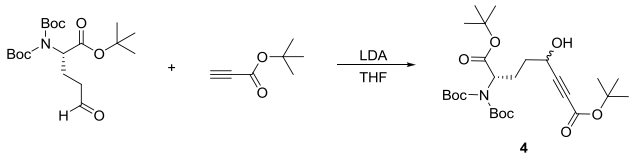
General: Reactions were run under a N_2 atmosphere in glassware dried at 150 °C prior to use; anhydrous solvents were obtained through standard laboratory protocols. Analytical thin-layer chromatography (TLC) was performed on SiO_2 60 F-254 plates available from Merck using the mobile phase indicated. Visualization was accomplished by UV irradiation at 254 or 304 nm, or by staining with one of the following reagents: 5% phosphomolybdic acid hydrate in EtOH (PMA), ninhydrin (0.3% w/v in glacial acetic acid/*n*-butanol 3:97), or vanillin (5% w/v in concentrated H_2SO_4/EtOH 1:99) stain. Flash chromatography was run on a CombiFLASH Companion^{TM} using 4, 12, 40, or 120 g SiO_2 columns and eluents were monitored at the wavelengths indicated or by an evaporative light scattering detector (ELSD). Proton and carbon NMR spectra were obtained on Brucker Avance 400 and 500 MHz NMR spectrometers. Mass spectra were obtained using the indicated ionization mode on an LCMS 2010 EV mass detector (Shimadzu). Reactions involving radioactive materials were run in a fully leaded hot-cell by trained personnel and in accordance with the guidelines established by the GR Radiation Safety Committee.



4

(7*S*)-di-*tert*-butyl 7-((bis-*tert*-butoxycarbonyl)amino)-4-hydroxyoct-2-ynedioate (4) A solution of *tert*-butyl propiolate in THF (5.68 mL) was cooled <-70 °C and monitored via an internal reaction thermocouple. LDA (2M in THF, 1.5 eq., 2.13 mL) was added and the mixture was stirred for 1 h at -70 ºC. Then (*S*)-*tert*-butyl 2-((bis-*tert*-butoxycarbonyl)amino)-5-oxopentanoate[1] in THF (9.3 mL) was added via a syringe pump at a rate such that the reaction temperature did not exceed -70 °C. The reaction was stirred for 1 h at -70 °C, quenched with 10 % citric acid solution (10 mL) and diluted with EtOAc (50 mL). The organic and aqueous layers were separated and the aqueous layer was extracted with two additional 20 mL portions of EtOAc. The combined organic extracts, back-extracted with two, 10 mL portions of saturated aqueous $NaHCO_3$, dried ($MgSO_4$), filtered and concentrated under reduced pressure to provide the crude product as a yellow oil. The crude material was dry loaded using silica gel and purified using a 40 g prepacked silica gel column. The product was purified at a flow rate of 40 mL/min. Initially the column was eluted with 4 column volumes of 10 % EtOAc-hexanes. We then executed a linear gradient to 25 % EtOAc-hexanes over 12 column volumes. Finally, we held the column at 25 % EtOAc-hexanes for an additional 4 column volumes. The column eluent was monitored by ELSD, and fractions that appeared to contain products were reanalyzed by TLC on silica gel and developed with 20 % EtOAc-hexanes. The developed plates were visualized by ninhydrin staining and fractions containing relevant materials were pooled. The purified product was a pale yellow oil (1.13 g, 77%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.46 (s, 9H), 1.50 (s, 9H), 1.52 (s, 18H), 1.83 (m, 2H), 2.04 (m, 2H), 2.27 (m, 1H), 4.53 (m, 1H), 4.76 (dt, J_1 = 9.2 Hz, J_2 = 5.2 Hz); ^{13}C NMR[2] ($CDCl_3$, 100 MHz) δ 24.72, 25.13, 27.93, 27.96, 28.02, 33.70, 33.75, 58.31, 58.47, 61.37, 31.90, 77.84, 77.89, 81.46, 81.48, 83.04, 83.09, 83.63, 84.94, 84.96, 152.34, 152.40, 152.47, 169.52, 169.63; LCMS (ESI) $(M+Na)^+$ 536.

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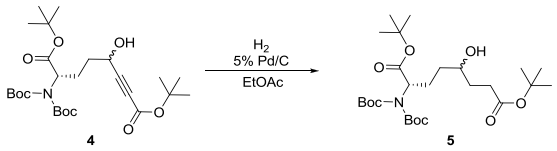
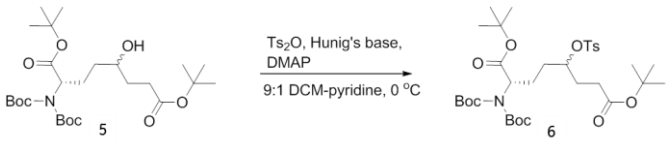
[1] (a) Yao, Y., Chen, P. Diao, J. Cheng, G. Deng, L. Anglin, J. L. Prasad, B. V. V. Song, Y. *J. Am. Chem. Soc.* **2011**, *133*(42), 16746-16749. b.) Ilies, M., Dowling, D. P.,Lombardi, P. M. Christianson, D. W. *Bioorg. Med. Chem. Lett.* **2011**, *21*(19), 5854-5858.

[2] Extra peaks observed in the ^{13}C NMR were a result of the product being a mixture of diastereomers, and did not indicate the presence of an impurity.

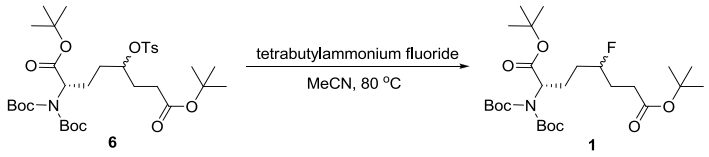


(2*S*)-di-*tert*-butyl 2-((bis-*tert*-butoxycarbonyl)amino)-5-hydroxyoctanedioate (5) To a solution of **4** (1.13 g, 2.2 mmol) in EtOAc (44 mL) was added solid 5% (wt.) Pd/C (0.14 g). The mixture was vacuum purged three times with H_2 gas and allowed to continue stirring for 48 h under a H_2 atmosphere. The reaction mixture was filtered through a Celite pad to remove the catalyst and the pad was rinsed with an additional 100 mL of EtOAc. The filtrate was concentrated under reduced pressure to provide a grey oil. The crude material was dry loaded using silica gel and purified with a 40 g prepacked silica gel column. The product was purified at a flow rate of 40 mL/min. Initially the column was eluted with 4 column volumes of 5 % EtOAc-hexanes. We subsequently executed a linear gradient to 25 % EtOAc-hexanes over 12 column volumes. Finally, we held the column at 25 % EtOAc-hexanes for an additional 4 column volumes. The column eluent was monitored by ELSD, and fractions that appeared to contain products were reanalyzed by TLC on silica gel and developed with 15 % EtOAc-hexanes. The developed plates were visualized by ninhydrin staining and fractions containing relevant materials were pooled. The product was a colorless oil. (1.1 g, 97%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.45 (m, 18H), 1.51 (m, 18H), 2.27–1.56 (m, 6H); 2.37 (m, 2H), 3.63 (m, 1H), 4.73 (m, 1H); ^{13}C NMR[2] ($CDCl_3$, 100 MHz) 25.55, 25.69, 27.94, 28.02, 28.07, 32.05, 32.15, 32.22, 32.30, 34.15, 34.37, 58.68, 58.92, 70.65, 71.19, 80.40, 80.42, 81.25, 81.28, 82.82, 82.86, 152.48, 152.58, 169.75, 170.01, 173.58, 173.60; LCMS (ESI) $(M+Na)^+$ 540.

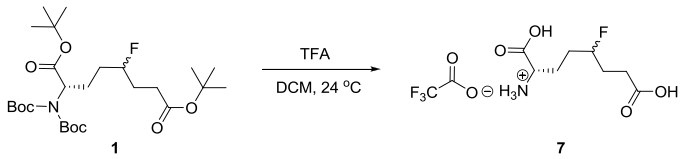


(2*S*)-di-*tert*-butyl 2-((bis-*tert*-butoxycarbonyl)amino)-5-(tosyloxy)octanedioate (6) A solution of **5** (240 mg, 0.46 mmol) in 1.4 mL of CH_2Cl_2 was treated with 155 µL of pyridine and 250 µL (1.39 mmol) of Hunig's base and cooled to 0 °C. To this was added 5.7 mg (46 µmol) of dimethylaminopyridine followed by 0.30 g (0.93 mmol) of toluene sulfonic anhydride. The stirred reaction mixture was allowed to warm to room temperature over 14 h. The reaction mixture was then poured into saturated aqueous $NaHCO_3$ (50 mL) and diluted with CH_2Cl_2 (25 mL). The organic and aqueous layers were separated and the aqueous layer was extracted twice with CH_2Cl_2 (20 mL). The organic extracts were combined and back extracted with one additional 20 mL portions of brine. The combined organic extracts were dried ($MgSO_4$) filtered and concentrated under reduced pressure to yield a purple oil. This was dry loaded using silica gel and purified with a 40 g prepacked silica gel column. The product was purified at a flow rate of 40 mL/min. Initially the column was eluted with 6 column volumes of 100 % hexanes with 0.5% Et_3N followed by a linear gradient to 30 % EtOAc-hexanes with 0.5% Et_3N over 20 column volumes and finally 4 column volumes of 30 % EtOAc-hexanes with 0.5% Et_3N. The eluent was monitored by UV at 254 nm, and fractions that appeared to contain products were reanalyzed by TLC on silica gel and developed with 20 % EtOAc-hexanes with 0.5% Et_3N. The plates were visualized by ninhydrin staining and fractions containing relevant materials were pooled. The product was a colorless oil that was aliquoted into 1-2 mg portions and stored at - 80 °C Until it was needed for radiolabeling (0.28 g, 90%): ^{1}H NMR (CD_2Cl_2, 400 MHz) δ 1.44-1.37 (m, 18H), 1.53-1.44 m, 19H), 1.71-1.53 (m, 3H), 2.06-1.72 (m, 4H),

2.27-2.07 (m, 2H), 2.44 (s, 3H), 4.71-4.49 (m, 2H), 7.36 (dd, J_1 = 8.0 Hz, J_2= 1.3 Hz, 2H), 7.77 (dd, J_1 = 8.1 Hz, J_2= 2 Hz, 2H); ^{13}C NMR[2] (CD_2Cl_2, 100 MHz) δ 20.78, 21.79, 24.59, 24.98, 28.07, 28.17, 29.34, 29.68, 30.86, 31.00, 31.28, 31.55, 58.63, 58.97, 80.61, 81.50, 81.54, 82.54, 82.79, 83.12, 128.03, 128.05, 130.27, 130.28, 134.61, 134.67, 145.27, 152.77, 152.80, 169.58, 171.96; LCMS (ESI) $(M+Na)^+$ 694.



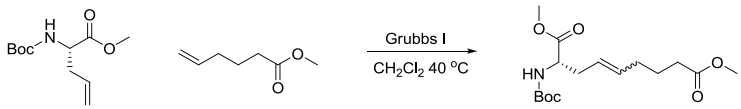
(2*S*)-di-*tert*-butyl 2-((bis-*tert*-butoxycarbonyl)amino)-5-fluorooctanedioate (1) To a solution of **6** (40 mg, 0.059 mmol) in CH_3CN (2 mL) was added TBAF (189 mg, 0.60 mmol). The resulting mixture was heated to 80 °C for 30 min. Following this time, volatile solvents were removed under reduced pressure and the crude product was partitioned against 10 mL of EtOAc and 10 mL of water. The organic and aqueous layers were separated and the aqueous layer was extracted with two additional 10 mL portions of EtOAc. The combined organic extracts were washed with 10 mL of brine, dried (Na_2SO_4), filtered and concentrated under reduced pressure to provide the crude product. The crude material was purified by flash chromatography on a 12 g silica gel column. We maintained an eluent flow rate of 30 mL/min. throughout the separation. Initially the column was eluted with 4 column volumes of 100% hexanes followed by a linear gradient to 40% EtOAc-hexanes over 20 column volumes and finally 6 column volumes of 40% EtOAc-hexanes. The eluent was monitored using an ELSD, and fractions that appeared to contain products were reanalyzed by TLC on silica gel and developed with 20% EtOAc-hexanes. The developed plates were visualized by ninhydrin staining and fractions containing relevant materials were pooled to afford the desired material as a mixture of diastereomers. The isolated material was a colorless, viscous oil (20 mg, 65%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.47–1.46 (m, 18H), 1.53 (m, 18H), 2.45–1.60 (m, 8H), 4.62–4.44 (m, 1H), 4.76–4.71 (m, 1H); ^{13}C NMR[3] ($CDCl_3$, 100MHz) δ25.14 (t, J = 4.8 Hz, 1C), 28.10, 28.18, 28.23, 30.54 (dd, J_1 = 14.8 Hz, J_2 = 21 Hz, 1C), 31.28 (dd, J_1 = 6.9 Hz, J_2 = 4.4 Hz, 1C), 32.15 (dd, J_1 = 20.5 Hz, J_2 = 4.7 Hz, 1C), 58.75 (d, J_1 = 59.1 Hz, 1C), 80.53 (d, J_1 = 0.8 Hz, 1C), 81.46 (d, J_1 = 2.5 Hz, 1C), 83.03 (d, J_1 = 3.3 Hz, 1C), 93.10 (dd, J_1 = 165 Hz, J_2 = 36.7 Hz, 1C), 152.59 ((d, J_1 = 3.0 Hz, 1C), 169.7 (d, J_1 = 11.9 Hz, 1C), 172.51 (d, J_1 = 0.6 Hz, 1C); ^{19}F NMR[3] ($CDCl_3$, 564 MHz) -182.59 – -182.89 (m, 1F), -183.32 – -183.61 (m, 1F); LCMS (ESI) $(M+Na)^+$ 542.



(1*S*)-1,6-dicarboxy-4-fluorohexan-1-amine 2,2,2-trifluoroacetate acid salt (7) In a 5 mL round bottom flask was added **1** (3.5 mg), CH_2Cl_2 (1.0 mL) and trifluoroacetic acid (1.0 mL) at room temperature. The clear solution was allowed to stir for 16 h at room temperature. Following the allotted time, the volatile materials were evaporated under reduced pressure and triturated with Et_2O to afford **7** as a colorless solid (1.3 mg, 60%). ^{1}H NMR (D_2O-TFA-D, 400 MHz) δ 1.83–1.33 (m, 8H), 2.16–2.09 (m, 2H), 3.74–3.73 (m, 1H), 4.22–4.35 (m,

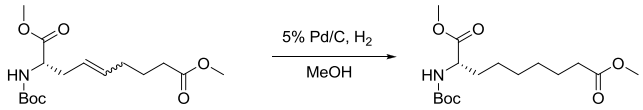
[3] Reported peaks were consistent with a diastereomeric mixture, C-F couplings were evident throughout.

1H); ^{13}C NMR[3] (D_2O, 100MHz) δ 25.64 (d, J_1 = 4.4 Hz, 1C), 29.8-29.1 (m, 3C), 52.86 (d, J_1 = 8.1 Hz, 1C), 93.05 (d, J_1 = 5.9 Hz, 0.5C), 94.70 (d, J_1 = 5.9 Hz, 0.5C), 116.23 (dd, J_1 = 505 Hz, J_2 = 291 Hz, 1C), 162.95 (dd, J_1 = 61.3 Hz, J_2 = 35.8 Hz, 1C), 172.32 (s, 1C), 177.95 (s, 1C) ^{19}F NMR ($CDCl_3$, 564 MHz) -75.66 (s, 3F), -183.00– -183.40 (m, 1F); LCMS (ESI) $(M+H)^+$ 208.



8

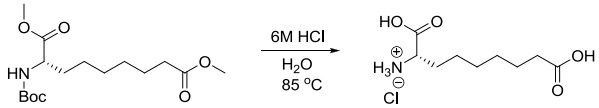
(*S*)-dimethyl 2-((*tert*-butoxycarbonyl)amino)non-4-enedioate (8) Methyl hex-5-enoate (0.56 g, 4.4 mmol) was dissolved in dichloromethane (22 mL) and (*S*)-methyl 2-((*tert*-butoxycarbonyl)amino)pent-4-enoate (0.5 g, 2.2 mmol) was added to the reaction mixture followed by 0.1 molar equivalents of benzylidene-bis(tricyclohexylphophine)dichlororuthenium (0.18g, 0.22 mmol). The reaction mixture was heated in an oil bath maintained at 40 °C for 14 h. Following the allotted time the reaction mixture was cooled to room temperature and immediately prepared for flash chromatography. The crude material was dry loaded using silica gel and purified with a 40 g prepacked silica gel column. The product was purified at a flow rate of 40 mL/min. Initially the column was eluted with 6 column volumes of 100 % hexanes. We then executed a linear gradient to 25 % EtOAc-hexanes over 20 column volumes. Finally, we held the column at 25 % EtOAc-hexanes for an additional 6 column volumes. The column eluent was monitored by UV at 220 nm, and fractions that appeared to contain products were reanalyzed by TLC on silica gel and developed with 25 % EtOAc-hexanes. The developed plates were visualized by ninhydrin and iodine and fractions containing relevant materials were pooled. A considerable amount of the allylglycine starting material (0.169g, 34%) and dimethyl dec-5-enedioate (0.19 g, 38%) were isolated from this procedure. The title compound was a mixture of E/Z isomers, isolated as a colorless oil (0.17 g, 24%): ^{1}H NMR (CD_2Cl_2, 400 MHz) δ 1.40 (s, 9H), 1.65 (pent, J_1 = 7.5 Hz, 2H), 2.04 (hex, J_1 = 7.5 Hz, 2H), 2.26 (q, J_1 = 7.2 Hz, 2H), 2.62-2.32 (m, 2H), 3.62 (m, 3H), 3.70 (m, 3H), 4.40-4.20 (m, 1H), 5.22-4.95 (m, 1H), 5.37-5.25 (m, 1H), 5.59-5.42 (m, 1H); ^{13}C NMR (CD_2Cl_2, 100 MHz) δ 24.79, 25.09, 26.93, 28.40, 30.50, 32.16, 33.51, 33.63, 35.87, 51.65, 51.69, 52.41, 52.49, 53.66, 79.85, 124.46, 125.20, 133.19, 134.38, 155.46, 172.97, 174.13; LCMS (ESI) $(M+Na)^+$ 352.



8 9

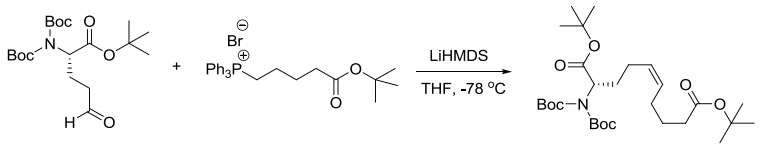
(*S*)-dimethyl 2-((*tert*-butoxycarbonyl)amino)nonanedioate (9) To a solution of **8** (0.17g, 0.53 mmol) in MeOH (11 mL) was added 28 mg of 5% Pd on C and the mixture was vacuum purged with H_2 three times and then permitted to stir under an atmosphere of hydrogen for 14 h. Following the allotted time, the reaction mixture was filtered through a Celite pad to remove the catalyst and the pad was rinsed with an additional 35 mL of EtOAc. The filtrate was concentrated under reduced pressure to provide a grey oil. The crude material was dry loaded using silica gel and purified with a 12 g prepacked silica gel column. The product was purified at a flow rate of 30 mL/min. Initially the column was eluted with 4 column volumes of 100 % hexanes. We then executed a linear gradient to 25 % EtOAc-hexanes over 25 column volumes. Finally, we held the column at 25 % EtOAc-hexanes for an additional 4 column volumes. The column eluent was monitored using an ELSD, and fractions that appeared to contain products were reanalyzed by TLC on silica gel and developed with 10 %

EtOAc-hexanes. The developed plates were visualized by ninhydrin staining and fractions containing relevant materials were pooled. The product was a colorless oil (0.136 g, 78%): ^{1}H NMR (CD_2Cl_2, 400 MHz) δ 1.37-1.23 (m, 6H), 1.41, (s, 9H), 1.66-1.50 (m, 3H), 1.82-1.67 (m, 1H), 2.27 (dd, J_1 = 7.5 Hz, J_2 = 7.5 Hz, 2H), 3.62 (s, 3H), 3.69 (s, 3H), 4.21 (dd, J_1 = 10.8 Hz, J_2 = 7.6 Hz, 1H), 5.06 (d, J_1 = 7.6 Hz, 1H); ^{13}C NMR (CD_2Cl_2, 100 MHz) δ 25.15, 25.50, 28.42, 29.17, 29.22, 32.88, 34.25, 51.61, 52.39, 79.81, 155.64, 173.73, 174.30; LCMS (ESI) $(M+Na)^+$ 354.



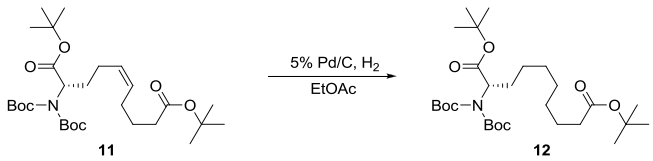
9 10

(*S*)-1,7-dicarboxyheptan-1-amine hydrochloride salt (10) The starting material **9** (0.136g, 0.41 mmol) was dissolved in 6M HCl (2 mL) and allowed to stir at 85 °C overnight. The residual solvent was blown off with an active nitrogen stream, and the resulting residue was redissolved in water, frozen and lyophilized. The isolated product was a colorless powder (0.084g, 85%): ^{1}H NMR (D_2O, 400 MHz) δ 1.38-1.10 (m, 6H), 1.68-1.40 (m, 4H), 2.35-2.00 (m, 2H), 3.28-3.04 (m, 1H); ^{13}C NMR (D_2O, 100 MHz) δ 24.85, 25.81, 28.49, 28.54, 34.68, 37.59, 55.99, 164.69, 184.30; LCMS (ESI) $(M+H)^+$ 204.

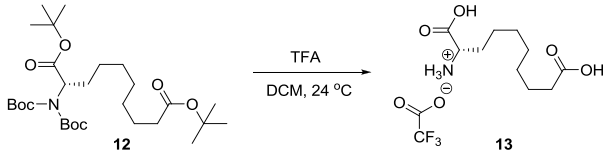


11

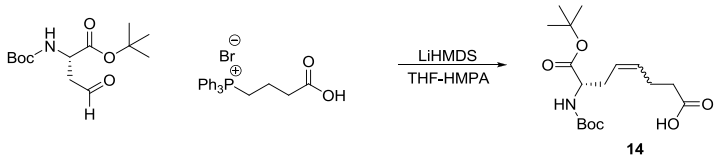
(*S*,Z)-9-(bis-*tert*-butoxycarbonyl)amino)-10-*tert*-butoxy-10-oxodec-5-enoic acid (11) A 1.0 M THF solution of LiHMDS (0.84 mmol, 0.84 mL) was added drop-wise to a suspension of (3-carboxybutyl)triphenyl-phosphonium bromide salt (171 mg, 0.39 mmol) in THF (5 mL) under nitrogen at -78 °C (acetone dry ice bath). The light yellow heterogeneous mixture was stirred 1 h at -78 °C and then was warmed to 0 °C by replacing the bath with an ice-MeOH bath (the reaction mixture turned from yellow to reddish orange). Once again the reaction mixture was cooled to -78 °C (by replacing the ice-MeOH bath with the acetone-dry ice bath), and then a solution of (*S*)-*tert*-butyl 2-((bis-*tert*-butoxycarbonyl)amino)-5-oxopentanoate[1] (100 mg, 0.26 mmol)) in dry THF (2.0 mL) was added. Following the addition, the reaction mixture was warmed to 0 °C and stirring was continued for another 30 min. Following the allotted time, the mixture was poured into a solution of 10% citric acid and was extracted with two 100 mL portions of diethyl ether. The combined ether extracts were washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure. The crude material was dry loaded using silica gel and purified with a 24 g prepacked silica gel column. The product was purified at a flow rate of 35 mL/min. Initially the column was eluted with 4 column volumes of 100 % hexanes. We then executed a linear gradient to 40 % EtOAc-hexanes with 6% acetic acid over 25 column volumes. Finally, we held the column at 40 % EtOAc-hexanes with 6% acetic acid for an additional 4 column volumes. The column eluent was monitored using an ELSD, and fractions that appeared to contain products were reanalyzed by TLC on silica gel and developed with 20 % EtOAc-hexanes. The developed plates were visualized by ninhydrin staining and fractions containing relevant materials were pooled. The title compound was a viscous oil. LCMS (ESI) $(M+Na)^+$ 494.



(*S*)-9-(bis(*tert*-butoxycarbonyl)amino)-10-*tert*-butoxy-10-oxodecanoic acid (12) A 25 mL round-bottomed flask was purged with N_2 and charged with **11** (0.06 g, 0.11 mmol), EtOAc (5 mL) and 5% Pd/C (~5.0 mg dry weight). The flask was evacuated, charged with H_2 from a balloon and stirred for 14 h at room temperature. After this time, the H_2 was evacuated and N_2 charged into the flask. The catalyst was removed by filtration through a pad of Celite 545 and the filter cake washed with 10 mL of EtOAc. The filtrate was concentrated under reduced pressure to afford the title compound as an oil (59 mg, 98%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.34–1.32 (m, 8H), 1.45 (s, 9H), 1.51 (s, 18H), 1.67–1.59 (m, 2H), 2.04–1.82 (m, 2H), 2.34 (t, J 7.58 Hz, 2H), 4.70 (dd, J_1 = 9.85 Hz, J_2= 5.05 Hz, 1H); LCMS (ESI) $(M+Na)^+$ 496.

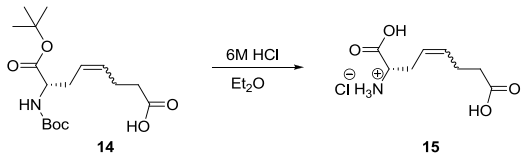


(*S*)-1,8-dicarboxyoctan-1-amine 2,2,2-trifluoroacetate salt (13) To a 5 mL round bottom flask was added **12** (58 mg, 0.11 mmol), CH_2Cl_2 (1.5 mL), and trifluoroacetic acid (1.5 mL) at room temperature. The clear solution was allowed to stir for 14 h at room temperature. The solvents were then removed under reduced pressure and triturated with Et_2O to afford the title compound **13** as an off-white solid (22 mg, 60%): ^{1}H NMR (D_2O-CD_3OD) δ 1.65–1.34 (m, 10H), 1.95 (m, 2H), 2.39 (t, J_1 = 7.33 Hz, 2H), 4.05 (t, J_1 = 5.31 Hz, 1H) LCMS (ESI) $(M+H)^+$ 218.



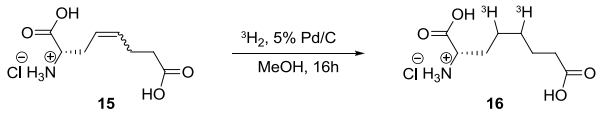
(*S*)-8-(*tert*-butoxy)-7-((*tert*-butoxycarbonyl)amino)-8-oxooct-4-enoic acid (14) A 1.0M THF solution of LiHMDS (19.1 mmol, 19.14 mL) was added drop-wise to a suspension of (3-carboxypropyl)triphenyl-phosphonium bromide (4.8g, 11.2 mmol) in 2:1 THF-HMPA (45 mL) under nitrogen at -78 °C (acetone-dry ice bath). The mixture was stirred 1 h at -78 °C and then was warmed to 0 °C by replacing the acetone-dry ice bath with an ice-MeOH bath. Subsequently, the reaction mixture was returned to -78 °C (by replacing the ice-MeOH bath with the acetone-dry ice bath), and then a solution of (*S*)-*tert*-butyl 2-((*tert*-butoxycarbonyl)amino)-4-oxobutanoate[1] (1.8 g, 6.6 mmol)) in dry THF (5.0 mL) was added. Following the addition, the reaction mixture was warmed to 0 °C (ice-MeOH bath) and stirring was continued for another 30 min. Following the allotted time, the mixture was poured into a solution of 10% citric acid and was extracted with two 100 mL portions of EtOAc. The combined ether extracts were washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure. The crude material was dry loaded using silica gel and purified with a 40 g prepacked silica gel column. The product was purified at a flow rate of 40 mL/min. Initially the column was eluted with 4 column volumes of 100 % hexanes. We then executed a linear gradient to 70 % EtOAc-hexanes with 6% acetic acid over 25 column volumes. Finally, we held the column at 70 % EtOAc-hexanes with

6% acetic acid for an additional 4 column volumes. The column eluent was monitored using an ELSD, and fractions that appeared to contain products were reanalyzed by TLC on silica gel and developed with 50 % EtOAc-hexanes with 6% acetic acid. The developed plates were visualized by $KMnO_4$ staining and fractions containing relevant materials were pooled (0.23g, 10%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.43 (s, 9H), 1.46 (s, 9H), 2.29-2.44 (m, 4H), 2.53-2.44 (m, 1H), 2.67-2.53 (m, 1H), 4.25 (dd, J_1 = 12.4 Hz, J_2 = 5.8 Hz, 1H), 5.12 (d, J_1 = 7.8 Hz, 1H), 5.36 (dd, J_1 = 16.4 Hz, J_2 = 7.4 Hz, 1H), 5.53 (dd, J_1 = 14.6 Hz, J_2 = 7.8 Hz, 1H); LCMS (ESI) $(M+Na)^+$ 366.



14 15

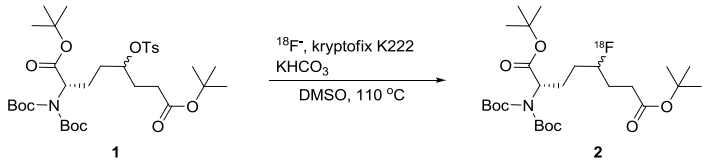
(*S*)-1,6-dicarboxyhex-3-en-1-amine hydrochloride (15) To a 5 mL round bottom flask was added **14** (100 mg, 0.29 mmol), diethyl ether (8 mL), and 1M hydrochloric acid (1.0 mL) at 0 °C. The mixture was stirred at 0 °C for 30 min. and was then allowed to warm to room temperature and continue stirring for an additional 18h. The aqueous and organic layers were then partitioned and the aqueous layer was collected and the solvent was removed under reduced pressure. The resulting material was triturated with two 10 mL portions of Et_2O and then the ether was carefully decanted off the solids. The resulting off-white solid was dried under high vacuum overnight (65 mg, 98%): ^{1}H NMR (CD_3OD, 400 MHz) δ 2.47-2.37 (m, 4H), 2.74 (dd, J_1 = 6.5 Hz, J_2 = 6.5 Hz, 2H), 4.05 (dd, J_1 = 6.1 Hz, J_2 = 6.1 Hz, 1H), 5.49-5.38 (m, 1H), 5.71-5.61 (m, 1H); ^{13}C NMR (MeOD, 100 MHz) δ 23.65, 29.16, 34.12, 53.68, 123.35, 135.20, 171.28, 176.86; LCMS (ESI) $(M+H)^+$ 188.



15 16

(*S*)-2-Amino 4,5-^{3}H-Suberic Acid (16) This material was prepared from **15** by Quotient Bioresearch, Cardiff, UK.

Radiosynthesis protocol employed at GE:



1 2

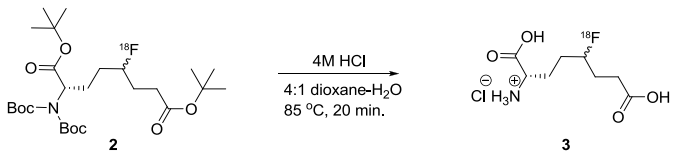
(2*S*)-di-*tert*-butyl 2-((bis-*tert*-butoxycarbonyl)amino)-5-[^{18}F]-fluorooctanedioate (2)

To a 5 mL conical vial was added 500 µL of K222 stock solution[4], 250 µL of $KHCO_3$ stock solution[5] and 3 mL of anhydrous CH_3CN. The solvent was removed under a stream of nitrogen to yield a colorless residue. To this

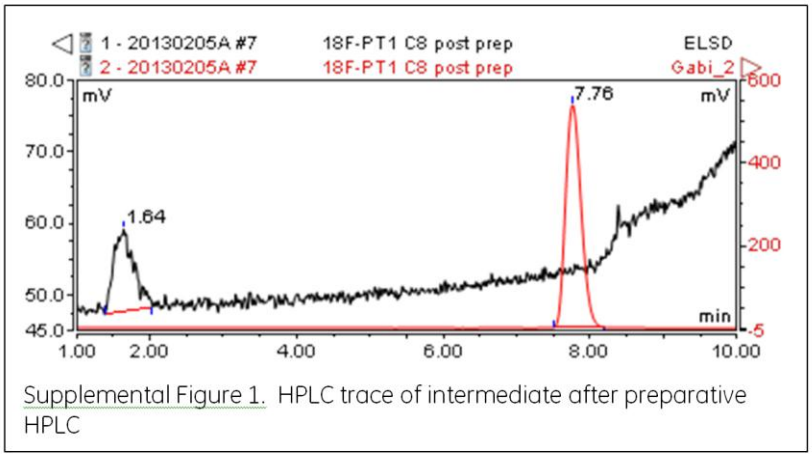
[4] Kryptofix stock solution prepared from 145 mg of Kryptofix K222 and 5.1 mL of anhydrous MeCN, yielding a 74 mM solution.

[5] $KHCO_3$ stock solution prepared from 165 mg of $KHCO_3$ solid and 11 mL of 16.8 MΩ water, yielding a 144 mM solution.

residue was added 3 mL of anhydrous CH_3CN and 0.5 mL of [^{18}F]- fluoride (48 mCi) in sterile water. The solvent was removed under N_2 flow at reduced pressure. An additional 1 mL of anhydrous CH_3CN was added to the dry-down vessel and the solvent was once again removed. The remaining residue from the dry-down was taken up in 700 µL of anhydrous DMSO and the vial was gently vortexed and activity of the solution was measured in a dosimeter (33 mCi). A volume of 600 µL of the DMSO solution was removed from the dry-down vessel and added to a 1.5 mL conical vial containing 2.8 mg of the precursor **1** deposited as a film on the walls of the vial. The quantity of activity transferred to the reaction vial was measured in the dosimeter (20.2 mCi) and the vial was placed in a lead block that had been preheated to 110 °C. The reaction mixture was allowed to remain in the heated block at 110 °C for 20 min. and was then removed and allowed to briefly cool to room temperature. The contents of the entire reaction mixture were immediately subjected to purification by reversed phase HPLC (XTerra Prep C_{18}, 5µm, 10 x 100 mm) at a constant flow rate of 8 mL/min. The mobile phase was comprised of water (weak solvent) and CH_3CN (strong solvent) each of which contained 0.05% trifluoroacetic acid by volume. The column was eluted according to the following gradient program. The column was initially held at 100% water for one minute. We then initiated a linear gradient to 98:2 CH_3CN-H_2O over 12 min. Subsequently, we maintained the column at 98% CH_3CN for an additional 4 min. The desired material **2** was collected as a single peak, eluting from the column from 11.6–12.4 min. following injection. The material isolated from the HPLC was measured in the dosimeter (2.4 mCi, 15% decay corrected yield , 12% uncorrected yield based on 20.2 mCi starting [^{18}F] fluoride). A small sample of the isolated fraction (20 µL) was added to 250 µL of 8:2 CH_3CN-water containing 0.05% trifluoroacetic acid by volume and was analyzed by analytical HPLC (XBridge C_{18}, 5 µm, 4.6 x 100 mm). The details of the gradient program used for analysis of this material are outlined in Supplemental Table 1 and a corresponding chromatogram of the isolated material is presented in Supplemental Figure 1. The material isolated from the HPLC was concentrated to ~100 µL under an active stream of N_2 at reduced pressure and was then taken immediately on to the next step.



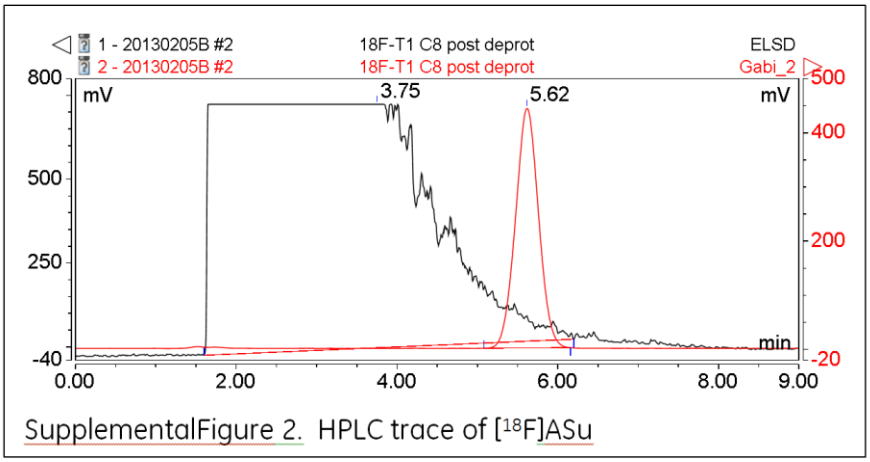
(1*S*)-1,6-dicarboxy-4-[^{18}F]-fluorohexan-1-amine hydrochloride (3) To the residue containing **2** in ~100 µL of water was added 500 µL of 4 N HCl in dioxane (Aldrich). The resulting solution was placed in a lead pig heated to 85 °C for 20 min. Then 20 µL was removed and added to a mixture containing 250 µL of water and 100 µL 0.33M sodium trifluoroacetate. This sample was subsequently taken for analysis by analytical HPLC (XBridge C_{18}, 5µm, 4.6 x 100 mm). The gradient program used for this purification is detailed in Supplemental Table 2. The analytical HPLC chromatogram is shown in Supplemental Figure 2; the large off-scale peak in the ELSD trace is due to the presence of nonvolatile salts resulting from the neutralization of HCl with sodium trifluoroacetate. To confirm the identity of the radioactive peak, an aliquot of **7** was added to the analytical HPLC vial containing the radiotracer for HPLC analysis (Supplemental Figure 3); the retention time delay of 16 seconds between the radioactivity detector and the ELSD is consistent with the time delayed measured for a control compound (results not shown). The remaining reaction mixture was concentrated to dryness under a stream of N_2 at reduced pressure to yield 1.10 mCi of **3 (**14 % decay-corrected yield, 5.4% uncorrected yield based on 20.2 mCi of starting [^{18}F]fluoride) for *in vivo* evaluation.



Supplemental Figure 1. HPLC trace of intermediate after preparative HPLC

Supplemental Table 1. Analytical HPLC method for intermediate

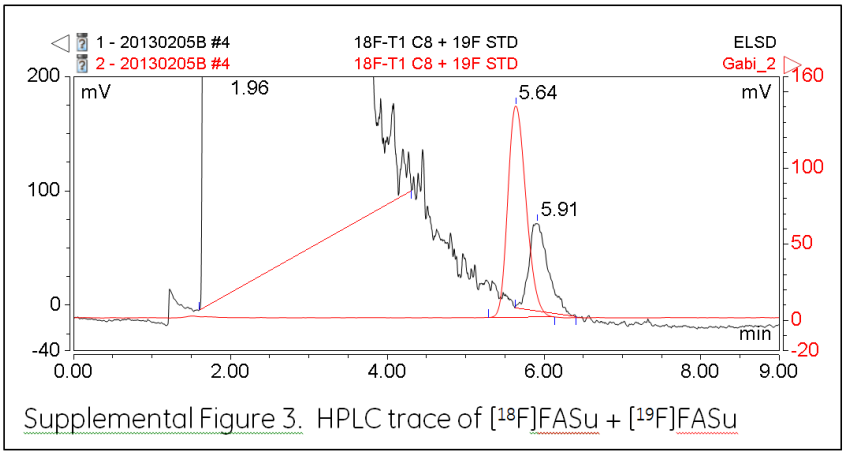
Time	Flow	%A	%B
min	ml/m		
-3.0	1.2	36%	64%
0.0	1.2	36%	64%
8.0	1.2	0%	100%
8.4	1.5	0%	100%
10.4	1.5	0%	100%
11.0	1.2	36%	64%
12.0	1.2	36%	64%



SupplementalFigure 2. HPLC trace of [^{18}F]ASu

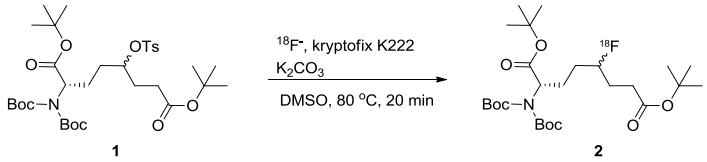
Supplemental Table 2. Analytical HPLC method for product

Time	Flow	%A	%B
min	ml/m		
-4.0	1.2	100%	0%
0.0	1.2	100%	0%
2.0	1.2	100%	0%
10.0	1.2	88%	12%
10.4	1.4	20%	80%
12.6	1.4	20%	80%
13.0	1.2	60%	40%
14.0	1.2	100%	0%



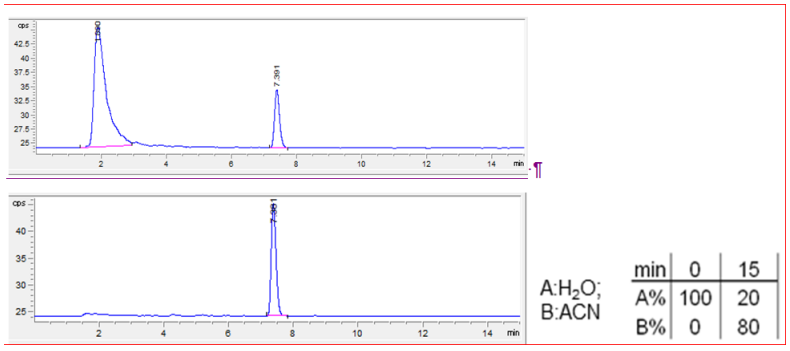
Supplemental Figure 3. HPLC trace of [^{18}F]FASu + [^{19}F]FASu

Radiosynthesis protocol employed at TRIUMF:

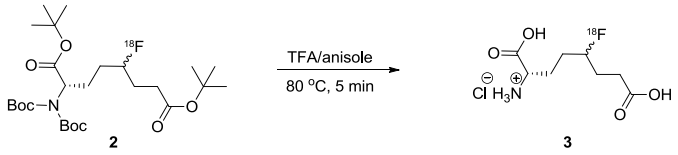


(2*S*)-di-*tert*-butyl 2-((bis-*tert*-butoxycarbonyl)amino)-5-[^{18}F]-fluorooctanedioate (2)

[^{18}F]F^- was isolated using a standard initial immobilization on a QMA column followed by elution from the column to a reaction vessel using K[2.2.2]/K_2CO_3 (K[2.2.2] 4.2mg in 0.075 mL acetonitrile mixed with K_2CO_3 0.8 mg in 0.075 mL H_2O). Azeotropic drying was achieved with three sequences of heating 1 mL of acetonitrile at 90 °C under a stream of nitrogen while applying a partial vacuum. A solution of 1 mg precursor in 0.2 mL DMSO was delivered to the reaction vessel and the reaction mixture heated at 80 °C for 20 min. The reaction was quenched with the addition of 2 mL distilled, deionized H_2O and transferred to a tC18 plus Sep-Pak column. The column was washed with 17 mL water and eluted with 1.5 mL acetonitrile. The acetonitrile eluent was dried under nitrogen flow at 90 °C in vacuo to obtain **2**. The decay corrected yield is 11±4% with the radiochemical purity >98%. HPLC tracers are shown in Supplemental Figure 4.

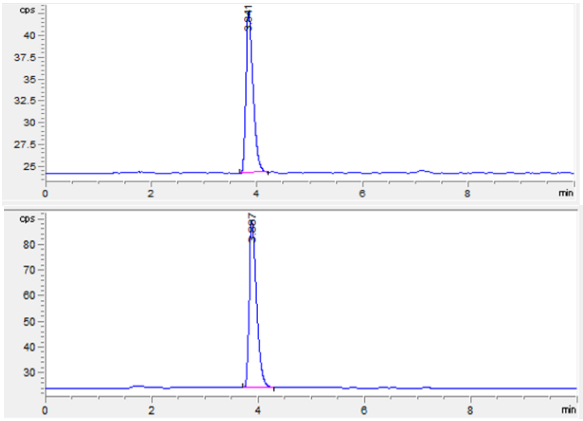


Supplemental Figure 4: HPLC γ traces of reaction mixture (top) and SepPak purified product (bottom).



(1*S*)-1,6-dicarboxy-4-[^{18}F]-fluorohexan-1-amine hydrochloride (3)

To the residue containing **2**, TFA/anisole (400 µL/8 µL) was added and heating continued for 5 min. followed by removal under a stream of nitrogen until the vessel was dry. The residue was dissolved in PBS buffer and passed through a tC18 light Sep-Pak column to obtain the final product. The radiofluorination process provided decay-corrected radiochemical yields of 55±12% with >98% radiochemical purity of the final product. HPLC tracers are shown in Supplemental Figure 5.



	min	0	15
A:0.1% TFA in H_2O	A%	100	20
B:0.1% TFA in ACN	B%	0	80

Supplemental Figure 5: HPLC γ traces of reaction mixture (top) and SepPak purified product (bottom).