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Syntheses of 6-fluoro-*meta*-tyrosine and of its metabolites

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Abstract

6-Fluoro-*meta*-tyrosine (**1**) was prepared from 2-fluoro-5-hydroxybenzaldehyde (**6**) based on an Erlenmeyer–Plöchl azlactone strategy. Products of expected metabolism of the amino acid, including 6-fluoro-*meta*-tyramine (**2**) and its *O*-sulfate conjugate (**3**), (2-fluoro-5-hydrxoyphenyl)acetic acid (**4**), and 6-fluoro-*meta*-octopamine (**5**) also were prepared from **1**. The use of a recently reported ultrasound-catalyzed Henry reaction facilitated the preparation of the tyramine derivative **2**. The compounds synthesized are available for high performance liquid chromatography (HPLC) standards in positron emission tomography (PET) studies employing 6-[^{18}F]fluoro-*meta*-tyrosine and as reference samples for metabolic studies of the amino acid.

Keywords: Fluorinated metabolites; PET scanning agents; HPLC standards

1. Introduction

Positron emission tomography (PET) involves the administering of a tracer molecule that is radio-labeled with a positron-emitting species, such as ^{11}C or ^{18}F. In one important application or PET, 6-[^{18}F]fluoro-3,4-dihydroxyphenylalanine (6-[^{18}F]fluoro-DOPA), functioning as a precursor to 6-[^{18}F]fluorodopamine, is used to visualize regional dopaminergic function in the brain. A complicating factor in the use of this agent is the fact that 6-[^{18}F]fluoro-DOPA is methylated by the enzyme catechol-*O*-methyltransferase (COMT) to produce radiofluorinated 3-methoxytyrosine. This action of COMT contributes to metabolic degradation of the tracer and bi-directional transport of the methylated product across the blood brain barrier contributes to significant background radioactivity [1]. 6-[^{18}F]fluoro-*meta*-tyrosine has been examined as a potential alternative for quantification of DA function, since the absence of the catechol ring obviates methylation by COMT. These and other issues regarding the use of 6-[^{18}F]fluoro-*meta*-tyrosine vis a vis 6-[^{18}F]fluoro-DOPA have been discussed in recent publications [1,2].

Pharmacological and metabolic studies are a necessary part of development of PET-scanning agents. To facilitate studies at NIH, we have used a readily available aldehyde precursor [3] to prepare authentic samples of 6-fluoro-*meta*-tyrosine (**1**) and several key metabolites thereof. The metabolites we have prepared include 6-fluoro-*meta*-tyramine (**2**) and its *O*-sulfate conjugate (**3**), 2-fluoro-5-hydroxyphenylacetic acid (**4**) [6], and 2-fluoro-5-hydroxyphenylethanolamine (**5**). These compounds function as standards for high performance liquid chromatography (HPLC) used in analyses of metabolites formed from administered 6-[^{18}F]fluoro-*meta*-tyrosine. In this report, we provide details for the syntheses of these compounds by the general strategy we had employed for a similar development of metabolites of 6-F-DOPA [4].

2. Results and discussion

2.1. Synthesis of 6-fluoro-meta-tyrosine

2-Fluoro-5-hydroxybenzaldehyde (**6**), prepared readily from 4-fluorophenol by our published procedure [3], provided a convenient precursor for our target molecules. The *O*-benzylation as described gives 2-benzyloxy-5-fluorobenzaldehyde **7**. Condensation of **7** with hippuric acid in the presence of acetic anhydride and sodium acetate gave the azlactone **8**. This was treated with methanol in the presence of sodium acetate to give unsaturated ester **9**. Hydrogenation over Pd/C reduced the double bond and removed the benzyl protecting group to give amido ester **10**. Acid hydrolysis provided 6-fluoro-*meta*-tyrosine (**1**) (Scheme 1). Luxen and coworkers have published an alternative synthesis of *S*-**1** based on alkylation of *S*-Boc-BMI, a chiral glycine equivalent, with 2-fluoro-4-methoxybenzylbromide prepared from

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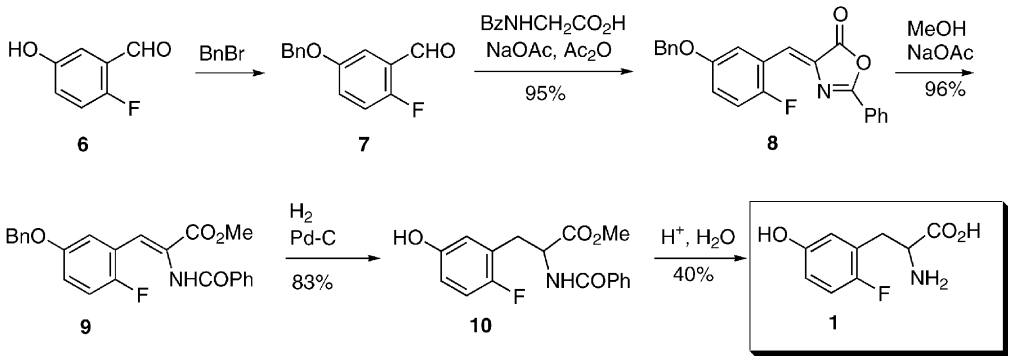


Scheme 1.

6 [5]. The [^{18}F]-labeled *S*-**1** was prepared by direct fluorination of *meta*-tyrosine with [^{18}F]acetyl hypofluorite [2].

2.2. Synthesis of metabolites

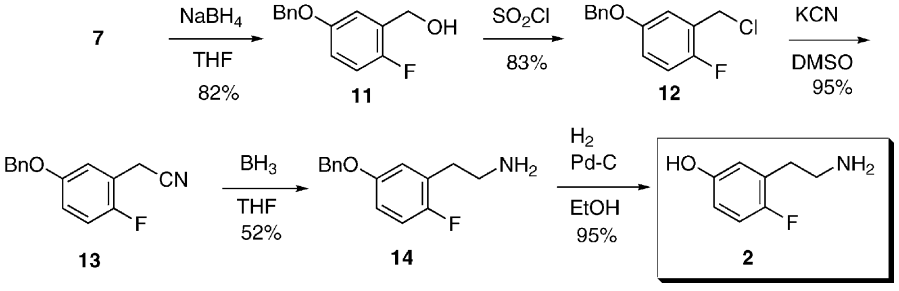
Reduction of **7** with sodium borohydride produced the benzyl alcohol **11**. The alcohol **11** was treated with thionyl chloride to give the benzyl chloride **12**. This was converted to 2-fluoro-5-benzyloxyphenylacetonitrile **13** by reaction with potassium cyanide in DMSO. Reduction of **13** with BH_3/THF to give amine **14** was followed by hydrogenolysis to give 6-fluoro-*meta*-tyramine (**2**) (Scheme 2).

A more convenient alternative synthesis of **2** is based on a recently reported usltrasound-catalyzed Henry reaction [6]. Condensation of **6** with nitromethane in the presence of ammonium acetate and acetic acid gave an excellent yield of the nitrostyrene **15**. Reduction with $LiAlH_4$ produced **2** (two-steps from **6**) (Scheme 3). The [^{18}F]-labeled **2** has been prepared previously by fluorination of *meta*-tyramine with [^{18}F]-F_2 in liquid HF [7].

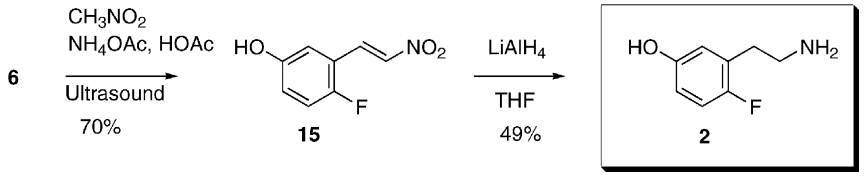
Attempts to hydrolyze **13** directly to the carboxylic acid proved difficult, giving the acid only in low yield. In contrast, treatment of **13** with methanolic HCl and ether, followed by hydrolysis of the intermediate iminoester gave methyl ester **16** in good yield. Saponification to the acid **17** followed by hydrogenolysis gave 2-fluoro-5-hydroxyphenylacetic acid **4**, providing a convenient alternative to direct hydrolysis of the cyano group (Scheme 4).

Sulfo-conugation of phenolic OH groups is an important process in metabolism of biogenic amines. An arylamine sulfotransferase that has especially high affinity for *meta*-tyramine has been isolated from human brain [8]. Accordingly, we have also prepared the sulfate ester of 6-fluoro-*meta*-tyramine. Selective *N*-acylation of **2** with CBZ-anhydride gave carbamate **18**. The phenoxide prepared by reaction with NaH in DMF was treated with trimethylamine-SO_3 [9] to give the sulfo-conjugate, **19**, hydrogenolysis of which produced the sulfo-conjugate **3** of 6-fluoro-*meta*-tyramine (Scheme 5).

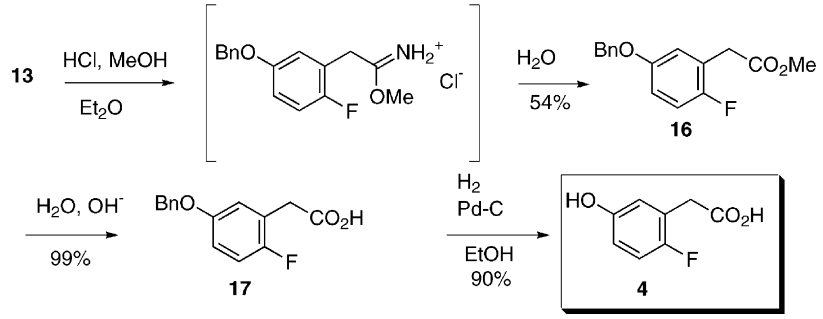
There is evidence that *meta*-tyramine serves as a substrate for dopamine *beta*-hydroxylase, thereby producing 3-hydroxyphenylethanolamine (*meta*-octopamine) as a minor metabolite [10]. Therefore, 4-benzyloxy-2-fluorophenylethanolamine (**20**), prepared previously as a precursor of



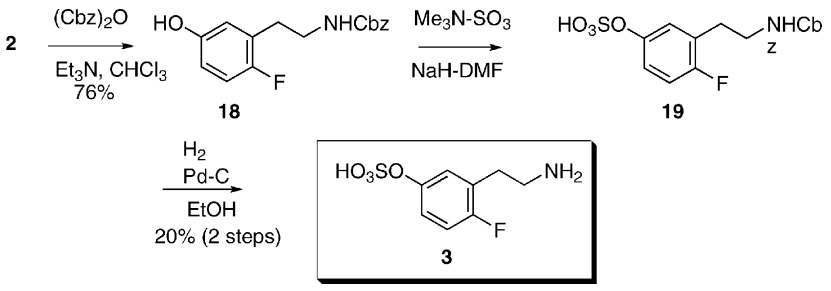
Scheme 2.



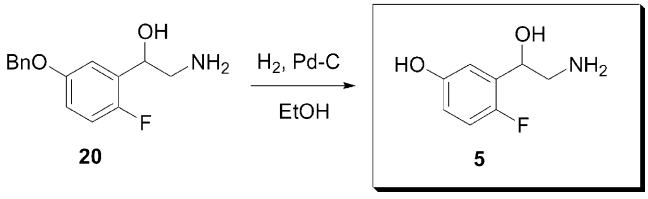
Scheme 3.



Scheme 4.



Scheme 5.



Scheme 6. 6-Fluoro-*meta*-tyrosine and key metabolites were synthesized.

6-fluorophenyleprhine [3], was subjected to Pd-catalyzed hydrogenolsysis to give 2-fluoro-4-hydroxyphenylethanolamine (**5**) (Scheme 6).

3. Summary

We have prepared 6-fluoro-*meta*-tyramine and several of its metabolites from a readily available aldehyde precursor. These compounds are now available for use as HPLC standards PET studies, and as reference samples for other metabolic studies of the amino acid.

4. Experimental

The ^{1}H NMR spectra were recorded at frequencies of 300 Hz and chemical shifts (δ) of protons are relative to TMS (0 ppm). Capillary tube melting points (mp) are not corrected. Low resolution MS were done with chemical ionization with ammonia gas. High resolution MS (HRMS) were done with FAB ionization with Xe gas. Elemental analyses were done by Atlantic Microlab Inc. silica gel Merck 60 (0.040–0.063 mm) was used for column chromatography, Uniplate^{TM} GF (Analtech) was used for preparative TLC. All reagents and dry solvents were purchased from Aldrich if not otherwise indicated and used without additional purification or drying.

*4.1. 2-Benzoylamino-3-(2-fluoro-5-benzyloxyphenyl)-acrylic acid azlactone (**8**)*

A mixture of 500 mg (2.17 mmol) of **7**, 430 mg (2.40 mmol) of hippuric acid, 200 mg of NaOAc, and 1.1 ml of Ac_2O was stirred at 80 °C for 2 h. The yellow reaction mixture was cooled and 5 ml of cold EtOH was added. The mixture was cooled in an ice bath for 15 min and then was poured into 15 ml of ice water, chilled, and the product was collected by filtration. This gave 770 mg (2.06 mmol, 95% yield) of **8** as a bright yellow crystalline solid, mp 156–157 °C. ^{1}H NMR ($CDCl_3$): δ 5.19 (2H, s, OCH_2Ar) 7.04–7.54 (m, ArH), 8.12 ppm (d, $J = 6.3$ Hz, CH), 8.53 (d, $J = 7.5$ Hz, CH). MS: NCI *m/z* (M^-) 373. HRMS. Calculated for $C_{23}H_{16}O_3NF$: 373.1114; found: 373.1106.

*4.2. 2-Benzoylamino-3-(2-fluoro-5-benzyloxyphenyl)-acrylic methyl ester (**9**)*

A solution of 530 mg (1.43 mmol) of **8** and 126 mg of NaOAc in 80 ml of MeOH was stirred at room temperature for 2 h. The solvent was removed by rotary evaporation and the residue was dissolved in 50 ml of EtOAc. The EtOAc

solution was washed two times with water and concentrated to give 557 mg (96%) of **9** as a white solid, mp 135–136 °C. ^{1}H NMR ($CDCl_3$): δ 3.89 (3H, s, OCH_3), 4.86 (2H, s, OCH_2Ar), 6.9–7.9 (13H, m, ArH), 7.47 (1H, s, CH) ppm. HRMS. Calculated for $C_{24}H_{20}O_4NF$: 405.1376; found: 405.1376.

4.3. N-benzoyl-3-(2-fluoro-5-hydroxyphenyl)-alanine methyl ester (*10*)

A solution of 470 mg (1.16 mmol) of **9** in 100 ml of MeOH was hydrogenated over 100 mg of 10% Pd/C at 40 psi for 20 h (Parr apparatus). After removal of the catalyst by filtration, the solvent was evaporated to give 306 mg (0.96 mmol, 83%) of **10**. The mp 139–140 °C. ^{1}H NMR ($CDCl_3$): δ 3.21 (2H, d, $J = 6.0$ Hz, CH_2), 3.78 (3H, s, OCH_3), 5.0 (1H, m, CH), 6.65–7.73 (m, ArH) ppm. HRMS. Calculated for $C_{17}H_{16}O_4NF$: 317.1063; found: 317.1048.

4.4. 3-(2-Fluoro-5-hydroxyphenyl)-alanine (*1*)

A solution 158 mg (0.5 mmol) of **10** in 10 ml of 3 N HCl was refluxed for 24 h. The solution was concentrated to dryness and the residue was dissolved in 5 ml of H_2O. After washing three times with ether, the solution was neutralized to pH 6 with dilute NaOH. The aqueous layer was concentrated to 3 ml and the white crystals that formed were collected by filtration to give 41 mg (40%) of **1**. ^{1}H NMR (D_2O/DCl): δ 3.28 (2H, m, CH_2), 4.30 (1H, m, CH), 6.78–6.86 (3H, m, ArH) ppm. MS: CI *m/z* ($M + 1$) 200, (M + 18) 217.

4.5. 2-Fluoro-5-benzyloxybenzyl alcohol (*11*)

A solution of 1.95 g (8.48 mmol) of **7** in 20 ml of dry THF was added dropwise to a stirred suspension of 800 mg of $NaBH_4$ in 50 ml of dry THF, cooled in ice. The reaction mixture was stirred at room temperature for 3.5 at which time TLC showed no remaining starting material. Water and a few crystals of NaH_2PO_4 were added to decompose excess $NaBH_4$ and the aqueous phase was extracted with three portions of ether. The combined organic extracts were washed twice with water, once with brine, and dried ($MgSO_4$). After removal of the solvent, silica gel chromatography (PE:EtOAc 10:1) gave 1.6 g (6.89 mmol, 82% yield) of **11** as a pale yellow crystalline solid, mp 62–63 °C. ^{1}H NMR ($CDCl_3$): δ 4.74 (2H, s, OCH_2Ar), 5.05 (2H, s, CH_2O), 6.86–7.41 (8H, m, ArH) ppm. HRMS. Calculated for $C_{14}H_{13}O_2F$: 232.0900; found: 232.0896.

4.6. 2-Fluoro-5-benzyloxybenzyl chloride (*12*)

A mixture of 1.50 g (6.46 mmol) of **11** and 1.50 g of thionyl chloride was refluxed for 1 h. CH_2Cl_2 was added and the excess thionyl chloride was evaporated. The residue was taken up in $CHCl_3$, washed twice with saturated aqueous $NaHCO_3$ and the washings were back-extracted twice with $CHCl_3$. The combined $CHCl_3$ extracts were washed twice with H_2O and dried ($MgSO_4$). Evaporation of the solvent gave 1.34 g (5.36 mmol, 83% yield) of **12** as a light brown liquid. ^{1}H NMR ($CDCl_3$): δ 4.60 (2H, s, OCH_2), 5.03 (2H, s, CH_2Cl, 6.86–7.44 (8H, m, ArH) ppm. MS: CI *m/z* (*M*) 250, ($M + 18$) 268, ($M + 35$) 285.

4.7. 2-Fluoro-5-benzyloxybenzyl cyanide (*13*)

To a solution of 2.0 g (8.0 mmol) of **12** in 30 ml of DMSO was added 0.50 g of NaCN. The mixture was stirred at room temperature for 3 h and then was poured over ice. The aqueous solution was extracted two times with EtOAc, then was partially saturated with NaCl and extracted twice more with the same solvent. The combined organic extracts were washed with brine and dried (Na_2SO_4). Evaporation of the solvent gave 1.8 g (7.47 mmol, 95% yield) of **13** as a thick yellow liquid. ^{1}H NMR ($CDCl_3$): δ 3.73 (2H, s, CH_2CN), 5.05 (2H, s, $ArCH_2O$), 6.95–7.42 (8H, m, ArH) ppm. MS: CI *m/z* ($M + 18$) 259, ($M + 35$) 276, ($M - 1$) 240.

4.8. 2-(2-Fluoro-5-benzyloxyphenyl)-ethylamine (*14*)

A solution of 500 mg (2.07 mmol) of **13** in 5 ml of THF was added dropwise to 5 ml of 1.0 M BH_3 in THF with ice bath cooling. After the reaction mixture then was refluxed for 1.5 h it was cooled in an ice bath, 5 ml of MeOH was added, and the mixture was refluxed for an additional 30 min. Solvent was removed, the residue was again dissolved in MeOH. After solvent removal, residual oil was redissolved in MeOH, 1 ml of 10% HCl was added and the mixture was refluxed for 30 min. The reaction mixture was evaporated to dryness and then dissolved in 50 ml of H_2O containing 1 ml of 10% HCl. After the aqueous solution was washed twice with ether it was made basic with 40% NaOH and extracted twice with ether. The aqueous layer was partially saturated with NaCl and extracted twice more with ether. The ether extracts were combined and dried ($MgSO_4$). Removal of the solvent gave 265 mg (1.08 mmol, 52% yield) of **14** pale yellow oil. ^{1}H NMR ($CDCl_3$): δ 2.74 (2H, t, $J = 7.70$ Hz, CH_2CH_2), 2.94 (2H, t, $J = 6.9$ Hz, CH_2CH_2), 5.02 (2H, s, OCH_2Ar), 7.32 –7.43 (8H, m, ArH) ppm. MS: CI *m/z* ($M + 1$) 246, ($M + 18$) 263.

4.9. 3-(2-Fluoro-5-hydroxy)phenylethyl amine (6-fluoro-meta-tyramine) (*2*)

A mixture of 123 mg (0.50 mmol) of **14** and 35 mg of 10% Pd/C in 35 ml of EtOH was stirred overnight in an atmosphere of hydrogen gas (balloon). Removal of catalyst and solvent gave 74 mg (0.48 mmol, 95% yield) of **2** as thick yellow oil. ^{1}H NMR (CD_3OD): δ 2.74 (2H, t, $J = 7.2$ Hz, CH_2CH_2), 2.86 (2H, t, $J = 6.9$ Hz, CH_2CH_2), 6.59–6.89 (3H, m, ArH) ppm. MS: CI *m/z* ($M + 1$) 156, ($M + 18$) 173.

4.10. 2-Fluoro-5-hydroxy-β-nitro-styrene(**15**)

A mixture of 700 mg (5 mmol) of aldehyde **6**, 3.25 ml (58 mmol) of nitromethane, 825 ml (14 mmol) of glacial HOAc, and 831 mg (16 mmol) of NH_4OAc was sonicated at 22–40 °C until the reaction was complete as shown by TLC. CH_2Cl_2 (20 ml) was added and the mixture was washed successively with water and brine. After drying (Na_2SO_4), the solvent was removed to give a yellow solid. This was purified by flash column chromatography (PE:EtOAc 2:1) to give 642 mg (3.5 mmol, 70%) of **15** as a yellow solid, mp 139–141 °C. ^{1}H NMR ($CDCl_3$): δ 4.97 (1H, s, ArOH), 6.92–6.96 (2H, m, ArH), 7.06 (1H, t, $J = 10.2$ Hz, ArH), 7.69(1H, d, $J = 14.1$ Hz, βH), 7.98 (1H, d, $J = 13.8$ Hz, αH) ppm. HRMS. Calculated for $C_8H_6NFO_3$: 183.0332; found:183.0326.

4.11. 6-Fluoro-meta-tyramine (**2**)

To a cooled solution of 500 mg (2.7 mmol) of **15** in 10 ml of anhydrous THF was cautiously added 124 mg (3.2 mmol) of $LiAlH_4$. The mixture was refluxed for 3 h and then cooled to 0 °C. To this was cautiously added 10 ml of 1.5 N H_2SO_4 with stirring. The aqueous layer was separated and its pH was adjusted to 6 with solid $(Li)_2CO_3$. The solution was heated to boiling and the precipitated $Al(OH)_3$ was removed by filtration with the aid of filter cell. The clear, hot filtrate was cooled to room temperature and was extracted three times with ether. The combined ether layer was washed with water and brine. After drying (Na_2SO_4), the solvent was removed to afford the 203 mg (1.3 mmol, 49%) of **2**, identical to the material prepared from **14**. HRMS. Calculated for $C_8H_{10}NFO$: 155.0746; found: 155.0744.

4.12. (2-Fluoro-5-benzyloxyphenyl)acetic acid methyl ester (**16**)

To a solution of 520 mg (2.15 mmol) of **13** in 6 ml of ether was added 0.93 ml of MeOH. Dry HCl gas was bubbled through the solution until saturation. The reaction mixture was stirred for 2 h at ice bath temperature and then was stored in a refrigerator for **7** days during which time fine white crystals of imino ester hydrochloride formed. To the reaction mixture was added 5 ml of water and the mixture was stirred at room temperature for 3 h. The layers were separated and the aqueous layer was extracted with four portions of ether. The organic layers were combined and washed successively with a saturated solution of $NaHCO_3$, water and brine. After drying (Na_2SO_4), the solvent was removed, the residue was dissolved in a 1:5 EtOAc:PE mixture and was filtered through silica gel. Evaporation of solvent gave 320 mg (1.16 mmol, 54%) of **16** as a clear liquid. ^{1}H NMR ($CDCl_3$): δ 3.64 (2H, s, CH_2CO_2), 3.71 (3H, s, OCH_3), 5.02 (2H, s, OCH_2Ar), 6.86–7.43 (8H, m, ArH) ppm. MS: FAB^- *m/z* ($M - 1$) 273, FAB^+ (*M*) 274.

4.13. 2-Fluoro-5-benzyloxyphenyl acetic acid (**17**)

A solution of 320 mg (1.17 mmol) of **16** in 5 ml of MeOH and 1.5 ml of 30% aqueous NaOH was stirred at room temperature for 4 h. The reaction mixture was washed twice with EtOAc, acidified with aqueous HCl, and extracted with three portions of EtOAc. The organic extracts were combined, washed with brine, and dried (Na_2SO_4). Evaporation of the solvent gave 300 mg (99%) of **17** as a white crystals, mp 126–127 °C. ^{1}H NMR (acetone-d_6): δ 3.66 (2H, s, CH_2CO_2), 5.09 (2H, s, OCH_2Ar), 6.9–7.6 (8H, m, ArH) ppm. MS: CI NH_3 *m/z* (*M*) 260, ($M + 18$) 278, ($M + 35$) 295.

4.14. 2-Fluoro-5-hydroxyphenylacetic acid (**4**)

A mixture of 132 mg (0.51 mmol) of **17** and 35 mg of 10% Pd/C in 35 ml of EtOH was stirred overnight in an atmosphere of hydrogen gas (balloon). Removal of catalyst and solvent gave 78 mg (0.45 mmol, 90%) of **4** as a pale solid. Recrystallization (toluene) gave white plates, mp 127–128 °C. ^{1}H NMR (CD_3OD): δ 3.56 (2H, s, CH_2CO_2), 6.62–6.91 (m, ArH) ppm. MS: CI *m/z* ($M + 18$) 188, ($M + 35$) 205.

4.15. N-cbz-6-fluoro-meta-tyramine (**18**)

To a solution of **2** (200 mg, 1.3 mmol) in 15 ml of $CHCl_3$ was added 0.24 ml (2.6 mmol) of Et_3N at room temperature. After 10 min, 243 mg (1.4 mmol) of benzyl chloroformate was added. After stirring the mixture for additional 3 h, the precipitated solid was removed by filtration and 30 ml of EtOAc was added to the filtrate. The organic layer was washed three times with chilled 1 N HCl, dried, and concentrated to give a yellow oil. Purification by flash column chromatography (PE:EtOAc 3:1) gave 285 mg (76%) of **18** as a viscous colorless oil. ^{1}H NMR ($CDCl_3$): δ 2.79 (2H, t, $J = 6.6$ Hz, CH_2CH_2), 3.40–3.47 (2H, m, CH_2CH_2), 5.09 (2H, s, $ArCH_2$), 6.61–6.65 (2H, m, ArH), 6.87 (1H, t, $J = 9.3$ Hz, ArH), 7.34 (5H, m, ArH) ppm. HRMS. Calculated for $C_{16}H_{16}NFO_3$: 289.1114; found: 289.1105.

4.16. 6-Fluoro-meta-tyramine O-sulfate (**3**)

A suspension of 60% NaH in oil (30 mg, 0.75 mmol) was added to a solution of **18** (145 mg, 0.5 mmol) in 5 ml of DMF. The mixture was stirred for 30 min at room temperature, at which time the NaH was completed consumed. The solution was cooled to 0 °C and Me_3N–SO_3 complex (278 mg, 1 mmol) was added. After 30 min, the solution was evaporated under reduced pressure at room temperature to give **19**, which was not further characterized. This was dissolved in 5 ml of EtOH, 10 mg of 10% Pd on carbon was added, and the mixture was hydrogenated for 30 min (balloon). After removal of catalyst and solvent, the residue was triturated with 95% EtOH (1 ml) and filtered. The crystals were dissolved in 2 ml of water, the solution was cooled to 5 °C and acidified with HCl to pH 3–4.

The resulting solid was collected by filtration, washed with a small amount of cold water and with EtOH, to give 24 mg of **3** (20%). ^{1}H NMR (D_2O): δ 2.96–3.24 (4H, m, CH_2CH_2), 6.79 (1H, d, $J = 4.8$ Hz, ArH), 7.02 (1H, t, $J = 9.9$, ArH), 7.25–7.20 (1H, m, ArH) ppm. MS: FAB$^-$ m/z ($M - 1$) 234.

4.17. 2-Fluoro-5-hydroxyphenyethanolamine (**5**)

To 150 mg (0.57 mmol) of **20** dissolved in 10 ml of EtOH was added 15 mg of 10% Pd/C and 77 mg (0.86 mmol) of oxalic acid dihydrate. After stirring under H_2 (balloon) for 3 h, catalyst and solvent were removed to give a solid yellow residue. Recrystallization from acetone/water afforded 35 mg (23%) of **5** as the oxalate, mp 209–210 °C. ^{1}H NMR (D_2O): δ 3.19–3.36 (2H, m, CH_2NH_2), 5.18–5.23 (1H, m, CHOH), 6.84–7.09 (3H, m, ArH) ppm. MS: CI m/z: ($M + 1$) 172. HRMS. Calculated for $C_8H_{10}NFO_2$: 171.0696; found: 171.0687.

References

[1] O.T. DeJesus, C.J. Endres, S.E. Shelton, R.J. Nickles, J.E. Holden, J. Nucl. Med. 38 (1997) 630–636.
[2] R. Chirakal, C. Nahmias, J. Labelled Comp. Radiopharm. 42 (1999) S489–S491.
[3] K.L. Kirk, O. Olubajo, K. Buchhold, G. Lewandowski, F. Gusovsky, D. McCulloh, J.W. Daly, C.R. Creveling, J. Med. Chem. 29 (1986) 1982–1988.
[4] J.-Y. Nie, K.L. Kirk, J. Fluorine Chem. 55 (1991) 259–269.
[5] M. Monclus, C. Masson, A. Luxen, J. Fluorine Chem. 70 (1995) 39–43.
[6] J. McNulty, J.A. Steers, S. Wolf, Tetrahedron Lett. 39 (1998) 8013–8016.
[7] R. Chirakal, C. Nahmias, J. Labelled Comp. Radiopharm. 42 (Suppl. 1) (1999) S489–491.
[8] P.H. Yu, B. Rozdilsky, A.A. Boulton, J. Neurochem. 45 (1985) 836–843.
[9] L. Konishi-Imamura, D.-H. Kim, K. Kobayashi, Chem. Pharm. Bull. 39 (1991) 2994–2998.
[10] W.C. Williams, M.W. Couch, Life Sci. 22 (1973) 2113–2120.