

MATERIALS AND METHODS

Radiochemical synthesis of [¹⁸F]FP-TZTP

This radiosynthesis (Fig. 1) was described in the supplementary materials of our previous communication (Kiesewetter et al., 1995a). A test tube was charged with 3 μmol of K_2CO_3 (30 μL of 0.1 M solution in water), 6 μmol of Kryptofix 2.2.2 (2.25 mg in 50 μL CH_3CN), and an aliquot of aqueous [¹⁸F]fluoride. The solvents were evaporated under a stream of nitrogen while heating the tube at approximately 100°C. Three 200 μL portions of acetonitrile were added and each in turn evaporated to dryness. To this residue, a solution of 5 μmol (1.92 mg) of 1,3-bis(toluenesulfonyloxy)propane in 400 μL CH_3CN was added, vortexed, and then heated at 100°C for 5 min. This reaction solution was transferred into a second tube containing 5 mg (16.5 μmol) of **2** (Fig. 1), 100 μL DMF, and 6 μL of 8 M KOH. This suspension was heated at 100°C for 5 min. At the end of the reaction, the mixture was diluted with 500 μL of buffer (5 mM NaH_2PO_4 , 5 mM Et_3N) and loaded onto a 1 mL BondElut C-18 column. The column was washed with 1 mL water and the product eluted with 1 mL 15% ethanol in CH_3CN . The eluate was loaded onto a semipreparative HPLC column (Axxiom C-18, 9.4 \times 250 mm), eluted at 7 mL/min with 50% CH_3CN , 50% buffer (5 mM NaH_2PO_4 , 5 mM Et_3N). The radioactive product was collected at about 35 min. The volume of the peak was approximately 15 to 20 mL. The eluate was concentrated to about 10 mL under an argon stream while heating in a 100°C block and then loaded onto a 3 mL BondElut C-18. The column was washed with 2 mL water and the product was eluted with 2 mL ether. The ether used for this elution was from a can that had been open for no more than 1 week. The radiochemical yield determined after the BondElut C-18 was 23 (66)% (n=21) at end of synthesis (not corrected for decay). The synthesis time averages 81 min, not including the time required to empty the cyclotron target. The product collected from the BondElut was concentrated until only a small amount of water remained. Ethanol (100 μL) was added to the residual liquid to facilitate efficient transfer. For rat studies, the ethanol/water solution was diluted with phosphate buffered saline to the appropriate dose. For monkey studies, the ethanol/water solution was diluted to about 10 mL with saline and filtered through a 0.22 μm filter. The specific activity for each batch was determined from an aliquot of the ethanol/water solution. The sample was injected onto an Axxiom C-18 column (4.63 \times 250 mm) and eluted with 65% CH_3CN and 35% buffer (retention time 11.2–11.7 min). The radiochemical purity (.95%) was determined from the HPLC radiochromatogram and by radio TLC on Whatman LK6DF Silica gel plates (eluted with 90:9:1 CHCl_3 :MeOH: NH_4OH). Identity was confirmed by coelution of the authentic standard and the radiochemical component by HPLC. The UV absorption at 230 nm was calibrated for mass per unit area with the authentic product. For the specific activity determination, the UV absorption was monitored at both 230 and 310. The specific activity is reported as a ratio of the quantity of radioactivity injected onto the column divided by the mass of the product peak. No correction is made for the presence of any other mass peak. The specific activity averaged 1378 (61045) mCi/ μmol (range 311–2,875) at EOB (n=18).

Radiochemical synthesis of [¹⁸F]FE-TZTP (**4**, Fig. 1)

This synthesis utilized 1,2-bis-toluenesulfonyloxy ethane and followed the same procedure as above except the HPLC eluant for the purification was 45% CH_3CN and 55% buffer. In eight successful runs (only one failed) the radiochemical yield at end of synthesis was 22.6%. Specific activity for the same runs averaged 855.6452 mCi/ μmol at EOB. HPLC analysis of specific activity utilized the same elution parameters as [¹⁸F]TP-TZTP. The elution time was about 8.5 min. Area per unit mass was calibrated at 310 nm. The radiochemical purity was determined from the HPLC radiochromatogram and by TLC (Whatman LK6DF Silica gel plates eluted with 90:9:1 CHCl_3 :MeOH: NH_4OH). Identity was confirmed by co-elution of the authentic standard and the radiochemical component by HPLC.