A Potent and Selective C-11 Labeled PET Tracer for Imaging Sphingosine-1-phosphate Receptor 2 in the CNS Demonstrates Sexually Dimorphic Expression

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Supporting Information

Copies of ¹H NMR spectra for known compounds and ¹H NMR, ¹³C NMR spectra for new compounds
Sample Name: T224-160
Data Collected on: Aug 26, 2015
Archive directory: /Users/username/Documents/Analysis_Data
Sample directory: T224-160_20150826_15
File Type: .edp

Pulse Sequence: Carbon (qspsp)
Solute: pm-pec
Data collected on: Aug 26, 2015
Temp. 25.0 °C / 298.1 K
Sample size: 486.0 g, Operator: vaar

Pulse delay: 1.000 sec
Pulse: 90.0 degrees
Acq. time: 1.000 sec
Width: 3510.0 Hz
1024 repetitions
OVERSAMP 1024, 5120464 MHz
SINE1 20, 399.3440 MHz
Power as for continuous acquisition
DATA PROCESS 1: 2048, 2048
Line broadening: 0.00 ppm
FT size: 2048
Total time: 1 min

Sample: 5e
CHN: N N N
OMOM

Sample: 18
CHN: N N N
Cl OH

ppm
18
Table S1. Conditions screening for the radiolabeling of compound 18.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reaction conditions</th>
<th>HPLC conditions</th>
<th>Product Collected (mCi)</th>
<th>Radiochemical purity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$[^{11}\text{C}]\text{MeOTf}$, 5 M$_{\text{(aq.)}}$ KOH 3 µL, DMF 200 µL, 85 °C, 5 min</td>
<td>45% acetonitrile in 0.1 M ammonium formate, pH 4.5</td>
<td>14.7</td>
<td>&gt; 99%</td>
</tr>
<tr>
<td>2</td>
<td>$[^{11}\text{C}]\text{MeOTf}$, 5 M$_{\text{(aq.)}}$ KOH 3 µL, DMF 200 µL, 60 °C, 5 min</td>
<td>45% acetonitrile in 0.1 M ammonium formate, pH 4.5</td>
<td>24.5</td>
<td>79%</td>
</tr>
<tr>
<td>3</td>
<td>$[^{11}\text{C}]\text{MeI}$, solid Cs$_2$CO$_3$, DMF 200 µL, 85 °C, 5 min</td>
<td>45% acetonitrile in 0.1 M ammonium formate, pH 4.5</td>
<td>2.1</td>
<td>&gt; 99%</td>
</tr>
<tr>
<td>4</td>
<td>$[^{11}\text{C}]\text{MeI}$, 5 M$_{\text{(aq.)}}$ KOH 3 µL, DMF 200 µL, 85 °C, 5 min</td>
<td>45% acetonitrile in 0.1 M ammonium formate, pH 4.5</td>
<td>26.9</td>
<td>71%</td>
</tr>
<tr>
<td>5</td>
<td>$[^{11}\text{C}]\text{MeI}$, 5 M$_{\text{(aq.)}}$ CsOH 3 µL, DMF 200 µL, 85 °C, 5 min</td>
<td>45% acetonitrile in 0.1 M ammonium formate, pH 6.5</td>
<td>15.8</td>
<td>&gt; 99%</td>
</tr>
<tr>
<td>6</td>
<td>$[^{11}C]$Mel, 5 M\textsubscript{(aq.)} KOH, DMF 200 \mu\text{L}, 85 \degree\text{C}, 5 min</td>
<td>45% acetonitrile in 0.1 M ammonium formate, pH 6.5</td>
<td>31.1</td>
<td>&gt; 99%</td>
</tr>
</tbody>
</table>

**Figure S1.** Analytical HPLC chromatograms of $[^{11}C]$5a precursor 18 (panel A), nonradiolabeled standard 5a (panel B), and co-injection of 18 and 5a (panel C). Analytical HPLC conditions: Agilent Zorbax SB-C18 column, 250 × 4.6 mm, mobile phase 55% acetonitrile in 0.1 M ammonium formate, pH 4.5, flow rate 1.2 mL/min, detection wavelength 254 nm.
Figure S2. Typical analytical HPLC trace of formulated $[^{18}\text{F}]$5a. Panel A shows UV trace for $[^{11}\text{C}]$5a with 10% EtOH in saline; panel B: $[^{11}\text{C}]$5a radiochemical trace; panel C: UV trace for co-injection of $[^{11}\text{C}]$5a and 5a; panel D: radiochemical trace for co-injection of $[^{11}\text{C}]$5a and 5a. Analytical HPLC conditions: Agilent Zorbax SB-C18 column, 250 × 4.6 mm, mobile phase 55% acetonitrile in 0.1 M ammonium formate, pH 4.5, flow rate 1.2 mL/min, detection wavelength 254 nm.