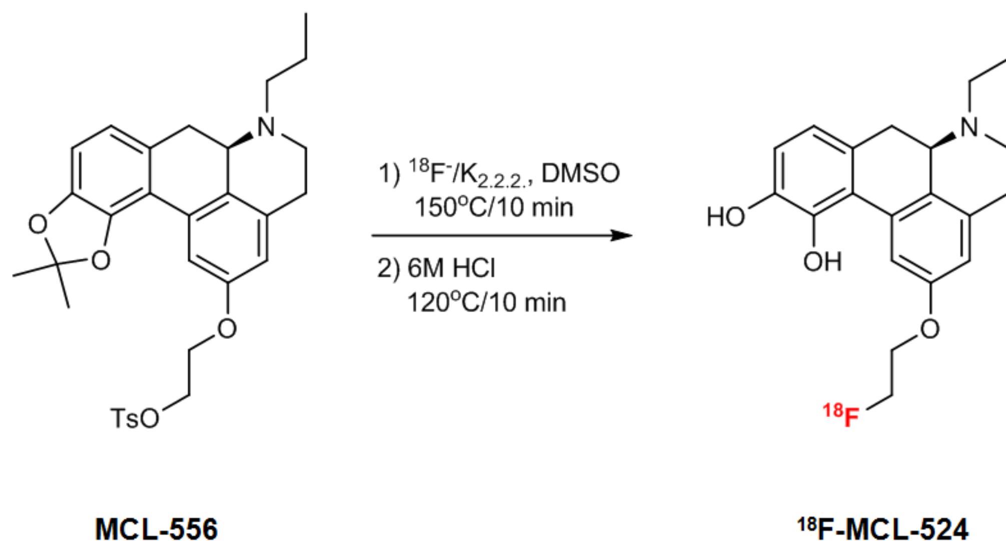
SUPPLEMENTAL MATERIALS AND METHODS



Preparation of (*R*)-(–)-2-^{18}F-fluoroethoxy-N-*n*-propylnorapomorphine (^{18}F-MCL-524): In short, aqueous $^{18}F^{-}$-fluoride was produced via the ^{18}O(p,n)^{18}F nuclear reaction using a GE Healthcare PETtrace cyclotron using silver fluorine-18 water target. The radionuclide was transferred from the target in a 1.5-mL bolus of ^{18}O-H_2O and trapped on a QMA light Sep-Pak cartridge (bicarbonate form). $^{18}F^{-}$-fluoride was then eluted into a reaction vessel using 2 mL of acetonitrile/water (96/4 *v*/*v*) containing 9.8 mg of Kryptofix 2.2.2 and 1.8 mg of K_2CO_3. The solvents were then evaporated under a stream of nitrogen by heating the reactor to 140°C. To the dried $^{18}F^{-}$-fluoride/$K_{2.2.2.}$ complex, 0.8–1.5 mg of MCL-556 in 600–700 µL of dry DMSO were added, and the reaction mixture was heated for 10 min at 150°C–160°C. After ^{18}F-fluorination, the reaction vessel was cooled to 50°C, 700 µL of 6 M aqueous HCl were added, and the reaction was heated to 90°C–110°C for an additional 10 min. After 10 min, the reaction vessel was cooled to room temperature, and the reaction mixture was diluted with 2 mL of water and injected directly onto a semipreparative high-performance liquid chromatography (HPLC) column and

purified using acetonitrile/phosphoric acid (0.01 M aqueous) (18/82 *v/v*) as the mobile phase at a flow of 6 mL/min, with the ultraviolet detector set to 220 nm. The desired fraction was collected into a vial containing 50 mL of water and 200 mg of sodium ascorbate. The resulting solution was pushed though a Sep-Pak tC18 Plus Short cartridge, and the product was then eluted from the cartridge with 1.0 mL of ethanol and collected in a sterile vial prefilled with 10 mL of sterile phosphate-buffered saline solution (PBS) and 25 mg of sodium ascorbate. The aliquot for the quality control analysis was then taken, and the product was filtered using a sterile Millex-GV 0.22-mm filter (Millipore) in a particle-free accepting environment. After filtration, the pH of the product was measured to confirm it was between pH 6.5 and 8. The radiochemical purity was determined using the HPLC system described below under the following conditions: acetonitrile/ammonium formate (0.1 M aqueous) (30/70 *v/v*); flow, 2 mL/min, with UV detector set at 254 nm. Specific activity was determined using the HPLC system described above under the following conditions: acetonitrile/phosphoric acid (0.05 M aqueous) (20/80 *v/v*); flow, 2 mL/min. Specific activity was calculated from ultraviolet adsorption versus ultraviolet adsorption of a known concentration of cold reference.

HPLC instrumentation for preparation of ^{18}F-MCL-524: The semipreparative HPLC system used for radioligand purification consisted of a pump (Smartline 100; Knauer) and automatic sample injector (Rheodyne-type) equipped with a 5-mL loop, ultraviolet detector (Smartline 2500; Knauer), and γ-radioactivity PIN diode detector (Caroll & Ramsey Associates). A μBondapak C18 column (300 × 7.8 mm, 10 μm Waters) was used for the purification.

The radioanalytical HPLC system included a pump (LaChrom L-7100; Merck-Hitachi), ultraviolet detector (LaChrom L-7400; Merck-Hitachi), interface (D-7000; Merck-Hitachi), and β-flow radiodetector (model 170; Beckman Instruments). The system was controlled by Merck-

Hitachi Chromatography Data Station software D-7000 (version 4.1). An ACE 5 C18-HL HPLC column (250 × 4.6 mm, 5 μm, Advances Chromatography Technologies) was used for determination of radiochemical purity. The specific activity was determined on a Hewlett-Packard series 1100 HPLC system using an ACE 5 C18-HL HPLC column.

Preparation of *R*-(−)-10,11-acetonido-N-*n*-propyl-2-tosyloxyethoxynoraporphine (MCL-556): To a 6-dram vial under nitrogen atmosphere were added *R*-(−)-10,11-acetonido-N-*n*-propyl-2-hydroxyethoxynoraporphine (230 mg, 0.582 mmol), DMAP (7.1 mg, 10%), and *p*-toluenesulfonyl chloride (2 equivalents, 222 mg, 1.16 mmol). The vial was capped with a Teflon septum and evacuated and flushed with nitrogen (3×), and then anhydrous dichloromethane (6 mL) was added. Next, triethylamine (0.142 mL) was added and the contents were stirred for 2 h. The reaction was quenched with water (10 mL), and the organic layer was separated. The aqueous layer was extracted with dichloromethane (2 × 6 mL). The combined extracts were filtered through sodium sulfate and concentrated, and the residue was purified by column chromatography to afford 105 mg of pure, light brown oil, 0.191 mmol, 38% isolated yield. The free base was then dissolved in DCM and treated with excess ethereal hydrogen chloride to afford the HCl salt as a tan solid, 38 mg, 19% yield, melting point of 122ºC–124ºC. HPLC showed a single peak.

Preparation of *R*-(−)-10,11-acetonido-N-*n*-propyl-2-hydroxyethoxynoraporphine: To a 6-dram vial were added *R*-(−)-10,11-acetonido-N-*n*-propyl-2-hydroxynoraporphine[i] (200 mg, 0.57 mmol) and 1-bromo-2-(tertbutyldimethylsilyl)ethyl ether (300 mg). Next, THF (6 mL) was added, and after the solids were dissolved, 5N NaOH (6 mL) was added and stirred. Next, Bu_4NI (70 mg) was added and the mixture was stirred at 85ºC for 8 h. An additional portion of 1-

bromo-2-(tertbutyldimethylsilyl)ethyl ether (200 mg) was added and stirred at 85ºC for another 8 h. The cooled mixture was diluted with water (40 mL) and extracted with DCM (3 × 20 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The brown residue was purified by column using 1:30 to 1:20 MeOH:DCM as the eluent to afford 138 mg of *R*-(−)-10,11-acetonido-N-*n*-propyl-2-hydroxyethoxynoraporphine, 0.349 mmol, 61% isolated yield.

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[i]Steiger C, Finnema SJ, Raus L, et al. A two-step one-pot radiosynthesis of the potent dopamine D_2/D_3 agonist PET radioligand [^{11}C]MNPA. *J Labelled Comp Radiopharm.* 2009;52:158–165.