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Green Approaches to Late-stage Fluorination: Radiosyntheses of ^{18}F-Labelled Radiopharmaceuticals in Ethanol and Water

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1. General Considerations

[^{18}F]Fluoride (100 – 1500 mCi / 3.7 – 55.5 GBq) was produced via the ^{18}O(p,n)^{18}F nuclear reaction using a GE PETTrace cyclotron and dried using a TRACERLab FX_{FN} automated radiochemistry synthesis module (General Electric, GE). Production of fluorine-18 labeled radiotracers was carried out using the reaction vessel of the TRACERLab FX_{FN} or in bullet vials using a sand bath. Precursor solutions were gently warmed with a heat-gun to aid dissolution as needed. Radio-TLC analyses were conducted using Merck Glass-backed TLC Silica Gel 60 F_{254} plates and analyzed using a Bioscan AR-2000 TLC scanner. Radio-HPLC analyses were conducted on a Shimadzu LC-2010A HT system equipped with a Bioscan B-FC-1000 radiation detector using HPLC conditions outlined below. The identity of all ^{18}F product peaks were confirmed by comparison to unlabeled ^{19}F reference standards.

Unless otherwise stated, reagents and solvents were commercially available and used without further purification: sodium chloride, 0.9% USP and Sterile Water for Injection, USP were purchased from Hospira; ethanol was purchased from American Regent; anhydrous acetonitrile, potassium carbonate, kryptofix-2.2.2, sodium hydroxide, hydrochloric acid, sodium dihydrogenphosphate, ammonium acetate and DMSO were purchased from Sigma Aldrich; HPLC grade acetonitrile was purchased from Fisher Scientific.

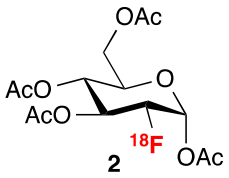
Precursors and standards were commercially available as follows: FDG precursor (mannose triflate), FET precursor (ditosyl methane) and reference standard, flubatine (standard and precursor), MPPF (standard and precursor) and nifene (standard and precursor) were purchased from ABX Advanced Biochemicals. FDG reference standard was purchased from Sigma Aldrich. FAZA precursor and reference standard were purchased from Prof. Friedrich Hammerschmidt (Universität Wien, Austria) and Prof. Hans-Jürgen Machulla (Steinbeis Transfer Center Radiopharmacy, Germany). All precursors and reference standards were used as received.

Other synthesis components were obtained as follows: sterile filters were obtained from Millipore; sterile product vials were purchased from Hollister-Stier; [^{18}O]H_2O was purchased from ABX Advanced Biochemical Compounds or Rotem Inc.; Alumina, C18-light and QMA-light Sep-Paks were purchased from Waters Corporation – C18-light and alumina Sep-Paks were flushed with 10 mL of ethanol followed by 10 mL of sterile water prior to use, while QMA-light Sep-Paks were flushed with 10 mL each of ethanol – water – 0.5 M sodium bicarbonate – water.

2. Synthesis Procedures

General Procedure for Drying [^{18}F]Fluoride

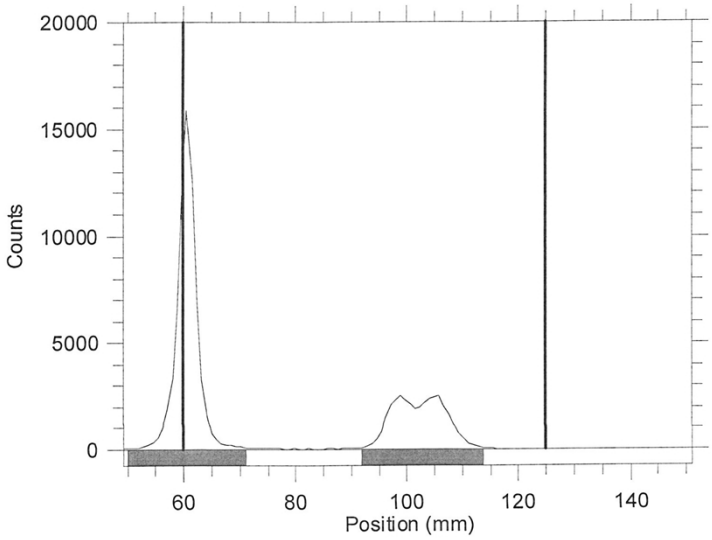
[^{18}F]Fluoride was delivered to the synthesis module (in a 1.5 mL bolus of [^{18}O]water) and trapped on a QMA-light Sep-Pak to remove [^{18}O]water. [^{18}F]Fluoride was then eluted into the reaction vessel using aqueous potassium carbonate (3.5 mg in 0.5 mL of water). A solution of kryptofix 2.2.2 (15 mg in 1 mL of acetonitrile or 1 mL of ethanol) was then added to the reaction vessel and the [^{18}F]fluoride was dried by evaporating the azeotrope. Azeotropic drying was achieved by heating the reaction vessel to 80 °C and drawing full vacuum for 4 min. After this time, the reaction vessel was cooled to 60 °C and subjected to both an argon stream and vacuum draw simultaneously for an additional 4 min.



[^{18}F]FDG-Ac4

Table 2, Entry 1

[^{18}F]Fluoride was dried using the general method described above. Following drying, a solution of mannose triflate (40 mg) in ethanol (1 mL) was added to the reaction vessel and heated at 100 ^{o}C for 30 min. After this time, the crude reaction mixture was cooled and analyzed by radio-TLC (plate: silica gel TLC plate, solvent system: MeCN : H_2O = 95 : 5; R_f 0.008 = [^{18}F]fluoride, 0.650 = [^{18}F]FDG-Ac4a typical chromatogram is shown in Figure S1). Typical RCC were 23±10% (n = 3).

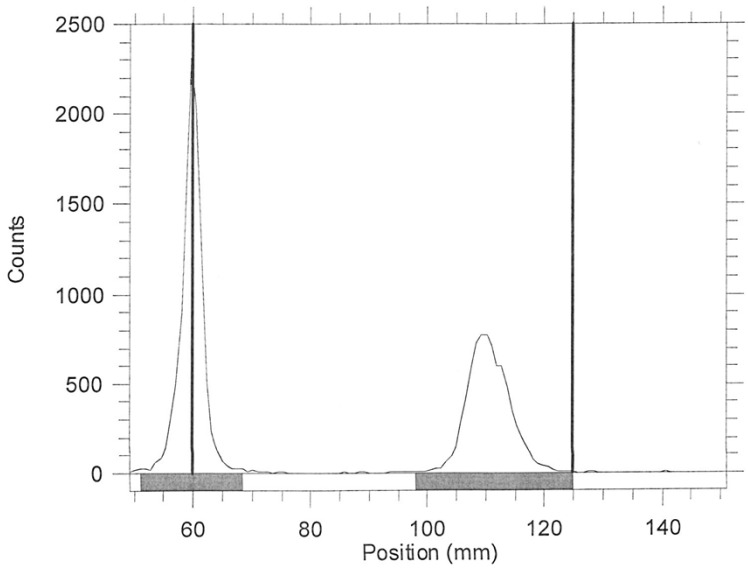


Reg	(mm) Start	(mm) Stop	(mm) Centroid	RF	Region Counts	Region CPM	% of Total	% of ROI
Rgn 1	50.2	71.0	60.5	0.008	68950.0	68950.0	64.90	66.35
Rgn 2	91.9	113.6	102.2	0.650	34975.0	34975.0	32.92	33.65
2 Peaks					103925.0	103925.0	97.82	100.00

Figure S1

Table 2, Entry 2

[^{18}F]Fluoride was dried using the general method described above. Following drying, a solution of mannose triflate (40 mg) in 15% water in ethanol (1 mL) was added to the reaction vessel and heated at 100 ^{o}C for 30 min. After this time, the crude reaction mixture was cooled and analyzed by radio-TLC (plate: silica gel TLC plate, solvent system: MeCN : H_2O = 95 : 5; R_f -0.004 = [^{18}F]fluoride, 0.779 = [^{18}F]FDG-Ac4; a typical chromatogram is shown in Figure S2). Typical RCC were 37±5% (n = 3).

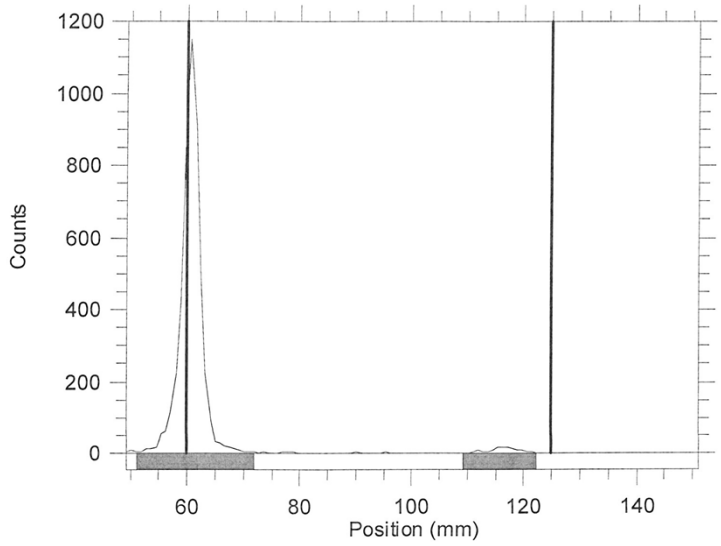


Reg	(mm) Start	(mm) Stop	(mm) Centroid	RF	Region Counts	Region CPM	% of Total	% of ROI
Rgn 1	51.0	68.4	59.7	-0.004	10170.0	10170.0	56.12	57.31
Rgn 2	98.0	125.0	110.6	0.779	7577.0	7577.0	41.81	42.69
2 Peaks					17747.0	17747.0	97.93	100.00

Figure S2

Table 2, Entry 3

A solution of [^{18}F]fluoride in [^{18}O]H_2O (0.15 mL) was added to the reaction vessel of the synthesis module. To this was added a mixture of potassium carbonate (3.5 mg), kryptofix (15 mg) and mannose triflate (40 mg) in ethanol (0.85 mL), and the reaction vessel was heated at 100 ^{o}C for 30 min. After this time, the crude reaction mixture was cooled and analyzed by radio-TLC (plate: silica gel TLC plate, solvent system: MeCN : H_2O = 95 : 5; R_f 0.009 = [^{18}F]fluoride, 0.864 = [^{18}F]FDG-Ac4; a typical chromatogram is shown in Figure S3). Typical RCC were 3±1% (n = 3).

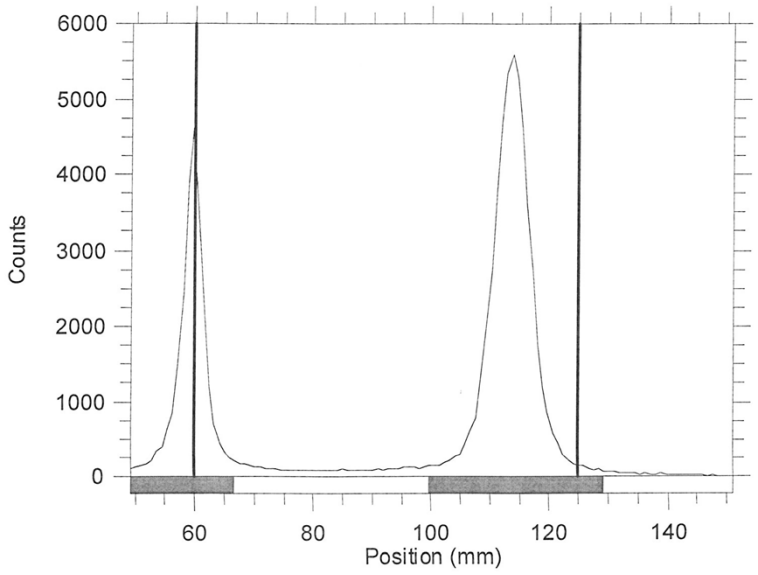


Reg	(mm) Start	(mm) Stop	(mm) Centroid	RF	Region Counts	Region CPM	% of Total	% of ROI
Rgn 1	51.0	71.9	60.6	0.009	4799.0	4799.0	96.11	97.68
Rgn 2	109.3	122.3	116.2	0.864	114.0	114.0	2.28	2.32
2 Peaks					4913.0	4913.0	98.40	100.00

Figure S3

Table 2, Entry 4

The [^{18}F]fluoride was delivered to the synthesis module (in a 1.5 mL bolus of [^{18}O]water) and trapped on a QMA-light Sep-Pak to remove [^{18}O]water. [^{18}F]Fluoride was then eluted into the reaction vessel using a solution of potassium carbonate (3.5 mg) and kryptofix (15 mg) in 15% water in ethanol (0.5 mL). A solution of mannose triflate (40 mg) in 15% water in ethanol (0.5 mL) was then added to the reaction vessel and the reaction was heated at 100 ^{o}C for 30 min. After this time, the crude reaction mixture was cooled and analyzed by radio-TLC (plate: silica gel TLC plate, solvent system: MeCN : H_2O = 95 : 5; R_f -0.011 = [^{18}F]fluoride, 0.824 = [^{18}F]FDG-Ac4; a typical chromatogram is shown in Figure S4). Typical RCC were 58±5% (n = 3).

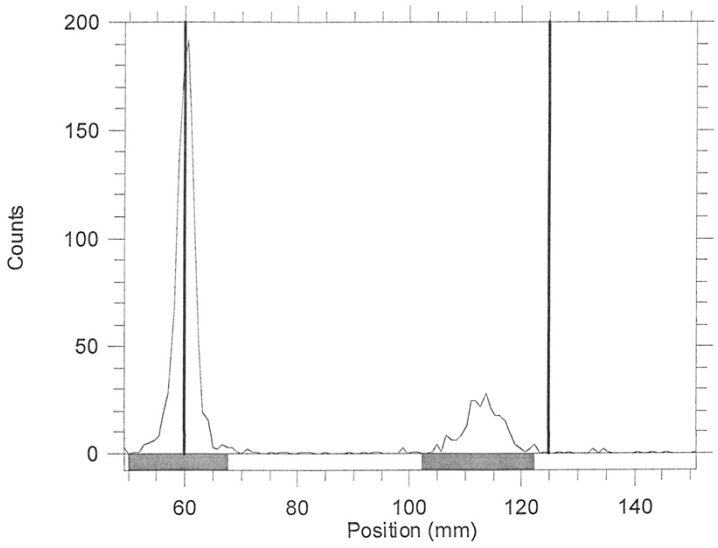


Reg	(mm) Start	(mm) Stop	(mm) Centroid	RF	Region Counts	Region CPM	% of Total	% of ROI
Rgn 1	49.3	66.7	59.3	-0.011	24128.0	24128.0	29.92	32.18
Rgn 2	99.7	129.3	113.6	0.824	50846.0	50846.0	63.05	67.82
2 Peaks					74974.0	74974.0	92.97	100.00

Figure S4

Table 2, Entry 5

The [^{18}F]fluoride was delivered to the synthesis module (in a 1.5 mL bolus of [^{18}O]water) and trapped on a QMA-light Sep-Pak to remove [^{18}O]water. [^{18}F]Fluoride was then eluted into the reaction vessel using a solution of potassium carbonate (3.5 mg) and kryptofix (15 mg) in 15% water in ethanol (1.0 mL). A solution of mannose triflate (40 mg) in 15% water in ethanol (1.0 mL) was then added to the reaction vessel and the reaction was heated at 100 ^{o}C for 30 min. After this time, the crude reaction mixture was cooled and analyzed by radio-TLC (plate: silica gel TLC plate, solvent system: MeCN : H_2O = 95 : 5; R_f -0.001 = [^{18}F]fluoride, 0.817 = [^{18}F]FDG-Ac4; a typical chromatogram is shown in Figure S5). Typical RCC were 16±4% (n = 3).

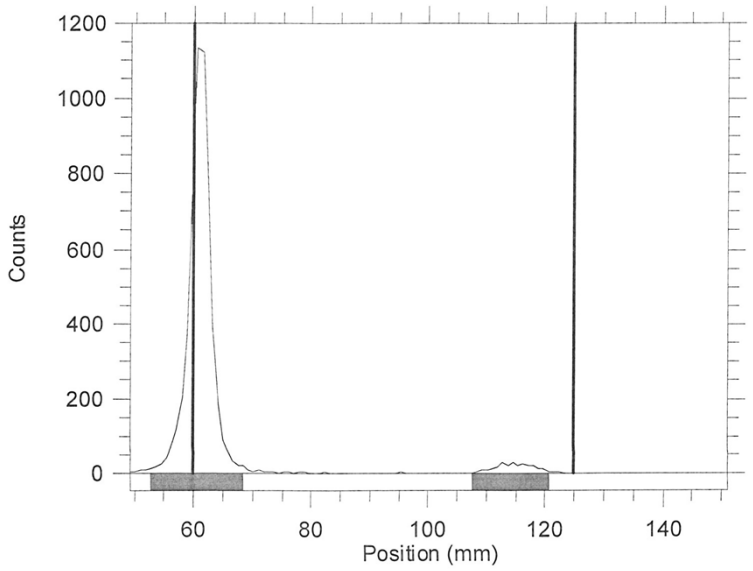


Reg	(mm) Start	(mm) Stop	(mm) Centroid	RF	Region Counts	Region CPM	% of Total	% of ROI
Rgn 1	50.2	67.5	59.9	-0.001	857.0	857.0	72.20	78.26
Rgn 2	102.3	122.3	113.1	0.817	238.0	238.0	20.05	21.74
2 Peaks					1095.0	1095.0	92.25	100.00

Figure S5

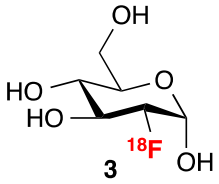
Table 2, Entry 6

The [^{18}F]fluoride was delivered to the synthesis module (in a 1.5 mL bolus of [^{18}O]water) and trapped on a QMA-light Sep-Pak to remove [^{18}O]water. [^{18}F]Fluoride was then eluted into the reaction vessel using a solution of potassium carbonate (3.5 mg) in 15% water in ethanol (0.5 mL). A solution of mannose triflate (40 mg) in 15% water in ethanol (0.5 mL) was then added to the reaction vessel and the reaction was heated at 100 ^{o}C for 30 min. After this time, the crude reaction mixture was cooled and analyzed by radio-TLC (plate: silica gel TLC plate, solvent system: MeCN : H_2O = 95 : 5; R_f 0.014 = [^{18}F]fluoride, 0.841 = [^{18}F]FDG-Ac4; a typical chromatogram is shown in Figure S6). Typical RCC were 4±1% (n = 3).



Reg	(mm) Start	(mm) Stop	(mm) Centroid	RF	Region Counts	Region CPM	% of Total	% of ROI
Rgn 1	52.8	68.4	60.9	0.014	5417.0	5417.0	92.39	95.81
Rgn 2	107.6	120.6	114.6	0.841	237.0	237.0	4.04	4.19
2 Peaks					5654.0	5654.0	96.44	100.00

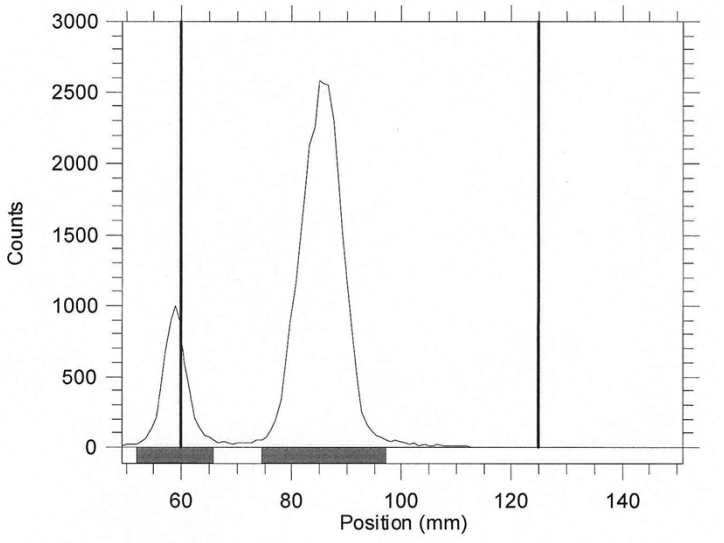
Figure S6



[^{18}F]FDG

Table 1, Entries 1 and 2

[^{18}F]Fluoride was dried using the general method described above. Following drying, a solution of mannose triflate (40 mg) in acetonitrile (1 mL) was added to the reaction vessel and heated at 100 ^{o}C for 30 min to yield [^{18}F]FDG-Ac4 (**2**). After this time, 1N NaOH was added and the reaction was stirred at room temperature (rt) for 5 min. Following neutralization (HCl/citrate buffer), the crude reaction mixture was analyzed by radio-TLC to determine RCC (plate: silica gel TLC plate, solvent system: MeCN : H_2O = 95 : 5, R_f -0.018 = [^{18}F]fluoride, 0.390 = [^{18}F]FDG; a typical chromatogram is shown in Figure S7). Typical RCC were 74±12% (H_2O-MeCN azeotrope, n = 3) or 70±10% (H_2O-EtOH azeotrope, n = 3).

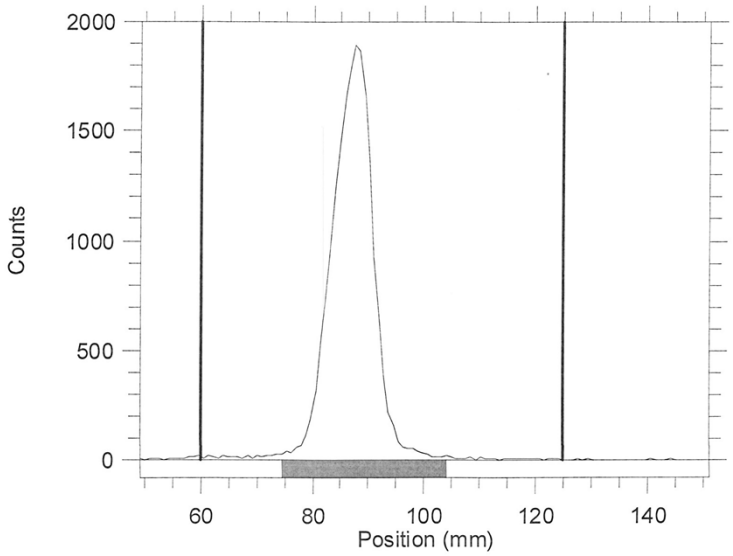


Reg	(mm) Start	(mm) Stop	(mm) Centroid	RF	Region Counts	Region CPM	% of Total	% of ROI
Rgn 1	51.9	65.8	58.9	-0.018	5838.0	5838.0	16.98	17.53
Rgn 2	74.5	97.1	85.3	0.390	27473.0	27473.0	79.93	82.47
2 Peaks					33311.0	33311.0	96.91	100.00

Figure S7

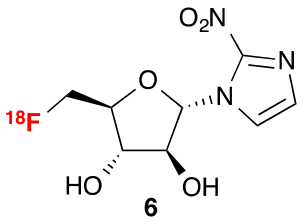
Fully-automated Synthesis of [^{18}F]FDG

The [^{18}F]fluoride was delivered to the synthesis module (in a 1.5 mL bolus of [^{18}O]water) and trapped on a QMA-light Sep-Pak to remove [^{18}O]water. [^{18}F]Fluoride was then eluted into the reaction vessel using a solution of potassium carbonate (3.5 mg) and kryptofix (15 mg) in 15% water in ethanol (0.5 mL). A solution of mannose triflate (40 mg) in 15% water in ethanol (0.5 mL) was then added to the reaction vessel and the reaction was heated at 100 ^{o}C for 30 min. After this time, 1N NaOH was added and the reaction was stirred at room temperature (rt) for 5 min. Following neutralization (HCl/citrate buffer), the crude reaction mixture was diluted and purified using alumina and C18 Sep-Paks, as previously described,[1] to yield [^{18}F]FDG in 33±2% radiochemical yield (decay-corrected, n = 3). Analysis of the final product by radio-TLC confirmed product purity (plate: silica gel TLC plate, solvent system: MeCN : H_2O = 95 : 5, R_f 0.417 = [^{18}F]FDG; a typical chromatogram is shown in Figure S8).



Reg	(mm) Start	(mm) Stop	(mm) Centroid	RF	Region Counts	Region CPM	% of Total	% of ROI
Rgn 1	74.5	104.1	87.1	0.417	18763.0	18763.0	97.16	100.00
1 Peaks					18763.0	18763.0	97.16	100.00

Figure S8



6

[^{18}F]FAZA

Table 1, Entries 3 and 4

[^{18}F]Fluoride was dried using the general method described above. [^{18}F]FAZA was then synthesized as previously described,[2] and typical non-corrected radiochemical yields were 6% (H_2O-MeCN azeotrope, n = 3) or 5% (H_2O-EtOH azeotrope, n = 3). Radiochemical purity and identity were confirmed by radio-HPLC (column: Phenomonex Luna C8(2) 5µ, 100 x 2.0 mm; mobile phase: 5% acetonitrile: 95% 20mM aqueous ammonium acetate, pH 4.5; flow rate: 0.5 mL/min; UV wavelength = 254 nm; t_R [^{18}F]FAZA = 6.2 min; a typical chromatogram is shown in Figure S9).

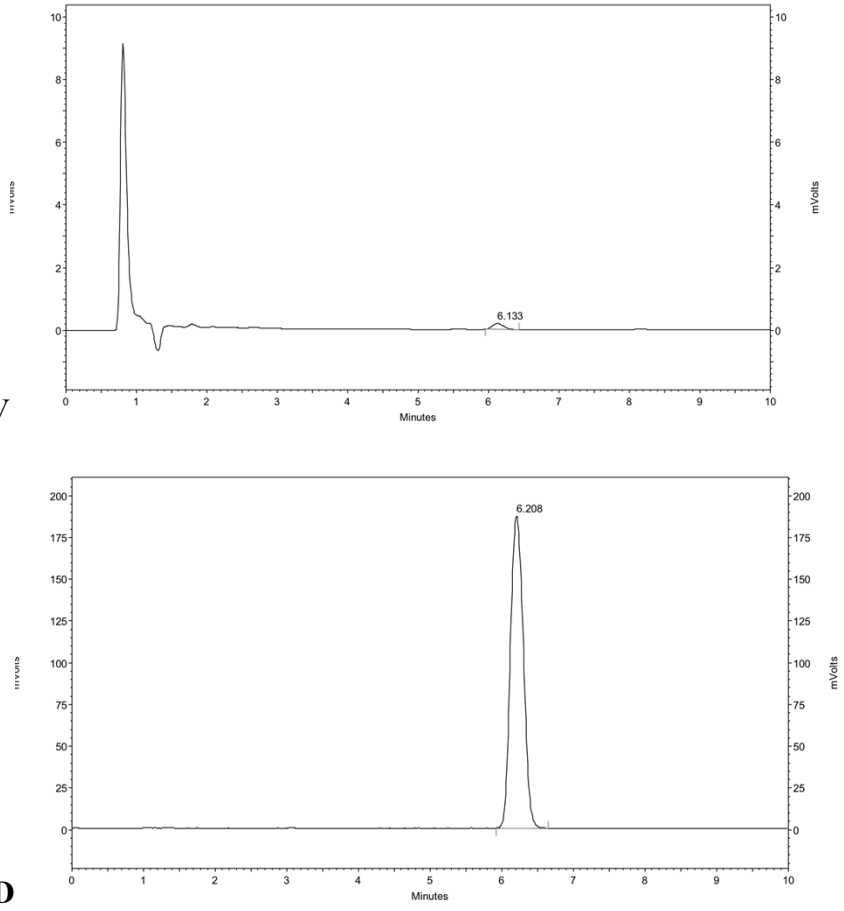
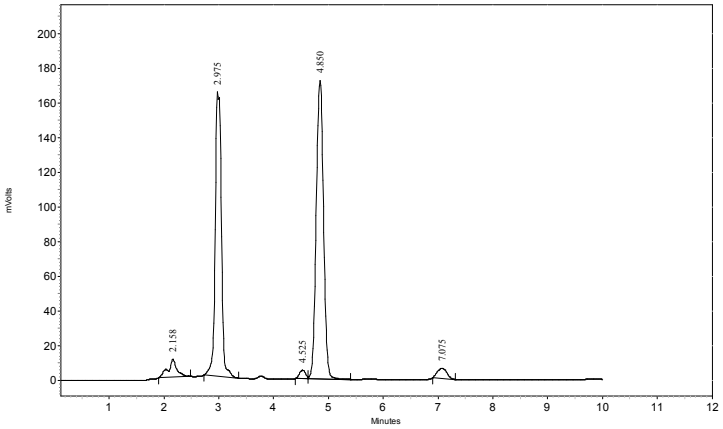


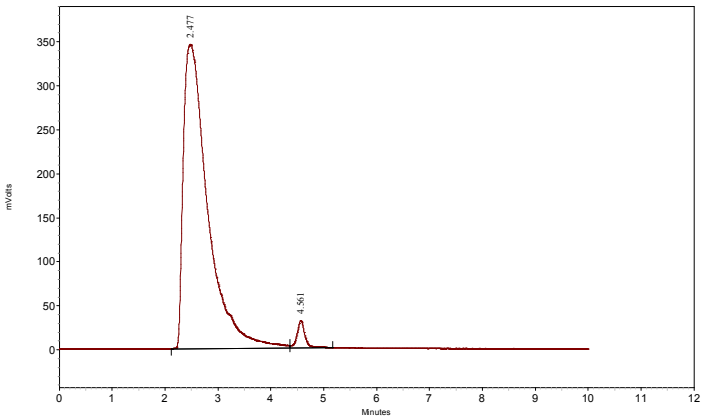
Figure S9

Table 2, Entry 7

[^{18}F]Fluoride was dried using the general method described above. Following drying, a solution of precursor **4** (8 mg) in 15% water in ethanol (2 mL) was added to the reaction vessel and heated at 100 ^{o}C for 10 min. After this time, the reaction was cooled to 40 ^{o}C and 0.1 M aqueous sodium hydroxide (1 mL) was added. The reaction was stirred for 5 min at 40 ^{o}C to hydrolyze the acetate protecting groups. The crude reaction mixture was then cooled and analyzed by radio-HPLC (column: Phenomonex Luna C8(2) 5µ, 100 x 2.0 mm; mobile phase: 15% acetonitrile: 85% 50mM aqueous ammonium acetate, pH 4.5; flow rate: 0.5 mL/min, UV = 254 nm, t_R [^{18}F]FAZA = 4.561 min; a typical chromatogram is shown in Figure S10). RCC was 3% (n = 1).

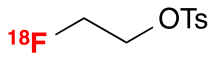


UV Detector Ch1-254nm Results Retention Time	Area	Area %	Height	Width	S/N (ASTM)
2.158	113813	4	10311	0.583	42.51
2.975	1283566	41	163832	0.625	675.45
4.525	38520	1	4877	0.233	4.71
4.850	1594457	51	171960	0.767	165.93
7.075	69664	2	5817	0.417	12.64



RAD Results Retention Time	Area	Area %	Width
2.477	11058513	97	2.24
4.561	321900	3	0.81

Figure S10

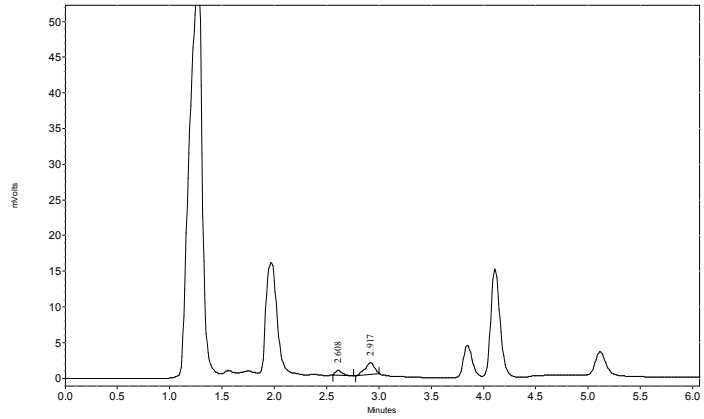


8

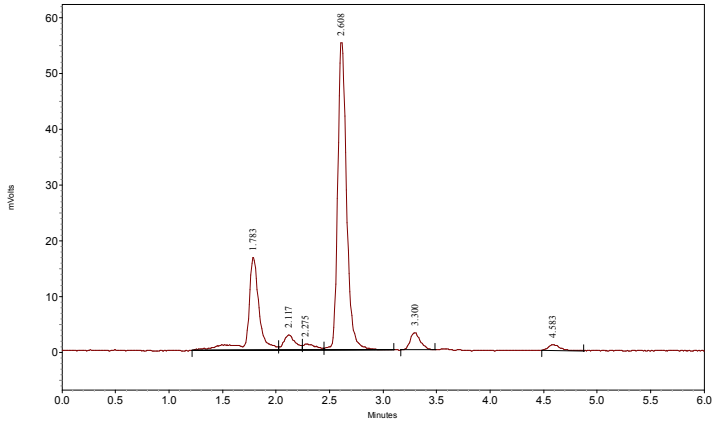
[^{18}F]Fluoroethyl tosylate ([^{18}F]FET)

Table 1, Entries 5 and 6

[^{18}F]Fluoride was dried using the general method described above. Following drying, a solution of ditosyl methane (5 mg) in acetonitrile (1 mL) was added to the reaction vessel and heated at 110 °C for 10 min. After this time, the crude reaction mixture was cooled and analyzed by radio-HPLC (column: Phenomenex Luna C18 150 x 4.6 mm, mobile phase: MeCN : H_2O = 60 : 40; flow rate: 1.0 mL/min; UV wavelength = 254 nm; t_R [^{18}F]FET = 2.608 min; a typical chromatogram is shown in Figure S11). Typical RCC were 70±10% (H_2O-MeCN azeotrope, n = 3) or 68±4% (H_2O-EtOH azeotrope, n = 2).



UV Detector Ch1-254nm Results Retention Time	Area	Area %	Height	Width	S/N (ASTM)
2.608	2998	23	647	0.200	0.04
2.917	10288	77	1635	0.225	0.1

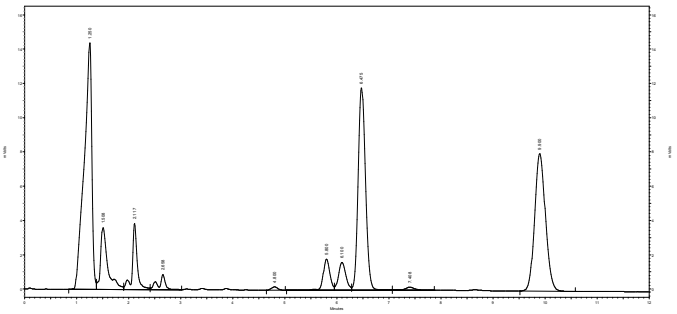


RAD Results Retention Time	Area	Area %	Width
1.783	119733	24	0.81
2.117	20910	4	0.22
2.275	8823	2	0.20
2.608	318364	64	0.65
3.300	20543	4	0.32
4.583	7845	2	0.39

Figure S11

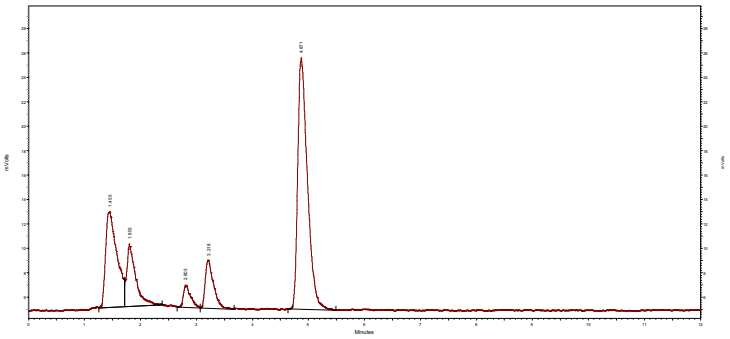
Table 2, Entry 8

[^{18}F]Fluoride was dried using the general method described above. Following drying, a solution of ditosyl methane (5 mg) in ethanol (1 mL) + 1 drop DMSO (to improve precursor solubility) was added to the reaction vessel and heated at 110 ^{o}C for 10 min. After this time, the crude reaction mixture was cooled and analyzed by radio-HPLC (column: Luna C18 150 x 4.6 mm, mobile phase: MeCN : H_2O = 50 : 50; t_R [^{18}F]FET = 4.87 min; chromatogram is shown in Figure S12). RCC was 52% (n = 1).



UV Detector Ch1-254nm
Results

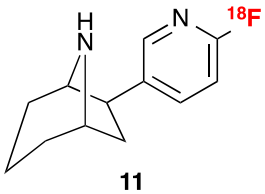
Retention Time	Area	Area %
1.25	145548	30.32
1.51	33779	7.04
2.12	25435	5.30
2.66	7517	1.57
4.80	1641	0.34
5.80	16368	3.41
6.10	16152	3.36
6.47	114957	23.95
7.41	2488	0.52
9.90	116162	24.20



RAD Results

Retention Time	Area	Area %
1.45	111013	23.49
1.80	56964	12.06
2.80	16155	3.42
3.22	40485	8.57
4.87	247916	52.47

Figure S12



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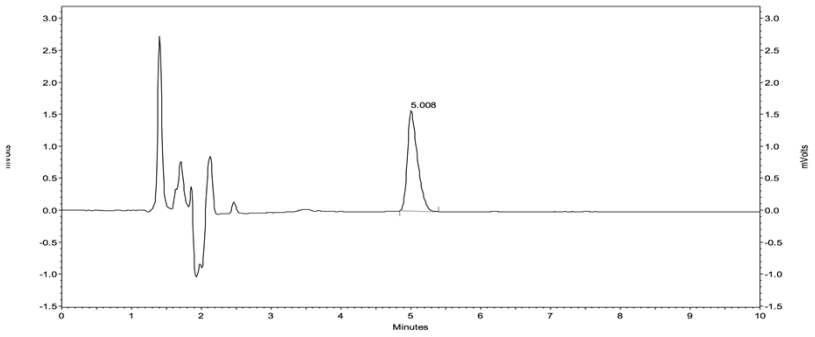
[^{18}F]Flubatine

Table 1, Entries 7 and 8

[^{18}F]Fluoride was dried using the general method described above. [^{18}F]Flubatine was then synthesized as previously described,[3] and typical non-corrected radiochemical yields were 25±10% (H_2O-MeCN azeotrope, n = 3) or 15±10% (H_2O-EtOH azeotrope, n = 20). Radiochemical purity and identity were confirmed by radio-HPLC (column: Phenomonex Synergi Polar-RP 4 µ, 150 × 4.6 mm; mobile phase: 50% acetonitrile : 50% 0.1 M acetic acid; pH, 4.5; flow rate: 1.0 mL/min; oven temp: 40°C; UV wavelength: 254 nm; t_R = 5.0 min; a typical chromatogram is shown in Figure S13).

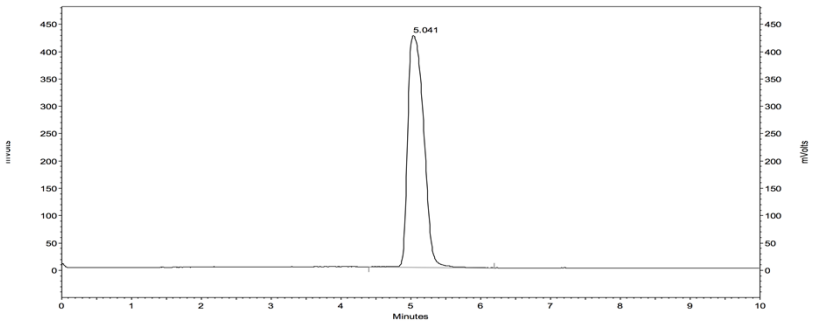
UV Detector Response



UV Detector Ch1-254nm Results

Retention Time	Area	Area %	Height	Width
5.008	15839	100.00	1570	0.57

Radioactivity Detector Response



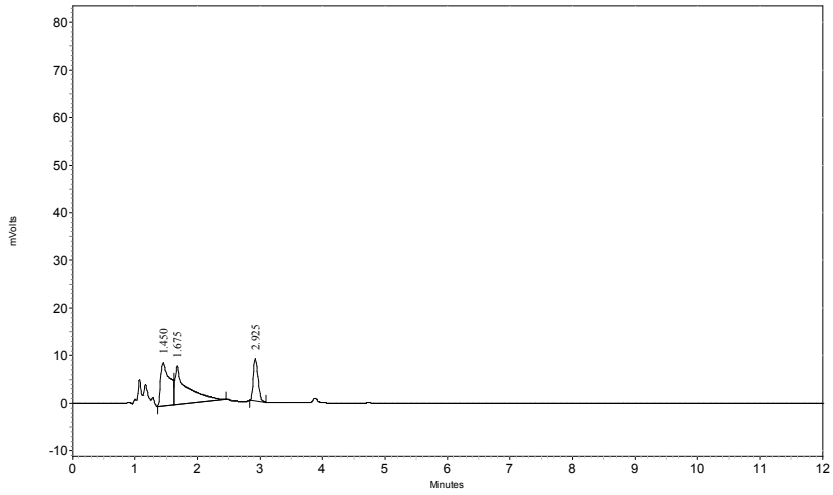
Bioscan RAD Results

Retention Time	Area	Area %
5.041	6721786	100.00

Figure S13

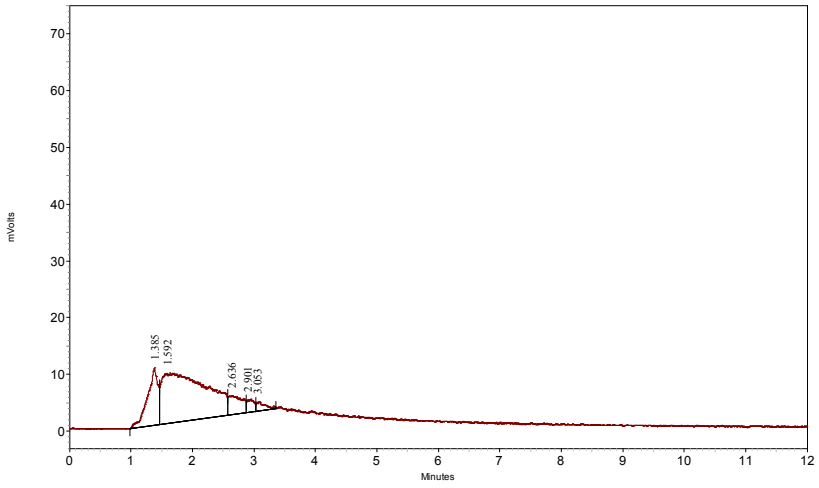
Table 2, Entry 9

[^{18}F]Fluoride was dried using the general method described above. It was then attempted to synthesize [^{18}F]flubatine as previously described,[3] but using ethanol or 15% H_2O : 85% EtOH as the reaction solvent (n = 3). In each case however, no product was formed as determined by radio-HPLC analysis (a typical chromatogram is shown in Figure S14, expected t_R of [^{18}F]flubatine = ~5 min).



UV Detector Ch1-254nm Results

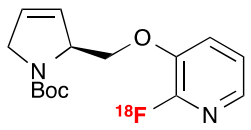
Retention Time	Area	Area %	Height	Width	S/N (ASTM)
1.450	90798	36	8990	0.267	2.97
1.675	113321	45	8025	0.833	2.66
2.925	46326	18	8848	0.267	2.93



RAD Results

Retention Time	Area	Area %	Width
1.385	118835	19	0.48
1.592	436345	68	1.12
2.636	49635	8	0.30
2.901	17060	3	0.15
3.053	16097	3	0.33

Figure S14

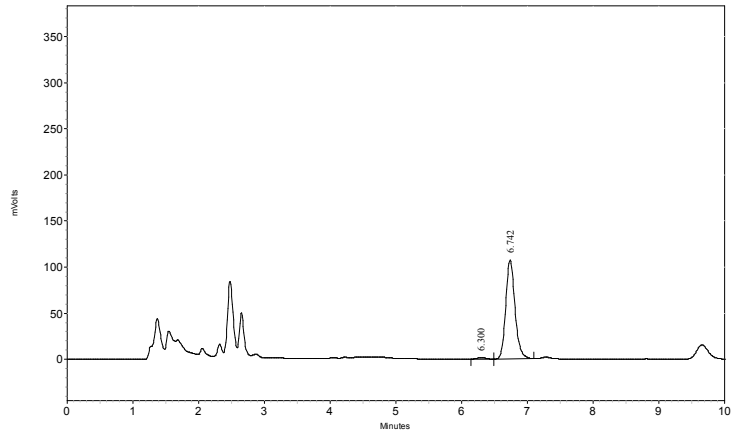


13

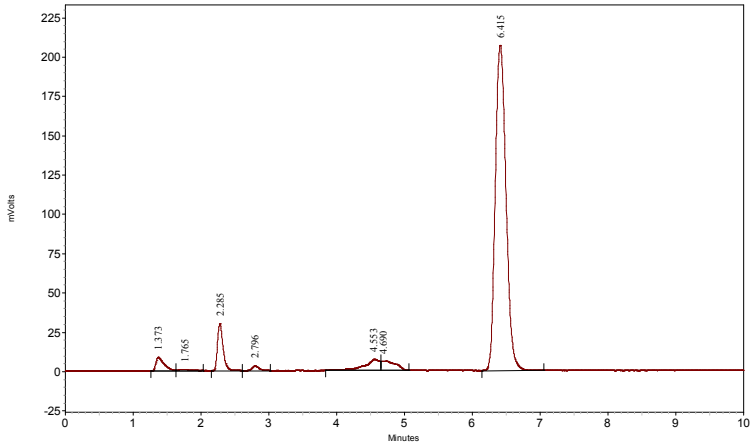
Boc-protected [^{18}F]Nifene

Table 1, Entries 9 and 10

[^{18}F]Fluoride was dried using the general method described above. Following drying, a solution of nifene precursor **12** (2 mg) in DMSO (1 mL) was added to the reaction vessel and heated at 125 ^{o}C for 30 min. After this time, the crude reaction mixture was cooled and analyzed by radio-HPLC (column: Phenomenex Synergi Polar RP 150 x 4.6 mm, mobile phase: MeCN : H_2O = 50 : 50 + 0.05% AcOH; flow rate: 1.0 mL/min; UV wavelength = 254 nm; t_R Bob-protected [^{18}F]nifene = 6.415 min; a typical chromatogram is shown in Figure S15). Typical RCC were 50% (H_2O-MeCN azeotrope, n = 1) or 83% (H_2O-EtOH azeotrope, n = 1).



UV Detector Ch1-254nm Results Retention Time	Area	Area %	Height	Width	S/N (ASTM)
6.300	14160	1	1659	0.342	0.12
6.742	1048493	99	107059	0.608	7.42

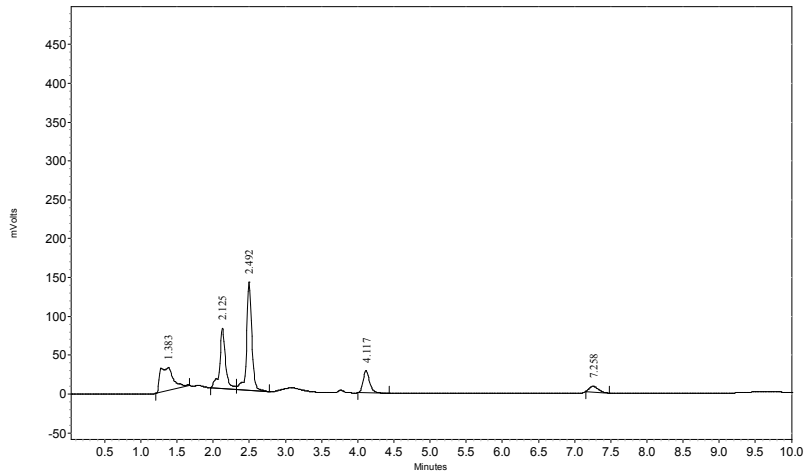


RAD Results Retention Time	Area	Area %	Width
1.373	71187	3	0.37
1.765	8801	0	0.40
2.285	171173	6	0.45
2.796	22772	1	0.42
4.553	118687	4	0.81
4.690	86963	3	0.41
6.415	2274486	83	0.91

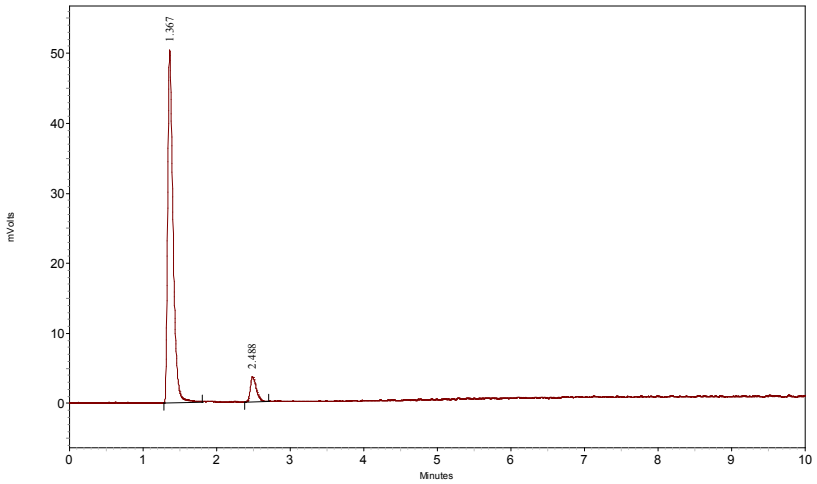
Figure S15

Table 2, Entry 10

[^{18}F]Fluoride was dried using the general method described above. It was then attempted to synthesize Bob-protected [^{18}F]nifene as described above, but using ethanol as the reaction solvent (n = 3). However, no product was formed as determined by radio-HPLC analysis (Figure S16, expected t_R of Boc-protected [^{18}F]nifene = ~6.4 min).

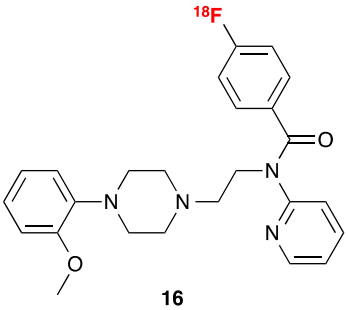


UV Detector Ch1-254nm Results Retention Time	Area	Area %	Height	Width	S/N (ASTM)
1.383	372700	21	29380	0.458	119.37
2.125	444136	25	77651	0.358	315.49
2.492	699441	40	139470	0.450	566.66
4.117	176449	10	28736	0.433	9.67
7.258	61599	4	7243	0.333	13.65



RAD Results Retention Time	Area	Area %	Width
1.367	254428	93	0.52
2.488	20328	7	0.33

Figure S16

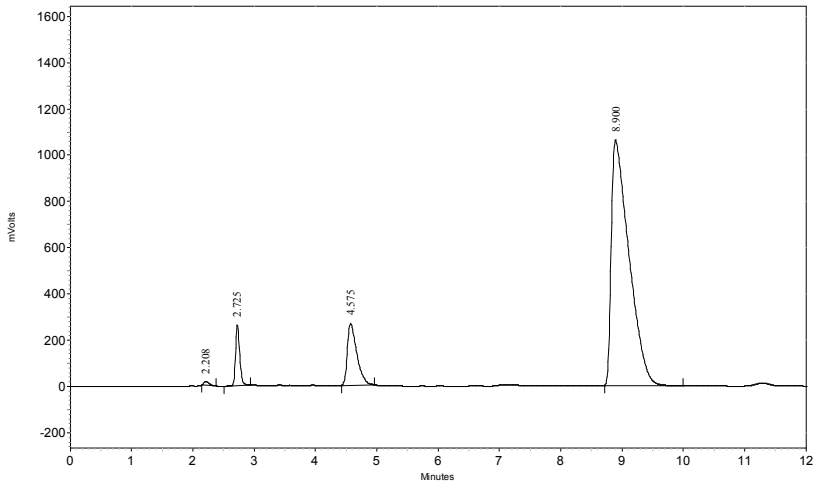


16

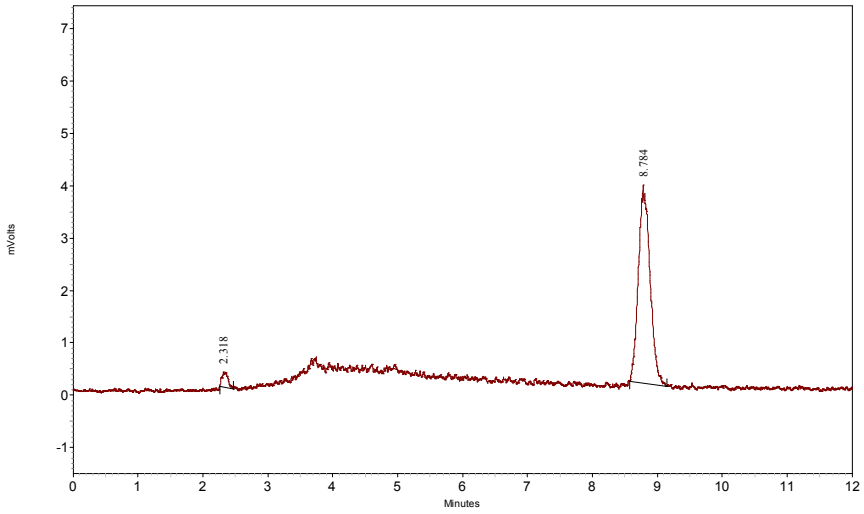
[^{18}F]MPPF

Table 1, Entries 11 and 12

[^{18}F]Fluoride was dried using the general method described above. MPPF precursor **15** (10 mg) in DMSO (0.5 mL) was added to the reactor, and the reaction was heated at 140 ^{o}C for 20 min. After this time, the crude reaction mixture was cooled and analyzed by radio-HPLC (column: Phenomenex Prodigy C8 5µ 150 x 4.6 mm; mobile phase: MeCN : 20 mM ammonium acetate = 35 : 50, pH 4.5; flow rate: 0.8 mL/min; oven temp: 40°C; UV wavelength: 254 nm; t_R [^{18}F]MPPF = 8.78 min; a typical chromatogram is shown in Figure S17). Typical RCC were 70±10% (H_2O-MeCN azeotrope, n = 3) or 78±18% (H_2O-EtOH azeotrope, n = 3).



UV Detector Ch1-254nm Results Retention Time	Area	Area %	Height	Width	S/N (ASTM)
2.208	97806	0	17202	0.233	22.13
2.725	1268980	5	263342	0.425	338.76
4.575	2867369	11	266439	0.542	97.83
8.900	21201104	83	1061339	1.275	615.01

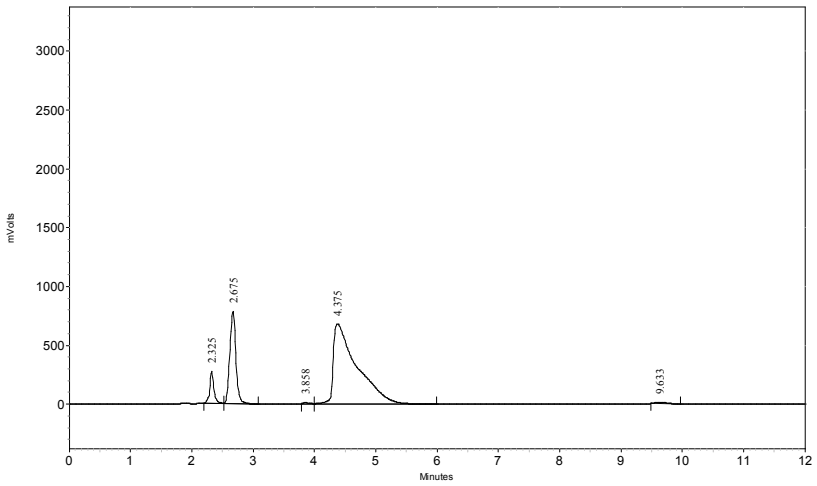


RAD Results Retention Time	Area	Area %	Width
2.318	1967	4	0.21
8.784	47150	96	0.57

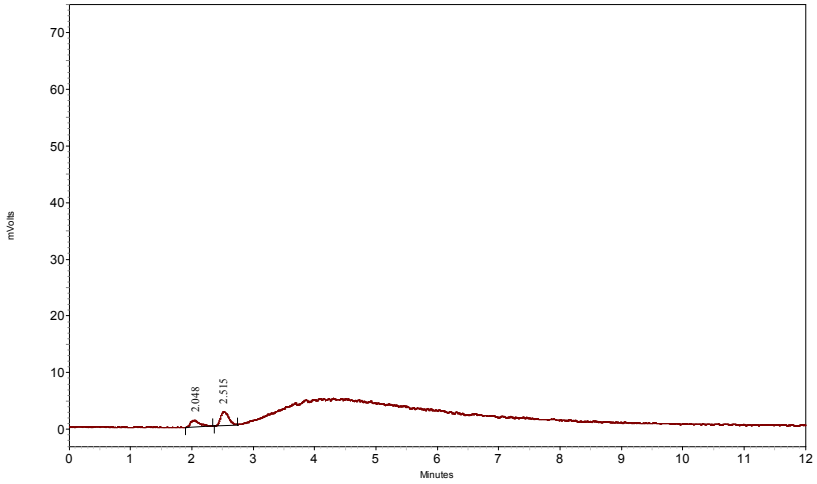
Figure S17

Table 2, Entry 11

[^{18}F]Fluoride was dried using the general method described above. It was then attempted to synthesize [^{18}F]MPPF as described above, but using ethanol (n = 3) or ethanol/DMSO [50:50] (n = 3) as the reaction solvent. However, no product was formed in either case as determined by radio-HPLC analysis (Figure S18, expected t_R of [^{18}F]MPPF = ~8.78 min).



UV Detector Ch1-254nm Results Retention Time	Area	Area %	Height	Width	S/N (ASTM)
2.325	1282831	5	271845	0.325	169.87
2.675	5381206	22	784338	0.558	490.12
3.858	54488	0	8850	0.208	4.01
4.375	18028968	72	680339	2.000	308.46
9.633	168280	1	13148	0.483	17.04



RAD Results Retention Time	Area	Area %	Width
2.048	13238	37	0.44
2.515	22386	63	0.37

Figure S18

3. References

[1] M. L. Richards and P. J. H. Scott. Synthesis of [^{18}F]Fluorodeoxyglucose ([^{18}F]FDG) in Radiochemical Syntheses Volume 1: Radiopharmaceuticals for Positron Emission Tomography by Peter J. H. Scott and Brian G. Hockley (Eds.), John Wiley and Sons Inc., Hoboken, New Jersey, 2012.

[2] X. Shao, R. Hoareau, B. G. Hockley, L. J. M. Tluczek, B. D. Henderson, H. C. Padgett and P. J. H. Scott, *J. Label. Compd. Radiopharm.* 2011, **54**, 292.

[3] B. G. Hockley, M. N. Stewart, P. Sherman, C. Quesada, M. R. Kilbourn, R. L. Albin, P. J. H. Scott, *J. Label. Compd. Radiopharm.* 2013, **56**, 595.