Supporting Information
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SUPPORTING INFORMATION

SYNTHESIS AND RADIO-SYNTHESIS OF PROSPECTIVE 2-NITROIMIDAZOLE HYPOXIA PET TRACERS VIA THIAZOLIDINE LIGATION WITH 5-FLUORODEOXYRIBOSE (FDR)

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Table of Contents

General Information ......................................................................................................... 4

Compounds Preparation .................................................................................................. 5

4-Carboxy-2,2-dimethylthiazolidin-3-ium chloride (6) .................................................. 5
3-(tert-Butoxy carbonyl)-2,2-dimethylthiazolidine-4-carboxylic acid (4a) ................. 5
tert-Butyl-4-(methoxy(methyl) carbamoyl)-2,2-dimethylthiazolidine-3-carboxylate (8) . 6
tert-Butyl-4-formyl-2,2-dimethylthiazolidine-3-carboxylate (9) ................................. 7
(E)-tert-Butyl-4-(3-methoxy-3-oxoprop-1-en-1-yl)-2,2-dimethylthiazolidine-3-carboxylate (10) .... 8
tert-Butyl-4-(3-methoxy-3-oxopropyl)-2,2-dimethylthiazolidine-3-carboxylate (11) ...... 8
3-(tert-Butoxy carbonyl)-2,2-dimethyl thiazolidin-4-yl propanoic acid (4b) .................. 9
tert-Butyl 4-(3-hydroxypropyl)-2,2-dimethyl thiazolidine-3-carboxylate (12) ............. 9
tert-Butyl-4-(3(1,3-dioxoisoindolin-2-yl)propyl)-2,2-dimethylthiazolidine-3-carboxylate (13) ... 10
tert-Butyl-4-(3-aminopropyl)-2,2-dimethyl thiazolidine-3-carboxylate (4c) ............... 11
2-(3-Bromopropyl)isoindoline-1,3-dione (16a) ......................................................... 11
2-(3-(2-Nitro-1H-imidazol-1-yl)propyl)isoindoline-1,3-dione (17a) ......................... 12
3-(2-Nitro-1H-imidazol-1-yl)propan-1-amine (14a) ................................................... 13
2-(5-Bromopentyl)isoindoline-1,3-dione (16b) ............................................................ 13
2-(5-(2-Nitro-1H-imidazol-1-yl)pentyl)isoindoline-1,3-dione (17b) ......................... 14
5-(2-Nitro-1H-imidazol-1-yl)pentan-1-amine (14b) ..................................................... 15
2-(3-Azidopropyl)isoindoline-1,3-dione (18) ............................................................... 15
2-nitro-1-((prop-2-yn-1-yl)-1H-imidazole (19) ........................................................... 16
2-(3-(4-((2-Nitro-1H-imidazol-1-yl)methyl)-1H-1,2,3-triazol-1-yl)propyl) isoindoline-1,3-dione (20) ................................................................. 17
3-(4-(2-Nitro-1H-imidazol-1-yl)methyl)-1H-1,2,3-triazol-1-yl)propan-1-amine (14c) .... 17
2-(2-Nitro-1H-imidazol-1-yl)acetic acid (14d) .............................................................. 18
tert-Butyl-2,2-dimethyl-4-((3-(2-nitro-1H-imidazol-1-yl)propyl) carbamoyl) thiazolidine-3-carboxylate (25a) ................................................................. 19
tert-Butyl-2,2-dimethyl-4-((5-(2-nitro-1H-imidazol-1-yl)pentyl) carbamoyl) thiazolidine-3-carboxylate (25b) ................................................................. 20
tert-Butyl-2,2-dimethyl-4-((3-4-((2-nitro-1H-imidazol-1-yl)methyl)-1H-1,2,3-triazol-1-yl)propyl) carbamoyl) thiazolidine-3-carboxylate (25c) ................................................................. 21
tert-Butyl-2,2-dimethyl-4-((3-(2-nitro-1H-imidazol-1-yl)propyl) amino)-3-oxopropylthiazolidine-3-carboxylate (25d) ................................................................. 21
tert-Butyl-2,2-dimethyl-4-((3-(2-nitro-1H-imidazol-1-yl)acetamido)propyl) thiazolidine-3-carboxylate (25e) ................................................................. 22
Radiosynthesis via conjugation with $[^{18}\text{F}]\text{FDR}$ .......................................................... 37

5-Deoxy-5-[$^{18}\text{F}]\text{-fluoro-}\alpha,\beta,\delta\text{-ribose} ([^{18}\text{F}]\text{FDR}) ([^{18}\text{F}]\text{F}2) ........................................ 37

Synthesis of $[^{18}\text{F}]\text{F}1 \text{a via thiazolidine ring formation} ................................. 38

Table S1 .................................................................................................................. 38

References .............................................................................................................. 39

$^1\text{H}, ^{13}\text{C}, ^{18}\text{F}$ NMR spectra .................................................................................. 40
**General Information**

All reagents and solvents were of highest grade from commercial sources, unless otherwise specified. Reactions were monitored by thin-layer chromatography (TLC), unless otherwise noted. TLCs were performed on Merck silica gel glass plates (60 F254). Visualisation was accomplished by irradiation with a UV lamp and/or staining with a ceric ammonium molybdate or KMnO4 solution. Flash chromatography was performed using Silica gel (60 Å, particle size 40-63 μm) purchased from Merck.

$^1$H-NMR, $^{19}$F-NMR and $^{13}$C-NMR spectra were recorded on a Bruker Advance AVIII 400 spectrometer and calibrated using residual undeuterated solvent as internal reference. Chemical shifts (δ) are reported in parts per million (ppm) and coupling constants (J) are given in Hertz (Hz). The following abbreviations are used for spin multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet-doublet, dt = doublet-triplet, m = multiplet, br = broad. When necessary, resonances were assigned using two-dimensional experiments (COSY, TOCSY, HMBC and HSQC).

Mass Analyses (MS) were performed using Agilent 1200 HPLC system coupled to Agilent G6120 single quadrupole detector equipped with an electrospray ionization (ESI) source in direct infusion modality. ESI-MS spectra were recorded in positive mode, unless otherwise noted. RP-(reverse phase)-HPLC-MS analyses were performed with an Agilent 1200 HPLC system equipped with a DAD and an ESI-MS detector. HPLC semi-preparative purifications were performed using an Agilent 1260 HPLC system with reverse phase column as indicated in individual experiment. HPLC analyses of radioactive compounds were performed using a Shimadzu HPLC system equipped with a SPD-M20A Prominence DAD UV detector and NaI radio-detector (Berthold Technologies). Semi-prep HPLC purification of radioactive compounds were performed using a lead shielded Shimadzu semiprep HPLC system equipped with a SPD-M20A Prominence DAD UV detector and NaI radio-detector (Berthold Technologies). RadioTLC were performed using a Raytest miniGITA RadioTLC scanner. The dose calibrators used to measure doses were CAPINTEC CRC 15R and CAPINTEC CRC 15PET.
Compounds Preparation

4- Carboxy-2,2-dimethylthiazolidin-3-ium chloride (6)

To a solution of cysteine 5 (3.10 g, 25.6 mmol) in acetone (150 mL), a conc. HCl solution (0.5 mL) was added and the reaction mixture was heated to reflux for 6 h. Then the mixture was cooled to r.t., the white precipitate formed was filtered off and the filtrate was concentrated under reduced pressure. The crude solid obtained was treated with Et₂O at 0°C to give 6 in mixture with 5% of dimer 7 as white solid (3.22 g, 63.6%). NMR data of the product correspond to literature information [1].

mp 156-154 °C. ¹H NMR (D₂O, 400 MHz) δ (ppm) 4.61 (dd, J = 8.0 Hz, 1H), 3.64 (dd, J = 12.3 Hz, J = 8.0 Hz, 1H), 3.48 (dd, J = 12.3 Hz, J = 8.0 Hz, 1H). ¹³C NMR (D₂O, 100 MHz) δ (ppm) 163.7 (2C), 134.7 (2C), 129.0 (2C), 123.7 (2C), 76.2, 31.6, 29.4. MS (ESI m/z) calcd for C₆H₁₂NO₂S: 163.1 [M+H]+, 184.1[M+Na]+; found: 163.1 [M+H]+, 184.1 [M+Na]+.

3-(tert-Butoxycarbonyl)-2,2-dimethylthiazolidine-4-carboxylic acid (4a)

Di-tert-butylidicarbonate (2.78 g, 12.7 mmol) was added portionwise within 15 min to a solution of 6 (2.10 g, 10.6 mmol) in pyridine (10 mL) cooled to 0 °C, under nitrogen atmosphere. After 72 h under stirring at r.t., toluene (30 mL) was added and the mixture
was extracted with 2 M NaOH aq solution (3 x 12 mL). The aqueous extracts were combined and washed with toluene (3 x 10 mL) and hexane (15 mL) before being acidified to pH = 3 with citric acid at 0 °C. The acidic solution was extracted with CH₂Cl₂ (3 x 20 mL) and the collected organic phases were washed with brine (20 mL), dried over Na₂SO₄ and evaporated to dryness. Crystallization of the crude material from hexane gave 4a as pale yellow solid (2.87 g, 86.5%). NMR data of the product correspond to literature information [1].

m.p. 112-114 °C. ¹H NMR (CDCl₃, 400 MHz, 2 rotamers, 1:1 ratio) δ (ppm) 9.87 (br, 2H), 4.97 (br, 1H) and 4.83 (br, 1H), 3.49-3.08 (m, 4H), 1.87 (br, 6H) and 1.79 (br, 6H), 1.51 (br, 9H) and 1.43 (br, 9H). ¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 177.1 and 175.2, 153.1 and 151.7, 81.9 and 81.0, 71.9 and 70.4, 65.9 and 65.3, 30.7 and 30.1 and 29.7 (2C) 28.7 and 28.3 (4C) and 28.0. MS (ESI m/z) calcd for C₁₄H₁₂N₄O₅: 317.1 [M+H]+, 339.1 [M+Na]+; found: 317.1 [M+H]+, 339.0 [M+Na]+.

\[
\begin{align*}
\text{MeO} & \quad \text{N} \\
\text{Boc} & \quad \text{N} \\
\hline
8
\end{align*}
\]

**tert-Butyl-4-(methoxy(methyl)carbamoyl)-2,2-dimethylthiazolidine-3-carboxylate** (8)

HATU (3.5 g, 9.18 mmol) was added at 0 °C to a solution of 4a (2.00 g, 7.65 mmol) and DIPEA (1.56 mL, 9.18 mmol) in dry DCM (60 mL). After 1 h under stirring at r.t. a solution of N,O-dimethylhydroxylamine hydrochloride (895 mg, 9.18 mmol) and DIPEA (1.56 mL, 9.18 mmol) in DCM (20 mL) were added and the mixture was allowed to react at r.t. for 18 h. Then the mixture was concentrated under reduced pressure and purified by FC on silica gel, eluting with EtOAc/Hex (1/3), giving 8 as a wax (1.72 g, 73.9%). NMR data of the product correspond to literature information [1].

¹H NMR (CD₂OD, 400 MHz, 2 rotamers, 1:1 ratio) δ (ppm) 5.27-5.05 (m, 2H), 3.86-3.73 (m, 6H), 3.44 (dd, J = 12.4 Hz, 8.0 Hz, 2H) and 3.00 (dd, J = 12.4 Hz, 3.8 Hz, 3.8 Hz,
\[ \text{tert-Butyl-4-formyl-2,2-dimethylthiazolidine-3-carboxylate (9)} \]

LiAlH\(_4\) (25 mg, 0.66 mmol) was added portionwise within 15 min to a solution of 8 (200 mg, 0.66 mmol) in Et\(_2\)O (3 mL) cooled to 0 °C, under nitrogen atmosphere. After 30 min under stirring at 0 °C the mixture was diluted with Et\(_2\)O (5 mL) and a 2.1 M aq. NaHSO\(_4\) solution (1 mL) was added dropwise under nitrogen atmosphere. The mixture was stirred at 0 °C and the precipitate formed was filtered off through a celite pad. The filtrate was washed with 0.1 M aq. HCl solution (1 mL), 10% aq. NaHCO\(_3\) solution (1 mL) and brine, dried over Na\(_2\)SO\(_4\) and concentrated under vacuum to give 9 as an oil (142 mg, 87.8% yield). Compound 9 was used in the next step without any further purification. NMR data of the product correspond to literature information \[1\].

\(^1\)H NMR (CDCl\(_3\), 400 MHz, 2 rotamers, 1:1 ratio) δ (ppm) 9.57 (s, 2H), 4.70 and 4.53 (br, 1H), 3.29-2.92 (m, 1H), 1.95-1.65 (m, 12H), 1.60-1.33 (m, 18H). \(^{13}\)C NMR (CDCl\(_3\), 100 MHz) δ (ppm) 200.0, 153.3 and 151.6, 81.5 and 81.1, 71.5 and 70.7, 38.9, 30.8 and 30.3 and 29.6, 28.4 and 28.3.
(E)-tert-Butyl-4-(3-methoxy-3-oxoprop-1-en-1-yl)-2,2-dimethylthiazolidine-3-carboxylate (10)

Methyl (triphenylphosphoranylidene)acetate (681 mg, 2.04 mmol) was added at r.t. to a solution of 9 (250 mg, 1.02 mmol) in anhydrous THF (6 mL) and the reaction mixture was heated to reflux for 18 h. Then the mixture was concentrated under reduced pressure and purified by FC on silica gel, eluting with Hex/EtOAc (4/1), giving 10 as a clear oil (267 mg, 86.8%). \(^1\)H NMR (CDCl\(_3\), 400 MHz) \(\delta\) (ppm) 6.92 (dd, 15.6 Hz, 6.4 Hz, 1H), 5.90 (d, \(J = 15.6\) Hz, 1H), 4.92 (br, 1H), 3.71 (s, 3H), 3.28 (dd, \(J = 12.1\) Hz, 6.5 Hz, 1H), 2.65 (dd, \(J = 12.1\) Hz, 1.4 Hz, 1H), 1.78 (br, 3H), 1.74 (s, 3H), 1.41 (br, 9H). \(^1\)C NMR (CDCl\(_3\), 100 MHz) \(\delta\) (ppm) 166.7, 152.1, 146.8, 121.9, 80.6, 70.4, 64.1, 51.6, 32.3 (2C), 29.6, 28.4 (3C). MS (ESI m/z) calcd for C\(_{14}\)H\(_{23}\)NO\(_4\)S: 324.1 [M+Na]\(^+\), 340.1 [M+K]\(^+\); found: 324.0 [M+Na]\(^+\), 340.1 [M+K]\(^+\).

tert-Butyl-4-(3-methoxy-3-oxopropyl)-2,2-dimethylthiazolidine-3-carboxylate (11)

5% w/w Pd/C (10% wt., 12 mg) was added to a solution of 10 (230 mg, 0.76 mmol) in MeOH (7 mL) and the mixture was stirred at r.t. under hydrogen atmosphere. After 24 h the mixture was filtered through a celite pad washing with MeOH (3 x 5 mL) and the filtrate was concentrated under reduced pressure to give 11 as a clear oil (227 mg, 98.1%). \(^1\)H NMR (CDCl\(_3\), 400 MHz) \(\delta\) (ppm) 4.34 (br, 1H), 3.66 (s, 3H), 3.15 (dd, \(J = 12.1\) Hz, 6.0 Hz, 1H), 2.56 (d, \(J = 12.1\) Hz, 1H), 2.41-2.25 (m, 2H), 2.13-2.00 (m,
2H), 1.73 (s, 6H), 1.46 (s, 9H). $^{13}$C NMR (CDCl$_3$, 100 MHz) δ (ppm) 173.0, 152.1, 79.7, 69.6, 63.1, 31.3, 31.1, 30.0, 28.9 (2C), 28.1 (3C). MS (ESI m/z) calcd for C$_{14}$H$_{25}$NO$_4$S: 326.1 [M+Na]$^+$, 342.1 [M+K]$^+$; found: 326.1 [M+Na]$^+$, 342.0 [M+K]$^+$.

3-(3-(tert-Butoxycarbonyl)-2,2-dimethylthiazolidin-4-yl)propanoic acid (4b)

A 1 M aq. LiOH solution (1.64 mL, 1.64 mmol) was added at r.t. to a solution of 11 (200 mg, 0.66 mmol) in THF (1.7 mL). The reaction mixture was stirred for 18 h at r.t. and neutralized with a 1 M aq. HCl solution, then extracted with EtOAc (3 x 2 mL), dried and concentrated under reduced pressure to give 4b as an oil (186 mg, 97.4%). $^1$H NMR (CDCl$_3$, 400 MHz) δ (ppm) 9.07 (br, 1H), 4.35 (br, 1H), 3.12 (dd, J = 11.9 Hz, 5.9 Hz, 1H), 2.58 (d, J = 11.9 Hz, 1H), 2.39-2.19 (m, 2H), 2.12-1.93 (m, 2H), 1.72 (s, 6H), 1.45 (s, 9H). $^{13}$C NMR (CDCl$_3$, 100 MHz) δ (ppm) 178.9, 152.7, 80.7, 69.6, 63.7, 51.2, 32.3, 31.3, 29.6 (2C), 28.4 (3C) MS (ESI m/z) calcd for C$_{13}$H$_{23}$NO$_4$S: 290.2 [M+H]$^+$, 312.1 [M+Na]$^+$; found: 290.2 [M+H]$^+$, 312.1 [M+Na]$^+$.

tert-Butyl 4-(3-hydroxypropyl)-2,2-dimethylthiazolidine-3-carboxylate (12)

LiAlH$_4$ (28 mg, 0.73 mmol) was added at 0 °C to a solution of 11 (200 mg, 0.66 mmol) in dry THF (5 mL) under nitrogen atmosphere. After 1 h under stirring at 0 °C the mixture was diluted with THF (5 mL), then a 2.1 M aq. NaHSO$_4$ solution (1.2 mL) was added dropwise. The mixture was stirred at 0 °C and the precipitate formed was filtered off through a celite pad. The filtrate was washed with a 0.1 M aq. HCl solution (1.2
mL), 10% aq. NaHCO₃ solution (1.2 mL) and brine, then dried over Na₂SO₄ and concentrated under reduced pressure to give 12 as an oil (181 mg, 99.6% yield). Compound 12 was used in the next step without any further purification. 

**1H NMR** (CD₃Cl 400 MHz) δ (ppm) 4.37 (br, 1H), 3.68 (br, 2H), 3.16 (dd, J = 11.7 Hz, 6.0 Hz, 1H) and 2.57 (d, J = 11.7 Hz, 1H), 1.94-1.67 (m, 2H), 1.73 (s, 6H), 1.65-1.42 (m, 2H), 1.46 (s, 9H). 

**13C NMR** (CDCl₃, 100 MHz) δ (ppm) 152.7, 80.2, 69.3, 64.0, 62.0, 31.8 (2C), 30.3, 30.0 and 29.6, 28.4 (3C). 


**tert-Butyl-4-(3-(1,3-dioxoisoindolin-2-yl)propyl)-2,2-dimethylthiazolidine-3-carboxylate (13)**

Ph₃P (276 mg, 1.05 mmol) and phthalimide (154 mg, 1.05 mmol) were added to a solution of 12 (264 mg, 0.96 mmol) in THF (6 mL) under nitrogen atmosphere. After 30 min under stirring at r.t. the mixture was cooled to 0 °C and DIAD (207 µL, 1.05 mmol) was added dropwise. After further 16 h under stirring at r.t., the mixture was concentrated under reduced pressure and purified by FC on silica gel, eluting with Hex/EtOAc (from 100/0 to 95/5) giving 13 as a wax (365 mg, 94.1%). 

**1H NMR** (CDCl₃, 400 MHz, mixture of rotamers) δ (ppm) 7.75-7.67 (m, 2H), 7.65-7.56 (m, 2H), 4.19 (br, 1H), 3.67-3.50 (m, 2H), 3.04 (dd, J = 11.8 Hz, 6.0 Hz, 1H), 2.48 (d, J = 11.8 Hz, 1H) 1.82-1.54 (m, 4H), 1.62 (s, 6H), 1.32 (s, 9H). 

**13C NMR** (CDCl₃, 100 MHz) δ (ppm) 168.1 (2C), 152.2, 133.8 (2C), 132.0 (2C) 123.1 (2C), 79.9, 70.0, 63.8, 37.7, 31.4, 31.0, 29.3, 28.4 (3C), 26.0. 

**tert-Butyl-4-(3-aminopropyl)-2,2-dimethylthiazolidine-3-carboxylate (4c)**

Hydrazine monohydrate (124 μL, 2.52 mmol) was added to a solution of 13 (340 mg, 0.84 mmol) in EtOH (5 mL) and the reaction mixture was refluxed for 3 h. After cooling to 0 °C the resulting white precipitate was filtered and the filtrate was concentrated under reduced pressure. The residue was dissolved with Et₂O (5 mL) and the resulting white precipitate was filtered and the filtrate was concentrated under reduced pressure to afford 4c as a yellow oil (448 mg, 98.4%). \(^1\)H NMR (CDCl₃, 400 MHz)  δ (ppm) 4.16 (br, 1H), 3.00 (dd, J = 11.6 Hz, 6.1 Hz, 1H), 2.65-2.54 (m, 2H), 2.47 (d, J = 11.6 Hz, 1H), 1.73-1.49 (m, 4H), 1.60 (s, 6H), 1.44-1.41 (m, 2H), 1.33 (s, 9H). \(^{13}\)C NMR (CDCl₃, 100 MHz)  δ (ppm) 152.3, 79.8, 69.4, 64.1, 41.8, 31.3, 30.9, 30.2, 29.6 (2C), 28.4 (3C). MS (ESI m/z) calcd for C₁₃H₂₆N₂O₂S: 275.1 [M+H]⁺, 297.2 [M+Na]⁺, 303.2 [M+K]⁺; found: 275.2 [M+H]⁺, 297.2 [M+Na]⁺, 303.1 [M+K]⁺.

**2-(3-Bromopropyl)isoindoline-1,3-dione (16a)**

1,3-Dibromopropane 15a (1.39 mL, 13.6 mmol) and TEA (946 µL, 6.80 mmol) were added at r.t. to a solution of phthalimide (1.0 g, 6.80 mmol) in DMF (5 mL). The reaction mixture was stirred at r.t. for 48 h and then the precipitate formed was filtered off, then the filtrate was diluted with water (50 mL) and extracted with Et₂O (3 x 30 mL). The organic phases were combined, washed with brine (20 mL), dried over Na₂SO₄ and concentrated under vacuum. The residue was purified by FC on silica gel.
eluting with Hex/EtOAc from 95/5 to 70/30 to give \( \textbf{16a} \) as a white solid (1.28 g, 70.0%). NMR data of the product correspond to literature information \(^2\).

mp 71-73 °C. \(^1\)H NMR (CDCl\(_3\), 400 MHz) \( \delta \) (ppm) 7.87-7.79 (m, 2H), 7.74-7.67 (m, 2H), 3.82 (t, \( J = 6.8 \) Hz, 2H), 3.40 (t, \( J = 6.8 \) Hz, 2H), 2.25 (q, \( J = 6.8 \) Hz, 2H). \(^{13}\)C NMR (CDCl\(_3\), 100 MHz) \( \delta \) (ppm) 168.3 (2C), 134.1 (2C), 132.0 (2C), 123.3 (2C), 36.7, 31.6, 29.8. MS (ESI m/z) calcd for C\(_{11}\)H\(_{10}\)BrNO\(_2\): 267.9 [M+H]\(^+\), 269.9 [M+2+H]\(^+\), 289.9 [M+Na]\(^+\), 291.9 [M+2+Na]\(^+\); found: 268.0 [M+H]\(^+\), 270.0 [M+2+H]\(^+\), 290.0 [M+Na]\(^+\), 292.0 [M+2+Na]\(^+\).

\( \textbf{2-(3-(2-Nitro-1H-imidazol-1-yl)propyl)isoindoline-1,3-dione (17a)} \)

2-Nitroimidazole (136 mg, 1.20 mmol) and K\(_2\)CO\(_3\) (276 mg, 1.79 mmol) were added to a solution of \( \textbf{16a} \) (300 mg, 1.12 mmol) in dry DMF (3 mL) under N\(_2\) atmosphere. The reaction mixture was heated to 110 °C for 3 h under N\(_2\) atmosphere, then cooled to r.t., diluted with water (50 mL) and extracted with EtOAc (3 x 40 mL). The organic phases were combined, washed with brine and dried over Na\(_2\)SO\(_4\), filtered and evaporated under reduced pressure. The crude was treated with MeOH at 0 °C to give \( \textbf{17a} \) as a white solid (287 mg, 85.3%). NMR data of the product correspond to literature information \(^3\). M.p. 199-201 °C. \( \textbf{17a} \) was used in the next step without any further purification. \(^1\)H NMR (CDCl\(_3\), 400 MHz) \( \delta \) (ppm) 7.90-7.83 (m, 2H), 7.78-7.71 (m, 2H), 7.35 (d, \( J = 1.0 \) Hz, 1H), 7.15 (d, \( J = 1.0 \) Hz, 1H), 4.46 (t, \( J = 7.0 \) Hz, 2H), 3.82-3.72 (m, 2H), 2.33-2.21 (m, 2H). \(^{13}\)C NMR (CDCl\(_3\), 100 MHz) \( \delta \) (ppm) 168.4 (2C), 134.3 (2C), 131.8 (2C), 128.5, 126.3, 123.5 (2C), 47.7, 34.7, 29.8. MS (ESI m/z) calcd for C\(_{14}\)H\(_{12}\)N\(_4\)O\(_4\): 301.0 [M+H]\(^+\), 323.0 [M+Na]\(^+\), 339.0 [M+K]\(^+\); found: 301.1 [M+H]\(^+\), 323.1 [M+Na]\(^+\), 339.0 [M+K]\(^+\).
3-(2-Nitro-1H-imidazol-1-yl)propan-1-amine (14a)

Hydrazine monohydrate (700 μL, 13.99 mmol) was added to a solution of 17a (1.40 g, 4.66 mmol) in ethanol (40 mL) and the reaction mixture was heated to reflux for 3 h. After cooling to 0 °C the resulting white precipitate was filtered off and the filtrate was concentrated under reduced pressure to give a crude oil. This crude oil was dissolved in Et₂O (4 mL) and the resulting white precipitate was filtered and the filtrate was concentrated under vacuum to afford 14a as a yellow oil (710 mg, 88.8%). 14a was used in the next step without any further purification. NMR data of the product correspond to literature information [3].

\[ ^1H \text{ NMR (CDCl}_3, 400\text{MHz}) \delta (\text{ppm}) 7.15 (d, J = 1.0 \text{ Hz}, 1H), 7.13 (d, J = 1.0 \text{ Hz}, 1H), 4.54 (t, J = 7.0 \text{ Hz}, 2H), 2.76 (t, J = 6.6 \text{ Hz}, 2H), 2.02-1.92 (m, 2H), 1.42 (br, 2H). \]

\[ ^13C \text{ NMR (CDCl}_3, 100\text{MHz}) \delta (\text{ppm}) 128.3, 126.2, 47.7, 38.4, 33.5. \]

MS (ESI m/z) calcd for C₆H₁₀N₄O₂: 171.1 [M+H]⁺; found: 171.1 [M+H]⁺.

2-(5-Bromopentyl)isoindoline-1,3-dione (16b)

1,5-Dibromopentane 15b (1.85 mL, 13.6 mmol) and TEA (946 µL, 6.80 mmol) were added at r.t. to a solution of phthalimide (1.0 g, 6.80 mmol) in DMF (5 mL). The reaction mixture was stirred at r.t. for 48 h and then the precipitate formed was filtered off and the filtrate was diluted with water (50 mL) and extracted with Et₂O (3 x 30 mL). The organic phases were combined, washed with brine (20 mL), dried over Na₂SO₄ and concentrated under reduced pressure. The residue was purified by FC on
silica gel eluting with Hex/EtOAc from 95/5 to 85/15 to give 16b as a white solid (1.41 g, 70.1%). NMR data of the product correspond to literature information [2].

mp 84-86°C. $^1$H NMR (CDCl$_3$, 400 MHz) δ (ppm) 7.76-7.70 (m, 2H), 7.66-7.59 (m, 2H), 3.59 (t, $J = 7.2$ Hz, 2H), 3.30 (t, $J = 6.8$ Hz, 2H), 1.86-1.76 (m, 2H), 1.67-1.57 (m, 2H), 1.45-1.35 (m, 2H). $^{13}$C NMR (CDCl$_3$, 100 MHz) δ (ppm) 168.1 (2C), 133.8 (2C), 132.0 (2C), 123.0 (2C), 37.5, 33.3, 32.1, 27.6, 25.3. MS (ESI m/z) calcd for C$_{13}$H$_{14}$BrNO$_2$: 296.0 [M+H]$^+$, 298.0 [M+2+H]$^+$, 318.0 [M+Na]$^+$, 320.0 [M+2+Na]$^+$; found: 296.0 [M+H]$^+$, 298.0 [M+2+H]$^+$, 318.0 [M+Na]$^+$, 320.0 [M+2+Na]$^+$.

2-$\text{N}(2-$Nitro-$1\text{H}$-imidazol-1-$yl$)$pentyl$)$isoindoline-1,3-dione (17b)

2-Nitroimidazole (422 mg, 3.72 mmol) and K$_2$CO$_3$ (841 mg, 6.08 mmol) were added to a solution of 16b (1.00 g, 3.38 mmol) in dry DMF (11 mL) under N$_2$ atmosphere. The reaction mixture was heated to 110 °C for 3 h under N$_2$ atmosphere, then cooled to r.t., diluted with water (50 mL) and extracted with EtOAc (3 x 40 mL). The organic phases were combined, washed with brine (20 mL) and dried over Na$_2$SO$_4$, filtered and evaporated under reduced pressure to give 17b as an oil (715 mg, 64.4%). Compound 17b was used without any further purification. $^1$H NMR (CDCl$_3$, 400 MHz) δ (ppm) 7.86-7.82 (m, 2H), 7.75-7.70 (m, 2H), 7.11 (d, $J = 1.0$ Hz, 1H), 7.07 (d, $J = 1.0$ Hz, 1H), 4.40 (m, $J = 7.3$ Hz, 2H), 3.70 (t, $J = 7.0$ Hz, 2H), 3.87 (s, 2H), 1.97-1.87 (m, 2H), 1.79-1.69 (m, 2H), 1.45-1.35 (m, 2H). $^{13}$C NMR (CDCl$_3$, 100 MHz) δ (ppm) 168.4 (2C), 134.0 (2C), 132.0 (2C), 128.4, 125.8, 123.3 (2C), 50.1, 37.3, 29.9, 27.9, 23.6. MS (ESI m/z) calcd for C$_{16}$H$_{16}$N$_4$O$_4$: 329.1 [M+H]$^+$, 351.1 [M+Na]$^+$; found: 329.1 [M+H]$^+$, 351.1 [M+Na]$^+$. 

![image]
5-(2-Nitro-1H-imidazol-1-yl)pentan-1-amine (14b)

Hydrazine monohydrate (284 μL, 5.85 mmol) was added to a solution of 17b (640 mg, 1.95 mmol) in EtOH (15 mL) and the reaction mixture was heated to reflux for 3 h. After cooling to 0 °C the resulting white precipitate was filtered off and the filtrate was concentrated under reduced pressure to give a crude oil. This crude oil was dissolved with Et₂O (2 mL) and the resultant white precipitate was filtered off, then the filtrate was concentrated under reduced pressure to afford 14b as a yellow oil (357 mg, 92.3%). Compound 14b was used in the next step without any further purification.

NMR data of the product correspond to literature information [4].

\[ ^1H \text{NMR (CD}_3\text{OD, 400 MHz) } \delta \text{ (ppm) 7.43 (d, } J = 1.0 \text{ Hz, } 1\text{H}), 7.04 (d, } J = 1.0 \text{ Hz, } 1\text{H}), 4.37 (t, } J = 7.3 \text{ Hz, } 2\text{H}), 2.59 (t, } J = 7.1 \text{ Hz, } 2\text{H}), 1.84-1.71 \text{ (m, } 2\text{H}), 1.52-1.38 \text{ (m, } 2\text{H}) 1.36-1.22 \text{ (m, } 2\text{H}). \]

\[ ^13C \text{NMR (CD}_3\text{OD, 100 MHz) } \delta \text{ (ppm) 128.7, 128.5, 51.1, 42.0, 32.5, 31.2, 24.7. MS (ESI } m/z) \text{ calcd for C}_8\text{H}_14\text{N}_4\text{O}_2: 199.1 \text{ [M+H]}^+, 221.1 \text{ [M+Na]}^+; \text{ found: 199.1 [M+H]}^+, 221.1 \text{ [M+Na]}^+. \]

2-(3-Azidopropyl)isoindoline-1,3-dione (18)

Sodium azide (136 mg, 1.20 mmol) was added to a solution of 16a (490 mg, 1.83 mmol) in dry DMF (3 mL) and the mixture was heated to 100 °C for 18 h. Then the mixture was cooled to r.t., poured into a saturated aq. NH₄Cl solution (30 mL) and extracted with EtO₂ (3 x 30 mL). The organic phases were combined, washed with
brine and dried over Na$_2$SO$_4$, filtered and evaporated under reduced pressure to give 18 as a white solid (388 mg, 92.1%). Compound 18 was used in the next step without any further purification. NMR data of the product correspond to literature information.$^5$ mp 66-68 °C. $^1$H NMR (CDCl$_3$, 400 MHz) δ (ppm) 7.87-7.81 (m, 2H), 7.75-7.68 (m, 2H), 3.78 (t, $J$ = 6.8 Hz, 2H), 3.37 (t, $J$ = 6.8 Hz, 2H), 1.95 (p, $J$ = 6.8 Hz, 2H). $^{13}$C NMR (CDCl$_3$, 100 MHz) δ (ppm) 168.3 (2C), 134.1 (2C), 132.0 (2C), 123.3 (2C), 49.1, 35.4, 28.0. MS (ESI m/z) calc. for C$_{11}$H$_{10}$N$_4$O$_2$: 253.1 [M+Na]$^+$; found: 253.1 [M+Na]$^+$.

2-nitro-1-(prop-2-yn-1-yl)-1H-imidazole (19)

To a solution of 2-nitroimidazole (170 mg, 1.50 mmol) and K$_2$CO$_3$ (436 mg, 3.16 mmol) in acetone (2.5 mL), was added a solution of propargyl bromide (80% in toluene, 200 µl, 1.8 mmol). The reaction mixture was allowed to react at rt overnight under stirring. Then the reaction mixture was dilute with EtOAc (5mL) and filtered through a small pad of silica gel. Purification by FC on silica gel eluting with Hex/EtOAc (1/1) gave 19 as a brown oil (171 mg, 75.4%). NMR data of the product correspond to literature information.$^6$ $^1$H NMR (CDCl$_3$, 400MHz) δ (ppm) 7.43 (s, 1H), 7.19 (s, 1H), 5.24 (d, $J$ = 2.5 Hz 2H), 2.63 (t, $J$ = 2.5 Hz, 1H). $^{13}$C NMR (CDCl$_3$, 400MHz) δ (ppm) 128.4, 125.1, 76.7, 74.9, 39.9. MS (ESI m/z) calc. for C$_6$H$_5$N$_3$O$_2$: 152.0 [M+H]$^+$, 174.0 [M+Na]$^+$; found: 152.1 [M+H]$^+$, 174.1 [M+Na]$^+$. 

16
2-(3-(4-((2-Nitro-1H-imidazol-1-yl)methyl)-1H-1,2,3-triazol-1-yl)propyl)isoindoline-1,3-dione (20)

1-Propargyl-2-nitroimidazole 19 (263 mg, 1.74 mmol), CuSO$_4$ (27 mg, 0.17 mmol) and sodium ascorbate (69 mg, 0.35 mmol) were added to a solution of 18 (440 mg, 1.74 mmol) in $t$-BuOH/H$_2$O (1/1 v/v, 10 mL) under nitrogen atmosphere and the mixture was stirred at r.t. for 16 h. Then CHCl$_3$ (10 mL) was added to the mixture and the organic layer was separated, washed with water (3 mL), dried over Na$_2$SO$_4$, filtered and concentrated under reduced pressure. Purification by FC on silica gel, eluting with EtOAc/Hex (from 9/1 to 10/0) gave 20 as a yellow oil (521 mg, 78.5%). $^1$H NMR (CDCl$_3$, 400 MHz) δ (ppm) 7.90 (s, 1H), 7.87-7.83 (m, 2H), 7.76-7.72 (m, 2H), 7.35 (d, $J = 1.0$ Hz, 1H), 7.15 (d, $J = 1.0$ Hz, 1H), 5.70 (s, 1H), 4.40 (t, $J = 7.0$ Hz, 2H), 3.72 (t, $J = 6.6$ Hz, 2H), 2.40-2.29 (m, 2H). $^{13}$C NMR (CDCl$_3$, 100 MHz) δ(ppm) 168.2 (2C), 141.1, 134.2 (2C), 131.8 (2C), 128.5, 126.5, 124.1, 123.3 (2C), 48.0, 44.7, 34.8, 29.2. MS (ESI m/z) calcd for C$_{17}$H$_{15}$N$_5$O$_4$: 382.1 [M+H]$^+$, 404.1 [M+Na]$^+$, 420.1 [M+K]$^+$; 382.1 [M+H]$^+$, 404.1 [M+Na]$^+$, 420.1 [M+K]$^+$.

3-(4-((2-Nitro-1H-imidazol-1-yl)methyl)-1H-1,2,3-triazol-1-yl)propan-1-amine (14c)

Hydrazine monohydrate (93 μL, 1.89 mmol) was added to a solution of 20 (240 mg, 0.63 mmol) in EtOH (4 mL) and the reaction mixture was heated to reflux for 3 h.
After cooling to 0 °C the resulting white precipitate was filtered off and the filtrate was concentrated under reduced pressure to give 14c as a clear oil (136 mg, 86.2%). Compound 14c was used in the next step without any further purification. 1H NMR (CD3OD, 400 MHz) δ (ppm) 8.09 (s, 1H), 7.58 (d, J = 1.2 Hz, 1H), 7.14 (d, J = 1.2 Hz, 1H), 5.78 (s, 2H), 4.48 (t, J = 7.2 Hz, 2H), 2.65 (t, J = 7.1 Hz, 2H), 2.09-1.99 (m, 2H). 13C NMR (CD3OD, 100 MHz) δ (ppm) 141.8, 127.6, 127.1, 123.9, 47.8, 44.4, 38.0, 32.5. MS (ESI m/z) calcd for C9H13N7O2: 252.1 [M+H]+, 275.1 [M+Na]+; found: 252.1 [M+H]+, 275.1 [M+Na]+.

2-(2-Nitro-1H-imidazol-1-yl)acetic acid (14d)

2-Iodoethanol 21 (1.36 mL, 17.4 mmol) was added to a solution of 2,3-dihydropyran (7.95 mL, 8.70 mmol) and p-toluenesulfonic acid monohydrate (3.3 mg 0.02 mmol) in DCM cooled to 0 °C, under N2 atmosphere. The mixture was allowed to react at r.t. for 16 h and then was concentrated under reduced pressure. The brown oil obtained was dissolved in Et2O (40 mL) and washed with sat NaHCO3 aq solution (20 mL), H2O (20 mL) and brine (20 mL). The crude was purified by FC on silica gel eluting with Hex to give 2-(3-iodopropoxy)tetrahydro-2H-pyran (22) as a pale yellow oil (2.67 g, 56.8%). NMR data of the product correspond to literature information [3]. 1H NMR (CDCl3, 400 MHz) δ (ppm) 4.67 (t, J = 3.5 Hz, 1H), 4.01-3.84 (m, 2H), 4.01-3.84 (m, 1H), 3.78-3.67 (m, 1H), 3.56-3.47 (m, 2H), 3.34-3.23 (m, 2H), 1.90-1.77 (m, 1H), 1.76-1.67 (m, 1H), 1.66-1.47 (m, 1H). 13C NMR (CDCl3, 100 MHz) δ (ppm) 98.7, 77.2, 68.3, 62.3, 30.5, 25.4, 19.3, 3.5.

A mixture of 22 (2.5 g, 9.26 mmol), 2-nitroimidazole (1.05 g, 9.26 mmol) and K2CO3 (1.35 g, 9.37 mmol) in DMF (20 mL) was heated to 110 °C for 4 h. Then the mixture was cooled to r.t., poured into water (50 mL) and extracted with Et2O (3 x 40 mL).
The collected organic phases were washed with water (60 mL), brine (60 mL), dried over Na₂SO₄ and concentrated under reduced pressure to give 23 as an oil. The crude 23 was dissolved in MeOH (10 mL) and a 6M aq. HCl solution (1 mL) was added, then the mixture was stirred at r.t. for 16 h. The resulting mixture was concentrated under reduced pressure and the residue was dissolved in acetone (25 mL), then cooled to 0 °C. Jones’s reagent (prepared by dissolving 5.3 g of CrO₃ in 4.5 mL of concentrated H₂SO₄) was added dropwise until the orange colour persisted. After 12 h under stirring at r.t. propan-2-ol was added dropwise and a green precipitate was formed. The mixture was neutralized with BaCO₃ and then filtered through a celite pad. The filtrate was concentrate under reduced pressure by FC on silica gel, eluting with EtOAc/MeOH 97/3 to give 14d as a white solid (657 mg, 41.3%). NMR data of the product correspond to literature information [3]. M.p. 173-175 °C. ¹H NMR (CD₃OD, 400 MHz) δ (ppm) 7.48 (d, J = 1.0 Hz, 1H), 7.19 (d, J = 1.0 Hz, 1H), 5.26 (s, 1H). ¹³C NMR (CD₃OD, 100 MHz) δ (ppm) 168.5, 144.9, 127.6, 127.1, 50.4. MS (ESI m/z) calcd for C₁₅H₁₅N₃O₄: 172.0 [M+H]⁺, 194.0 [M+Na]⁺; found: 172.1 [M+H]⁺, 194.1 [M+Na]⁺.

![25a](image)

**tert-Butyl-2,2-dimethyl-4-((3-(2-nitro-1H-imidazol-1-yl)propyl)carbamoyl)thiazolidine-3-carboxylate (25a)**

DIPEA (156 μL, 0.92 mmol) and HATU (350 mg, 0.92 mmol) were added to a solution of 4a (200 mg, 0.77 mmol) in dry DCM (10 mL) at 0 °C and the mixture was allowed to react at r.t. for 1 h. Then 14a (260 mg, 1.53 mmol) dissolved in DCM (2 mL) was added to the mixture. After 16 h under stirring the mixture was washed with a 0.5 M aq. NaOH solution (3 x 6 mL) and then with a 0.1 M aq. HCl solution (3 x 6 mL), dried over Na₂SO₄ and concentrated under reduced pressure. Purification by FC on
silica gel, eluting with Hex/EtOAc (from 8/2 to 7/3), gave 25a as a yellow oil (229 mg, 72.3%). ¹H NMR (CDCl₃, 400 MHz, mixture of rotamers) δ (ppm) 7.32 (s, 1H), 7.08 (s, 1H), 6.55 (br, 1H), 4.72 (br, 1H), 3.42-3.11 (m, 4H), 1.82 (s, 3H), 1.73 (s, 3H), 1.42 (s, 9H). ¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 171.7, 153.3, 144.7, 128.4, 127.0, 81.8, 71.4, 67.5, 47.4, 36.0, 31.0, 29.3, 28.9, 28.4 (3C). MS (ESI m/z) calcd for C₁₇H₂₇N₅O₅S: 436.2 [M+Na]⁺, 452.0 [M+K]⁺; found: 436.1 [M+Na]⁺, 452.0 [M+K]⁺.

**tert-Butyl-2,2-dimethyl-4-((5-(2-nitro-1H-imidazol-1-yl)pentyl)carbamoyl)thiazolidine-3-carboxylate (25b)**

DIPEA (156 μL, 0.92 mmol) and HATU (350 mg, 0.92 mmol) were added to a solution of 4a (200 mg, 0.77 mmol) in dry DCM (10 mL) at 0 °C and the mixture was allowed to react at r.t. for 1 h. Then 14b (303 mg, 1.53 mmol) dissolved in DCM (5 mL) was added to the mixture. After 16 h under stirring the mixture was washed with a 0.5 M aq. NaOH solution (3 x 7 mL) and then with a 0.1 M aq. HCl solution (3 x 7 mL), dried over Na₂SO₄ and concentrated under reduced pressure. Purification by FC on silica gel, eluting with Hex/EtOAc (4/1), gave 25b as a yellow oil (260 mg, 77.1%). ¹H NMR (CDCl₃, 400 MHz, mixture of rotamers) δ (ppm) 7.06 (s, 1H), 6.97 (s, 1H), 6.29 (br, 1H), 4.58 (br, 1H), 4.28 (t, J = 7.3 Hz, 2H), 3.27-2.90 (m, 4H), 1.82-1.65 (m, 5H), 1.62 (s, 3H), 1.48-1.37 (m, 2H), 1.36-1.20 (s, 11H). ¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 171.0, 152.8, 144.6, 128.2, 126.2, 81.3, 71.4, 67.2, 50.0, 38.9, 30.5, 29.3, 29.0, 28.7, 28.2 (3C), 23.4. MS (ESI m/z) calcd for C₁₉H₂₃N₅O₅S: 442.2 [M+H]⁺, 464.2 [M+Na]⁺; found: 442.1 [M+H]⁺, 464.1 [M+Na]⁺.
tert-Butyl-2,2-dimethyl-4-((3-(4-((2-nitro-1H-imidazol-1-yl)methyl)-1H-1,2,3-triazol-1-yl)propyl)carbamoyl)thiazolidine-3-carboxylate (25c)

DIPEA (94 μL, 0.55 mmol) and HATU (209 mg, 0.55 mmol) were added to a solution of 4a (120 mg, 0.46 mmol) in dry DCM (5 mL) at 0 °C and the mixture was allowed to react at r.t. for 1 h. Then 14c (231 mg, 0.92 mmol) was dissolved in DCM (3 mL) and added to the mixture. After 18 h under stirring the mixture was washed with a 0.5 M aq. NaOH solution (3 x 2 mL) and then with a 0.1 M aq. HCl solution (3 x 2 mL), dried over Na₂SO₄ and concentrated under reduced pressure. Purification by FC on silica gel, eluting with EtOAc/MeOH (from 10/0 to 8/2), gave 25c as a yellow oil (152 mg, 66.6%). ¹H NMR (CDCl₃, 400 MHz, 2 rotamers) δ (ppm) 7.83 (s, 1H), 7.32 (s, 1H), 7.09 (s, 1H), 6.61 (s, 2H), 5.66 (s, 2H), 5.71 (s, 2H), 4.50-4.20 (m, 2H), 3.48-2.99 (m, 4H), 2.17-1.92 (m, 2H), 1.83 (s, 3H), 1.73 (s, 3H), 1.41 (s, 9H). ¹³C NMR (CDCl₃, 100 MHz) δ (ppm) 171.5, 162.5 153.1, 144.2, 141.0, 128.3, 126.3, 124.1, 81.4, 71.3, 67.4, 47.3, 44.7, 36.4, 30.1, 29.5, 28.8, 28.3 (3C). MS (ESI m/z) calcd for C₂₀H₃₀N₈O₅S: 517.2 [M+Na]⁺, 533.1 [M+K]⁺; found: 517.2 [M+Na]⁺, 533.0 [M+K]⁺.

tert-Butyl-2,2-dimethyl-4-((3-(2-nitro-1H-imidazol-1-yl)propyl)amino)-3-oxopropyl)thiazolidine-3-carboxylate (25d)
DIPEA (186 μL, 1.04 mmol) and HATU (350 mg, 0.76 mmol) were added to a solution of 4b (200 mg, 0.69 mmol) in dry THF (5 mL) at 0 °C and the mixture was allowed to react at r.t. for 1 h. Then 14a (235 mg, 1.53 mmol) dissolved in THF (2 mL) was added to the mixture. After 18 h under stirring the mixture was washed with a 0.5 M aq. NaOH solution (3 x 3 mL) and then with a 0.1 M aq. HCl solution (3 x 3 mL), dried over Na₂SO₄ and concentrated under reduced pressure. Purification by FC on silica gel, eluting with Hex/EtOAc (from 8/2 to 7/3), gave 25d as a yellow oil (196 mg, 64.3%). ¹H NMR (CD₃OD, 400 MHz, 2 rotamers) δ (ppm) 7.57 (s, 1H), 7.16 (s, 1H), 4.53 (t, J = 7.4 Hz, 1H), 4.33 (br, 1H), 3.31-4.19 (m, 4H), 2.72 (d, J = 12.0 Hz, 1H), 2.35-2.17 (m, 2H), 2.17-2.95 (m, 4H), 1.76 (s, 3H), 1.75 (s, 3H), 1.49 (s, 9H). ¹³C NMR (CD₃OD, 100 MHz) δ (ppm) 174.1, 152.7, 144.6, 127.2, 127.0, 80.3, 69.4, 64.0, 47.5, 35.9, 33.1, 30.6, 29.9, 29.4, 28.9, 28.5, 27.4 (3C). MS (ESI m/z) calcd for C₁₉H₃₁N₅O₅S: 442.2 [M+H]⁺, 464.2 [M+Na]⁺; found: 442.1 [M+H]⁺, 465.0 [M+Na]⁺.

tert-Butyl-2,2-dimethyl-4-(3-(2-nitro-1H-imidazol-1-yl)acetamido)propyl thiazolidine-3-carboxylate (25e)

DIPEA (383 μL, 2.25 mmol) and HATU (860 mg, 2.25 mmol) were added to a solution of 14d (350 mg, 2.05 mmol) in dry THF (7 mL) at 0 °C and the mixture was allowed to react at r.t. for 1 h. Then 4c (726 mg, 2.65 mmol) dissolved in THF (7 mL) was added to the mixture. After 16 h under stirring the mixture was washed with a 0.5 M aq. NaOH solution (3 x 7 mL) and then with a 0.1 M aq. HCl solution (3 x 7 mL), dried over Na₂SO₄ and concentrated under reduced pressure. Purification by FC on silica gel, eluting with Hex/EtOAc (from 7/3 to 1/2), gave 25e as a yellow oil (565 mg, 64.5%). ¹H NMR (CDCl₃, 400 MHz, mixture of rotamers) δ (ppm) 7.75 (br, 1H), 7.13 (d, J = 0.8 Hz, 1H), 7.07 (d, J = 0.8 Hz, 1H), 4.98 (s, 2H), 4.24 (br, 1H), 3.39-3.16 (m,
tert-Butyl-2,2-dimethyl-4-(3-(3-(2-nitro-1H-imidazol-1-yl)propyl)ureido)propyl thiazolidine-3-carboxylate (25f)

A solution of 4c (152 mg, 0.56 mmol) in DCM (2 mL) was added dropwise to a solution of CDI (90 mg, 0.56 mmol) in dry DCM (3 mL) at 0 °C under nitrogen atmosphere, then the mixture was allowed to react at r.t. for 1 h. After 16 h under stirrer, the mixture was added by syringe to a solution of 14a (226 mg, 1.33 mmol) in DCM (3 mL) under N₂ atmosphere. After 16 h under stirring the mixture was concentrated under reduced pressure. Purification by FC on silica gel, eluting with Hex/EtOAc (from 7/3 to 3/7 ), gave 25f as a yellow oil (148 mg, 56.7%). ¹H NMR (CDCl₃, 400 MHz, 2 rotamers) δ (ppm) 7.35 (br, 1H), 7.02 (br, 1H), 5.55 (br, 2H), 4.40 (t, J = 6.9 Hz, 2H), 4.19 (br, 1H), 3.24-2.94 (m, 5H), 2.49 (d, J = 11.8 Hz, 1H), 2.05-1.86 (m, 2H), 1.81-1.66 (m, 2H), 1.63 (s, 3H), 1.61 (s, 3H), 1.48-1.26 (m, 11H). ¹³C NMR (CDCl₃, 100 MHz, 2 rotamers) δ (ppm) 159.0, 152.7, 144.6, 128.2, 127.1, 80.3, 69.4, 64.0, 47.8, 39.8, 36.6, 31.6, 31.4, 30.6, 30.1, 29.6, 28.4 (3C), 27.3. MS (ESI m/z) calcd for C₂₀H₃₄N₅O₅S: 471.2 [M+H]⁺, 493.2 [M+Na]⁺; found: 471.2 [M+H]⁺, 493.2 [M+Na]⁺.
3-Mercapto-1-((3-(2-nitro-1H-imidazol-1-yl)propyl)amino)-1-oxopropan-2-aminium 2,2,2-trifluoroacetate (3a)

Compound 25a (80 mg, 0.19 mmol) was dissolved in a TFA:H₂O:MeOH 3:2:1 mixture and heated to 65 °C for 2 h. Solvents were then concentrated under reduced pressure at 60 °C and the residue was dissolved in ethanol and passed through a SiliaBond® carbonate pad to give crude 3a as trifluoroacetate salt (55.7 mg, 74.8%). Compound 3a was used in the next reaction without any further purification. ¹H NMR (CD₃OD, 400 MHz, in mixture with the dimer) δ (ppm) 7.62-7.54 (m, 1H), 7.20-7.15 (m, 1H), 4.60-4.42 (m, 2H), 4.31-4.19 (m, 1H), 3.52-3.33 (m, 2H), 3.24-3.09 (m, 2H), 2.19-2.00 (m, 2H). ¹³C NMR (CD₃OD, 100 MHz, in mixture with the dimer) δ (ppm) 167.4, 144.6, 127.4, 127.2, 51.7, 47.4, 37.8, 36.3, 29.7. MS (ESI m/z) calcld for C₉H₁₅N₅O₃S: 274.1 [M+H]+, 296.1 [M+Na]+; found: 274.0 [M+H]+, 296.0 [M+Na]+.

3-Mercapto-1-((5-(2-nitro-1H-imidazol-1-yl)pentyl)amino)-1-oxopropan-2-aminium 2,2,2-trifluoroacetate (3b)

Compound 25b (75 mg, 0.17 mmol) was dissolved in a TFA:H₂O:MeOH 3:2:1 mixture and heated to 65 °C for 2 h. Solvents were then concentrated under reduced pressure at 60 °C and the residue was dissolved in ethanol and passed through a SiliaBond® carbonate pad to give crude 3b as trifluoroacetate salt (54.7 mg, 77.4%). Compound 3b was used in the next reaction without any further purification. ¹H NMR (CD₃OD,
400 MHz, in mixture with the dimer) δ (ppm) 7.56-7.49 (m, 1H), 7.20-7.12 (m, 1H), 4.57-4.42 (m, 2H), 4.36-4.18 (m, 1H), 3.43-2.87 (m, 4 H), 1.97-1.81 (m, 2H), 1.72-1.49 (m, 2H) 1.48-1.27 (m, 2H). 13C NMR (CD3OD, 100 MHz, in mixture with the dimer) δ (ppm) 167.1, 144.6, 127.2, 127.1, 54.8 51.8, 49.7, 39.1, 29.6, 28.2, 23.2. MS (ESI m/z) calcd for C11H19N5O3S: 302.1 [M+H]^+, 324.1 [M+Na]^+; found: 302.1 [M+H]^+, 324.1 [M+Na]^+.

\[ \text{3-Mercapto-1-} \left((3-(4-((2-nitro-1H-imidazol-1-yl)methyl)-1H-1,2,3-triazol-1-yl)propyl)amino)-1-oxopropan-2-aminium 2,2,2-trifluoroacetate (3c) } \]

Compound 25c (93 mg, 0.20 mmol) was dissolved in a TFA:H2O:MeOH 3:2:1 mixture and heated to 65 °C for 2 h. Solvents were then concentrated under reduced pressure at 60 °C to give crude 3c as n-trifluoroacetate salt (60.7 mg). Compound 3c was used in the next reaction without any further purification. 1H NMR (D2O, 400 MHz, in mixture with the corresponding dimer) δ (ppm) 7.84 (br, 1H), 7.32 (b, 1H), 6.95 (b, 1H), 5.50 (b, 2H), 4.21-4.02 (m, 2H), 3.88-3.86 (m, 1H), 3.16-2.86 (m, 1H), 2.84-2.69 (m, 1H), 1.99-1.68 (m, 2H). 13C NMR (D2O, 100 MHz, in mixture with the corresponding dimer) δ (ppm) 166.1, 141.3, 127.8, 124.8 (3C), 54.3, 51.8, 47.8, 44.2, 36.3, 28.5. MS (ESI m/z) calcd for C12H18N8O3S: 355.1 [M+H]^+, 377.1 [M+Na]^+; found: 355.1 [M+H]^+, 377.1 [M+Na]^+. 

25
1-Mercapto-5-((3-(2-nitro-1H-imidazol-1-yl)propyl)amino)-5-oxopentan-2-aminium 2,2,2-trifluoroacetate (3d)

Compound 25d (69 mg, 0.16 mmol) was dissolved in a TFA:H₂O:MeOH 3:2:1 mixture and heated to 65 °C for 4 h. Solvents were then concentrated under reduced pressure at 60 °C and the residue was dissolved in ethanol and passed through a SiliaBond® carbonate pad to give crude 3d as trifluoroacetate salt (20.5 mg, 30.8%). Compound 3d was used in the next reaction without any further purification. ¹H NMR (CD₃OD, 400 MHz, in mixture with the corresponding dimer) δ (ppm) 7.55 (d, J = 0.9, 1H), 7.17 (d, J = 0.9, 1H), 4.58-4.47 (m, 2H), 4.18-3.97 (m, 1H), 3.71-3.09 (m, 2H), 2.98-2.86 (m, 1H), 2.80-2.69 (m, 2H), 2.42-2.24 (m, 2H), 2.13-2.00 (m, 2H), 2.00-1.83 (m, 2H). ¹³C NMR (CD₃OD, 100 MHz, in mixture with the corresponding dimer) δ (ppm) 179.5, 144.7, 127.3, 127.0, 53.8, 47.4, 44.1, 35.9, 29.6, 29.4, 25.5. MS (ESI m/z) calcd for C₁₁H₁₉N₅O₃S: 302.1 [M+H]⁺, 324.1 [M+Na]⁺, 340.1 [M+K]⁺; found: 302.1 [M+H]⁺, 324.0 [M+Na]⁺, 340.0 [M+K]⁺.

1-Mercapto-5-(2-(2-nitro-1H-imidazol-1-yl)acetamido)pentan-2-aminium 2,2,2-trifluoroacetate (3e)

Compound 25e (86 mg, 0.20 mmol) was dissolved in a TFA:H₂O:MeOH 3:2:1 mixture and heated to 65 °C for 3 h. Solvents were then concentrated under reduced pressure at 60 °C and the residue was dissolved in ethanol and passed through a SiliaBond®
carbonate pad to give crude 3e as trifluoroacetate salt (54.2 mg, 67.1%). Compound 3e was used in the next reaction without any further purification. $^1$H NMR (CD$_3$OD, 400 MHz, in mixture with the dimer) $\delta$ (ppm) 7.48 (br, 1H), 7.19 (br, 1H), 5.18 (s, 1H), 3.31-3.16 (m, 2H), 3.10-3.04 (m, 1H), 2.98-2.87 (m, 1H), 2.68-2.54 (m, 1H), 1.90-1.73 (m, 1H), 1.76-1.46 (m, 4H). $^{13}$C NMR (CD$_3$OD, 100 MHz, in mixture with the dimer) $\delta$ (ppm) 166.6, 145.0, 128.1, 127.0, 51.5, 39.1, 32.7, 29.4, 25.5. MS (ESI m/z) calcd for C$_{10}$H$_{17}$N$_5$O$_3$S: 288.1 [M+H]$^+$, 310.1 [M+Na]$^+$, 326.1 [M+K]$^+$; found: 288.1 [M+H]$^+$, 310.1 [M+Na]$^+$, 326.1 [M+K]$^+$.

\[ \text{O}_2\text{N} \]
\[ \text{N} \]
\[ \text{N} \]
\[ \text{O} \]
\[ \text{NH} \]
\[ \text{NH} \]
\[ \text{SH} \]
\[ \text{CH}_3^+ \text{CF}_3\text{COO}^- \]

1-Mercapto-5-(3-(2-nitro-1H-imidazol-1-yl)propyl)ureido)pentan-2-aminium 2,2,2-trifluoroacetate (3f)

Compound 25f (73 mg, 0.15 mmol) was dissolved in a TFA:H$_2$O:MeOH 3:2:1 mixture and heated to 65 °C for 4 h. Solvents were then concentrated under reduced pressure at 60 °C and the residue was dissolved in ethanol and passed through a SiliaBond$^\circledR$ carbonate pad to give crude 3f as trifluoroacetate salt (54.0 mg, 78.3%). Compound 3f was used in the next reaction without any further purification. $^1$H NMR (CD$_3$OD, 400 MHz, in mixture with the corresponding dimer) $\delta$ (ppm) 7.55 (d, $J = 1.1$ Hz, 1H), 7.16 (d, $J = 1.1$ Hz, 1H), 4.52 (t, $J = 7.1$ Hz, 2H), 3.26-3.10 (m, 4H), 3.06 (br, 1H), 2.98-2.84 (m, 1H), 2.69-2.58 (m, 1H), 2.10-1.98 (m, 2H), 1.67-1.52 (m, 4H). $^{13}$C NMR (CD$_3$OD, 400 MHz, in mixture with the corresponding dimer) $\delta$ (ppm) 159.8, 144.7, 127.3, 127.1, 49.6, 47.6, 46.6, 39.6, 36.5, 32.9, 30.9, 26.5. MS (ESI m/z) calcd for C$_{12}$H$_{22}$N$_6$O$_3$S: 331.1 [M+H]$^+$, 353.1 [M+Na]$^+$; found: 331.1 [M+H]$^+$, 353.1 [M+Na]$^+$. 

27
2-((1R,2R,3S)-4-Fluoro-1,2,3-trihydroxybutyl)-4-((3-(2-nitro-1H-imidazol-1-yl)propyl)carbamoyl)thiazolidin-3-ium 2,2,2-trifluoroacetate (1a)

[^1F]FDR ([^19F]2) (5 mg, 0.033 mmol) was added to a solution of 3a (32.0 mg, 0.083 mmol) and DTT (12.8 mg, 0.083 mmol) in 1 M sodium acetate buffer solution (pH = 4.5) and the mixture was allowed to react at 30 °C for 20 min. Purification by RP-HPLC (Column: Phenomenex Luna C18 250 × 10.00 mm, 5µm; mobile phase: A (H₂O + 0.05% TFA), B (ACN + 0.05% TFA); gradient: from 5% B to 6% B in 15 min; flow: 5 mL min⁻¹; tR: 12.5 min) gave 1a as trifluoroacetate salt (10.6 mg, 61.3 %). NMR analyses were performed after treatment of 1a with SiliaBond® carbonate (10w/w) in EtOH, under gentle stirring for 1 h in order to freebase the trifluoroacetate salt. ¹H NMR (CD₂OD, 400 MHz, 4 diastereoisomers – two major isomers in ~3/2 ratio were identified) δ (ppm) first isomer: 7.55 (d, J = 1.2 Hz, 1H), 7.16 (d, J = 1.2 Hz, 1H), 4.89-4.83 (m, 1H), 4.62-4.42 (m, 4H), 4.25 (dd, J = 7.0 Hz, 6.8 Hz, 1H), 4.09-4.04 (m, 1H), 3.91 (dd, J = 7.4 Hz, 4.6 Hz, 1H), 3.66 (dd, J = 7.4 Hz, 5.8 Hz, 1H), 3.39-3.23 (m, 3H), 3.02-2.91 (m, 1H), 2.16-2.05 (m, 2H); second isomer: 7.57 (d, J = 1.2 Hz, 1H), 7.17 (d, J = 1.2 Hz, 1H), 4.92 (d, J = 2.6 Hz, 1H), 4.67 (dd, J = 9.8 Hz, 3.0 Hz, 1H), 4.63-4.42 (m, 3H), 4.25 (dd, J = 7.0 Hz, 6.8 Hz, 1H), 4.04-3.95 (m, 1H), 3.85-3.75 (m, 2H), 3.39-3.14 (m, 3H), 3.02-2.91 (m, 1H), 2.16-2.05 (m, 2H). ¹³C NMR (CD₂OD, 100 MHz, 4 diastereoisomers – two major isomers in ~3/2 ratio were identified) δ (ppm) first isomer: 172.5, 144.7, 127.2, 127.1, 84.1 (d, J_CF = 167 Hz), 73.6 (d, J_CF = 7 Hz), 72.3, 72.1, 71.8 (d, J_CF = 18 Hz), 71.4, 65.8, 35.8, 34.9, 30.0; second isomer: 172.4, 144.7, 127.2, 127.1, 84.3 (d, J_CF = 167 Hz), 73.6 (d, J_CF = 7 Hz), 72.3, 72.0, 71.9, 71.9 (d, J_CF = 18 Hz), 70.2, 66.2, 36.6, 34.9. ¹⁹F NMR (376 MHz, CD₂OD) δ (ppm) first isomer: -233.0 (dt, J = 48.0 Hz, J = 22.7 Hz), second isomer: -233.6 (dt, J = 48.0
Hz, $J_2 = 22.3$ Hz) MS (ESI m/z) calcd for: C$_{14}$H$_{22}$FN$_5$O$_6$S: 408.1 [M+H]$^+$, 430.1 [M+Na]$^+$; found: 408.0 [M+H]$^+$, 430.0 [M+Na]$^+$.

4-((1S,2S,3S)-4-Fluoro-1,2,3-trihydroxybutyl)-2-((5-(2-nitro-1H-imidazol-1-yl)pentyl)carbamoyl)thiazolidin-3-ium 2,2,2-trifluoroacetate (1b)

$[^{19}$F]$^2$FDR ($[^{19}$F]$^2$F2) (5 mg, 0.033 mmol) was added to a solution of 3b (34.3 mg, 0.083 mmol) and DTT (12.8 mg, 0.083 mmol) in 1 M sodium acetate buffer solution (pH = 4.5) and the mixture was allowed to react at 30 °C for 20 min. Purification by RP-HPLC (Column: Phenomenex Luna C18 250 × 10.00 mm, 5µm; mobile phase: A (H$_2$O + 0.05% TFA), B (ACN + 0.05% TFA); isocratic 7% B from 0 to 10 min, then gradient: from 7% B to 11% B in 21 min; flow: 5 mL min$^{-1}$; $t_R$: 27.3 min, 28.4 min) gave 1b as trifluoroacetate salt (12.2 mg, 67.9%). MS (ESI m/z) calcd for: C$_{16}$H$_{26}$FN$_5$O$_6$S: 436.1 [M+H]$^+$, 458.1 [M+Na]$^+$; found: 436.0 [M+H]$^+$, 458.1 [M+Na]$^+$.

2-((1R,2R,3S)-4-Fluoro-1,2,3-trihydroxybutyl)-4-((3-(4-((2-nitro-1H-imidazol-1-yl)methyl)-1H-1,2,3-triazol-1-yl)propyl)carbamoyl)thiazolidin-3-ium 2,2,2-trifluoroacetate (1c)
[\textsuperscript{19}F]FDR ([\textsuperscript{19}F]2) (5 mg, 0.033 mmol) was added to a solution of 3c (38.6 mg, 0.083 mmol) and DTT (12.8 mg, 0.083 mmol) in 1 M sodium acetate buffer solution (pH = 4.5), and the mixture was allowed to react at 30 °C for 20 min. RP-HPLC analysis: (Column: Phenomenex Luna C18 250 × 10.00 mm, 5µm; mobile phase: A (H\textsubscript{2}O + 0.1% TFA), B (ACN + 0.1% TFA); 1\textsuperscript{st} isocratic: 6% B from 0 min to 20 min, then gradient: from 6% B to 10% B from 20 min to 23 min and 2\textsuperscript{nd} isocratic: 10% B from 23 min to 28 min flow: 5 mL min\textsuperscript{-1}; t\textsubscript{R}: 23.3 min).

\[ \text{2-((1R,2R,3S)-4-Fluoro-1,2,3-trihydroxybutyl)-4-((3-((2-nitro-1H-imidazol-1-yl)propyl)amino)-3-oxopropyl)thiazolidin-3-ium 2,2,2-trifluoroacetate (1d)} \]

[\textsuperscript{19}F]FDR ([\textsuperscript{19}F]2) (5 mg, 0.033 mmol) was added to a solution of 3d (34.3 mg, 0.083 mmol) and DTT (12.8 mg, 0.083 mmol) in 1 M sodium acetate buffer solution (pH = 4.5) and the mixture was allowed to react at 30 °C for 20 min. Purification by RP-HPLC (Column: Phenomenex Luna C18 250 × 10.00 mm, 5µm; mobile phase: A (H\textsubscript{2}O + 0.05% TFA), B (ACN + 0.05% TFA); 1\textsuperscript{st} isocratic: 6% B from 0 min to 15 min, then gradient: from 7% B to 10% B from 15 min to 18 min and 2\textsuperscript{nd} isocratic: 10% B for 4 min; flow: 5 mL min\textsuperscript{-1}; t\textsubscript{R}: 22.4 – 23.4 min) gave 1d as trifluoroacetate salt (2.0 mg, 11.2%). MS (ESI m/z) calcd for: C\textsubscript{16}H\textsubscript{26}FN\textsubscript{5}O\textsubscript{6}S: 436.1 [M+H]\textsuperscript{+}, 458.1 [M+Na]\textsuperscript{+}; found: 436.2 [M+H]\textsuperscript{+}, 458.2 [M+Na]\textsuperscript{+}. 

\[ 1d \]
2-((1R,2R,3S)-4-Fluoro-1,2,3-trihydroxybutyl)-4-(3-(2-(2-nitro-1H-imidazol-1-yl)acetamido)propyl)thiazolidin-3-ium 2,2,2-trifluoroacetate (1e)

[^19]F]FDR ([^19]F]2) (5 mg, 0.033 mmol) was added to a solution of 3e (38.7 mg, 0.083 mmol) and DTT (12.8 mg, 0.083 mmol) in 1 M sodium acetate buffer solution (pH = 4.5) and the mixture was allowed to react at 30 °C for 20 min. Purification by RP-HPLC (Column: Phenomenex Luna C18 250 × 10.00 mm, 5µm; mobile phase: A (H2O + 0.05% TFA), B (ACN + 0.05% TFA); isocratic: 4% B for 18 min, then gradient from 4% B to 10% B in 4 min; flow: 5 mL min⁻¹; tR: 15.6 – 18.4 min) gave 1e as trifluoroacetate salt (5.7 mg, 31.8%). MS (ESI m/z) calcd for: C15H24FN5O6S: 422.1 [M+H]^+, 444.1 [M+Na]^+; found: 422.1 [M+H]^+, 444.1 [M+Na]^+.

2-((1R,2R,3S)-4-Fluoro-1,2,3-trihydroxybutyl)-4-(3-(3-(2-nitro-1H-imidazol-1-yl)ureido)propyl)thiazolidin-3-ium 2,2,2-trifluoroacetate (1f)

[^19]F]FDR ([^19]F]2) (5 mg, 0.033 mmol) was added to a solution of 3f (36.7 mg, 0.083 mmol) and DTT (12.8 mg, 0.083 mmol) in 1 M sodium acetate buffer solution (pH = 4.5) and the mixture was allowed to react at 30 °C for 20 min. Purification by RP-HPLC (Column: Phenomenex Luna C18 250 × 10.00 mm, 5µm; mobile phase: A (H2O + 0.05% TFA), B (ACN + 0.05% TFA); 1st isocratic: 5% B from 0 min to 10 min, then gradient: from 5% B to 8% B from 10 min to 20 min and 2nd isocratic: 8% B for 10
min; flow: 5 mL min⁻¹; tᵣ: 27.7 – 29.4 min) gave 3f as trifluoroacetate salt (8.0 mg, 42.3%). MS (ESI m/z) calcd for: C₁₇H₂₀FN₆O₆S: 465.1 [M+H]⁺, 487.1 [M+Na]⁺; found: 465.2 [M+H]⁺, 487.2 [M+Na]⁺.
Competitive thiazolidine formation experiments between L-ribose 26 and $[^{19}\text{F}]2$

2.5 eq of 1,2-aminothiol derivatives 3a-f and 2.5 eq of DTT were mixed with 1 eq of $[^{19}\text{F}]$FDR $[^{19}\text{F}]2$ and 10 eq of L-ribose 26 using 1 M acetate buffer at pH 4.5 as reaction medium. The mixture was stirred for 20 min at 30 °C.

Reaction mixtures were purified by RP-HPLC using the conditions optimised for the synthesis of derivatives 1a-f reported above.
RP-HPLC profiles 1a vs 27a

RP-HPLC profiles 1b vs 27b
RP-HPLC profiles 1c vs 27c

[Diagram of HPLC profiles showing compounds 1c and 27c with respective retention times and by-products]

RP-HPLC profiles 1d vs 27d

[Diagram of HPLC profiles showing compounds 1d and 27d with respective retention times]
RP-HPLC profiles 1e vs 27e

RP-HPLC profiles 1f vs 27f
Radiosynthesis via conjugation with $[^{18}\text{F}]\text{FDR}$

5-Deoxy-5-$[^{18}\text{F}]$-fluoro-$\alpha$/$\beta$-$D$-ribose ($[^{18}\text{F}]\text{FDR}$) ($[^{18}\text{F}]2$)

The automated radiosynthesis of $[^{18}\text{F}]\text{FDR}$ ($[^{18}\text{F}]2$) was accomplished and optimised using an Eckert & Ziegler Eurotope Modular-Lab. After the end of bombardment, $[^{18}\text{F}]$fluoride dissolved in heavy water ($[^{18}\text{O}]\text{H}_2\text{O}$) was driven by a flow of helium gas to the synthesis module contained in a lead shielded hot cell. Subsequently a $[^{18}\text{F}]$fluoride solution passing through a CHROMAFIX anion exchange cartridge (Macherey Nagel, Germany) was retained by and the heavy water was collected in a proper vial. Then $[^{18}\text{F}]$fluoride was eluted into the reaction vessel with $\text{K}_2\text{CO}_3$ (0.5 mL of a 6 mg/mL water solution, 21.7 µmol) and a solution of Kriptofix 2.2.2 (16.2 mg, 43.0 µmol) in dry ACN was added. The azotropic mixture was evaporated heating to 90 °C using a stream of helium to form the dried complex [K/$\text{K}_{222}^{18}\text{F}$] (the drying process was performed twice with 1 mL of ACN). Precursor A dissolved in 1 mL of ACN was added and the reaction mixture was heated at 100 °C for 20 min. ACN was removed with a stream of helium, and the fluorinated intermediate compound B formed was hydrolysed with 1 M HCl (0.9 mL) heating to 100 °C for 10 min to give $[^{18}\text{F}]\text{FDR}$ ($[^{18}\text{F}]2$). After cooling, the solution was transferred onto a CHROMABOND IV purification cartridge (Macherey Nagel, Germany) and the cartridge was washed with water (3 mL). The $[^{18}\text{F}]\text{FDR}$ ($[^{18}\text{F}]2$) was obtained from a further elution of the cartridge with sterile water (10 mL) and collected into a vial placed in a second lead shielded hot cell. The radiochemical purity of ($[^{18}\text{F}]2$) was > 90%, estimated by Radio TLC (RAYTEST mini GITA, Raytest Isotopenmessgeraete GmbH, Germany; eluent eluent: ACN:H$_2$O 95:5) and Radio HPLC analysis (Column: Phenomenex Luna C18 250 × 4.6 mm, 5µm; mobile phase: A (H$_2$O), B (ACN); gradient 3% B for 4 min and then from 3% to 60% in 10 min; flow: 1 mL min$^{-1}$; $t_R$:}
4.0 min). The radiochemical yield for ([\(^{18}\text{F}\)]^2) was 38.3\% ± 7.0 decay corrected (the value was obtained on average of seven production runs). The bio-conjugation reactions via thiazolidine bond formation were not affected by the presence of \([^{18}\text{F}]\)fluoride, which was completely removed by RP-HPLC during the radiotracers purification.

![Chemical Structure](image)

**Synthesis of [\(^{18}\text{F}\)]1a via thiazolidine ring formation**

A solution of sodium acetate buffer (6 M, pH = 4.5) was added to a solution of 3a (2.5 mg, 6.4 \(\mu\)mol), DTT (1 mg, 6.4 \(\mu\)mol) and \([^{18}\text{F}]\)FDR ([\(^{18}\text{F}\)]^2) (2.5-10 MBq) in 0.5-1.0 mL of H\(_2\)O to form a 70\% v/v sodium acetate buffer solution (final concentration 4.2 M). After ~20 min the mixture was purified by RP-HPLC (Column: Phenomenex Luna C18 250 \(\times\) 10.00 mm, 5\(\mu\)m) using the conditions optimised in cold – for the purification of \([^{19}\text{F}]1a\) – to give \([^{18}\text{F}]1a\) in 29.2\% RYC (decay corrected). Identity of the products was confirmed by superimposition of the semi-prep RP-HPLC Radio-chromatogram of \([^{18}\text{F}]1a\) with the UV-chromatogram of the cold reference \([^{19}\text{F}]1a\) acquired before the purification of the radiotracer by using the same RP-HPLC gradient mobile phase.

**Table S1**

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<th>Conditions</th>
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*Decay corrected RCY

References

$^1$H, $^{13}$C, $^{19}$F NMR spectra
$^1$H NMR CDCl$_3$ (400 MHz)
$^{13}$C NMR CDCl$_3$ (100 MHz)
$^{13}$C NMR CDCl$_3$ (100 MHz)
\(^1\)H NMR CDCl\(_3\) (400 MHz)
$^{13}$C NMR CDCl$_3$ (100 MHz)
$^1$H NMR CDCl₃ (400 MHz)
$^{13}$C NMR CDCl$_3$ (100 MHz)
$^1$H NMR CDCl$_3$ (400 MHz)
$^{13}$C NMR CDCl$_3$ (100 MHz)
$^1$H NMR CDCl$_3$ (400 MHz)

![NMR Spectrum](image)

- ppm values: 10.68, 9.51, 0.95, 1.84, 1.01, 0.91, 0.91, 1.01, 1.84, 0.95, 9.51, 10.68
$^{13}$C NMR CDCl$_3$ (100 MHz)
$^1$H NMR CDCl$_3$ (400 MHz)
$^{13}$C NMR CDCl$_3$ (100 MHz)
$^1$H NMR CD$_3$OD (400 MHz)
$^{13}$C NMR CD$_3$OD (100 MHz)

H$_2$N$\begin{array}{c}\text{NO}_2 \\
\text{N}
\end{array}$

$^{14b}$

- 24.69 ppm
- 31.19 ppm
- 32.54 ppm
- 42.03 ppm
- 51.08 ppm
- 128.47 ppm
- 128.68 ppm
$^1$H NMR CDCl$_3$ (400 MHz)
$^{13}$C NMR CDCl$_3$ (100 MHz)
$^1$H NMR CD$_3$OD (400 MHz)
$^{13}$C NMR CD$_3$OD (100 MHz)
$^1$H NMR CDCl$_3$ (400 MHz)
$^{13}$C NMR CDCl$_3$ (400 MHz)
$^1$H NMR CDCl$_3$ (400 MHz)
$^{13}$C NMR CDCl$_3$ (400 MHz)

![Chemical Structure](image)

25b
$^1\text{H NMR CDCl}_3 (400 \text{ MHz})$
$^{13}$C NMR CDCl$_3$ (100 MHz)

![NMR spectrum image]
$^1$H NMR CD$_3$OD (400 MHz)

![NMR Spectrum]

- 13.78 ppm
- 8.92 ppm
- 5.43 ppm
- 2.75 ppm
- 1.39 ppm
- 4.41 ppm
- 1.39 ppm
- 2.15 ppm
- 1.03 ppm
- 1.00 ppm
$^{13}$C NMR CD$_3$OD (100 MHz)
$^1$H NMR CDCl$_3$ (400 MHz)
$^{13}$C NMR CDCl$_3$ (100 MHz)
$^1$H NMR CDCl$_3$ (400 MHz)
$^{13}$C NMR CDCl$_3$ (100 MHz)
$^1$H NMR CDCl$_3$ (400 MHz)

\[ \text{Diagram of molecule} \]
$^{13}$C NMR CDCl$_3$ (100 MHz)
$^{18}$F NMR CDCl$_3$ (376 MHz)