6, 134.3, 131.2, 128.3, 84.0, 83.2, 79.5, 45.2, 28.4, 28.2, 25.0 (Signal due to carbon bearing the boron is not observed). Data consistent with literature values.[9]

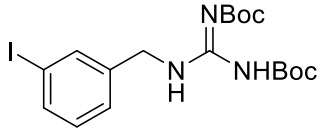
***tert*-Butyl *N*-[(1*Z*)-{bis[(*tert*-butoxy)carbonyl]amino}({[(*tert*butoxy)carbonyl]({[3-(tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]methyl})amino})methylidene] carbamate (1n):**



To a stirred solution of commercially available (3-(3,3,4,4-tetramethylborolan-1-yl)phenyl)methanaminium chloride (1.00 g, 3.8 mmol) in DCM (10 mL) was added triethylamine (1.00 mL, 7.6 mmol). After 5 minutes stirring, N,N'-bis(tert-butoxycarboyl)-N''-triflylguanidine (1.45 g, 3.8 mmol) was added before leaving the reaction mixture to stir for 30 min. Upon completion, the excess solvent was removed in vacuo before adding water (50 mL) and extracting the organic layer with DCM (3 × 30 mL). The organic layers were combined, washed with water (2 × 50 mL) and brine (50 mL), dried with MgSO4, filtered and the solvent removed in vacuo affording *tert*-butyl-N-[(1E)-{[(tertbutoxy)carbonyl]imino}({[3-(tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]methyl}amino) methyl]carbamate as a white solid (1.75 g, 99%).

^{1}H NMR (400 MHz, CDCl3): δ = 11.54 (bs, 1H), 8.52 (s, 1H), 7.76 – 7.71 (m, 2H), 7.43 (dt, 1H, J = 7.6, 1.4 Hz), 7.35 (t, 1H, J = 7.6 Hz), 4.62 (d, 2H, J = 5.1 Hz), 1.52 (s, 9H), 1.46 (s, 9H), 1.34 (s, 12H); **^{13}C NMR** (100 MHz, CDCl3): δ = 163.8, 156.2, 153.3, 136.7, 134.6, 134.3, 131.2, 128.3, 84.0, 83.2, 79.5, 45.2, 28.4, 28.2, 25.0 (note: C_{Ar}-B was not observed). Data consistent with literature values.[9]

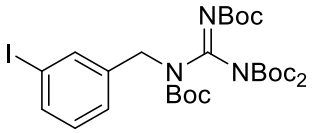
***tert*-Butyl{(*Z*)-[(3-iodobenzyl)amino][(*tert*-butoxycarbonyl)amino]methylidene} carbamate**.



To a stirred solution of 3-iodobenzylamine (0.50 g, 1.05 mmol) in DCM (10 mL) was added triethylamine (0.43 mL, 3.15 mmol). After 5 minutes stirring, *N,N*′-bis(*tert*-butoxycarboyl)-*N*′′-triflylguanidine (0.411 g, 1.05 mmol) was added before leaving the reaction mixture to stir for 30 mins. Upon completion, the excess solvent was removed *in vacuo* before adding water (10 mL) and extracting the organic layer with DCM (3 × 10 mL). The organic layers were combined, washed with water (2 × 10 mL) and brine (10 mL), dried with $MgSO_4$, filtered and the solvent removed *in vacuo* affording the title compound *tert*-Butyl{(*Z*)-[(3-iodobenzyl)amino][(*tert*-butoxycarbonyl)amino]methylidene} carbamate as a white solid (0.40 g 81%).

Mp: 95 – 97 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 11.53 (s, 1H), 8.59 (bs, 1H), 7.66 (s, 1H), 7.61 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.27 (d, *J* = 7.8, 1H), 7.07 (t, *J* = 7.8 Hz, 1H), 4.57 (d, *J* = 5.4 Hz, 2H), 1.51 (s, 9H), 1.48 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 163.6, 156.3, 153.3, 139.9, 137.0, 136.8, 130.6, 127.2, 94.7, 83.5, 79.7, 44.2, 28.4, 28.2; **IR** (*v,* cm^{-1}): 2980, 1720, 1639, 1617, 1457, 1327, 1157, 1133; **HRMS** (ESI) for $C_{18}H_{27}N_3O_4{}^{127}I$ $[M+H]^+$ requires 476.1040 found 476.1039.

***tert*-Butyl-*N*-[(1*Z*)-{bis[(*tert*-butoxy)carbonyl]amino}({[(tert-butoxy)carbonyl][(3-iodophenyl) methyl]amino})methylidene]carbamate**.

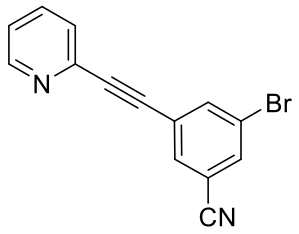


To a round bottom flask was added, *tert*-butyl{(*Z*)-[(3-iodobenzyl)amino][(*tert*-butoxycarbonyl)amino]methylidene}carbamate (0.61 g, 1.28 mmol), di-*tert*-butyl dicarbonate (0.89 g, 5.12 mmol), dimethyl amino pyridine (0.47 g, 3.84 mmol), triethylamine (0.71 mL, 5.12 mmol) and THF (10 mL). The reaction was then left to stir at room temperature 17 hours. Upon completion, the solvent was removed *in vacuo* and the product purified via flash column chromatography (8:2 cyclohexane: EtOAc) affording the title compound *tert*-butyl-*N*-[(1*Z*)-{bis[(*tert*-butoxy)carbonyl]amino}({[(*tert*-butoxy)carbonyl][(3-iodophenyl)methyl]amino})methylidene] carbamate as a colourless oil (0.59 g, 68%).

Mp: 61 – 63 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.74 (t, *J* = 1.5 Hz, 1H), 7.61 – 7.53 (m, 1H), 7.39 (d, *J* = 7.8, 1H), 7.02 (t, *J* = 7.8 Hz, 1H), 4.96 (s, 2H), 1.49 (s, 9H), 1.46 (s, 18H), 1.41 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 157.4, 151.2, 147.4, 144.3, 140.0, 136.9, 136.4, 130.1, 127.4, 94.1, 84.2, 83.9, 82.2, 49.5, 28.1, 28.0, 28.0; **IR** (*v,* cm^{-1}): 2980, 1808, 1727, 1652, 1368, 1279, 1252, 1127, 1102; **HRMS** (ESI) for $C_{28}H_{42}N_3O_8{}^{127}I^{23}Na$ $[M+Na]^+$ requires 698.1909 found 698.1906.

3-Iodo-5-(pyridine-2-ylethynyl)benzonitrile: IPEB

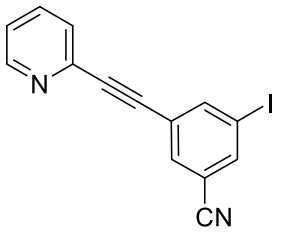
3-Bromo-5-(pyridine-2-ylethynyl)benzonitrile



A mixture slurry of 2-ethynylpyridine (0.5 mL, 5.0 mmol), 3,5-dibromobenzonitrile (3.9 g, 15.0 mmol), trans-dichlorobis(triphenyl-phosphine)palladium (350 mg, 0.5 mmol), CuI (475 mg, 2.5 mmol) and PPh_3 (262 mg, 1.0 mmol) in Et_3N (14.0 mL, 99.9 mmol) was heated in a Schlenk tube at 80 °C for 1.5 h. After cooling to rt the resulting reaction mixture was diluted with sat. NH_4Cl (100 mL) and extracted with Et_2O (3 x 80 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated in vacuum. The residue was dissolve in hexane/EtOAc (4/1) and filtered through a small silica-gel column (washed several times) and concentrated in vacuum. The crude product was purified by crystallization from hot hexane/EtOAc (placed in the freezer) to afford the product as a white solid (852 mg, 60%).

^{1}H NMR (400 MHz, CDCl3): δ = 8.65 (ddd, J = 4.9, 1.8, 1.0 Hz, 1H), 7.95 (dd, J = 1.9, 1.5 Hz, 1H), 7.80 – 7.76 (m, 2H), 7.73 (td, J = 7.7, 1.8 Hz, 1H), 7.54 (dt, J = 7.8, 1.1 Hz, 1H), 7.31 (ddd, J = 7.7, 4.9, 1.2 Hz, 1H); **^{13}C NMR** (126 MHz, CDCl3): δ = 150.4, 142.2, 138.9, 136.4, 134.7, 133.8, 127.6, 125.7, 123.8, 122.9, 116.6, 114.5, 92.0, 84.9. Data consistent with literature values. Data consistent with literature values.[9]

3-Iodo-5-(pyridine-2-ylethynyl)benzonitrile

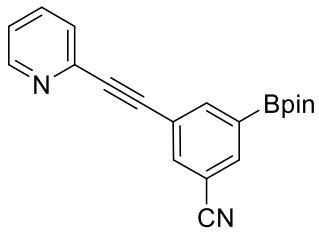


To a dried schlenk tube under an atmosphere of argon was added, 3-Bromo-5-(pyridine-2-ylethynyl)benzonitrile (200 mg, 0.71 mmol), copper iodide (6 mg, 0.032 mmol), *N*,*N*'-dimethylethylenediamine (10 µL, 0.071 mmol) and sodium iodide (212 mg, 1.41 mmol). The reaction flask was then heated to 90 °C before dioxane (14 mL) was added. The reaction was then left to stir at 90 °C overnight. After stirring for 16 hr, the reaction was cooled and filtered through celite. To the crude mixture was added H_2O (30 mL) before extraction was performed with DCM (3 x 30 mL). The organic layers were then combined, dried with $MgSO_4$ and excess solvent removed *in vacuo*. The crude product was initially purified *via* flash column chromatography (10 : 3 Petane: EtOAc) affording a mixture of 3-bromo-5-(pyridine-2-ylethynyl)benzonitrile and 3-Iodo-5-(pyridine-2-ylethynyl)benzonitrile after which reverse phase HPLC purification was carried out affording the title compound as a white solid (55 mg, 23%, 0.17 mmol)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.66 (d, *J* = 5.0 Hz, 1H), 8.17 (s, 1H), 7.97 (s, 1H), 7.82 (s, 1H), 7.74 (td, *J* = 7.5. 1.0 Hz, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.32 (dd, *J* = 7.5, 5.5 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ =

150.7, 145.0, 142.5, 140.6, 136.8, 134.6, 127.8, 125.8, 124.0, 116.7, 114.8, 93.9, 92.2, 85.2. Data consistent with literature values.[10]

3-(Pyridin-2-ylethynyl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile (1o):

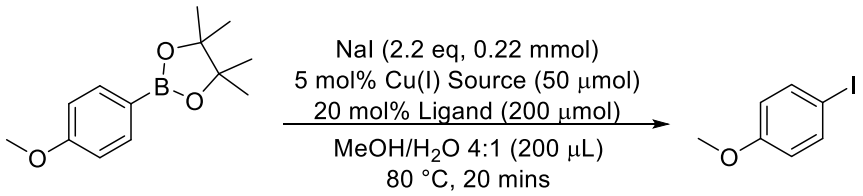


Nitrogen was bubbled through a mixture of 3-bromo-5-(pyridin-2-ylethynyl)benzonitrile (640.0 mg, 2.26 mmol), bis(pinacolato)diboron (631 mg, 2.49 mmol), potassium acetate (887.0 mg, 9.04 mmol), dichloro[1,1'-bis(diphenylphosphino)ferrocene]-palladium(II) dichloromethane adduct (110.8 mg, 0.14 mmol) and N,N-dimethylacetamide (7 mL) for 1 h. Then the reaction was heated at 110° C for 40 min, cooled to room temperature and diluted with H_2O (100 mL), and extracted with EtOAc (4 x 35 mL). The combined organic extracts were washed with brine (35 mL), dried ($MgSO_4$), filtered, and concentrated in vacuum to give a residue that was dissolve in Et_2O/hexane (5/1) and filtered through a small silica-gel column. The filtrate was concentrated in vacuum and the residue was purified by crystallization from hot acetonitrile (placed in the freezer) to afford the product as a white solid (332 mg, 45%).

^{1}H NMR (400 MHz, CD_2Cl_2): δ = 8.65 – 8.56 (m, 1H), 8.21 (s, 1H), 8.04 (t, *J* = 1.3 Hz, 1H), 7.92 (t, *J* = 1.6 Hz, 1H), 7.72 (td, *J* = 7.8 Hz, 1.8, 1H), 7.55 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.29 (ddd, *J* = 7.5, 4.9, 1.2 Hz, 1H), 1.35 (s, 12H); **^{13}C NMR** (126 MHz, CD_2Cl_2): δ = 150.6, 143.1, 142.3, 138.4, 137.4, 136.6, 127.8, 123.7, 123.7, 118.3, 113.0, 91.0, 86.4, 85.2, 25.0 (note: the aromatic carbon bound to the BPin was not observed). Data consistent with literature values.[9]

2.0 Optimisation for the Iodination of Aryl Boron Reagents

2.1 Screening of Copper(I) Sources

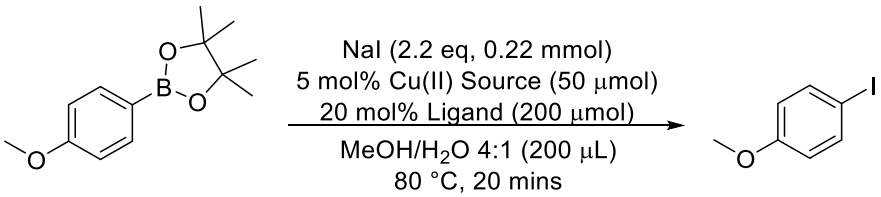


0.1 mmol

Copper (I) Source	Ligand	NMR Yield/%[a]
Cu_2O	1,10-Phenanthroline	58
$Cu(OTf)(C_6H_6)$	1,10-Phenanthroline	4
$Cu(OTf)(C_6H_6)$	-	2
$Cu(OTf)(MeCN)_4$	1,10-Phenanthroline	24
$Cu(OTf)(MeCN)_4$	-	2
Cu(TC)	1,10-Phenanthroline	24

[a]NMR yields measured using *tert*-butyl methyl ether as internal standard.

2.2 Screening of Copper(II) Sources

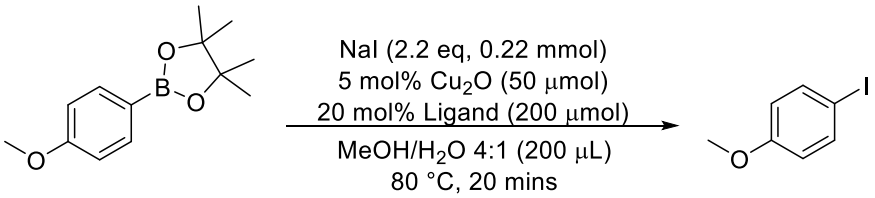


0.1 mmol

Copper (II) Source	Ligand	NMR Yield/%[a]
$Cu(OAc)_2$	-	8
$Cu(OAc)_2$	1,10-Phenanthroline	48
$Cu(OTf)_2(py)_4$	1,10-Phenanthroline	0
$Cu(OTf)_2$	1,10-Phenanthroline	5
$Cu(OCOCF_3)_2$	1,10-Phenanthroline	60

[a]NMR yields measured using *tert*-butyl methyl ether as internal standard.

2.3 Screening of Ligands



0.1 mmol

Ligand	NMR Yield/%[a]
1,10-Phenanthroline	58
1,2-Bis(diphenylphosphino)ethane	0
2,2'-bipyridine	7
Bathophenanthroline	-
Pyridine	2
TMEDA	3

[a]NMR yields measured using *tert*-butyl methyl ether as internal standard.

3.0 Radiochemistry

3.1 General Information and Procedures

General information for radiochemical procedures at the Chemistry Research Laboratory, University of Oxford. Sodium [^{123}I]Iodide was produced by GE Healthcare as none carrier added [^{123}I]Sodium Iodide in 0.05 M NaOH. In each case this was diluted in methanol until the total volume came to 200 µL. HPLC analysis was performed with a Dionex Ultimate 3000 dual channel HPLC system equipped with shared autosampler, parallel UV-detectors and with Flowram analog output. Radio-TLC was performed on Merck Kiesegel 60 F254 plates. Analysis was performed using a LabLogic NaI/PMT-radiodetectors. All radiochemical conversions quoted are decay corrected and are calculated by radioTLC, taking into account the radiochemical purity observed by radio-HPLC.

3.1.1 General procedure for the ^{123}I-Iodination of Aryl Bpin or B(OH)$_2$ substrates (2a – 2k):

To a V-vial containing a magnetic stirrer bar, arylBpin (15 µmol) or arylB(OH)$_2$ (15 µmol) and [^{123}I]NaI (ca. 4 MBq, 5 µL MeOH approx.) was added Cu(OCOCF$_3$)$_2$ (0.30 µmol), 1,10-phenanthroline (0.30 µmol) in MeOH:H$_2$O (4:1, 200 µL) from a stock solution. The reaction vial was then heated to 80 °C for 20 minutes. The reaction was quenched by addition of 10 mol% sodium thiosulfate (200 µL) and MeCN (100 µL). An aliquot was removed for analysis by radioTLC and HPLC to calculate the radiochemical conversion (RCC) and purity respectively.

3.1.2 Procedure for the ^{123}I-Iodination of ArylBpin Tracers: [^{123}I]DPA-713, [^{123}I]IMPY, Boc Protected [^{123}I]MIBG and [^{123}I]IPEB (5l – 5o):

The optimised method started with the preparation of a V-vial containing a magnetic stirrer bar and [^{123}I]NaI (ca. 4 MBq, 5 µL MeOH approx.) to which arylBpin (5 µmol), Cu(OCOCF$_3$)$_2$ (0.25 µmol), 1,10-phenanthroline (0.25 µmol) in MeOH:H$_2$O (4:1, 200 µL). The reaction vial was then heated to 80 °C for 20 minutes. The reaction was quenched by addition of 10 mol% sodium thiosulfate (400 µL) and MeCN (100 µL). An aliquot was removed for analysis by thin-layer chromatography (radioTLC) and high performance liquid chromatography (radioHPLC) to calculate the radiochemical conversion and purity respectively.

3.1.3 Procedure for the ^{123}I-Iodination and determination of RCY of ArylBpin Tracers: [^{123}I]DPA-713, [^{123}I]IMPY, and [^{123}I]IPEB (5l – 5o):

The optimised method started with the preparation of a V-vial containing a magnetic stirrer bar, arylBpin (5 µmol) and [^{123}I]NaI (ca. 4 – 36 MBq, 5 - 15 µL MeOH approx.) to which Cu(OCOCF$_3$)$_2$ (0.25 µmol), 1,10-phenanthroline (0.25 µmol) in MeOH:H$_2$O (4:1, 200 µL). The reaction vial was then heated to 80 °C for 20 minutes. The reaction was diluted in H$_2$O (6 mL) and loaded onto a C-18 SepPak Plus cartridge. This was then flushed with H$_2$O (2 mL) and air (2 mL)followed by elution of the ^{123}I-iodinated product with MeCN (2 mL). The radiochemical yield was then calculated as a percentage of activity (MBq) found in the MeCN elute compared to the starting activity (MBq). An aliquot was removed for analysis by HPLC to calculate the radiochemical yield and purity respectively.

3.1.4 Procedure for the ^{123}I-iodination, deprotection and determination of RCY of [^{123}I]MIBG (5o):

The optimised method started with the preparation of a V-vial containing a magnetic stirrer bar, arylBpin (5 µmol) and [^{123}I]NaI (ca. 3 – 7 MBq, 5 µL MeOH approx.) to which Cu(OCOCF$_3$)$_2$ (0.25 µmol), 1,10-phenanthroline (0.25 µmol) in 4:1 MeOH:H$_2$O (200 µL). The reaction vial was then heated to 80 °C for 20 minutes. The reaction was diluted in H$_2$O containing 10% MeOH (6 mL) and loaded onto a C-18 SepPak Plus cartridge and flushed with H$_2$O:MeOH (9:1, 6 mL). [^{123}I[MIBG was then eluted with

DCM (2 x 1 mL) followed by air (2 x 1 mL). At this point the radiochemical yield was calculated as a percentage of activity (MBq) found in the DCM collected compared to the starting activity (MBq). Following this, the DCM was removed at 50 °C under a stream of N_2. Once dry, either; 300 µL of 57% HI was added and the reaction stirred for 10 minutes at 125 °C, or 300 µL of TFA was added and the reaction stirred for 10 minutes at 80 °C or. After 10 minutes, an aliquot was removed for analysis by high performance liquid chromatography (radioHPLC) to calculate the conversion of the deprotection step and the purity respectively.

3.1.5 HPLC gradient A: water/acetonitrile, 1 mL/min, Waters Nova-Pak C18 Column, 4 µm, 3.9 x 150 mm

0-1 min (5% MeCN) isocratic
1-10 min (5% MeCN to 95% MeCN) linear increase
10-14 min (95% MeCN) isocratic
14-15 min (95% MeCN to 5% MeCN) linear decrease
15-17 min (5% MeCN) isocratic

3.1.6 HPLC gradient B: water/acetonitrile containing 0.1 mg/mL TFA, 1 mL/min, Waters Nova-Pak C18 Column, 4 µm, 3.9 x 150 mm

0-2 min (5% MeCN containing 0.1 mg/mL TFA) isocratic
1-10 min (5% MeCN containing 0.1 mg/mL TFA to 95% MeCN containing 0.1 mg/mL TFA) linear increase
10-14 min (95% MeCN containing 0.1 mg/mL TFA) isocratic
14-15 min (95% MeCN containing 0.1 mg/mL TFA to 5% MeCN containing 0.1 mg/mL TFA) linear decrease
15-17 min (5% MeCN containing 0.1 mg/mL TFA) isocratic

3.1.7 Calculation of Radiochemical Yields for [^{123}I]DPA-713, [^{123}I]IMPY, and [^{123}I]IPEB:

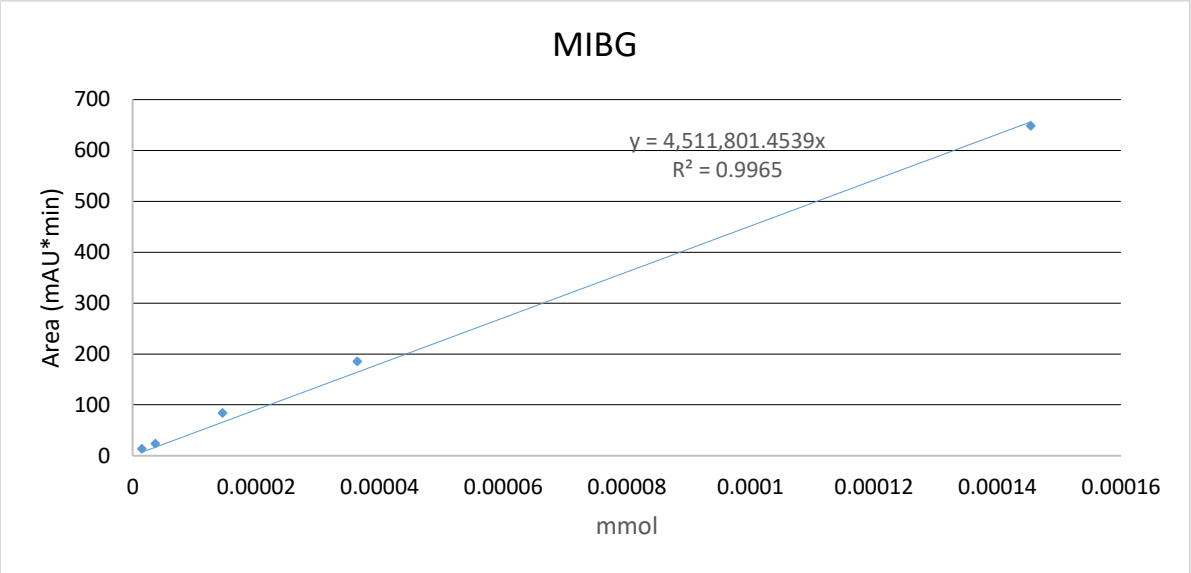
Compound	**Starting Activity (MBq)**	**MeCN Flush Activity (MBq)**	**H_2O Flush Activity (MBq)**	**QMA Activity (MBq)**	**Radiochemical Purity (%)**	**Radiochemical Yield (%)***
[^{123}I]DPA-713	36.5	32.0	0.7	1.0	> 99%	88%
[^{123}I]IMPY	15.2	11.8	1.5	1.7	> 99%	78%
[^{123}I]IPEB	15.9	8.4	2.8	0.0	> 99%	53%
[^{123}I]IPEB	4.9	2.2	2.7	0.0	> 99%	45%

3.1.8 Calculation of Radiochemical Yields for Boc Protected [^{123}I]MIBG and [^{123}I]MIBG:

Starting Activity (MBq)	MeOH Flush Activity (MBq)	H_2O Flush Activity (MBq)	Radiochemical Purity (%)	Radiochemical Yield* (%) (Protected Species)	Deprotection Condition	Conversion (%)	Radiochemical Conversion (%) ([^{123}I]MIBG Salt)
15.8	7.1	3.5	> 99	45	-	-	-
8.1	3.6	1.1	-	44	57% HI (300 µL), 125 °C, 10 mins	79	35
41.9	18.1	11.1	-	43	TFA (300 µL), 80 °C, 10 mins	86	37

*Radiochemical yield calculated as a percentage of activity in the MeOH or DCM flush (MBq) compared to the starting activity. Loss in activity due to transfer losses.

3.2 Specific Activity



Injection Number	Activity (MBq)	Area (mAu*min)	Mmol injected	Specific Activity (GBq)
1	0.6	0.1368	3.03205E-08	19.8

3.3 Radio-HPLC Tracers

HPLC Traces:

Radio-HPLC traces with authentic UV references (blue line) overlaid Crude Radio-HPLC (black line) traces of the crude mixture following the general procedure, with authentic UV references overlaid are shown below. The solid blue line indicates the UV trace for cold reference material and the solid black line is the crude radio-HPLC trace. All samples were run using HPLC gradient A unless otherwise specified. In each case, a table presenting all individual radiochemical conversions is presented. For each pair of reactions, only one HPLC run is carried out for which the purity of the second reaction is then assumed to be equal.

3.3.1 Radiochemical Conversion:

To determine the radiochemical conversion (RCC) the reaction mixture is quenched with 10% sodium thiosulfate, after which an aliquot is analysed by radio-TLC and radio-PHLC. The conversion of Na[^{123}I]I can be determined by radio-TLC, choosing a suitable eluent and comparing the activity on the base-line, from unreacted Na[^{123}I]I, with the activity from the ^{123}I-containing organic material at higher R_f. The RCC can then be determined by taking into account the purity of the ^{123}I-containing product. This is usually determined as the average of at least two experiments, with the error defined as the standard deviation of the mean and is corrected for decay of ^{123}I.

3.3.2 Equation used for the calculation of the standard deviation of mean:

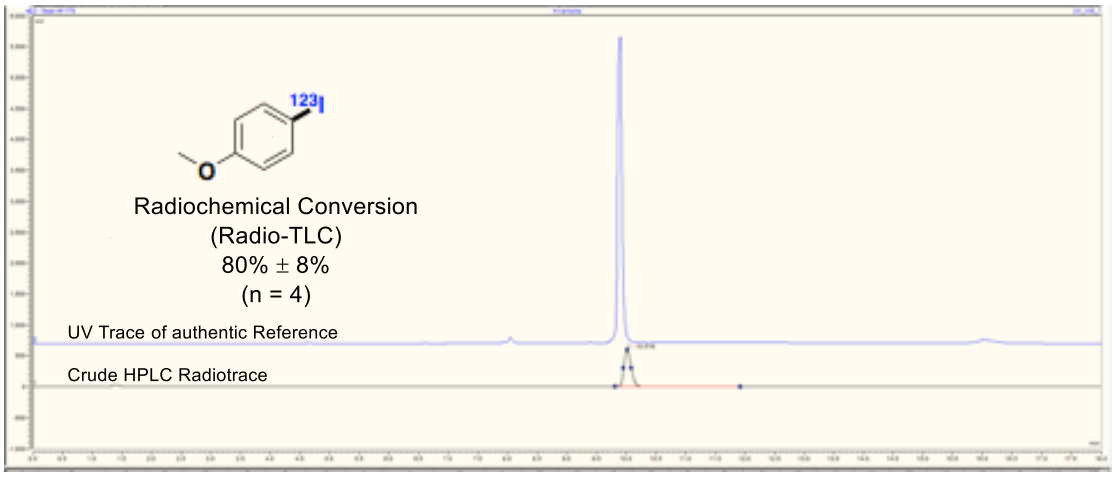
$$Mean = \bar{x} = \frac{1}{n}\sum_{i=1}^{n} x_i = \frac{1}{n}(x_1 + x_2 + \cdots + x_n)$$

$$Standard\ Deviation\ (of\ the\ population) = \sigma = \sqrt{\frac{1}{n}\sum_{i=1}^{n}(x_i - \bar{x})^2}$$

$$Standard\ Deviation\ of\ the\ Mean = \frac{\sigma}{\sqrt{n}}$$

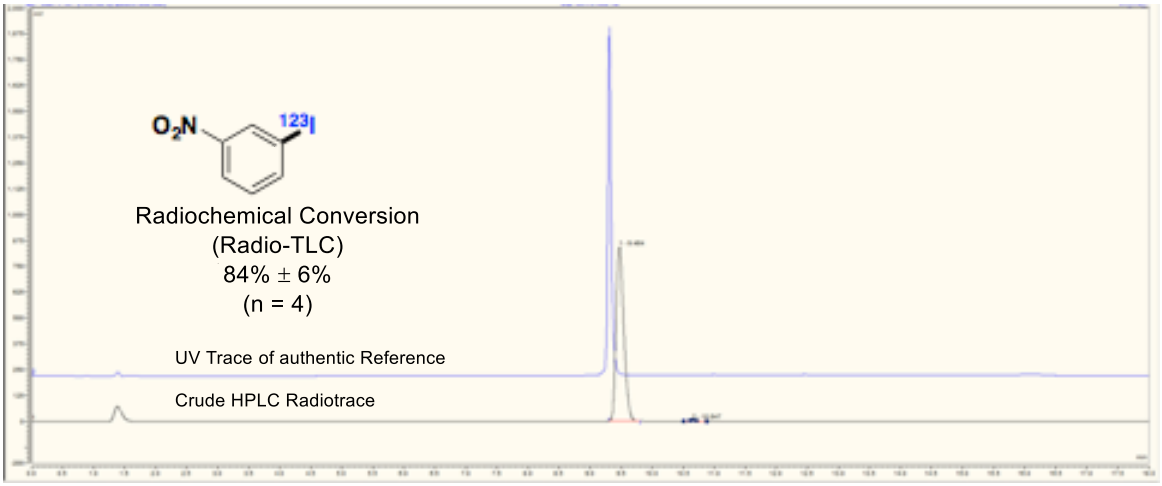
3.3.3 HPLC Traces Derived from Boron Pinacol Ester Starting Material (2a – 2k):

Radiotrace and RCC Calculation for 5a:



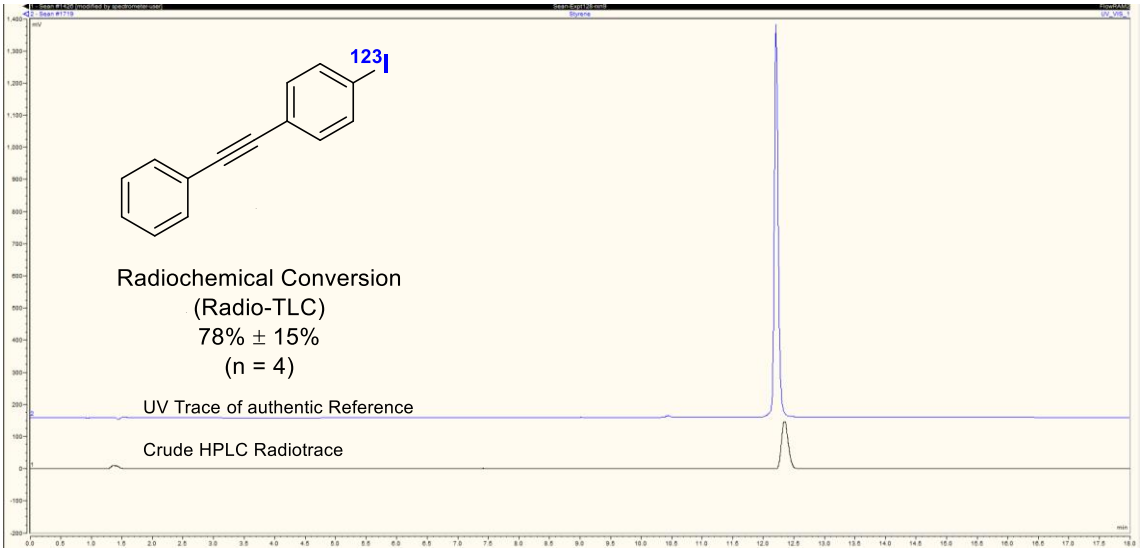
Reaction Number	Radio-TLC (%)	Radiochemical Purity (%)	Radiochemical Conversion (%)
1	56%	>99%	56%
2	89%	-	89%
3	87%	>99%	87%
4	87%	-	87%
RCC and Standard Deviation of the Mean			80% ± 8%

Radiotrace and RCC Calculation for 5b:



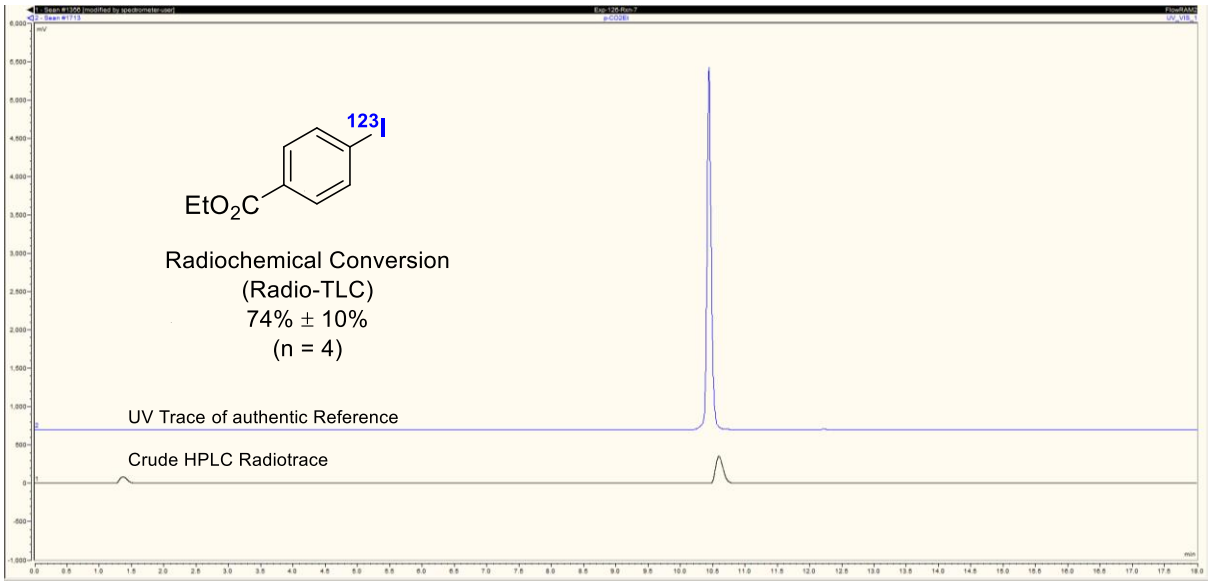
Reaction Number	Radio-TLC (%)	Radiochemical Purity (%)	Radiochemical Conversion (%)
1	67%	>99%	67%
2	89%	-	89%
3	97%	>99%	97%
4	84%	-	84%
RCC and Standard Deviation of the Mean			84% ± 6%

Radiotrace and RCC Calculation for 5c:



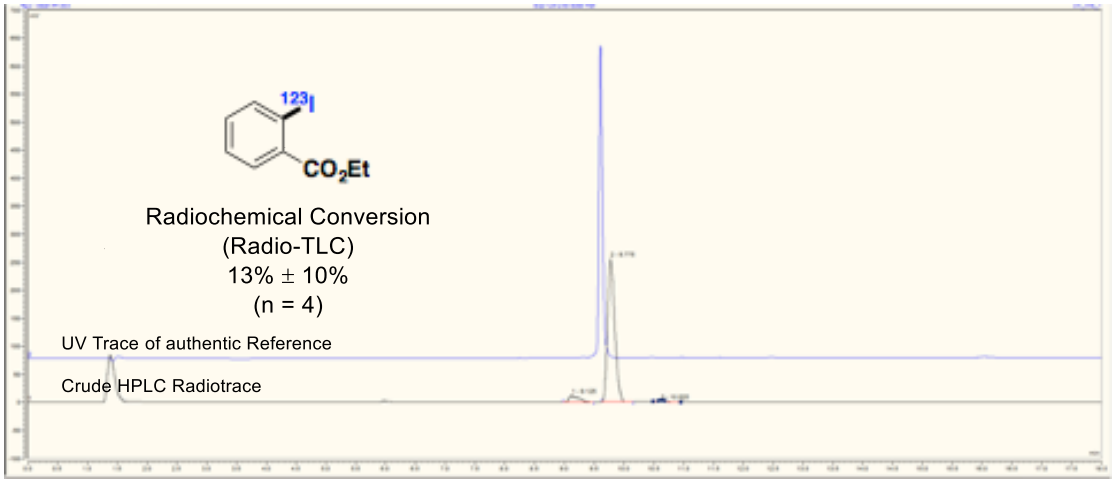
Reaction Number	Radio-TLC	Radiochemical Purity	RCC
1	81%	>99%	81%
2	65%	-	65%
3	93%	>99%	93%
4	93%	-	93%
RCC and Standard Deviation of the Mean			78% ± 15%

Radiotrace and RCC Calculation for 5d:



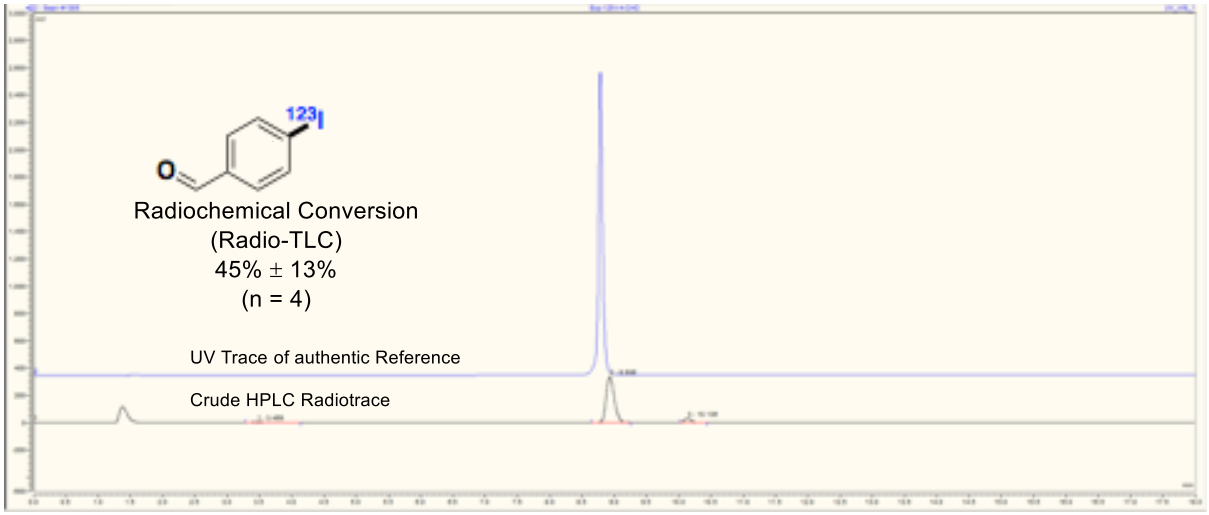
Reaction Number	Radio-TLC (%)	Radiochemical Purity (%)	Radiochemical Conversion (%)
1	46%	>99%	46%
2	92%	-	92%
3	72%	>99%	72%
4	87%	-	87%
RCC and Standard Deviation of the Mean			74% ± 10%

Radiotrace and RCC Calculation for 5e:



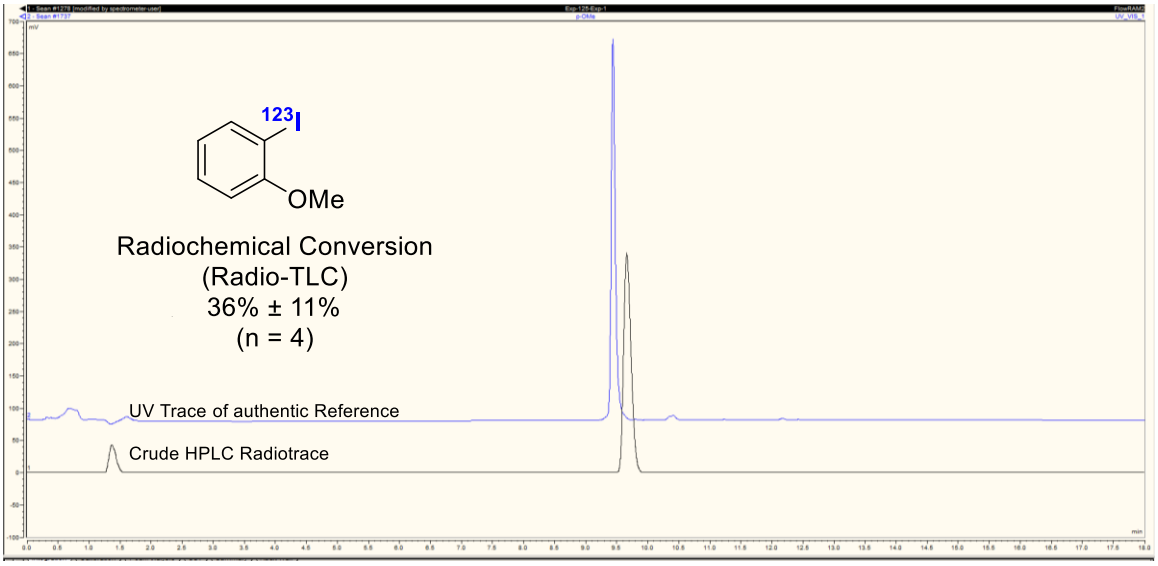
Reaction Number	Radio-TLC (%)	Radiochemical Purity (%)	Radiochemical Conversion (%)
1	0%	>99%	0%
2	5%	-	5%
3	46%	94%	43%
4	2%	-	2%
RCC and Standard Deviation of the Mean			13% ± 10%

Radiotrace and RCC Calculation for 5f:



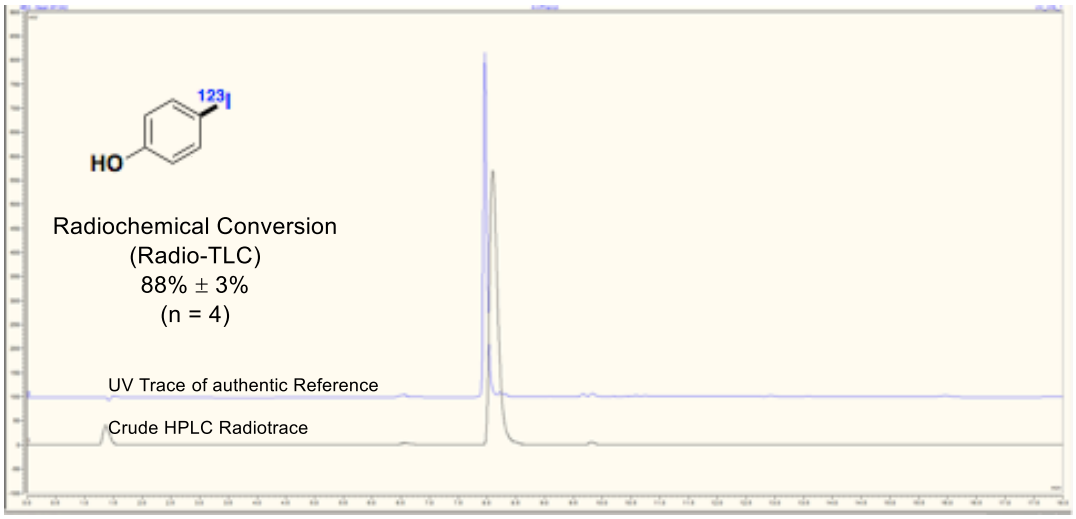
Reaction Number	Radio-TLC (%)	Radiochemical Purity (%)	Radiochemical Conversion (%)
1	37%	91%	33%
2	92%	-	83%
3	98%	93%	91%
4	99%	-	92%
RCC and Standard Deviation of the Mean			75% ± 14%

Radiotrace and RCC Calculation for 5g:



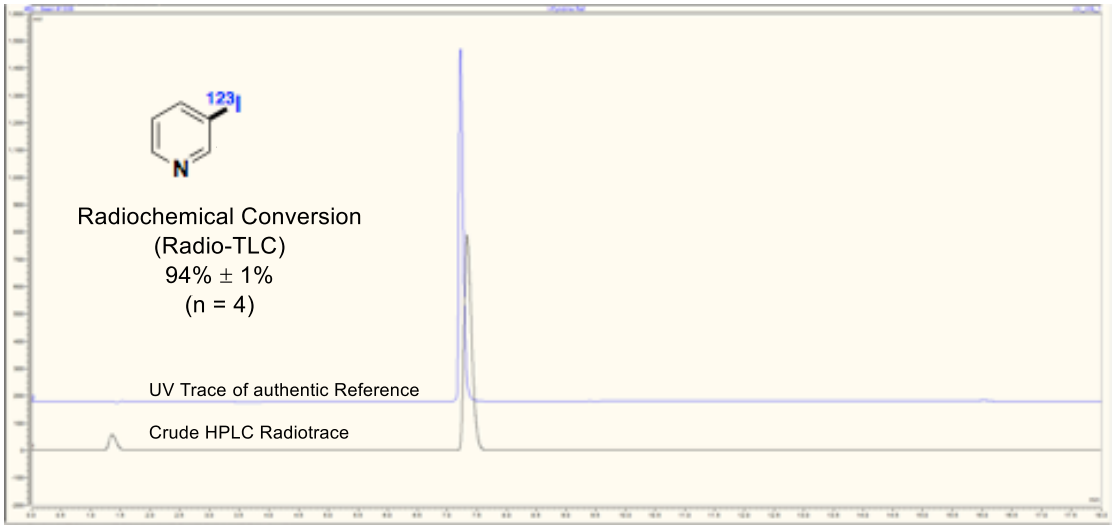
Reaction Number	Radio-TLC (%)	Radiochemical Purity (%)	Radiochemical Conversion (%)
1	70%	98%	69%
2	33%	-	32%
3	19%	>99%	19%
4	23%	-	23%
RCC and Standard Deviation of the Mean			36% ± 11%

Radiotrace and RCC Calculation for 5h:



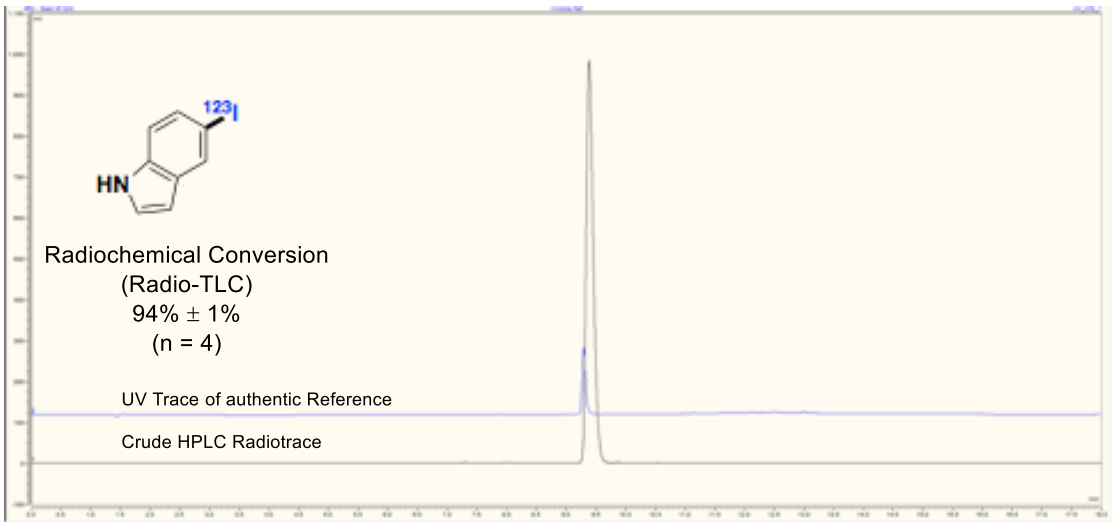
Reaction Number	Radio-TLC (%)	Radiochemical Purity (%)	Radiochemical Conversion (%)
1	85%	>99%	85%
2	90%	-	90%
3	91%	98%	89%
4	98%	-	96%
RCC and Standard Deviation of the Mean			88% ± 3%

Radiotrace and RCC Calculation for 5i:



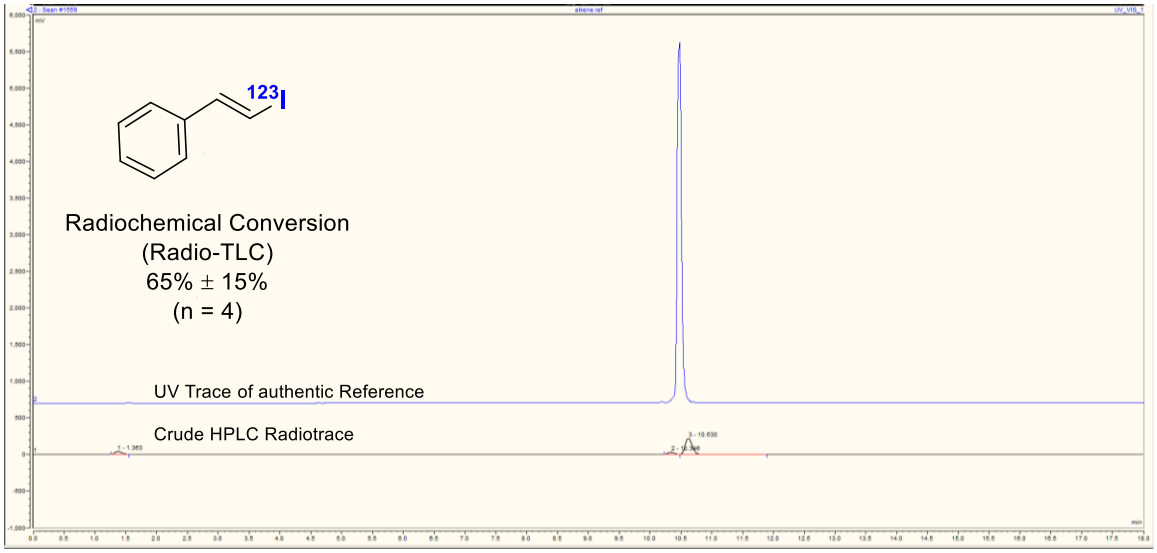
Reaction Number	Radio-TLC (%)	Radiochemical Purity (%)	Radiochemical Conversion (%)
1	95%	>99%	95%
2	93%	-	93%
3	90%	>99%	90%
4	99%	-	99%
RCC and Standard Deviation of the Mean			94% ± 1%

Radiotrace and RCC Calculation for 5j:



Reaction Number	Radio-TLC (%)	Radiochemical Purity (%)	Radiochemical Conversion (%)
1	92%	>99%	92%
2	93%	-	93%
3	94%	>99%	94%
4	95%	-	95%
RCC and Standard Deviation of the Mean			94% ± 1%

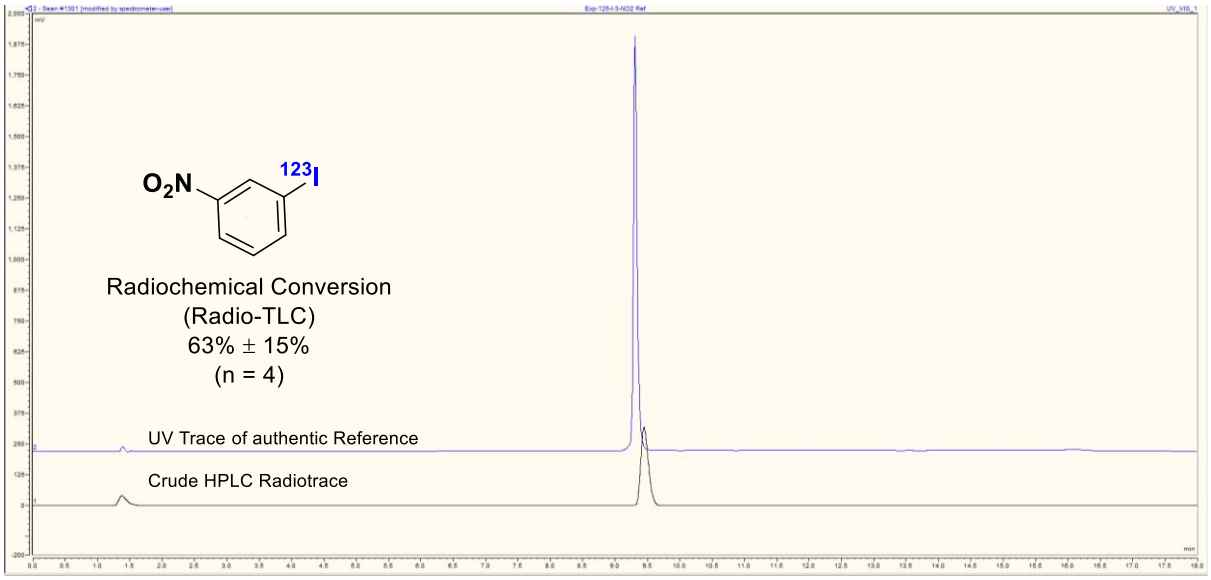
Radiotrace and RCC Calculation for 5k:



Reaction Number	Radio-TLC (%)	Radiochemical Purity (%)	Radiochemical Conversion (%)
1	89%	90%	80%
2	54%	-	49%
3	75%	92%	69%
4	84%	-	77%
RCC and Standard Deviation of the Mean			65% ± 15%

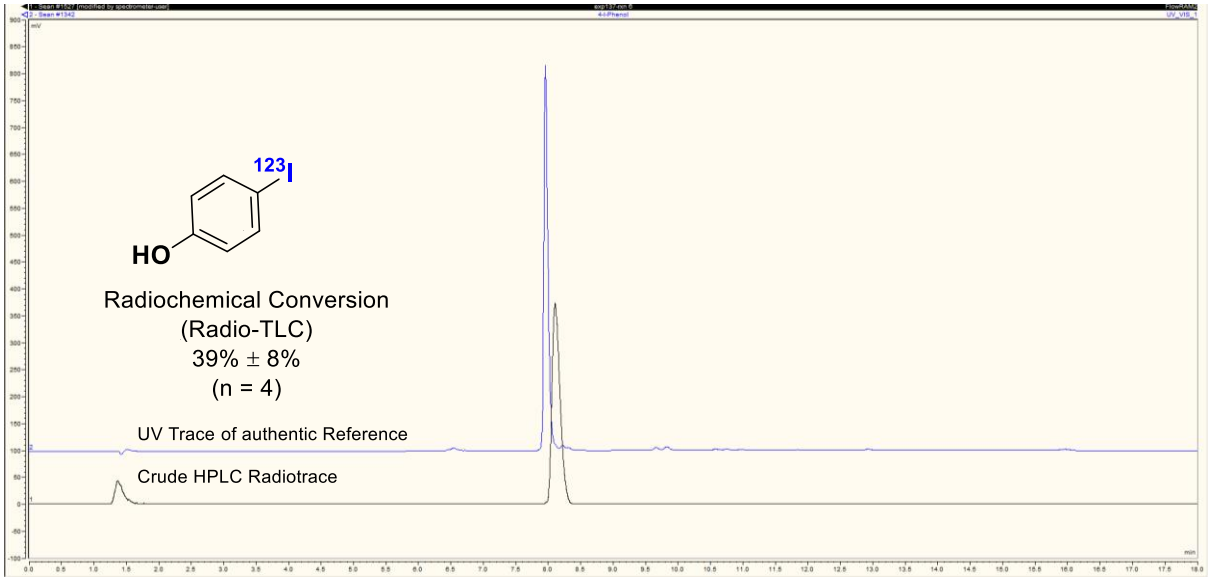
3.3.4 HPLC Traces Derived from Boronic Acid Starting Material (2b, 2h, 2j)

Radiotrace and RCC Calculation for 5b: Trace recorded using HPLC gradient B



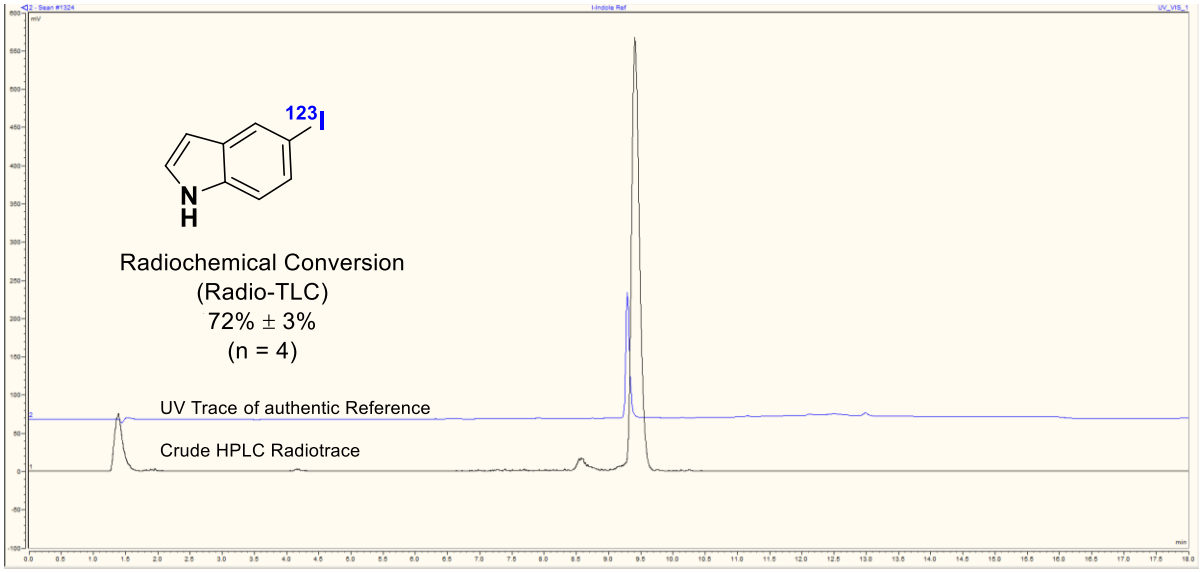
Reaction Number	Radio-TLC (%)	Radiochemical Purity (%)	Radiochemical Conversion (%)
1	60%	>99%	60%
2	85%	-	85%
3	35%	>99%	35%
4	40%	-	40%
RCC and Standard Deviation of the Mean			63% ± 15%

Radiotrace and RCC Calculation for 5h: Trace recorded using HPLC gradient B



Reaction Number	Radio-TLC (%)	Radiochemical Purity (%)	Radiochemical Conversion (%)
1	35%	>99%	35%
2	63%	-	63%
3	29%	>99%	29%
4	28%	-	28%
RCC and Standard Deviation of the Mean			39% ± 8%

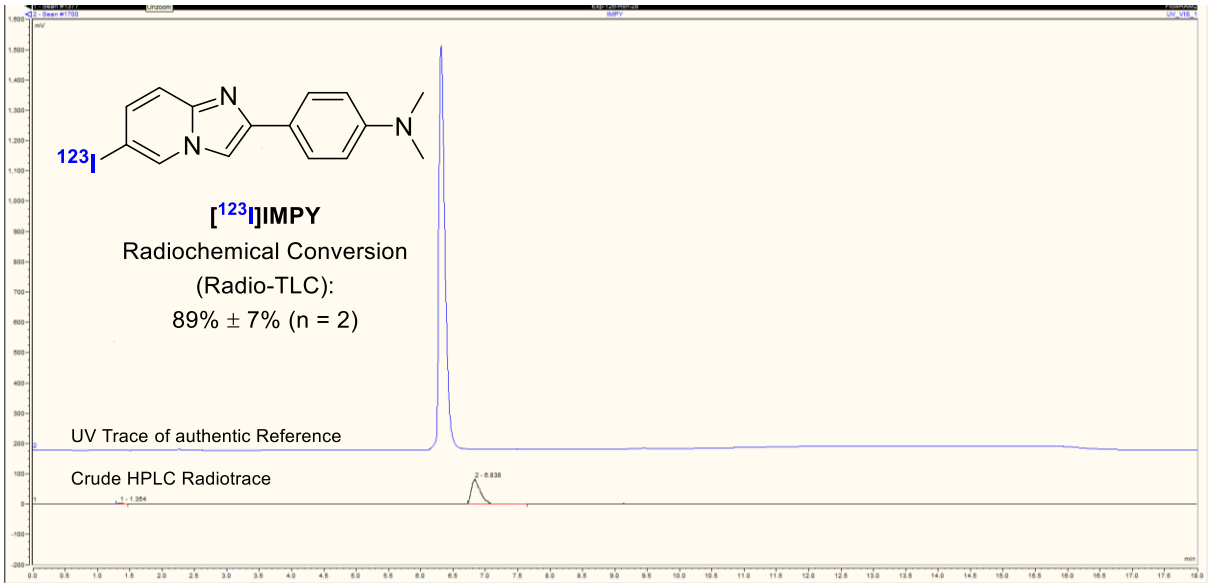
Radiotrace and RCC Calculation for 5j: Trace recorded using HPLC gradient B



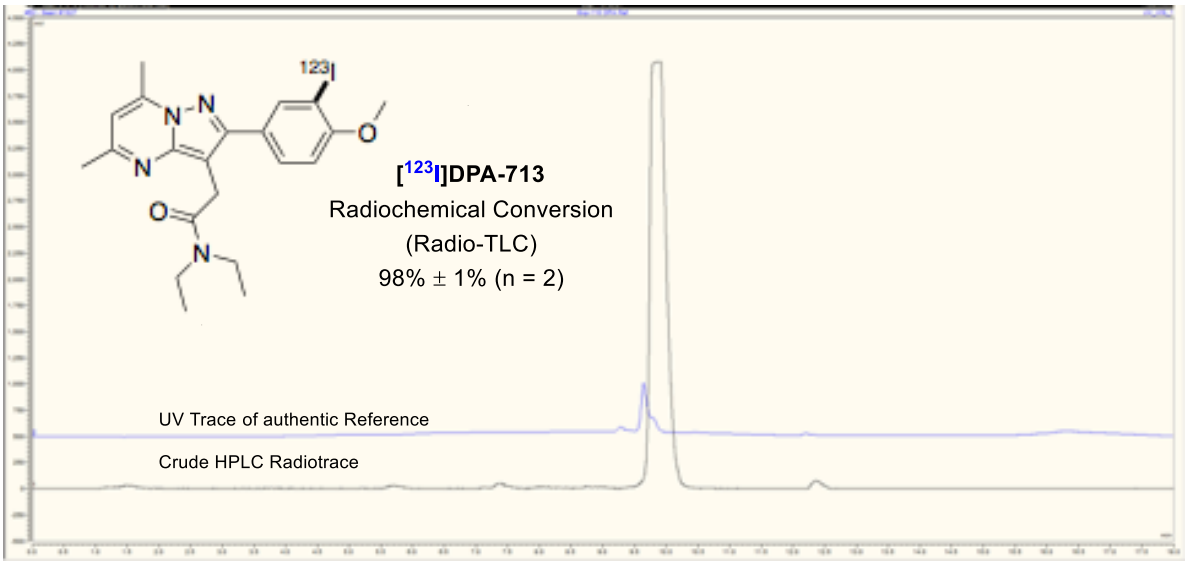
Reaction Number	Radio-TLC (%)	Radiochemical Purity (%)	Radiochemical Conversion (%)
1	70%	>96%	67%
2	77%	-	74%
3	75%	>86%	65%
4	64%	-	55%
RCC and Standard Deviation of the Mean			72% ± 3%

3.3.5 HPLC Traces of SPECT Traces (all traces taken using HPLC gradient A unless otherwise specified)

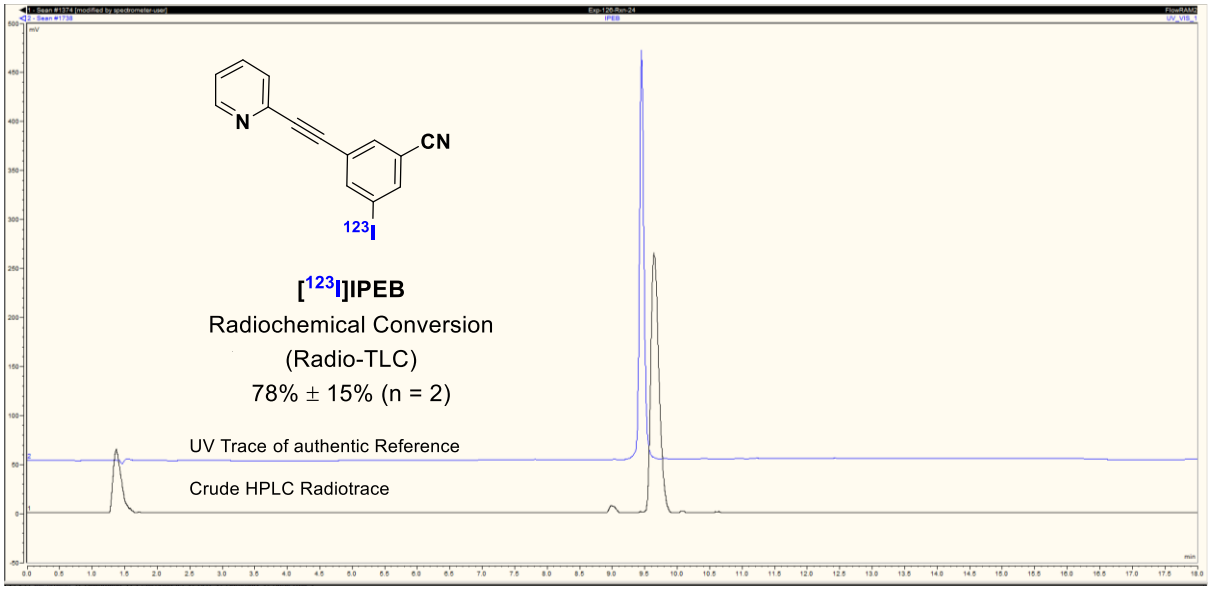
Radiotrace and RCC Calculation for [^{123}I]IMPY (5l): Trace recorded using HPLC gradient B



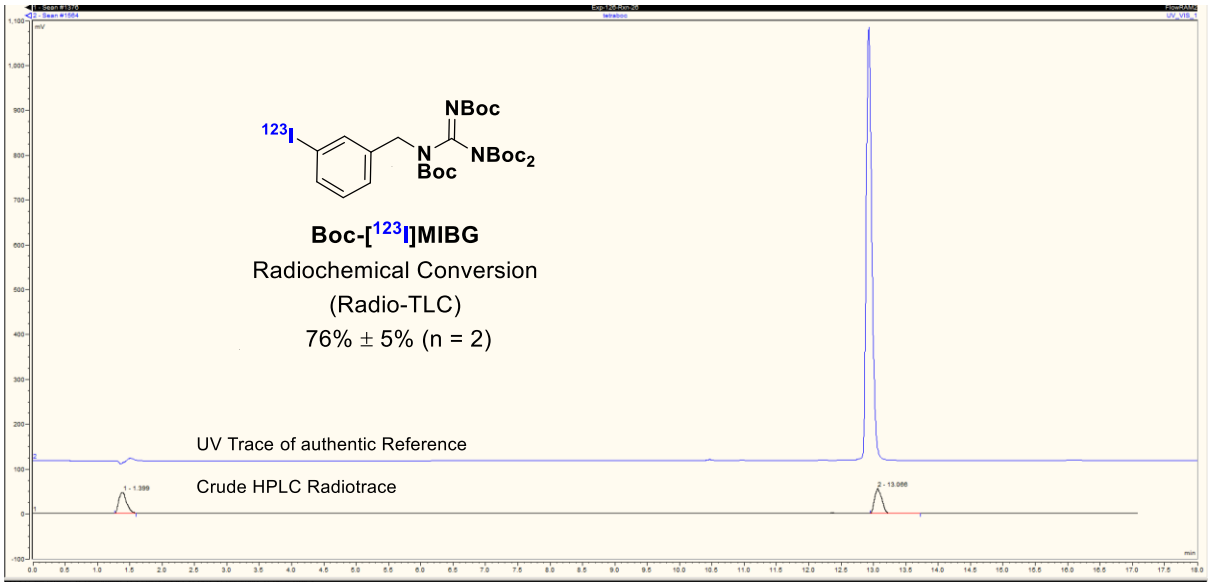
Radiotrace and RCC Calculation for [^{123}I]DPA-713 (5m):



Radiotrace and RCC Calculation for [^{123}I]IPEB (5n):

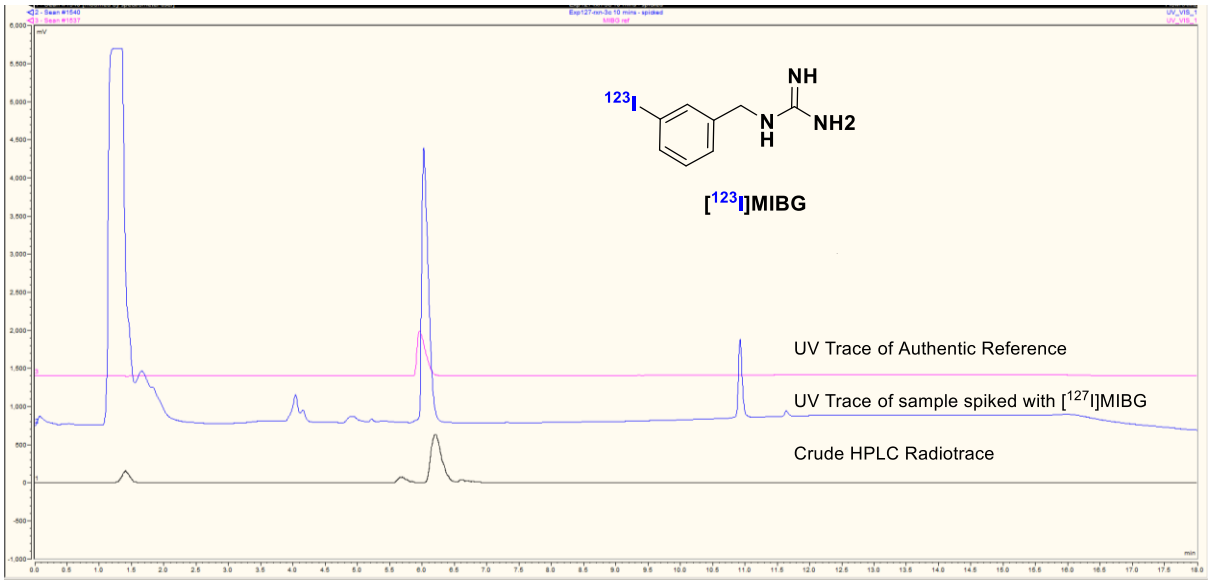


Radiotrace and RCC Calculation for Protected [^{123}I]MIBG (5o):



Radiotrace and RCC Calculation for MIBG (5o):

MIBG Salt: The product injected onto an analytical column overlaid with a UV spectra spiked with an authentic reference sample. Trace carried out using HPLC gradient B.



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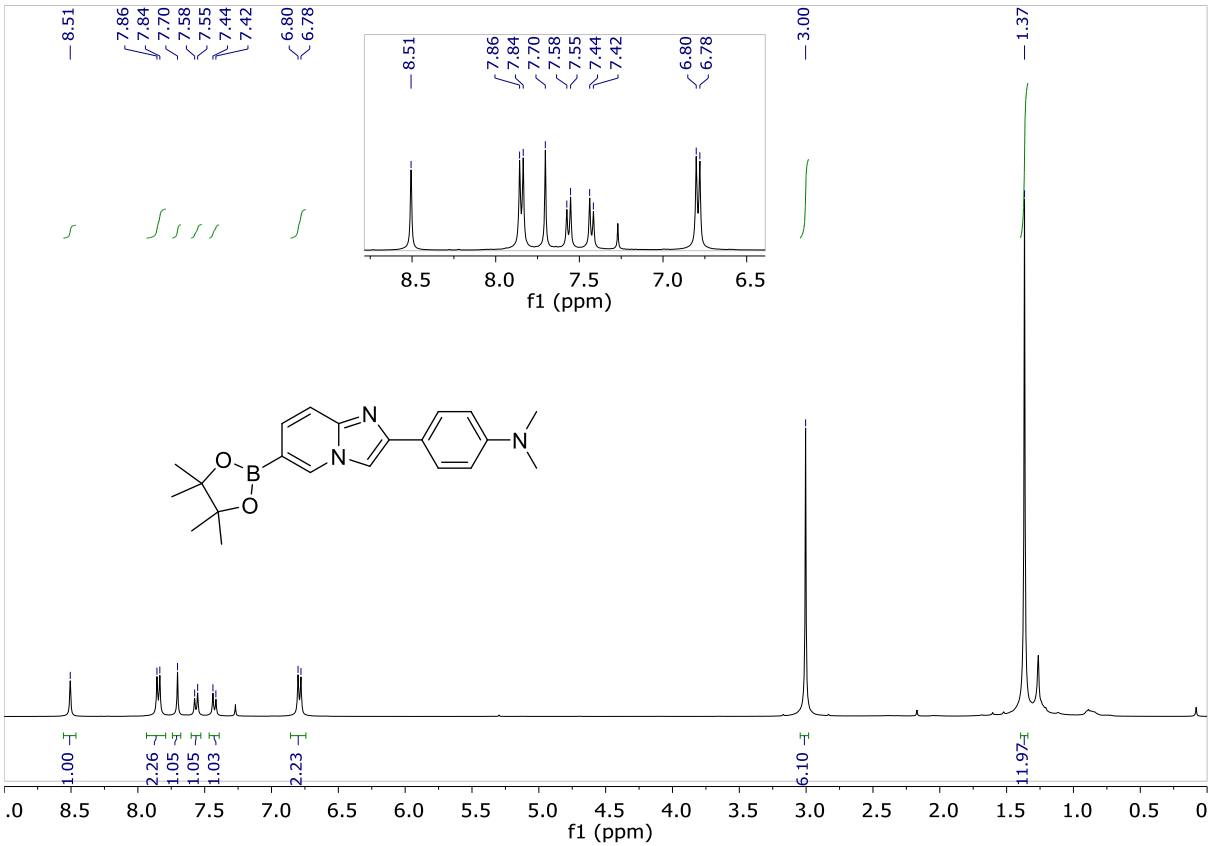
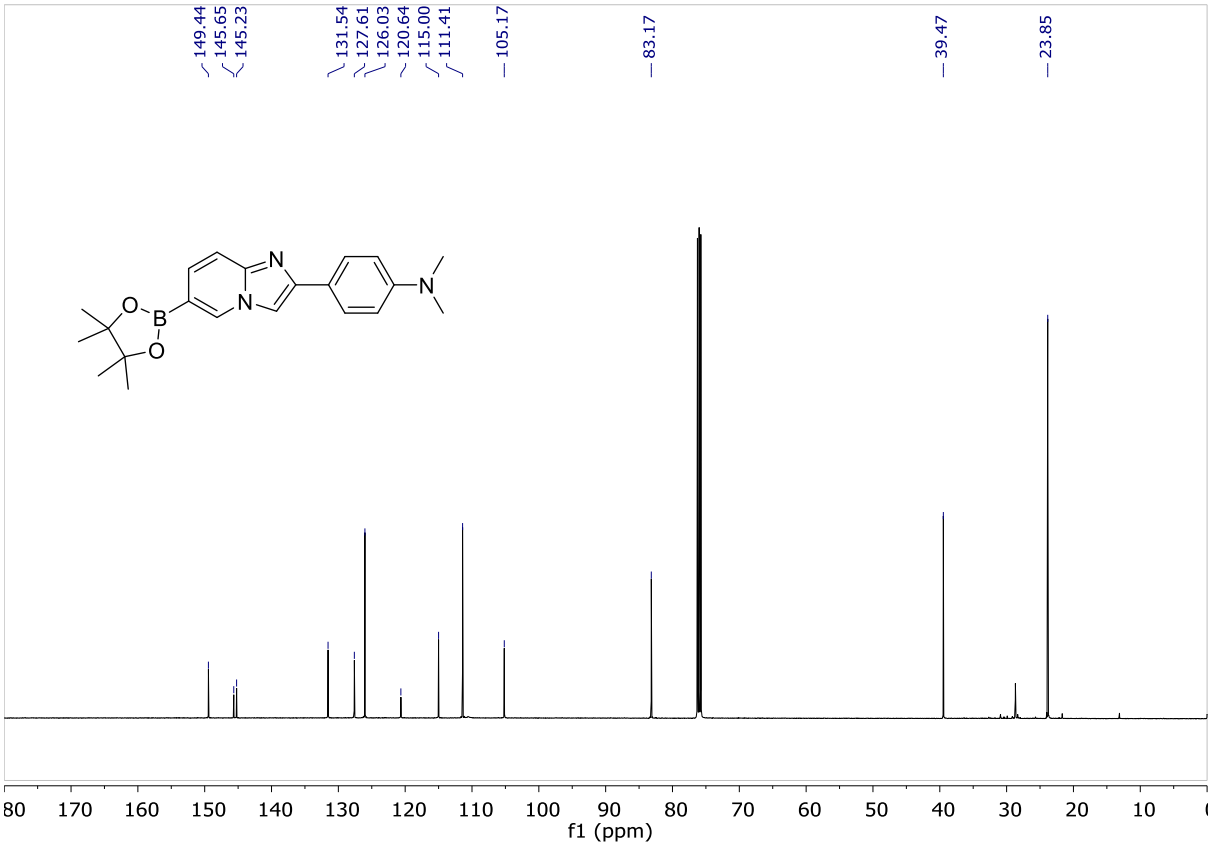
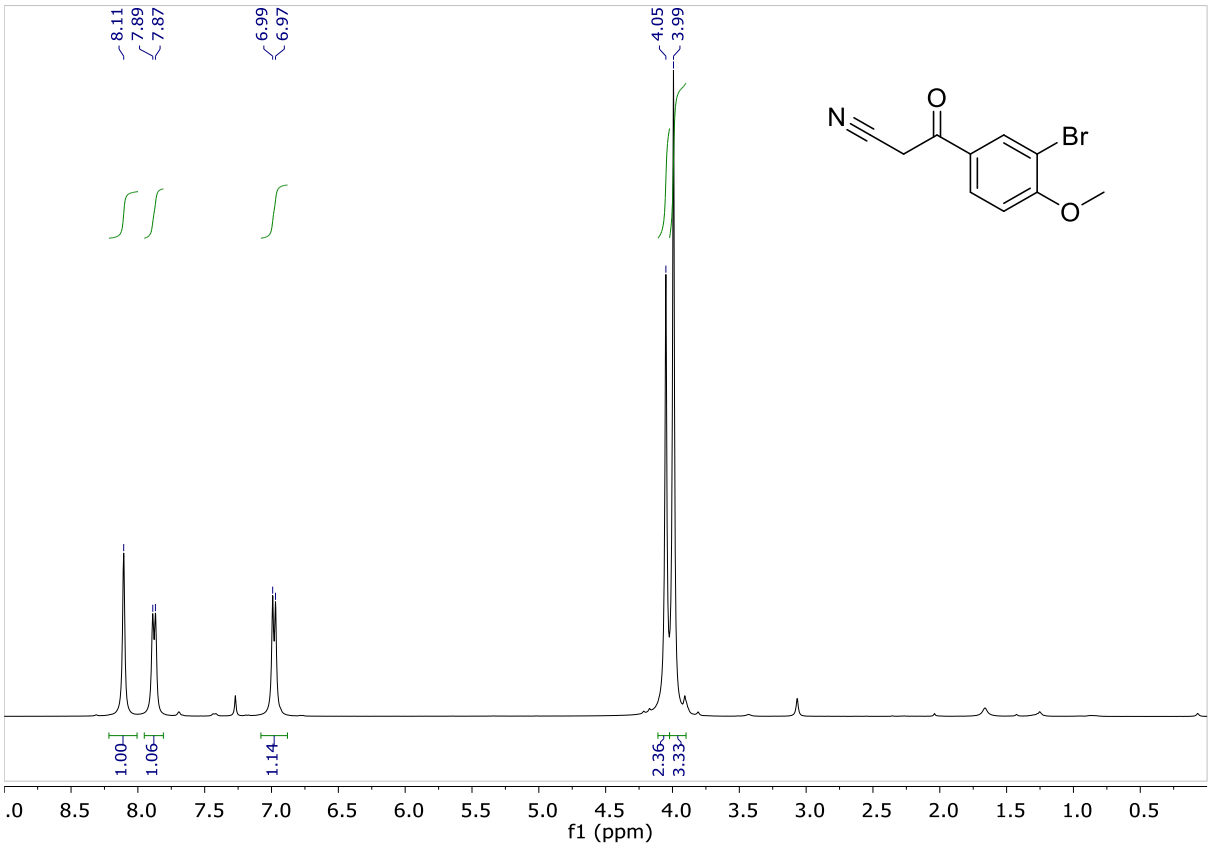
5. NMR Spectra of Novel Compounds

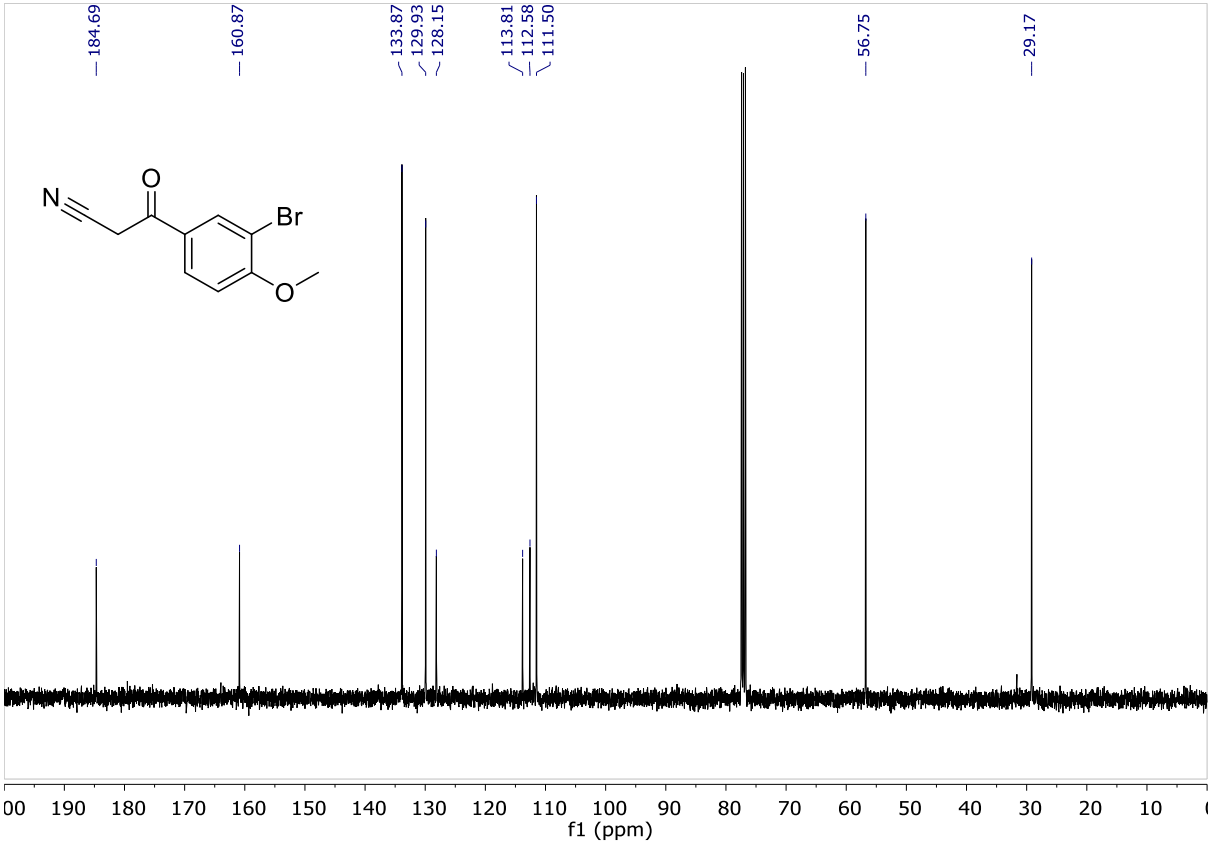
***N*,*N*-dimethyl-4-(6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)imidazo[1,2-*a*]pyridin-2-yl)aniline**



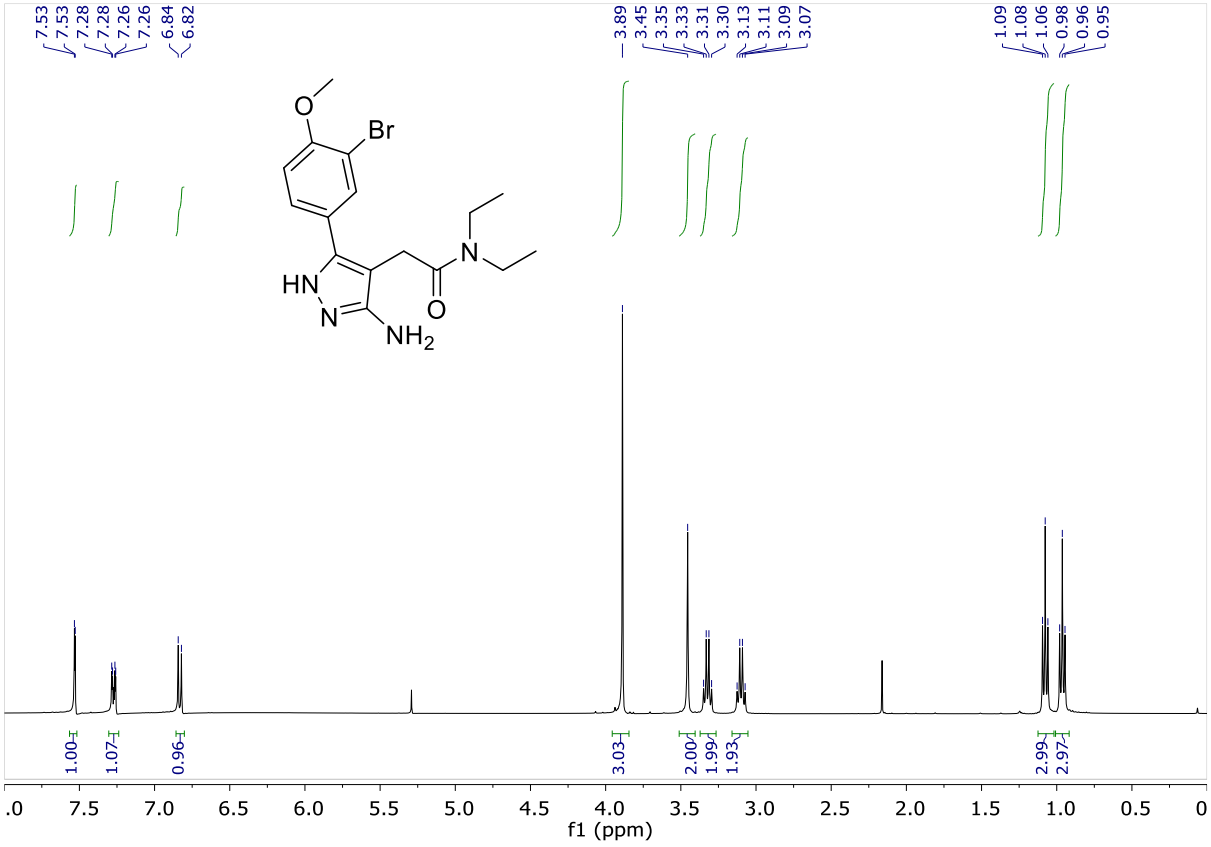


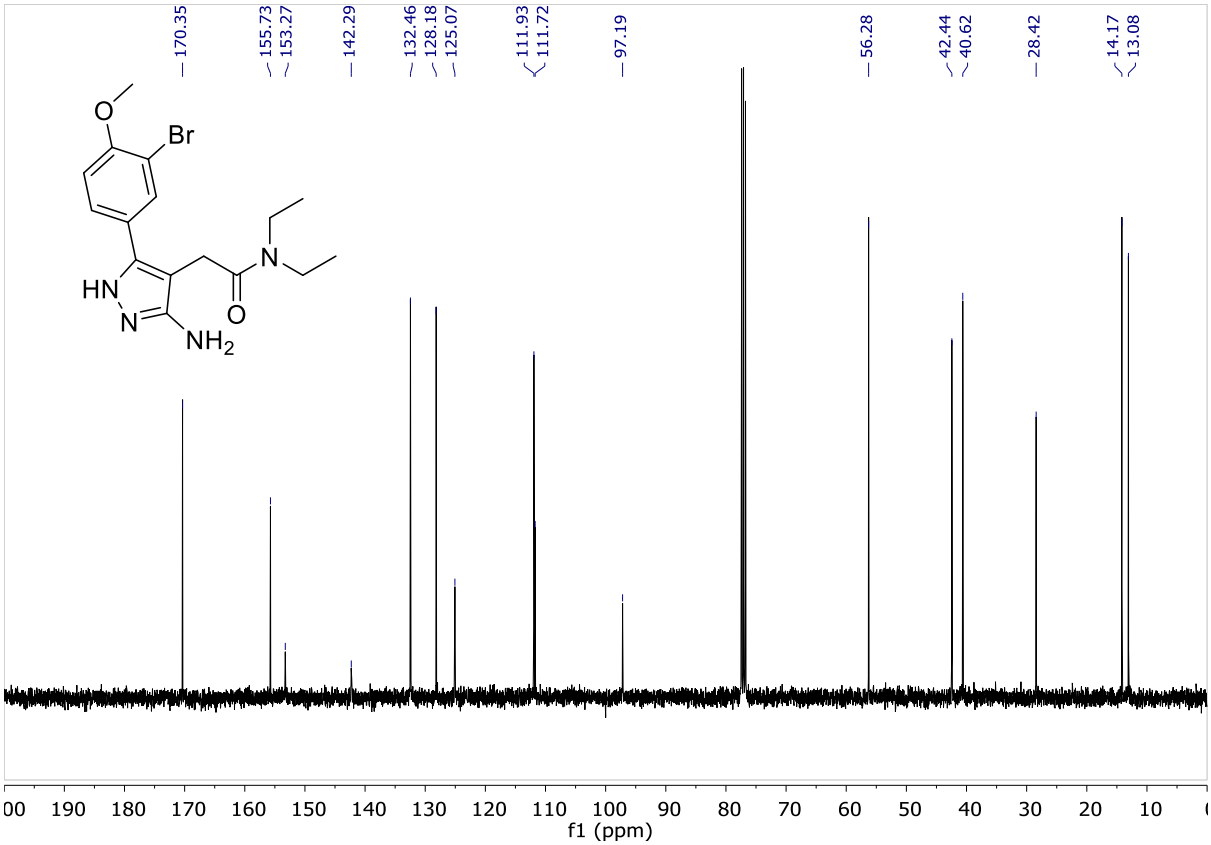
3-(3-bromo-4-methoxyphenyl)-3-oxopropanenitrile



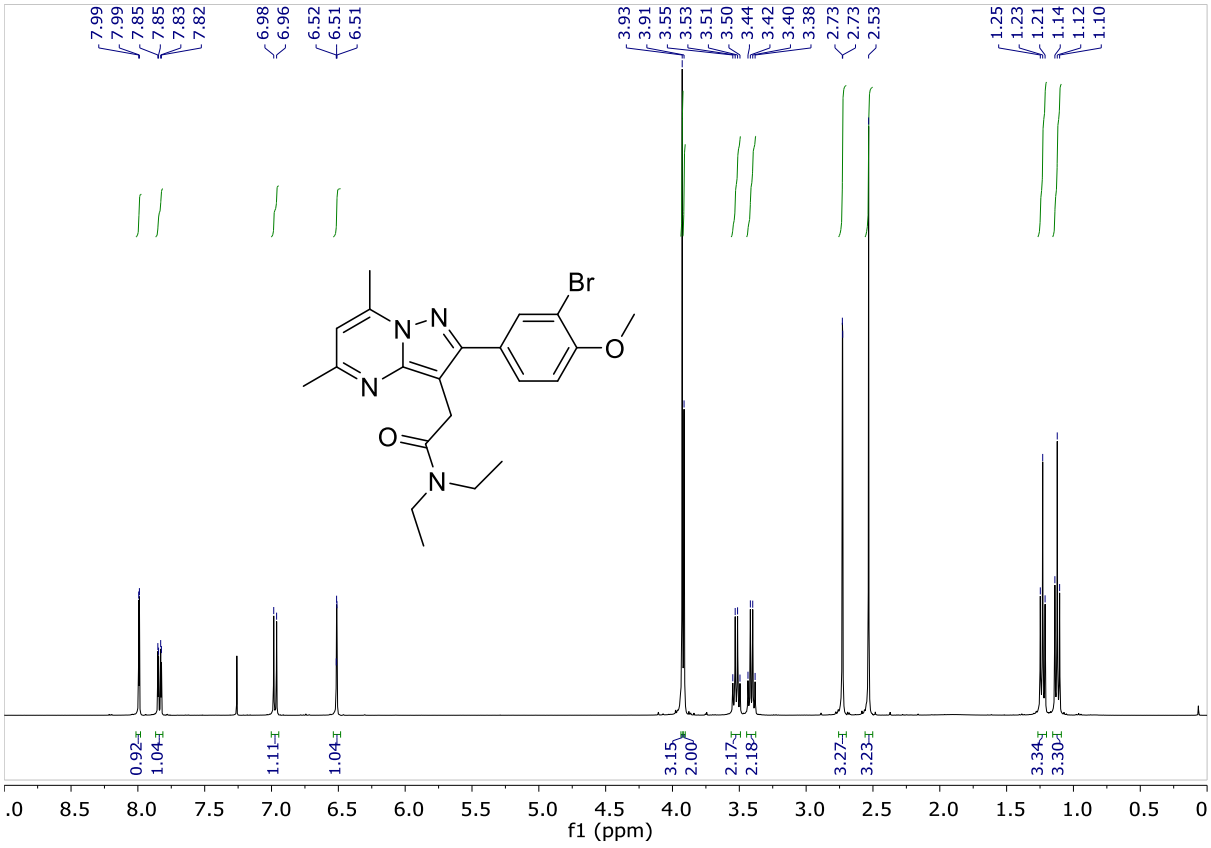


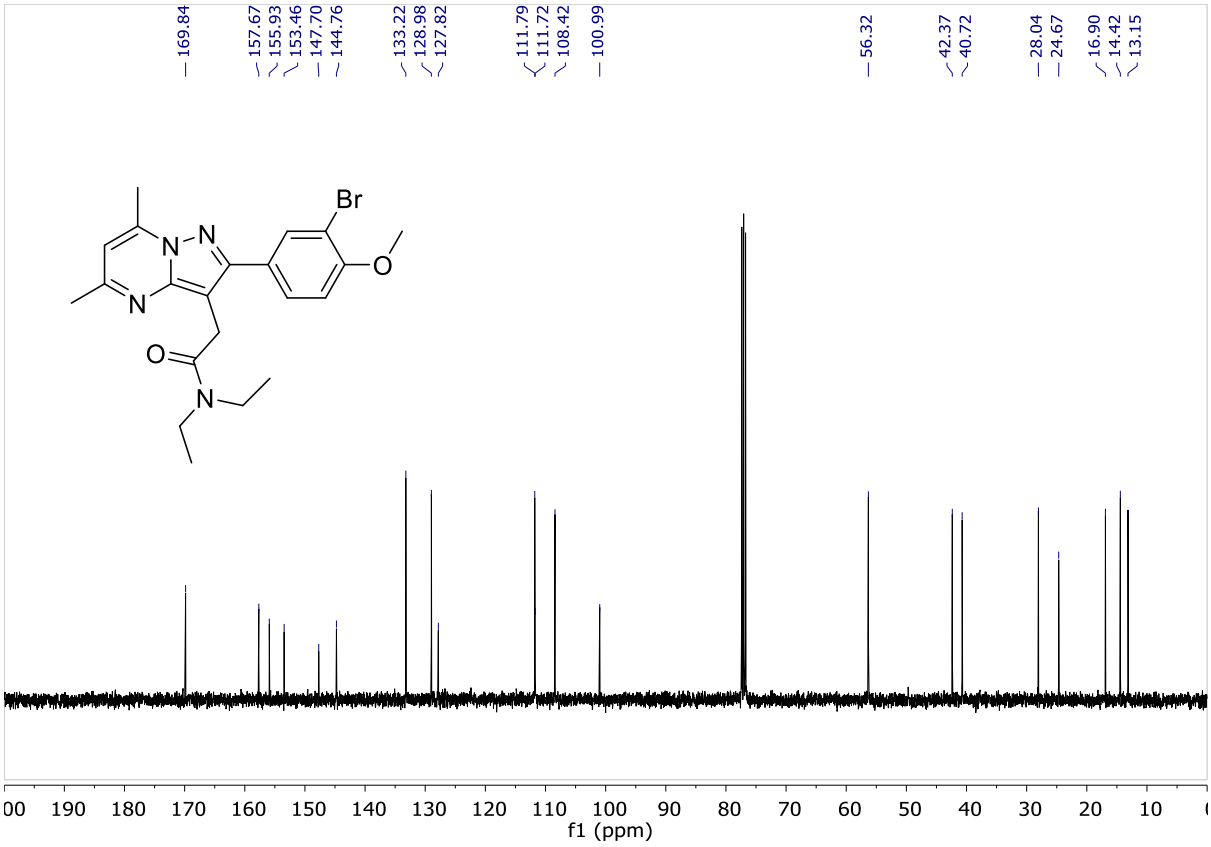
2-(3-amino-5-(3-bromo-4-methoxyphenyl)-1*H*-pyrazol-4-yl)-*N*,*N*-diethylacetamide



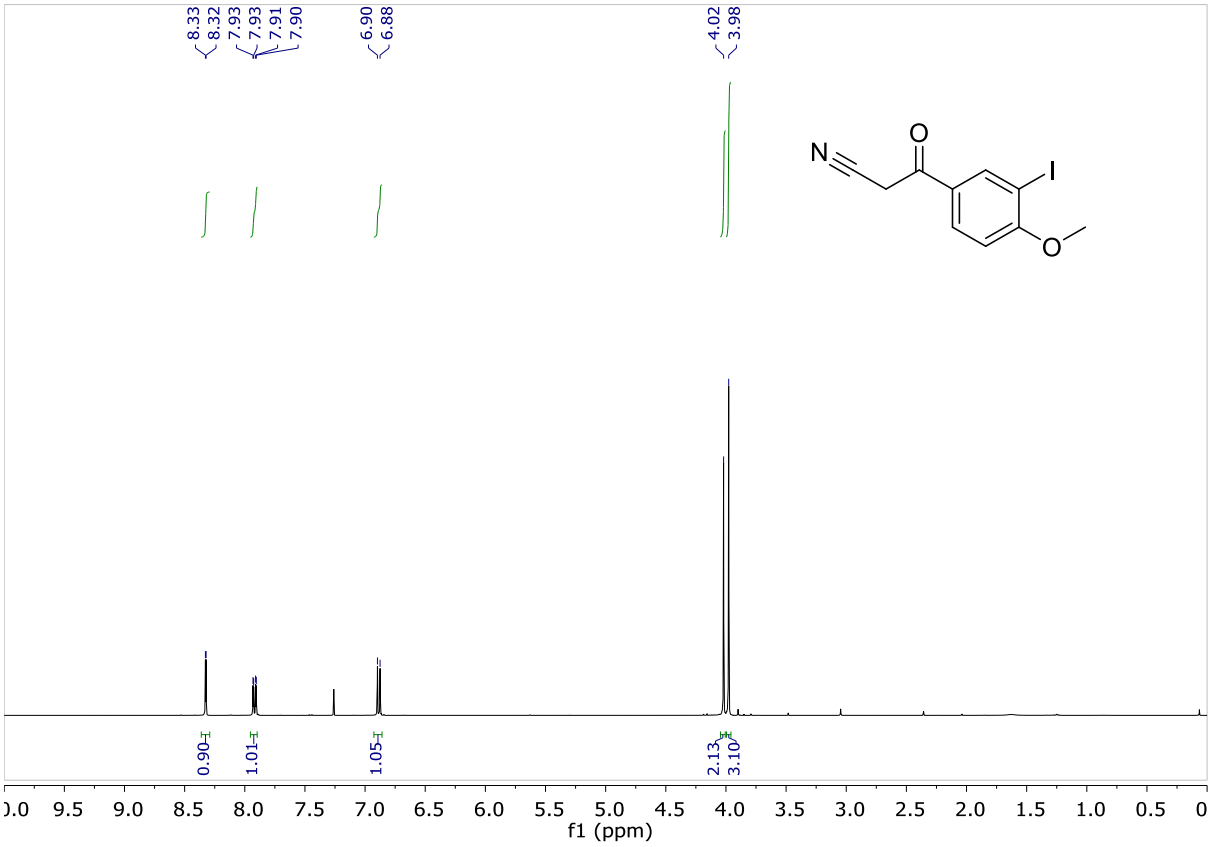


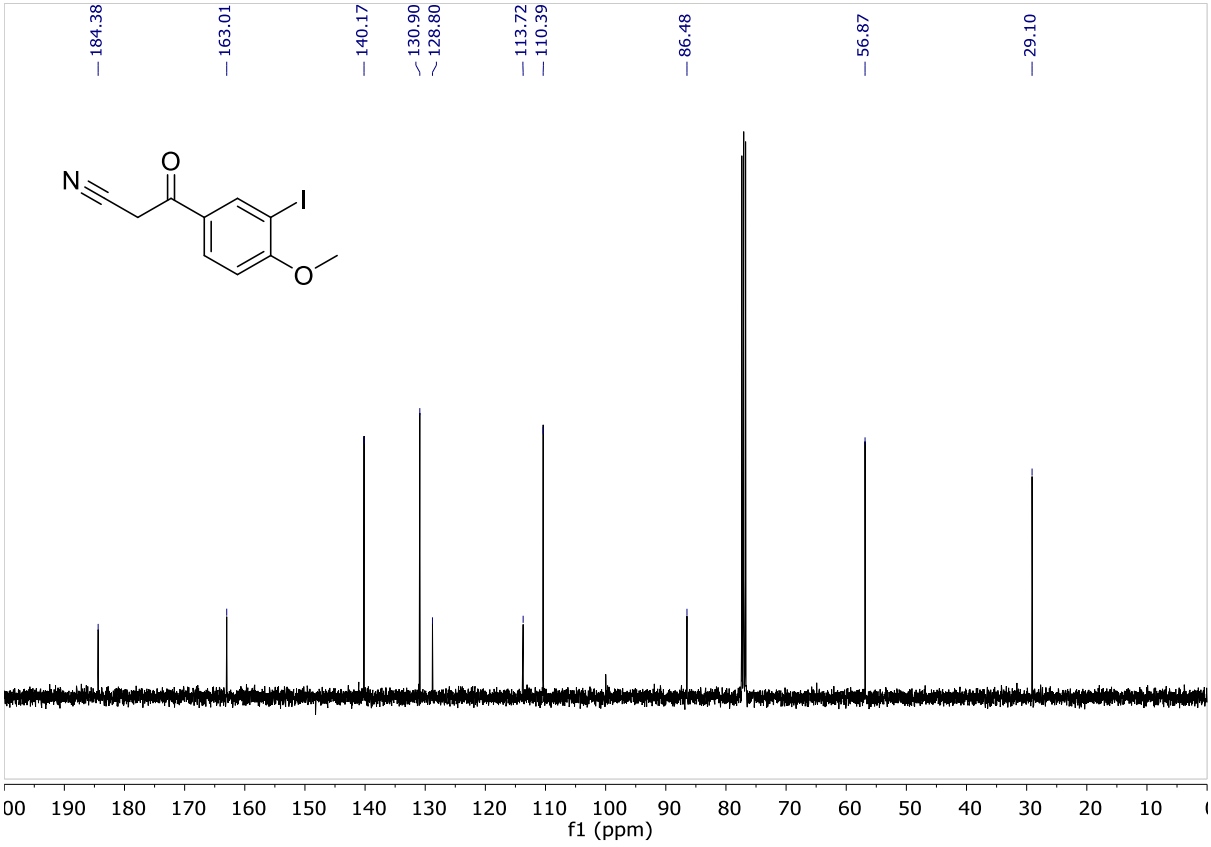
2-(2-(3-bromo-4-methoxyphenyl)-5,7-dimethylpyrazolo[1,5-*a*]pyrimidin-3-yl)-*N*,*N*-diethyl acetamide



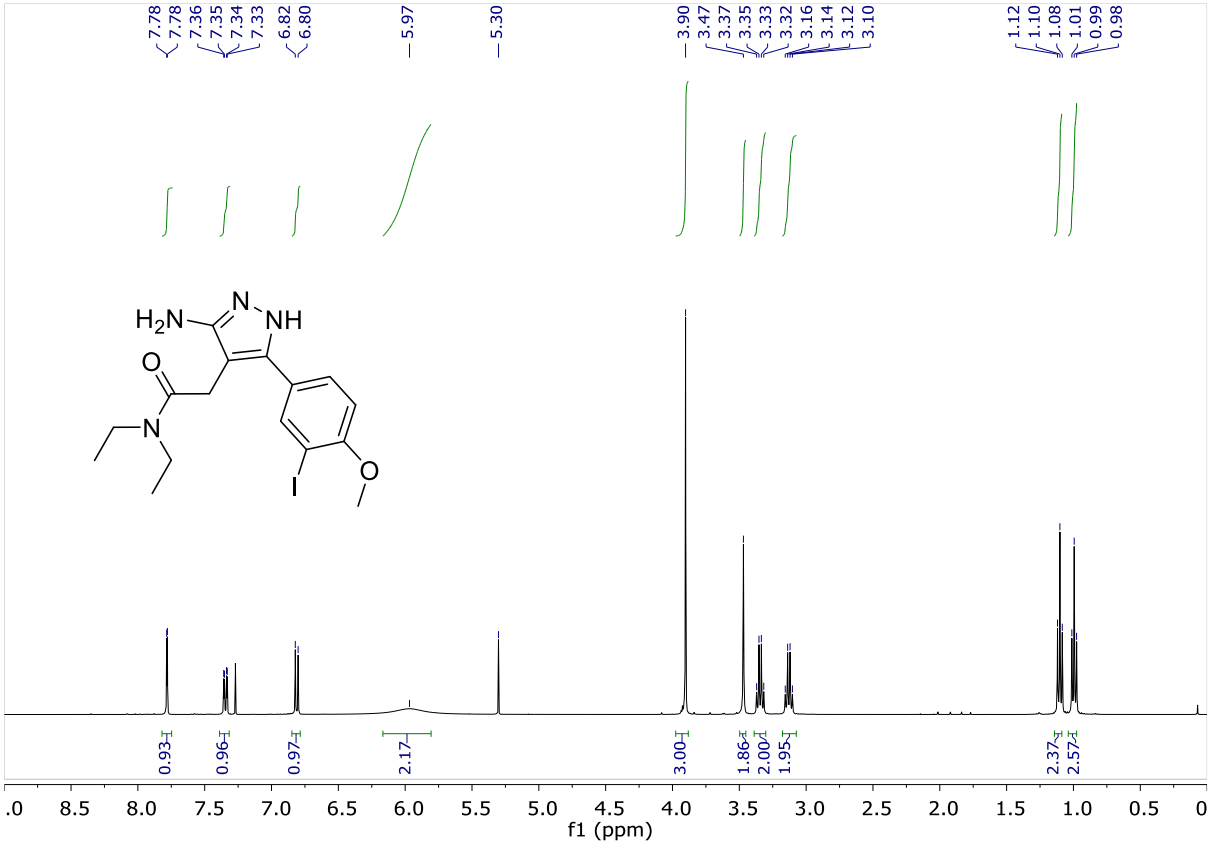


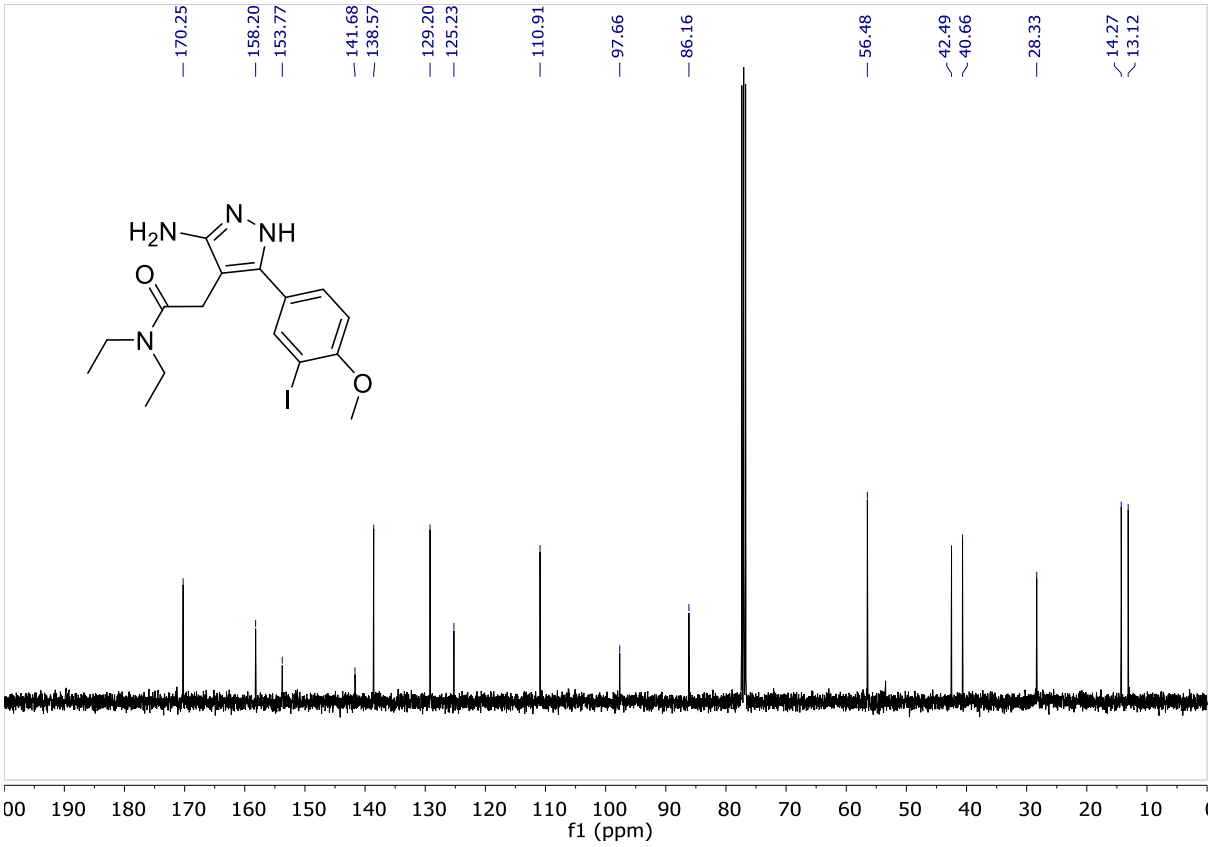
3-(3-iodo-4-methoxyphenyl)-3-oxopropanenitrile



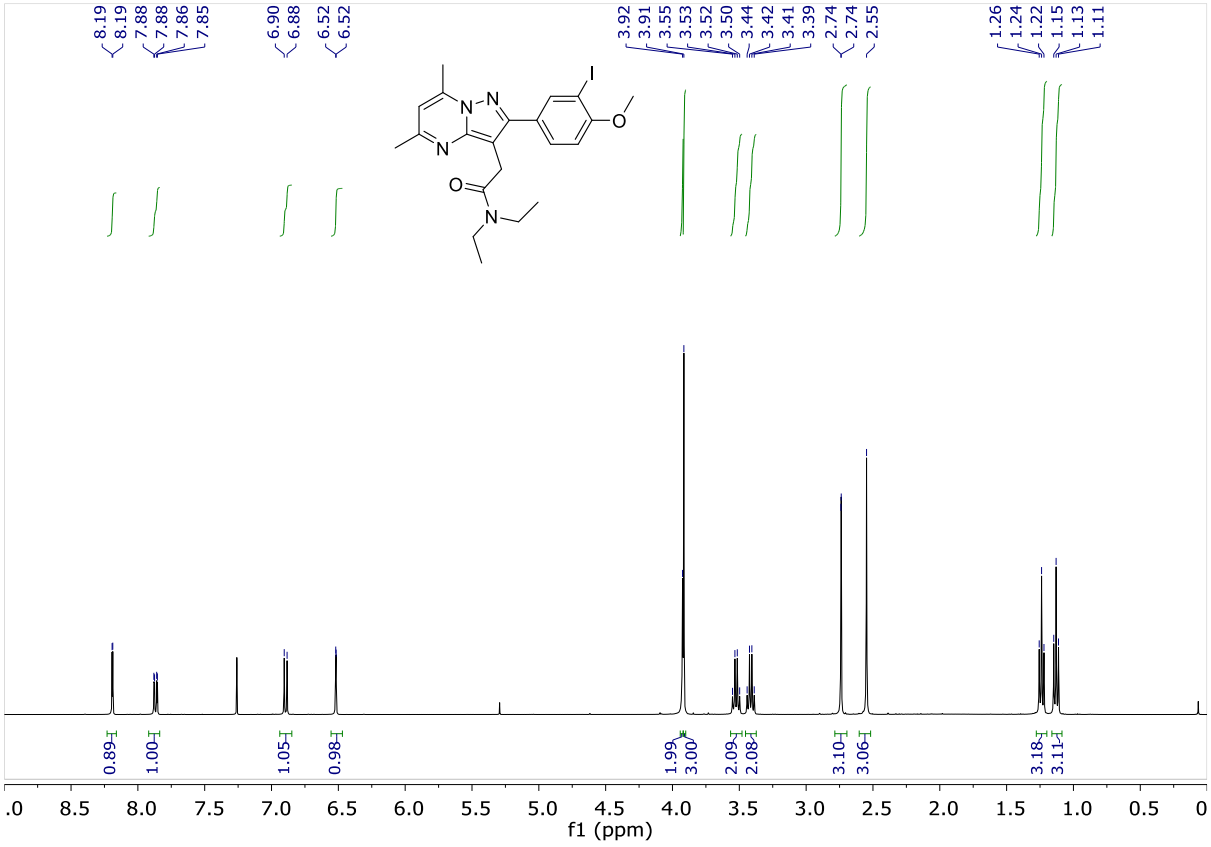


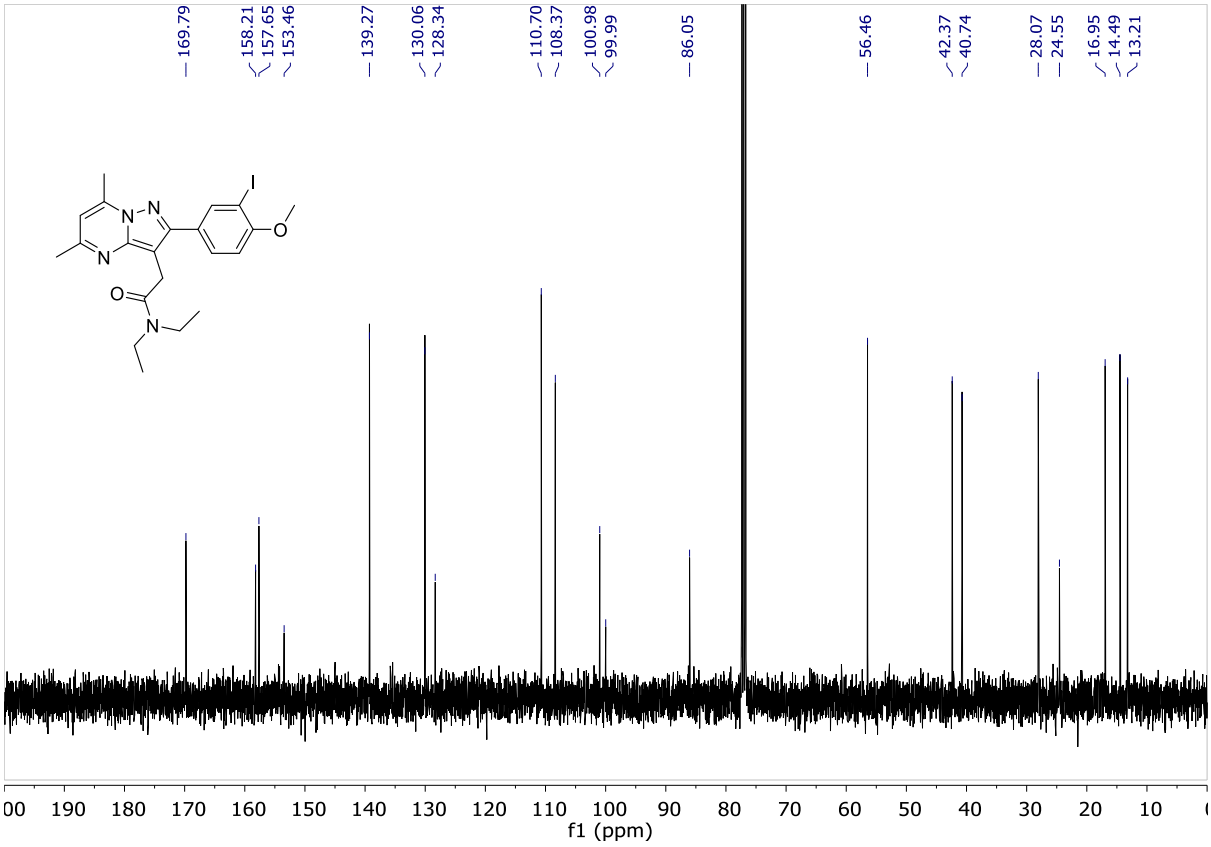
2-(3-amino-5-(3-iodo-4-methoxyphenyl)-1*H*-pyrazol-4-yl)-*N*,*N*-diethylacetamide



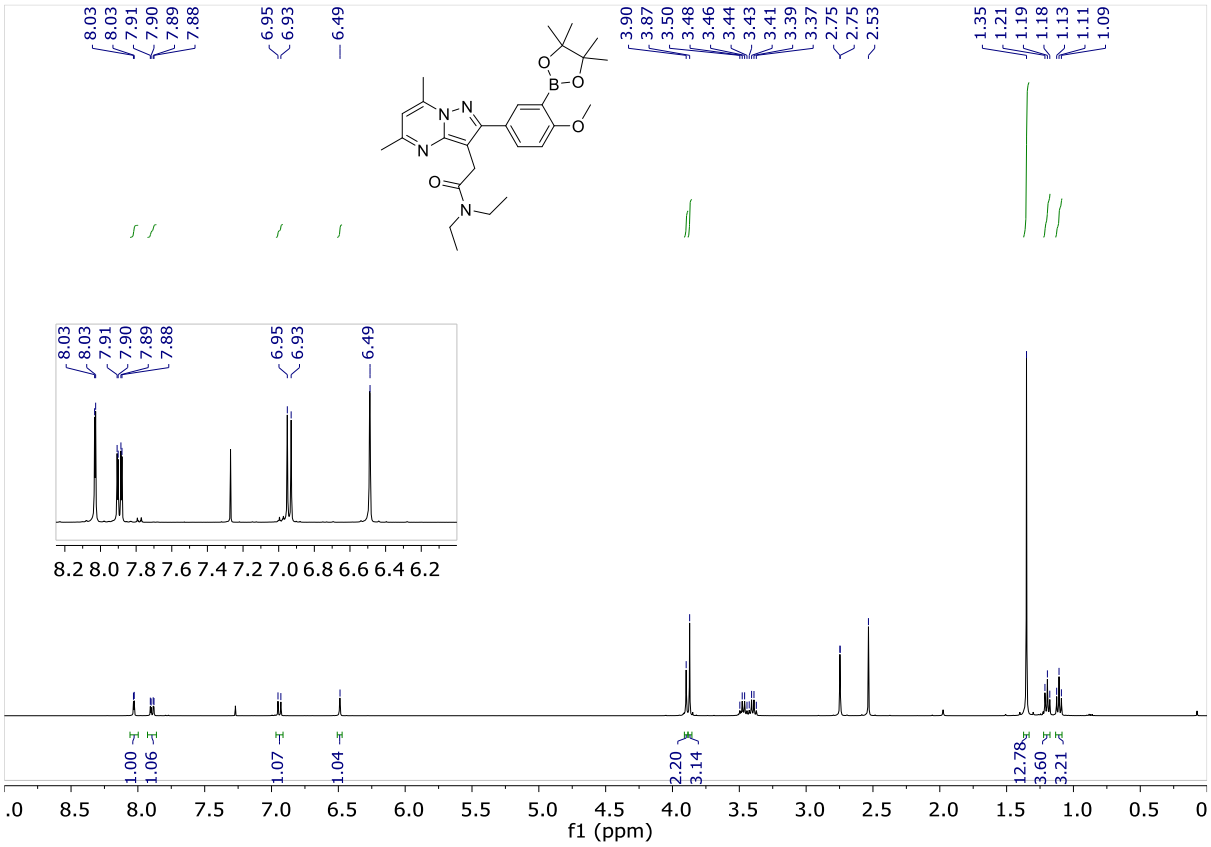


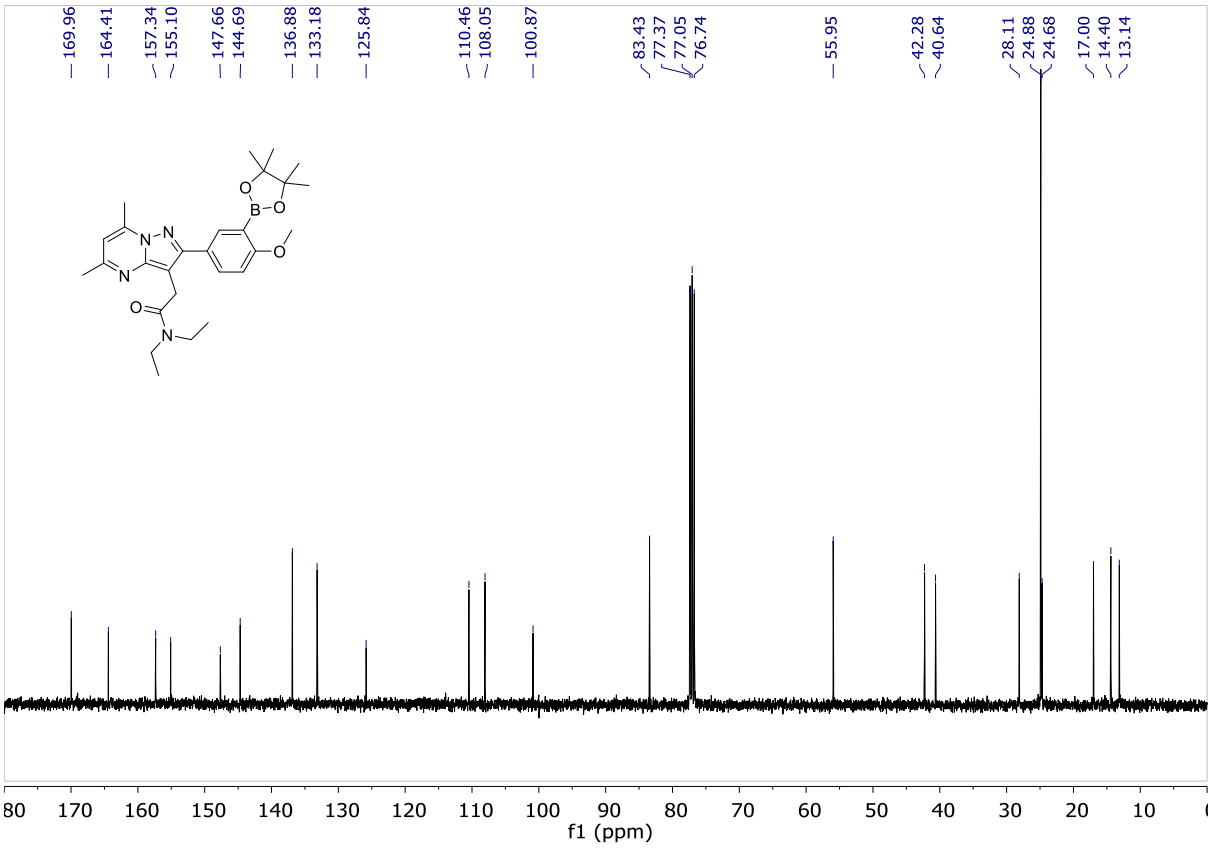
***N*,*N*-diethyl-2-(2-(3-iodo-4-methoxyphenyl)-5,7-dimethylpyrazolo[1,5-*a*]pyrimidin-3-yl)acetamide**



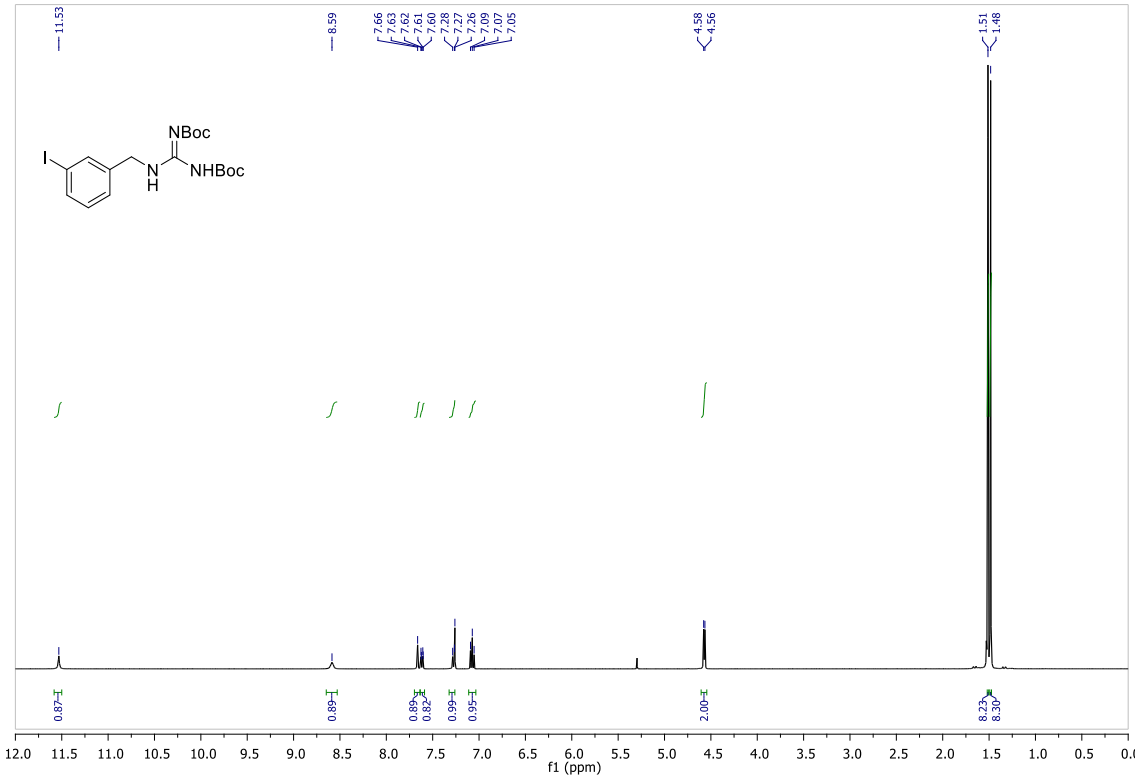


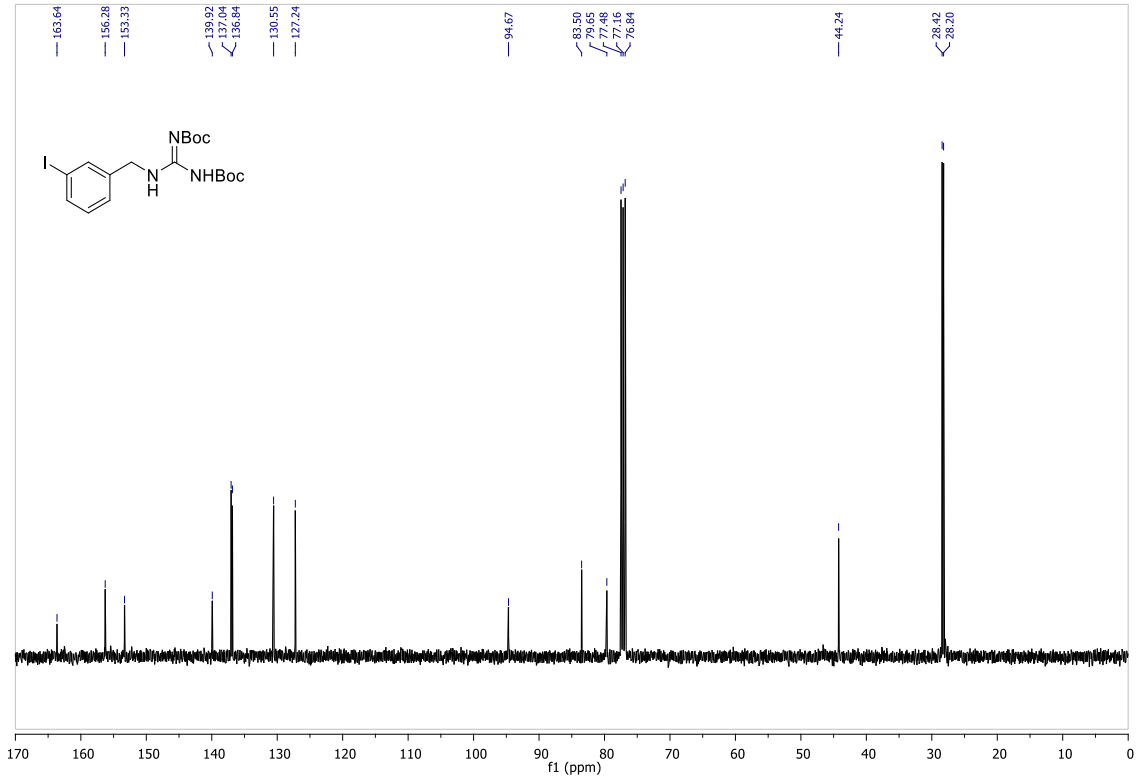
***N*,*N*-diethyl-2-(2-(4-methoxy-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-5,7-dimethylpyrazolo[1,5-*a*]pyrimidin-3-yl)acetamide**





Butyl{(*Z*)-[(3-iodobenzyl)amino][(*tert*-butoxycarbonyl)amino]methylidene} carbamate





***tert*-Butyl-N-[(1Z)-{bis[(tert-butoxy)carbonyl]amino}({[(tert-butoxy)carbonyl][(3-iodophenyl)methyl]amino})methylidene]carbamate**