Supporting Information

for

A Multi-Pronged Evaluation of Aldehyde-Based Tripeptidyl Main Protease Inhibitors as SARS-CoV-2 Antivirals

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Materials. We purchased yeast extract from Thermo Fisher Scientific, tryptone from Gibco, Sub3 from Bachem, HEK 293T/17 cells from ATCC, DMEM with GlutaMax from Gibco, FBS from Gibco, polyethyleneimine from Polysciences, the trypsin-EDTA solution from Gibco. Chemicals used in this work were acquired from Sigma Aldrich, Chem Impex, Ambeed, A2B, etc.

M^{Pro} Expression and Purification. The expression plasmid pET28a-His-SUMO-M^{Pro} was constructed in a previous study. We used this construct to transform *E. coli* BL21(DE3) cells. A single colony grown on a LB plate containing 50 μg/mL kanamycin was picked and grown in 5 mL LB media supplemented with 50 μg/mL kanamycin overnight. We inoculated this overnight culture to 6 L 2YT media with 50 μg/mL kanamycin. Cells were grown to OD_{600} as 0.8. At this point, we added 1 mM IPTG to induce the expression of His-SUMO-M^{Pro}. Induced cells were let grown for 3 h and then harvested by centrifugation at 12,000 rpm, 4 °C for 30 min. We resuspended cell pellets in 150 mL lysis buffer (20 mM Tris-HCl, 100 mM NaCl, 10 mM imidazole, pH 8.0) and lysed the cells by sonication on ice. We clarified the lysate by centrifugation at 16,000 rpm, 4 °C for 30 min. We decanted the supernatant and mixed with Ni-NTA resins (GenScript). We loaded the resins to a column, washed the resins with 10 volumes of lysis buffer, and eluted the bound protein using elution buffer (20 mM Tris-HCl, 100 mM NaCl, 250 mM imidazole, pH 8.0). We exchanged buffer of the elute to another buffer (20 mM Tris-HCl, 100 mM NaCl, 10 mM imidazole, 1 mM DTT, pH 8.0) using a HiPrep 26/10 desalting column (Cytiva) and digested the elute using 10 units SUMO protease overnight at 4 °C. The digested elute was subjected to Ni-NTA resins in a column to remove His-tagged SUMO protease, His-tagged SUMO tag, and undigested His-SUMO-M^{Pro}. We loaded the flow-through onto a Q-Sepharose column and purified M^{Pro} using FPLC by running a linear gradient from 0 to 500 mM NaCl in a buffer (20 mM Tris-HCl, 1 mM DTT, pH 8.0). Fractions eluted from the Q-Sepharose column was concentrated and loaded onto a HiPrep 16/60 Sephacryl S-100 HR column and purified using a buffer containing 20 mM Tris-HCl, 100 mM NaCl, 1 mM DTT, and 1 mM EDTA at pH 7.8. The final purified was concentrated and stored in a -80 °C freezer.

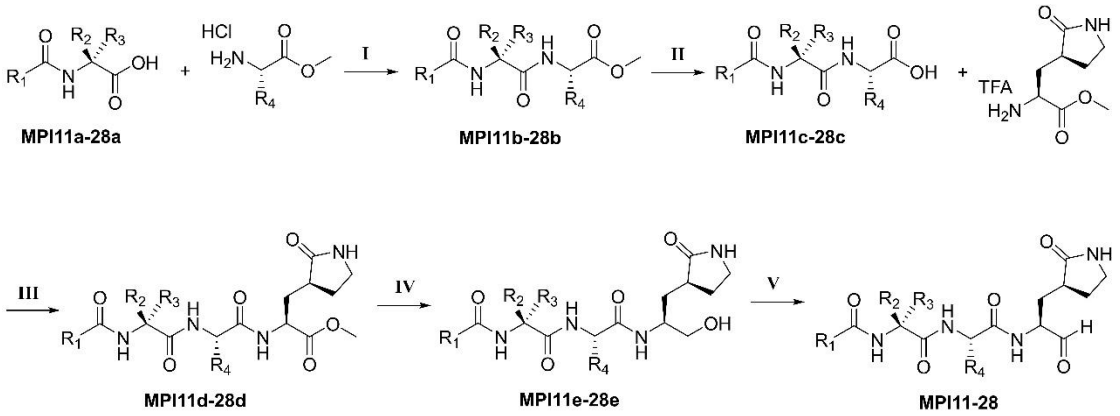
***In Vitro* M^{Pro} Inhibition Potency Characterizations of MPIs.** For most MPIs, we conducted the assay using 20 nM M^{Pro} and 10 μM Sub3. For MPI13-14, 10 nM M^{Pro} was used. We dissolved all inhibitors in DMSO as 10 mM stock solutions. Sub3 was dissolved in DMSO as a 1 mM stock solution and diluted 100 times in the final assay buffer containing 10 mM $Na_xH_yPO_4$, 10 mM NaCl, 0.5 mM EDTA, and 1.25% DMSO at pH 7.6. We incubated M^{Pro} and an inhibitor in the final assay buffer for 30 min before adding the substrate to initiate the reaction catalyzed by M^{Pro}. The production format was monitored in a fluorescence plate reader with excitation at 336 nm and emission at 455 nm. More assay details can be found in a previous study.[1]

X-Ray Crystallography Analysis of M^{Pro}-Inhibitor Complexes. The production of crystals of M^{pro}-inhibitor complexes wasfollowing the previous protocols.[1] The data of M^{pro} with MPI11, MPI12 and MPI24 were collected on a Rigaku R-AXIS IV++ image plate detector. The data of M^{pro} with MPI16, MPI18, MPI19, MPI22, MPI23, MPI25 and MPI27 were collected on a Bruker Photon II detector. The data of M^{pro} with MPI14, MPI20, MPI21, MPI26 and MPI28 were collected at the Advanced Light Source (ALS) beamline 5.0.2 using a Pilatus3 6M detector. The diffraction data were indexed, integrated and scaled with iMosflm or PROTEUM3.[2] All the structures were determined by molecular replacement using the structure model of the free enzyme of the SARS-CoV-2 M^{pro} [Protein Data Bank (PDB) ID code 7JPY] as the search model

using Phaser in the Phenix package.[1,3] *JLigand* and *Sketcher* from the CCP4 suite were employed for the generation of PDB and geometric restraints for the inhibitors. The inhibitors were built into the Fo-Fc density by using *Coot*.[4] Refinement of all the structures was performed with Real-space Refinement in Phenix.[3] Details of data quality and structure refinement are summarized in Table S1. All structural figures were generated with PyMOL (https://www.pymol.org).

Cellular M^{Pro} Inhibition Potency Characterizations of MPIs. We grew HEK 293T/17 cells in high-glucose DMEM with GlutaMAX supplement and 10% FBS in 10 cm culture plates under 37 °C and 5% CO_2 to 80-90% confluency and then transfected cells with the pLVX-M^{Pro}-eGFP-2 plasmid. 30 mg/mL polyethyleneimine and the total of 8 µg of the plasmid in 500 µL opti-MEM media were used for transfection. We incubated transfected cells overnight. On the second day, we collected cells using 0.05% trypsin-EDTA to detach them from plates, resuspended collected cells in the original growth media, adjusted the cell density to $5 \cdot 10^5$ cells/mL, added 500 µL adjusted cells to each well of a 48-well plate, and then added 100 µL of a drug solution in DMEM. We incubated treated cells under 37 °C and 5% CO_2 for 72 h. After 72 h incubation, cells were collected using trypsinization and centrifugation. We resuspended collected cells in 200 ⌈L PBS and analyzed cells with fluorescence using a Cytoflex Research Flow Cytometer based on the size scatters (SSC-A and SSC-H) and forward scatter (FSC-A). We gated cells based on SSC-A and FSC-A then with SSC-A and SSC-H. Fluorescence was detected with excitation at 488 nm and emission at 525 nm. All collected data were converted to csv files and analyzed using a self-prepared MATLAB script for massive data processing. We sorted the FITC-A column from lowest to highest. A 10^6 cutoff was set to separate the column to two groups with higher than 10^6 as positive and lower than 10^6 as negative. We integrated the positive group and divided the total integrated fluorescence intensity by the total cell positive cell counts as Flu. Int. shown in all graphs. The standard deviation of positive fluorescence was calculated as well. All processed data were plotted and fitted to a four-parameter Hill equation in GraphPad 9.0 to obtain determined EC_{50} values.

The Synthesis of MPIs. All reagents and solvents for the synthesis were purchased from commercial sources and used without purification. All glassware was flame-dried prior to use. Thin-layer chromatography (TLC) was carried out on aluminum plates coated with 60 F254 silica gel. TLC plates were visualized under UV light (254 or 365 nm) or stained with 5% phosphomolybdic acid. Normal phase column chromatography was carried out using a Yamazen Small Flash AKROS system. Analytical reverse phase HPLC was carried out on a Shimazu LC20 HPLC system with an analytical C18 column. Semipreparative HPLC was carried out the same system with a semipreparative C18 column. The mobile phases were H_2O with 0.1% formic acid (A) and acetone with 0.1% formic acid (B). NMR spectra were recorded on a Bruker AVANCE Neo 400 MHz or Varian INOVA 300 MHz spectrometer in specified deuterated solvents. High-resolution electrospray mass spectrometry was carried out on a Thermo Scientific Q Exactive Focus system. The purity of all compounds was confirmed by NMR and analytic HPLC-UV as ε 95%.



Scheme S1. General synthetic route to MPI11-28. Reagents and conditions: (I) HATU, DIPEA, DMF; (II) LiOH•H_2O, THF/H_2O; (III) HATU, DIPEA, DMP; (IV) $LiBH_4$, THF; (V) DMP, DCM

(S)-methyl 2-((S)-2-(((benzyloxy)carbonyl)amino)-3-methylbutanamido)-4,4-dimethylpentanoate (MPI11b). Methyl (S)-2-amino-4,4-dimethylpentanoate hydrochloride (0.4 g, 2.27 mmol, 1.1 equiv) and *N*-Cbz-L-valine (0.52 g, 2.07 mmol, 1.0 equiv) were dissolved in dry DMF (20 mL) and the reaction was cooled to 0 °C. HATU (1.01 g, 2.69 mmol, 1.3 equiv) and DIPEA (1.46 mL, 8.28 mmol, 4.0 equiv) were added, and the reaction mixture was allowed warm up to room temperature and stirred for 12 h. The mixture was then poured into water (50 mL) and extracted with ethyl acetate (4×20 mL). The organic layer was washed with aqueous hydrochloric acid 10% v/v (2×20 mL), saturated aqueous $NaHCO_3$ (2×20 mL), brine (2×20 mL) and dried over Na_2SO_4. The organic phase was evaporated to dryness and the crude material purified by silica gel column chromatography (15-50% EtOAc in n-hexane as the eluent) to afford pure **MPI11b** as a white solid (0.6 g, 73%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 (m, 5H), 6.39 (m, 1H), 5.43 (t, *J* = 10.6 Hz, 1H), 5.12 (s, 2H), 4.65 (td, *J* = 8.5, 3.6 Hz, 1H), 4.04 (q, *J* = 7.2 Hz, 1H), 3.73 (s, 3H), 2.24 – 2.01 (m, 1H), 1.80 (dd, *J* = 14.2, 3.5 Hz, 1H), 1.50 (dd, *J* = 14.3, 8.7 Hz, 1H), 1.07 – 0.90 (m, 15H). ^{13}C NMR (100 MHz, Chloroform-*d*): δ 173.5, 170.9, 156.4, 136.26, 128.5, 128.2, 128.0, 77.4, 77.0, 76.7, 67.0, 60.3, 52.3, 49.8, 46.0, 31.1, 30.7, 29.5, 19.1, 17.9.

(S)-2-((S)-2-(((benzyloxy)carbonyl)amino)-3-methylbutanamido)-4,4-dimethylpentanoic acid (MPI11c). The **MPI11b** (600 mg, 1.53 mmol, 1.0 equiv) was dissolved in THF/H_2O (1:1, 10 mL). LiOH•H_2O (153 mg, 3.82 mmol, 2.5 equiv) was added at 0 °C. The mixture was stirred at room temperature overnight. Then THF was removed on vacuum and the aqueous layer was acidified with 1 M HCl and extracted with dichloromethane (3 x 10 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated to yield **MPI11c** as a white solid (415 mg, yield 70%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.42 (s, 1H), 7.26 (tdd, *J* = 9.1, 5.5, 2.5 Hz, 5H), 6.69 (d, *J* = 8.2 Hz, 1H), 5.82 (d, *J* = 9.3 Hz, 1H), 5.10 – 4.96 (m, 2H), 4.54 (td, *J* = 8.6, 3.2 Hz, 1H), 4.13 – 3.88 (m, 1H), 1.83 – 1.73 (m, 1H), 1.43 (dd, *J* = 14.7, 8.9 Hz, 1H), 1.18 (dt, *J* = 12.4, 7.1 Hz, 1H), 0.91 (s, 3H), 0.85 (m, 12H).

(5S,8S,11S)-methyl 5-isopropyl-8-neopentyl-3,6,9-trioxo-11-(((S)-2-oxopyrrolidin-3-yl)methyl)-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (MPI11d). The methyl (S)-2-amino-3-((S)-2-oxopyrrolidin-3-yl)propanoate hydrochloride (110 mg, 0.494 mmol, 1.1 equiv) and the **MPI11c** (170 mg, 0.45 mmol, 1.0 equiv) were dissolved in anhydrous DMF (10 mL) and the reaction was cooled to

0 °C. HATU (222 mg, 0.585 mmol, 1.3 equiv) and DIPEA (0.32 mL, 1.81 mmol, 4.0 equiv) were added, and the reaction mixture was allowed to warm up to room temperature and stirred for 12 h. The mixture was then poured into water (20 mL) and extracted with ethyl acetate (4×20 mL). The organic layer was washed with aqueous hydrochloric acid 10% v/v (2×20 mL), saturated aqueous $NaHCO_3$ (2×20 mL), brine (2×20 mL) and dried over Na_2SO_4. The organic phase was evaporated to dryness and the crude material purified by silica gel column chromatography to afford pure **MPI11d** as a white solid (200 mg, yield 81%). ^{1}H NMR (400 MHz, Chloroform-*d*): δ 7.72 (d, *J* = 7.7 Hz, 1H), 7.32 – 7.21 (m, 5H), 6.88 – 6.60 (m, 2H), 5.47 (d, *J* = 9.2 Hz, 1H), 5.00 (s, 2H), 4.58 - 4.56 (m, 1H), 4.46 – 4.43 (m, 1H), 3.91 – 3.88 (m, 1H), 3.61 (s, 3H), 3.27 – 3.24 (m, 2H), 2.34 – 2.24 (m, 2H), 2.15 – 2.12 (m, 1H), 2.01 – 1.97 (m, 1H), 1.78 –1.75 (m, 3H), 1.19 – 1.11 (m, 1H), 0.91 – 0.81 (m, 16H).

Benzyl ((S)-1-(((S)-1-(((S)-1-hydroxy-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)-4,4-dimethyl-1-oxopentan-2-yl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (MPI11e). To a stirred solution of **MPI11d** (150 mg, 0.27 mmol, 1.0 equiv) in anhydrous THF (8 mL) was added $LiBH_4$ (2.0 M in THF, 0.412 mL, 0.54 mmol, 2.0 equiv) in several portions at 0 °C. The reaction mixture was then allowed to warm up to room temperature and stirred for an additional 2 h. The reaction was quenched by the dropwise addition of 1.0 M HCl (aq) (1.2 mL) with cooling in an ice bath. Removed THF in vacuo, and the mixture was diluted with H_2O and extracted with EtOAc, washed with sat. NaCl, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (6% MeOH in CH_2Cl_2 as the eluent) to afford the pure product **MPI11e** as a white solid (102 mg, yield 71%). ^{1}H NMR (400 MHz, Chloroform-*d*): δ 7.84 (d, *J* = 9.3 Hz, 1H), 7.71 (d, *J* = 7.5 Hz, 1H), 7.28 – 7.24 (m, 5H), 6.86 (d, *J* = 4.4 Hz, 1H), 5.66 (d, *J* = 8.7 Hz, 1H), 5.07 – 4.94 (m, 2H), 4.60 – 4.58 (m, 1H), 4.08 (t, *J* = 8.2 Hz, 1H), 3.89 (dq, *J* = 11.9, 5.6 Hz, 1H), 3.77 (s, 1H), 3.59 (d, *J* = 10.9 Hz, 1H), 3.32 – 3.06 (m, 2H), 2.46 – 2.14 (m, 3H), 1.99 – 1.96 (m, 2H), 1.72 – 1.69 (m, 2H), 1.64 – 1.40 (m, 2H), 0.94 – 0.77 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.8, 173.6, 171.0, 156.6, 136.2, 128.5, 128.2, 128.0, 67.1, 65.3, 60.3, 51.1, 50.4, 46.6, 40.6, 38.2, 32.2, 31.4, 30.6, 29.6, 28.2, 19.1, 18.3.

Benzyl ((S)-1-(((S)-4,4-dimethyl-1-oxo-1-(((S)-1-oxo-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)pentan-2-yl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (MPI11). To a solution of **MPI11e** (90 mg, 0.17 mmol, 1.0 equiv) in anhydrous CH_2Cl_2 (6 mL) was added $NaHCO_3$ (60 mg, 0.68 mmol, 4 equiv) and the Dess-Martin reagent (225 mg, 0.51 mmol, 3 equiv). The resulting mixture was stirred at RT for 12 h. Then the reaction was quenched with a saturated $NaHCO_3$ solution containing 10 % $Na_2S_2O_3$. The layers were separated. The organic layer was then washed with saturated brine solution, dried over anhydrous Na_2SO_4 and concentrated *on vacuum*. The residue was purified by column chromatography (6% MeOH in CH_2Cl_2 as the eluent) to afford the pure product **MPI11** as a white solid (58 mg, yield 65%). ^{1}H NMR (400 MHz, Chloroform-*d*): δ 9.42 (s, 1H), 7.32 – 7.23 (m, 5H), 6.64 – 6.41 (m, 1H), 5.91 (d, *J* = 26.3 Hz, 1H), 5.43 (d, *J* = 8.9 Hz, 1H), 5.31 (d, *J* = 8.6 Hz, 1H), 5.03 (d, *J* = 7.8 Hz, 2H), 4.51 (dt, *J* = 8.6, 4.4 Hz, 1H), 4.26 (d, *J* = 7.0 Hz, 1H), 4.18 – 4.01 (m, 1H), 3.92 (dd, *J* = 8.4, 6.3 Hz, 1H), 3.29-3.26 (m, 2H), 2.44 – 2.25 (m, 2H), 2.16 – 2.05 (m, 1H), 1.91 – 1.87 (m, 2H), 1.80 – 1.73 (m, 1H), 1.58 – 1.54 (m, 2H), 1.02 – 0.73 (m, 15H). ^{13}C NMR (100 MHz, Chloroform-*d*): δ 199.5, 180.0, 173.8, 171.1, 156.6, 136.2, 128.5, 128.2, 128.0, 67.1, 60.6, 57.2, 50.9, 46.4, 40.6, 37.9, 31.0, 30.6, 29.9, 29.6, 28.2, 19.2, 18.1.

(S)-methyl 2-((S)-2-(((benzyloxy)carbonyl)amino)-3-methylbutanamido)-4-methylpent-4-enoate (MPI12b). MPI112b was prepared with methyl (S)-2-amino-4-methylpent-4-enoate hydrochloride and *N*-Cbz-L-valine as a white solid following a similar procedure to **MPI11b** (yield 40%). ^{1}H NMR (400 MHz, Chloroform-*d*): δ 7.41-7.28 (m, 5H), 6.19 (t, *J* = 5.8 Hz, 1H), 5.33 (d, *J* = 9.2 Hz, 1H), 5.11 (s, 2H), 4.83 (s, 1H), 4.73 (s, 1H), 4.67 (td, *J* = 8.0, 5.6 Hz, 1H), 4.08 – 3.95 (m, 1H), 3.72 (s, 3H), 2.55 (dd, *J* = 14.1, 5.4 Hz, 1H), 2.40 (dd, *J* = 14.0, 8.4 Hz, 1H), 2.14 (dt, *J* = 13.4, 7.0 Hz, 1H), 1.71 (s, 3H), 1.69 -1.66 (m, 1H), 0.95 (dd, *J* = 18.8, 6.7 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*): δ 172.3, 170.9, 156.3, 140.2, 136.2, 128.6, 128.2, 128.1, 114.9, 67.1, 60.2, 52.3, 50.5, 40.4, 31.2, 21.8, 21.1, 19.1, 17.7.

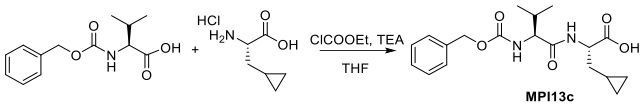
(S)-2-((S)-2-(((benzyloxy)carbonyl)amino)-3-methylbutanamido)-4-methylpent-4-enoic acid (MPI12c). MPI12c was prepared as a white solid following a similar procedure to **MPI11c** (yield 83%). ^{1}H NMR (400 MHz, Chloroform-*d*): δ 7.41 – 7.28 (m, 5H), 6.41 (d, *J* = 7.3 Hz, 1H), 5.44 (d, *J* = 9.1 Hz, 1H), 5.11 (s, 2H), 4.83 (s, 1H), 4.75 (s, 1H), 4.73 – 4.63 (m, 1H), 2.62 (dd, *J* = 14.2, 5.2 Hz, 1H), 2.43 (dd, *J* = 14.2, 8.7 Hz, 1H), 1.94 – 1.84 (m, 1H), 1.72 (s, 3H), 0.94 (dd, *J* = 16.9, 6.8 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*): δ 174.8, 171.7, 156.6, 140.2, 136.1, 128.6, 128.3, 128.0, 127.0, 114.9, 68.0, 67.2, 60.3, 50.5, 40.0, 31.0, 25.6, 21.8, 19.1, 17.9.

(5S,8S,11S)-methyl 5-isopropyl-8-(2-methylallyl)-3,6,9-trioxo-11-(((S)-2-oxopyrrolidin-3-yl)methyl)-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (MPI12d). MPI12d was prepared as a white solid following a similar procedure to **MPI11d** (yield 63%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.82 (d, *J* = 7.7 Hz, 1H), 7.41 – 7.28 (m, 5H), 7.06 (d, *J* = 8.5 Hz, 1H), 6.67 (s, 1H), 5.45 (d, *J* = 8.8 Hz, 1H), 5.09 (s, 2H), 4.75 (s, 1H), 4.71 (s, 1H), 4.54 (ddd, *J* = 11.6, 7.8, 3.4 Hz, 1H), 4.05 – 3.95 (m, 1H), 3.70 (s, 3H), 3.31 (p, *J* = 8.1, 6.7 Hz, 2H), 2.58 (dd, *J* = 14.1, 4.8 Hz, 1H), 2.45 – 2.28 (m, 3H), 2.25 – 2.05 (m, 2H), 1.90 – 1.73 (m, 2H), 1.72 (s, 3H), 0.91 (dd, *J* = 18.8, 6.8 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*): δ 179.8, 172.0, 171.8, 171.2, 156.5, 140.9, 136.2, 128.6, 128.2, 128.0, 114.3, 67.1, 60.6, 52.4, 51.3, 41.1, 40.5, 38.3, 33.3, 30.9, 28.1, 21.9, 19.2, 18.6, 17.3.

Benzyl ((S)-1-(((S)-1-(((S)-1-hydroxy-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)-4-methyl-1-oxopent-4-en-2-yl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (MPI12e). MPI12e was prepared as a white solid following a similar procedure to **MPI11e** (yield 70%). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.36 – 7.15 (m, 5H), 5.01 (q, *J* = 12.5 Hz, 2H), 4.69 (d, *J* = 8.8 Hz, 2H), 4.41 (dd, *J* = 9.5, 5.6 Hz, 1H), 3.84 (dd, *J* = 16.3, 7.9 Hz, 2H), 3.44 (dd, *J* = 11.2, 5.4 Hz, 1H), 3.36 (dd, *J* = 11.0, 6.4 Hz, 1H), 3.20 – 3.12 (m, 2H), 2.50 – 2.16 (m, 4H), 2.00 – 1.80 (m, 2H), 1.65 (s, 4H), 1.45 (ddd, *J* = 14.2, 11.1, 3.1 Hz, 1H), 0.84 (dd, *J* = 11.7, 6.8 Hz, 6H). ^{13}C NMR (100 MHz, Methanol-d_4) δ 181.2, 172.8, 172.6, 157.5, 141.0, 136.8, 128.1, 127.6, 127.5, 112.9, 66.5, 64.1, 61.0, 52.0, 49.3, 40.1, 39.4, 38.1, 32.2, 30.4, 27.6, 20.8, 18.3, 17.1.

Benzyl ((S)-3-methyl-1-(((S)-4-methyl-1-oxo-1-(((S)-1-oxo-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)pent-4-en-2-yl)amino)-1-oxobutan-2-yl)carbamate (MPI12). MPI12 was prepared as a white solid following a similar procedure to **MPI11** (yield 60%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.48 (s, 1H), 8.33 – 8.20 (m, 1H), 7.42 – 7.29 (m, 5H), 6.63 (d, *J* = 7.8 Hz, 1H), 6.05 (s, 1H), 5.34 (d, *J* = 8.2 Hz, 1H), 5.10 (s, 2H), 4.82 (t, *J* = 1.7 Hz, 1H), 4.75 (s, 1H), 4.68 (td, *J* = 8.5, 5.7 Hz, 1H), 4.33 (d, *J* = 8.5 Hz, 1H), 4.02 (dd, *J* = 8.2, 5.8 Hz, 1H), 3.33 (dt, *J* = 8.9, 4.3 Hz, 2H), 2.62 (dd, *J* = 14.1, 5.5 Hz, 1H), 2.53 – 2.32 (m, 3H), 2.21 – 2.09 (m, 1H), 2.05 – 1.88 (m, 2H), 1.87 – 1.82 (m, 1H), 1.75 (s, 3H), 0.93 (dd, *J* = 23.8, 6.8 Hz, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*): δ 199.7, 180.0, 172.4, 171.4, 156.6, 140.8, 136.2, 128.5, 128.2, 128.0, 114.4, 67.1, 60.6, 57.5, 51.4, 41.0, 40.6, 38.0, 30.9, 29.9, 28.3, 21.9, 19.2, 17.7.



MPI13c

(S)-2-((S)-2-(((benzyloxy)carbonyl)amino)-3-methylbutanamido)-3-cyclopropylpropanoic acid (MPI13c). *N*-Cbz-L-valine (500 mg, 2.0 mmol, 1.0 equiv), ethyl chloroformate (268 μL, 2.8 mmol, 1.4 equiv) and TEA (836 μL, 6.0 mmol, 3.0 equiv) were dissolved in anhydrous THF (30 mL). After stirring at 0 °C for 0.5 h, L-cyclopropylalanine (386 mg, 4.0 mmol, 1.5 equiv) in water was added. The reaction mixture was stirred for 0.5 h at 0 °C. The THF was removed in vacuo and the aqueous layer was acidified with 1.0 M HCl. The aqueous layer was extracted with ethyl acetate. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was recrystallized from $CHCl_3$ and hexane to yield the pure product **MPI13c** as a white solid (380 mg, yield 52%).

Methyl (5S,8S,11S)-8-(cyclopropylmethyl)-5-isopropyl-3,6,9-trioxo-11-(((S)-2-oxopyrrolidin-3-yl)methyl)-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (MPI13d). MPI13d was prepared as a white solid following a similar procedure to **MPI11d** (yield 51%).

Benzyl ((S)-1-(((S)-3-cyclopropyl-1-(((S)-1-hydroxy-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)-1-oxopropan-2-yl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (MPI13e). MPI13e was prepared as a white solid following a similar procedure to **MPI11e** (yield 75%). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.3 – 7.1 (m, 5H), 5.0 (d, *J* = 4.1 Hz, 2H), 4.3 (t, *J* = 7.3 Hz, 1H), 3.9 (d, *J* = 7.3 Hz, 2H), 3.5 – 3.3 (m, 2H), 3.1 (dt, *J* = 16.3, 5.5 Hz, 2H), 2.4 (dd, *J* = 14.7, 6.6 Hz, 1H), 2.2 (dt, *J* = 15.7, 7.8 Hz, 1H), 2.0 – 1.8 (m, 2H), 1.6 (dq, *J* = 20.5, 7.7, 7.0 Hz, 2H), 1.5 – 1.3 (m, 2H), 0.8 (dd, *J* = 9.4, 6.7 Hz, 6H), 0.7 (p, *J* = 6.9 Hz, 1H), 0.3 (t, *J* = 10.5 Hz, 2H), 0.0 (dq, *J* = 7.5, 4.0 Hz, 2H). ^{13}C NMR (100 MHz, Methanol-d_4) δ 181.3, 172.9, 172.7, 157.4, 136.8, 128.1, 127.6, 127.5, 66.4, 64.1, 60.7, 54.3, 49.1, 40.1, 38.1, 36.6, 32.2, 30.6, 27.6, 18.4, 17.3, 7.3, 3.8, 3.6.

Benzyl ((S)-1-(((S)-3-cyclopropyl-1-oxo-1-(((S)-1-oxo-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)propan-2-yl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (MPI13). MPI13 was prepared as a white solid following a similar procedure to **MPI11** (yield 50%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.4 (s, 1H), 8.3 (d, *J* = 6.5 Hz, 1H), 7.2 (s, 5H), 7.2 (s, 1H), 6.6 (d, *J* = 23.9 Hz, 1H), 5.7 – 5.5 (m, 1H), 5.1 – 4.9 (m, 2H), 4.6 (dq, *J* = 18.1, 9.9, 8.6 Hz, 1H), 4.4 – 4.2 (m, 1H), 4.0 (h, *J* = 6.9, 5.7 Hz, 1H), 3.3 (s, 1H), 3.2 (d, *J* = 10.8 Hz, 1H), 2.4 (t, *J* = 8.4 Hz, 1H), 2.3 (s, 1H), 2.1 (s, 1H), 2.0 (dp, *J* = 25.6, 9.2, 7.8 Hz, 2H), 1.9 – 1.6 (m, 2H), 1.5 – 1.4 (m, 1H), 0.8 (dd, *J* = 12.2, 6.6 Hz, 6H), 0.7 – 0.5 (m, 1H), 0.3 (t, *J* = 9.5 Hz, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 199.5, 180.0, 172.7, 171.3, 156.6, 136.2, 128.5, 128.2, 128.0, 67.1, 60.5, 53.7, 50.7, 40.6, 38.0, 37.6, 31.1, 29.8, 28.4, 19.2, 17.9, 7.3, 4.5, 4.4.

Methyl (S)-2-((S)-2-(((benzyloxy)carbonyl)amino)-3-methylbutanamido)-3-(furan-2-yl)propanoate (MPI14b). MPI14b was prepared with methyl (S)-2-amino-3-(furan-2-yl)propanoate hydrochloride and *N*-Cbz-L-valine as a white solid following a similar procedure to **MPI11b** (yield 80%). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.32 – 7.09 (m, 6H), 6.15 (dd, *J* = 3.2, 1.9 Hz, 1H), 6.02 (d, *J* = 3.2 Hz, 1H), 4.99 (s, 2H), 4.59 (dd, *J* = 8.1, 5.5 Hz, 1H), 3.84 (d, *J* = 7.1 Hz, 1H), 3.59 (s, 3H), 3.14 – 2.90 (m,

2H), 2.02 – 1.77 (m, 1H), 0.82 (dd, *J* = 11.5, 6.8 Hz, 6H). ^{13}C NMR (100 MHz, Methanol-d_4) δ 172.73, 171.40, 150.58, 141.76, 128.09, 127.46, 109.92, 107.20, 48.25, 48.04, 47.82, 47.61, 47.40, 47.19, 46.97, 30.61, 29.49, 18.25.

(S)-2-((S)-2-(((benzyloxy)carbonyl)amino)-3-methylbutanamido)-3-(furan-2-yl)propanoic acid (MPI14c). MPI14c was prepared as a white solid following a similar procedure to **MPI11c** (yield 88%). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.30 – 7.14 (m, 6H), 6.19 – 6.08 (m, 1H), 6.02 (d, *J* = 3.2 Hz, 1H), 4.98 (s, 2H), 4.58 (dd, *J* = 8.2, 5.0 Hz, 1H), 3.92 – 3.76 (m, 1H), 3.11 (dd, *J* = 15.3, 5.1 Hz, 1H), 2.97 (dd, *J* = 15.3, 8.2 Hz, 1H), 1.99 – 1.82 (m, 1H), 0.82 (dd, *J* = 14.3, 6.8 Hz, 6H). ^{13}C NMR (100 MHz, Methanol-d_4) δ 172.61, 172.49, 150.87, 141.63, 128.10, 127.63, 127.45, 109.89, 107.09, 66.31, 60.59, 48.27, 48.06, 47.84, 47.63, 47.42, 47.21, 46.99, 30.63, 18.32.

Methyl (5S,8S,11S)-8-(furan-2-ylmethyl)-5-isopropyl-3,6,9-trioxo-11-(((S)-2-oxopyrrolidin-3-yl)methyl)-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (MPI14d). MPI14d was prepared as a white solid following a similar procedure to **MPI11d** (yield 80%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.67 (d, *J* = 7.2 Hz, 1H), 7.38 – 7.22 (m, 5H), 6.90 (d, *J* = 7.9 Hz, 1H), 6.23 – 6.11 (m, 1H), 6.03 (d, *J* = 3.2 Hz, 1H), 5.86 (s, 1H), 5.26 (d, *J* = 8.0 Hz, 1H), 5.04 (d, *J* = 5.1 Hz, 2H), 4.74 (d, *J* = 7.3 Hz, 1H), 4.45 (s, 1H), 3.95 (t, *J* = 7.1 Hz, 1H), 3.64 (s, 3H), 3.24 (d, *J* = 8.8 Hz, 1H), 3.17 – 3.01 (m, 2H), 2.31 (s, 1H), 2.19 (s, 1H), 2.07 (dd, *J* = 13.3, 6.9 Hz, 2H), 1.86 – 1.68 (m, 2H), 1.60 (s, 3H), 1.41 (d, *J* = 22.6 Hz, 4H), 0.96 – 0.74 (m, 6H).

Benzyl ((S)-1-(((S)-3-(furan-2-yl)-1-(((S)-1-hydroxy-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)-1-oxopropan-2-yl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (MPI14e). MPI14e was prepared as a white solid following a similar procedure to **MPI11e** (yield 37%). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.25 (s, 6H), 6.24 – 6.14 (m, 1H), 6.05 (d, *J* = 3.1 Hz, 1H), 5.09 – 4.86 (m, 2H), 4.52 (d, *J* = 7.9 Hz, 2H), 3.80 (t, *J* = 9.6 Hz, 2H), 3.48 – 3.25 (m, 2H), 3.11 – 2.88 (m, 2H), 2.39 – 2.02 (m, 2H), 2.03 – 1.73 (m, 2H), 1.73 – 1.55 (m, 1H), 1.51 – 1.32 (m, 1H), 1.26 (dd, *J* = 6.8, 2.3 Hz, 1H), 0.80 (dd, *J* = 9.1, 6.5 Hz, 6H). ^{13}C NMR (100 MHz, Methanol-d_4) δ 181.23, 172.74, 171.62, 157.61, 151.02, 141.73, 136.74, 128.10, 127.66, 127.57, 109.96, 107.24, 66.57, 64.01, 61.10, 52.89, 48.26, 48.05, 47.83, 47.62, 47.41, 47.20, 46.98, 40.11, 38.05, 32.13, 29.99 (d, *J* = 65.0 Hz), 27.59, 18.23, 17.08.

Benzyl ((S)-1-(((S)-3-(furan-2-yl)-1-oxo-1-(((S)-1-oxo-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)propan-2-yl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (MPI14). MPI14 was prepared as a white solid following a similar procedure to **MPI11** (yield 80%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.34 (s, 1H), 8.22 (d, *J* = 6.8 Hz, 1H), 7.27 (q, *J* = 7.8, 5.8 Hz, 5H), 7.02 (d, *J* = 8.1 Hz, 1H), 6.16 (d, *J* = 2.5 Hz, 2H), 6.03 (d, *J* = 3.1 Hz, 1H), 5.40 (t, *J* = 11.0 Hz, 1H), 5.03 (d, *J* = 6.8 Hz, 2H), 4.79 (q, *J* = 6.7 Hz, 1H), 4.22 (d, *J* = 10.4 Hz, 1H), 4.00 – 3.88 (m, 1H), 2.25 (s, 2H), 2.17 – 2.02 (m, 1H), 1.76 (d, *J* = 35.2 Hz, 5H), 0.84 (dd, *J* = 25.3, 6.8 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 199.96, 179.97, 171.32, 171.18, 150.71, 142.04, 136.11, 128.60, 128.29, 128.11, 110.41, 108.07, 67.26, 52.41, 50.86, 40.56, 30.70, 28.57, 19.26, 17.59.

Methyl (S)-2-((S)-2-(((benzyloxy)carbonyl)amino)-3-methylbutanamido)-3-(thiophen-2-yl)propanoate (MPI15b). MPI15b was prepared with methyl (S)-2-amino-3-(thiophen-2-yl)propanoate and *N*-Cbz-L-valine as a white solid following a similar procedure to **MPI11b** (yield 72%). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.37 – 7.13 (m, 5H), 7.11 – 7.03 (m, 1H), 6.78 (dd, *J* = 4.6, 2.9 Hz, 2H), 4.99 (d, *J* = 2.9 Hz, 2H), 4.58 (dd, *J* = 7.9, 5.3 Hz, 1H), 3.90 – 3.74 (m, 1H), 3.60 (s, 3H), 3.27 (dd, *J* = 14.9, 5.3 Hz, 1H), 3.21 – 3.12 (m, 3H), 1.91 (s, 1H), 0.82 (dd, *J* = 8.4, 6.7 Hz, 6H). ^{13}C

NMR (100 MHz, Methanol-d_4) δ 172.79, 171.25, 138.12, 136.86, 128.10, 127.63, 127.47, 66.30, 60.62, 53.75, 51.40, 48.26, 48.04, 47.83, 47.62, 47.41, 47.19, 46.98, 31.05, 30.62, 18.28, 17.13.

(S)-2-((S)-2-(((benzyloxy)carbonyl)amino)-3-methylbutanamido)-3-(thiophen-2-yl)propanoic acid (MPI15c). MPI15c was prepared as a white solid following a similar procedure to **MPI11c** (yield 60%). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.44 – 7.29 (m, 5H), 7.19 (dd, *J* = 4.9, 1.5 Hz, 1H), 6.97 – 6.83 (m, 2H), 5.12 (d, *J* = 2.6 Hz, 2H), 4.69 (dd, *J* = 7.9, 4.9 Hz, 1H), 3.99 (d, *J* = 7.1 Hz, 1H), 3.43 (dd, *J* = 15.0, 4.8 Hz, 1H), 3.31 – 3.22 (m, 1H), 2.14 – 1.93 (m, 1H), 1.08 – 0.86 (m, 6H).

Methyl (5S,8S,11S)-5-isopropyl-3,6,9-trioxo-11-(((S)-2-oxopyrrolidin-3-yl)methyl)-1-phenyl-8-(thiophen-2-ylmethyl)-2-oxa-4,7,10-triazadodecan-12-oate (MPI15d). MPI15d was prepared as a white solid following a similar procedure to **MPI11d** (yield 90%). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.35 – 7.18 (m, 5H), 7.08 (dd, *J* = 5.0, 1.3 Hz, 1H), 6.84 – 6.70 (m, 1H), 5.03 – 4.95 (m, 2H), 4.58 – 4.48 (m, 1H), 4.44 – 4.32 (m, 1H), 3.88 – 3.73 (m, 1H), 3.60 (d, *J* = 6.3 Hz, 3H), 3.14 (d, *J* = 3.4 Hz, 2H), 2.39 – 2.25 (m, 1H), 2.24 – 2.09 (m, 1H), 2.10 – 2.01 (m, 1H), 1.99 – 1.83 (m, 1H), 1.67 (s, 2H), 1.19 (d, *J* = 3.6 Hz, 2H), 0.89 (dd, *J* = 9.1, 6.8 Hz, 2H), 0.78 (dd, *J* = 8.4, 6.7 Hz, 4H). ^{13}C NMR (100 MHz, Methanol-d_4) δ 180.21, 172.65, 172.01, 171.69, 157.27, 138.44, 136.84, 128.14, 127.66, 127.51, 126.54, 126.36, 124.01, 66.40, 51.58, 50.54, 48.32, 48.11, 47.90, 47.69, 47.47, 47.26, 47.05, 32.51, 31.41, 27.30, 18.40, 17.21.

Benzyl ((S)-1-(((S)-1-(((S)-1-hydroxy-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)-1-oxo-3-(thiophen-2-yl)propan-2-yl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (MPI15e). MPI15e was prepared as a white solid following a similar procedure to **MPI11e** (yield 53%). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.32 – 7.15 (m, 5H), 7.10 (d, *J* = 4.8 Hz, 1H), 6.80 (d, *J* = 4.9 Hz, 2H), 5.08 – 4.88 (m, 2H), 4.48 (s, 1H), 3.80 (d, *J* = 6.7 Hz, 2H), 3.30 (d, *J* = 23.7 Hz, 2H), 3.17 – 3.00 (m, 3H), 2.24 (dd, *J* = 24.9, 14.9 Hz, 2H), 2.02 – 1.69 (m, 2H), 1.70 – 1.54 (m, 1H), 1.50 – 1.24 (m, 1H), 1.19 (s, 1H), 0.78 (t, *J* = 7.2 Hz, 6H).

Benzyl ((S)-3-methyl-1-oxo-1-(((S)-1-oxo-1-(((S)-1-oxo-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)-3-(thiophen-2-yl)propan-2-yl)amino)butan-2-yl)carbamate (MPI15). MPI15 was prepared as a white solid following a similar procedure to **MPI11** (yield 60%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.30 (s, 1H), 8.24 (s, 1H), 7.38 – 7.22 (m, 4H), 7.04 (d, *J* = 5.0 Hz, 1H), 6.91 (d, *J* = 8.4 Hz, 1H), 6.87 – 6.65 (m, 2H), 5.97 (s, 1H), 5.33 (d, *J* = 8.2 Hz, 1H), 5.03 (s, 2H), 4.80 (d, *J* = 7.7 Hz, 1H), 4.20 (s, 1H), 3.97 (t, *J* = 7.2 Hz, 1H), 3.49 – 3.03 (m, 4H), 2.24 (s, 2H), 2.14 – 1.93 (m, 2H), 1.76 (d, *J* = 33.7 Hz, 3H), 0.83 (dd, *J* = 25.9, 6.7 Hz, 6H).

Methyl (S)-2-((2S,3R)-2-(((benzyloxy)carbonyl)amino)-3-(tert-butoxy)butanamido)-4,4-dimethylpentanoate (MPI16b). MPI16b was prepared with Z-Thr(tBu)-OH and methyl (S)-2-amino-4,4-dimethylpentanoate hydrochloride as a white solid following a similar procedure to **MPI11b** (yield 83%).^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.5 (d, *J* = 8.1 Hz, 1H), 7.3 (d, *J* = 4.2 Hz, 5H), 5.9 (d, *J* = 4.3 Hz, 1H), 5.1 – 4.9 (m, 2H), 4.5 (td, *J* = 9.0, 3.2 Hz, 1H), 4.1 (d, *J* = 5.0 Hz, 2H), 3.6 (s, 3H), 1.7 (dd, *J* = 14.5, 3.2 Hz, 1H), 1.4 (dd, *J* = 14.5, 9.4 Hz, 1H), 1.1 (d, *J* = 74.2 Hz, 12H), 0.9 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.2, 169.2, 156.1, 136.3, 128.5, 128.1, 127.9, 75.6, 66.9, 66.8, 58.4, 52.2, 50.3, 45.7, 30.7, 29.7, 28.2, 16.2.

(S)-2-((2S,3R)-2-(((benzyloxy)carbonyl)amino)-3-(tert-butoxy)butanamido)-4,4-dimethylpentanoic acid (MPI16c). MPI16c was prepared as a white solid following a similar procedure to **MPI11c** (yield 82%).

Methyl (5S,8S,11S)-5-((R)-1-(tert-butoxy)ethyl)-8-(cyclopropylmethyl)-3,6,9-trioxo-11-(((S)-2-oxopyrrolidin-3-yl)methyl)-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (MPI16d). MPI16d was prepared as a white solid following a similar procedure to **MPI11d** (yield 66%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.9 (d, *J* = 7.5 Hz, 1H), 7.5 (d, *J* = 8.4 Hz, 1H), 7.2 (q, *J* = 8.0, 6.1 Hz, 5H), 7.2 (s, 1H), 6.0 (d, *J* = 5.5 Hz, 1H), 5.0 (q, *J* = 12.3 Hz, 2H), 4.5 (td, *J* = 8.4, 4.1 Hz, 1H), 4.4 (ddd, *J* = 11.9, 7.4, 3.5 Hz, 1H), 4.1 (p, *J* = 4.2 Hz, 2H), 3.6 (s, 3H), 3.2 (dd, *J* = 20.8, 9.1 Hz, 2H), 2.3 (qd, *J* = 9.9, 3.9 Hz, 1H), 2.2 – 2.1 (m, 2H), 1.8 – 1.6 (m, 3H), 1.4 (dd, *J* = 14.5, 8.6 Hz, 1H), 1.3 – 0.9 (m, 12H), 0.9 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 179.6, 172.5, 172.0, 168.9, 155.9, 136.0, 128.3, 128.0, 127.8, 75.3, 66.7, 66.7, 58.6, 52.0, 50.9, 50.7, 45.8, 40.3, 38.0, 32.8, 30.2, 29.6, 28.0, 27.6, 16.8.

Benzyl ((2S,3R)-3-(tert-butoxy)-1-(((S)-1-(((S)-1-hydroxy-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)-4,4-dimethyl-1-oxopentan-2-yl)amino)-1-oxobutan-2-yl)carbamate (MPI16e). MPI16e was prepared as a white solid following a similar procedure to **MPI11e** (yield 66%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.1 (d, *J* = 8.7 Hz, 1H), 7.5 (d, *J* = 8.0 Hz, 1H), 7.3 – 7.1 (m, 6H), 6.8 (s, 1H), 5.1 – 4.9 (m, 2H), 4.4 (q, *J* = 6.9 Hz, 2H), 4.1 (dd, *J* = 6.3, 3.8 Hz, 1H), 4.0 – 3.9 (m, 1H), 3.9 (q, *J* = 10.1, 9.2 Hz, 1H), 3.6 – 3.4 (m, 2H), 3.1 (dtd, *J* = 17.2, 9.3, 8.7, 5.0 Hz, 2H), 2.4 – 2.1 (m, 3H), 1.8 – 1.6 (m, 2H), 1.3 (dd, *J* = 14.3, 6.9 Hz, 2H), 1.2 (s, 9H), 0.9 (d, *J* = 6.3 Hz, 3H), 0.8 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 181.7, 172.7, 169.0, 156.3, 136.3, 128.4, 128.0, 127.9, 75.6, 67.2, 66.7, 65.2, 58.6, 53.4, 51.2, 49.1, 45.4, 40.5, 38.5, 33.9, 30.2, 29.5, 28.1, 16.5.

Benzyl ((2S,3R)-3-(tert-butoxy)-1-(((S)-4,4-dimethyl-1-oxo-1-(((S)-1-oxo-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)pentan-2-yl)amino)-1-oxobutan-2-yl)carbamate (MPI16). MPI16 was prepared as a white solid following a similar procedure to **MPI11** (yield 40%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.4 (s, 1H), 8.1 (d, *J* = 6.6 Hz, 1H), 7.5 (d, *J* = 8.3 Hz, 1H), 7.3 – 7.2 (m, 5H), 6.8 (s, 1H), 5.9 (d, *J* = 5.1 Hz, 1H), 5.0 (q, *J* = 12.2 Hz, 2H), 4.5 (td, *J* = 8.5, 4.1 Hz, 1H), 4.3 (dq, *J* = 10.8, 5.4, 4.8 Hz, 1H), 4.1 (d, *J* = 5.8 Hz, 2H), 3.3 – 3.1 (m, 2H), 2.3 (p, *J* = 8.3 Hz, 1H), 2.3 – 2.2 (m, 1H), 1.9 (td, *J* = 12.4, 10.2, 5.7 Hz, 1H), 1.8 (ddt, *J* = 11.8, 8.3, 3.9 Hz, 2H), 1.7 (tt, *J* = 12.3, 6.2 Hz, 1H), 1.4 (dd, *J* = 14.4, 8.6 Hz, 1H), 1.1 (d, *J* = 81.8 Hz, 12H), 0.9 (d, *J* = 7.3 Hz, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 199.6, 180.0, 173.3, 169.3, 156.2, 136.2, 128.6, 128.2, 128.1, 75.6, 67.0, 66.8, 58.9, 57.3, 51.2, 46.1, 40.5, 37.8, 30.5, 29.9, 29.8, 29.7, 28.2, 17.0.

Methyl (S)-2-((2S,3R)-2-(((benzyloxy)carbonyl)amino)-3-(tert-butoxy)butanamido)-3-cyclopropylpropanoate (MPI17b). MPI17b was prepared with Z-Thr(tBu)-OH and methyl (S)-2-amino-3-cyclopropylpropanoate hydrochloride as a white solid following a similar procedure to **MPI11b** (yield 79%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.7 (d, *J* = 7.5 Hz, 1H), 7.3 (d, *J* = 4.3 Hz, 5H), 5.9 (d, *J* = 5.3 Hz, 1H), 5.1 – 5.0 (m, 2H), 4.6 (q, *J* = 6.3 Hz, 1H), 4.2 – 4.1 (m, 2H), 3.7 (s, 3H), 1.6 (ddt, *J* = 27.6, 13.9, 7.1 Hz, 2H), 1.2 (s, 8H), 1.0 (d, *J* = 6.4 Hz, 4H), 0.6 (p, *J* = 6.3 Hz, 1H), 0.4 (d, *J* = 8.1 Hz, 2H), -0.0 (q, *J* = 8.7, 7.3 Hz, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.2, 169.0, 156.0, 136.2, 128.4, 128.0, 127.9, 75.4, 66.8, 66.7, 58.5, 52.7, 52.0, 36.9, 28.1, 16.5, 6.9, 4.2, 4.0.

(S)-2-((2S,3R)-2-(((benzyloxy)carbonyl)amino)-3-(tert-butoxy)butanamido)-3-cyclopropylpropanoic acid (MPI17c). MPI17c was prepared as a white solid following a similar procedure to **MPI11c** (yield 90%).

Methyl (5S,8S,11S)-5-((R)-1-(tert-butoxy)ethyl)-8-(cyclopropylmethyl)-3,6,9-trioxo-11-(((S)-2-oxopyrrolidin-3-yl)methyl)-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (MPI17d). MPI17d was prepared as a white solid following a similar procedure to **MPI11d** (yield 60%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.8 (d, *J* = 7.4 Hz, 1H), 7.6 (d, *J* = 7.9 Hz, 1H), 7.2 (d, *J* = 12.4 Hz, 5H), 7.0 (s, 1H), 5.9 (d, *J* = 6.0 Hz, 1H), 5.0 (t, *J* = 10.8 Hz, 2H), 4.5 (q, *J* = 7.1 Hz, 1H), 4.4 (ddd, *J* = 11.4, 7.7, 3.8 Hz, 1H), 4.1 – 4.0 (m, 2H), 3.6 (s, 3H), 3.2 (dt, *J* = 16.5, 9.1 Hz, 2H), 2.3 (ddq, *J* = 28.6, 13.9, 7.6 Hz, 2H), 2.1 (ddd, *J* = 15.6, 11.7, 4.2 Hz, 1H), 1.8 – 1.6 (m, 2H), 1.6 (q, *J* = 7.7 Hz, 2H), 1.2 (s, 8H), 1.0 (d, *J* = 6.2 Hz, 4H), 0.7 (td, *J* = 8.0, 4.2 Hz, 1H), 0.4 (dd, *J* = 8.1, 5.0 Hz, 2H), 0.0 (d, *J* = 4.9 Hz, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 179.8, 172.1, 171.7, 169.2, 156.1, 136.2, 128.5, 128.1, 128.0, 75.2, 66.8, 58.9, 53.6, 53.5, 52.2, 50.9, 40.4, 38.2, 37.6, 33.0, 28.2, 27.9, 17.3, 7.1, 4.4, 4.2.

Benzyl ((2S,3R)-3-(tert-butoxy)-1-(((S)-3-cyclopropyl-1-(((S)-1-hydroxy-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)-1-oxopropan-2-yl)amino)-1-oxobutan-2-yl)carbamate (MPI17e). MPI17e was prepared as a white solid following a similar procedure to **MPI11e** (yield 85%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.6 (t, *J* = 7.0 Hz, 2H), 7.3 (d, *J* = 4.3 Hz, 5H), 7.0 (s, 1H), 6.1 (d, *J* = 6.3 Hz, 1H), 5.1 – 4.9 (m, 2H), 4.4 (t, *J* = 7.2 Hz, 1H), 4.2 (d, *J* = 6.6 Hz, 1H), 4.2 – 4.0 (m, 2H), 4.0 (ddt, *J* = 13.4, 9.3, 4.5 Hz, 1H), 3.6 – 3.4 (m, 2H), 3.2 (s, 2H), 2.4 – 2.2 (m, 2H), 2.0 (d, *J* = 12.4 Hz, 1H), 1.8 – 1.4 (m, 4H), 1.1 (d, *J* = 66.6 Hz, 12H), 0.6 (t, *J* = 7.0 Hz, 1H), 0.4 (q, *J* = 8.3, 7.4 Hz, 2H), 0.0 (s, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 181.0, 171.8, 169.4, 156.2, 136.1, 128.4, 128.1, 128.0, 75.1, 67.8, 66.8, 65.1, 59.1, 54.0, 49.7, 40.5, 38.2, 37.3, 32.4, 28.1, 28.0, 17.6, 7.2, 4.3, 4.3.

Benzyl ((2S,3R)-3-(tert-butoxy)-1-(((S)-3-cyclopropyl-1-oxo-1-(((S)-1-oxo-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)propan-2-yl)amino)-1-oxobutan-2-yl)carbamate (MPI17). MPI17 was prepared as a white solid following a similar procedure to **MPI11** (yield 54%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.4 (s, 1H), 8.1 (d, *J* = 6.3 Hz, 1H), 7.5 (t, *J* = 8.6 Hz, 1H), 7.3 (s, 5H), 6.4 – 6.1 (m, 1H), 5.9 (d, *J* = 5.4 Hz, 1H), 5.0 (q, *J* = 12.3 Hz, 2H), 4.4 (dt, *J* = 34.9, 6.6 Hz, 1H), 4.3 (p, *J* = 5.6, 4.6 Hz, 1H), 4.1 (t, *J* = 5.9 Hz, 2H), 3.3 (d, *J* = 8.6 Hz, 1H), 3.2 – 3.2 (m, 1H), 2.3 (d, *J* = 14.0 Hz, 1H), 2.2 (s, 2H), 2.0 – 1.9 (m, 1H), 1.9 (t, *J* = 6.8 Hz, 1H), 1.7 (dt, *J* = 15.4, 8.5 Hz, 1H), 1.6 (dd, *J* = 12.9, 6.3 Hz, 1H), 1.1 (d, *J* = 72.7 Hz, 12H), 0.7 (d, *J* = 9.1 Hz, 1H), 0.4 (q, *J* = 8.5 Hz, 2H), 0.0 (d, *J* = 5.1 Hz, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 199.7, 180.1, 172.4, 169.6, 156.3, 136.2, 128.7, 128.4, 128.2, 75.5, 67.1, 66.9, 59.2, 57.7, 55.0, 40.6, 38.0, 37.5, 29.9, 28.6, 28.3, 17.7, 7.4, 4.7, 4.5.

(S)-methyl 2-((S)-2-(((benzyloxy)carbonyl)amino)-3,3-dimethylbutanamido)-4,4-dimethylpentanoate (MPI18b). MPI18b was prepared with Cbz-L-tert-leucine and methyl (S)-2-amino-4,4-dimethylpentanoate hydrochloride as a white solid following a similar procedure to **MPI11b** (yield 81%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.19 (m, 5H), 6.51 – 6.17 (m, 1H), 5.64 – 5.46 (m, 1H), 5.09 (s, 2H), 4.74 – 4.54 (m, 1H), 4.06 – 3.96 (m, 1H), 3.70 (d, *J* = 2.5 Hz, 3H), 1.83 – 1.74 (m, 1H), 1.52 – 1.38 (m, 1H), 1.00 (d, *J* = 2.4 Hz, 9H), 0.91 (d, *J* = 2.6 Hz, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*): δ 173.5, 170.2, 156.4, 136.3, 128.5, 128.1, 127.92, 127.90, 66.9, 60.4, 52.3, 49.7, 46.1, 34.8, 30.7, 29.4, 26.4, 21.1.

(S)-2-((S)-2-(((benzyloxy)carbonyl)amino)-3,3-dimethylbutanamido)-4,4-dimethylpentanoic acid (MPI18c). MPI18c was prepared as a white solid following a similar procedure to **MPI11c** (yield 79%). ^{1}H NMR (400 MHz, Chloroform-*d*): δ 7.40 – 7.27 (m, 5H), 7.03 – 6.56 (m, 1H), 5.85 (s, 1H), 5.08 (q, *J* = 12.5 Hz, 2H), 4.64 – 4.42 (m, 1H), 4.14 – 3.94 (m, 1H), 1.85 – 1.72 (m, 1H), 1.59 – 1.43 (m, 1H), 0.94 (s, 9H), 0.89 (s, 9H).

(5S,8S,11S)-methyl 5-(tert-butyl)-8-neopentyl-3,6,9-trioxo-11-(((S)-2-oxopyrrolidin-3-yl)methyl)-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (MPI18d). MPI18d was prepared as a white solid following a similar procedure to **MPI11d** (yield 60%). ^{1}H NMR (400 MHz, Chloroform-*d*): δ 7.73 (d, *J* = 8.2 Hz, 1H), 7.60 (d, *J* = 9.0 Hz, 1H), 7.38 – 7.27 (m, 5H), 7.18 – 7.08 (m, 1H), 5.62 (d, *J* = 9.8 Hz, 1H), 5.06 (d, *J* = 2.4 Hz, 2H), 4.75 – 4.61 (m, 1H), 4.61 – 4.50 (m, 1H), 4.00 (dd, *J* = 9.6, 5.3 Hz, 1H), 3.67 (s, 3H), 3.41 – 3.21 (m, 2H), 2.51 – 2.32 (m, 2H), 2.29 – 2.16 (m, 1H), 1.94 – 1.74 (m, 3H), 1.49 – 1.44 (m, 1H), 0.96 (s, 9H), 0.89 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*): δ 179.9, 173.0, 171.9, 170.2, 156.6, 136.3, 128.5, 128.5, 128.2, 128.1, 127.9, 67.0, 62.7, 55.5, 52.3, 50.8, 50.5, 46.8, 40.6, 38.2, 34.6, 30.6, 29.5, 27.8, 26.5, 26.4.

Benzyl ((S)-1-(((S)-1-(((S)-1-hydroxy-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)-4,4-dimethyl-1-oxopentan-2-yl)amino)-3,3-dimethyl-1-oxobutan-2-yl)carbamate (MPI18e). MPI18e was prepared as a white solid following a similar procedure to **MPI11e** (yield 67%). ^{1}H NMR (400 MHz, Chloroform-*d*): δ 8.73 – 8.45 (m, 1H), 8.15 – 7.94 (m, 1H), 7.62 – 7.43 (m, 1H), 7.42 – 7.25 (H), 5.83 – 5.63 (m, 1H), 5.07 (d, *J* = 4.2 Hz, 2H), 4.93 – 4.75 (m, 1H), 4.49 – 4.33 (m, 1H), 4.01 – 3.85 (m, 1H), 3.85 – 3.67 (m, 1H), 3.51 – 3.22 (m, 3H), 3.22 – 3.03 (m, 1H), 2.35 – 2.23 (m, 1H), 22.20 – 2.10 (m, 1H), 1.90 – 1.55 (m, 4H), 1.55 – 1.37 (m, 1H), 0.93 (s, 9H), 0.90 (s, 9H).^{13}C NMR (100 MHz, Chloroform-*d*): δ 180.3, 173.5, 169.8, 156.5, 136.2, 128.6, 128.5, 128.2, 128.1, 128.0, 67.2, 65.0, 61.7, 53.4, 50.5, 47.2, 40.5, 38.2, 35.3, 34.8, 30.6, 29.6, 26.5.

Benzyl ((S)-1-(((S)-4,4-dimethyl-1-oxo-1-(((S)-1-oxo-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)pentan-2-yl)amino)-3,3-dimethyl-1-oxobutan-2-yl)carbamate (MPI18). MPI18 was prepared as a white solid following a similar procedure to **MPI11** (yield 67%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.50 (s, 1H), 8.16 – 7.99 (m, 1H), 7.42 – 7.28 (m,, 5H), 6.90 – 6.74(m, 1H), 5.55 (dd, *J* = 22.5, 9.6 Hz, 1H), 5.08 (d, *J* = 2.7 Hz, 2H), 4.72 – 4.58 (m, 1H), 4.38 (dd, *J* = 10.6, 5.9 Hz, 1H), 3.96 (dd, *J* = 13.1, 9.4 Hz, 1H), 3.47 – 3.25 (m, 2H), 2.51 – 2.29 (m, 2H), 2.09 – 1.77 (m, 4H), 1.53 – 1.43 (m, 1H), 1.13 – 0.71 (m, 18H). ^{13}C NMR (100 MHz, Chloroform-*d*): δ 199.3, 18.0, 173.7, 170.3, 156.5, 136.3, 128.5, 128.2, 127.9, 67.1, 62.6, 57.0, 50.8, 46.6, 40.5, 37.8, 36.5, 34.7, 30.6, 29.9, 29.5, 28.0, 26.5.

Methyl (S)-2-((S)-2-(((benzyloxy)carbonyl)amino)-3,3-dimethylbutanamido)-3-cyclopropylpropanoate (MPI19b). MPI19b was prepared with Cbz-L-tert-leucine and methyl (S)-2-amino-3-cyclopropylpropanoate hydrochloride as a colorless oil following a similar procedure to **MPI11b** (yield 73%).

(S)-2-((S)-2-(((benzyloxy)carbonyl)amino)-3,3-dimethylbutanamido)-3-cyclopropylpropanoic acid (MPI19c). MPI19c was prepared as a white solid following a similar procedure to **MPI11c** (yield 82%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.28 (m, 5H), 6.89 (d, *J* = 7.6 Hz, 1H), 5.85 (d, *J* = 9.7 Hz, 1H), 5.10 (s, 2H), 4.67 (q, *J* = 7.7, 6.3 Hz, 1H), 4.16 (d, *J* = 9.7 Hz, 1H), 1.72 (dtd, *J* = 27.3,

13.9, 6.4 Hz, 2H), 0.99 (s, 9H), 0.67 (pd, *J* = 7.5, 3.7 Hz, 1H), 0.42 (td, *J* = 8.1, 5.0 Hz, 2H), 0.07 (td, *J* = 4.7, 2.3 Hz, 2H).

Methyl (5S,8S,11S)-5-(tert-butyl)-8-(cyclopropylmethyl)-3,6,9-trioxo-11-(((S)-2-oxopyrrolidin-3-yl)methyl)-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (MPI19d). MPI19d was prepared as a white solid following a similar procedure to **MPI11d** (yield 64%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.80 (d, *J* = 7.4 Hz, 1H), 7.41 – 7.28 (m, 5H), 6.96 (d, *J* = 8.3 Hz, 1H), 6.33 (d, *J* = 9.9 Hz, 1H), 5.55 (t, *J* = 10.4 Hz, 1H), 5.09 (s, 2H), 4.67 – 4.48 (m, 2H), 3.96 (t, *J* = 9.2 Hz, 1H), 3.71 (s, 3H), 3.43 – 3.27 (m, 2H), 2.53 – 2.32 (m, 2H), 2.17 (ddd, J = 16.5, 12.2, 4.8 Hz, 1H), 1.87 (dddd, J = 17.6, 11.4, 8.6, 2.9 Hz, 1H), 1.80 – 1.68 (m, 2H), 1.60 (dt, *J* = 13.9, 7.0 Hz, 1H), 0.99 (s, 9H), 0.73 (td, *J* = 7.5, 3.9 Hz, 1H), 0.42 (ddq, *J* = 11.4, 7.7, 3.8 Hz, 2H), 0.16 – 0.01 (m, 2H).

Benzyl ((S)-1-(((S)-3-cyclopropyl-1-(((S)-1-hydroxy-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)-1-oxopropan-2-yl)amino)-3,3-dimethyl-1-oxobutan-2-yl)carbamate (MPI19e). MPI19e was prepared as a white solid following a similar procedure to **MPI11e**. It was used in the next step without further purification.

Benzyl ((S)-1-(((S)-3-cyclopropyl-1-oxo-1-(((S)-1-oxo-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)propan-2-yl)amino)-3,3-dimethyl-1-oxobutan-2-yl)carbamate (MPI19). MPI19 was prepared as a white solid following a similar procedure to **MPI11** (yield 48%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.51 (s, 1H), 8.20 (d, *J* = 6.7 Hz, 1H), 7.32 (d, *J* = 4.2 Hz, 5H), 7.17 (d, *J* = 8.3 Hz, 1H), 6.67 (s, 1H), 5.68 (d, J = 9.4 Hz, 1H), 5.08 (s, 2H), 4.67 (q, J = 7.3 Hz, 1H), 4.42 (p, *J* = 4.9 Hz, 1H), 4.02 (d, *J* = 9.4 Hz, 1H), 3.31 (dq, *J* = 17.4, 9.5 Hz, 2H), 2.44 (p, *J* = 8.1 Hz, 1H), 2.34 (dt, *J* = 14.9, 8.5 Hz, 1H), 2.07 – 1.86 (m, 2H), 1.86 – 1.74 (m, 1H), 1.65 (ddt, J = 20.5, 13.6, 6.9 Hz, 2H), 0.98 (s, 9H), 0.70 (h, *J* = 7.1, 6.6 Hz, 1H), 0.43 (d, *J* = 8.0 Hz, 2H), 0.08 (d, *J* = 5.1 Hz, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 199.3, 180.0, 172.6, 170.4, 156.6, 136.3, 128.5, 128.2, 128.0, 77.3, 67.1, 62.9, 57.4, 53.7, 40.6, 37.9, 37.7, 34.7, 29.9, 28.4, 26.5, 7.3, 4.5, 4.3.

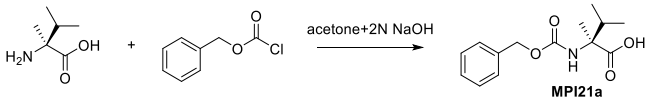
(S)-methyl 2-((S)-2-(((benzyloxy)carbonyl)amino)-2-cyclopropylacetamido)-4,4-dimethylpentanoate (MPI20b). MPI20b was obtained from methyl (S)-2-amino-4,4-dimethylpentanoate hydrochloride and (S)-2-(((benzyloxy)carbonyl)amino)-2-cyclopropylacetic acid following a similar procedure to **MPI11b.** The crude product was purified by silica gel column chromatography (15-50% EtOAc in n-hexane) to afford the **MPI20b** as a white solid (yield 80%). ^{1}H NMR (400 MHz, Chloroform-*d*): δ 7.42 – 7.28 (m, 5H), 6.53 – 6.37 (m, 1H), 5.63 – 5.44 (m, 1H), 5.09 (s, 2H), 4.64 (td, *J* = 8.7, 3.5 Hz, 1H), 3.71 (s, 3H), 3.68 – 3.60 (m, 1H), 1.77 (dd, *J* = 14.4, 3.6 Hz, 1H), 1.48 (dd, *J* = 14.4, 8.8 Hz, 1H), 1.22 – 1.07 (m, 1H), 0.93 (s, 9H), 0.72 – 0.41 (m, 4H). ^{13}C NMR (100 MHz, Chloroform-*d*): δ 173.59, 170.61, 156.26, 136.20, 128.54, 128.17, 128.03, 67.06, 60.43, 52.39, 49.90, 46.06, 30.72, 29.50, 14.21, 3.60, 2.99.

(S)-2-((S)-2-(((benzyloxy)carbonyl)amino)-2-cyclopropylacetamido)-4,4-dimethylpentanoic acid (MPI20c). MPI20c was prepared as a white solid following a similar procedure to **MPI11c** (yield 83%)**.** ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.29 (m, 5H), 6.61 (d, *J* = 8.2 Hz, 1H), 5.72 (d, *J* = 7.6 Hz, 1H), 5.09 (s, 2H), 4.62 (td, *J* = 8.7, 3.0 Hz, 1H), 3.72 – 3.55 (m, 1H), 1.91 – 1.81 (m, 1H), 1.51 (dd, *J* = 14.5, 9.1 Hz, 1H), 1.20 – 1.06 (m, 1H), 0.94 (s, 9H), 0.69 – 0.36 (m, 4H). ^{13}C NMR (100 MHz, Chloroform-*d*): δ 176.37, 171.31, 156.49, 136.06, 128.56, 128.24, 128.06, 67.97, 67.24, 50.01, 45.68, 30.77, 29.49, 25.61, 13.90, 3.66, 3.15.

(5S,8S,11S)-methyl 5-cyclopropyl-8-neopentyl-3,6,9-trioxo-11-(((S)-2-oxopyrrolidin-3-yl)methyl)-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (MPI20d). MPI20d was prepared as a white solid following a similar procedure to **MPI11d** (yield 49%). ^{1}H NMR (400 MHz, Chloroform-*d*): δ 7.89 – 7.74 (m, 1H), 7.30 – 7.19 (m, 5H), 6.75 (s, 1H), 5.85 – 5.67 (m, 1H), 5.00 (d, *J* = 5.2 Hz, 2H), 4.55 (td, *J* = 8.7, 3.5 Hz, 1H), 4.49 – 4.34 (m, 1H), 3.61 (s, 3H), 3.60 – 3.52 (m, 1H), 3.28 – 3.14 (m, 2H), 2.39 – 2.19 (m, 2H), 2.11 (td, *J* = 12.7, 11.7, 4.1 Hz, 1H), 1.87 – 1.61 (m, 3H), 1.12 – 0.98 (m, 1H), 0.85 (s, 9H), 0.57 – 0.23 (m, 4H). ^{13}C NMR (100 MHz, Chloroform-*d*): δ 179.90, 173.11, 172.07, 170.88, 156.30, 136.24, 128.52, 128.15, 128.00, 67.02, 58.86, 55.27, 52.36, 50.89, 45.93, 40.57, 38.33, 30.55, 29.60, 28.01, 12.47, 3.30, 3.18.

Benzyl ((S)-1-cyclopropyl-2-(((S)-1-(((S)-1-hydroxy-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)-4,4-dimethyl-1-oxopentan-2-yl)amino)-2-oxoethyl)carbamate (MPI20e). MPI20e was prepared as a white solid following a similar procedure to **MPI11e** (yield 79%). ^{1}H NMR (400 MHz, Chloroform-*d*): δ 7.70 – 7.42 (m, 2H), 7.38 – 7.21 (m, 5H), 6.79 (d, *J* = 5.1 Hz, 1H), 6.16 – 5.91 (m, 1H), 5.05 (q, *J* = 12.4 Hz, 2H), 4.62 – 4.43 (m, 1H), 4.06 – 3.87 (m, 1H), 3.63 – 3.54 (m, 2H), 3.24 (t, *J* = 9.2 Hz, 2H), 2.44 – 2.22 (m, 2H), 1.91 – 1.68 (m, 2H), 1.62 – 1.44 (m, 2H), 1.17 – 1.02 (m, 1H), 0.90 (s, 9H), 0.57 – 0.42 (m, 3H), 0.42 – 0.30 (m, 1H).

Benzyl ((S)-1-cyclopropyl-2-(((S)-4,4-dimethyl-1-oxo-1-(((S)-1-oxo-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)pentan-2-yl)amino)-2-oxoethyl)carbamate (MPI20). MPI20 was prepared as a white solid following a similar procedure to **MPI11** (yield 62%). ^{1}H NMR (400 MHz, Chloroform-*d*): δ 9.48 (s, 1H), 8.22 (s, 1H), 7.40 – 7.27 (m, 5H), 7.06 – 6.87 (m, 1H), 6.51 – 6.29 (m, 1H), 5.78 (s, 1H), 5.07 (s, 2H), 4.68 – 4.52 (m, 1H), 4.36 – 4.24 (m, 1H), 3.56 (ddd, *J* = 9.2, 7.0, 2.4 Hz, 1H), 3.36 – 3.19 (m, 2H), 2.50 – 2.28 (m, 2H), 2.07 – 1.84 (m, 4H), 1.84 – 1.72 (m, 1H), 1.21 – 1.07 (m, 1H), 0.95 (s, 9H), 0.66 – 0.35 (m, 4H). ^{13}C NMR (100 MHz, Chloroform-*d*): δ 199.77, 180.13, 173.80, 171.01, 156.44, 136.16, 128.55, 128.21, 128.04, 67.10, 59.12, 57.47, 51.03, 45.90, 40.59, 38.03, 30.62, 30.01, 29.64, 28.29, 13.85, 3.29, 3.22.



(S)-2-(((benzyloxy)carbonyl)amino)-2,3-dimethylbutanoic acid (MPI21a). H-L-(αMe)Val-OH (1.0 g, 7.63 mmol, 1.0 equiv) was dissolved in a 1:1 mixture of 1N NaOH (20 mL) : acetone (20 mL) and kept at 0 °C . Z-Cl (1.25 mL, 0.877 mmol, 0.1 equiv), diluted in acetone (5 mL), was added drop wise in 40 min and the pH was adjusted to 10.8-11.0 with 2N NaOH. After stirring the reaction mixture at room temperature for 5 h, Acetone was evaporated under reduce pressure and NaOH 2 N was added (20 mL). The unreacted Z-Cl was extracted with Et_2O. The aqueous solution was acidified with $KHSO_4$, the product was extracted with EtOAc (4x30 mL). The organic phase was washed with water (3x30 mL), and the solvent was evaporated at reduced pressure. The solid colorless product was obtained in 76% yield. ^{1}H NMR (400 MHz, Chloroform-*d*): δ 10.38, 7.38, 7.37, 7.36, 7.36, 7.35, 7.34, 7.33, 5.46, 5.12, 1.61, 1.03, 1.01, 0.99, 0.98.

(S)-methyl 2-((S)-2-(((benzyloxy)carbonyl)amino)-2,3-dimethylbutanamido)-4,4-dimethylpentanoate (MPI21b). MPI21b was obtained from methyl (S)-2-amino-4,4-dimethylpentanoate hydrochloride and **MPI21a** following a similar procedure to **MPI11b.** The crude product was purified by silica gel column chromatography (15-

50% EtOAc in n-hexane) to afford the **MPI21b** as a white solid (yield 78%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.53 – 7.30 (m, 5H), 6.93 (s, 1H), 5.24 (s, 1H), 5.13 – 5.01 (m, 2H), 4.68 – 4.51 (m, 1H), 3.68 (s, 3H), 1.77 (dd, *J* = 14.4, 3.6 Hz, 1H), 1.50 (dd, *J* = 14.5, 8.9 Hz, 1H), 1.45 (s, 3H), 1.08 – 0.67 (m, 15H).

(S)-2-((S)-2-(((benzyloxy)carbonyl)amino)-2,3-dimethylbutanamido)-4,4-dimethylpentanoic acid (MPI21c). MPI21c was prepared as a white solid following a similar procedure to **MPI11c**. The crude **MPI21c** was used in the next step without further purification.

(5S,8S,11S)-methyl 5-isopropyl-5-methyl-8-neopentyl-3,6,9-trioxo-11-(((S)-2-oxopyrrolidin-3-yl)methyl)-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (MPI21d). MPI21d was prepared as a white solid following a similar procedure to **MPI11d** (yield 63%). ^{1}H NMR (400 MHz, Methanol-d_4) δ 8.35 (d, *J* = 8.1 Hz, 1H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.37 – 7.13 (m, 5H), 6.93 (s, 1H), 5.14 – 4.93 (m, 2H), 4.43 – 4.19 (m, 2H), 3.60 (s, 3H), 3.20 – 3.10 (m, 2H), 2.45 – 2.33 (m, 1H), 2.28 – 2.18 (m, 1H), 1.97 – 1.87 (m, 1H), 1.77 – 1.61 (m, 3H), 1.50 (dd, *J* = 14.4, 8.3 Hz, 1H), 1.32 (s, 3H), 0.93 – 0.62 (m, 15H). ^{13}C NMR (100 MHz, Methanol-d_4): δ 180.36, 174.44, 174.38, 172.08, 156.83, 136.80, 128.18, 128.09, 127.65, 127.62, 66.51, 62.93, 54.47, 51.65, 51.37, 50.73, 44.60, 42.43, 40.04, 38.06, 30.08, 28.71, 17.34, 17.12, 16.55, 16.16, 15.90.

Benzyl ((S)-1-(((S)-1-(((S)-1-hydroxy-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)-4,4-dimethyl-1-oxopentan-2-yl)amino)-2,3-dimethyl-1-oxobutan-2-yl)carbamate (MPI21e). MPI21e was prepared as a white solid following a similar procedure to **MPI11e** (yield 70%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.27 (m, 5H), 6.56 (d, *J* = 6.3 Hz, 1H), 5.99 (s, 1H), 5.47 (s, 1H), 5.22 – 5.07 (m, 2H), 4.23 (ddd, *J* = 9.1, 6.2, 2.4 Hz, 1H), 4.03 (s, 1H), 3.74 – 3.64 (m, 1H), 3.63 – 3.54 (m, 1H), 3.36 – 3.19 (m, 2H), 2.46 – 2.29 (m, 2H), 2.22 – 1.96 (m, 2H), 2.01 – 1.88 (m, 2H), 1.76 (dd, *J* = 12.2, 9.0 Hz, 1H), 1.41 (s, 3H), 1.29 (dd, *J* = 14.7, 9.6 Hz, 1H), 1.02 – 0.77 (m, 15H). ^{13}C NMR (100 MHz, Chloroform-*d*): δ 180.44, 173.62, 173.41, 156.25, 135.91, 128.67, 128.46, 128.37, 67.62, 65.70, 63.37, 53.46, 53.04, 50.63, 45.80, 40.33, 35.36, 32.36, 30.69, 29.69, 28.38, 17.45, 17.33, 17.11, 17.00.

Benzyl ((S)-1-(((S)-4,4-dimethyl-1-oxo-1-(((S)-1-oxo-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)pentan-2-yl)amino)-2,3-dimethyl-1-oxobutan-2-yl)carbamate (MPI21). MPI21 was prepared as a white solid following a similar procedure to **MPI11** (yield 78%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.52 (s, 1H), 8.07 (d, *J* = 7.7 Hz, 1H), 7.50 – 7.26 (m, 5H), 6.77 (d, *J* = 7.4 Hz, 1H), 6.39 – 6.20 (m, 1H), 5.47 (s, 1H), 5.07 (d, *J* = 3.2 Hz, 2H), 4.57 – 4.37 (m, 1H), 4.33 – 4.16 (m, 1H), 3.35 – 3.18 (m, 2H), 2.44 – 2.29 (m, 2H), 2.14 – 2.05 (m, 2H), 1.98 – 1.92 (m, 1H), 1.90 – 1.81 (m, 1H), 1.74 (t, *J* = 9.8 Hz, 1H), 1.40 (s, 3H), 0.97 – 0.85 (m, 15H). ^{13}C NMR (100 MHz, Chloroform-*d*): δ 200.59, 173.83, 173.43, 173.17, 156.23, 136.06, 128.70, 128.63, 128.35, 128.16, 67.48, 67.28, 63.36, 57.12, 51.83, 45.78, 40.35, 37.64, 34.88, 30.65, 30.24, 29.67, 28.12, 17.44, 17.36, 17.09, 17.04.

Methyl (S)-2-(2-(((benzyloxy)carbonyl)amino)-2-methylpropanamido)-4,4-dimethylpentanoate (MPI22b). MPI22b was obtained from methyl (S)-2-amino-4,4-dimethylpentanoate hydrochloride and Z-Aib-OH following a similar procedure to **MPI11b.** The crude product was purified by silica gel column chromatography (15-50% EtOAc in hexanes as the eluent) to afford the **MPI22b** as a colorless oil (yield 79%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 (s, 5H), 6.68 (s, 1H), 5.31 (s, 1H),

5.08 (s, 2H), 4.57 (t, *J* = 8.4 Hz, 1H), 3.69 (s, 3H), 1.91 – 1.64 (m, 2H), 1.53 (d, *J* = 6.0 Hz, 6H), 0.94 (s, 9H).

(S)-2-(2-(((benzyloxy)carbonyl)amino)-2-methylpropanamido)-4,4-dimethylpentanoic acid (MPI22c). MPI22c was prepared as a white solid following a similar procedure to **MPI11c** (yield 85%).

Methyl (8S,11S)-5,5-dimethyl-8-neopentyl-3,6,9-trioxo-11-(((S)-2-oxopyrrolidin-3-yl)methyl)-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (MPI22d). MPI22d was prepared as a white solid following a similar procedure to **MPI11d** (yield 66%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.81 (d, *J* = 7.8 Hz, 1H), 7.41 – 7.29 (m, 5H), 6.67 (d, *J* = 8.2 Hz, 1H), 5.77 (s, 1H), 5.43 (s, 1H), 5.17 – 5.01 (m, 2H), 4.63 – 4.43 (m, 2H), 3.71 (s, 3H), 3.40 – 3.16 (m, 2H), 2.48 – 2.32 (m, 2H), 2.30 – 2.16 (m, 1H), 2.15 – 1.95 (m, 1H), 1.95 – 1.82 (m, 2H), 1.52 (d, *J* = 11.7 Hz, 6H), 1.49 – 1.36 (m, 1H), 0.95 (s, 9H).

Benzyl (1-(((S)-1-(((S)-1-hydroxy-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)-4,4-dimethyl-1-oxopentan-2-yl)amino)-2-methyl-1-oxopropan-2-yl)carbamate (MPI22e). MPI22e was prepared as a white solid following a similar procedure to **MPI11e**. The crude **MPI22e** was used in the next step without further purification.

Benzyl (1-(((S)-4,4-dimethyl-1-oxo-1-(((S)-1-oxo-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)pentan-2-yl)amino)-2-methyl-1-oxopropan-2-yl)carbamate (MPI22). MPI22 was prepared as a white solid following a similar procedure to **MPI11** (yield 50%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.52 (s, 1H), 8.15 (d, *J* = 7.6 Hz, 1H), 7.33 (s, 5H), 6.83 (d, *J* = 8.0 Hz, 1H), 6.12 (s, 1H), 5.71 (s, 1H), 5.05 (q, *J* = 12.2 Hz, 2H), 4.58 – 4.42 (m, 1H), 4.23 (ddd, *J* = 11.3, 7.6, 3.9 Hz, 1H), 3.33 – 3.16 (m, 2H), 2.49 – 2.29 (m, 2H), 2.13 – 1.97 (m, 2H), 1.96 – 1.82 (m, 2H), 1.82 – 1.68 (m, 1H), 1.47 (d, *J* = 6.8 Hz, 6H), 0.94 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 200.5, 180.0, 173.8, 156.0, 136.0, 128.6, 128.3, 128.1, 67.2, 57.3, 57.1, 51.6, 45.5, 40.4, 37.7, 30.7, 30.2, 29.6, 28.3, 26.0.

Methyl (S)-2-(1-(((benzyloxy)carbonyl)amino)cyclopropane-1-carboxamido)-3-cyclohexylpropanoate (MPI23b). MPI23b was obtained from H-Cha-OMe hydrochloride and 1-(((benzyloxy)carbonyl)amino)cyclopropane-1-carboxylic acid following a similar procedure to **MPI11b.** The crude product was purified by silica gel column chromatography (50-100% EtOAc in hexanes as the eluent) to afford the **MPI23b**. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.29 (d, *J* = 3.9 Hz, 5H), 6.72 (s, 1H), 5.05 (d, *J* = 12.0 Hz, 2H), 4.60 – 4.33 (m, 1H), 3.63 (s, 3H), 1.78 – 0.66 (m, 18H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.61, 171.53, 135.97, 128.63, 52.27, 50.58, 40.06, 34.09, 33.38, 32.57, 26.35, 26.15, 25.98.

(S)-2-(1-(((benzyloxy)carbonyl)amino)cyclopropane-1-carboxamido)-3-cyclohexylpropanoic acid (MPI23c). MPI23c was prepared as a white solid following a similar procedure to **MPI11c**. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.26 (s, 5H), 6.84 (d, *J* = 11.3 Hz, 1H), 5.80 (s, 1H), 5.25 – 4.94 (m, 2H), 4.49 (s, 1H), 1.59 (dd, *J* = 13.3, 6.7 Hz, 6H), 1.51 – 1.24 (m, 3H), 1.20 (s, 2H), 1.06 – 0.91 (m, 4H), 0.81 (s, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 176.01, 172.64, 128.63, 128.35, 67.96, 50.83, 34.07, 33.40, 32.43, 29.72, 26.34, 26.13, 25.95, 25.60.

Methyl (S)-2-((S)-2-(1-(((benzyloxy)carbonyl)amino)cyclopropane-1-carboxamido)-3-cyclohexylpropanamido)-3-((S)-2-oxopyrrolidin-3-yl)propanoate (MPI23d). MPI23d was prepared as a white solid following a similar

procedure to **MPI11d** (yield 62%). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.32 – 7.13 (m, 5H), 5.14 – 4.94 (m, 2H), 4.47 – 4.26 (m, 2H), 3.62 (s, 3H), 3.13 (d, *J* = 7.5 Hz, 2H), 2.39 (d, *J* = 10.3 Hz, 1H), 2.22 – 2.02 (m, 2H), 1.82 – 1.43 (m, 9H), 1.43 – 1.30 (m, 2H), 1.17 (d, *J* = 12.4 Hz, 2H), 1.11 (q, *J* = 8.4, 7.6 Hz, 2H), 0.96 (d, *J* = 8.3 Hz, 2H), 0.89 – 0.70 (m, 2H).

Benzyl (1-(((S)-3-cyclohexyl-1-(((S)-1-hydroxy-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)-1-oxopropan-2-yl)carbamoyl)cyclopropyl)carbamate (MPI23e). MPI23e was prepared as a white solid following a similar procedure to **MPI11e** (yield 61%). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.32 – 7.09 (m, 5H), 5.09 (d, *J* = 12.4 Hz, 1H), 4.98 (d, *J* = 12.4 Hz, 1H), 4.35 (dd, *J* = 10.4, 4.9 Hz, 1H), 3.96 – 3.74 (m, 1H), 3.42 (dd, *J* = 11.5, 5.9 Hz, 2H), 2.37 – 2.14 (m, 2H), 1.87 (t, *J* = 12.5 Hz, 1H), 1.70 – 1.41 (m, 9H), 1.42 – 1.28 (m, 2H), 1.28 – 1.19 (m, 3H), 1.19 – 0.97 (m, 4H), 0.97 – 0.72 (m, 3H). ^{13}C NMR (100 MHz, Methanol-d_4) δ 181.30, 173.80, 173.46, 136.60, 128.14, 127.59, 66.73, 64.06, 48.26, 48.05, 47.84, 47.63, 47.41, 47.20, 46.99, 40.16, 38.24, 35.21, 34.08, 33.57, 27.55, 26.19, 26.04, 25.80.

Benzyl (1-(((S)-3-cyclohexyl-1-oxo-1-(((S)-1-oxo-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)propan-2-yl)carbamoyl)cyclopropyl)carbamate (MPI23). MPI23 was prepared as a white solid following a similar procedure to **MPI11** (yield 41%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.43 (d, *J* = 24.1 Hz, 1H), 8.30 (s, 1H), 7.27 (d, *J* = 4.2 Hz, 5H), 6.86 (d, *J* = 56.9 Hz, 1H), 6.25 (s, 1H), 5.88 (d, *J* = 34.9 Hz, 1H), 5.18 – 4.90 (m, 2H), 4.56 (q, *J* = 4.1 Hz, 1H), 4.51 – 4.35 (m, 1H), 4.20 (s, 1H), 3.24 (d, *J* = 10.0 Hz, 2H), 2.45 – 2.20 (m, 2H), 2.03 – 1.66 (m, 7H), 1.52 – 1.35 (m, 3H), 1.22 (d, *J* = 9.4 Hz, 1H), 1.14 – 1.00 (m, 4H), 0.98 – 0.67 (m, 4H).

(S)-methyl 2-((S)-2-(((benzyloxy)carbonyl)amino)-2-cyclopropylacetamido)-3-cyclopropylpropanoate (MPI24b). MPI24b was obtained from methyl (S)-2-amino-3-cyclopropylpropanoate hydrochloride and (S)-2-(((benzyloxy)carbonyl)amino)-2-cyclopropylacetic acid following a similar procedure to **MPI11b.** The crude product was purified by silica gel column chromatography (15-50% EtOAc in hexanes as the eluent) to afford the **MPI24b** (yield 80%). ^{1}H NMR (400 MHz, Chloroform-*d*): δ 7.58 – 7.21 (m, 5H), 6.77 (s, 1H), 5.68 – 5.49 (m, 1H), 5.10 (s, 2H), 4.66 (q, *J* = 6.4 Hz, 1H), 3.75 (s, 3H), 3.71 – 3.59 (m, 1H), 1.70 (q, *J* = 6.4 Hz, 2H), 1.20 – 1.04 (m, 1H), 0.68 – 0.41 (m, 6H), 0.20 – -0.02 (m, 2H).^{13}C NMR (100 MHz, Chloroform-*d*): δ 172.51, 171.10, 156.27, 136.21, 128.52, 128.15, 127.98, 67.05, 58.58, 52.79, 52.36, 36.91, 14.30, 6.82, 4.20, 4.10, 3.57, 3.16.

(S)-2-((S)-2-(((benzyloxy)carbonyl)amino)-2-cyclopropylacetamido)-3-cyclopropylpropanoic acid (MPI24c). MPI24c was prepared as a white solid following a similar procedure to **MPI11c** (yield 85%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.96 (d, *J* = 7.9 Hz, 1H), 7.43 (d, *J* = 8.2 Hz, 1H), 7.34 – 7.16 (m, 5H), 4.96 (s, 2H), 4.23 (td, *J* = 7.8, 5.3 Hz, 1H), 3.57 (t, *J* = 8.3 Hz, 1H), 1.64 – 1.35 (m, 2H), 1.07 – 0.87 (m, 1H), 0.82 – 0.64 (m, 1H), 0.50 – 0.19 (m, 6H), 0.12 – -0.09 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 173.78, 171.30, 156.15, 137.51, 128.78, 128.22, 128.13, 65.83, 58.15, 52.78, 36.62, 14.20, 8.04, 4.85, 4.53, 3.54, 3.00.

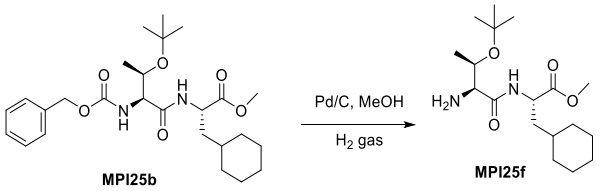
(5S,8S,11S)-methyl 5-cyclopropyl-8-(cyclopropylmethyl)-3,6,9-trioxo-11-(((S)-2-oxopyrrolidin-3-yl)methyl)-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (MPI24d). MPI24d was prepared as a white solid following a similar procedure to **MPI11d** (yield 50%). ^{1}H NMR (400 MHz, Chloroform-*d*): δ 8.03 (d, *J* = 7.2 Hz, 1H), 7.37 – 7.26 (m, 5H), 7.19 (d, *J* = 8.0 Hz, 1H), 6.53 (s, 1H), 5.83 (d, *J* = 7.4 Hz, 1H), 5.08 (d, *J* = 3.0 Hz, 2H), 4.63 (q, *J* = 7.1 Hz, 1H), 4.57 – 4.43 (m, 1H), 3.70 (s, 4H),

3.40 – 3.18 (m, 2H), 2.51 – 2.28 (m, 2H), 2.26 – 2.09 (m, 1H), 1.95 – 1.76 (m, 2H), 1.76 – 1.55 (m, 2H), 1.52 – 1.38 (m, 1H), 1.20 – 1.03 (m, 1H), 0.79 – 0.66 (m, 1H), 0.65 – 0.33 (m, 6H), 0.17 – -0.03 (m, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*): δ 179.99, 172.09, 171.94, 170.97, 156.32, 136.26, 128.53, 128.15, 128.03, 67.01, 54.81, 53.65, 52.43, 51.53, 40.60, 38.51, 37.45, 33.14, 28.31, 14.36, 7.10, 4.49, 4.22, 3.49, 3.20.

Benzyl ((S)-1-cyclopropyl-2-(((S)-3-cyclopropyl-1-(((S)-1-hydroxy-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)-1-oxopropan-2-yl)amino)-2-oxoethyl)carbamate (MPI24e). MPI24e was prepared as a white solid following a similar procedure to **MPI11e** (yield 79%). ^{1}H NMR (400 MHz, Methanol-d_4): δ 7.34 – 6.98 (m, 5H), 5.06 – 4.87 (m, 2H), 4.23 (d, *J* = 7.3 Hz, 1H), 3.85 (d, *J* = 10.5 Hz, 1H), 3.48 – 3.27 (m, 3H), 3.16 – 3.09 (m, 1H), 2.41 – 2.25 (m, 1H), 2.27 – 2.13 (m, 1H), 1.88 – 1.77 (m, 1H), 1.70 – 1.31 (m, 4H), 1.05 – 0.90 (m, 1H), 0.73 – 0.59 (m, 1H), 0.53 – 0.20 (m, 6H), 0.15 – -0.11 (m, 2H).

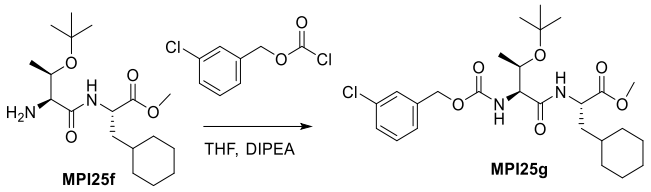
Benzyl ((S)-1-cyclopropyl-2-(((S)-3-cyclopropyl-1-oxo-1-(((S)-1-oxo-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)propan-2-yl)amino)-2-oxoethyl)carbamate (MPI24). MPI24 was prepared as a white solid following a similar procedure to **MPI11** (yield 66%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.35 (s, 1H), 8.38 (d, *J* = 7.7 Hz, 1H), 7.91 (dd, *J* = 22.3, 7.8 Hz, 1H), 7.57 (s, 1H), 7.52 – 7.42 (m, 1H), 7.35 – 7.16 (m, 5H), 4.94 (s, 2H), 4.34 – 4.20 (m, 1H), 4.20 – 4.07 (m, 1H), 3.57 – 3.41 (m, 1H), 3.15 – 2.91 (m, 2H), 2.30 – 2.14 (m, 1H), 2.14 – 1.99 (m, 1H), 1.81 (q, *J* = 16.5, 14.7 Hz, 1H), 1.64 – 1.27 (m, 4H), 1.04 – 0.85 (m, 1H), 0.74 – 0.55 (m, 1H), 0.48 – 0.16 (m, 6H), 0.08 – -0.11 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 201.20, 178.70, 172.56, 171.22, 156.23, 137.50, 128.79, 128.24, 128.15, 65.84, 58.23, 56.67, 53.57, 37.63, 29.81, 27.74, 14.07, 8.05, 4.88, 4.69, 3.59, 2.87.

(S)-methyl 2-((2S,3R)-2-(((benzyloxy)carbonyl)amino)-3-(tert-butoxy)butanamido)-3-cyclohexylpropanoate (MPI25b). MPI25b was obtained from methyl (S)-2-amino-3-cyclohexylpropanoate hydrochloride and N-((benzyloxy)carbonyl)-O-(tert-butyl)-L-allothreonine following a similar procedure to **MPI11b.** The crude product was purified by silica gel column chromatography (15-50% EtOAc in hexanes as the eluent) to afford the **MPI25b** (yield 84%).^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.65 (d, *J* = 7.7 Hz, 1H), 7.43 – 7.29 (m, 5H), 5.94 (d, *J* = 5.0 Hz, 1H), 5.27 – 4.90 (m, 2H), 4.52 (td, *J* = 8.4, 5.0 Hz, 1H), 4.27 – 4.16 (m, 2H), 3.72 (s, 3H), 1.79 – 1.61 (m, 7H), 1.60 – 1.47 (m, 1H), 1.30 (s, 9H), 1.22 – 1.14 (m, 3H), 1.11 (d, *J* = 6.0 Hz, 3H), 1.01 – 0.85 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.07, 169.43, 156.15, 136.28, 128.55, 128.15, 127.96, 75.57, 66.83, 60.42, 58.37, 52.16, 50.51, 39.76, 34.30, 33.51, 32.56, 28.20, 26.32, 26.18, 25.99, 21.07, 16.41.



(S)-methyl 2-((2S,3R)-2-amino-3-(tert-butoxy)butanamido)-3-cyclohexylpropanoate (MPI25f). To a solution of **MPI25b** (2.73 mmol, 1.3 g) in methanol (20 mL) was added 10 % Pd/C (150 mg). The mixture was then stirred with hydrogen balloon at room temperature for 12 h. The catalyst was then filtered off and the solution was evaporated on vacuum to afford **MPI25f** as white solid, which was used without purification. ^{1}H NMR (400 MHz, Methanol-d_4) δ 4.49 (dd, *J* = 9.4, 5.4

Hz, 1H), 4.01 – 3.90 (m, 1H), 3.73 (s, 3H), 3.41 – 3.28 (m, 1H), 3.20 (d, *J* = 4.5 Hz, 1H), 1.90 – 1.59 (m, 7H), 1.51 – 1.37 (m, 1H), 1.23 (d, *J* = 9.9 Hz, 15H), 1.11 – 0.89 (m, 2H). ^{13}C NMR (100 MHz, MeOD): δ 174.31, 173.15, 73.93, 68.77, 59.84, 51.23, 50.10, 38.97, 33.92, 33.35, 32.03, 27.59, 26.10, 25.94, 25.70, 18.68.



(S)-methyl 2-((2S,3R)-3-(tert-butoxy)-2-((((3-chlorobenzyl)oxy)carbonyl)amino)butanamido)-3-cyclohexylpropanoate (MPI25g). To 3,5-dichlorobenzyl alcohol (0.201 g, 1.39 mmol) in THF (5 mL) were added K_2CO_3 (193 mg, 1.39 mmol) and Triphosgene (166 mg, 0.56 mmol) and the mixture was stirred at room temperature for 1 h. The mixture was then poured into water (10 mL) and extracted with ethyl acetate (2×20 mL), combine organic layers and dried over Na_2SO_4. The organic phase was evaporated to dryness and the crude material was used directly in the next step. 3,5-Dichlorobenzyl Chloroformate in THF (5 mL) was added to drop wise to a mixture of compound **MPI25f** (400 mg,1.39mmol) and DIPEA (0.47 ml, 2.78mmol). The reaction mixture stirred for 12 h. The mixture was then poured into water (30 mL) and extracted with ethyl acetate (4×20 mL). The organic layer was washed with aqueous hydrochloric acid 10% v/v (2×20 mL), saturated aqueous $NaHCO_3$ (2×20 mL), brine (2×20 mL) and dried over Na_2SO_4. The organic phase was evaporated to dryness and the crude material purified by silica gel column chromatography (15-50% EtOAc in n-hexane as the eluent) to afford **MPI25g** white solid (410 mg, 70%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.69 (d, *J* = 7.7 Hz, 1H), 7.44 – 7.22 (m, 4H), 6.00 (d, *J* = 4.9 Hz, 1H), 5.19 – 5.03 (m, 2H), 4.55 (td, *J* = 8.4, 5.1 Hz, 1H), 4.22 (q, *J* = 6.9, 5.5 Hz, 2H), 3.75 (s, 3H), 1.88 – 1.60 (m, 7H), 1.46 – 1.11 (m, 16H), 1.04 – 0.89 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.04, 171.18, 169.33, 155.86, 138.37, 134.42, 129.83, 128.24, 127.85, 125.81, 75.62, 66.84, 65.85, 60.42, 58.34, 52.17, 50.54, 39.75, 34.68, 34.31, 33.51, 32.56, 31.61, 28.19, 26.32, 26.18, 16.36.

(S)-2-((2S,3R)-3-(tert-butoxy)-2-((((3-chlorobenzyl)oxy)carbonyl)amino)butanamido)-3-cyclohexylpropanoic acid (MPI25c). MPI25c was prepared as a white solid following a similar procedure to **MPI11c** (yield 82%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.57 (d, *J* = 7.3 Hz, 1H), 7.39 – 7.04 (m, 4H), 6.09 (d, *J* = 5.8 Hz, 1H), 5.16 – 4.83 (m, 2H), 4.36 (td, *J* = 8.1, 7.6, 4.7 Hz, 1H), 4.20 – 4.01 (m, 2H), 1.72 – 1.46 (m, 7H), 1.33 – 0.95 (m, 16H), 0.95 – 0.76 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.40, 170.06, 156.11, 138.37, 134.39, 129.82, 128.21, 127.85, 125.84, 75.56, 67.03, 65.96, 58.65, 39.41, 34.33, 33.65, 32.35, 28.20, 26.34, 26.20, 25.97, 16.82.

(5S,8S,11S)-methyl 5-((R)-1-(tert-butoxy)ethyl)-1-(3-chlorophenyl)-8-(cyclohexylmethyl)-3,6,9-trioxo-11-(((S)-2-oxopyrrolidin-3-yl)methyl)-2-oxa-4,7,10-triazadodecan-12-oate (MPI25d). MPI25d was prepared as a white solid following a similar procedure to **MPI11d** (yield 64%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.48 (dd, *J* = 52.5, 7.6 Hz, 2H), 7.36 – 7.01 (m, 4H), 6.30 (s, 1H), 5.90 (d, *J* = 5.1 Hz, 1H), 5.01 (q, *J* = 12.6 Hz, 2H), 4.54 – 4.33 (m, 2H), 4.11 (d, *J* = 5.7 Hz, 2H), 3.65 (s, 3H), 3.39 – 3.18 (m, 2H), 2.46 – 2.25 (m, 2H), 2.20 – 2.03 (m, 1H), 1.87 – 1.40 (m, 9H), 1.11 (d, *J* = 72.3 Hz, 16H), 0.97 – 0.79 (m, 2H). ^{13}C NMR (100 MHz,

$CDCl_3$) δ 179.92, 172.23, 172.12, 169.47, 155.95, 138.30, 134.42, 129.86, 128.28, 127.93, 125.93, 75.51, 66.73, 65.97, 58.82, 52.43, 51.49, 51.19, 40.55, 39.95, 38.64, 38.24, 34.10, 33.62, 33.13, 32.66, 28.30, 28.23, 26.39, 26.23, 26.07, 17.15.

3-chlorobenzyl ((2S,3R)-3-(tert-butoxy)-1-(((S)-3-cyclohexyl-1-(((S)-1-hydroxy-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)-1-oxopropan-2-yl)amino)-1-oxobutan-2-yl)carbamate (MPI25e). MPI25e was prepared as a white solid following a similar procedure to **MPI11e** (yield 67%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54 (d, *J* = 7.6 Hz, 1H), 7.34 – 7.10 (m, 4H), 6.10 (d, *J* = 5.4 Hz, 1H), 5.89 (s, 1H), 5.01 (q, *J* = 12.6 Hz, 2H), 4.32 (q, *J* = 7.7 Hz, 1H), 4.18 – 4.03 (m, 2H), 3.94 (s, 1H), 3.55 (t, *J* = 4.0 Hz, 2H), 3.36 – 3.12 (m, 2H), 2.44 – 2.23 (m, 4H), 2.05 – 1.90 (m, 1H), 1.78 – 1.41 (m, 8H), 1.11 (d, *J* = 68.1 Hz, 15H), 0.93 – 0.77 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.95, 172.81, 169.73, 156.11, 138.27, 134.42, 129.88, 128.31, 127.97, 125.97, 75.52, 66.73, 66.06, 65.92, 59.13, 51.89, 40.52, 39.74, 38.21, 34.25, 33.62, 32.61, 28.63, 28.24, 26.36, 26.23, 26.03, 17.44.

3-chlorobenzyl ((2S,3R)-3-(tert-butoxy)-1-(((S)-3-cyclohexyl-1-oxo-1-(((S)-1-oxo-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)propan-2-yl)amino)-1-oxobutan-2-yl)carbamate (MPI25). MPI25 was prepared as a white solid following a similar procedure to **MPI11** (yield 72%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.44 (s, 1H), 7.99 (d, *J* = 6.4 Hz, 1H), 7.41 (d, *J* = 7.8 Hz, 1H), 7.29 (s, 1H), 7.22 (d, *J* = 4.6 Hz, 2H), 7.16 (t, *J* = 4.5 Hz, 1H), 6.11 (s, 1H), 5.89 (d, *J* = 5.1 Hz, 1H), 5.01 (q, *J* = 12.7 Hz, 2H), 4.48 – 4.37 (m, 1H), 4.35 – 4.25 (m, 1H), 4.11 (d, *J* = 5.5 Hz, 2H), 3.36 – 3.19 (m, 2H), 2.44 – 2.26 (m, 2H), 1.98 – 1.86 (m, 2H), 1.78 – 1.70 (m, 2H), 1.60 – 1.47 (m, 3H), 1.30 – 1.15 (m, 12H), 1.16 – 1.08 (m, 3H), 1.02 (d, *J* = 6.0 Hz, 3H), 0.96 – 0.82 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.57, 179.96, 172.90, 169.62, 155.99, 138.26, 134.43, 129.88, 128.32, 127.95, 125.95, 75.51, 66.72, 66.02, 58.93, 57.58, 51.50, 40.54, 40.03, 37.92, 34.24, 33.65, 32.62, 29.81, 29.71, 28.62, 28.24, 26.35, 26.22, 26.02, 17.29.

(S)-methyl 2-((2S,3R)-2-(((benzyloxy)carbonyl)amino)-3-(tert-butoxy)butanamido)-4-methylpentanoate (MPI26b). MPI26b was obtained from methyl L-leucinate hydrochloride and N-((benzyloxy)carbonyl)-O-(tert-butyl)-L-allothreonine following a similar procedure to **MPI11b.** The crude product was purified by silica gel column chromatography (15-50% EtOAc in hexanes as the eluent) to afford the **MPI26b** (yield 78%).^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.66 (d, *J* = 7.8 Hz, 1H), 7.51 – 7.31 (m, 5H), 5.94 (d, *J* = 4.9 Hz, 1H), 5.26 – 4.95 (m, 2H), 4.57 – 4.42 (m, 1H), 4.28 – 4.16 (m, 2H), 3.72 (s, 3H), 1.75 – 1.52 (m, 3H), 1.30 (s, 9H), 1.11 (d, *J* = 6.2 Hz, 3H), 0.94 (dd, *J* = 6.1, 3.8 Hz, 6H).^{13}C NMR (100 MHz, $CDCl_3$): δ 172.95, 169.43, 156.11, 136.28, 128.54, 128.14, 127.95, 75.57, 66.89, 66.82, 60.40, 58.36, 52.15, 51.07, 41.27, 28.18, 25.01, 22.80, 21.95, 21.06, 16.39, 14.21.

(S)-methyl 2-((2S,3R)-2-amino-3-(tert-butoxy)butanamido)-4-methylpentanoate (MPI26f). MPI26f was prepared as a white solid following a similar procedure to **MPI125f**. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.88 (d, *J* = 8.1 Hz, 1H), 4.61 – 4.43 (m, 1H), 4.19 – 4.06 (m, 1H), 3.72 (s, 3H), 3.21 (d, *J* = 3.2 Hz, 1H), 1.75 – 1.51 (m, 3H), 1.18 (s, 12H), 1.04 – 0.86 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.53, 173.48, 74.14, 67.85, 59.58, 52.11, 50.73, 41.23, 28.53, 24.90, 22.85, 21.91, 19.27.

(S)-methyl 2-((2S,3R)-3-(tert-butoxy)-2-((((3-chlorobenzyl)oxy)carbonyl)amino)butanamido)-4-methylpentanoate (MPI126g). MPI26g was prepared as a white solid following a similar procedure to **MPI125g** (yield

51%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.61 (d, *J* = 7.8 Hz, 1H), 7.36 – 7.09 (m, 4H), 5.91 (d, *J* = 5.0 Hz, 1H), 5.11 – 4.93 (m, 2H), 4.52 – 4.38 (m, 1H), 4.24 – 3.98 (m, 2H), 3.66 (s, 3H), 1.70 – 1.54 (m, 2H), 1.51 (q, *J* = 9.0, 8.4 Hz, 1H), 1.24 (s, 9H), 1.05 (d, *J* = 6.2 Hz, 3H), 0.87 (dd, *J* = 6.1, 3.6 Hz, 6H).^{13}C NMR (100 MHz, $CDCl_3$): δ 172.95, 169.36, 155.83, 138.36, 134.41, 129.83, 128.23, 127.85, 125.81, 75.64, 66.83, 65.84, 58.32, 52.19, 51.10, 41.24, 28.16, 25.02, 22.81, 21.95, 16.34.

(S)-2-((2S,3R)-3-(tert-butoxy)-2-((((3-chlorobenzyl)oxy)carbonyl)amino)butanamido)-4-methylpentanoic acid (MPI126c). MPI26c was prepared as a white solid following a similar procedure to **MPI11c.** ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.63 (d, *J* = 7.5 Hz, 1H), 7.37 – 7.09 (m, 4H), 5.97 (d, *J* = 5.4 Hz, 1H), 5.01 (q, *J* = 12.7 Hz, 2H), 4.44 (q, *J* = 7.2, 6.0 Hz, 1H), 4.25 – 4.07 (m, 2H), 1.72 – 1.59 (m, 2H), 1.59 – 1.43 (m, 1H), 1.22 (s, 9H), 1.02 (d, *J* = 6.3 Hz, 3H), 0.95 – 0.80 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.19, 169.79, 155.91, 138.31, 134.41, 129.83, 128.25, 127.86, 125.82, 75.70, 67.95, 66.91, 65.92, 58.35, 51.08, 40.96, 28.14, 25.03, 22.84, 21.84, 16.42.

(5S,8S,11S)-methyl 5-((R)-1-(tert-butoxy)ethyl)-1-(3-chlorophenyl)-8-isobutyl-3,6,9-trioxo-11-(((S)-2-oxopyrrolidin-3-yl)methyl)-2-oxa-4,7,10-triazadodecan-12-oate (MPI126d). MPI26d was prepared as a white solid following a similar procedure to **MPI11d** (yield 60%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.61 (d, *J* = 7.4 Hz, 1H), 7.42 (d, *J* = 7.9 Hz, 1H), 7.33 – 7.12 (m, 4H), 6.58 (s, 1H), 5.88 (d, *J* = 5.3 Hz, 1H), 5.01 (q, *J* = 12.6 Hz, 2H), 4.54 – 4.33 (m, 2H), 4.10 (d, *J* = 5.5 Hz, 2H), 3.65 (s, 3H), 3.36 – 3.18 (m, 2H), 2.52 – 2.25 (m, 2H), 2.17 – 2.05 (m, 1H), 1.87 – 1.71 (m, 2H), 1.67 – 1.59 (m, 2H), 1.49 (q, *J* = 8.9, 8.4 Hz, 1H), 1.20 (s, 9H), 1.00 (d, *J* = 6.0 Hz, 3H), 0.88 (dd, *J* = 11.7, 6.0 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.96, 172.16, 172.07, 169.48, 155.92, 138.30, 134.41, 129.87, 128.29, 127.93, 125.94, 75.50, 66.73, 65.97, 58.83, 54.58, 52.43, 41.51, 40.82, 38.35, 33.08, 28.21, 24.78, 22.86, 22.12, 18.53, 17.18, 17.14.

3-chlorobenzyl ((2S,3R)-3-(tert-butoxy)-1-(((S)-1-(((S)-1-hydroxy-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)-4-methyl-1-oxopentan-2-yl)amino)-1-oxobutan-2-yl)carbamate (MPI126e). MPI26e was prepared as a white solid following a similar procedure to **MPI11e** (yield 73%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.66 (d, *J* = 7.9 Hz, 1H), 7.40 (d, *J* = 7.8 Hz, 1H), 7.33 – 7.10 (m, 4H), 6.28 – 6.06 (m, 2H), 5.08 – 4.88 (m, 2H), 4.34 (td, *J* = 8.2, 5.2 Hz, 1H), 4.14 – 4.06 (m, 1H), 4.02 – 3.80 (m, 1H), 3.74 (t, *J* = 6.4 Hz, 1H), 3.61 – 3.50 (m, 2H), 3.30 – 3.13 (m, 2H), 2.33 (dt, *J* = 8.6, 5.1 Hz, 2H), 2.15 – 1.96 (m, 1H), 1.82 – 1.68 (m, 1H), 1.64 – 1.32 (m, 4H), 1.20 (s, 9H), 1.00 (d, *J* = 6.3 Hz, 3H), 0.84 (dd, *J* = 9.0, 6.1 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 181.06, 172.62, 169.58, 156.06, 138.34, 134.40, 129.86, 128.27, 127.94, 125.94, 75.52, 66.85, 65.97, 65.85, 58.98, 52.37, 50.31, 41.29, 40.55, 38.29, 32.66, 28.47, 28.21, 24.90, 22.77, 22.14, 17.21.

3-chlorobenzyl ((2S,3R)-3-(tert-butoxy)-1-(((S)-4-methyl-1-oxo-1-(((S)-1-oxo-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)pentan-2-yl)amino)-1-oxobutan-2-yl)carbamate (MPI126). MPI26 was prepared as a white solid following a similar procedure to **MPI11** (yield 79%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.50 (s, 1H), 8.39 – 7.96 (m, 1H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.35 (s, 1H), 7.29 (d, *J* = 4.7 Hz, 2H), 7.23 (s, 1H), 6.19 – 5.86 (m, 2H), 5.07 (q, *J* = 12.6 Hz, 2H), 4.55 – 4.34 (m, 2H), 4.18 (d, *J* = 5.3 Hz, 2H), 3.37 – 3.26 (m, 2H), 2.56 – 2.26 (m, 3H), 2.01 – 1.92 (m, 1H), 1.87 – 1.77 (m, 1H), 1.77 – 1.64 (m, 2H), 1.59 (t, *J* = 9.0 Hz, 1H), 1.27 (s, 9H), 1.08 (d, *J* = 5.9 Hz, 3H), 0.96 (dd, *J* = 10.9, 5.7 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.64,

172.82, 169.54, 169.33, 155.98, 138.29, 134.42, 129.88, 128.31, 127.95, 125.96, 75.53, 66.74, 66.00, 58.91, 57.66, 52.11, 41.48, 40.61, 28.60, 28.22, 24.93, 22.92, 22.08, 17.21.

(((3-chlorobenzyl)oxy)carbonyl)-L-valine (MPI27a). MPI27a was prepared as a white solid following a similar procedure to **MPI125g** and followed by **MPI111c** protocol. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.58 (s, 1H), 7.55 (d, *J* = 8.6 Hz, 1H), 7.47 – 7.25 (m, 4H), 5.18 – 4.98 (m, 2H), 3.87 (dd, *J* = 8.6, 5.8 Hz, 1H), 2.15 – 1.96 (m, 1H), 0.89 (t, *J* = 6.5 Hz, 6H).

Methyl (S)-2-((S)-2-((((3-chlorobenzyl)oxy)carbonyl)amino)-3-methylbutanamido)-3-cyclohexylpropanoate (MPI127b). MPI27b was prepared as a white solid following a similar procedure to **MPI11b** (yield 56%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.25 (d, *J* = 7.5 Hz, 1H), 7.48 – 7.22 (m, 5H), 5.11 – 4.95 (m, 2H), 4.33 (q, *J* = 7.7, 7.2 Hz, 1H), 3.88 (t, *J* = 8.1 Hz, 1H), 3.60 (s, 3H), 2.01 – 1.89 (m, 1H), 1.72 – 1.44 (m, 7H), 1.34 (s, 1H), 1.22 – 1.00 (m, 3H), 0.98 – 0.69 (m, 8H).

(S)-2-((S)-2-((((3-chlorobenzyl)oxy)carbonyl)amino)-3-methylbutanamido)-3-cyclohexylpropanoic acid (MPI127c). MPI27c was prepared as a white solid following a similar procedure to **MPI11c** (yield 83%).

Methyl (5S,8S,11S)-1-(3-chlorophenyl)-8-(cyclohexylmethyl)-5-isopropyl-3,6,9-trioxo-11-(((S)-2-oxopyrrolidin-3-yl)methyl)-2-oxa-4,7,10-triazadodecan-12-oate (MPI127d). MPI27d was prepared as a white solid following a similar procedure to **MPI11d** (yield 56%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.81 (d, *J* = 7.2 Hz, 1H), 7.35 (s, 1H), 7.32 – 7.18 (m, 3H), 6.60 (d, *J* = 8.4 Hz, 1H), 6.02 (s, 1H), 5.42 (d, *J* = 8.6 Hz, 1H), 5.15 – 5.00 (m, 2H), 4.58 (td, *J* = 8.8, 5.5 Hz, 1H), 4.49 (d, *J* = 6.6 Hz, 1H), 3.99 (dd, *J* = 8.6, 6.2 Hz, 1H), 3.72 (s, 3H), 3.41 – 3.24 (m, 2H), 2.48 – 2.35 (m, 2H), 2.23 – 2.05 (m, 2H), 2.01 – 1.58 (m, 8H), 1.56 – 1.46 (m, 1H), 1.40 – 1.04 (m, 5H), 1.04 – 0.77 (m, 8H).

3-chlorobenzyl ((S)-1-(((S)-3-cyclohexyl-1-oxo-1-(((S)-1-oxo-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)propan-2-yl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (MPI127). MPI27 was prepared as a white solid following a similar procedure of **MPI11e** followed b**y MPI11** procedure (yield 52%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.49 (s, 1H), 8.25 (d, *J* = 6.6 Hz, 1H), 7.39 – 7.11 (m, 4H), 7.02 (d, *J* = 8.3 Hz, 1H), 6.56 (s, 1H), 5.64 (d, *J* = 8.5 Hz, 1H), 5.06 (q, *J* = 12.6 Hz, 2H), 4.74 – 4.61 (m, 1H), 4.37 (s, 1H), 4.03 (t, *J* = 7.6 Hz, 1H), 3.41 – 3.22 (m, 2H), 2.50 – 2.27 (m, 2H), 2.19 – 2.07 (m, 1H), 2.07 – 1.86 (m, 3H), 1.86 – 1.48 (m, 8H), 1.39 – 1.04 (m, 5H), 1.04 – 0.81 (m, 8H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.5, 180.0, 173.3, 171.2, 156.4, 138.2, 134.4, 129.9, 128.3, 128.0, 126.0, 66.2, 60.6, 57.5, 51.1, 40.6, 40.2, 38.0, 34.2, 33.5, 32.5, 31.0, 29.9, 29.7, 28.4, 26.3, 26.2, 26.0, 19.2, 17.8.

Methyl (S)-2-((S)-2-((S)-2-amino-3-methylbutanamido)-4-methylpentanamido)-3-((S)-2-oxopyrrolidin-3-yl)propanoate (MPI128f). MPI28f was prepared as a white solid following a similar procedure to **MPI125f** (yield 90%).

Methyl (S)-2-((S)-2-((S)-2-(1H-indole-2-carboxamido)-3-methylbutanamido)-4-methylpentanamido)-3-((S)-2-oxopyrrolidin-3-yl)propanoate (MPI128d). MPI28d was prepared as a white solid following a similar procedure to **MPI11d** (yield 53%). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.62 (d, *J* = 8.0 Hz, 1H), 7.49 – 7.39 (m, 1H), 7.22 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.18 (d, *J* = 0.8 Hz, 1H), 7.11 – 7.01 (m, 1H), 4.53 (dd, *J* = 11.8, 3.9 Hz, 1H), 4.42 (dd, *J* = 13.8, 7.7 Hz, 2H), 3.72 (s, 3H), 2.56 (qd, *J* = 10.4, 4.0 Hz, 1H), 2.35 – 2.14 (m, 3H), 1.87 – 1.69 (m, 3H), 1.63 (t, *J* = 7.2 Hz,

2H), 1.04 (d, *J* = 6.7 Hz, 6H), 0.94 (dd, *J* = 19.4, 6.5 Hz, 6H).

N-((S)-3-methyl-1-(((S)-4-methyl-1-oxo-1-(((S)-1-oxo-3-((S)-2-oxopyrrolidin-3-yl)propan-2-yl)amino)pentan-2-yl)amino)-1-oxobutan-2-yl)-1H-indole-2-carboxamide (MPI128). MPI28 was prepared as a white solid following a similar procedure of **MPI11e** followed b**y MPI11** procedure (yield 60%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.59 (d, *J* = 2.2 Hz, 1H), 9.42 (s, 1H), 8.48 (d, *J* = 7.8 Hz, 1H), 8.23 (dd, *J* = 19.8, 8.1 Hz, 2H), 7.71 – 7.57 (m, 2H), 7.50 – 7.39 (m, 1H), 7.29 (d, *J* = 2.1 Hz, 1H), 7.18 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.03 (ddd, *J* = 8.0, 6.9, 1.0 Hz, 1H), 4.44 – 4.32 (m, 2H), 4.24 (ddd, *J* = 11.6, 7.8, 3.9 Hz, 1H), 3.21 – 3.11 (m, 1H), 3.07 (td, *J* = 9.2, 7.0 Hz, 1H), 2.31 (qd, *J* = 10.3, 3.9 Hz, 1H), 2.13 (dt, *J* = 14.3, 7.9 Hz, 2H), 1.96 – 1.85 (m, 1H), 1.73 – 1.58 (m, 3H), 1.58 – 1.43 (m, 2H), 1.02 – 0.79 (m, 12H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 201.2, 178.8, 173.1, 171.5, 161.5, 137.0, 131.8, 127.5, 123.9, 122.0, 120.2, 112.7, 104.2, 58.8, 56.6, 51.6, 41.2, 37.6, 30.9, 29.8, 27.7, 24.7, 23.3, 22.3, 19.6, 19.2

Table S1. Statistics of crystallographic analysis of M^{Pro} in complexed with different inhibitors.

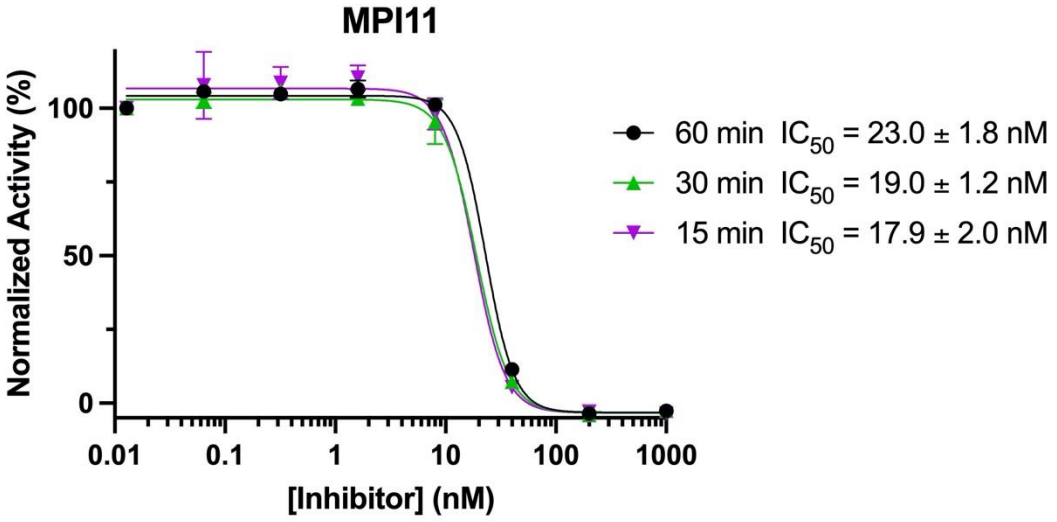
Protein/Ligand (PDI entry)	**MPI11** (7RVM)	**MPI12** (7RVN)	**MPI13** (7RVO)	**MPI14** (7RVP)
Data Collection				
Space group	C121	C121	P1	P1
cell dimensions				
a, *b*, *c* (Å)	98.71, 81.35, 51.98	98.92, 81.18, 51.92	55.51, 60.54, 63.15	55.58, 60.80, 63.45
α, β, γ (°)	90.00, 115.46, 90.00	90.00, 115.15, 90.00	79.98, 68.24, 70.25	80.06, 68.16, 70.12
Resolution (Å)	46.93-1.95 (2.00-1.95)	47.00-1.63 (1.66-1.63)	44.34-1.80 (1.84-1.80)	58.81-1.90 (1.94-1.90)
R_{merge}	9.2 (72.0)	6.6 (77.6)	20.8 (57.9)	10.4 (145.9)
$I/\sigma I$	9.3 (1.5)	12.5 (1.6)	3.5 (1.6)	5.9 (0.9)
Completeness (%)	97.4 (95.8)	95.8 (90.5)	89.8 (90.6)	95.5 (94.5)
Redundancy	6.9 (6.9)	5.9 (5.5)	3.7 (3.9)	3.6 (3.7)
Refinement				
Resolution (Å)	46.93-1.95	47.00-1.63	44.34-1.80	43.48-1.90
No. Reflections	26267 (2594)	44233 (4238)	59690 (6029)	54436 (5351)
R_{work}/R_{free}	0.2055/0.2383	0.1972/0.2124	0.2444/0.2750	0.2368/0.2736
No. atoms				
Protein	2400	2426	4798	4802
Water	230	183	246	173
B factors				
Protein	23.652	40.122	31.900	44.602
Water	30.233	43.562	36.757	44.891
R.m.s deviations				
Bond lengths (Å)	0.009	0.009	0.010	0.010
Bond angles (°)	1.67	1.38	2.38	1.41
Protein/Ligand (PDI entry)	**MPI16** (7RVQ)	**MPI18** (7RVR)	**MPI19** (7RVS)	**MPI20** (7RVT)
Data Collection				
Space group	P1	P1	C121	P 1
cell dimensions				
a, *b*, *c* (Å)	56.34, 62.85, 63.57	54.70, 61.66, 62.10	98.80, 81.80, 52.03	55.51, 60.70, 63.34
α, β, γ (°)	80.34, 68.56, 69.65	81.13, 69.31, 69.71	90.00, 115.5, 90.00	80.42, 68.42, 70.59
Resolution (Å)	24.91-2.47 (2.58-2.47)	24.27-2.46 (2.56-2.46)	24.41-1.85 (1.89-1.85)	58.83-2.10 (2.16-2.10)
R_{merge}	41.3 (419.6)	21.7 (231.3)	6.9 (118.7)	30.0 (54.2)
$I/\sigma I$	3.5 (0.3)	8.0 (0.5)	17.8 (1.6)	3.8 (2.6)
Completeness (%)	98.1 (84.8)	98.4 (86.8)	99.9 (100.0)	95.8 (96.3)
Redundancy	8.9 (5.1)	13.1 (7.8)	10.1 (7.5)	2.9 (3.1)
Refinement				
Resolution (Å)	24.91-2.49	24.27-2.46	24.41-1.85	32.85 - 2.10
No. Reflections	13243 (1018)	12359 (758)	31512 (3128)	40069 (4014)
R_{work}/R_{free}	0.2386/0.3222	0.2529/0.3231	0.2000/0.2265	0.2702/0.3076
No. atoms				
Protein	2431	2401	2427	2433
Water	45	37	176	144
B factors				
Protein	50.449	50.903	37.652	31.883
Water	45.343	46.359	41.474	34.449
R.m.s deviations				
Bond lengths (Å)	0.010	0.010	0.009	0.009
Bond angles (°)	1.25	1.24	1.31	1.13

Table S1 – continued

Protein/Ligand (PDI entry)	**MPI21** (7RVU)	**MPI22** (7RVV)	**MPI23** (7RVW)	**MPI24** (7RVX)
Data Collection				
Space group	P1	P1	C1	P1
cell dimensions				
a, *b*, *c* (Å)	55.60, 60.93, 62.87	46.46, 52.26, 64.12	95.91, 81.31, 54.47	56.06, 61.15, 63.76
α, β, γ (°)	79.27, 68.84, 69.73	108.82, 97.3, 98.14	90.00, 116.98, 90.00	79.94, 68.33, 70.17
Resolution (Å)	57.76-2.50 (2.60-2.50)	48.52-3.00 (3.18-3.00)	24.27-1.85 (1.89-1.85)	49.69-1.85 (1.89-1.85)
R_{merge}	47.1 (91.8)	10.5 (170.0)	13.6 (98.3)	8.3 (51.4)
$I/\sigma I$	2.1 (0.8)	6.1 (4.0)	13.3 (2.1)	7.6 (1.5)
Completeness (%)	98.9 (98.7)	93.2 (95.9)	99.9 (100.0)	89.1 (85.9)
Redundancy	5.4 (5.6)	2.8 (2.9)	11.4 (9.1)	3.8 (3.8)
Refinement				
Resolution (Å)	43.51-2.50	48.52-3.00	24.27-1.85	49.69-1.85
No. Reflections	12573 (1249)	10372 (1108)	31811 (3152)	56153 (5444)
R_{work}/R_{free}	0.2515/0.3285	0.3414/0.4279	0.1898/0.2175	0.2353/0.2651
No. atoms				
Protein	2378	2376	2401	4840
Water	43	0	223	229
B factors				
Protein	29.165	22.608	30.173	40.269
Water	26.273	0	34.473	42.174
R.m.s deviations				
Bond lengths (Å)	0.010	0.010	0.009	0.012
Bond angles (°)	1.28	1.38	1.24	1.50
Protein/Ligand (PDI entry)	**MPI25** (7RVY)	**MPI26** (7RVZ)	**MPI27** (7RV0)	**MPI28** (7RV1)
Data Collection				
Space group	C1	C121	C1	P1
cell dimensions				
a, *b*, *c* (Å)	96.50, 81.24, 54.48	98.33, 80.95, 51.82	95.66, 80.81, 54.44	55.64, 61.09, 63.87
α, β, γ (°)	90.00, 117.06, 90.00	90.00, 115.19, 90.00	90.00, 116.96, 90.00	79.27, 68.06, 69.37
Resolution (Å)	24.21-1.85 (1.89-1.85)	59.88-1.90 (1.94-1.90)	24.26-1.85 (1.89-1.85)	59.13-2.50 (2.60-2.50)
R_{merge}	6.5 (38.7)	10.1 (141.9)	12.2 (90.8)	26.2 (37.8)
$I/\sigma I$	12.2 (2.5)	8.7 (1.3)	8.8 (1.7)	4.7 (2.8)
Completeness (%)	92.6 (81.3)	96.1 (95.6)	99.8 (98.9)	97.1 (97.4)
Redundancy	4.2 (3.7)	6.4 (6.5)	6.8 (4.0)	2.9 (3.1)
Refinement				
Resolution (Å)	24.21-1.85	43.45-1.90	24.26-1.85	46.10 - 2.50
No. Reflections	29597 (2613)	27763 (2745)	31429 (3102)	24135 (2442)
R_{work}/R_{free}	0.2309/0.2680	0.1911/0.2199	0.2220/0.2534	0.2566/0.3160
No. atoms				
Protein	2407	2358	2403	4722
Water	232	103	200	122
B factors				
Protein	22.457	44.839	28.397	16.575
Water	25.228	44.799	31.384	15.514
R.m.s deviations				
Bond lengths (Å)	0.009	0.008	0.011	0.010
Bond angles (°)	1.19	1.73	1.39	1.24

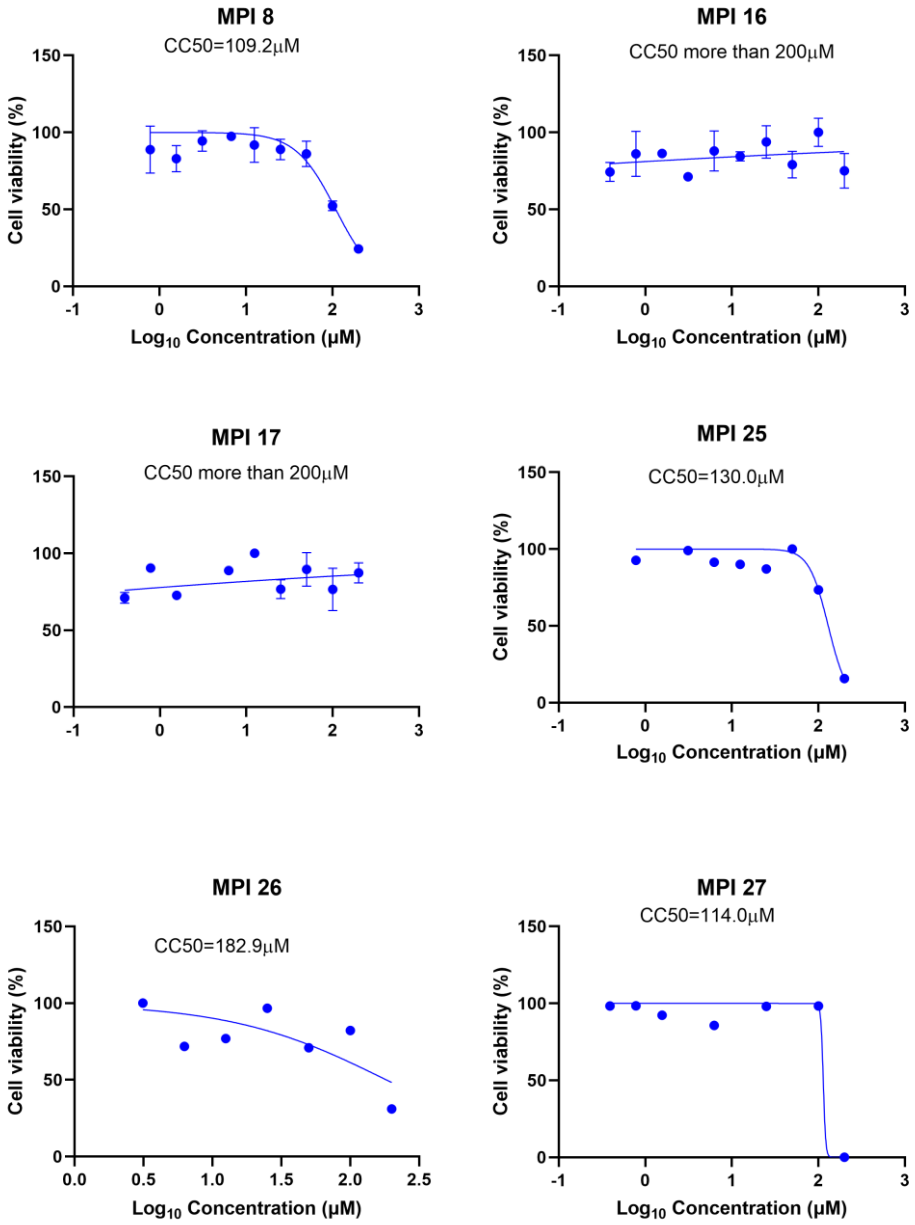
Supplementary Figure 1

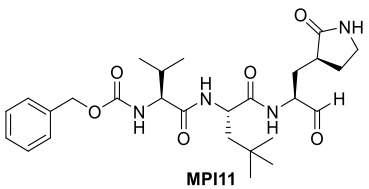
M^{Pro} was incubated with different concentrations of MPI11 for 15, 30 and 60 min and then its activity was determined by adding Sub3.



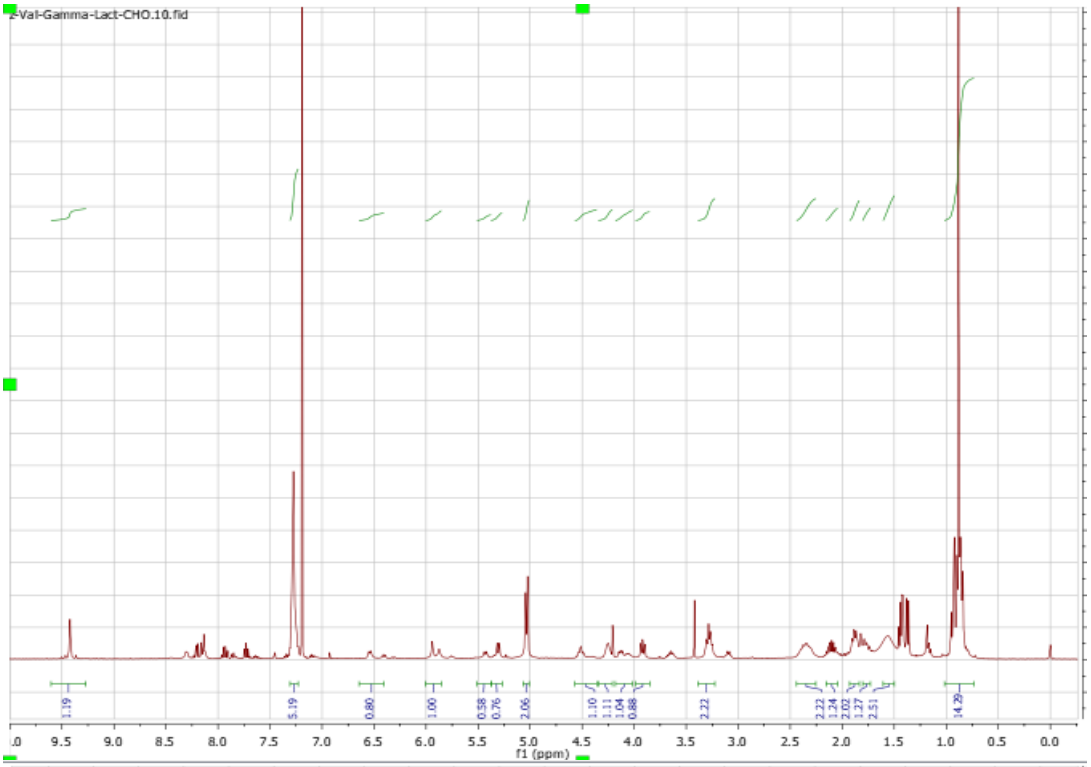
Supplementary Figure S2

To assess the half-maximal cytotoxic concentration (CC_{50}), stock solutions of the tested compounds were dissolved in DMSO and diluted further to the working solutions with DMEM. Briefly, the 293T cells were seeded in 96 well-plates and incubated at 37 °C and 5% CO_2 for 24 h. After that, the cells were treated with different concentrations (200 µM, 100 µM, 50 µM, 25 µM, 12.5 µM, 6.25 µM, 3.125 µM, 1.5625 µM, 0.78125 µM, 0 µM) of the tested compounds in triplicates for 48 h. Cell viability was assessed by MTT assay to determine the CC_{50}. All data reported was normalized on a per-plate basis to wells that contained cells in the presence of 200 µM doxorubincin (0% cell viability). The concentration caused a 50% cytotoxicity (CC_{50}) was obtained by plotting the normalization % cell viability versus log10 sample concentration.





MPI11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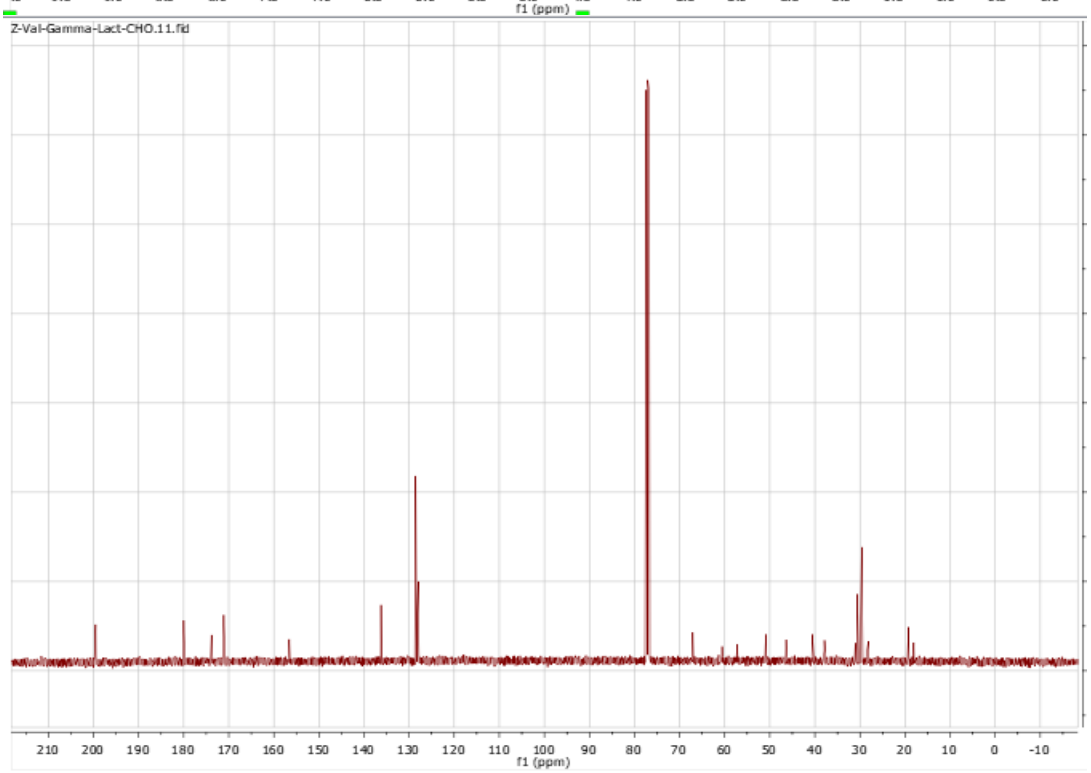
1.10
1.11
1.04
0.88
2.22
2.22
1.24
2.02
1.27
2.51
14.29
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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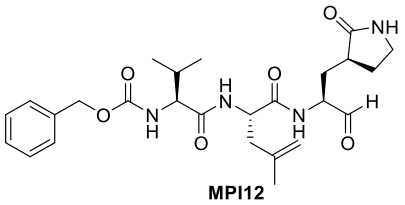
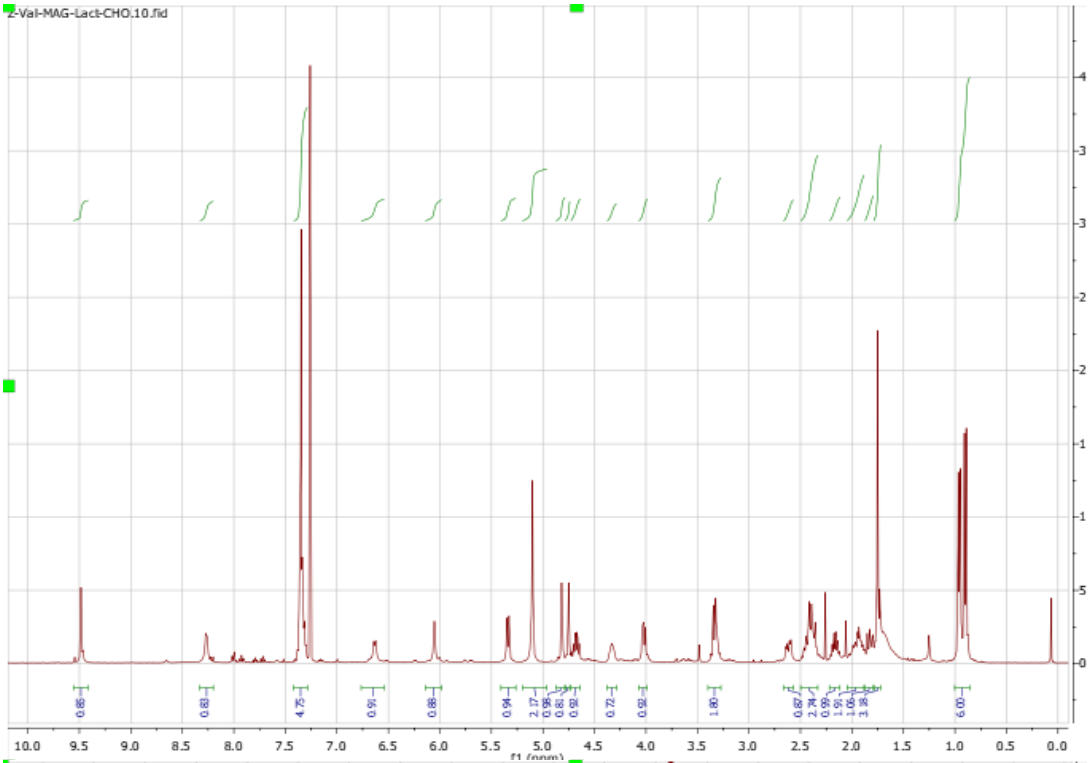
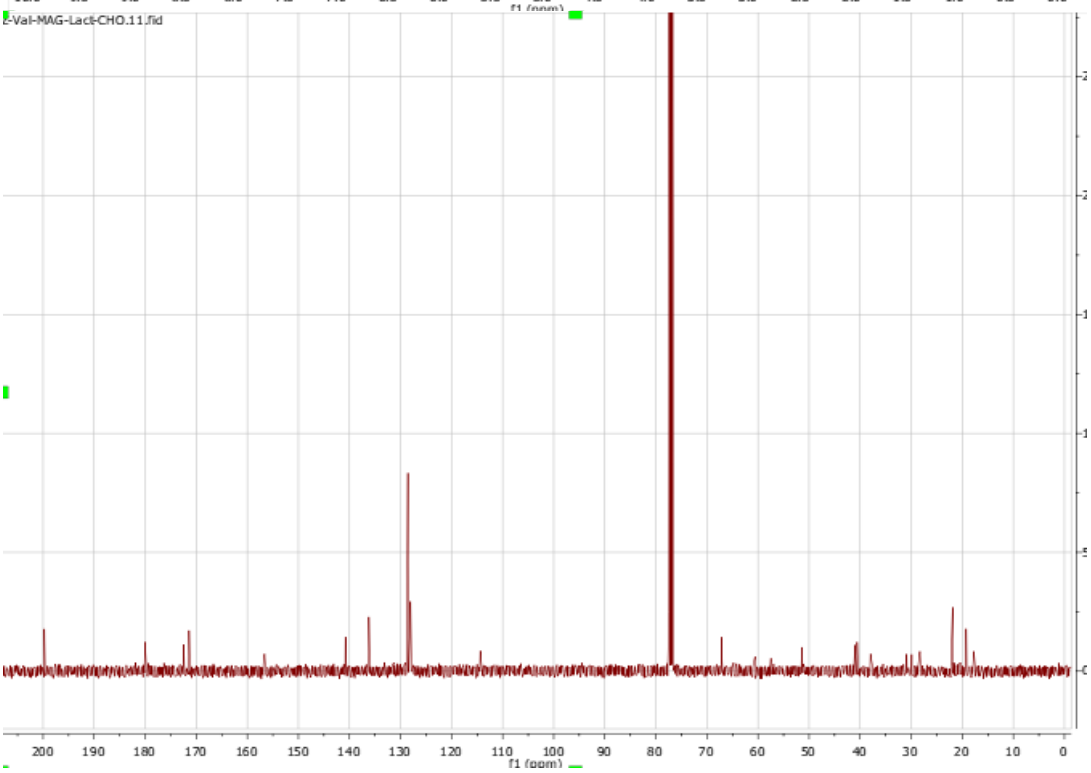
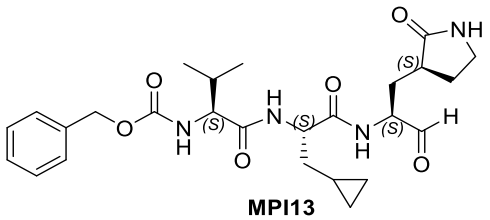
f1 (ppm)



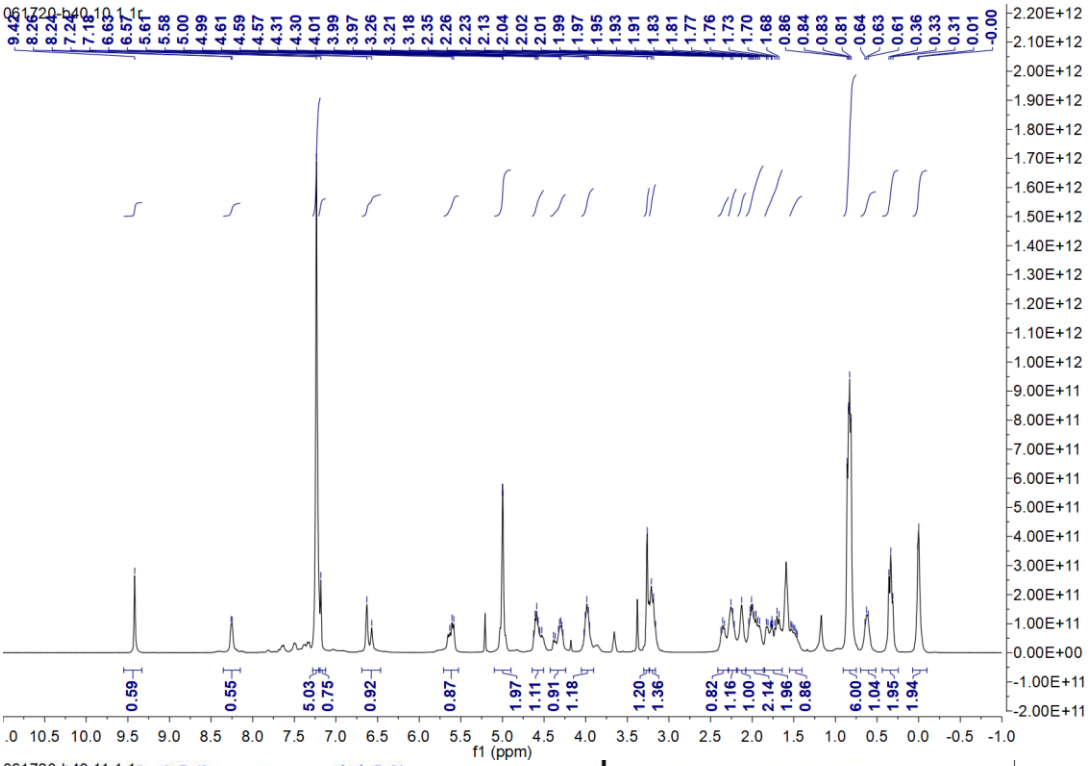
MPI12







MPI13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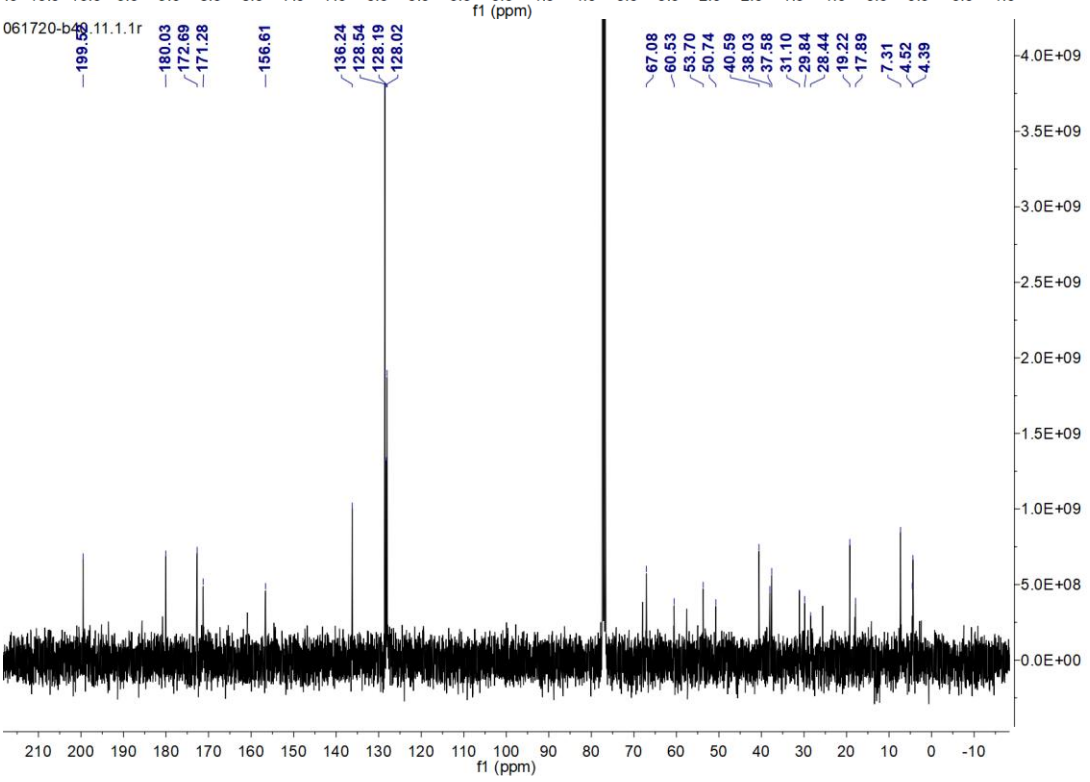
0.59 0.55 5.03 0.75 0.92 0.87 1.97 1.11 0.91 1.18 1.20 1.36 0.82 1.16 1.00 2.14 1.96 0.86 6.00 1.04 1.95 1.94
f1 (ppm)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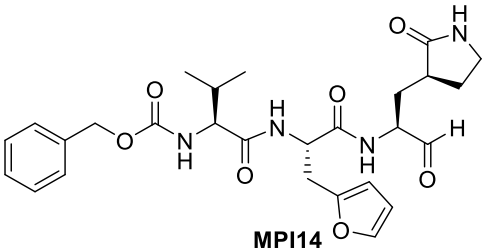
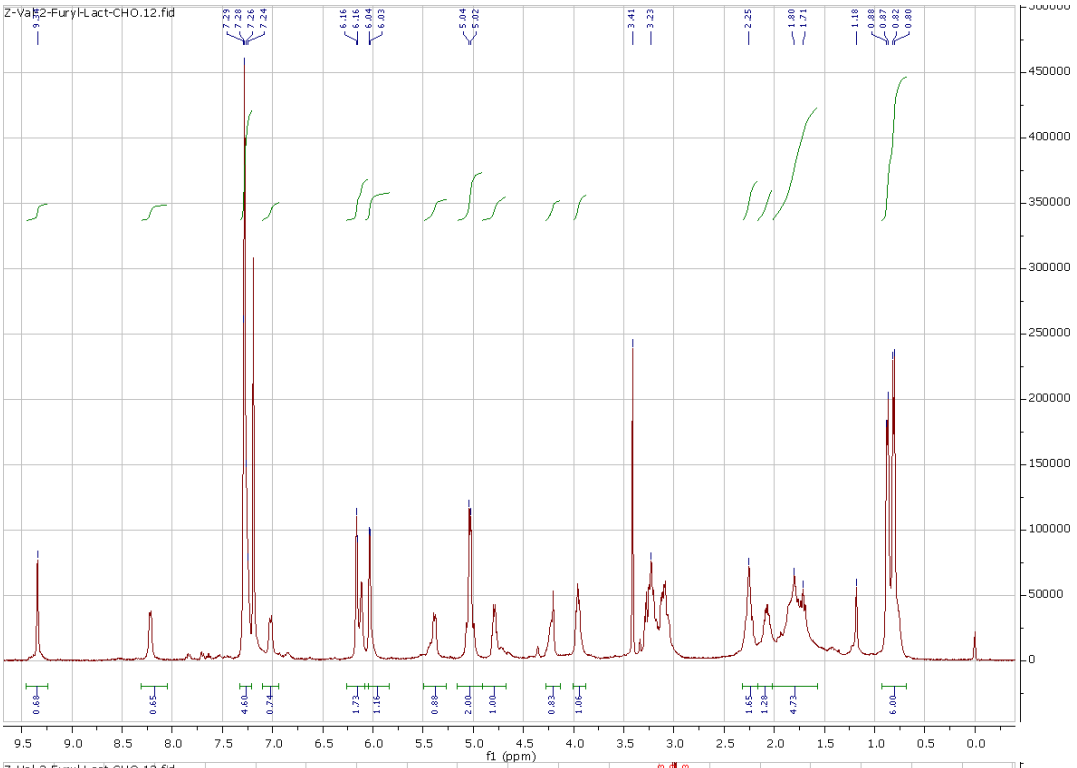
f1 (ppm)



MPI14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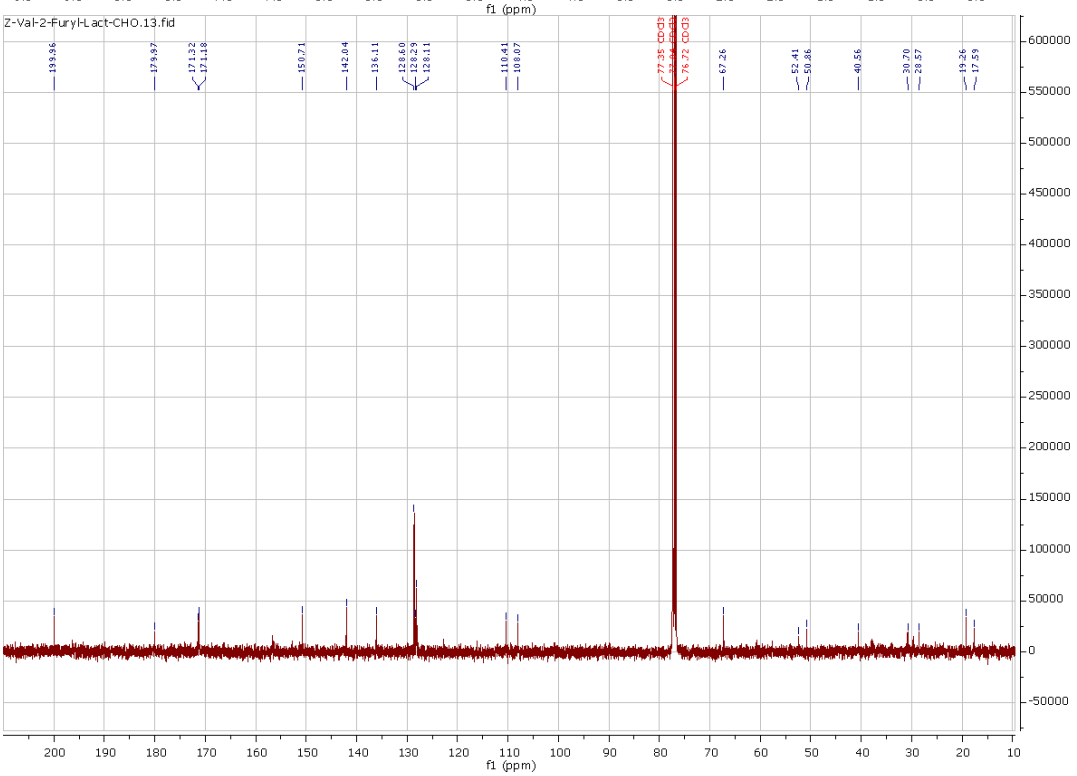
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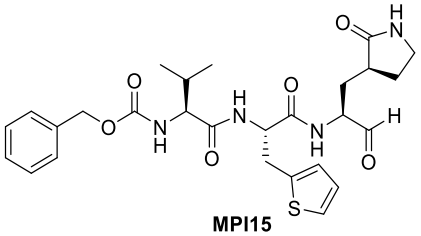
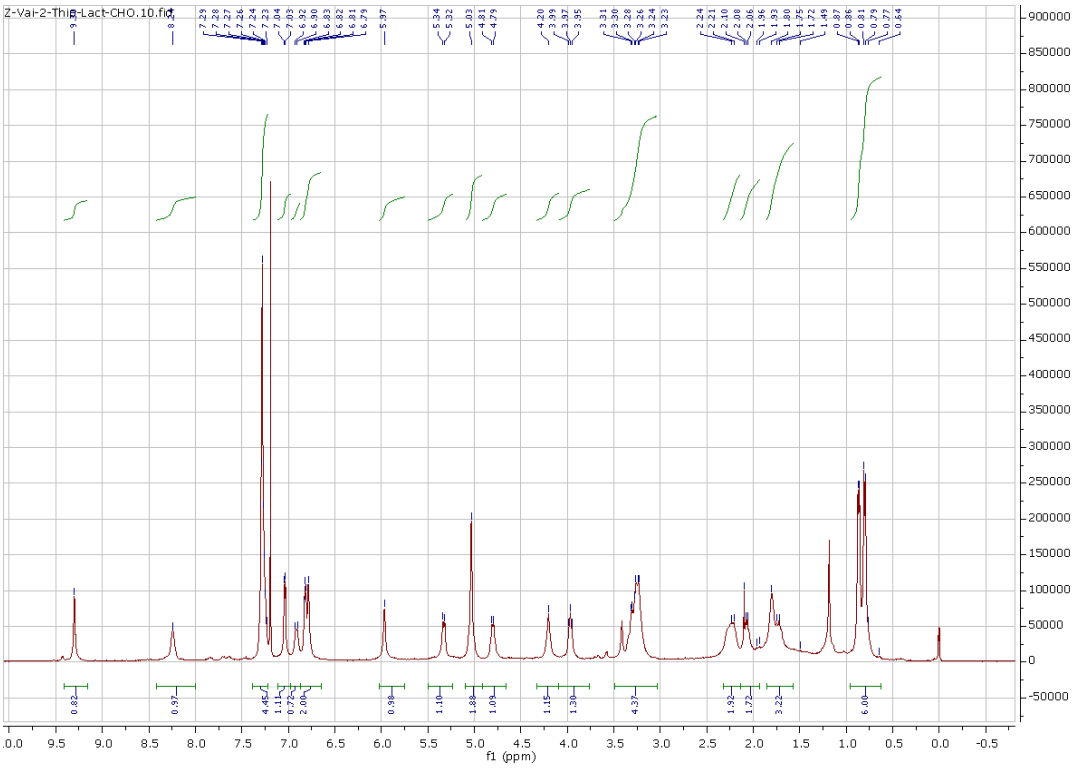
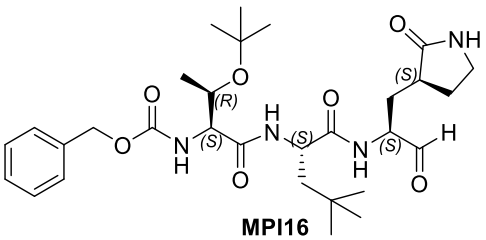
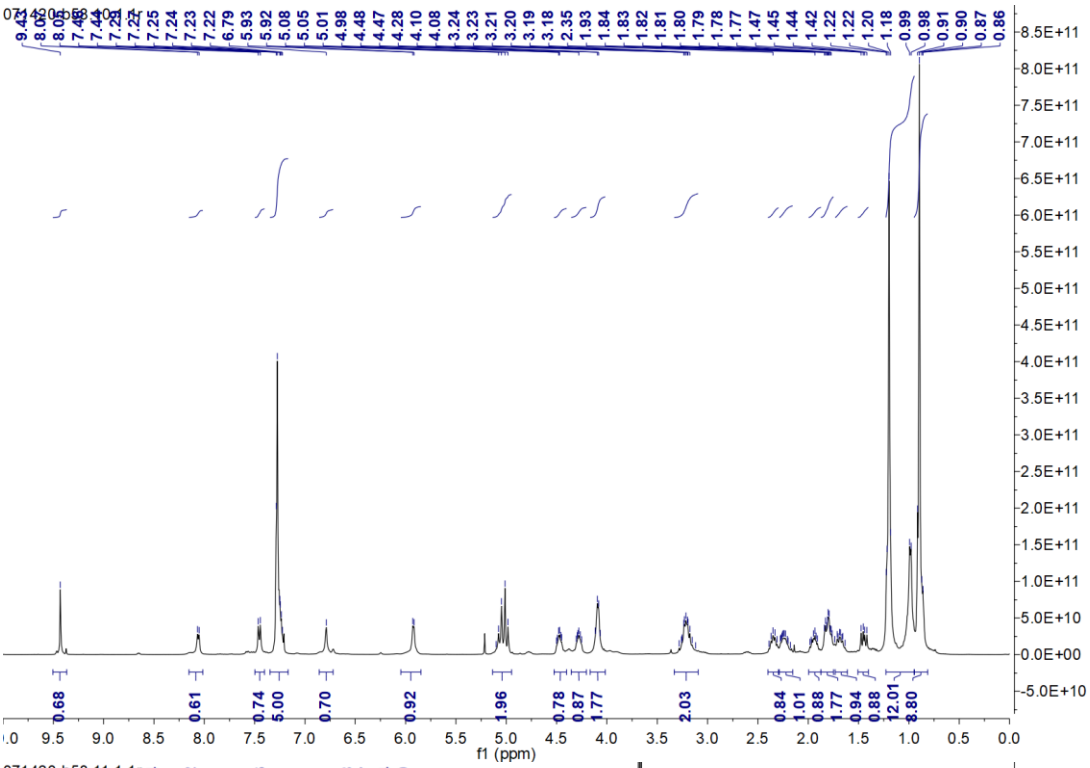


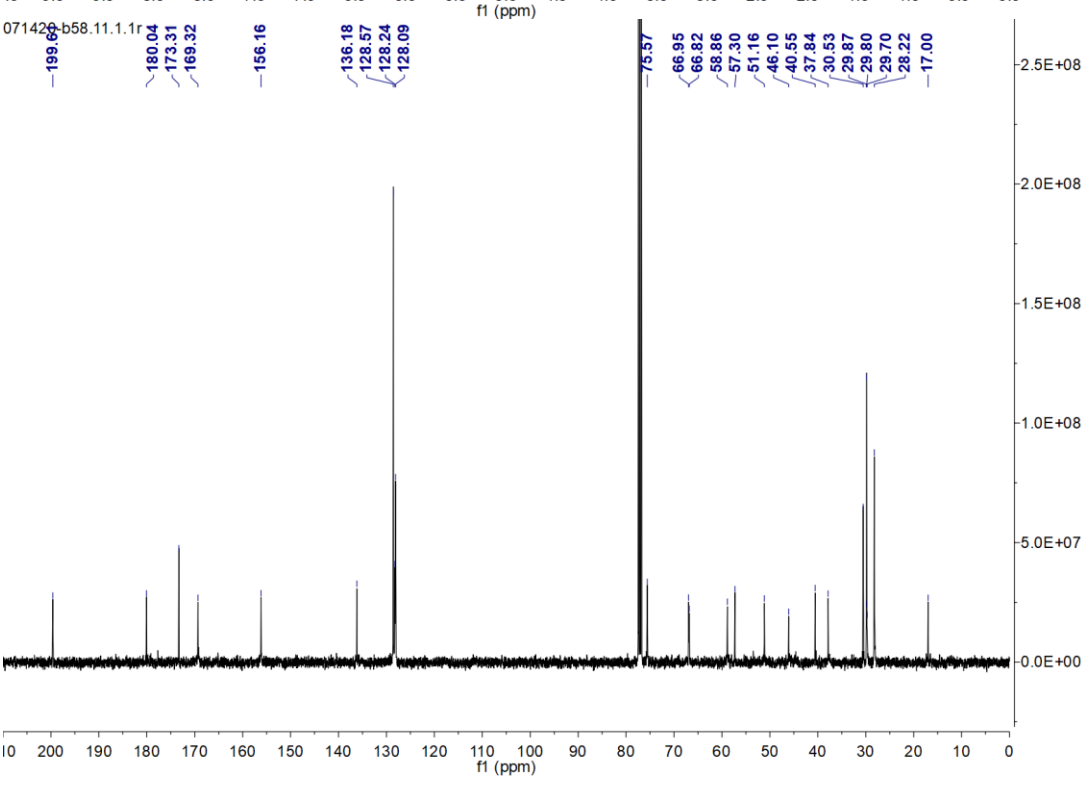
MPI15

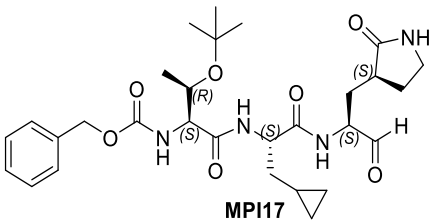




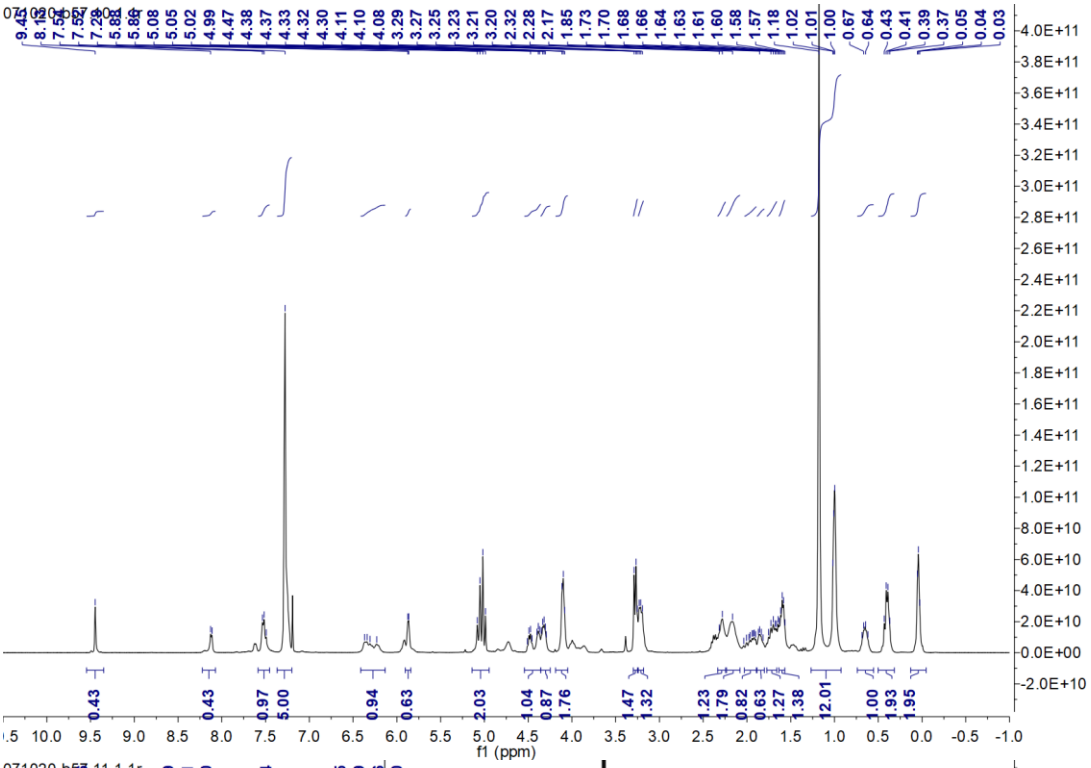
MPI16

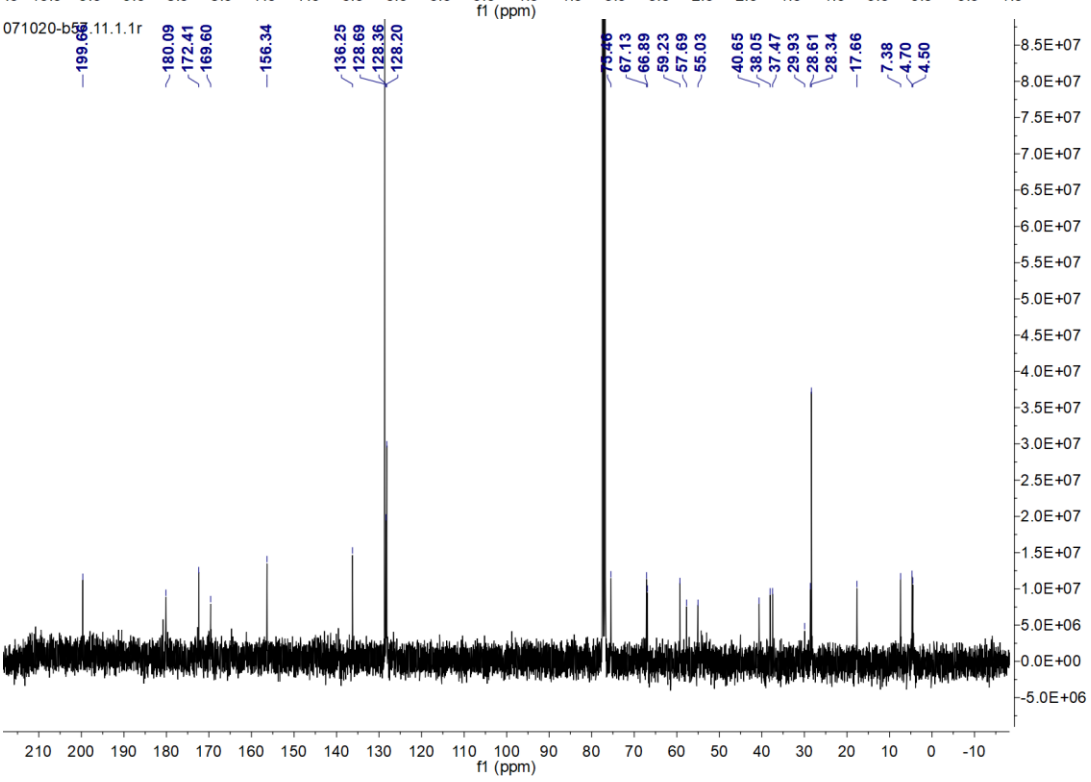


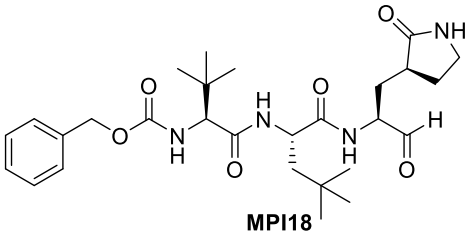




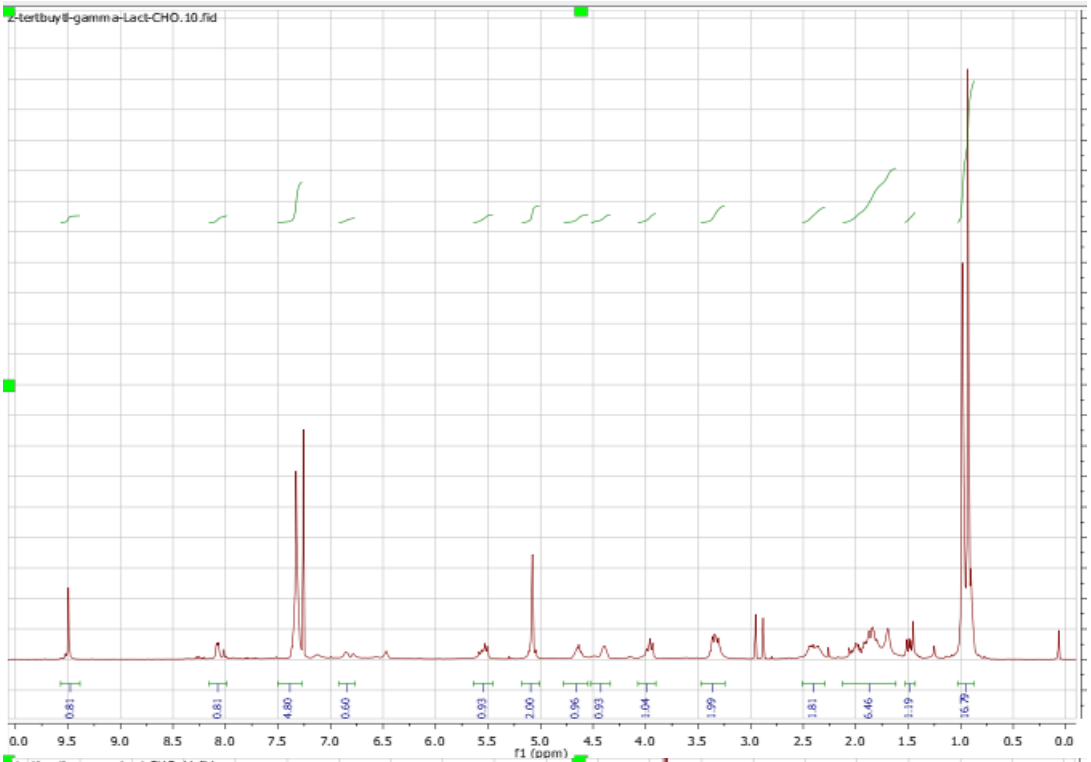
MPI17

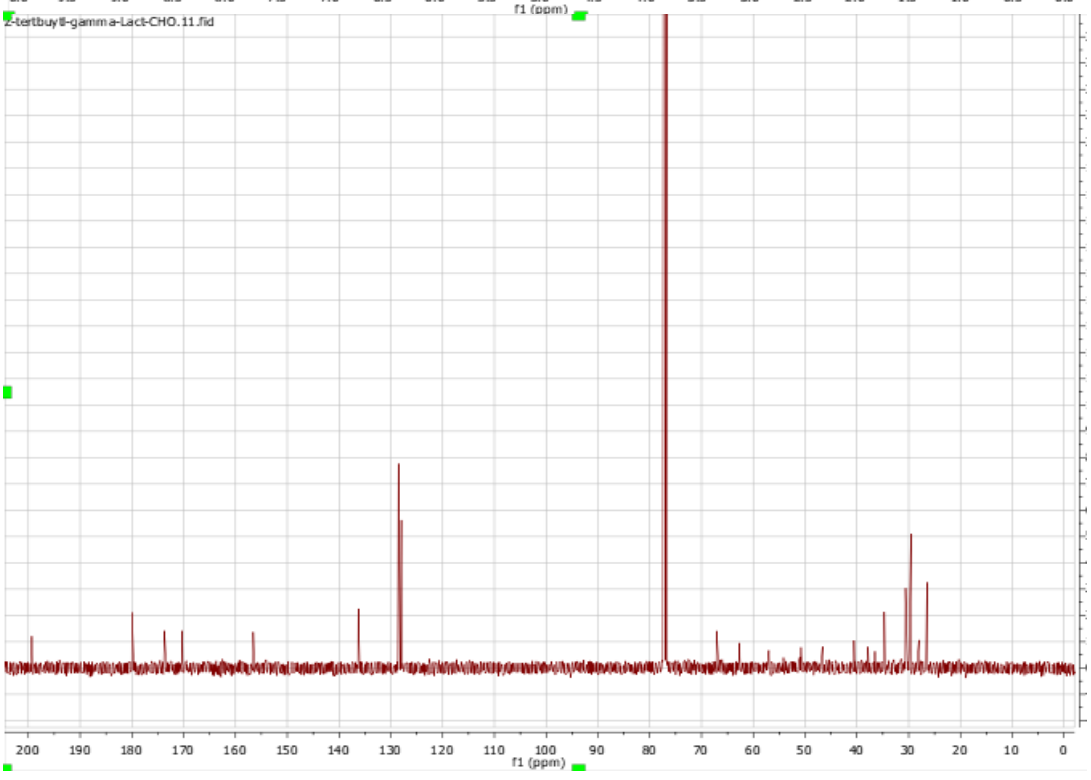


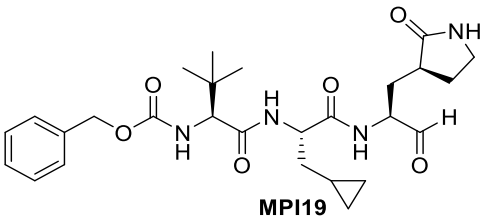



O
NH
O
H
N
H
O
N
H
O
O
N
H
O
H

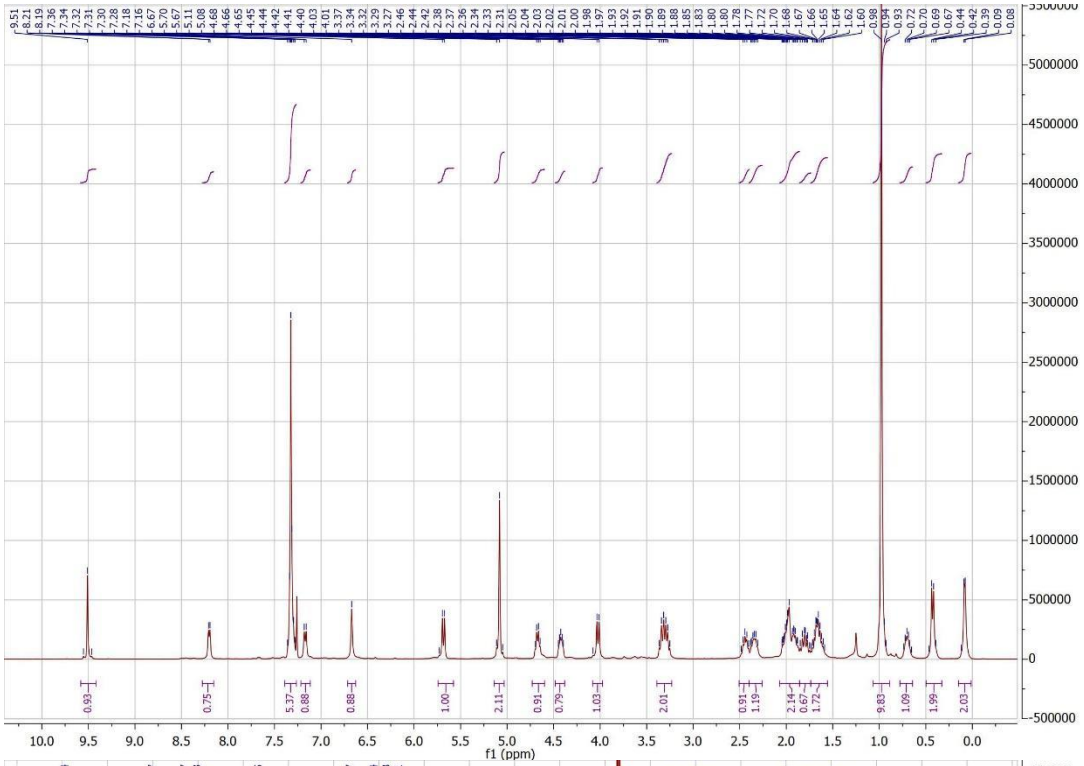
MPI18

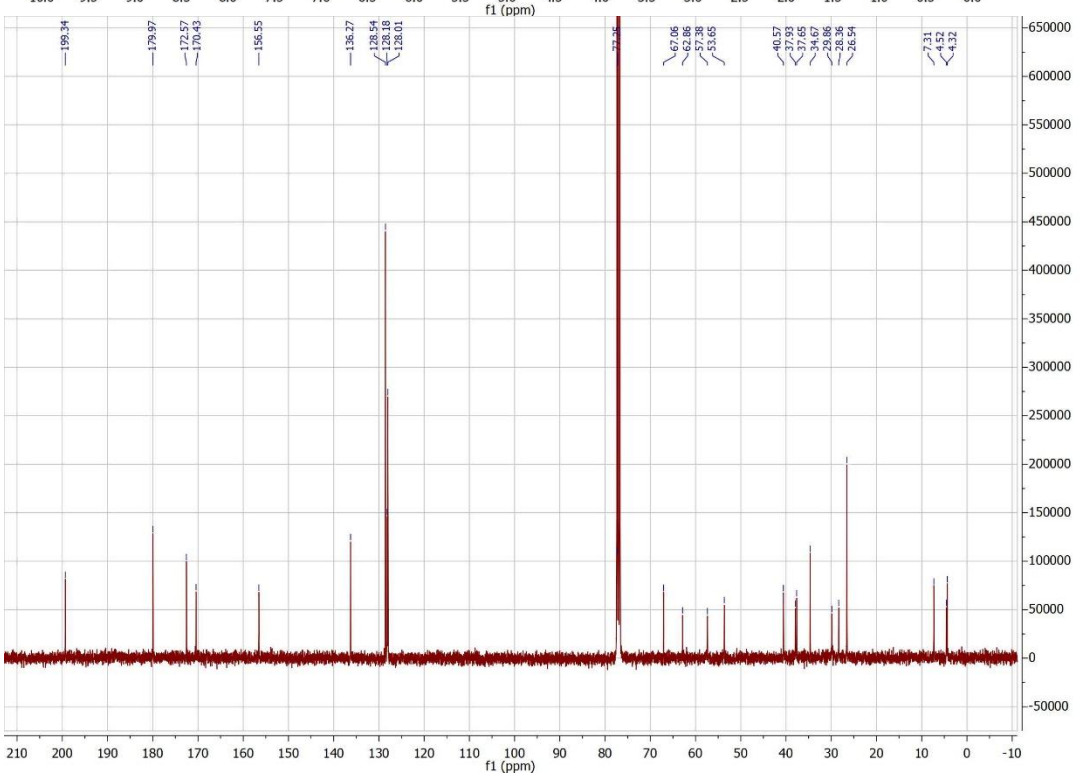

Z-tertbuyll-gamma-Lact-CHO.10.fid
0.81
0.81
4.80
0.60
0.93
2.00
0.96
0.93
1.04
1.99
1.81
6.46
3.19
16.79
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

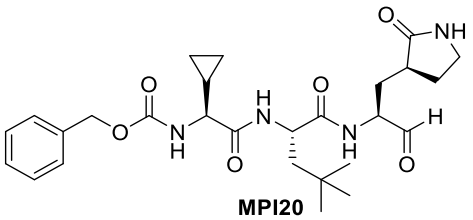

Z-tertbuyll-gamma-Lact-CHO.11.fid
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



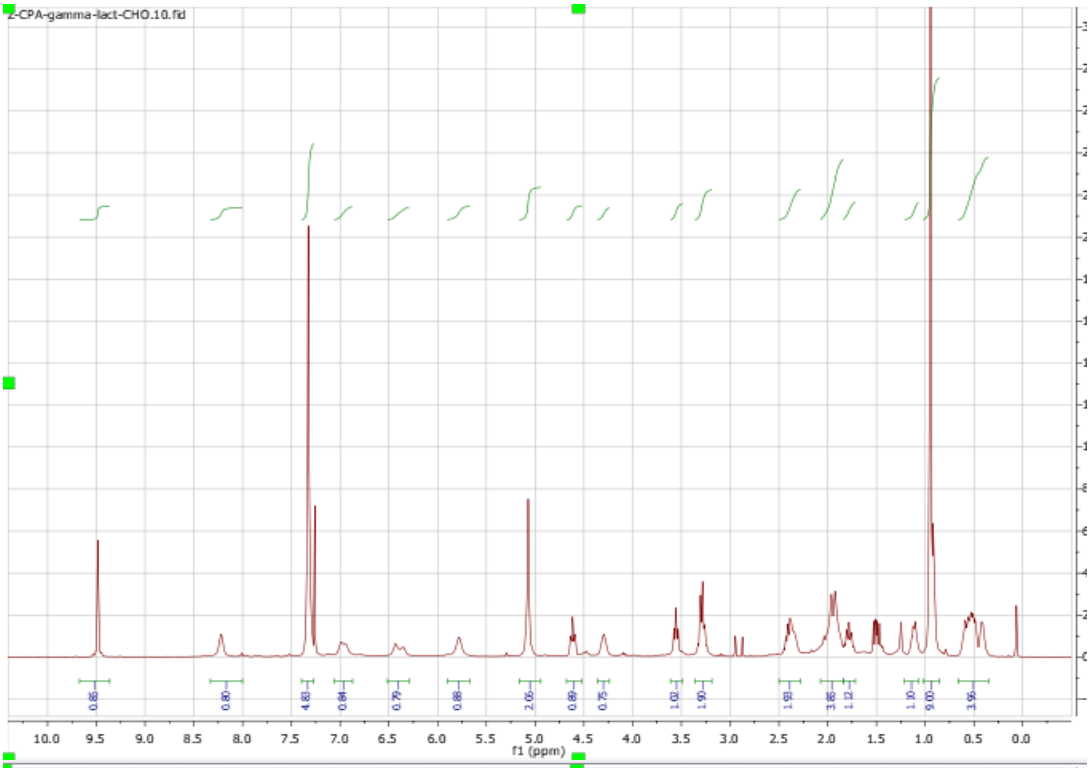
MPI19

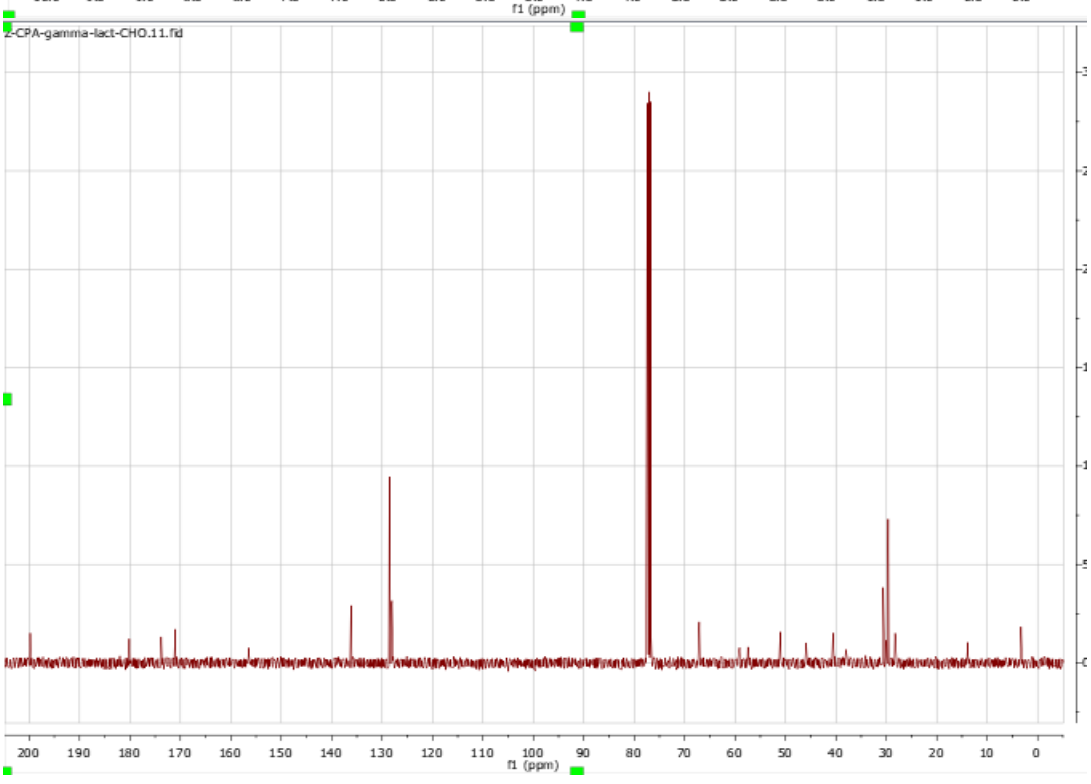


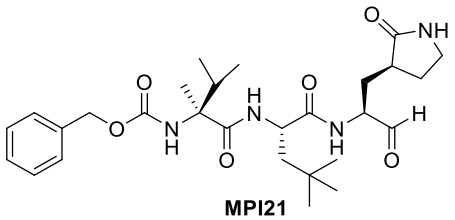




MPI20

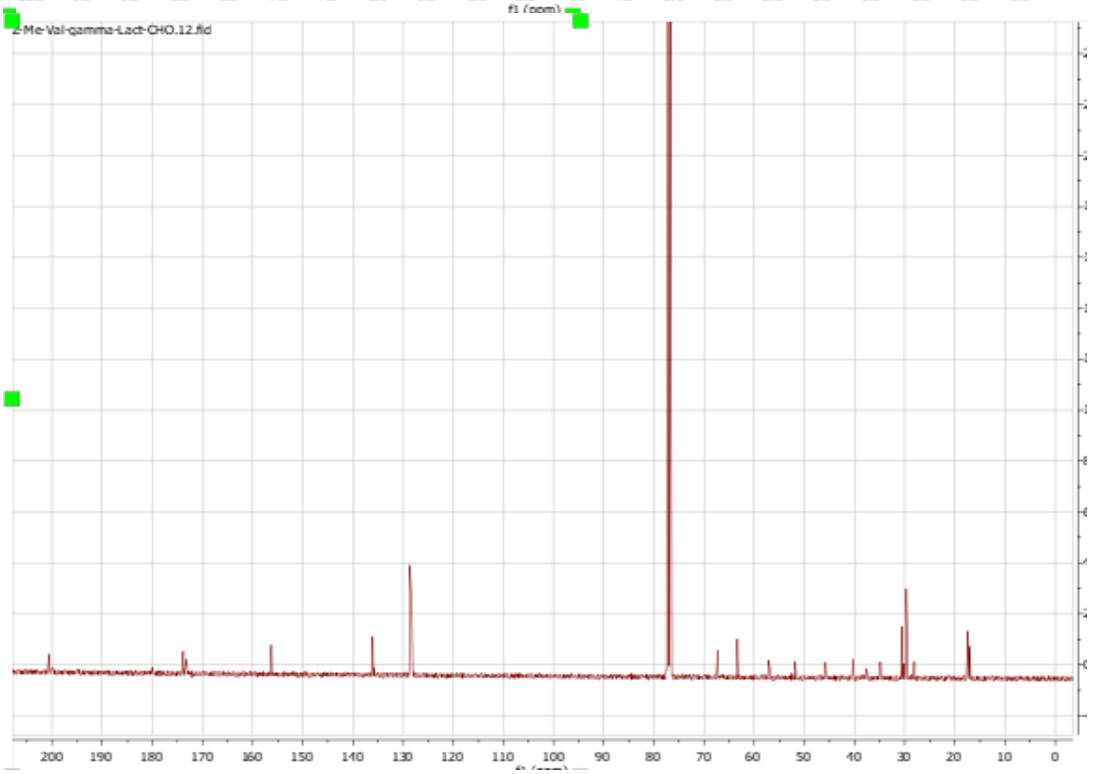

Z-CPA-gamma-lact-CHO.10.fid
f1 (ppm)

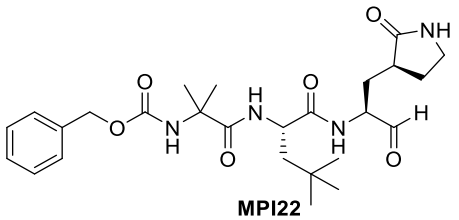

Z-CPA-gamma-lact-CHO.11.fid
f1 (ppm)


O
NH
O
H
N
H
O
N
H
O
O
H

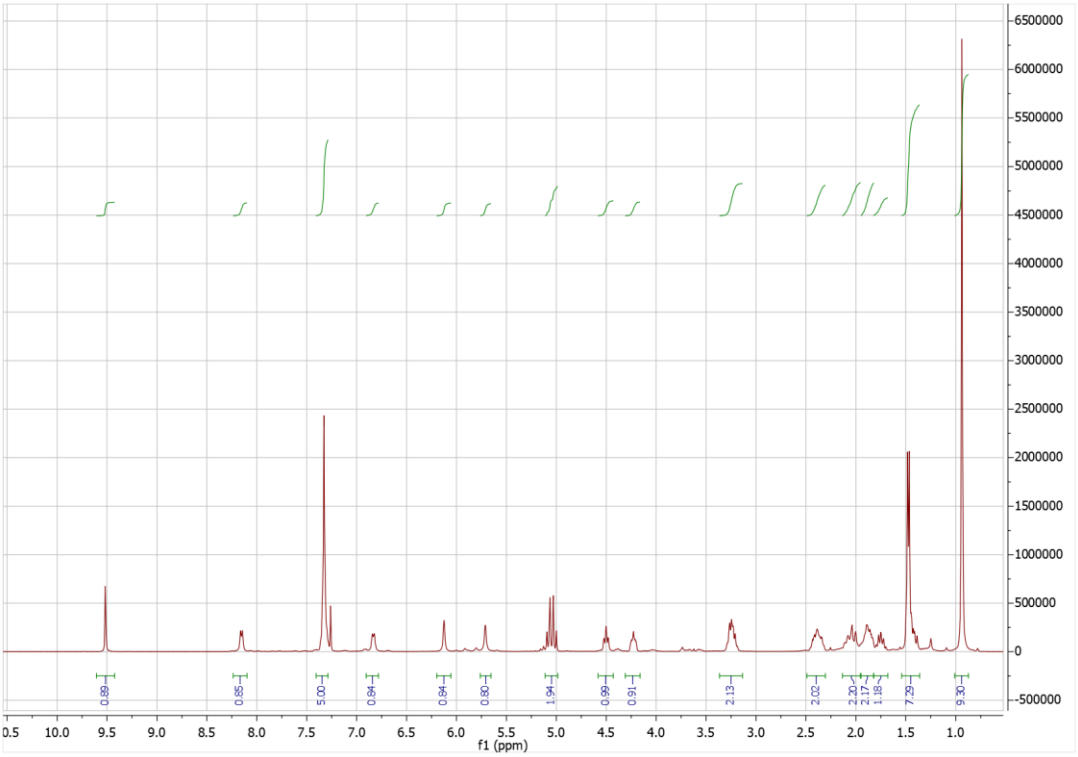
MPI21

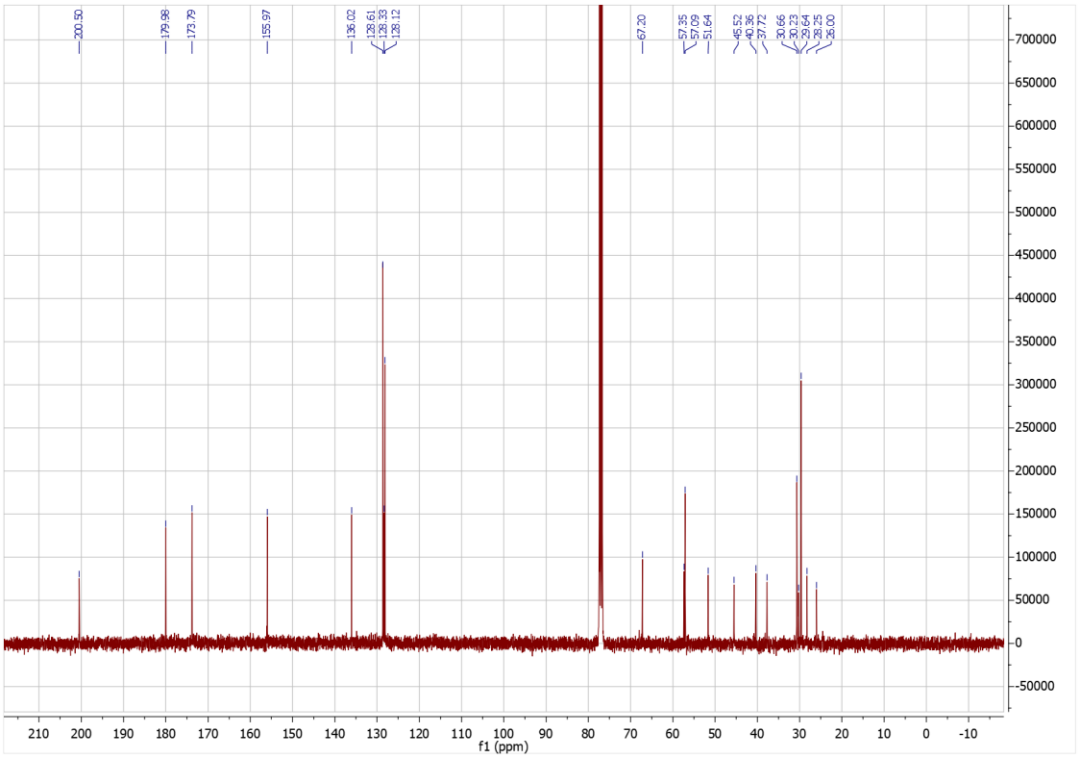

Z-Me-Val-gamma-Lact-CHO.11.fid
f1 (ppm)

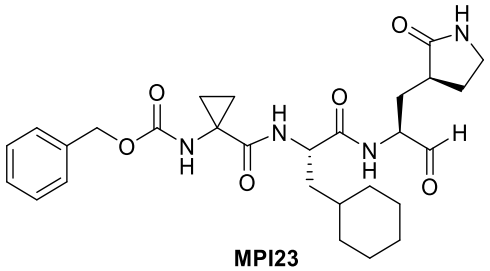

Z-Me-Val-gamma-Lact-CHO.12.fid



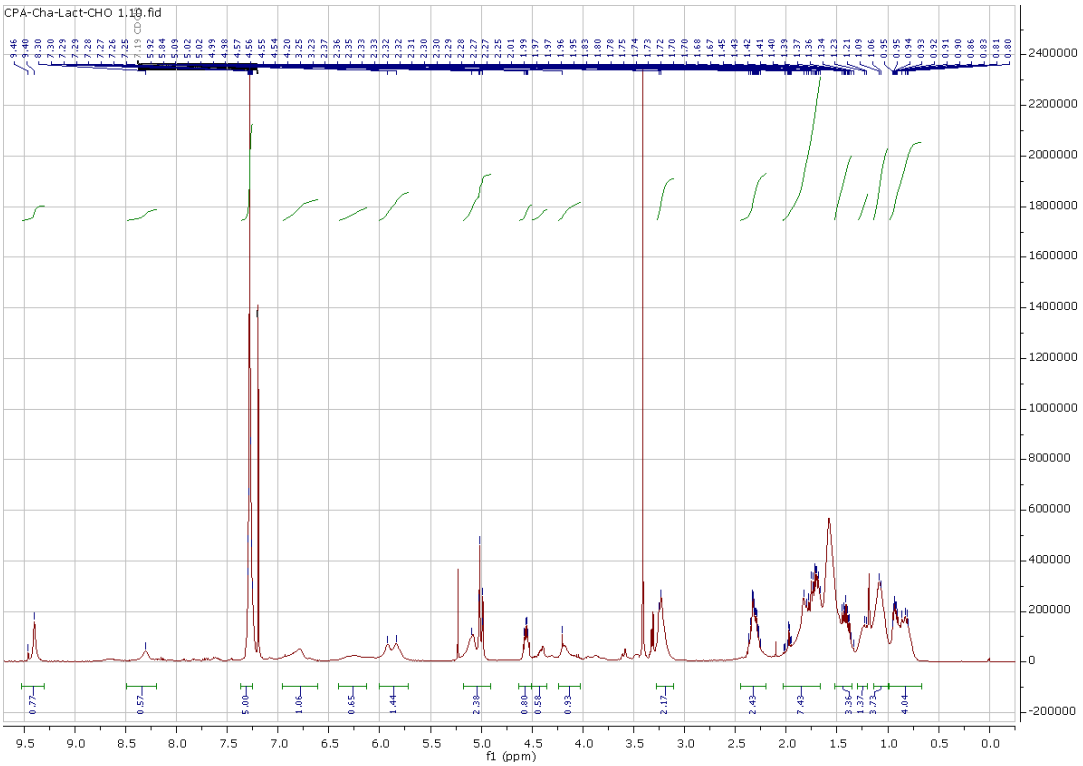
MPI22

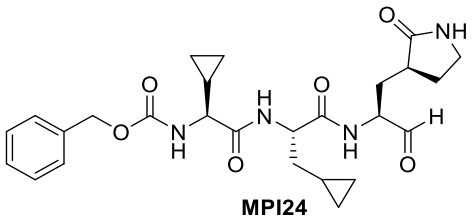

0.89
0.85
5.00
0.94
0.94
0.80
1.94
0.99
0.91
2.13
2.02
2.20
2.17
1.18
7.29
9.30
f1 (ppm)


200.50
179.98
173.79
155.97
136.02
128.61
128.33
128.12
67.20
57.35
57.09
51.64
45.52
40.36
37.72
30.66
30.23
29.64
28.25
26.00
f1 (ppm)

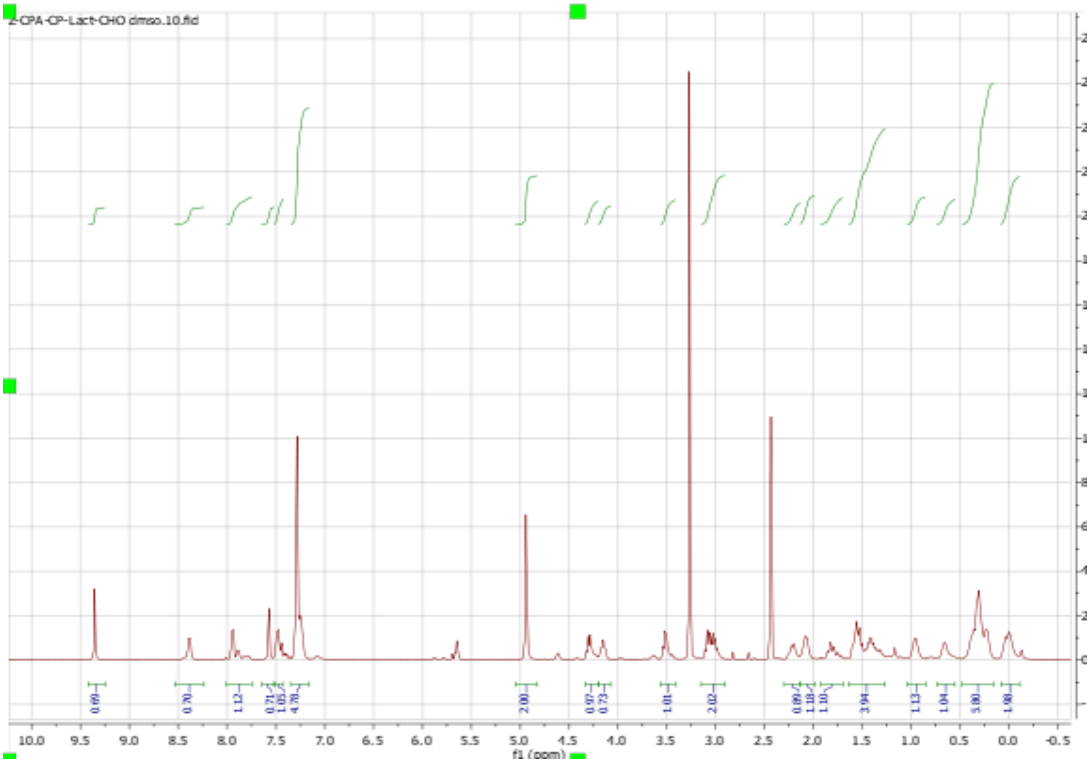


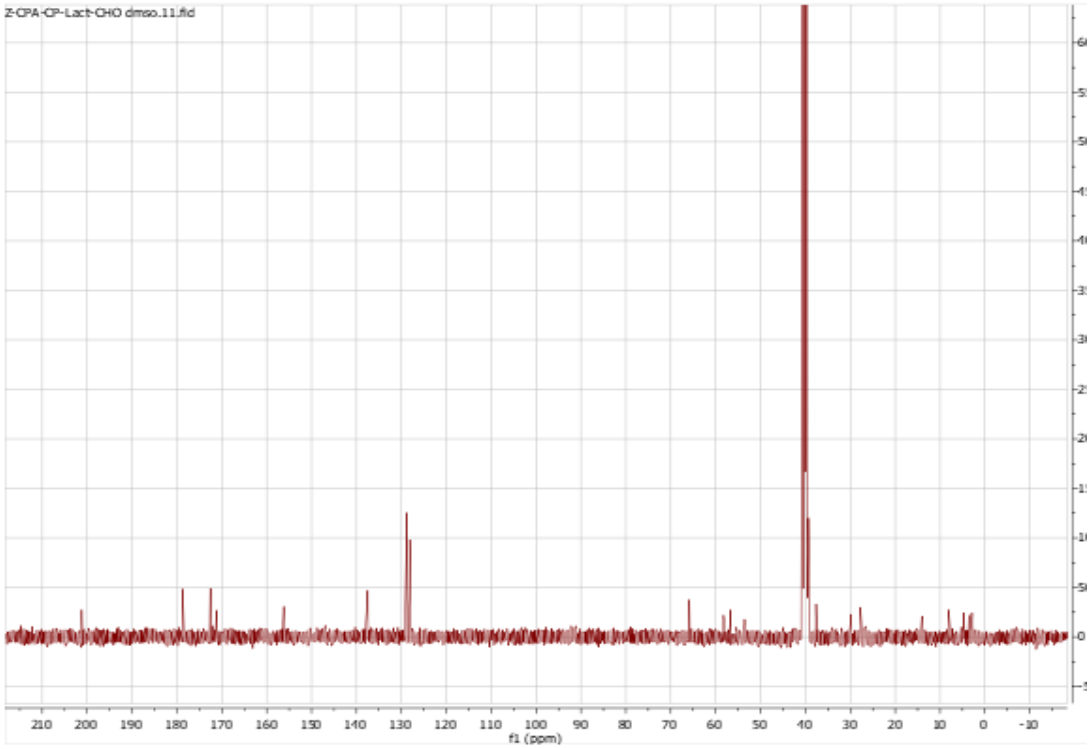
MPI23

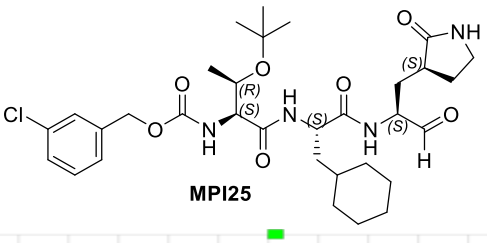




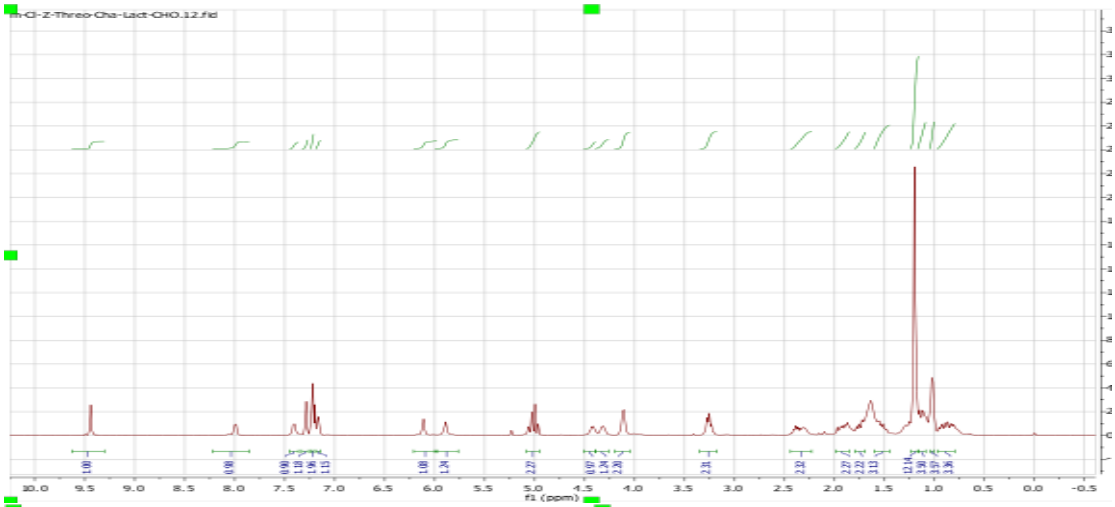
MPI24

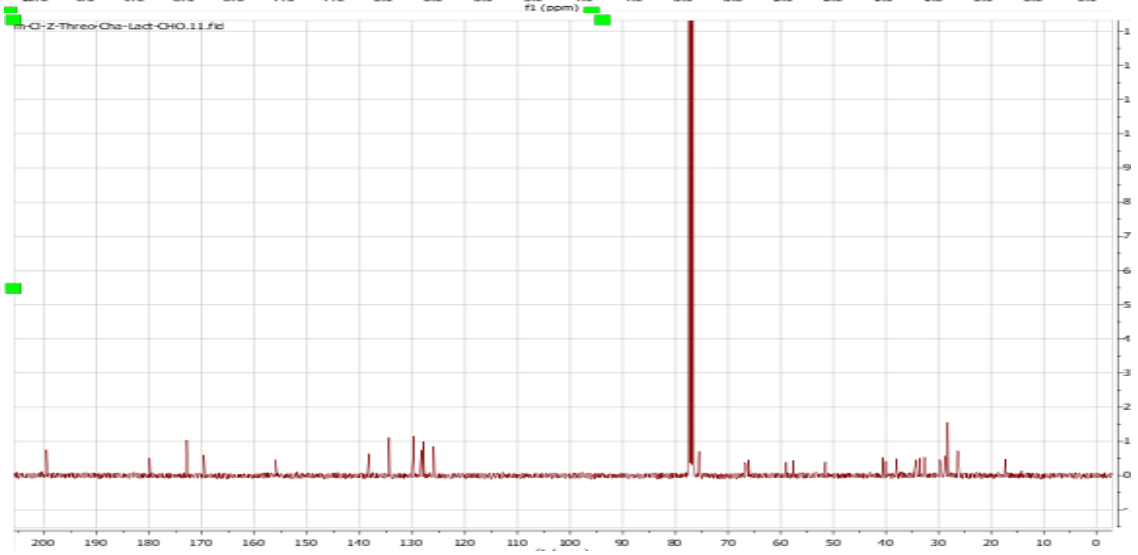

Z-CPA-CP-Lact-CHO dmso.10.fid
f1 (ppm)

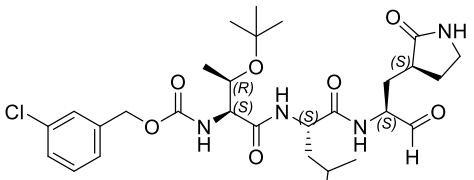

Z-CPA-CP-Lact-CHO dmso.11.fid
f1 (ppm)


Cl
O
O
N
H
O
(R)
(S)
O
H
N
(S)
O
N
H
(S)
O
NH
(S)
O
H

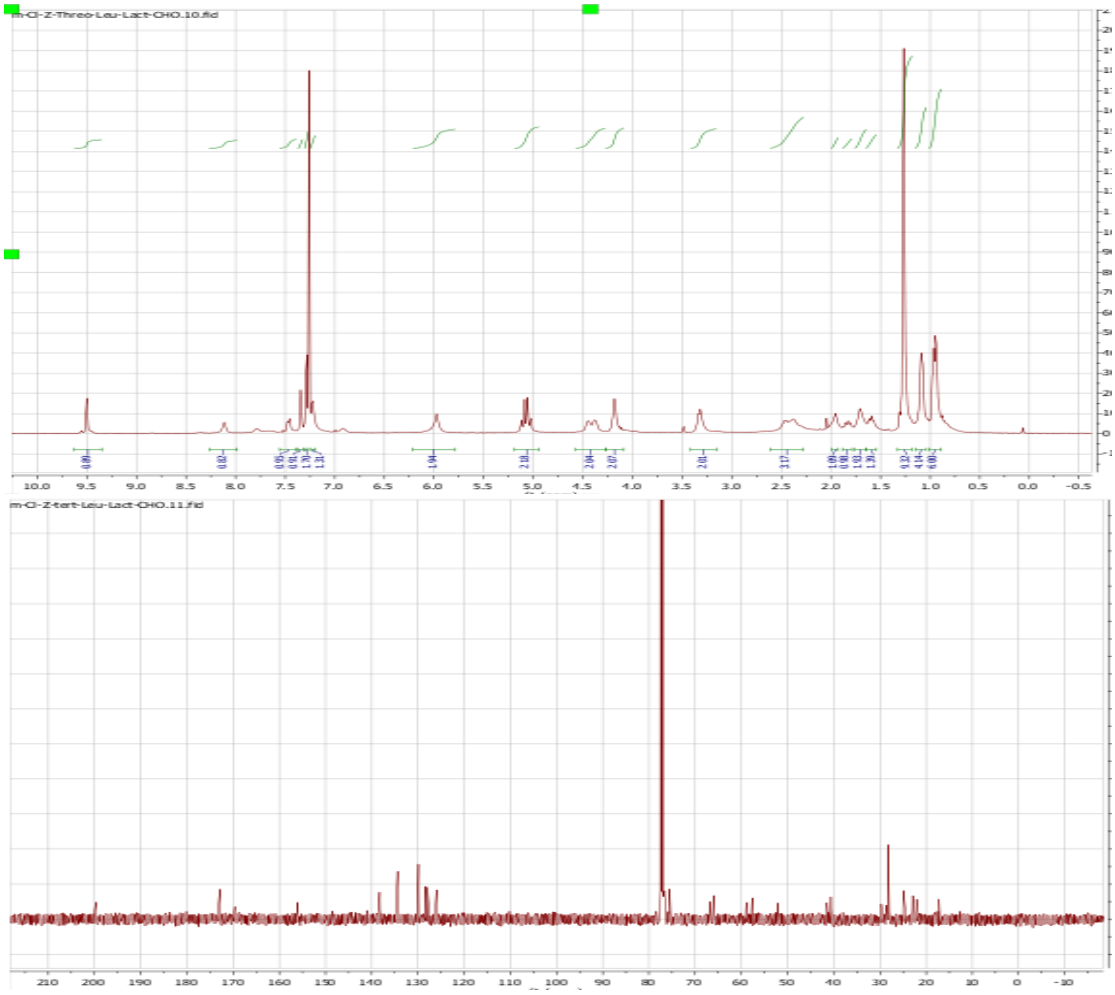
MPI25

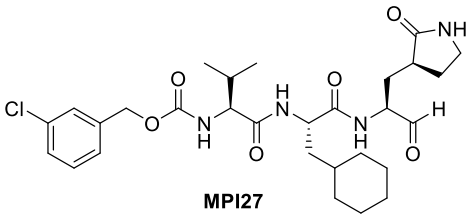

m-Cl-Z-Threo-Cha-Lact-CHO.12.fid
f1 (ppm)


m-Cl-Z-Threo-Cha-Lact-CHO.11.fid

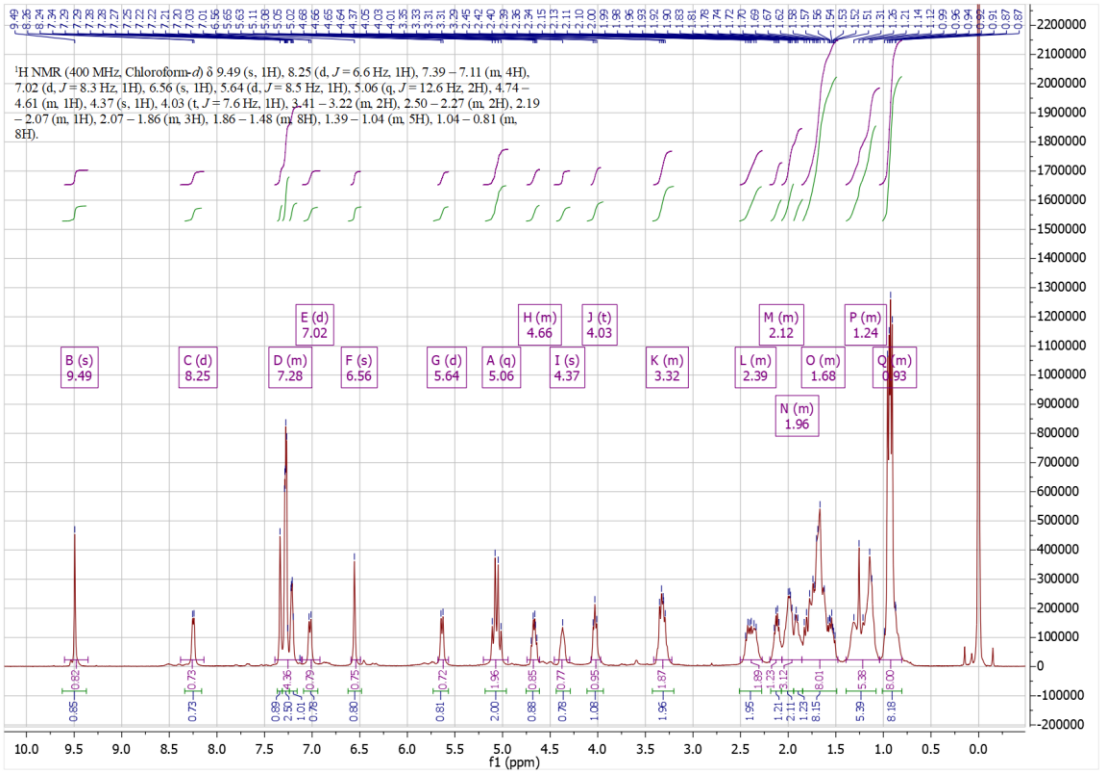

Cl
O
O
N
H
O
(R)
(S)
H
N
(S)
O
N
H
(S)
O
NH
(S)
O
H

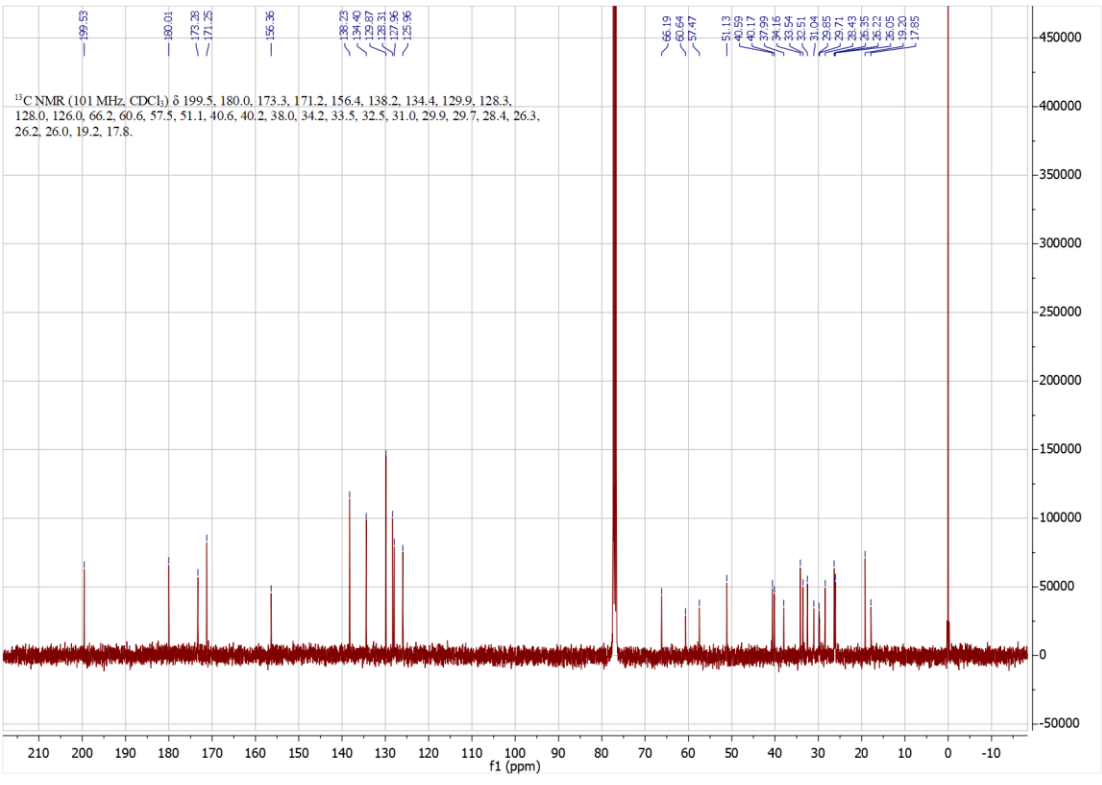
MPI26

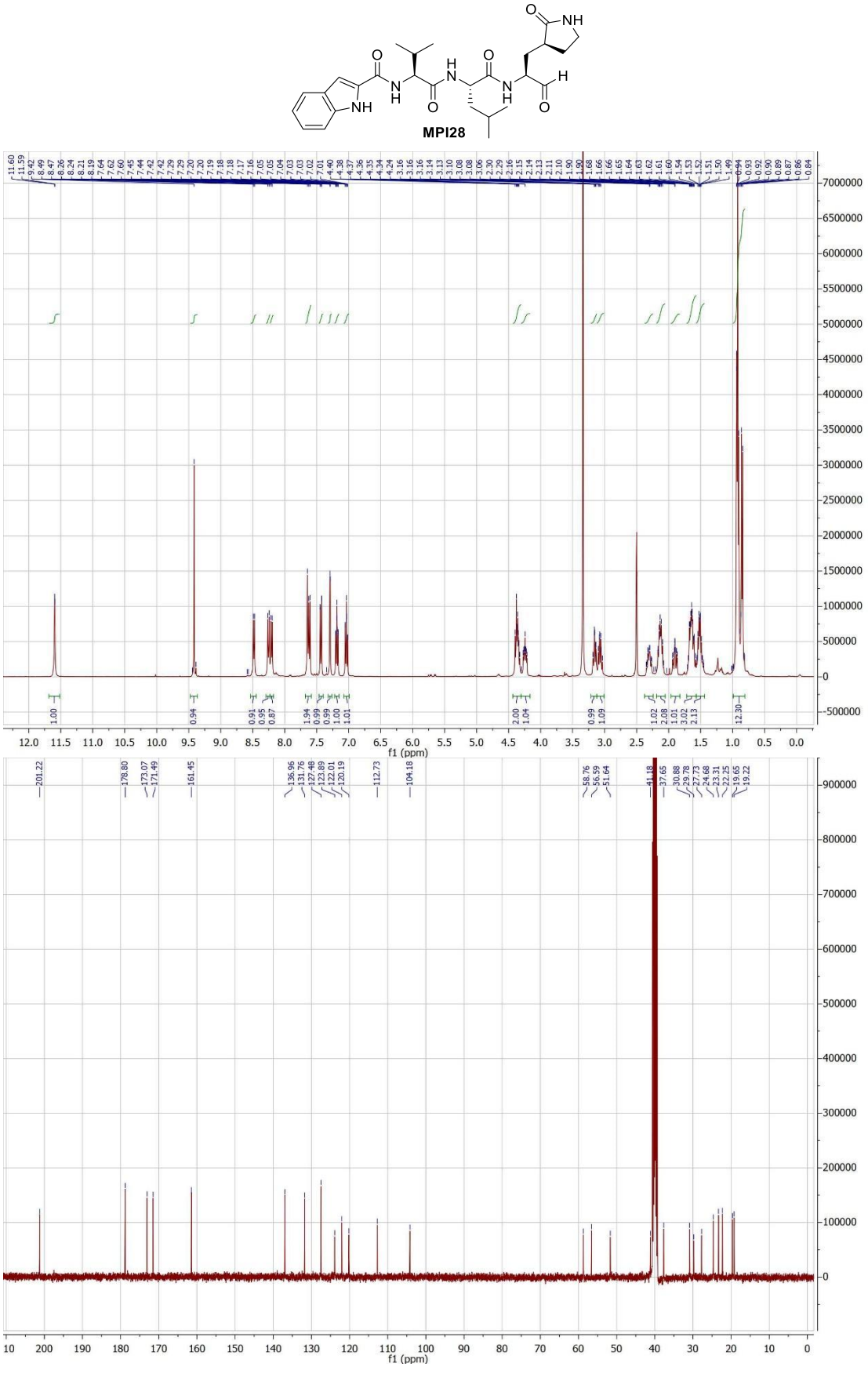

m-Cl-Z-Threo-Leu-Lact-CHO.10.fid
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
m-Cl-Z-tert-Leu-Lact-CHO.11.fid
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10



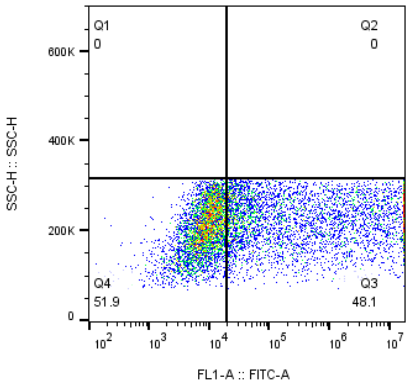
MPI27


[1]H NMR (400 MHz, Chloroform-d) δ 9.49 (s, 1H), 8.25 (d, J = 6.6 Hz, 1H), 7.39 – 7.11 (m, 4H), 7.02 (d, J = 8.3 Hz, 1H), 6.56 (s, 1H), 5.64 (d, J = 8.5 Hz, 1H), 5.06 (q, J = 12.6 Hz, 2H), 4.74 – 4.61 (m, 1H), 4.37 (s, 1H), 4.03 (t, J = 7.6 Hz, 1H), 3.41 – 3.22 (m, 2H), 2.50 – 2.27 (m, 2H), 2.19 – 2.07 (m, 1H), 2.07 – 1.86 (m, 3H), 1.86 – 1.48 (m, 8H), 1.39 – 1.04 (m, 5H), 1.04 – 0.81 (m, 8H).
B (s) 9.49
C (d) 8.25
D (m) 7.28
E (d) 7.02
F (s) 6.56
G (d) 5.64
A (q) 5.06
H (m) 4.66
I (s) 4.37
J (t) 4.03
K (m) 3.32
L (m) 2.39
M (m) 2.12
N (m) 1.96
O (m) 1.68
P (m) 1.24
Q (m) 0.93
f1 (ppm)

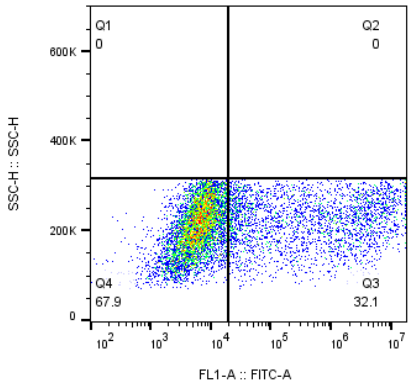

[13]C NMR (101 MHz, CDCl3) δ 199.5, 180.0, 173.3, 171.2, 156.4, 138.2, 134.4, 129.9, 128.3, 128.0, 126.0, 66.2, 60.6, 57.5, 51.1, 40.6, 40.2, 38.0, 34.2, 33.5, 32.5, 31.0, 29.9, 29.7, 28.4, 26.3, 26.2, 26.0, 19.2, 17.8.
f1 (ppm)



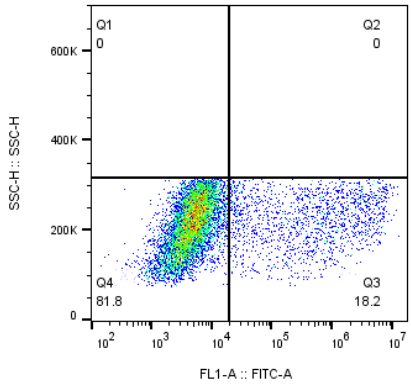
Flow cytometry images for MPI11, compound concentration labeled.



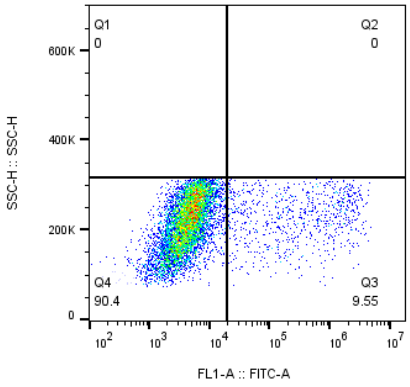
MPI11-10uM
HEK
8503



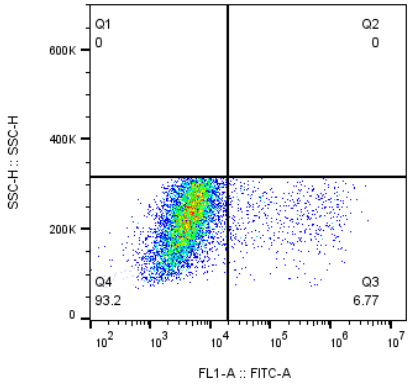
MPI11-2uM
HEK
8864



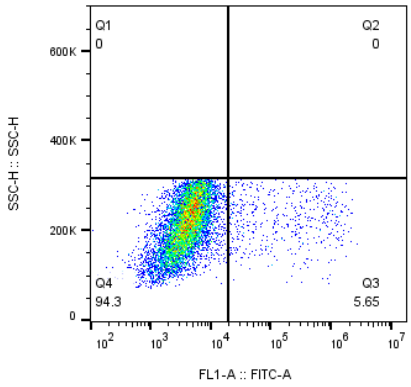
MPI11-400nM
HEK
8814



MPI11-80nM
HEK
8437

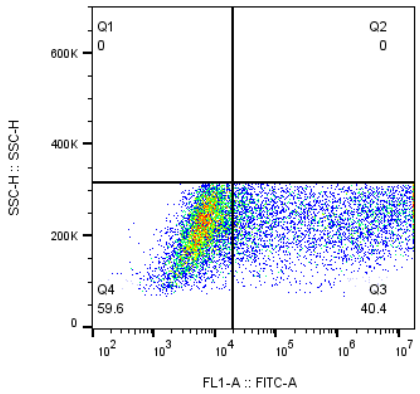


MPI11-16nM
HEK
8238

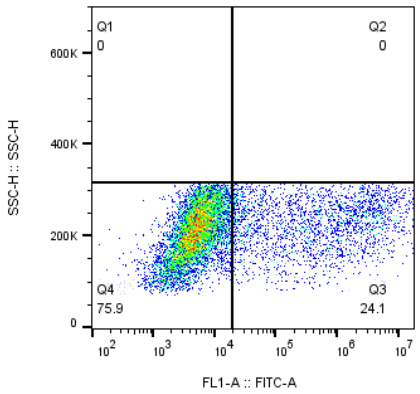


MPI11-3.2nM
HEK
8566

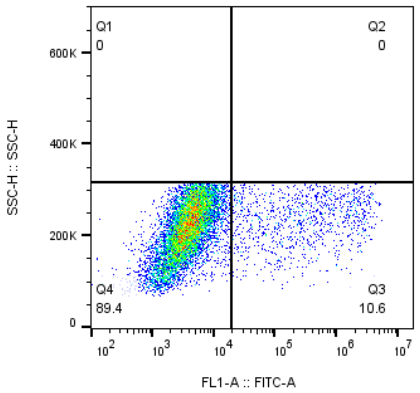
MPI12



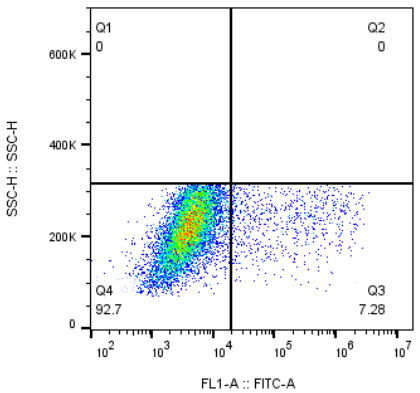
MPI12-10uM
HEK
9939



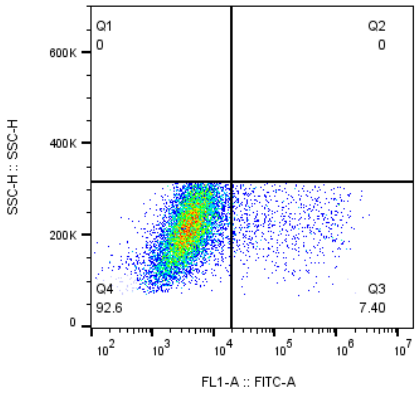
MPI12-2uM
HEK
10342



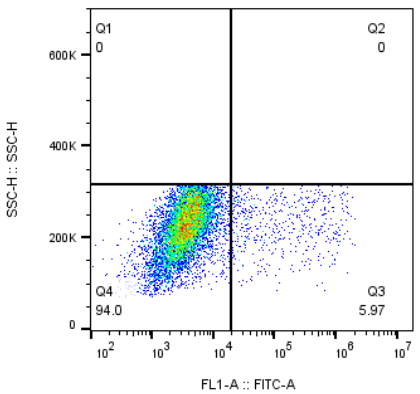
MPI12-400nM
HEK
9916



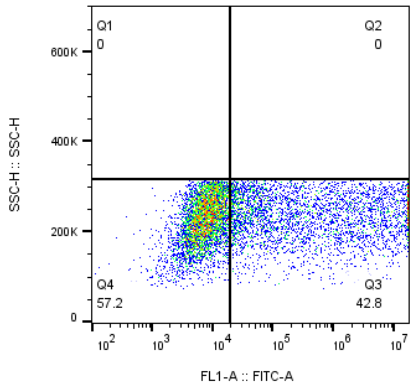
MPI12-80nM
HEK
10198



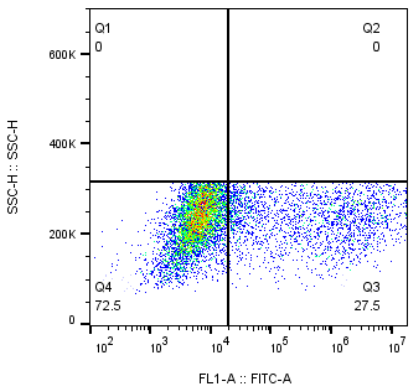
MPI12-16nM
HEK
10331



MPI12-3.2nM
HEK
8893



MPI13-10uM
HEK
8217



MPI13-2uM
HEK
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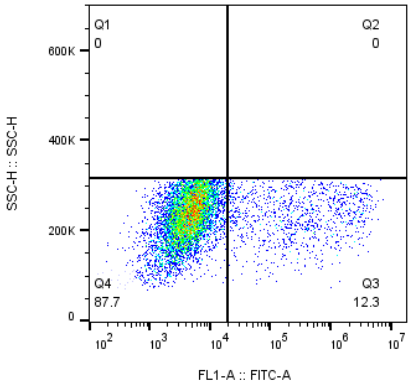
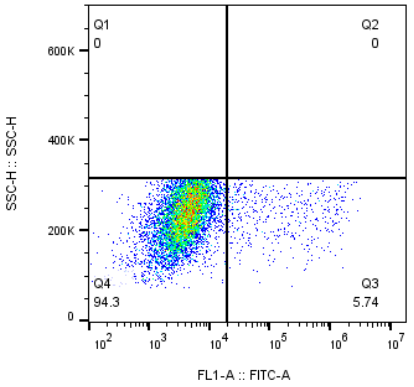
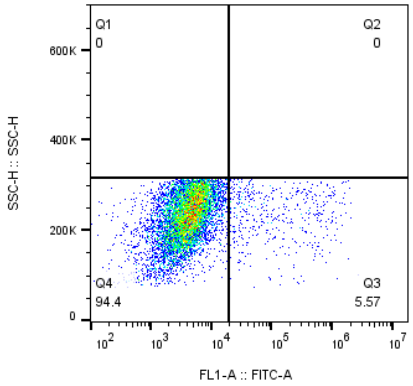


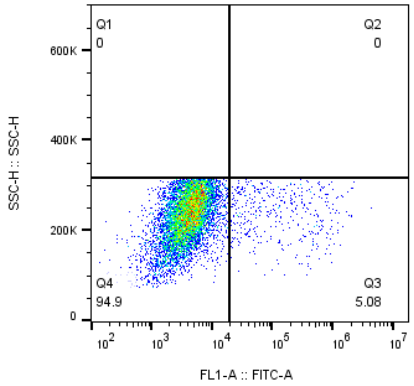
MPI13-400nM
HEK
8537



MPI13-80nM
HEK
8138

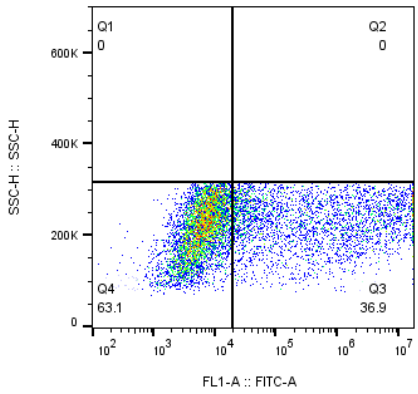


MPI13-16nM
HEK
8397

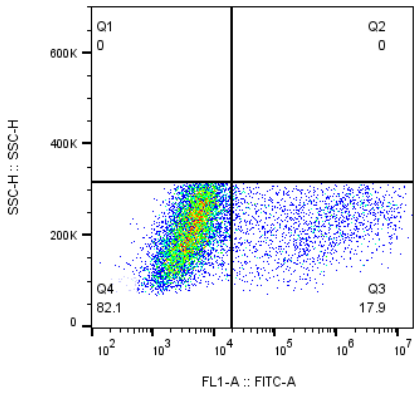


MPI13-3.2nM
HEK
8191

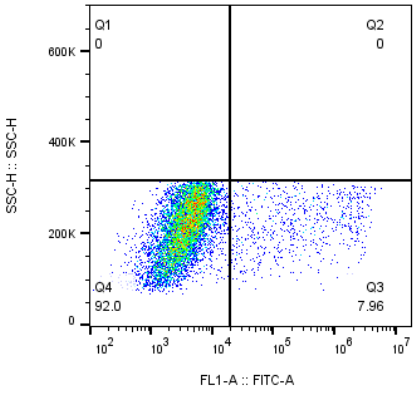
MPI14



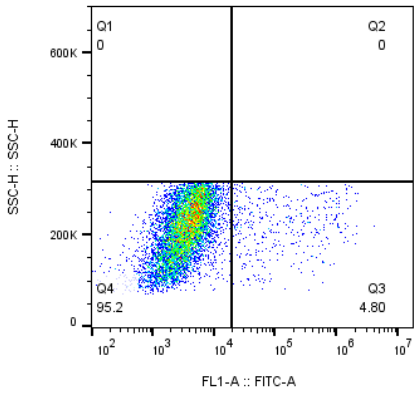
MPI14-10uM
HEK
8663



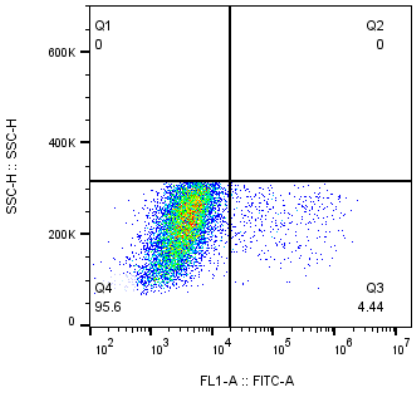
MPI14-2uM
HEK
9318



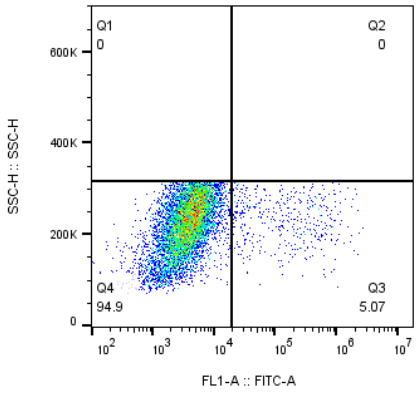
MPI14-400nM
HEK
8899



MPI14-80nM
HEK
8954

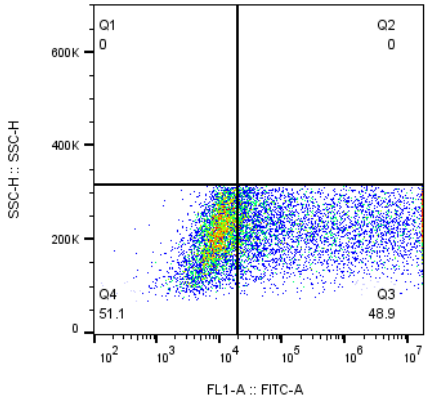


MPI14-16nM
HEK
8937

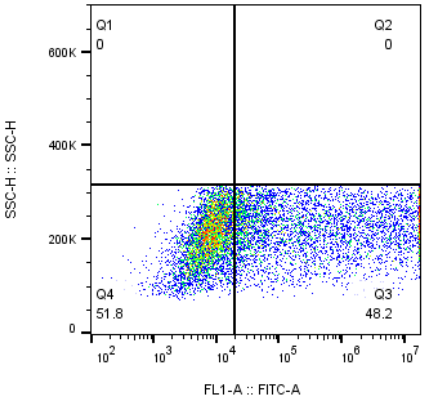


MPI14-3.2nM
HEK
8421

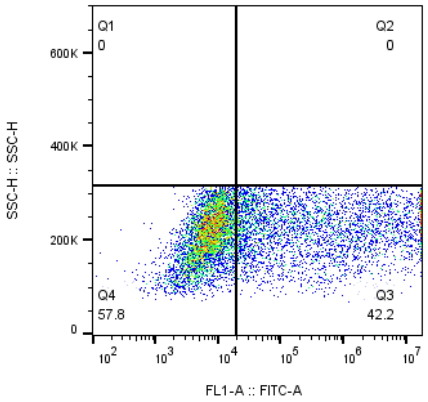
MPI16



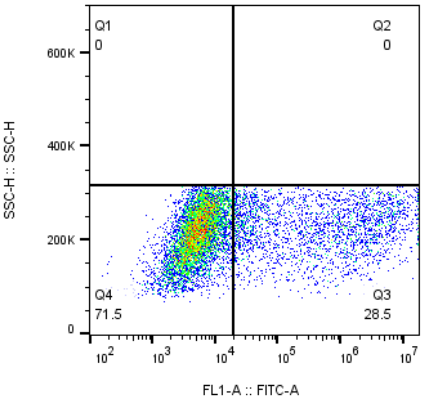
MPI16-10uM
HEK
9121



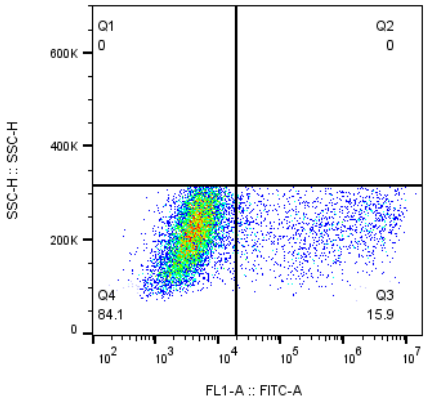
MPI16-2uM
HEK
9316



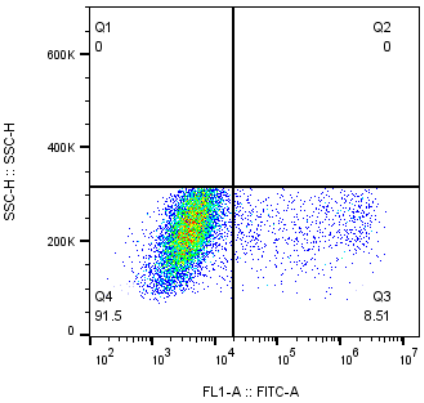
MPI16-400nM
HEK
9078



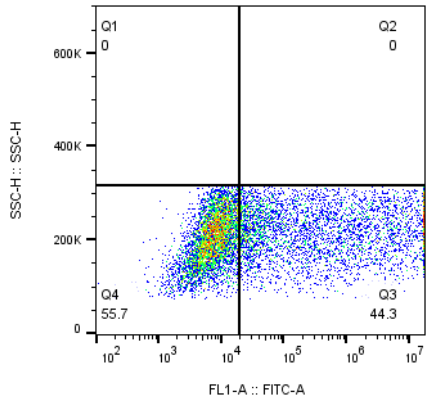
MPI16-80nM
HEK
9190



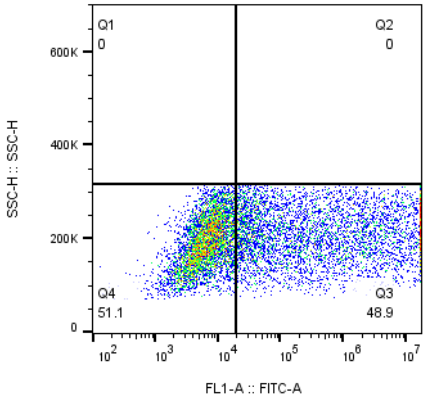
MPI16-16nM
HEK
9193



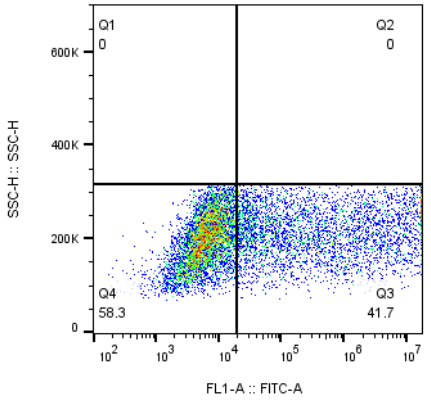
MPI16-3.2nM
HEK
8670



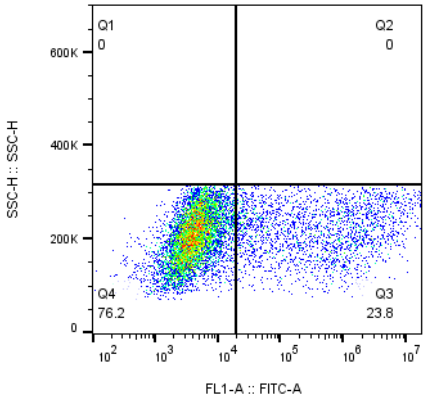
MPI17-10uM
HEK
9139



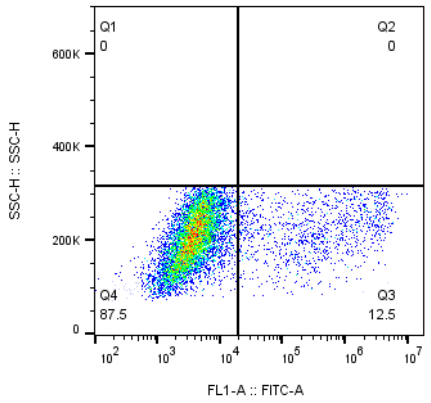
MPI17-2uM
HEK
9915



MPI17-400nM
HEK
9653



MPI17-80nM
HEK
9446



MPI17-16nM
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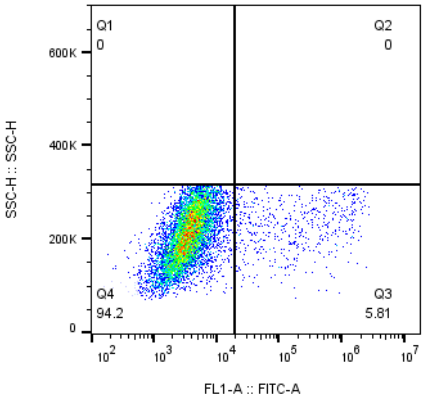
9369



MPI17-3.2nM
HEK
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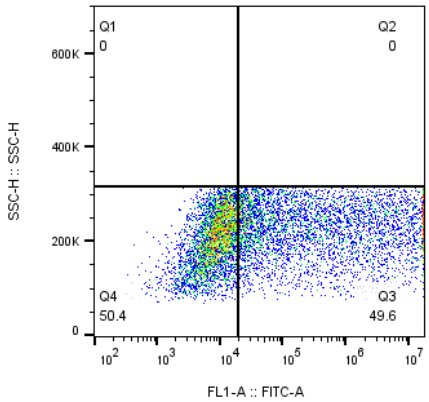
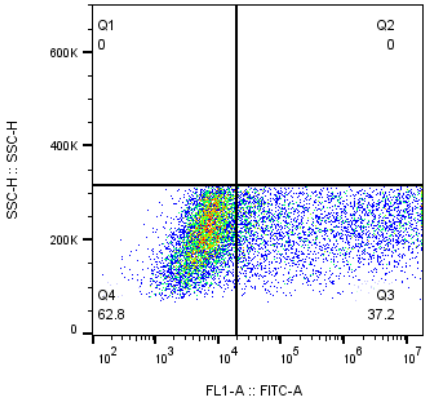
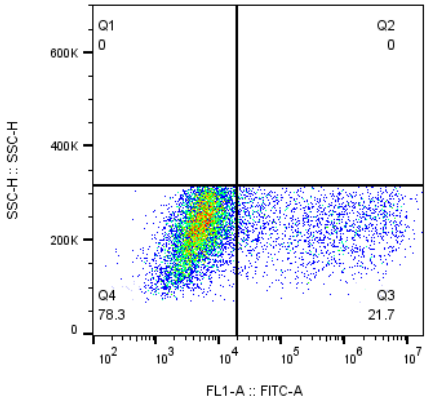


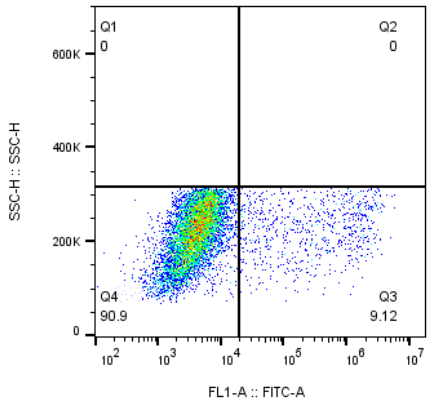
MPI18-10uM
HEK
9023



MPI18-2uM
HEK
9158



MPI18-400nM
HEK
8579



MPI18-80nM
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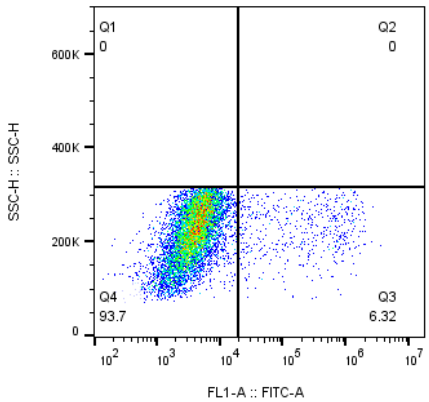
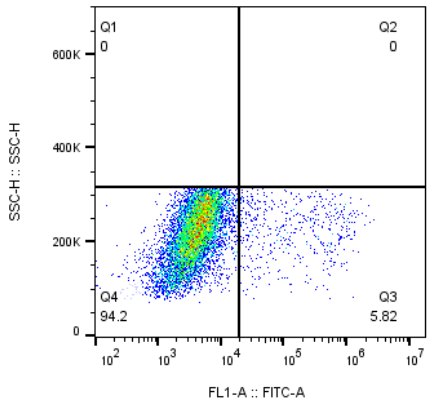
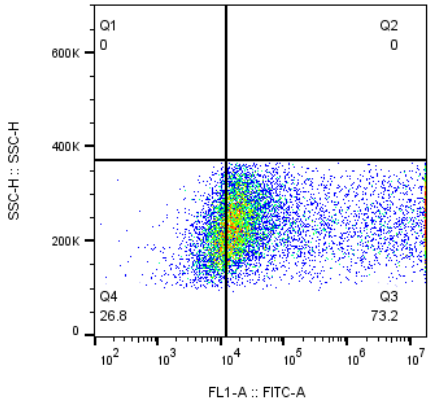


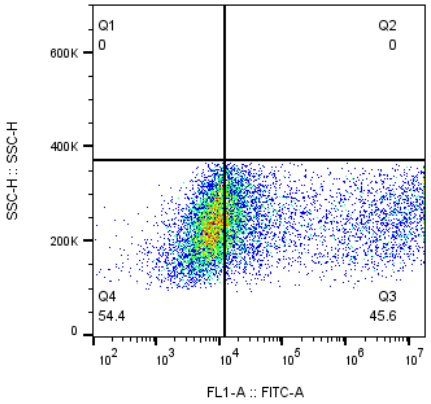
MPI18-80nM
HEK
8317



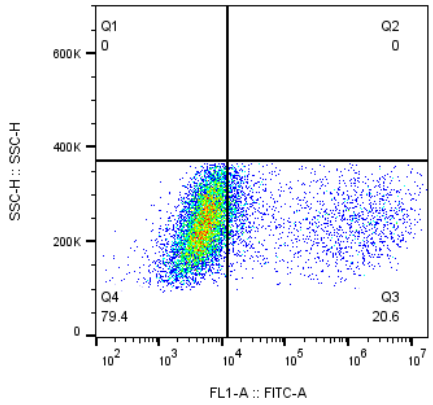
MPI18-3.2nM
HEK
8421



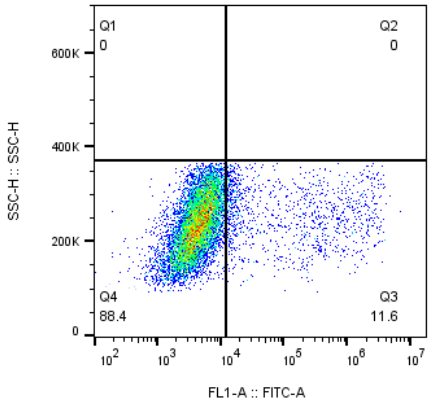
MPI19-10uM
HEK
9577



MPI19-2uM
HEK
9958



MPI19-400nM
HEK
9672



MPI19-80nM
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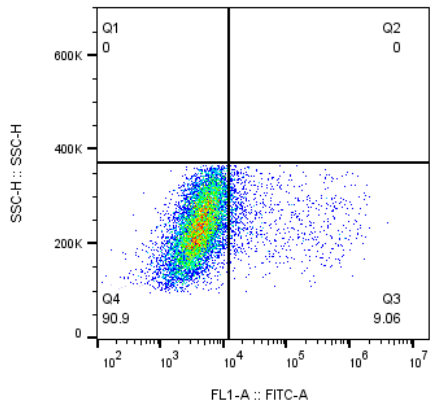
9771



MPI19-16nM
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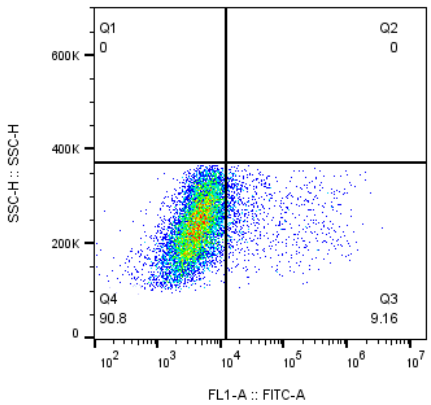

MPI19-3.2nM
HEK
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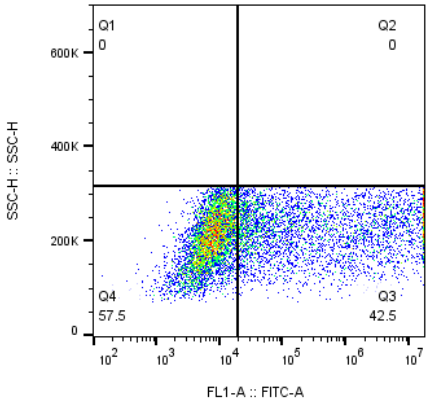
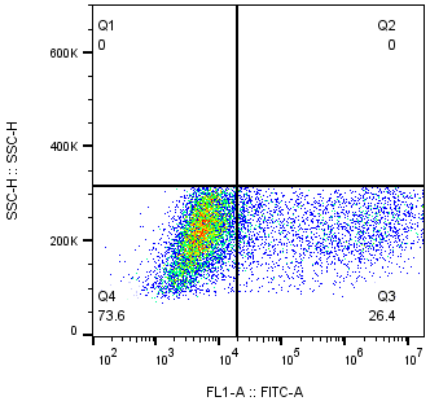
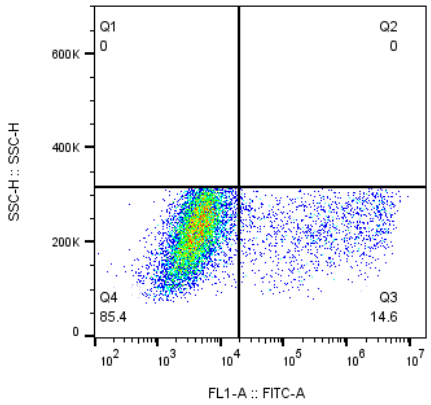


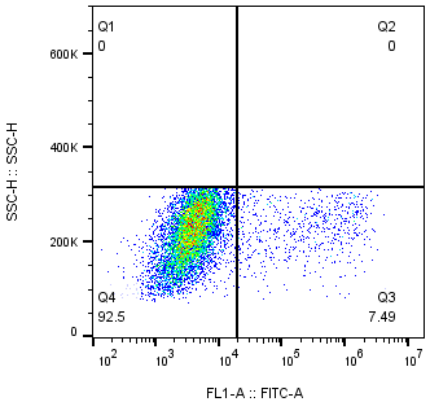
MPI20-10uM
HEK
9252



MPI20-2uM
HEK
9242



MPI20-400nM
HEK
8719



MPI20-80nM
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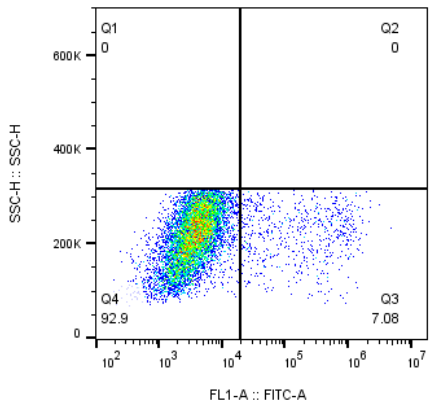

MPI20-16nM
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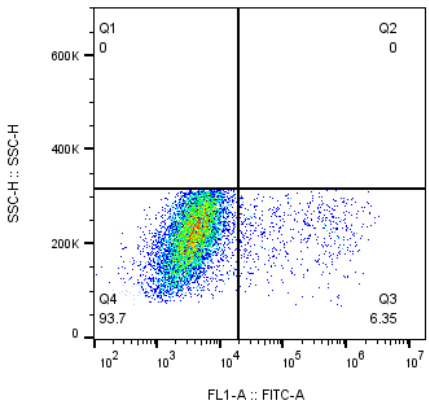
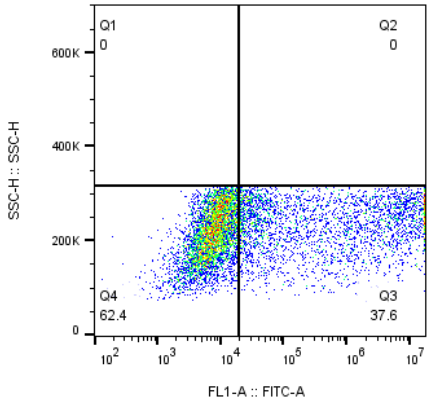
8988



MPI20-3.2nM
HEK
8886



MPI21-10uM
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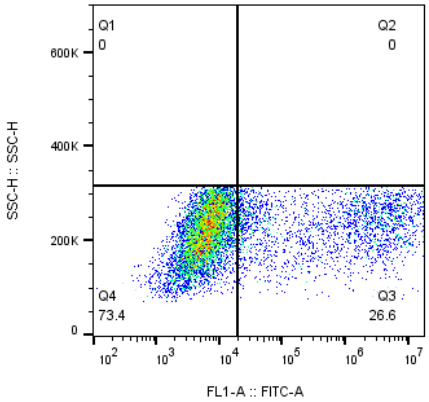
8396



MPI21-2uM
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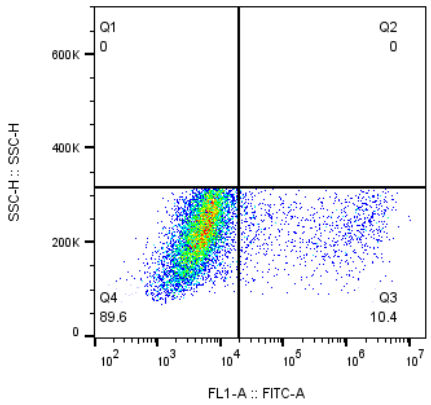
8758



MPI21-400nM
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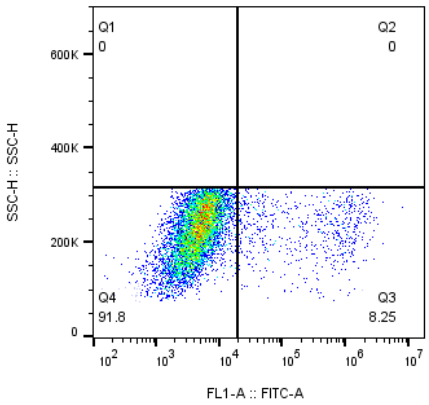

MPI21-80nM
HEK
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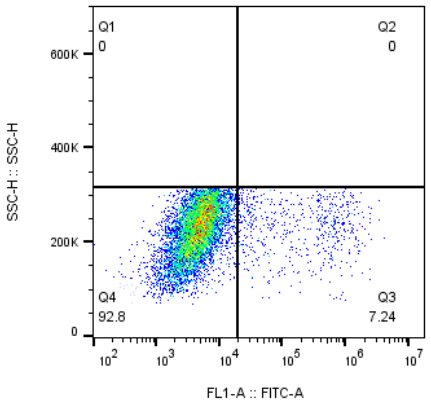
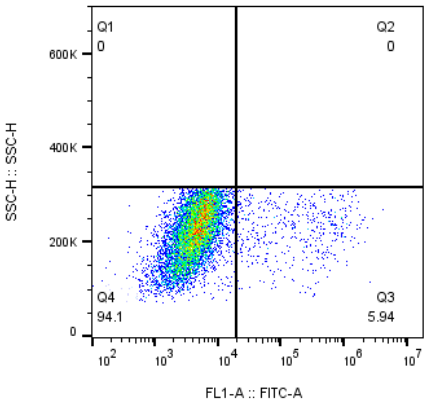
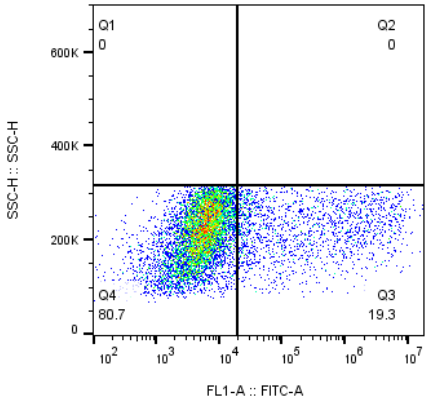


MPI21-16nM
HEK
8162

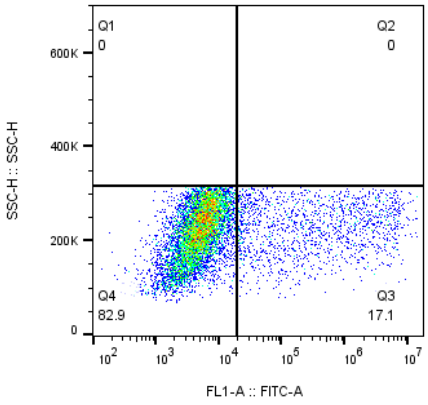


MPI21-3.2nM
HEK
8402

MPI22



MPI22-10uM
HEK
9010



MPI22-2uM
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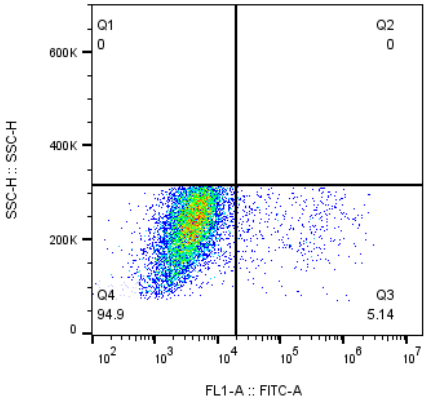

MPI22-400nM
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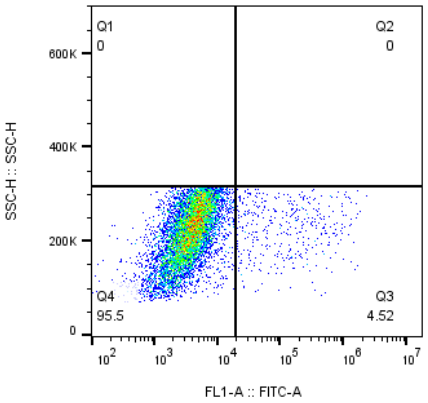
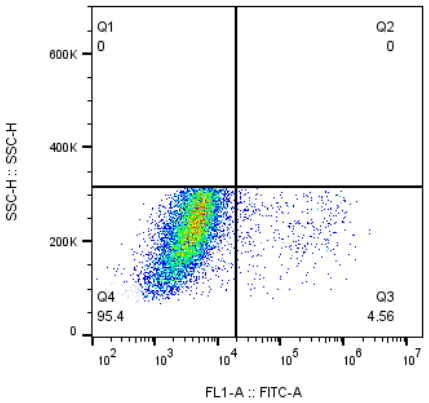
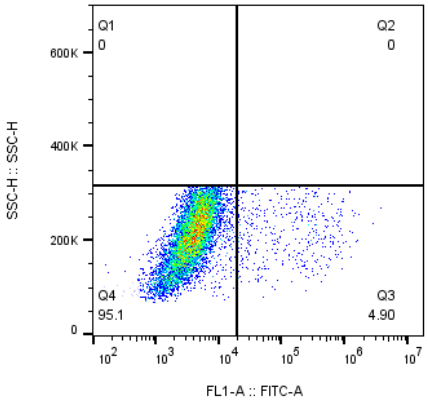


MPI22-80nM
HEK
8718



MPI22-16nM
HEK
8647



MPI22-3.2nM
HEK
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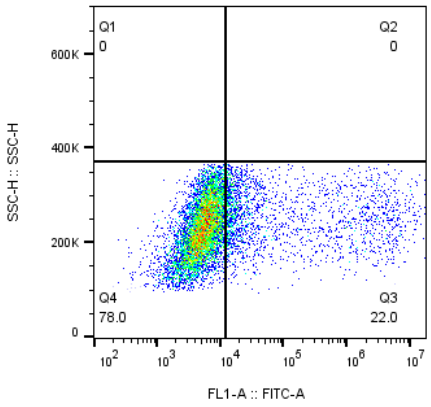
MPI23



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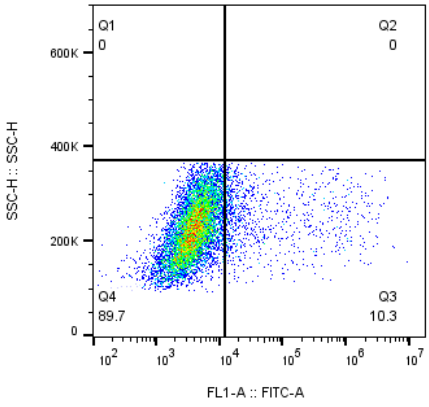

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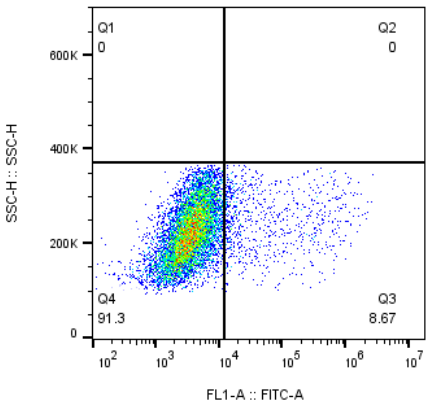

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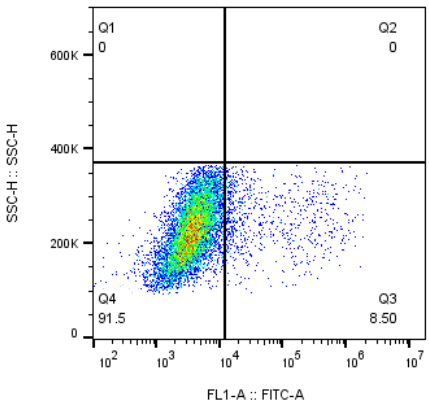

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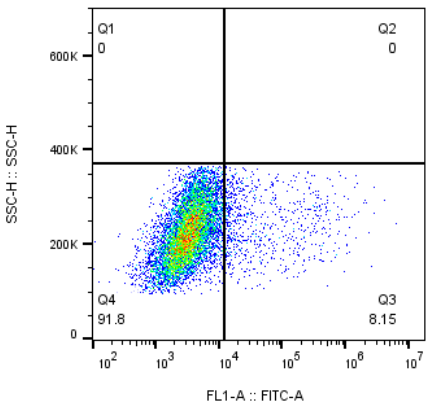

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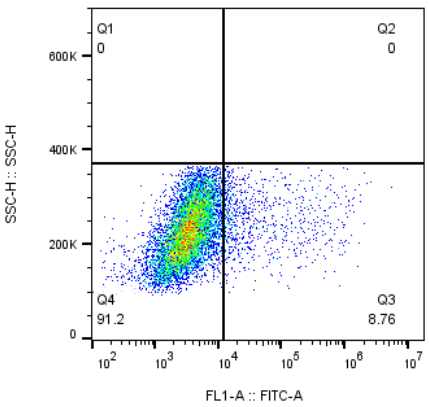

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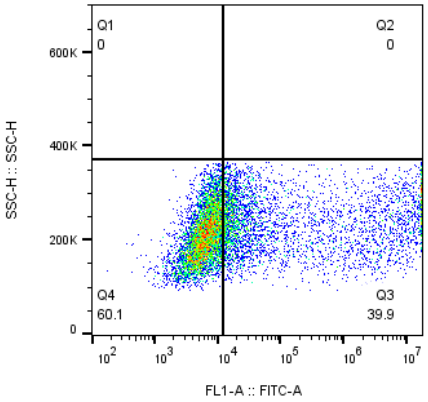

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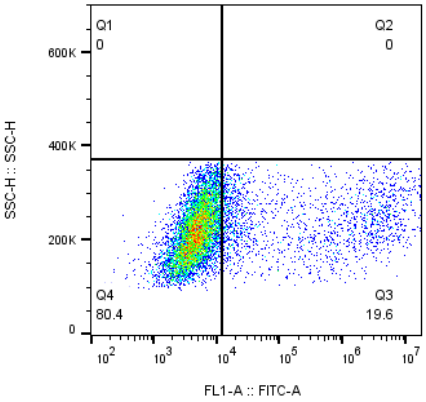

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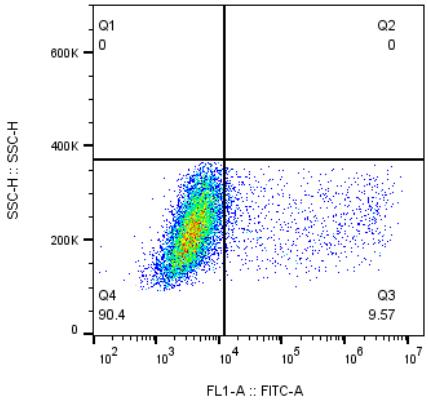

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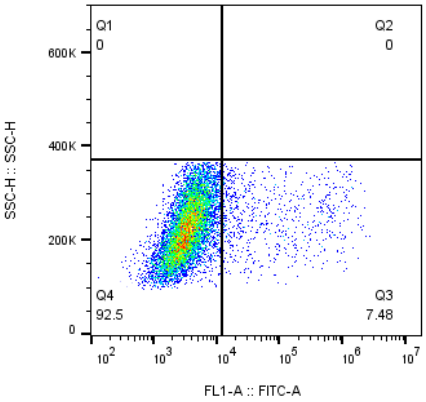
9745



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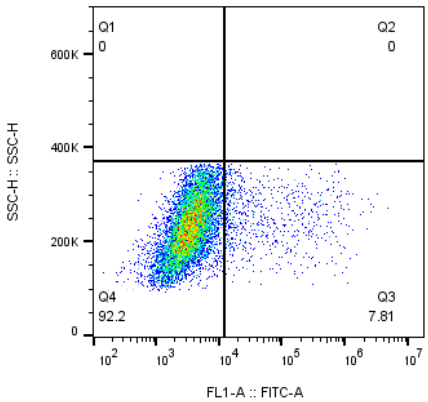
9736



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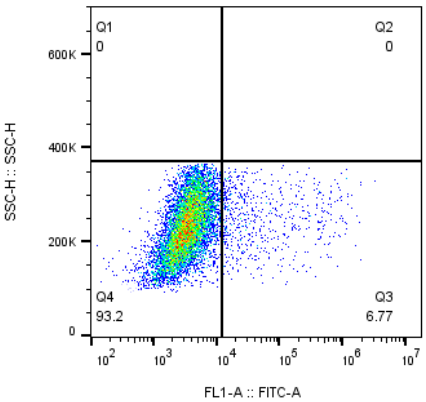
9710



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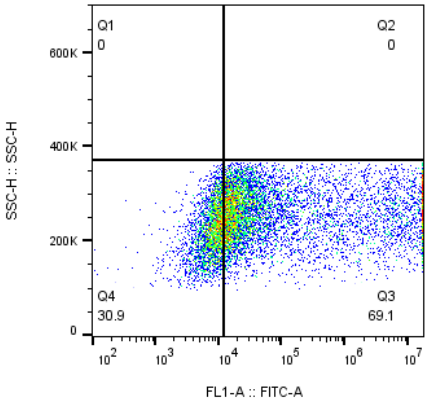
MPI25



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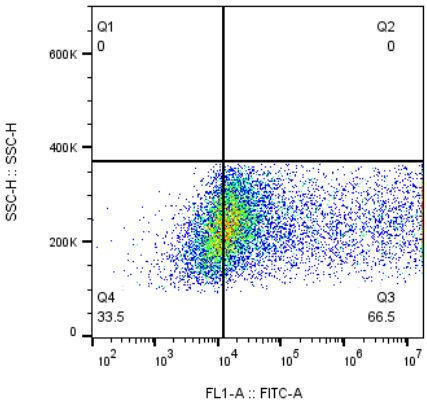

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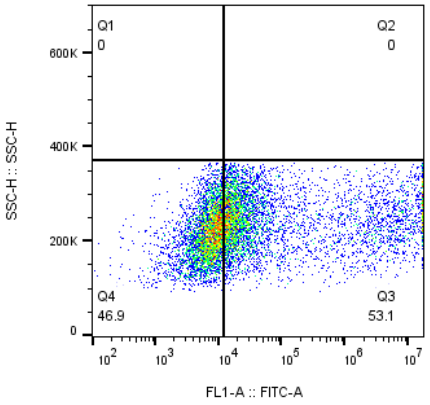

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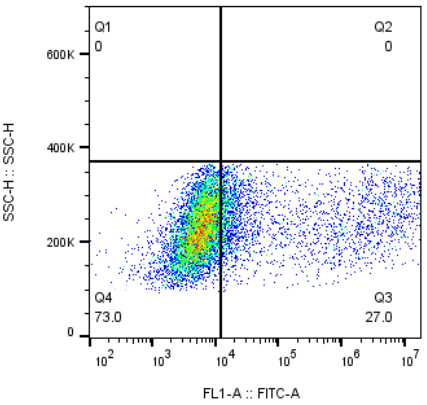

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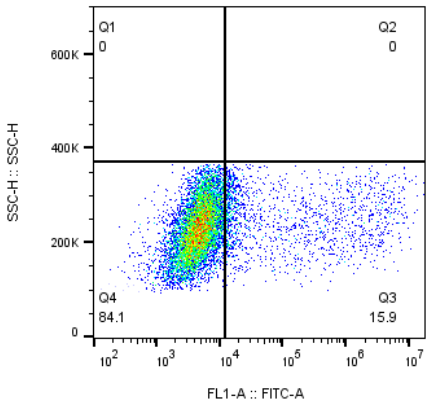

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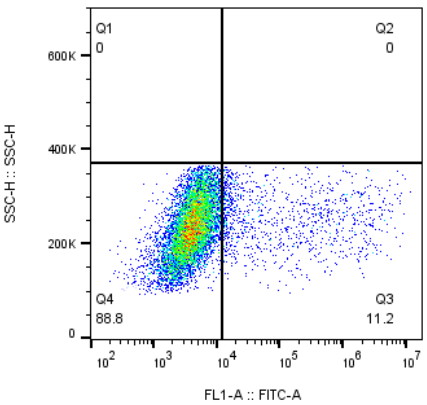

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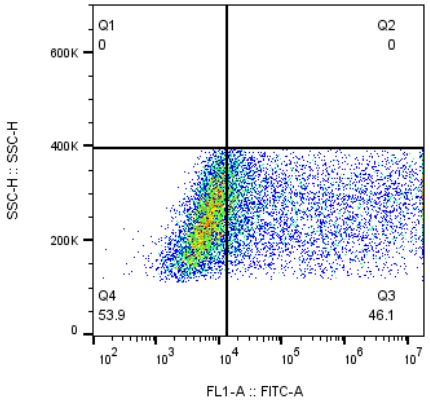

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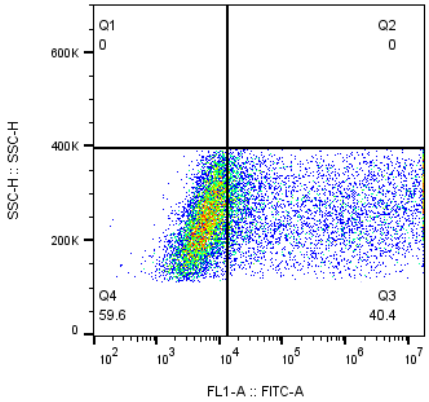

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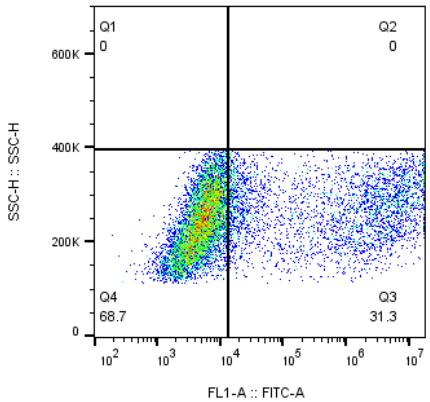

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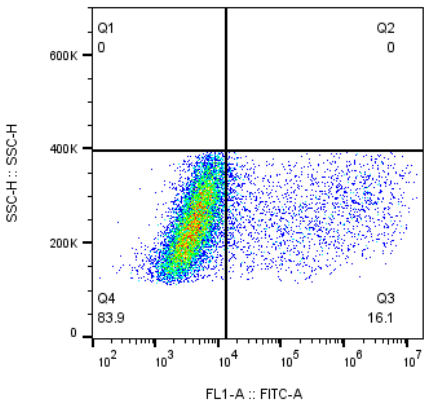

MPI26-80nM]
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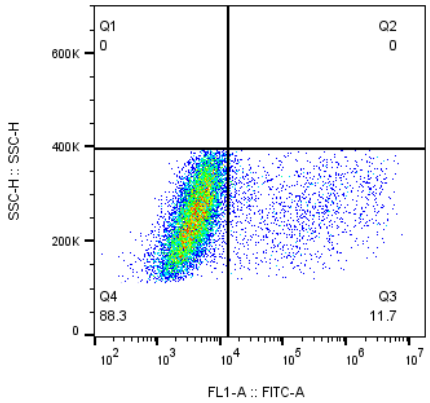

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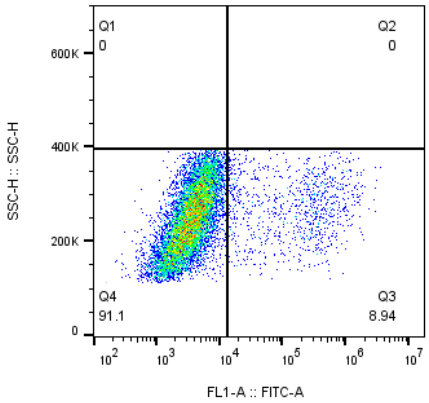

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HEK
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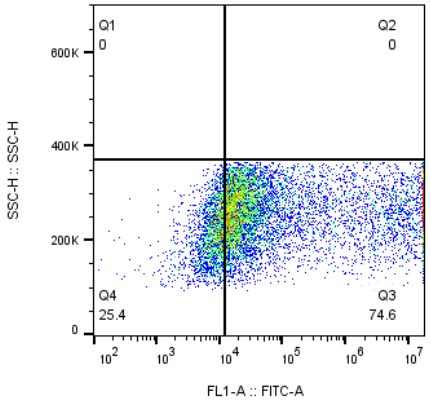

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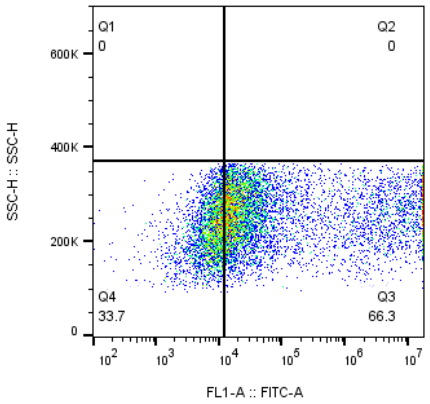

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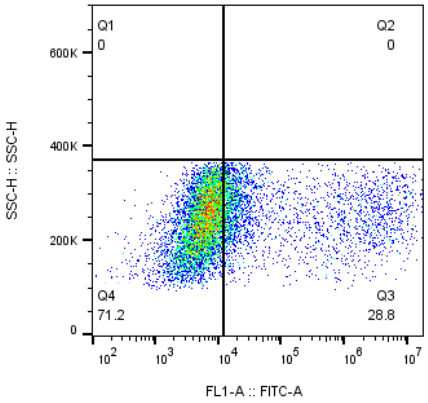

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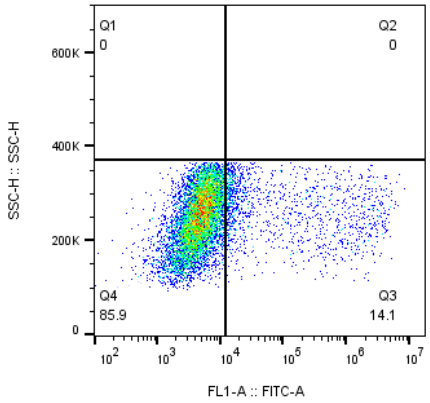

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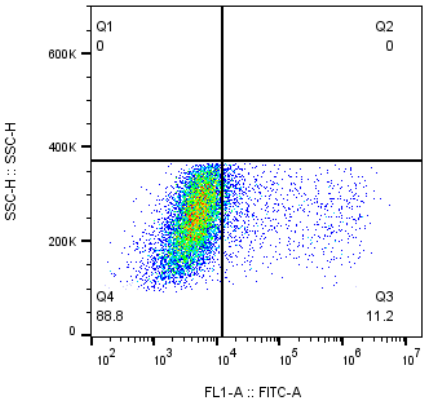

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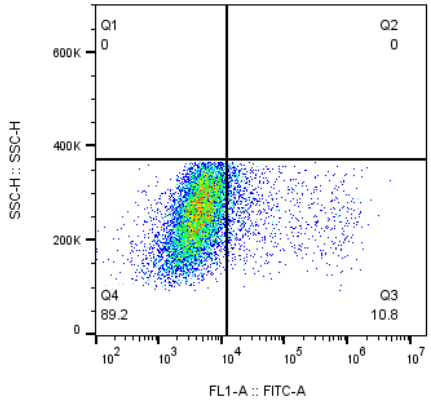
9631



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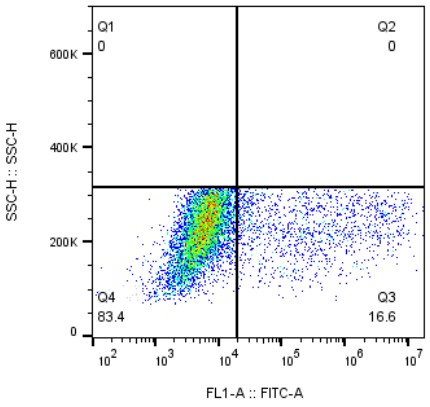
9598

MPI28



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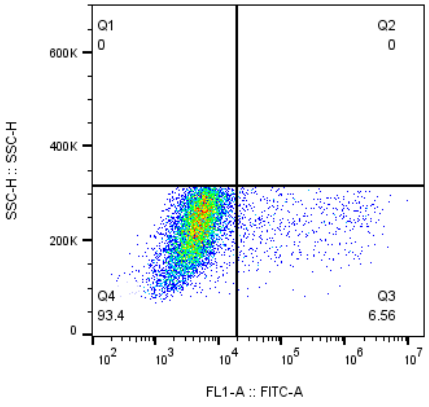

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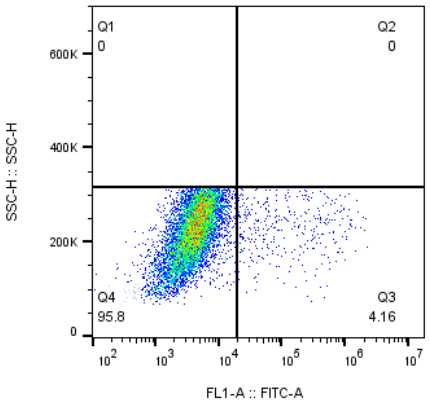

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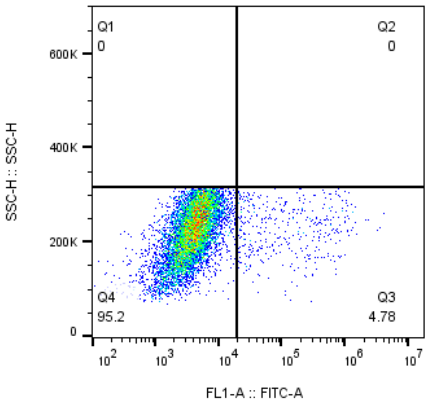

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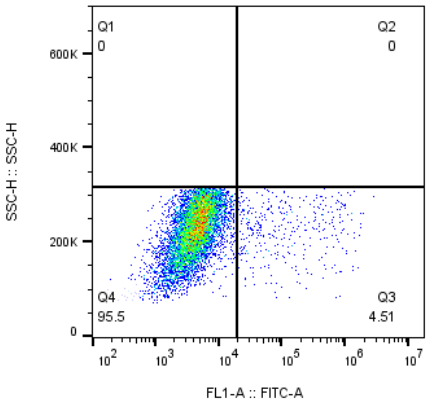
8396



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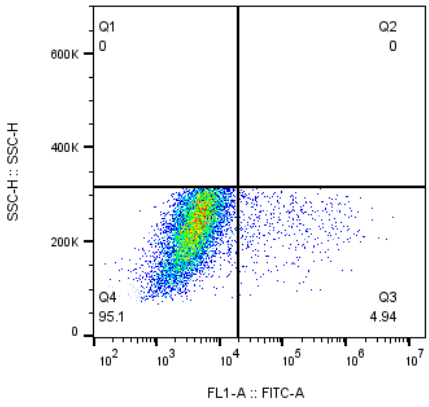

MPI28-3.2nM
HEK
8466

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