Electronic Supplementary Material (ESI) for ChemComm.

[^{11}C]Cyanation of Arylboronic Acids in Aqueous Solution

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GENERAL INFORMATION

All solvents were of reagent or anhydrous grade quality and purchased from Sigma-Aldrich, Alfa Aesar, or Fisher Scientific. All reagents were purchased from Sigma-Aldrich, Alfa Aesar, Fisher Scientific, or Oakwood Chemical, unless otherwise stated. Boronic acids **1b-1j**, **1l** were purchased from Sigma-aldrich; boronic acid **1a** was purchased from Combi-Blocks and **1k** was purchased from Alfa Aesar. All deuterated solvents were purchased from Cambridge isotopes. Analytical thin-layer chromatography (TLC) was performed on pre-coated glass-backed plates (EMD TLC Silica gel 60 F_{254}) and visualized using a UV lamp (254 nm), potassium permanganate stain. Flash column chromatography was performed using a Biotage Isolera One system and preloaded Biotage Zip silica gel columns. Silica gel for flash chromatography was high purity grade 40-63 μm pore size and purchased from Sigma-Aldrich. Yields refer to purified and spectroscopically pure compounds.

RADIOCHEMISTRY

General Methods for Radioisotope Preparation

Radioactivity was produced by an Eclipse HP 11 MeV cyclotron (Siemens Healthcare, Munich, Germany) using a ^{11}C gas target (N_2 gas containing 2.5% O_2) irradiated at 52 μA to generate $[^{11}C]CO_2$. The $[^{11}C]CO_2$ was delivered to a Siemens Healthcare Explora CN synthesis module and first converted to $[^{11}C]CH_4$ with H_2 on Ni at 400 °C, and then to $[^{11}C]HCN$ with NH_3 on Pt at 900 °C. He was used as a carrier gas. The $[^{11}C]HCN$ was trapped in a solution of Cs_2CO_3 in 1.7 mL water (0.32 g/mL). We measured the amount of $[^{11}C]CN$ that is captured by attaching the vent line of the reaction vial to a charcoal trap. Passing the $[^{11}C]HCN$ gas mixture through Cs_2CO_3 aqueous solution leads to approximately 150 mCi of $[^{11}C]HCN$ captured in solution at 10 min post bombardment. The point at which the addition of $[^{11}C]HCN$ concluded was designated as the start of synthesis, and the moment when the radioactivity of the final purified product was measured was designated as the end of synthesis. The isolated radiochemical yields are non-decay corrected.

General Procedure for the [^{11}C]Cyanation of Arylboronic Acids

Arylboronic acid (4 mg), CuI (1 mg) and DMEDA (2 μL) were mixed in 0.15 mL DMF in a V-shaped vial sealed with a teflon-lined septum. $[^{11}C]HCN$ trapped in Cs_2CO_3 solution (50 μL, 0.32 g/mL) was added the V-shaped reaction vial and the vial was heated to 150 °C for 5 min. The reaction mixture was then cooled to room temperature and the contents were resolubilized in 0.1 mL 1:1 acetonitrile and water solution for analysis.

General Methods for Analysis of [^{11}C]Cyanation Reactions

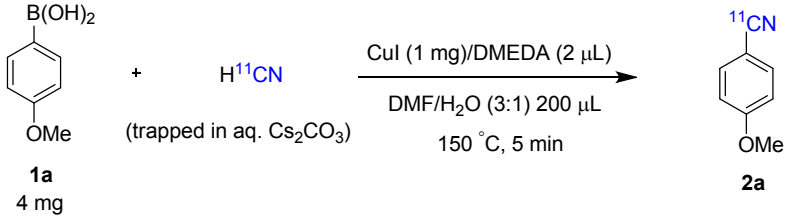
Radiochemical conversions were determined by radioTLC. EMD TLC Silica gel 60 plates (10 x 2 cm) were spotted with an aliquot (1-5 μL) of crude reaction mixture approximately 1.5 cm from the bottom of the plate (baseline). TLC plates were developed in a chamber containing ethyl acetate (EtOAc) until within 2 cm of the top of the plate (front). Analysis was performed using a Bioscan AR-2000 radioTLC imaging scanner and WinScan software.

Radiochemical identity and purity were determined by comparing the radio-detector (γ-ray) peak with the UV peak of standard compound. A Phenomenex (Luna C18, 250 x 4.6 mm, 5 μm) HPLC column was used for the analytical analysis with a an Agilent 1200 series HPLC equipped with a quaternary pump, vacuum degasser, diode-array detector, Carroll & Ramsey radiation detector

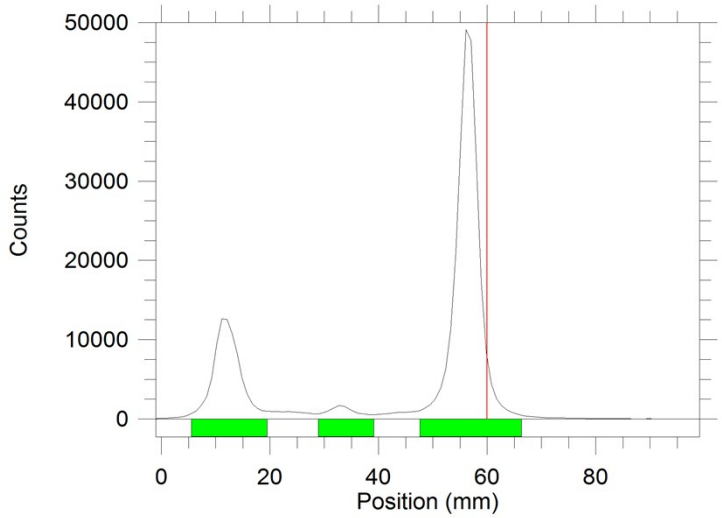
(Model 105S). Semi-preparative HPLC was performed on an Agilent 1200 HPLC equipped with a VICI sample injector, quaternary pump, vacuum degasser, variable wavelength detector, and semi-preparative HPLC column (Phenomenex Gemini® C18-110 Å, LC Column 250 x 10 mm, 5 µm). Radioactive analytes were detected with a Carroll & Ramsey radiation detector (Model 105S).

Radiochemical Synthesis of 2a-2l:

Synthesis of compound **2a:**

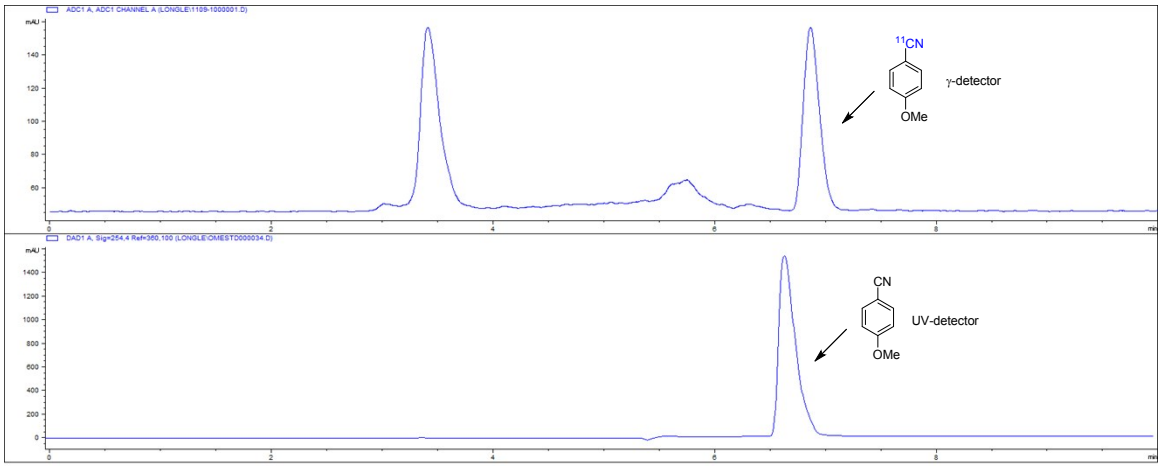


RadioTLC Chromatogram of the Reaction Mixture:



	1	2	3	mean	standard deviation
RCC (%)	77	70	63	70	7

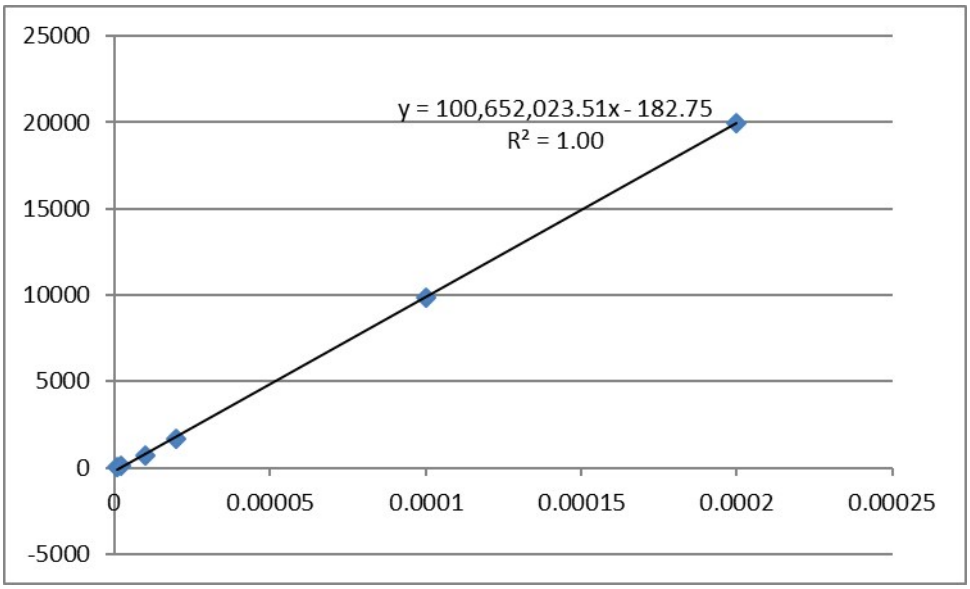
RadioHPLC Chromatogram:
Column: Phenomenex Luna, C18, 250 x 4.6 mm, 5 µm
Mobile phase: A = Water (0.1% TFA), B = MeCN (0.1% TFA)
Gradient method: 5% B 0-1 min, 5-90 % B 1-3 min, 90-95 % B 3-10 min
Flow rate: 1 mL/min
Injection volume: 50 µL



*Isolation of **2a** with semi-Preparative HPLC and Specific Activity (SA) Determination*

Standard Curve of **2a** (UV-absorption plot vs. 6 concentrations)

2a was dissolved in 80:20 (v:v) acetonitrile/water solvent to make solutions at 6 concentrations: $2x10^{-4}$ M, $1x10^{-4}$ M, $2x10^{-5}$ M, $1x10^{-5}$ M, $2x10^{-6}$ M, $1x10^{-6}$ M. The UV-absorbance was recorded on an Agilent 1200 series HPLC with a Phenomenex (Luna C18, 250 x 4.6 mm, 5 µm) HPLC column.

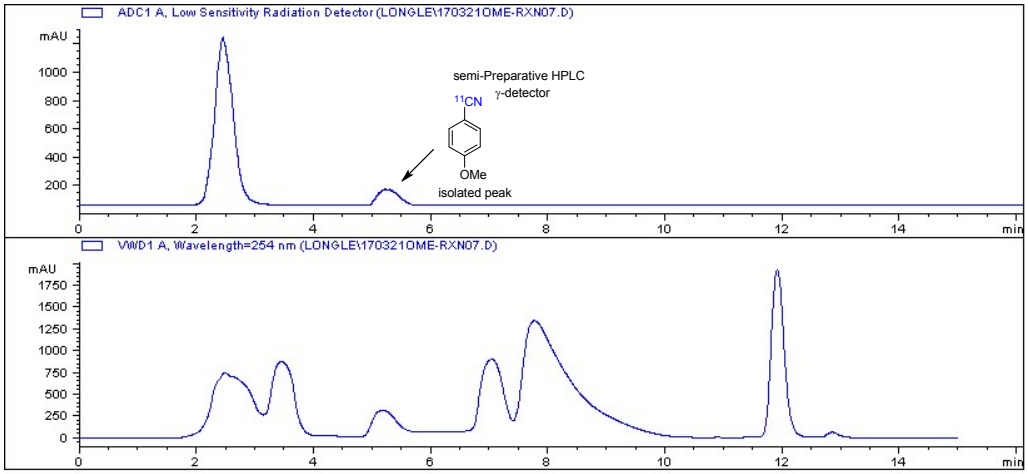


Synthesis of and Purification of **2a** Using semi-Preparative HPLC

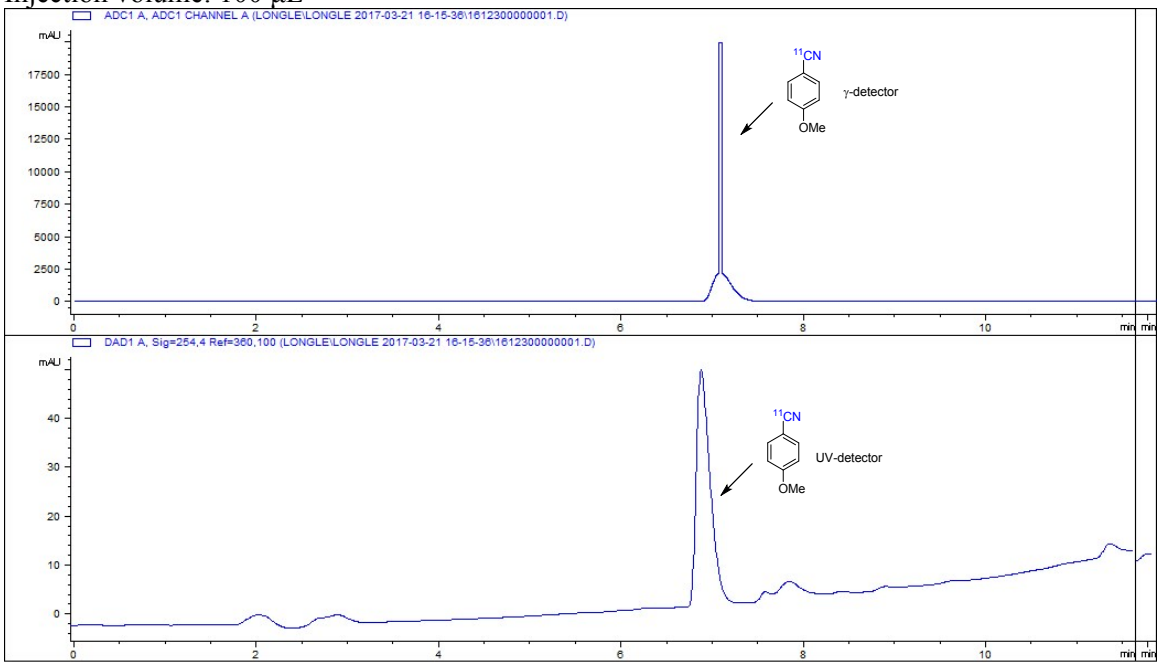
Arylboronic acid (4 mg), CuI (1 mg) and DMEDA (2 µL) were mixed in 0.15 mL DMF in a V-shaped vial sealed with a teflon-lined septum. [^{11}C]HCN produced from cyclotron was trapped in a solution of DMF/water mixture (0.15 mL/0.1mL) containing 16 mg Cs_2CO_3. The trapping was stopped at 10 min post bombardment and the solution with [^{11}C]HCN was transferred to the reaction V-shaped vial. The resulting reaction mixture was heated at 150 °C for 5 min and quenched with 1.1 mL 1:1 acetonitrile/water solution. The quenched reaction mixture was injected to semi-preparative HPLC for purification. The chemical and radiochemical purities of **2a** was determined to be 99% and >99% via analytical HPLC. The specific activity of **2a** was

determined to be 433 mCi/μmol (n=2) based on isolated radioactivity (non-decay corrected) at the end of synthesis (26 min) and concentration derived from the standard curve.

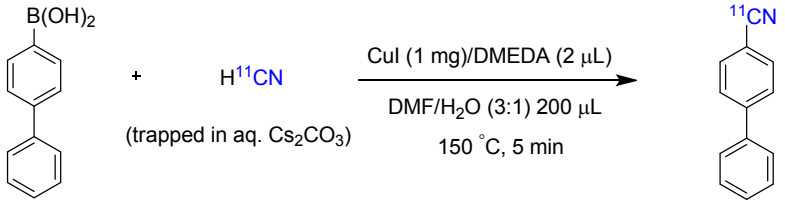
Semi-Preparative RadioHPLC Chromatogram:
Column: Phenomenex Gemini, C18, 250 x 10 mm, 5 μm
Mobile phase: A = Water (0.1% TFA), B = MeCN (0.1% TFA)
Gradient method: 20% B 0-1 min, 20-95 % B 1-20 min
Flow rate: 5 mL/min
Injection volume: 1.5 mL



*Analytical RadioHPLC chromatogram of Isolated **2a**:*
Column: Phenomenex Luna, C18, 250 x 4.6 mm, 5 μm
Mobile phase: A = Water (0.1% TFA), B = MeCN (0.1% TFA)
Gradient method: 30-95% B 0-10 min
Flow rate: 1.5 mL/min
Injection volume: 100 μL



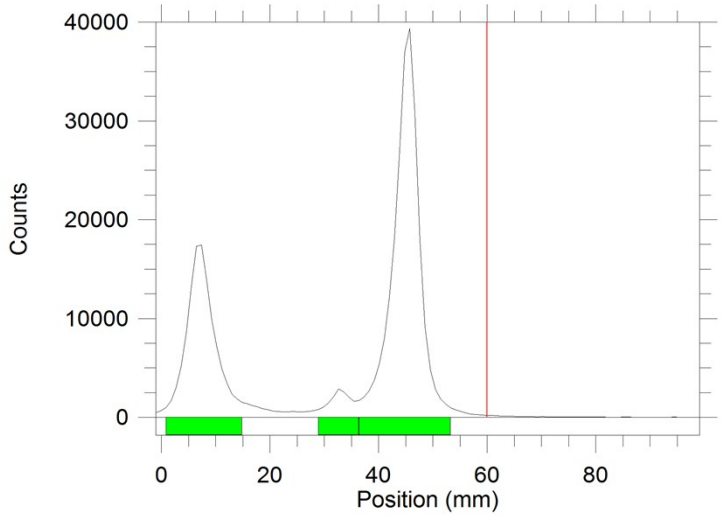
Synthesis of compound **2b:**



1b
4 mg

2b

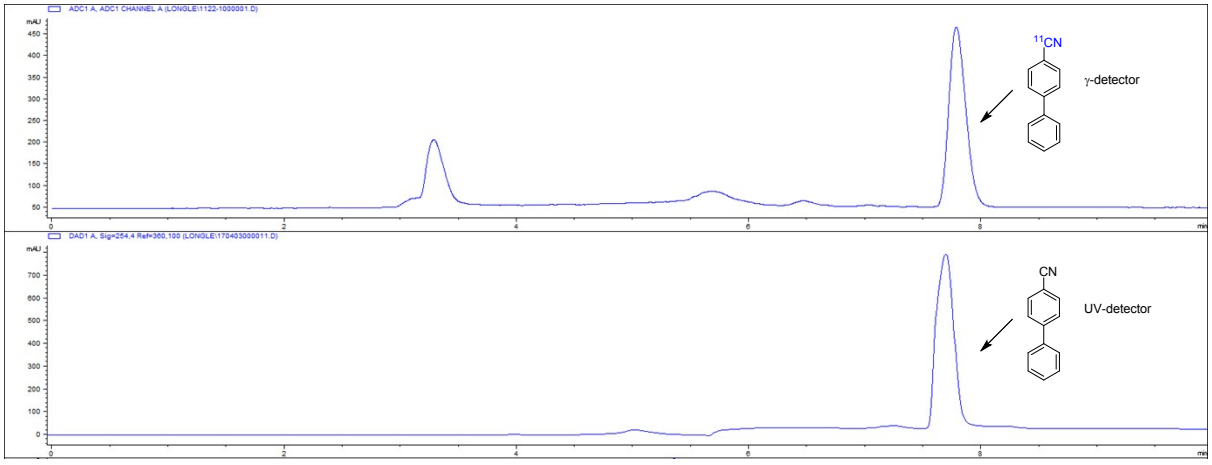
RadioTLC Chromatogram of the Reaction Mixture:



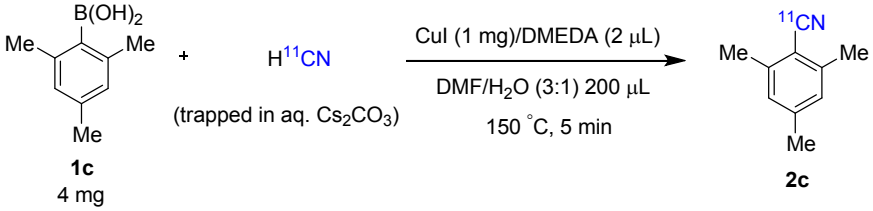
	1	2	mean	standard deviation
RCC (%)	64	65	65	1

RadioHPLC Chromatogram:

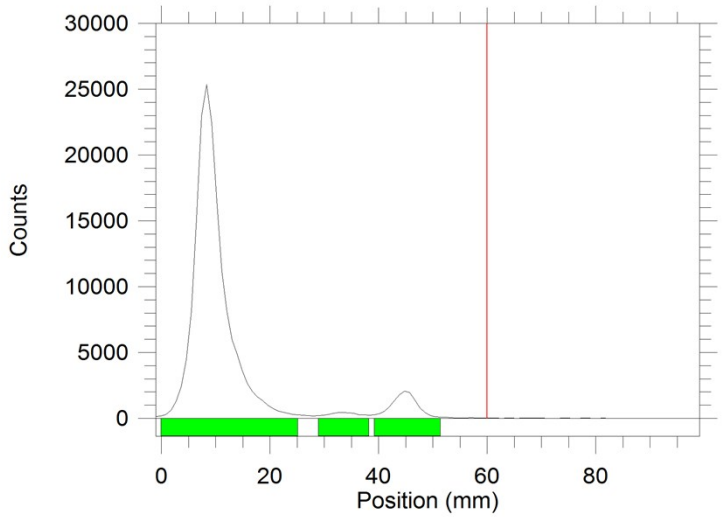
Column: Phenomenex Luna, C18, 250 x 4.6 mm, 5 µm
Mobile phase: A = Water (0.1% TFA), B = MeCN (0.1% TFA)
Gradient method: 5% B 0-1 min, 5-90 % B 1-3 min, 90-95 % B 3-10 min
Flow rate: 1 mL/min
Injection volume: 50 µL



Synthesis of compound **2c:**



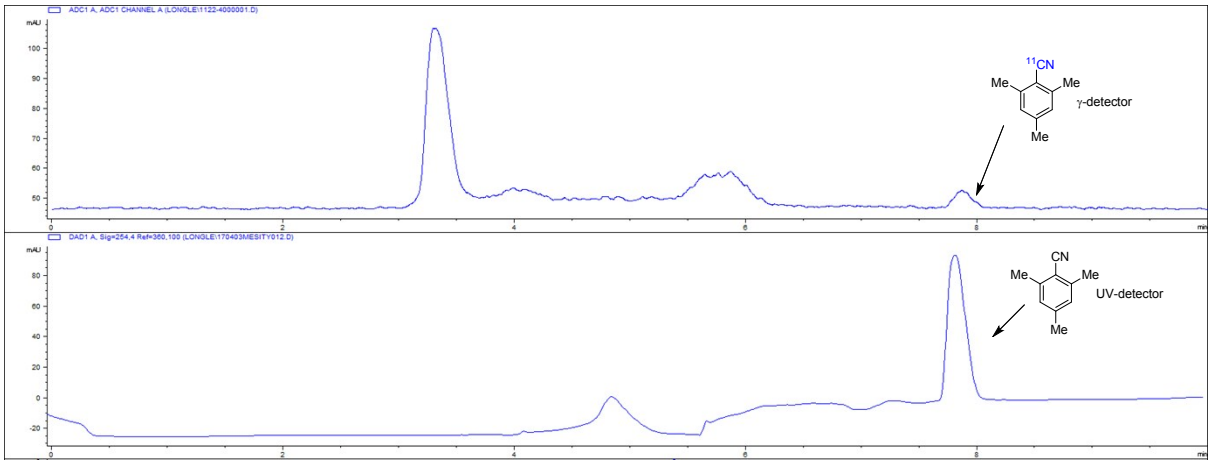
RadioTLC Chromatogram of the Reaction Mixture:



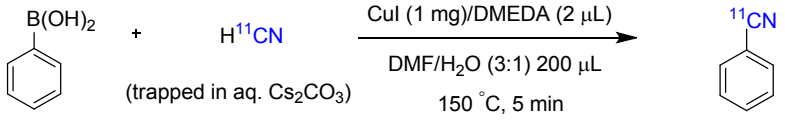
	1	2	mean	standard deviation
RCC (%)	7	8	8	1

RadioHPLC chromatogram:

Column: Phenomenex Luna, C18, 250 x 4.6 mm, 5 µm
Mobile phase: A = Water (0.1% TFA), B = MeCN (0.1% TFA)
Gradient method: 5% B 0-1 min, 5-90 % B 1-3 min, 90-95 % B 3-10 min
Flow rate: 1 mL/min
Injection volume: 50 µL



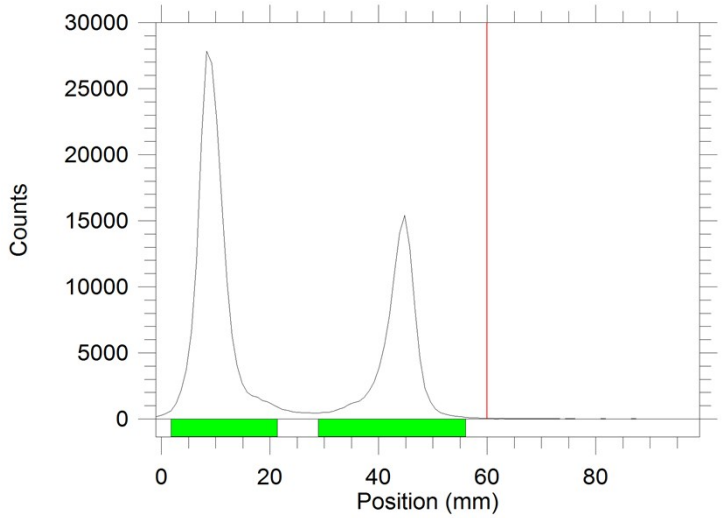
Synthesis of compound **2d:**



1d
4 mg

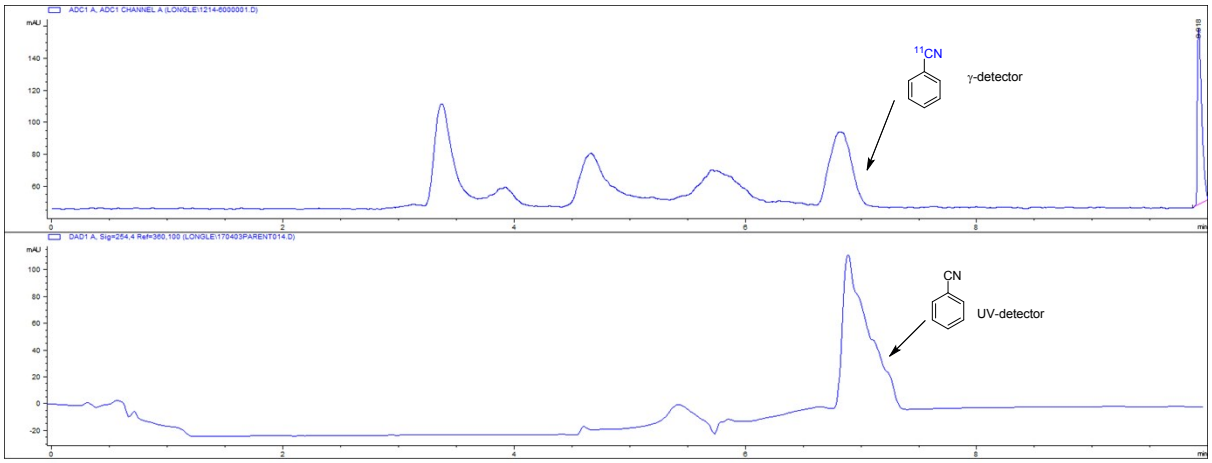
2d

RadioTLC chromatogram of the Reaction Mixture:

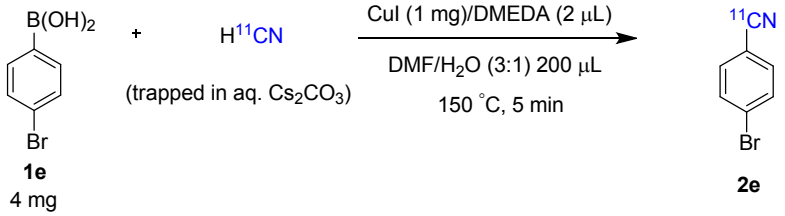


	1	2	mean	standard deviation
RCC (%)	40	34	37	4

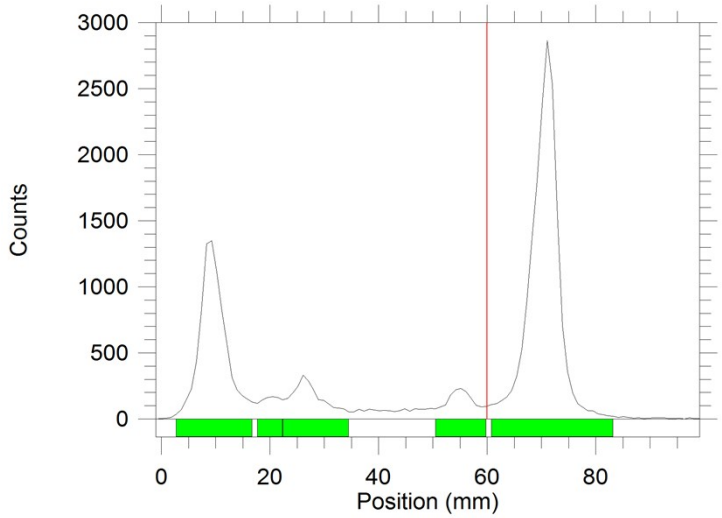
RadioHPLC Chromatogram:
Column: Phenomenex Luna, C18, 250 x 4.6 mm, 5 µm
Mobile phase: A = Water (0.1% TFA), B = MeCN (0.1% TFA)
Gradient method: 5% B 0-1 min, 5-90 % B 1-3 min, 90-95 % B 3-10 min
Flow rate: 1 mL/min
Injection volume: 50 µL



Synthesis of compound **2e:**



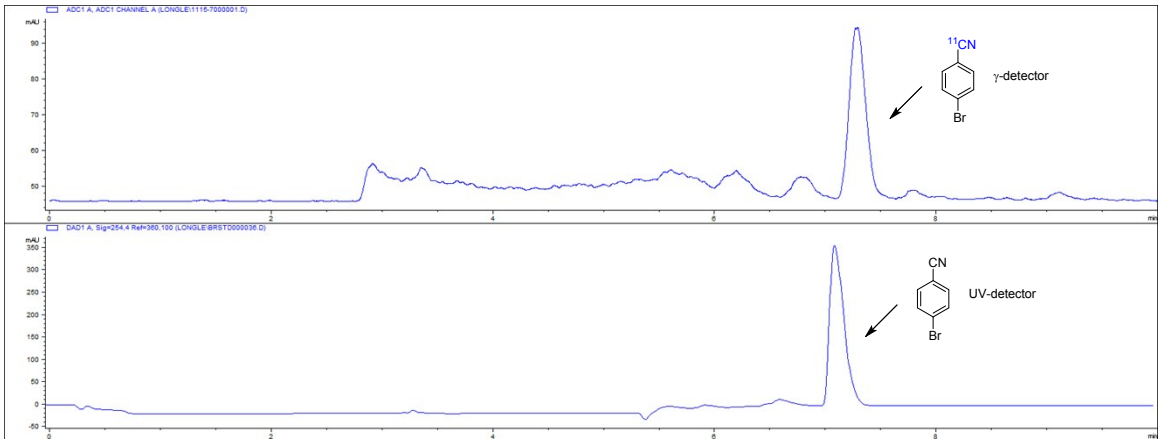
RadioTLC chromatogram of the Reaction Mixture:



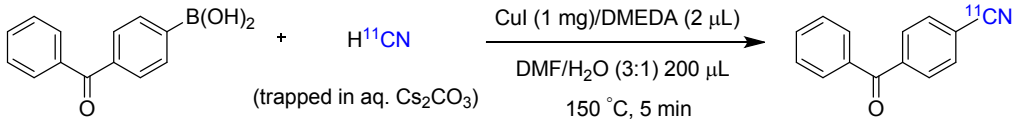
	1	2	3	mean	standard deviation
RCC (%)	58	44	61	54	9

RadioHPLC Chromatogram:

Column: Phenomenex Luna, C18, 250 x 4.6 mm, 5 µm
Mobile phase: A = Water (0.1% TFA), B = MeCN (0.1% TFA)
Gradient method: 5% B 0-1 min, 5-90 % B 1-3 min, 90-95 % B 3-10 min
Flow rate: 1 mL/min
Injection volume: 50 µL



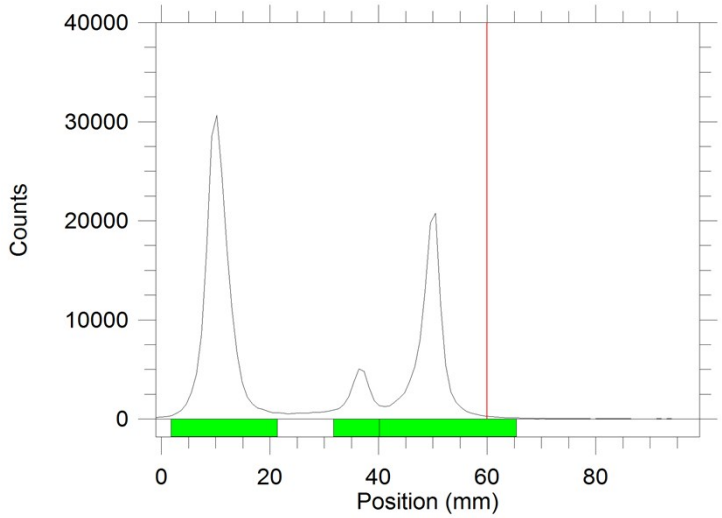
Synthesis of compound **2f:**



1f
4 mg

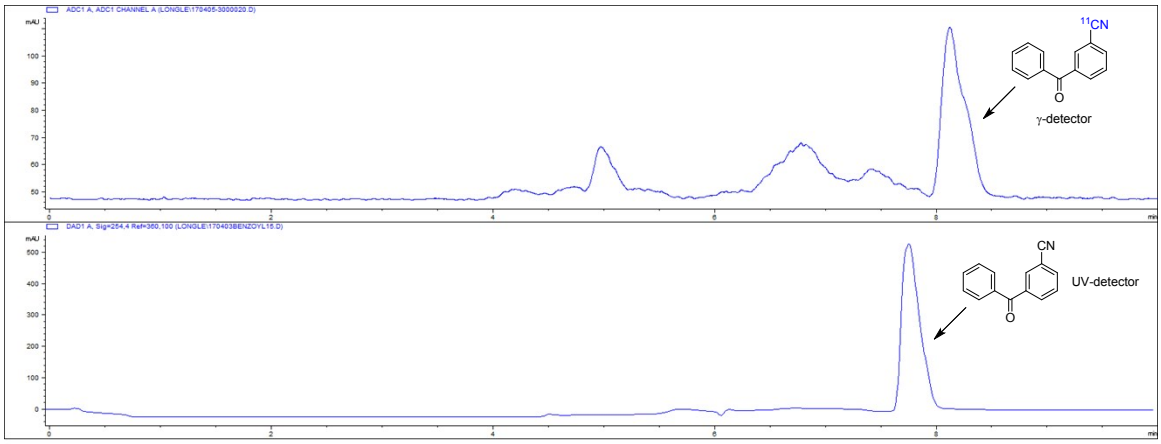
2f

RadioTLC Chromatogram of the Reaction Mixture:

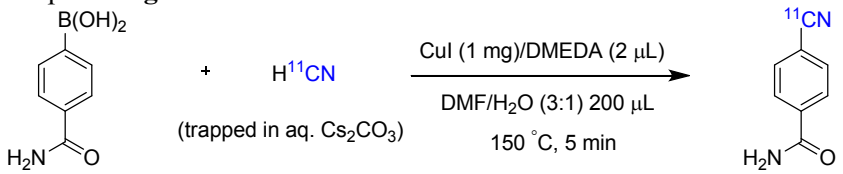


	1	2	mean	standard deviation
RCC (%)	36	32	34	3

RadioHPLC Chromatogram:
Column: Phenomenex Luna, C18, 250 x 4.6 mm, 5 µm
Mobile phase: A = Water (0.1% TFA), B = MeCN (0.1% TFA)
Gradient method: 5% B 0-1 min, 5-90 % B 1-3 min, 90-95 % B 3-10 min
Flow rate: 1 mL/min
Injection volume: 50 µL



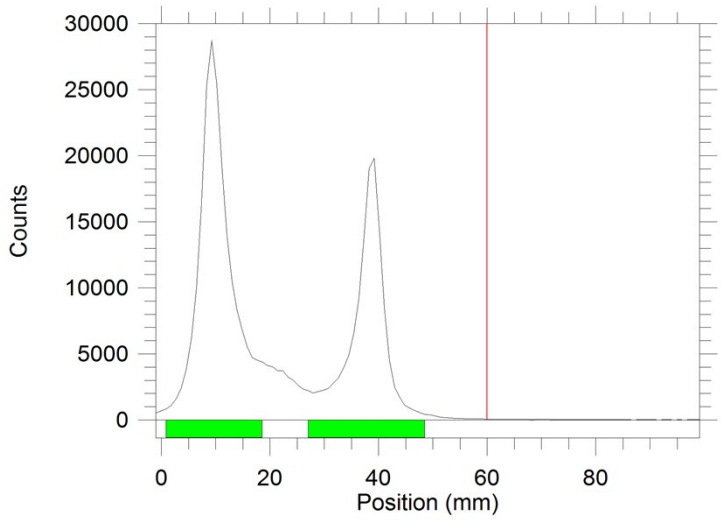
Synthesis of compound **2g:**



1g
4 mg

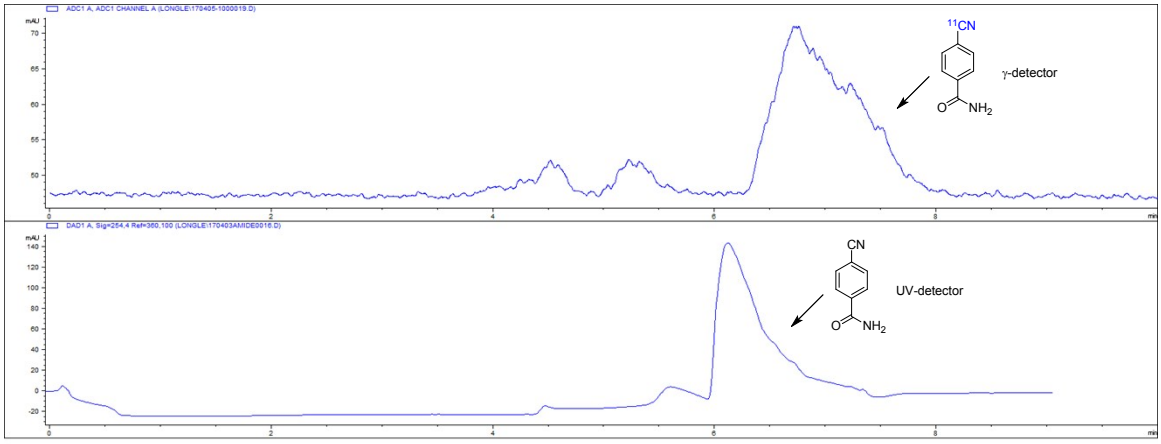
2g

RadioTLC Chromatogram of the Reaction Mixture:

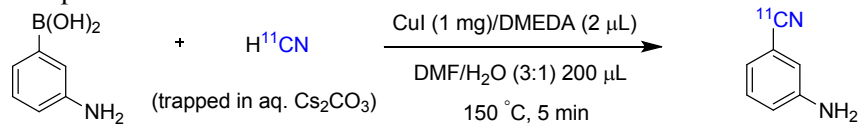


	1	2	mean	standard deviation
RCC (%)	40	32	36	6

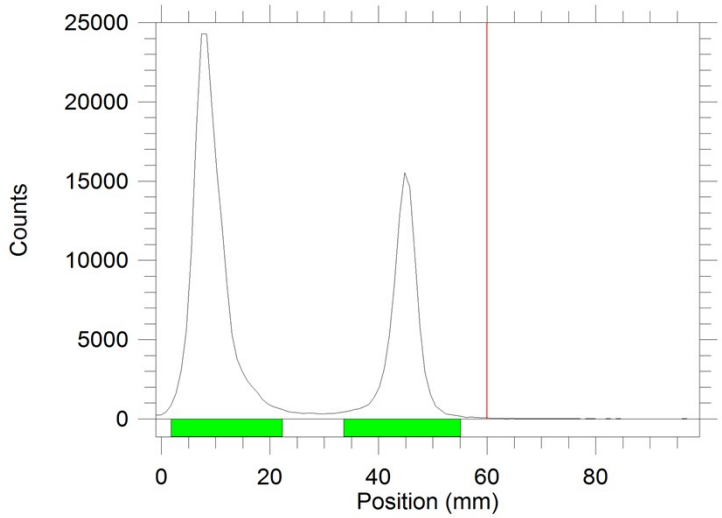
RadioHPLC Chromatogram:
Column: Phenomenex Luna, C18, 250 x 4.6 mm, 5 µm
Mobile phase: A = Water (0.1% TFA), B = MeCN (0.1% TFA)
Gradient method: 5% B 0-1 min, 5-90 % B 1-3 min, 90-95 % B 3-10 min
Flow rate: 1 mL/min
Injection volume: 50 µL



Synthesis of compound **2h:**



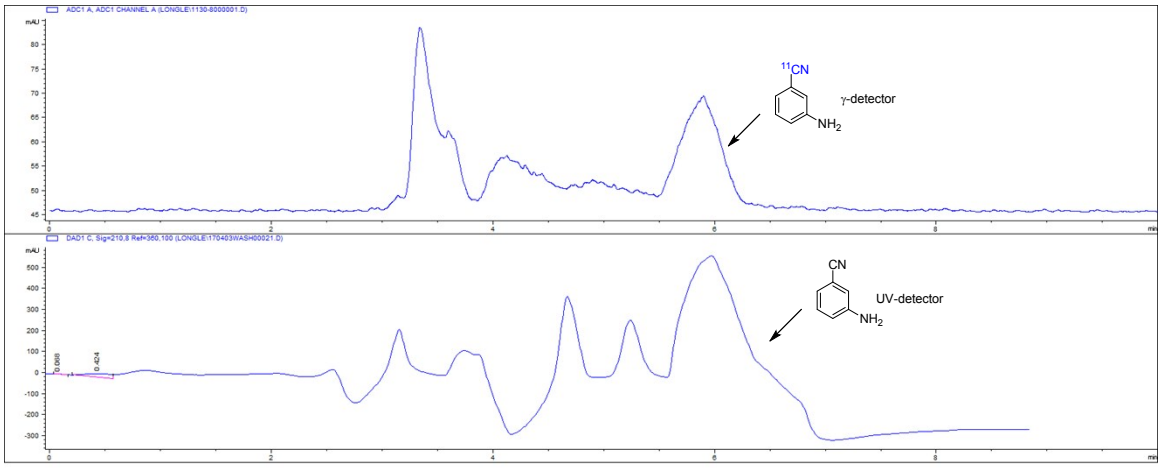
RadioTLC Chromatogram of the Reaction Mixture:



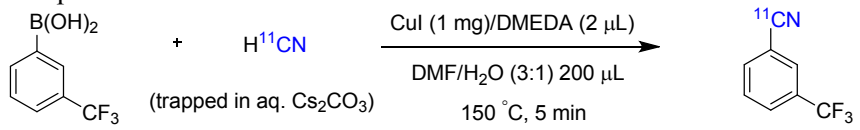
	1	2	mean	standard deviation
RCC (%)	36	32	34	3

RadioHPLC Chromatogram:

Column: Phenomenex Luna, C18, 250 x 4.6 mm, 5 µm
Mobile phase: A = Water (0.1% TFA), B = MeCN (0.1% TFA)
Gradient method: 5% B 0-1 min, 5-90 % B 1-3 min, 90-95 % B 3-10 min
Flow rate: 1 mL/min
Injection volume: 50 µL



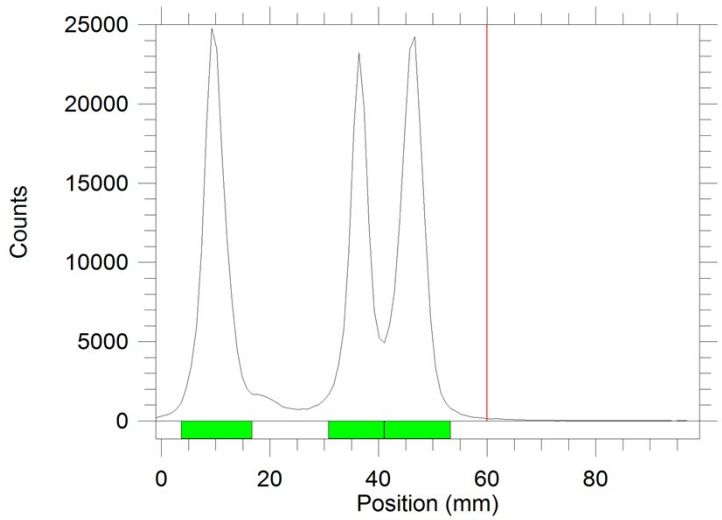
Synthesis of compound **2i:**



1i
4 mg

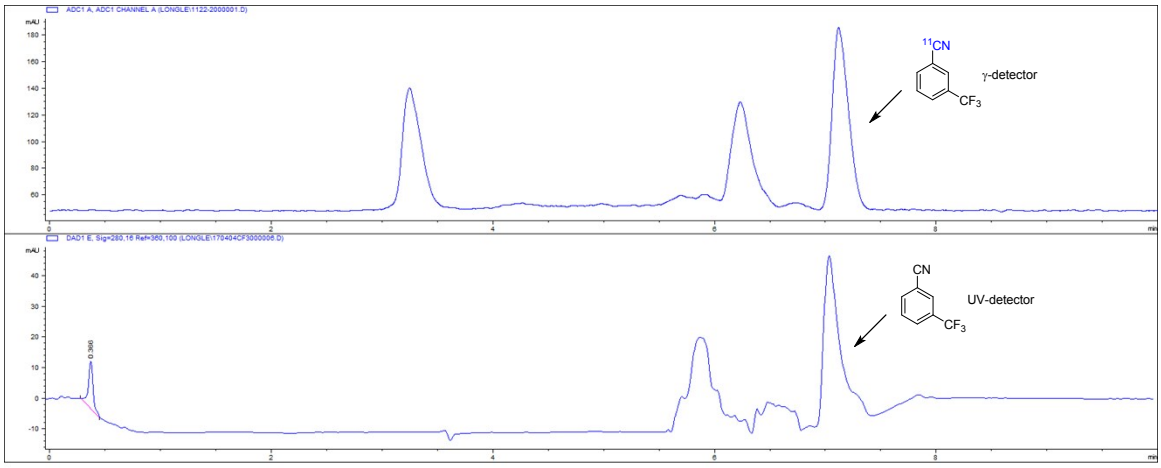
2i

RadioTLC Chromatogram of the Reaction Mixture:

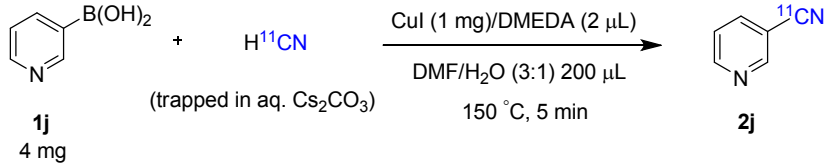


	1	2	mean	standard deviation
RCC (%)	36	38	37	1

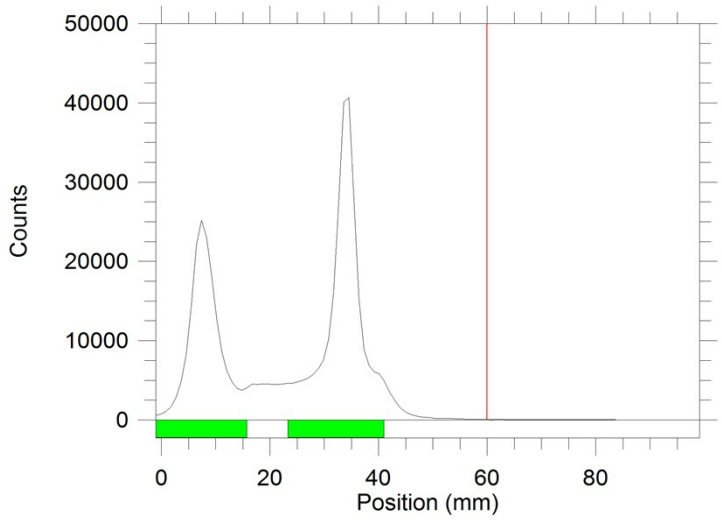
RadioHPLC Chromatogram:
Column: Phenomenex Luna, C18, 250 x 4.6 mm, 5 µm
Mobile phase: A = Water (0.1% TFA), B = MeCN (0.1% TFA)
Gradient method: 5% B 0-1 min, 5-90 % B 1-3 min, 90-95 % B 3-10 min
Flow rate: 1 mL/min
Injection volume: 50 µL



Synthesis of compound **2j:**

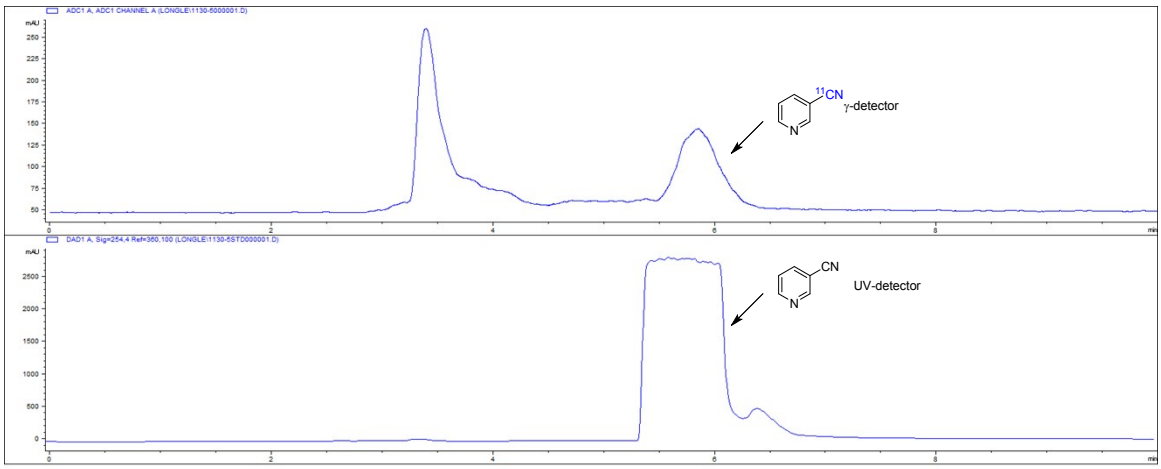


RadioTLC Chromatogram of the Reaction Mixture:

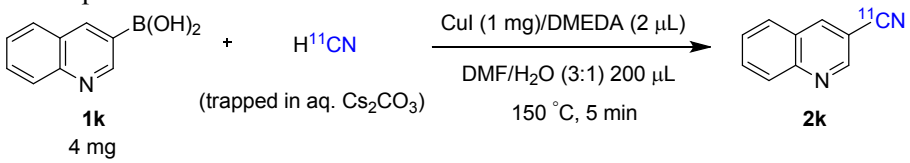


	1	2	mean	standard deviation
RCC (%)	63	43	53	14

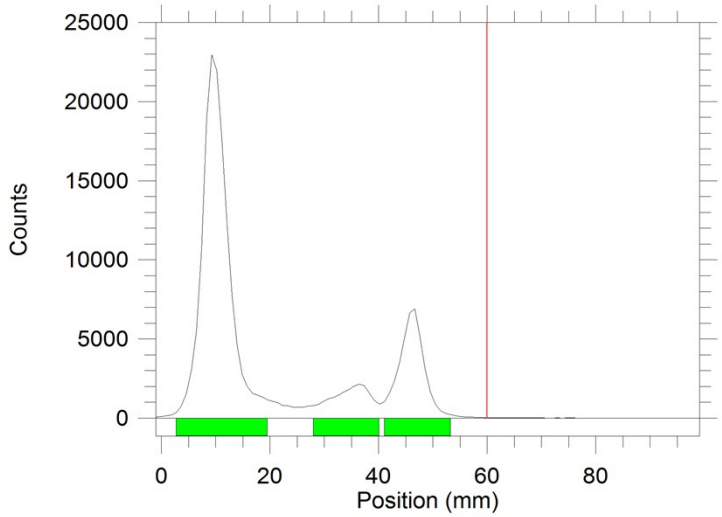
RadioHPLC Chromatogram:
Column: Phenomenex Luna, C18, 250 x 4.6 mm, 5 µm
Mobile phase: A = Water (0.1% TFA), B = MeCN (0.1% TFA)
Gradient method: 5% B 0-1 min, 5-90 % B 1-3 min, 90-95 % B 3-10 min
Flow rate: 1 mL/min
Injection volume: 50 µL



Synthesis of compound **2k:**



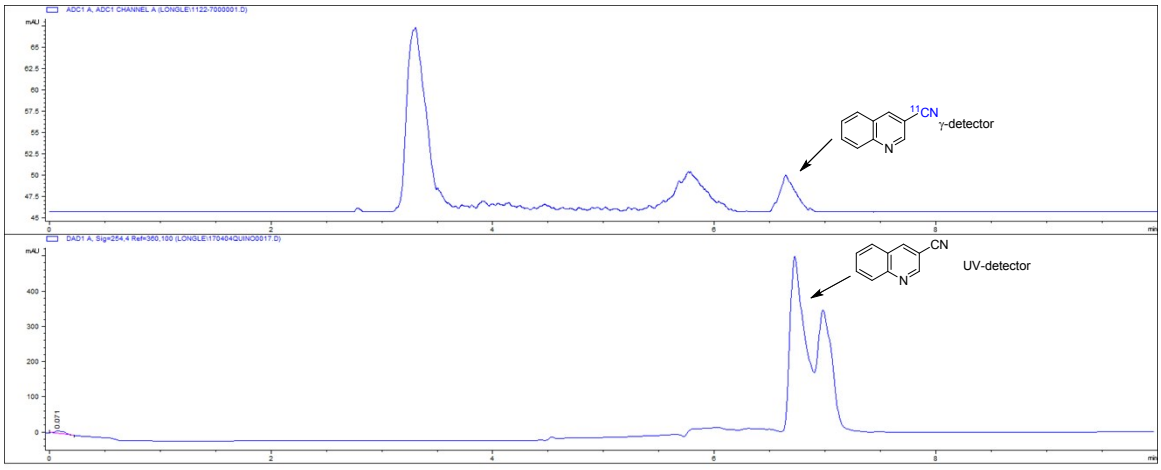
RadioTLC Chromatogram of the Reaction Mixture:



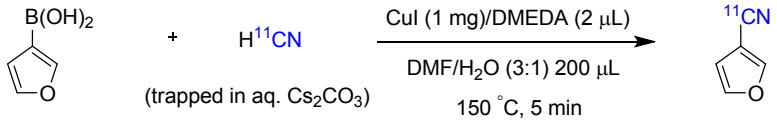
	1	2	mean	standard deviation
RCC (%)	20	16	18	3

RadioHPLC Chromatogram:

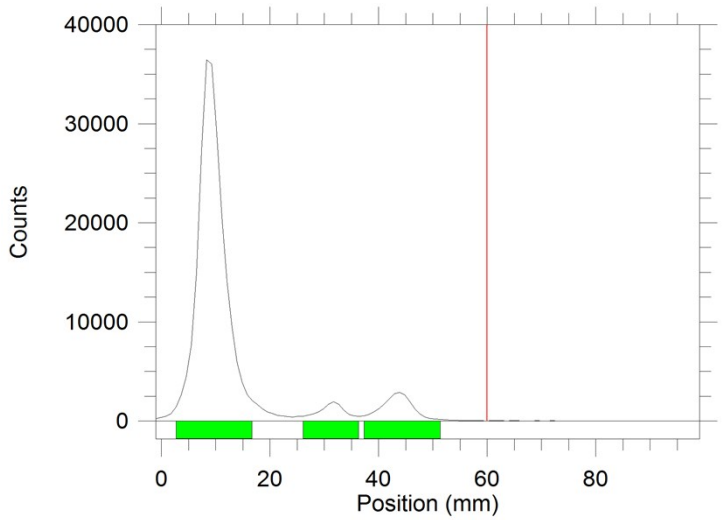
Column: Phenomenex Luna, C18, 250 x 4.6 mm, 5 µm
Mobile phase: A = Water (0.1% TFA), B = MeCN (0.1% TFA)
Gradient method: 5% B 0-1 min, 5-90 % B 1-3 min, 90-95 % B 3-10 min
Flow rate: 1 mL/min
Injection volume: 50 µL



Synthesis of compound **2l:**



RadioTLC Chromatogram of the Reaction Mixture:



	1	2	mean	standard deviation
RCC (%)	8	9	9	1

RadioHPLC Chromatogram:

Column: Phenomenex Luna, C18, 250 x 4.6 mm, 5 µm
Mobile phase: A = Water (0.1% TFA), B = MeCN (0.1% TFA)
Gradient method: 5% B 0-1 min, 5-90 % B 1-3 min, 90-95 % B 3-10 min
Flow rate: 1 mL/min
Injection volume: 50 µL