Experimental Procedures

General

All commercial reagents and solvents were purchased from Sigma-Aldrich or Merck, were of analytical grade, and were used without further purification. The ^{1}H and ^{13}C NMR spectra were recorded on a JEOL ECA-500 FT-NMR spectrometer (Advanced Radiation Technology Institute, Korea Atomic Energy Research Institute). All chemical shifts were reported on the ppm scale with tetramethylsilane as an internal standard. Mass spectra were recorded on a JEOL JMS-AX505WA spectrometer. Compounds were measured by electrospray ionization (ESI) and fast atom bombardment (FAB) methods at the National Center for Interuniversity Research Facilities (NCIRF). Gravity column chromatography was performed on Merck silica gel 60 (70-230 mesh ASTM). Thin layer chromatography (TLC) was performed on Merck silica gel 60 F_{254} glass plates and was visualized by UV light. Purification was achieved by HPLC, with a SP930D pump, UV730D UV detector (Young-Lin Inc., Korea), and FC-3200 high energy gamma detector (Bioscan, USA) to measure the radioactive flow. The UV detection wavelength was 254 nm for all experiments. Both semipreparative (Phenomenex Luna, C18, 10 mm × 250 mm) and analytical (Waters Atlantis C18, 4.6 mm × 250 mm) reverse-phase HPLC columns were used. A CRC-712MH radioisotope calibrator (Capintec Instruments, USA) was used for radioactivity measurements. ^{18}F analysis was performed with a 1480 WIZARD 3 gamma counter (Perkin Elmer, USA), and ^{3}H was measured with an LS 6500 liquid scintillation counter (Beckman, USA). No-carrier-added (n.c.a) ^{18}F fluoride was produced on a PETtrace cyclotron (16.4 MeV, General Electric Company, USA) by irradiation of a ^{18}O-H_2O water target.

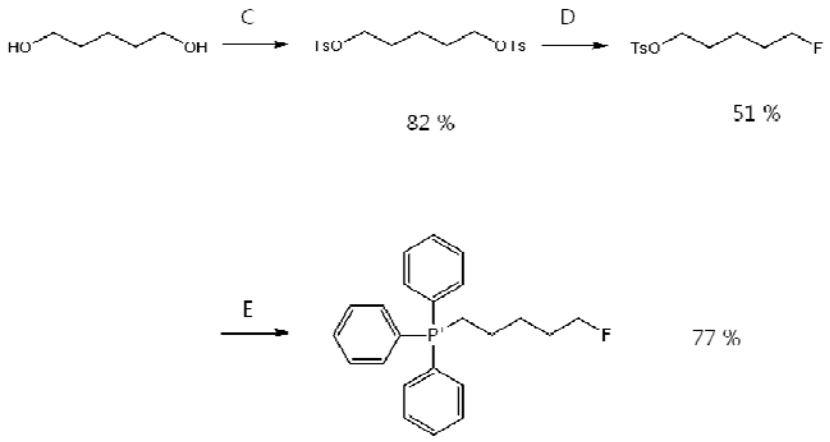
Chemistry

Synthesis of pentane-1,5-diyl bis(4-methylbenzenesulfonate) Pentane-1,5-diol (1.56 g, 15.0 mmol) in 30.0 mL of anhydrous pyridine was added to 4-methylbenzene-1-sulfonyl chloride (8.58 g , 45.0 mmol) at 0 °C. The mixture was stirred at room temperature for 3 h, quenched with 3.0 mL of water and stirred for a further 30 min. Methylene chloride and 1.0 M HCl were added to reaction mixture and the pyridine was extracted from organic phase. The organic phase was washed twice with water and brine, dried over sodium sulfate and filtered. After evaporation of the solvent, the solution was purified by column chromatography (methylene

chloride : *n*-hexane : acetone = 48 : 50 : 2) recrystallized from methylene chloride : *n*-hexane to yield 5.07 g (82 %) of pentane-1,5-diyl bis(4-methylbenzenesulfonate). mp 81-83 °C; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.3 Hz, 4H), 7.34 (d, *J* = 8.0 Hz, 4H), 3.97 (t, *J* = 6.3 Hz, 4H), 2.44 (s, 6H), 1.59 (m, 4H), 1.35 (m, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 144.96, 133.01, 130.00, 127.96. 70.08, 28.26, 21.75, 21.60; HRMS (ESI) *m/z* calculated for $C_{19}H_{24}O_6S_2Na$ $[M+Na]^+$ 435.0987, found 435.0982.

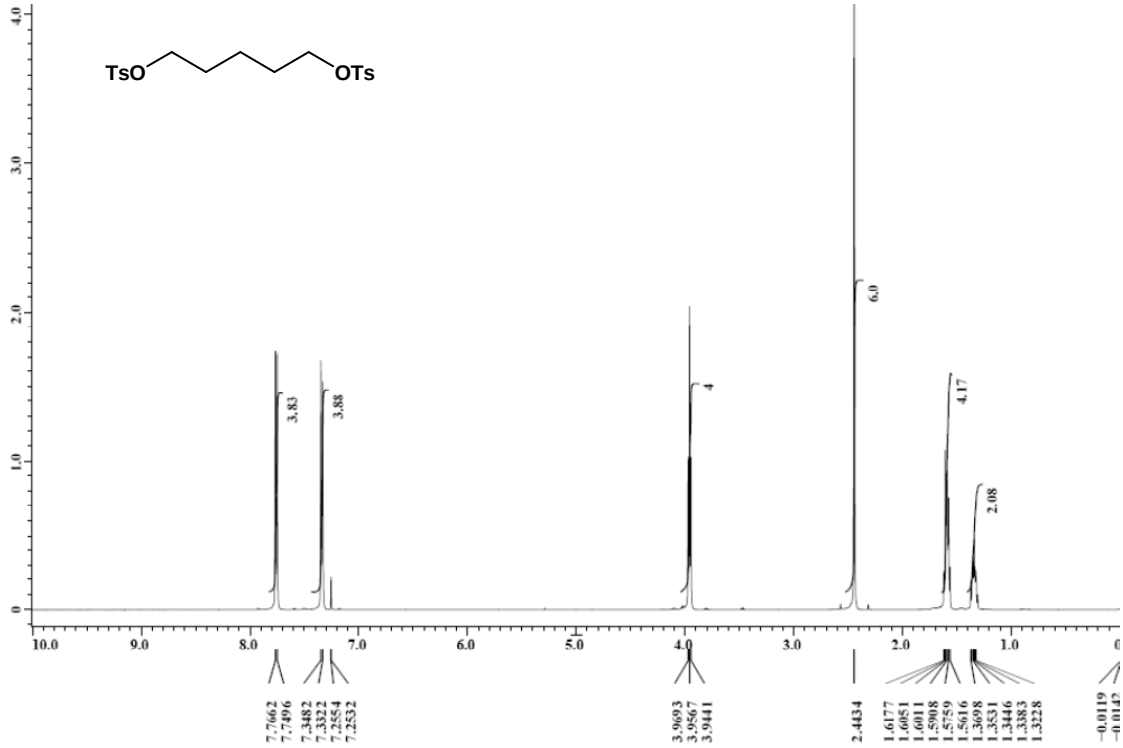
Synthesis of 5-fluoropentyl 4-methylbenzenesulfonate Anhydrous acetonitrile (3.0 mL) was added to tetrabutylammonium fluoride trihydrate (TBAF, 1.43 g, 4.54 mmol). The mixture was evaporated under reduced pressure to remove the water. This procedure was repeated twice. Pentane-1,5-diyl bis(4-methylbenzenesulfonate) (1.87 g, 4.54 mmol) in 10.0 mL of anhydrous acetonitrile was added to the reaction flask. The mixture was stirred for 4 h at 85 °C in a closed tube. The solvent was evaporated under reduced pressure. Column chromatography (methylene chloride : *n*-hexane : acetone = 49 : 50 : 1) provided 0.60 g (51 %) of 5-fluoropentyl 4-methylbenzenesulfonate as a yellow oil. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 4.39 (dt, *J* = 47.2, 6.05 Hz, 2H), 4.03 (t, *J* = 6.3 Hz, 2H), 2.44 (s, 3H), 1.64 (m, 4H), 1.44 (m, 2H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 144.87, 133.15, 129.94, 127.97, 83.75, 70.32, 29.85, 28.53, 21.73, 21.46; MS (FAB) *m/z* 261 $[M+H]^+$, 173 (100); HRMS (FAB) *m/z* calculated for $C_{12}H_{18}FO_3S$ $[M+H]^+$ 261.0961, found 261.0958.

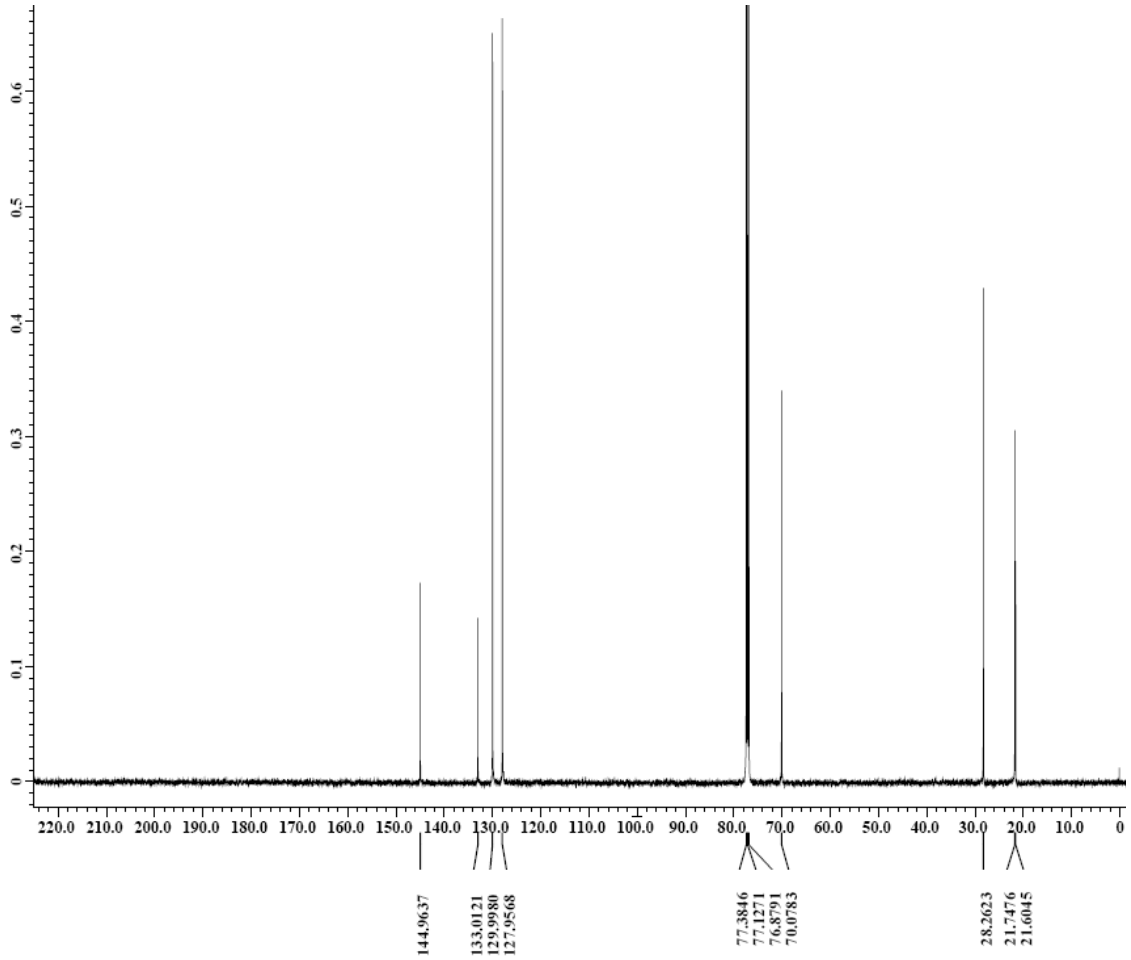
Synthesis of (5-fluoropentyl)triphenylphosphonium salt Triphenylphosphine (1.0 g, 3.81 mmol) dissolved in 10.0 mL anhydrous acetonitrile was added to 5-fluoropentyl 4-methylbenzenesulfonate (0.99 g, 3.81 mmol). The solution was refluxed 19 h. The solvent was evaporated under reduced pressure, the solution was purified by column chromatography (methylene chloride : methanol : ethyl acetate = 8 : 1 :1) provided 1.03 g (77 %) of (5-fluoropentyl)triphenylphosphonium salt as a powder. mp 218-220 °C; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.72 (m, 17H), 7.06 (d, *J* = 8.0 Hz, 2H), 4.33 (dt, *J* = 47.6, 5.7 Hz, 2H), 3.63 (m, 2H), 2.29 (s, 3H), 1.66 (m, 6H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 144.58, 138.58, 135.01, 133.71, 130.49, 128.37, 126.22, 118.82, 118.14, 84.05, 29.54, 26.25, 22.27, 21.49; MS (FAB) *m/z* 351 $[M]^+$, 351 (100); HRMS (FAB) *m/z* calculated for $C_{23}H_{25}FP$ $[M]^+$ 351.1678, found 351.1685.



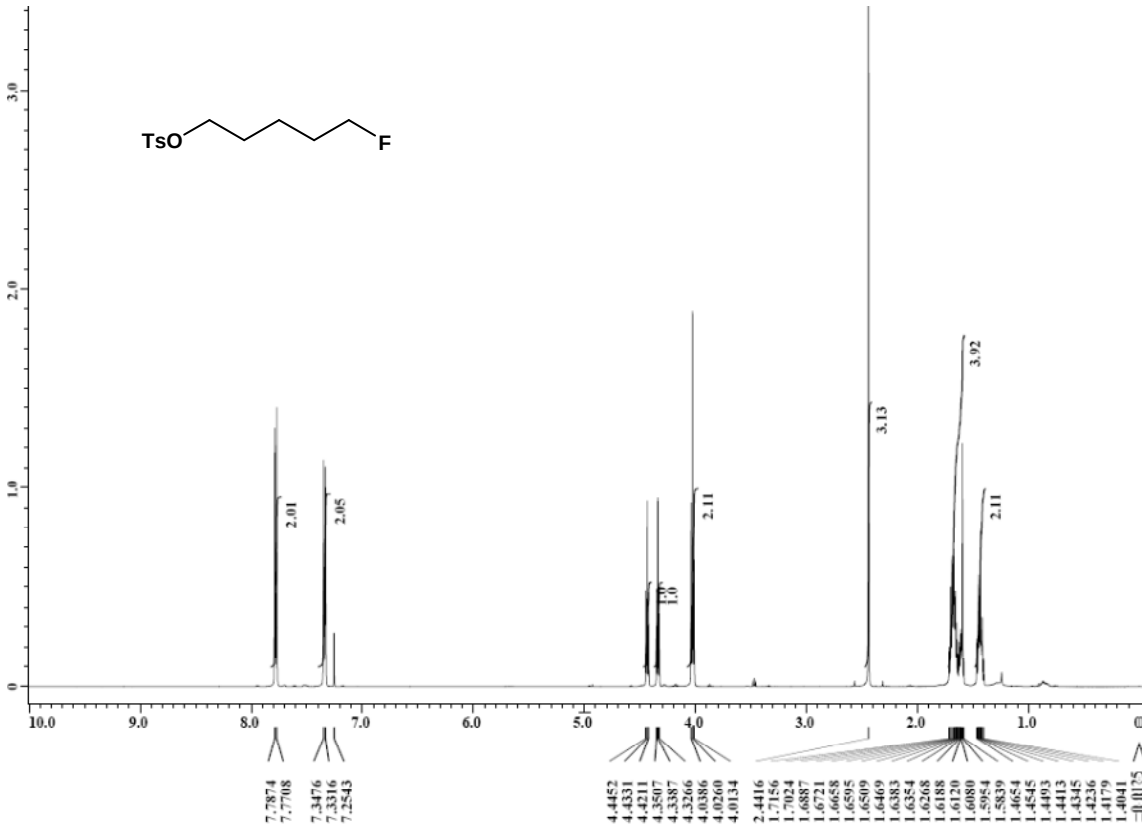
Supplemental Figure 1. Reagents and conditions : (C) 4-methylbenzene-1-sulfonyl chloride, pyridine, room temp, 3 h; (D) tetra butyl ammonium fluoride, acetonitrile, 85 °C, 4 h; (E) triphenylphosphine, acetonitrile, reflux, 19 h.

^{1}H and ^{13}C NMR spectra of all compounds





Supplemental Figure 2. (A) ^{1}H spectra of pentane-1,5-diyl bis(4-methylbenzenesulfonate). (B) ^{13}C spectra of pentane-1,5-diyl bis(4-methylbenzenesulfonate).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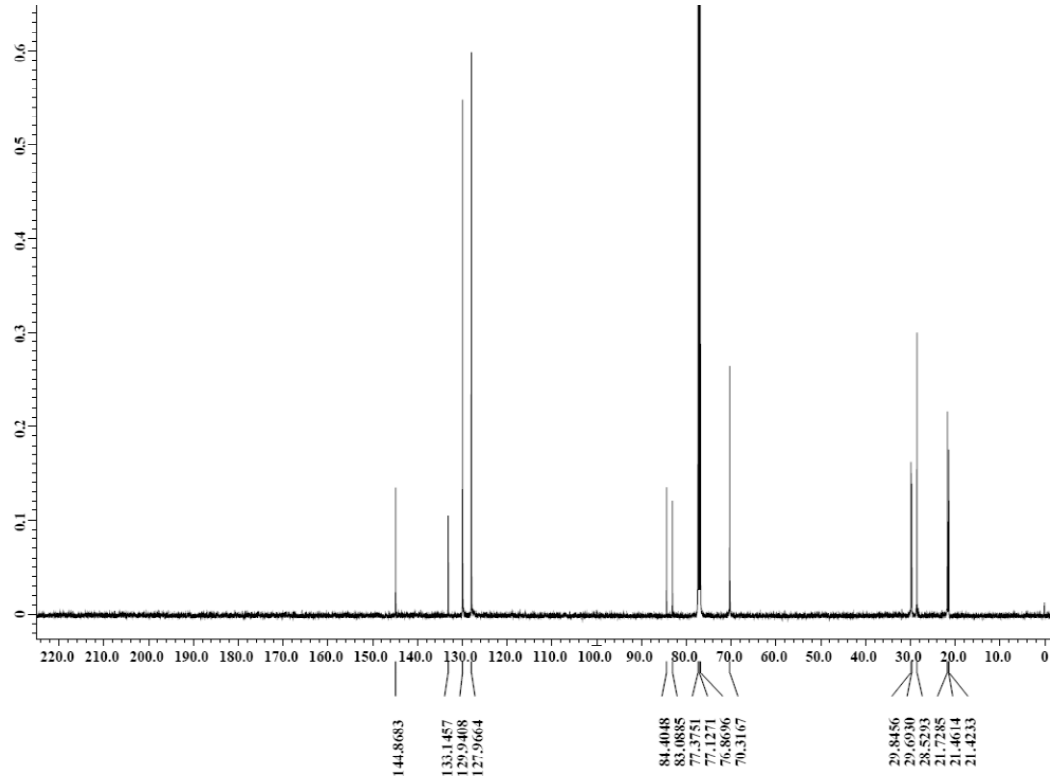
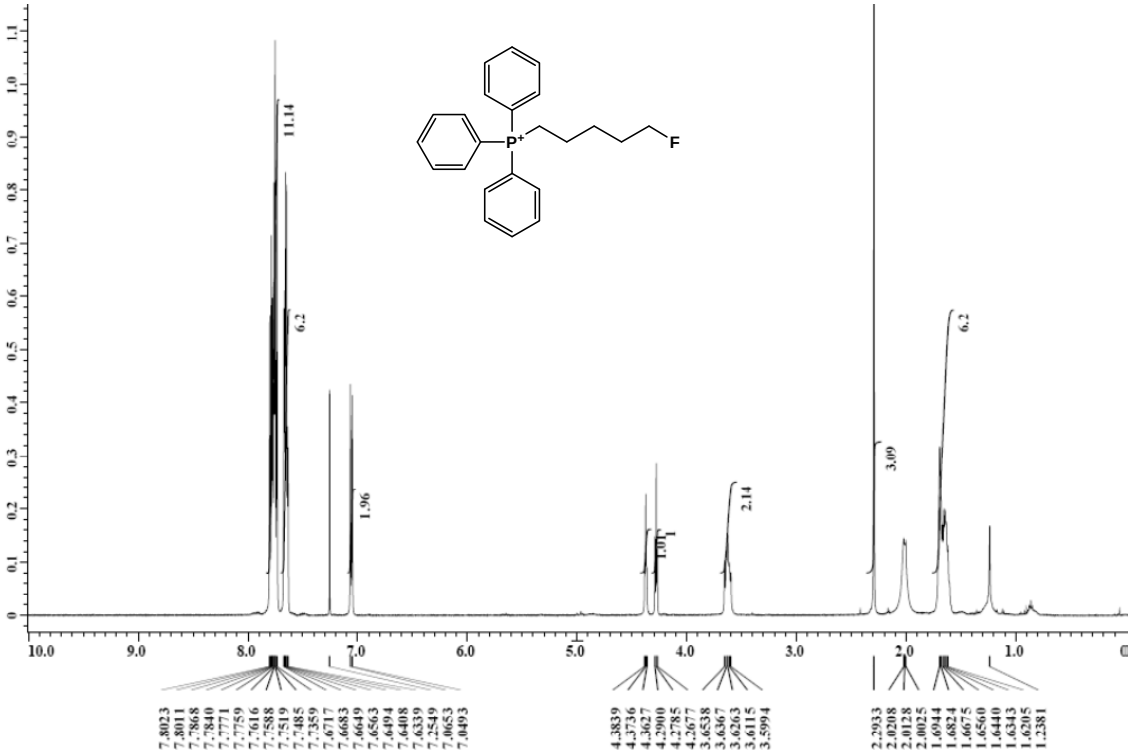


Supplemental Figure 3. (A) ^{1}H spectra of 5-fluoropentyl 4-methylbenzenesulfonate. (B) ^{13}C spectra of 5-fluoropentyl 4-methylbenzenesulfonate.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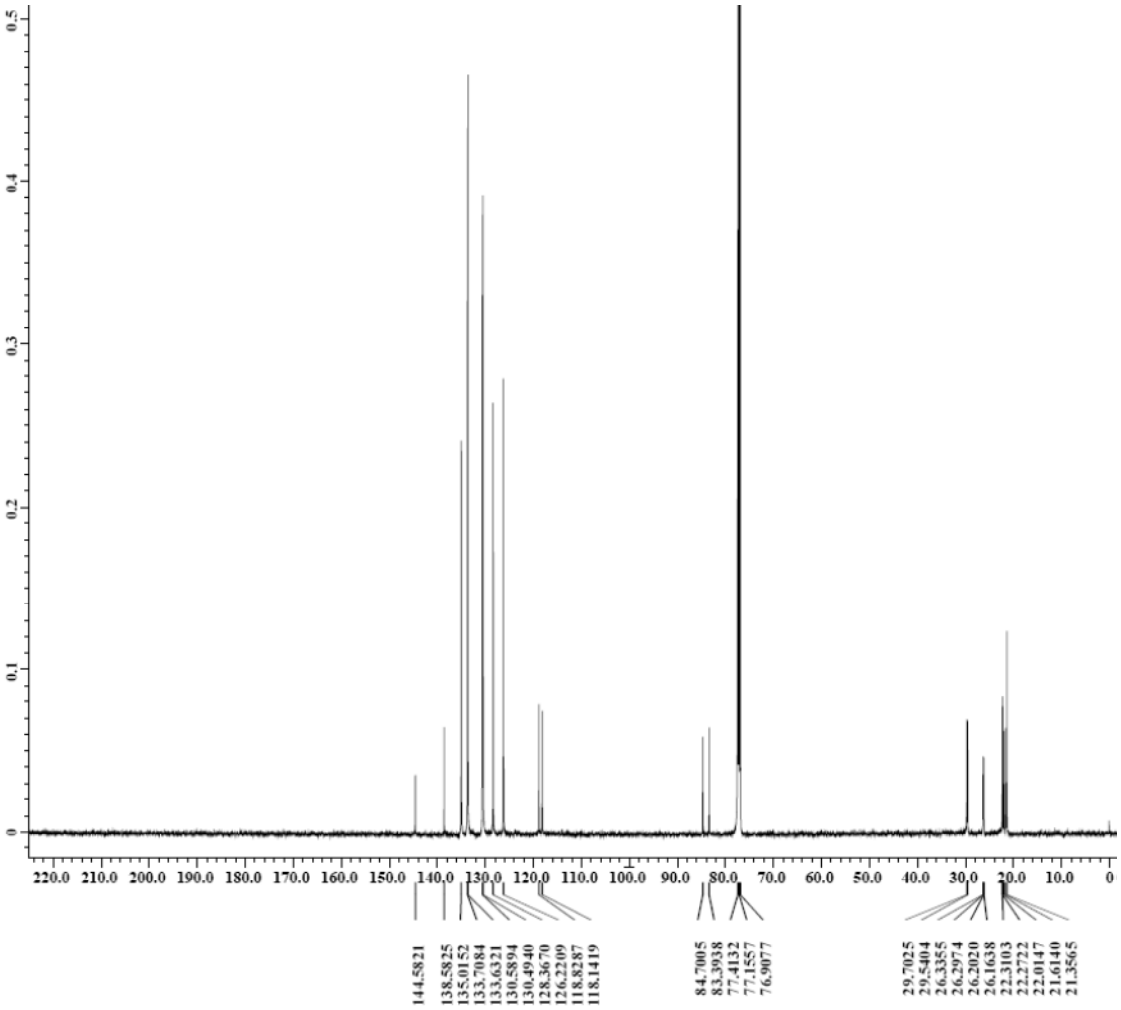
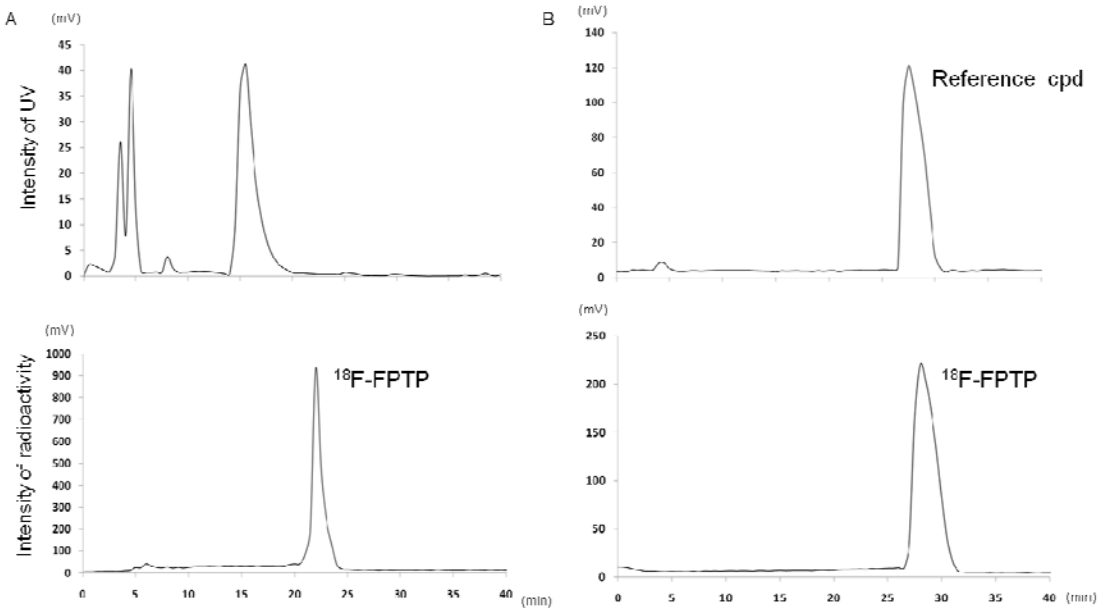
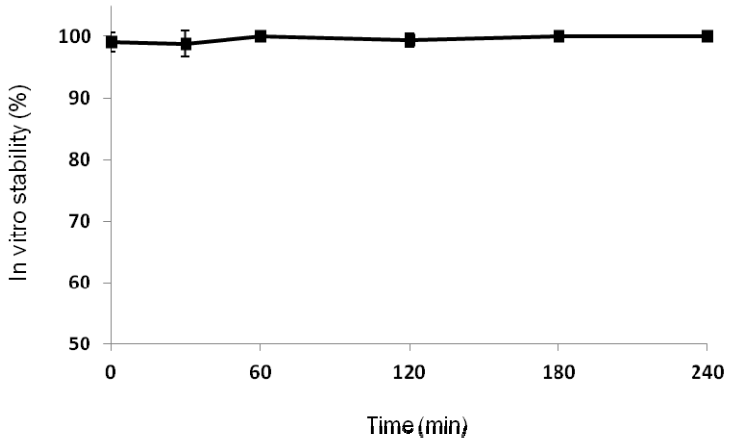


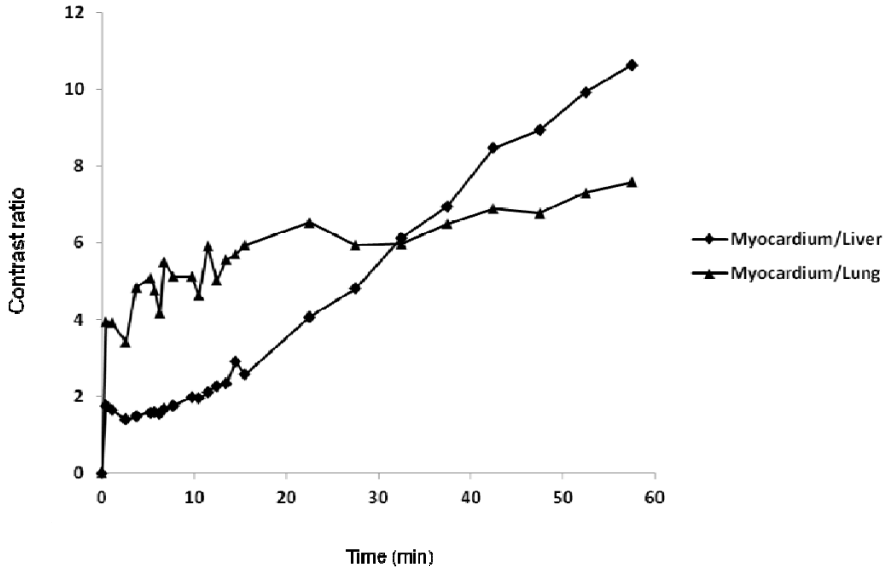
Supplemental Figure 4. (A) ^{1}H spectra of (5-fluoropentyl)triphenylphosphonium salt. (B) ^{13}C spectra of (5-fluoropentyl)triphenylphosphonium salt.



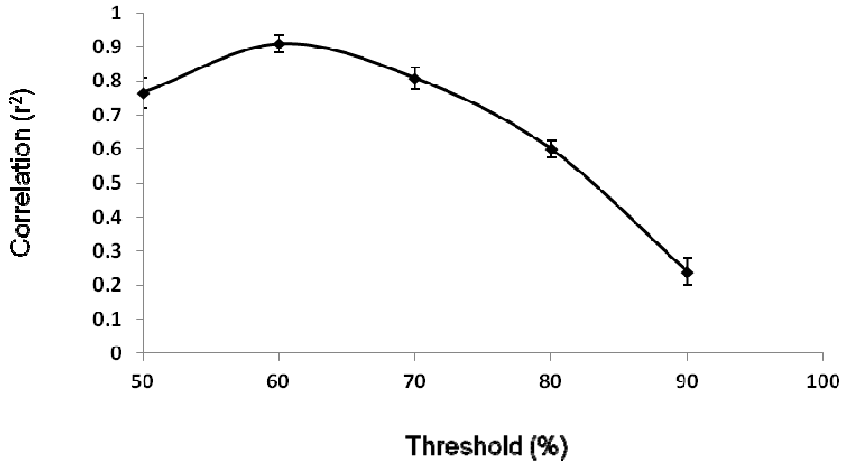
Supplemental Figure 5. (A) Purification of ^{18}F-FPTP on semi-preparative HPLC. The reaction mixture was injected on a C18 column and was eluted with acetonitrile : phosphate-buffered saline = 45 : 55 at a flow rate of 3.0 mL/min. (B) Analytical HPLC chromatogram of ^{18}F-FPTP coinjected with its non-radioactive compound (acetonitrile : phosphate-buffered saline = 45 : 55 at a flow rate of 1.0 mL/min).



Supplemental Figure 6. In vitro human serum stability of ^{18}F-FPTP.



Supplemental Figure 7. Contrast ratio of myocardium to liver and lung for 1.0 h after tail vein injection of ^{18}F-FPTP.



Supplemental Figure 8. Variation of correlation coefficient (r^2) with the different threshold used in the analysis of the microPET polar map. Correlation coefficient (r^2) of 50, 60 and 70% threshold was 0.77 ± 0.04, 0.91 ± 0.02, 0.81 ± 0.03, respectively. The *P* value was < 0.005, < 0.001, and < 0.005 in 50, 60 and 70 % respectively. The *P* value of each threshold was significant, while the slope of each regression equation was 0.73 ± 0.03, 0.77 ± 0.02, 0.70 ± 0.02, thus indicating that 60% threshold provided the best correlation with the MI size determined by TTC staining.

Supplemental Movie. Dynamic microPET imaging of rats after i.v. injection of ^{18}F-FPTP. Dynamic images were displayed for 60 min (40 s × 15 frames, 100 s × 30 frames).