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Supplemental Information

Dataset**Author(s):**

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Publication date:

2018-07

Permanent link:

<https://doi.org/10.3929/ethz-b-000266284>

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Identification and Preclinical Evaluation of a Radiofluorinated Benzazepine Derivative for Imaging the GluN2B Subunit of the Ionotropic NMDA Receptor

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Supplemental Information

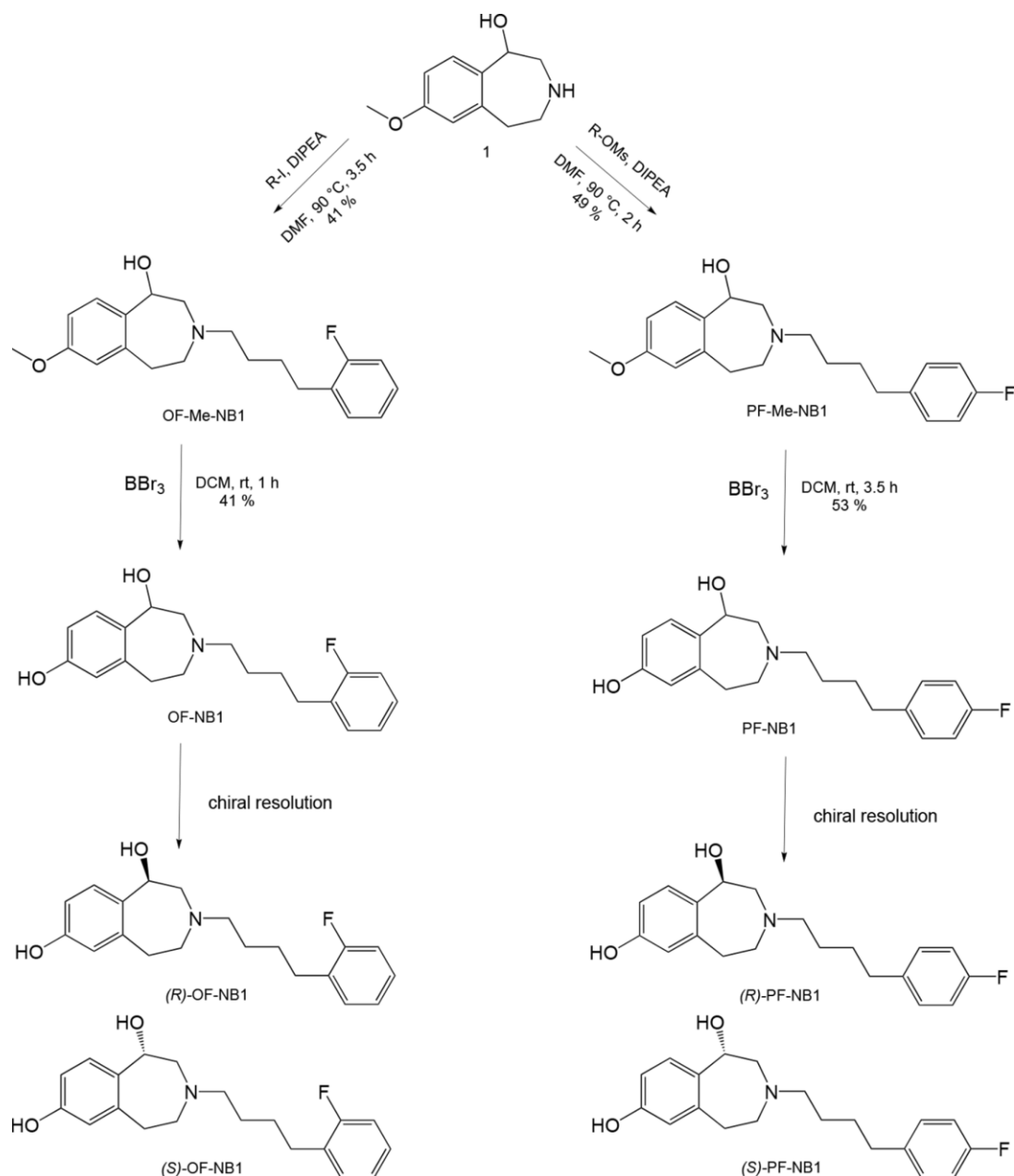
Chemistry

Reagents were purchased from Acros Organics, Amatek Chemical, ABCR, Fluorochem, Merck, Sigma Aldrich as well as Perkin Elmer and were used without any further purification. Solvents for thin-layer chromatography (TLC), flash column chromatography and extractions were of technical grade. Dry solvents for all non-aqueous reactions were purchased from Acros Organics (dried over molecular sieves, H₂O < 0.005 %). High performance liquid chromatography (HPLC) grade solvents were provided by Fisher Scientific. Non-aqueous reactions were carried out in flame-dried glassware under N₂-atmosphere using standard Schlenk techniques and organic reactions were generally monitored by TLC using silica gel 60 F₂₅₄ coated glass plates supplied by Sigma Aldrich with visualization under UV light ($\lambda = 254$ nm) or through staining with potassium permanganate KMnO₄. Flash column

chromatographies were carried out with silica gel (60 Å pore size, 230–400 mesh particle size) from Sigma Aldrich as a stationary phase, while preparative HPLC purifications were conducted on a Merck-Hitachi system (D-7000 interface, L-7400 UV detector and L-7100 pump) with a Ultimate XB-C18 reversed-phase column (5 μm, 21.2 x 150 mm), using a mixture of aqueous NH₄HCO₃ (10 mM, solvent A) and MeCN (solvent B) and a gradient system as follows: 0–5 min: 80 % A, 5–15 min: 80–50 % A, 15–20 min: 50 % A, 20–28 min: 50–5 % A, 28–35 min: 5 % A, 35–37 min: 5–80 % A, 37–45 min: 80 % A. The flow rate was 10 mL/min. Enantiomeric purifications were performed by semi-preparative normal phase HPLC using a Reprosil Chiral-NR column (8 μm, 250 x 10 mm) with an isocratic system of hexane/isopropanol 4:1 for OF-NB1 and PF-NB1 and hexane/isopropanol 98:2 for precursor **7**. Carbon-11 labeled probes were purified by semi-preparative HPLC on a Merck-Hitachi system equipped with a L-6200A Intelligent pump, a Knauer Variable Wavelength Monitor UV-detector and a Veenstra Instrument VRM-202 radioactivity detector. A Sunfire C18 reversed-phase column (5 μm, 10 x 150 mm) and the following system were used: Aqueous H₃PO₄ (0.1%, solvent A) and MeCN (solvent B) 0–8 min: 10–25 % B, 8–19 min: 25–75 % B, 19–20 min: 75–10 % B, 20–30 min: 10 % B. The flow rate was 5 mL/min. For quality control, an aliquot of the final formulation was injected into an analytical Agilent 1100 HPLC system equipped with a Raytest Gabi Star radiodetector and an Atlantis T3 C18 reversed-phase column (3 μm, 4.6 x 150 mm). Conditions: 0.1% TFA in H₂O (solvent A), MeCN (solvent B); 0-10 min, 40-60% B; 10-11 min, 60-40% B; 11-15 min, 40% B, flow rate 1 mL/min, UV detection at 230 nm. Tracer identities were confirmed by co-injection of the corresponding reference compounds and comparison of the retention times.

¹H and ¹³C nuclear magnetic resonance (NMR) spectra were recorded at ambient temperature on a Bruker Avance FT-NMR (400 MHz) using CDCl₃ as a solvent. Chemical shifts (δ) are reported in parts per million (ppm) relative to tetramethylsilane (0.00 ppm) with the respective solvent signals as internal standard (δ_H = 7.26 ppm and δ_C = 77.16 for CDCl₃). ¹H-NMR spectra resonance multiplicities are abbreviated as follows: s = singlet, d = doublet, t = triplet, m = multiplet, dd = doublet of doublet, and br = broad peak, whereas coupling constants (*J*) are given in hertz (Hz). High resolution mass spectrometry (HRMS) was carried out on a Bruker maXis - ESI-Qq-TOF-MS spectrometer and the

corresponding mass/charge (m/z) ratios are given in atom mass units. Binding affinities of **OF-Me-NB1** and **PF-Me-NB1** were determined as previously reported (1).



Supplemental Figure 1: Synthesis of reference compounds **OF-Me-NB1** and **PF-Me-NB1** as well as the respective phenolic precursors **OF-NB1** and **PF-NB1**. Chiral separation was carried out by semipreparative HPLC under isochratic normal phase conditions using a system of hexane/isopropanol (4:1).

3-(4-(2-fluorophenyl)butyl)-7-methoxy-2,3,4,5-tetrahydro-1H-benzo[d]azepin-1-ol (OF-Me-NB1)

To a solution of commercially available amine **1** (276 mg, 1.43 mmol) in DMF (5.2 mL) was added dropwise DIPEA (0.2 mL, 1.15 mmol) and a solution of 1-fluoro-2-(4-iodobutyl)benzene (794 mg, 2.85 mmol) in DMF (4 mL). After refluxing for 3.5 h at 90 °C, the reaction mixture was diluted with aq. NaOH (1 mM) and extracted with DCM (3 x 300 mL). Combined organic layers were back-extracted with aq. NaOH (1 mM), dried over MgSO₄. Volatiles were removed under reduced pressure. The crude product was purified by flash column chromatography (gradient elution using hexane/ethyl acetate 4:1 to hexane/ethyl acetate 1:1, all mobile phases containing 0.1 % ammonia) to afford **OF-Me-NB1** (198 mg, 0.58 mmol, 41 % yield). ¹H-NMR (400 MHz, CDCl₃): δ 7.22–7.13 (m, 2H), 7.13–6.96 (m, 3H), 6.68–6.61 (m, 2H), 4.57 (d, *J* = 6.7 Hz, 1H), 3.77 (s, 3H), 3.26 (t, *J* = 13.4 Hz, 1H), 3.16 (m, 1H), 2.99 (m, 1H), 2.63 (m, 5H), 2.51 (d, *J* = 12.0 Hz, 1H), 2.40 (t, *J* = 11.7 Hz, 1H), 1.59 (m, 4H). ¹³C-NMR (400 MHz, CDCl₃): δ 162.5, 160.1, 159.0, 141.4, 135.7, 130.7, 129.9, 127.6, 124.1, 116.7, 115.3, 110.3, 72.6, 61.0, 59.6, 56.2, 55.3, 37.1, 29.0, 28.0, 26.8. HRMS: *m/z* 344.2020 (M+H⁺).

3-(4-(4-fluorophenyl)butyl)-7-methoxy-2,3,4,5-tetrahydro-1H-benzo[d]azepin-1-ol (PF-Me-NB1)

To a solution of amine **1** (426 mg, 2.20 mmol) in DMF (5 ml), DIPEA (0.35 ml, 2.05 mmol) and the respective tosylate (1085 mg, 4.41 mmol) were added dropwise and the solution was stirred for 2 h at 90 °C. The mixture was diluted with DCM and extracted with aq. NaOH (1 mM). The combined organic layers were back-extracted with water and the volatiles removed under reduced pressure. The crude residue was purified by flash column chromatography using a hexane/ethyl acetate gradient (4:1 to 1:1, mobile phases containing 0.1-0.25 % ammonia) to afford **PF-Me-NB1** (367 mg, 1.00 mmol, 49 %). ¹H-NMR (400 MHz, CDCl₃): δ 7.11 (m, 3H), 6.96 (t, *J* = 8.1, 2H), 6.65 (dd, *J* = 10.8, 2H), 4.57 (d, *J* = 6.7, 1H), 3.77 (s, 3H), 3.26 (t, *J* = 13.4, 1H), 3.15 (m, 1H), 2.99 (m, 1H), 2.62 (m, 5H), 2.50 (d, *J* = 12.0, 1H), 2.39 (t, *J* = 11.7, 1H), 1.59 (m, 4H). ¹³C-NMR (400 MHz, CDCl₃): δ 159.0, 141.2, 137.9, 135.6, 129.8, 129.7, 129.6, 116.7, 115.2, 115.0, 110.2, 72.5, 60.8, 59.6, 56.2, 55.3, 37.0, 35.0, 29.3, 26.6.

3-(4-(2-fluorophenyl)butyl)-2,3,4,5-tetrahydro-1H-benzo[d]azepine-1,7-diol (OF-NB1)

To a solution of **OF-Me-NB1** (84 mg, 0.25 mmol) in DCM (3.6 mL) was added dropwise BBr₃ (1M in DCM, 1.8 mL, 1.80 mmol) at -78 °C. Upon stirring for 1h at ambient temperature, the mixture was quenched with aq. NaOH (1 mM) and the pH adjusted to 7 using aq. NaOH (5 M). Volatiles were evaporated under reduced pressure and the resulting brown solid washed by trituration with water. The crude residue was purified by HPLC to afford **OF-NB1** (33 mg, 0.10 mmol, 41 % yield). ¹H-NMR (400 MHz, CDCl₃): δ 7.21–7.13 (m, 2H), 7.09–6.94 (m, 3H), 6.59–6.48 (m, 2H), 4.60 (d, *J* = 6.7 Hz, 1H), 3.30–3.12 (m, 2H), 3.07–2.92 (m, 1H), 2.71–2.51 (m, 6H), 2.44 (t, *J* = 11.7 Hz, 1H), 1.68–1.53 (m, 4H). ¹³C-NMR (400 MHz, CDCl₃): δ 162.5, 160.1, 155.6, 141.2, 134.8, 130.7, 130.1, 127.7, 124.1, 117.6, 115.3, 112.7, 72.3, 60.6, 59.5, 56.0, 36.2, 28.9, 27.9, 26.4. HRMS: *m/z* 330.1862 (M+H⁺).

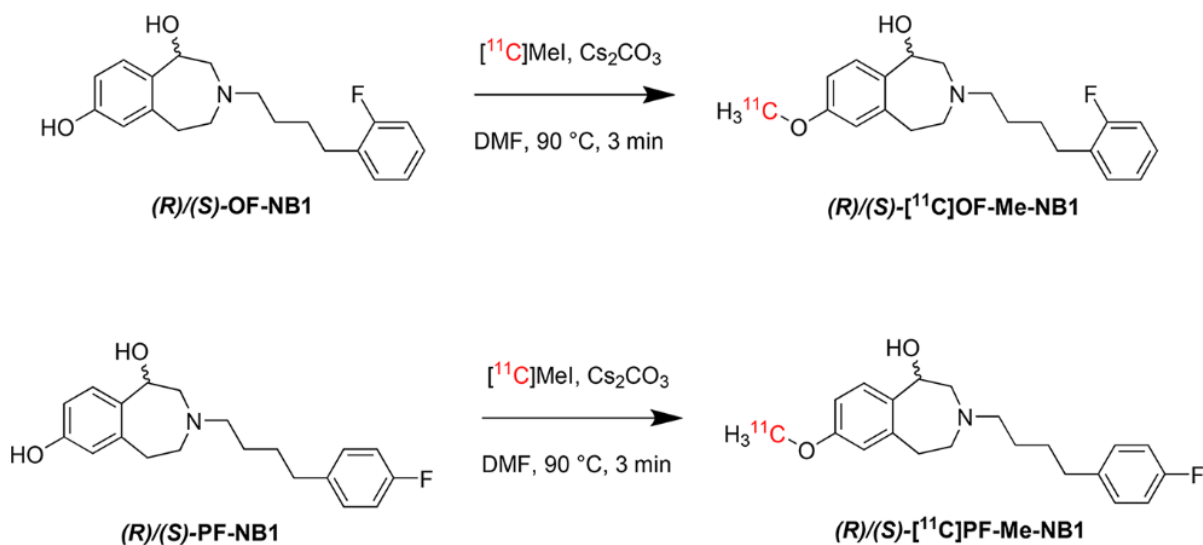
3-(4-(4-fluorophenyl)butyl)-2,3,4,5-tetrahydro-1H-benzo[d]azepin-1,7-diol (PF-NB1)

To a solution of **PF-Me-NB1** (118 mg, 0.343 mmol) in DCM (5 ml) was added dropwise a solution of BBr₃ in DCM (1M, 2.5 ml, 2.50 mmol) at -78 °C. The reaction mixture was stirred for 3.5h at ambient temperature and subsequently quenched by addition of ice water. Volatiles were removed under reduced pressure and the aqueous phase alkalized with aq. NaOH (1M). The mixture was extracted with ethyl acetate (3x 150 mL) and the combined organic layers were concentrated under reduced pressure. The resulting precipitate was purified by preparative HPLC to give the title compound (59 mg, 0.18 mmol, 53 %). ¹H-NMR (400 MHz, CDCl₃): δ 7.11 (m, 2H), 6.95 (m, 3H), 6.50 (m, 2H) 5.44 (m, 2H), 4.58 (d, *J* = 6.7, 1H), 3.14 (m, 2H), 2.94 (m, 1H), 2.59 (t, *J* = 11.7, 4H), 2.53 (t, *J* = 12.0, 1H), 2.41 (t, *J* = 11.87, 1H), 1.58 (m, 4H). ¹³C-NMR (400 MHz, CDCl₃): δ 162.4, 159.9, 155.7, 141.0, 137.9, 134.5, 129.6, 117.8, 115.2, 114.9, 112.6, 72.1, 60.6, 59.5, 56.1, 36.1, 34.9, 29.3, 26.3. HRMS: *m/z* 330.1864 (M+H⁺).

Radiochemistry (Carbon-11 Labeling)

Carbon-11 labeling was performed as previously reported (1). Briefly, $[^{11}\text{C}]\text{CO}_2$ was produced *via* the $^{14}\text{N}(\text{p},\alpha)^{11}\text{C}$ nuclear reaction by proton bombardment of N_2 gas containing 0.5 % O_2 in a Cyclone 18/9 cyclotron (18 MeV; IBA, Belgium). Nickel-based catalytic reduction of $[^{11}\text{C}]\text{CO}_2$ afforded $[^{11}\text{C}]\text{CH}_4$ followed by gas phase iodination to give $[^{11}\text{C}]\text{CH}_3\text{I}$, which was added to a mixture containing 1 mg precursor of either (*S*)-OF-NB1, (*R*)-OF-NB1, (*S*)-PF-NB1 or (*R*)-PF-NB1 with cesium carbonate (5 mg) in DMF (0.4 mL). After stirring for 3 min at 90 °C, the mixture was diluted with H_2O (1.6 mL) and the crude residue was purified by semi-preparative HPLC. Radiotracers were collected in H_2O (8 mL) and trapped on a C18 light cartridge (Waters; preconditioned with 5 mL EtOH and 5 mL H_2O). The cartridge was washed with H_2O (5 mL) and the tracer subsequently eluted with EtOH (0.8 mL). The product was formulated in aqueous saline containing 8 % EtOH.

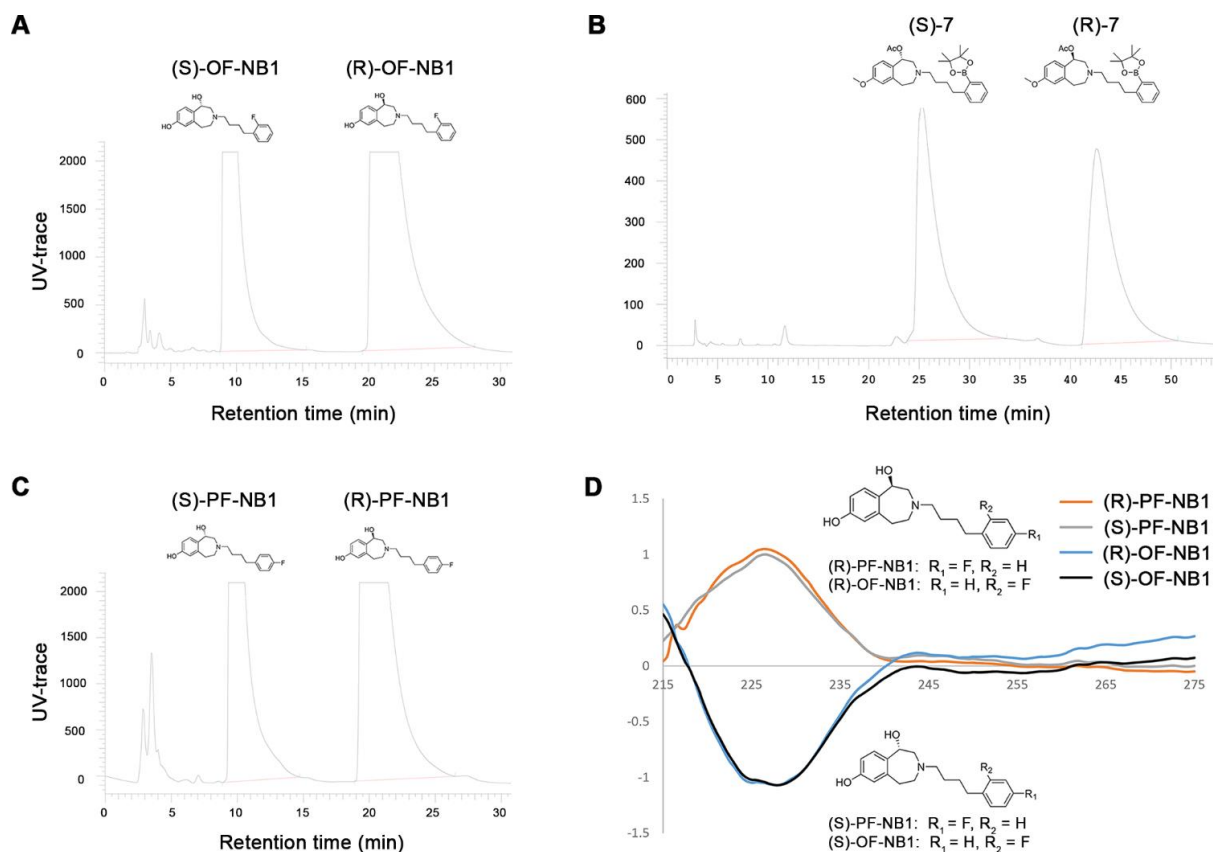
The radiosynthetic conditions are summarized in **Supplemental Figure 2**. Carbon-11 labeled probes were afforded in radiochemical yields from 7 – 36% (decay-corrected), molar activities between 54 and 220 GBq/ μmol and radiochemical purities greater than 99%.



Supplemental Figure 2: Radiosynthesis of (*R*)- $[^{11}\text{C}]\text{PF-Me-NB1}$, (*S*)- $[^{11}\text{C}]\text{PF-Me-NB1}$, (*R*)- $[^{11}\text{C}]\text{OF-Me-NB1}$ and (*S*)- $[^{11}\text{C}]\text{OF-Me-NB1}$.

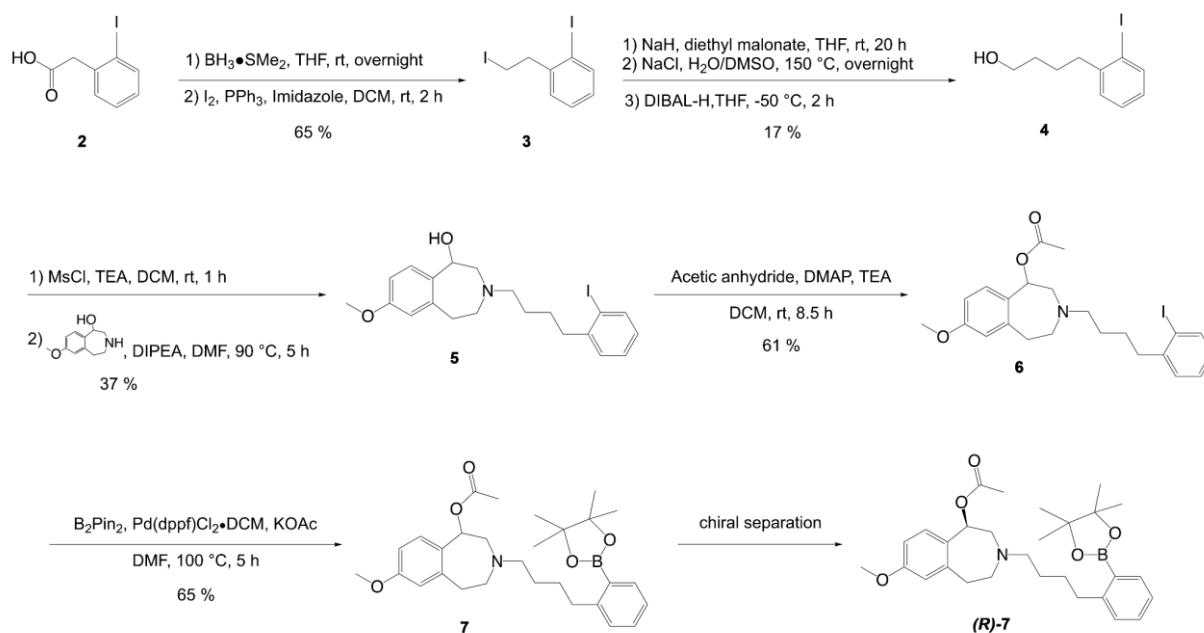
Chiral HPLC and Circular Dichroism

Chiral separations were performed by semi-preparative normal phase HPLC using a Reprisil Chiral-NR column (8 μm , 250 x 10 mm) with an isocratic system of hexane/isopropanol 4:1 for OF-NB1 as well as PF-NB1 and hexane/isopropanol 98:2 for aryl boronic ester precursor **7**. *S*-enantiomers generally eluted first and *R*-enantiomers second, as confirmed by circular dichroism analysis and comparison to a derivative with known absolute configuration. Circular dichroism spectra were recorded in MeOH with a concentration of 0.1 mg/mL of the respective benzazepine.



Supplemental Figure 3: Chiral resolution and circular dichroism spectra. **A.** Chiral resolution of precursor OF-NB1. **B.** Chiral resolution of precursor PF-NB1. **C.** Chiral resolution of aryl boronic ester precursor **7**. **D.** Circular dichroism spectra of (*R*)- and (*S*)-PF-NB1 as well as (*R*)- and (*S*)-OF-NB1.

Synthesis of Precursor 7 for Radiofluorination



Supplemental Figure 4: Synthesis of aryl boronic ester precursor 7 for radiofluorination. Chiral resolution was performed by semipreparative HPLC.

The synthesis of compound 3 and 4 were performed according to published procedure (2).

3-(4-(2-iodophenyl)butyl)-7-methoxy-2,3,4,5-tetrahydro-1H-benzo[d]azepin-1-ol (5)

To a mixture of 4-(2-iodophenyl)butan-1-ol (340 mg, 1.23 mmol) and Et_3N (224 mg, 2.21 mmol) in DCM (12.4 mL) was added dropwise mesyl chloride (137 mg, 1.20 mmol) at 0°C . The mixture was stirred for 1 h at ambient temperature, subsequently diluted with water (10 mL) and extracted with DCM (3 x 50 mL). Combined organic layers were back-extracted with brine, dried over MgSO_4 and concentrated under reduced pressure. The crude residue was dissolved in DMF (3 mL) and added to a solution of amine 1 (207 mg, 1.07 mmol) and DIPEA (0.17 mL, 0.99 mmol) in DMF (7.8 mL) and the mixture was stirred at 90°C for 5 h. The crude residue was purified by flash column chromatography (gradient elution with hexane/ethyl acetate 4:1 to 1:1, containing 0.1% NH_3) to afford the title compound (180 mg, 0.40 mmol, 37% yield for 2 steps). $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ 7.81 (dd, $J = 7.9, 1.1$ Hz, 1H), 7.31–7.23 (m, 1H), 7.20 (dd, $J = 7.6, 1.7$ Hz, 1H), 7.11 (d, $J = 7.9$ Hz, 1H), 6.88 (m, 1H), 6.68–6.62 (m, 2H), 4.59 (d, $J = 6.7$ Hz, 1H), 3.78 (s, 3H), 3.32–3.24 (m, 1H), 3.19 (m, 1H), 3.08–2.98 (m,

1H), 2.79–2.59 (m, 5H), 2.53 (d, $J = 12.1$ Hz, 1H), 2.43 (t, $J = 11.9$ Hz, 1H), 1.68–1.60 (m, 4H). ^{13}C -NMR (400 MHz, CDCl_3): δ 159.0, 144.9, 139.5, 136.6, 129.8, 129.4, 128.4, 127.7, 116.6, 110.2, 100.6, 72.4, 60.8, 59.5, 56.2, 55.2, 40.7, 36.9, 29.7, 28.0, 26.8. HRMS: m/z 474.0892 ($\text{M}+\text{Na}^+$).

3-(4-(2-iodophenyl)butyl)-7-methoxy-2,3,4,5-tetrahydro-1H-benzo[d]azepin-1-yl acetate (6)

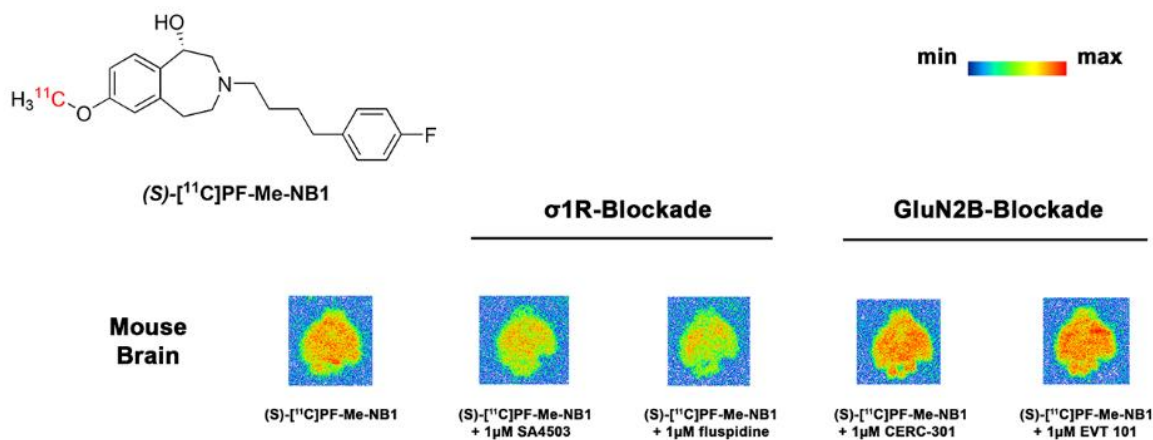
DMAP (9 mg, 0.07 mmol), Et_3N (76 mg, 0.75 mmol), acetic anhydride (76 mg, 0.74 mmol) and benzazepine **5** (165 mg, 0.37 mmol) were dissolved in DCM (8.8 mL). After stirring for 8.5h at ambient temperature, the mixture was diluted with sat. NaHCO_3 and extracted with DCM (3 x 100 mL). Combined organic layers were back-extracted with brine, dried over MgSO_4 and volatiles were removed under reduced pressure. The crude residue was purified by flash column chromatography (hexane/ethyl acetate 7:3) to afford the title compound (110 mg, 0.22 mmol, 61% yield). ^1H -NMR: δ 7.80 (dd, $J = 7.9$, 1.1 Hz, 1H), 7.29–7.23 (m, 1H), 7.22–7.16 (m, 2H), 6.86 (m, 1.8 Hz, 1H), 6.71–6.65 (m, 2H), 5.87 (d, $J = 6.5$, 1H), 3.79 (s, 3H), 3.12 (dd, $J = 12.1$, 8.8 Hz, 1H), 2.99 (dd, $J = 12.1$, 7.5 Hz, 1H), 2.87–2.79 (dd, $J = 14.0$, 8.4 Hz, 1H), 2.77–2.65 (m, 5H), 2.58 (t, $J = 6.7$ Hz, 2H), 2.11 (s, 3H), 1.67–1.50 (m, 4H). ^{13}C -NMR: δ 170.3, 159.3, 145.20, 142.5, 139.6, 131.7, 129.5, 128.7, 128.4, 127.8, 116.0, 110.5, 100.7, 75.1, 58.6 (2C), 55.4, 55.3, 40.8, 36.1, 28.2, 26.7, 21.5. HRMS: m/z 494.1179 ($\text{M}+\text{H}^+$).

7-methoxy-3-(4-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)butyl)-2,3,4,5-tetrahydro-1H-benzo[d]azepin-1-yl acetate (7)

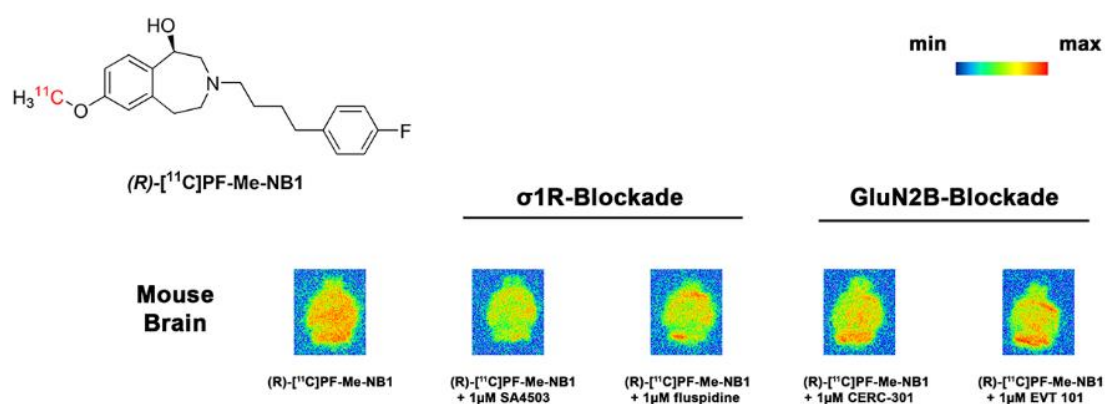
Compound **6** (102 mg, 0.21 mmol), 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (65 mg, 0.26 mmol), potassium acetate (81 mg, 0.83 mmol) and $\text{Pd}(\text{dppf})\text{Cl}_2 \cdot \text{DCM}$ (8 mg, 0.011 mmol) were combined in one flask and dissolved in DMF (2.1 mL). After stirring for 5 h at 100 °C, the mixture was diluted with water (10 mL) and extracted with MTBE (3 x 40 mL). Combined organic layers were back-extracted with brine, dried over MgSO_4 and volatiles were evaporated under reduced pressure. The crude product was purified by flash column chromatography (hexane/ethyl acetate 7:3) to afford the title

compound (66 mg, 0.13 mmol, 65 % yield). ¹H-NMR: δ 7.76 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.38–7.31 (m, 1H), 7.17 (t, *J* = 7.7 Hz, 3H), 6.72–6.65 (m, 2H), 5.88 (d, *J* = 7.0 Hz, 1H), 3.79 (s, 3H), 3.16–3.04 (m, 1H), 3.03–2.93 (m, 1H), 2.92–2.79 (m, 3H), 2.77–2.64 (m, 3H), 2.61–2.50 (m, 2H), 2.12 (s, 3H), 1.60–1.52 (m, 4H), 1.34 (s, 12H). ¹³C-NMR: δ 170.3, 159.3, 149.9, 142.5, 136.2, 131.6, 131.0, 129.3, 128.7, 125.1, 116.0, 110.5, 83.5 (2C), 75.1, 59.0, 58.6, 55.4, 55.2, 36.1, 35.8, 31.4, 27.0, 25.0 (4C), 21.5. HRMS: *m/z* 494.3084 (M+H⁺).

In vitro autoradiography (carbon-11 labeled probes)



Supplemental Figure 5: Representative *in vitro* autoradiogram of (S)-[¹¹C]PF-Me-NB1 on coronal mouse brain sections. GluN2B ligands (CERC-301, EVT 101) and σ₁R ligands (SA4503, fluspidine) were used to assess GluN2B-specificity and selectivity over the σ₁R.



Supplemental Figure 6: Representative *in vitro* autoradiogram of (R)-[¹¹C]PF-Me-NB1 on coronal mouse brain sections. GluN2B ligands (CERC-301 and EVT 101) as well as σ₁R ligands (SA4503 and fluspidine) were used to assess GluN2B-specificity and selectivity over the σ₁R.

Determination of Distribution Coefficient at pH 7.4

The distribution coefficient of (*R*)-[¹⁸F]OF-Me-NB1 at pH 7.4 ($\log D_{7.4}$) was determined with the shake-flask method (3). The radiotracer (5 MBq) was partitioned between 1-octanol (saturated with aq. phosphate buffer pH 7.4, 250 μ L) and aq. phosphate buffer pH 7.4 (saturated with 1-octanol, 250 μ L) by shaking for 15 min in an overhead-shaker at ambient temperature and subsequent centrifugation for 3 min at 5000 rpm. Aliquots (50 μ L) of both phases were measured in a γ -counter (Perkin Elmer, Schwerzenbach, CH). The $\log D_{7.4}$ value was calculated as logarithmic ratio of radioactivity in the 1-octanol and the aq. phosphate buffer phase as previously described (1).

Receptor Occupancy Calculations

Receptor occupancy studies with GluN2B-antagonist CP101,606 were conducted using bolus injections of doses ranging from 0.1 mg/kg up to 10 mg/kg. Receptor occupancy was calculated from the applied blocker dose and the respective time-activity curves (area under the curve) according to **equations 1** and **2** (4).

$$AUC = (AUC_{max} - AUC_{min}) * \frac{D_{50}}{D + D_{50}} + AUC_{min} \quad \text{equation 1}$$

$$RO = \frac{AUC_{max} - AUC}{AUC_{max} - AUC_{min}} * 100 \quad \text{equation 2}$$

AUC is the area under the curve of the respective PET scan standardized uptake values (from 4-90 min), whereas D_{50} is the dose required for 50 % receptor occupancy, D is the actual dose and RO is the receptor occupancy in %. AUC_{max} and AUC_{min} are the maximum and minimum binding, respectively.

Ex vivo biodistribution

Supplemental Table 1: Organ biodistribution of (*R*)-[¹⁸F]OF-Me-NB1 in Wistar rats (n=4), reported as averaged % normalized injected dose per gram body weight ± SD.

<i>organ</i>	<i>30 min p.i.</i>	<i>30 min p.i + eliprotil 2 mg/kg</i>	<i>specificity %</i>
<i>spleen</i>	0.244 ± 0.013	0.190 ± 0.018	22
<i>liver</i>	0.315 ± 0.040	0.199 ± 0.032	37
<i>kidney</i>	0.578 ± 0.113	0.197 ± 0.038	66
<i>adrenal gland</i>	1.926 ± 0.457	0.328 ± 0.071	83
<i>lung</i>	0.242 ± 0.021	0.276 ± 0.048	no specificity
<i>femur</i>	0.067 ± 0.017	0.052 ± 0.001	22
<i>heart</i>	0.047 ± 0.004	0.060 ± 0.006	no specificity
<i>fat</i>	0.056 ± 0.024	0.047 ± 0.008	16
<i>intestine</i>	0.653 ± 0.083	0.913 ± 0.078	no specificity
<i>testicle</i>	0.093 ± 0.001	0.068 ± 0.009	27
<i>blood</i>	0.010 ± 0.000	0.043 ± 0.059	no specificity
<i>urine</i>	0.454 ± 0.174	0.796 ± 0.608	no specificity
<i>muscle</i>	0.059 ± 0.006	0.066 ± 0.010	no specificity
<i>pancreas</i>	0.585 ± 0.093	0.211 ± 0.043	64
<i>skin</i>	0.059 ± 0.008	0.061 ± 0.009	no specificity

Supplemental Table 2: Regional biodistribution of (*R*)-[¹⁸F]OF-Me-NB1 in the Wistar rat brain (n=4), reported as averaged % normalized injected dose per gram body weight ± SD.

<i>brain region</i>	<i>30 min p.i.</i>	<i>30 min p.i + eliprotil 2 mg/kg</i>	<i>specificity %</i>
<i>olfactory bulb</i>	0.161 ± 0.024	0.085 ± 0.003	47
<i>hippocampus</i>	0.198 ± 0.020	0.111 ± 0.007	44
<i>thalamus</i>	0.195 ± 0.023	0.121 ± 0.005	38
<i>cerebellum</i>	0.146 ± 0.011	0.088 ± 0.003	40
<i>brain stem</i>	0.215 ± 0.024	0.102 ± 0.003	53
<i>colliculus superior/inferior</i>	0.199 ± 0.022	0.094 ± 0.006	53
<i>cortex</i>	0.201 ± 0.019	0.100 ± 0.005	50
<i>striatum</i>	0.190 ± 0.020	0.102 ± 0.009	46

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