

Research Article

Efficient methods for the synthesis of 5-(4-[¹⁸F]fluorophenyl)-10,15,20-*tris*(3-methoxyphenyl)porphyrin as a potential imaging agent for tumor[†]

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Summary

F-18-labeled porphyrins, the potential tracing and detecting agents for tumor have been synthesized and characterized by two convenient routes: one is a mixed aldehyde condensation, which involves acid-catalyzed condensation of pyrrole, *m*-anisaldehyde and 4-[¹⁸F]fluorobenzaldehyde. The other is the acid-catalyzed condensation of tetrapyrrene with 4-[¹⁸F]fluorobenzaldehyde. The synthetic methodologies including solvents, reaction concentrations and catalysts are optimized for radiolabeled porphyrins. The methods also provide the desired product in reasonable radiochemical yield (20–26%) compared with those of cold chemical synthesis (1–3%) and with high radiochemical purity (>95%). The methods described here would be effective and convenient ways to produce radiolabeled porphyrin. Copyright © 2005 John Wiley & Sons, Ltd.

Key Words: porphyrin; fluorine-18; ¹⁸F-porphyrin; tetrapyrrene; tumor imaging; PET

Introduction

The tetrapyrrolic macrocycles play highly diverse roles in biological systems.¹ The more recent and promising applications of porphyrin derivatives in

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[†]Part of this work was presented at the 15th ISRC, Conference, Australia.

Contract/grant sponsor: National Research Laboratory Program

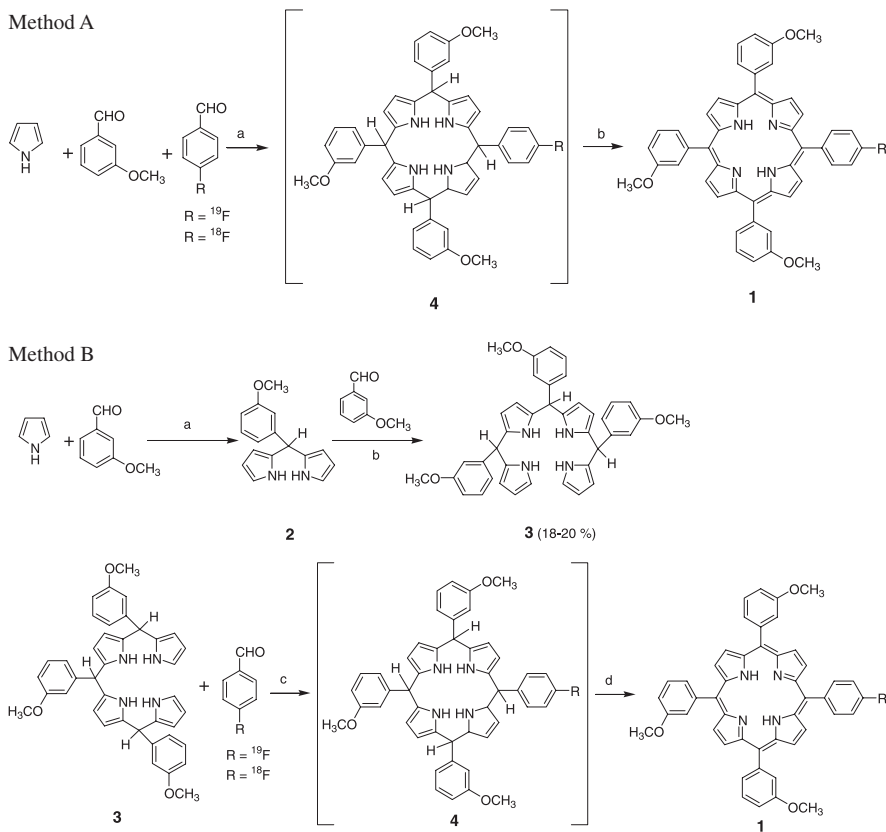
Contract/grant sponsor: Korea Institute of Radiological and Medical Sciences

medicine are in the diagnostic detection and treatment of tumors.^{2,3} The porphyrins have been recognized as one of the most important prosthetic groups in biological systems and the diverse chemistry performed by natural porphyrins has inspired works in various field of chemistry.^{4,5} Porphyrin derivatives have been synthesized in various way and their affinities for tumor tissues in relation with the nature of the side chain and the mechanism of their physico-chemical action have been studied.⁶ Among those reported porphyrins, 5,10,15,20-tetra(3-hydroxyphenyl)chlorin has shown promising activity and tissue selectivity in photonecrosis. The studies indicated that the *meta-isomer* of four *meso*-hydroxyphenyl groups shows 25–30 times more potency than haematoporphyrin derivatives in sensitizing tumors *in vivo*.⁷

Positron emission tomography (PET) is widely used for the medical imaging and fluorine-18 ($t_{1/2} = 110$ min) is a very attractive radionuclide for the labeling of organic molecules as PET radiotracers, because of its many favorable characteristics including small steric size, stable bonding to carbon, convenient half life, low positron energy and ease of production.^{8,9} Although many drugs based on porphyrin increase the radiosensitivity of hypoxic cells *in vitro* and some of them show marked therapeutic effects in tumor models, clinical applications have been failed because of insufficient uptake of drugs in solid tumors and neurotoxicity of the drugs.^{10–13} Thus the development of radiosensitizers with high tumor affinity and less neurotoxicity is essential for their clinical application. As the target compound has a structural resemblance to 5,10,15,20-tetra(3-hydroxyphenyl)chlorin, the target compound will have a chance to be useful radiopharmaceuticals. Herein, we report the practical and convenient synthesis of potential radiotracer, the fluorine-18-labeled title compound via two different approaches. Is it not only almost impossible to prepare 3-[¹⁸F]fluorobenzaldehyde, but also 4-[¹⁸F]fluorobenzaldehyde could easily be prepared, we used 4-[¹⁸F]fluorobenzaldehyde in two different approaches.

Results and discussion

An essential purpose in designing ¹⁸F-associated porphyrins is that these compounds could be used as a radiotracer and can play an important role in detecting tumor. Practically, there were no synthetic reports of the directly fluorine-18 radiolabeled porphyrins. The unlabeled porphyrin **1** could be synthesized as shown in Scheme 1 (Methods A and B). The synthesis has been achieved by two methods: one is a mixed aldehyde condensation (Method A) and another is a stepwise approach (Method B). Initially the cold authentic compound was prepared by Method A as shown in Scheme 1. Condensation of pyrrole (4 equiv), 3-methoxybenzaldehyde (3 equiv), and 4-fluorobenzaldehyde (1 equiv) in the presence of catalytic amount of trifluoroacetic acid (TFA) followed by 2,3-dichloro-5,6-dicyanoquinone (DDQ) oxidation afforded



Scheme 1. Method A: Reagents. (a) TFA, CH₂Cl₂, rt, 40 min (R = ¹⁹F); ice-bath 5 min, rt, 20 min (R = ¹⁸F); (b) DDQ, rt, 1 h (R = ¹⁹F); 20 min (R = ¹⁸F). **Method B. Reagents.** (a) TFA, rt, 10 min; (b) TFA, CH₂Cl₂, rt, 10 min; (c) TFA, rt, 40 min (R = ¹⁹F); ice-bath 5 min, rt, 20 min (R = ¹⁸F); (d) DDQ, rt, 1 h (R = ¹⁹F); 20 min (R = ¹⁸F)

5-(4-fluorophenyl)-10,15,20-*tris*(3-methoxyphenyl)porphyrin (**1**) in 1% yield. As an alternative approach, the step-by-step synthesis (Method B) was performed. The condensation of 3-methoxybenzaldehyde with pyrrole, a large excess of pyrrole present (40 equiv), catalyzed by TFA, afforded *meso*-(3-methoxyphenyl)dipyrromethane (**2**).^{14,15} Then the reaction of dipyrromethane **2** (2 equiv) with 3-methoxybenzaldehyde (1 equiv) catalyzed by TFA at rt gave tetrapyrane **3**^{16,17} in moderate yield (18–20%). This result indicates the cleavage of 5-(3-methoxyphenyl)dipyrromethane (**2**) by acid to generate free pyrrole. The product was easily separated by flash column chromatography on neutralized silica, using EtOAc/hexane (1:9) as an eluant. The use of neutralized silica (mildly basic) prevents the tetrapyrane from the

decomposition usually observed on slightly acidic conditions. The dipyrromethane **2** and tetrapyrrene **3** are stable in the purified form upon storage at 0°C under nitrogen atmosphere and absence of light. High-purity dipyrromethane and tetrapyrrene seems to be essential for their application in the synthesis of non-symmetrically *meso*-substituted porphyrins. The tetrapyrrene **3** is then condensed with the 4-fluorobenzaldehyde, catalyzed by TFA followed by DDQ oxidation, to afford the cold authentic **1** in 3%. All the spectroscopic data were in conformity with the cold authentic prepared by Method A. The radiolabeled porphyrins were synthesized by the same methodologies as shown in Scheme 1 (Methods A and B) and the yields were moderately low.

The preparation of 4- ^{18}F fluorobenzaldehyde has been achieved by the nucleophilic aromatic substitution of (4-formylphenyl)trimethylammonium triflate by ^{18}F fluoride ion in DMSO at 90°C within 5 min in overall 85% yield according to the known procedure.^{18,19} The formation of 4- ^{18}F fluorobenzaldehyde was characterized by radio-thin layer chromatography (TLC) and change of solvent from DMSO to CH_2Cl_2 was performed by C-18 Sep-Pak.^{18,19} We have carried out number of experiments to optimize the condition and solvents for the synthesis of radiolabeled porphyrin. The experimental results were illustrated in Tables 1 and 2. Table 1 summarizes the experiments carried out to optimize the reaction of synthesis of **4** conditions such as solvent concentrations, reaction time and temperature and compare with Methods A and B. We found that radiolabeled porphyrinogen **4** was prepared in an ice-bath for 5 min and rt for 20 min in 222.5 μl of CH_2Cl_2 and 2.5 μl of TFA. It was also found that the Method B gave a maximum radiochemical yield (22.8%, Table 1, entry 6). The radiochemical yield of the mixed aldehydes condensation (Method A) was lower than Method B (12.7%, Table 1, entry 2).

We attempted to check the formation of labeled porphyrins by tracing radioactivity in the intermediate before final DDQ oxidation. Indeed, we were able to detect the formation of porphyrinogen **4** by radio-TLC (4- ^{18}F fluorobenzaldehyde, $R_f = 0.8$; porphyrinogen, $R_f = 0.5$, EtOAc/hexane (2:8)). Hence, the optimized the solvent volume, reaction time, and temperature (Table 1, entry 6) were applied to the whole experiment with DDQ oxidation, which provided the title compound [^{18}F]**1** ($R_f = 0.6$, EtOAc/hexane (2:8), Table 2, entry 2). Deviation from the 2.5 μl of TFA did not improve the yield (Table 2, entries 1 and 3). Since we thought that the change of solvents might lead to increase in the yield of porphyrins, we also used various solvents such as CH_3CN , THF and toluene (Table 2, entries 6–8), but none of these solvents gave satisfactory results. The obtained results were represented in Table 2. The formation of the radiolabeled porphyrin was confirmed on the basis of radio-TLC ($R_f = 0.6$, EtOAc/hexane = 2/8) (Figure 1) which is well matched with that of the cold authentic. Some

Table 1. Optimization of reaction condition for the radiolabeled porphyrinogen 4

Entry	Precursor ^a	CH ₂ Cl ₂ (μ l)	Reaction time (min)				Products (%)		
			Ice-bath time	rt time	50°C time	Unknown peak ^b	4 ^b	Starting material recovered	
1	Pyrrole (<i>n</i> = 2)	200	5	10	–	72.8 \pm 3.3	5.4 \pm 1.9	21.2 \pm 2.0	
2	Pyrrole (<i>n</i> = 3)	200	5	20	–	86.7 \pm 0.6	12.7 \pm 0.9	–	
3	Pyrrole (<i>n</i> = 2)	200	5	–	–	46.8 \pm 1.0	–	51.2 \pm 0.6	
4	Pyrrole (<i>n</i> = 2)	200	25	–	–	34.9 \pm 0.1	4.9 \pm 0.1	59.5 \pm 0.2	
5	3 (<i>n</i> = 2)	200	5	10	–	66.2 \pm 3.8	12.7 \pm 0.9	20.0 \pm 2.1	
6	3 (<i>n</i> = 3)	200	5	20	–	74.6 \pm 2.2	22.8 \pm 2.8	–	
7	3 (<i>n</i> = 2)	400	5	20	–	17.9 \pm 0.7	–	81.6 \pm 0.8	
8	3 (<i>n</i> = 2)	400	5	20	5	24.1 \pm 0.5	–	74.2 \pm 1.1	
9	3 (<i>n</i> = 2)	1000	5	30	–	28.5 \pm 1.5	2.5 \pm 0.1	65.3 \pm 3.5	
10	3 (<i>n</i> = 2)	200	5	–	30	45.2 \pm 1.1	5.3 \pm 0.6	49.3 \pm 0.8	

^aMethod A was applied for pyrrole and Method B for 5,10,15-*tris*(3-methoxyphenyl)tetrapyrane **3**. Method A: *m*-anisaldehyde (2.3 μ l, 1.8 μ mol), pyrrole (2 μ l, 2.9 μ mol), and 4-[¹⁸F]fluorobenzaldehyde (233–370 MBq) and 2.5 μ l of TFA (25 μ l solution was taken from the mixture of 50 μ l TFA and 450 μ l of CH₂Cl₂) in dry CH₂Cl₂ (200 μ l) was added. Method B: 5,10,15-*tris*(3-methoxyphenyl)tetrapyrane **3** (2 mg, 0.3 μ mol), 4-[¹⁸F]fluorobenzaldehyde and 2.5 μ l of TFA (25 μ l solution was taken from the mixture of 50 μ l TFA and 450 μ l of CH₂Cl₂) in dry CH₂Cl₂ (200 μ l) was added.

^bYield was based on radio-TLC.

Table 2. Optimized condition and result of radiolabeled porphyrin

Entry	Precursor ^a	TFA (μ l)	Solvent (200 μ l)	Unknown peak (%) ^b	Product (%) ^b	Starting material (%) ^b
1	3 (<i>n</i> = 2)	0.5	CH ₂ Cl ₂	83.4 \pm 1.1	6.4 \pm 0.2	9.1 \pm 0.1
2	3 (<i>n</i> = 3)	2.5	CH ₂ Cl ₂	–	20.5 \pm 4.8 ^c	–
3	3 (<i>n</i> = 2)	5.0	CH ₂ Cl ₂	80.1 \pm 0.5	7.6 \pm 0.8	–
4	Pyrrole (<i>n</i> = 3)	2.5	CH ₂ Cl ₂	–	9.4 \pm 5.9 ^c	–
5	Pyrrole (<i>n</i> = 2)	5.0	CH ₂ Cl ₂	84.4	4.5	–
6	3	2.5	CH ₃ CN	36.9	Trace	49.3
7	3	2.5	THF	3.1	–	89.1
8	3	2.5	Toluene	58.2	Trace	9.2

^aSee footnote a in Table 1 with proper amounts of TFA. All reactions were carried out initially in an ice-bath (5 min) followed by 20 min at rt and oxidation with DDQ (3 mg, 13.2 μ mol) for 20 min at rt.

^bYield was based on radio-TLC.

^cIsolated yield by HPLC.

unknown radioactive peaks appeared on radio-TLC, but no attempts were made to analyze these unknown compounds. For further purification, the reaction mixture was then passed through a bed of Celite (1.5 cm/5 mm) using EtOAc (1 ml) to remove the unreacted DDQ and the unknown products

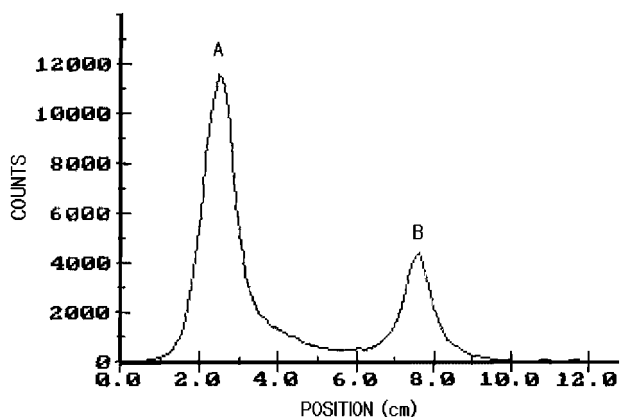


Figure 1. The radio-TLC of the reaction mixture of entry 2 in Table 2. A = unknown peak, B = [^{18}F]1

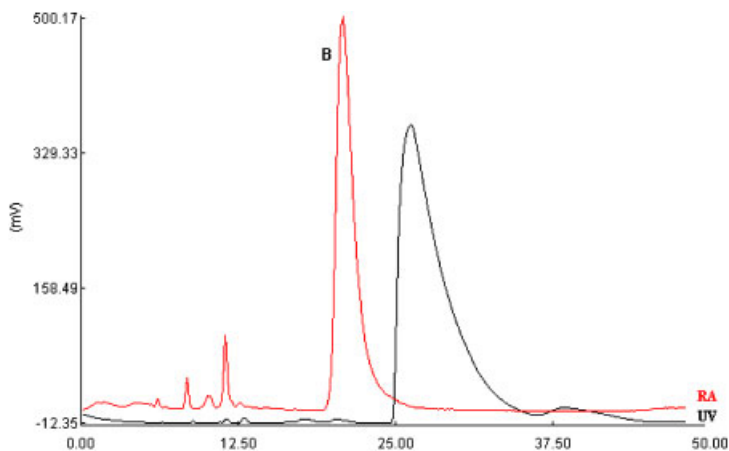


Figure 2. The HPLC analysis of the purified [^{18}F]1. UV (400 nm) and γ -detection (511 keV) profiles were recorded simultaneously. HPLC (Alltech Econosil silica gel, 10 μm , 10 \times 250 mm; Eluant: EtOAc: hexane = 3:7, at a flow rate of 2.5 ml/min) data of the reaction mixture of entry 2 in Table 2. A radioactive peak at 20.63 min marked with B is [^{18}F]1

before injecting into high-performance liquid chromatography (HPLC). The HPLC were performed on a semi-preparative column (Alltech Econosil silica gel, 10 μm , 10 \times 250 mm) simultaneously monitored by a UV detector (400 nm) and a γ -detector with the eluant of EtOAc/hexane (3:7) and a flow rate of 2.5 ml/min. The RA was recorded at $t_R = 20.63$ min (Figure 2). Identity of the product was confirmed by coelution with cold authentic compound.

Conclusion

We have described two effective and convenient methods of radiolabeling porphyrin. The approaches are condensation of aldehydes with pyrrole (Method A) and aldehyde with tetrapyrane (Method B). Both provided radiolabeled 5-(4-[^{18}F]fluorophenyl)-10,15,20-*tris*(3-methoxyphenyl)porphyrin ([^{18}F]1) in better radiochemical yields (9.4%, Method A and 20.5%, Method B) than the chemical yields of cold synthesis (1 and 3%, respectively). In the course of developing these practical syntheses a number of interesting observations were made and further applications to the synthesis of radiolabeled porphyrins are feasible.

Materials and methods

Chemicals were purchased from Sigma-Aldrich Chemical Company (Milwaukee, WI, USA) and HPLC solvents from Fisher Scientific (Pittsburgh, PA, USA) and other solvents were distilled and dried prior to use. HPLC was carried out on a Young-Lin System with a semi preparative column (Alltech Econosil silica gel, 10 μm , 10 \times 250 mm). The eluant was simultaneously monitored by a Young-Lin UV instrument (400 nm) and γ -detection a Raytest GABI instrument. TLC was performed on Merck F₂₅₄ silica plates and visualized by UV illumination. Flash column chromatography was performed on silica gel 230-400 mesh. For radiolabeled compounds TLC was analyzed on a Bioscan AC-3000 scanner (Washington, DC, USA). ^1H and ^{13}C NMR spectra were recorded on a Varian Gemini-200 and Varian Gemini-400 and chemical shifts were reported in δ units (ppm) from internal standard tetramethylsilane. Electron impact (EI) mass spectra were obtained on a GC/MS QP5050A spectrometer (Shimadzu, Kyoto, Japan) and MALDI-TOF mass spectra was performed on Voyager-DE STR MALDI-TOF mass spectrometer (San Francisco, USA).

Method A: condensation of aldehydes with pyrrole

5-(4-Fluorophenyl)-10,15,20-*tris*(3-methoxyphenyl)porphyrin (**1**). *m*-Anisaldehyde (660 mg, 4.8 mmol) and 4-fluorobenzaldehyde (200 mg, 1.6 mmol) and pyrrole (430 mg, 6.4 mmol) were dissolved in dry CH_2Cl_2 (20 ml) and the reaction flask was protected from light. Nitrogen gas was bubbled through this solution for 10 min. TFA (50 μl , 0.64 mmol) was added at 0°C and the reaction was stirred under nitrogen for about 40 min at rt DDQ (6.4 mmol) was added and the reaction was stirred for 60 min exposed to air. The reaction mixture was evaporated to dryness to produce black tarry solid. This crude product was adsorbed onto silica gel and purified by flash column chromatography using EtOAc/hexane (2:8) as an eluant. The major product was *meso*-tetramethoxyphenylporphyrin (10%). The desired product was collected as a purple solid (12 mg, 1%); ^1H NMR (200 MHz, CDCl_3) δ 3.99 (s, 9H), 7.21

(t, $J = 8.8$ Hz, 1H), 7.32–7.36 (m, 3H), 7.46 (t, $J = 8.6$ Hz, 2H), 7.65 (t, $J = 7.2$ Hz, 3H), 7.78–7.84 (m, 6H), 7.95–8.01 (m, 1H), 8.14–8.21 (m, 2H), 8.81 (d, $J = 5.2$ Hz, 2H), 8.91 (d, $J = 5.2$ Hz, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 55.5, 113.5, 113.6, 113.8, 115.7, 115.9, 118.1, 118.7, 119.9, 120.4, 124.8, 127.5, 127.6, 131.6, 131.7, 135.7, 135.7, 138.0, 143.4, 157.9. MALDI-TOF MS: 722.63 (MH^+); (calculated for $\text{C}_{47}\text{H}_{35}\text{FN}_4\text{O}_3$, 722.27).

Method B: condensation of aldehyde with tetrapyrrole

5-(3-Methoxyphenyl)dipyrromethane (2).^{14,15} A mixture of *m*-anisaldehyde (270 mg, 2.0 mmol) and pyrrole (5.40 g, 80 mmol) was degassed by bubbling with nitrogen for 10 min then TFA (15 μl , 0.2 mmol) was added and the solution was stirred for 10 min at rt. The mixture was diluted with CH_2Cl_2 (30 ml) then washed with 0.1 N NaOH (10 ml), washed with water, the organic layer separated and dried over anhydrous Na_2SO_4 . The solvent was removed under reduced pressure and the unreacted pyrrole was removed by vacuum distillation at rt. The resulting thick oily liquid was further distilled using Kugelrohr apparatus to get 5-(3-methoxyphenyl)dipyrromethane **2** as brown viscous liquid (64%): ^1H NMR (400 MHz, CDCl_3) δ 3.76 (s, 3H), 5.45 (s, 1H, *meso*-H), 5.91–5.93 (m, 2H), 6.13–6.15 (q, $J = 2.8$ Hz, 2H), 6.65–6.66 (m, 2H), 6.76–6.81 (m, 3H), 7.20–7.24 (m, 1H), 7.90 (brs, 2H, NH); ^{13}C NMR (100 MHz, CDCl_3) δ 43.9, 55.1, 107.2, 108.4, 112.2, 114.3, 17.2, 120.8, 129.6, 132.3, 143.6, 159.8; MS (EI) m/z : 252 (M^+).

5,10,15,-Tris(3-methoxyphenyl)tetrapyrrole (3).¹⁶ In dry CH_2Cl_2 (20 ml) was added a solution of *m*-anisaldehyde (75 mg, 0.55 mmol) and 5-(3-methoxyphenyl)dipyrromethane (**2**, 280 mg, 1.11 mmol) under nitrogen atmosphere. To this stirred solution, TFA (4 μl , 0.05 mmol) was added and stirred for 10 min at rt. Solvent was evaporated and the resulting crude thick liquid was purified by flash column chromatography over silica gel neutralized with 1% Et_3N in EtOAc /hexane (1:9) to get the product as pale brown semi-solid (20%): ^1H NMR (200 MHz, CDCl_3) δ 3.72 (s, 9H), 5.23 (s, 1H), 5.31 (s, 2H), 5.71–5.75 (m, 2H), 5.85–5.87 (m, 4H), 6.09–6.12 (m, 2H), 6.63–6.78 (m, 11H), 7.15–7.25 (m, 3H), 7.69 (brs, 2H, NH), 7.90 (brs, 2H, NH); ^{13}C (100 MHz, CDCl_3) δ 44.0, 44.1, 55.1, 55.1, 107.1, 107.3, 108.3, 112.2, 112.4, 113.8, 114.1, 117.1, 120.7, 120.7, 129.4, 129.5, 132.0, 132.0, 132.3, 143.6, 143.6, 159.7, 159.8.

5-(4-Fluorophenyl)-10,15,20-tris(3-methoxyphenyl)porphyrin (1). 5,10,15-*Tris*(3-methoxyphenyl)tetrapyrrole (**3**, 400 mg, 0.64 mmol), 4-fluorobenzaldehyde (80 mg, 0.64 mmol) and TFA (7 μl , 0.064 mmol) in dry CH_2Cl_2 (20 ml) were stirred under nitrogen for 40 min at rt. To this stirred solution was added DDQ (1.28 mmol) exposing the reaction mixture to air for 60 min. The resulting dark solution was adsorbed over silica gel and further purified over

silica gel flash chromatography using EtOAc/hexane (2:8) as an eluant to get the product as purple crystals (14 mg, 3%).

Synthesis of radiolabeled porphyrin

4-[¹⁸F]Fluorobenzaldehyde.^{18,19} [¹⁸F]Fluoride was produced in a cyclotron by the ¹⁸O(p,n) ¹⁸F reaction. A volume of 100–300 μl of [¹⁸F]fluoride (370–1800 MBq) in water was added to a vacutainer containing *n*-Bu₄NOH (40% aq., 3.5 μl, 5.44 μmol). The azeotropic distillation was carried out each time with 200 μl of aliquote of CH₃CN at 85°C under a stream of nitrogen. A [¹⁸F]fluoride ion nucleophilic aromatic substitution on (4-formylphenyl)trimethylammonium triflate (2 mg, 6.4 μmol) with *n*-Bu₄N[¹⁸F]F in DMSO (200 μl) was carried out in a reaction vial at 90°C for 5 min. The reaction vessel was cooled in an ice-bath, and HCl (0.2 M, 2 ml) was added to the mixture. The crude mixture was loaded on C-18 Sep-Pak and then washed with H₂O (5 ml) and CH₂Cl₂ (1 ml). The solvent CH₂Cl₂ was passed through a bed of Na₂SO₄ and the solvent collected. The collected solvent contained the [¹⁸F]fluorobenzaldehyde.

5-(4-[¹⁸F]Fluorophenyl)-10,15,20-tris(3-methoxyphenyl)porphyrin (1). *Method A:* To *m*-anisaldehyde (2.3 μl, 1.8 μmol), pyrrole (2 μl, 2.9 μmol), and 4-[¹⁸F]fluorobenzaldehyde (233–370 MBq) in dry CH₂Cl₂ (200 μl) was added 2.5 μl of TFA (25 μl solution was taken from the mixture of 50 μl TFA and 450 μl of CH₂Cl₂). The mixture was stirred in an ice-bath for 5 min. This solution was further stirred at rt for 20 min. The reaction vial was protected from light. DDQ (3 mg, 13.2 μmol) was added and the reaction was stirred further for 20 min at rt. The resulting black mixture was filtered through a bed of Celite and washed with EtOAc (1 ml). The formation of product was conformed by radio-TLC (*R*_f = 0.6, EtOAc/hexane (2:8)).

Method B: 5,10,15-Tris(3-methoxyphenyl)tetrapyrane (**3**, 2 mg, 0.3 μmol), 4-[¹⁸F]fluorobenzaldehyde (233–370 MBq) and TFA (2.5 μl) in dry CH₂Cl₂ (200 μl) was stirred in an ice-bath for 5 min. This solution was further stirred at rt for 20 min. The reaction vial was protected from light. DDQ (3 mg, 13.2 μmol) was added and the reaction was stirred further for 20 min at rt. The resulting black mixture was filtered through a bed of Celite and washed with EtOAc (1 ml). The formation of product was conformed by radio-TLC (*R*_f = 0.6, EtOAc/hexane (2:8)).

HPLC condition. The mixture solvent of EtOAc and CH₂Cl₂ was removed with a gentle stream of nitrogen. After removing the solvent, the mixture was dissolved with an eluant of HPLC solvent (EtOAc/hexane = 3:7). The crude compound was injected onto HPLC with a semi-preparative column (Alltech Econosil silica gel, 10 μm, 10 × 250 mm). An eluant EtOAc/hexane (3:7) with a

flow rate of 2.5 ml/min was simultaneously monitored by a UV detector (400 nm) and a γ -detector. The desired compound was collected from HPLC $t_R = 20.63$ min with a radiochemical yield (20–26%) and radiochemical purity (>95%). Authenticity of the product was confirmed by coelution with cold compound.

Acknowledgements

This work was supported by the National Research Laboratory Program in Korea and Korea Institute of Radiological and Medical Sciences.

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