**Supporting Information: Experimentals**

**General Methods:**

All reactions were performed in heat gun or oven dried glass ware under nitrogen or argon using dry solvents unless otherwise noted. Dry diethyl ether, tetrahydrofuran, toluene, dichlormethane were obtained by passing inhibitor free, HPLC grade solvents through activated alumina columns. Methanol was distilled from magnesium turnings under and atmosphere of dry nitrogen. Triethylamine, pyridine, TMEDA were distilled from KOH under and atmosphere of dry nitrogen. Diisopropylethylamine was distilled from sodium hydride under and atmosphere of dry nitrogen. Ti(OEt)$_4$ was distilled under reduced pressure (0.5 torr). Commercially available chemicals were used as received unless noted otherwise. Reactions were monitored by thin-layer chromatography carried out on 250 µm Merck silica gel plates (TLC silicagel 60 F254) and visualized using UV light, or appropriate stains: ninhydrin, potassium permanganate, phosphomolybdic acid, vanillin. Concentrations *in vacuo* were performed by a rotary evaporator at 40 ºC. Compounds 1, 42, 44, 46 were synthesized according to literature procedures. Compounds (3, 4, 5, 6, and 7) were synthesized according to general procedure G. $^1$H NMR spectra were recorded on a VARIAN Mercury 300 MHz or a Gemini 300 MHz spectrometer in the indicated deuterated solvent. $^1$H NMR chemical shifts are reported relative to residual CHCl$_3$ (7.26 ppm) or C$_6$D$_6$ (7.15 ppm). $^{13}$C-NMR spectra were recorded with $^1$H-decoupling on a VARIAN Mercury 75 MHz spectrometer in the indicated deuterated solvent. $^{13}$C-NMR chemical shifts were reported relative to the central line of CDCl$_3$ (77.23 ppm) or C$_6$D$_6$ (128.62 ppm). Infrared spectra were recorded neat on a Varian 800 FT-IR Scimilar Series spectrophotometer or a Perkin Elmer Spectrum BX FT-IR. Optical rotations were measured on a JASCO DIP-1000 digital polarimeter. High resolution mass spectrometric measurements were performed by the mass spectrometry service of the Laboratorium für Organische Chemie at the ETH Zürich. ESI measurements were performed on a Bruker Daltonics maxis and Varian Ionspec ESI-FT-ICR.
General Procedure A: Conjugate Addition of Protected Amino Acid to 3-(nitromethylene)oxetane. The synthesis of (S)-5-tert-butyl 1-propyl 2-((3-(nitromethyl)oxetan-3-yl)amino)pentanedioate (9): To a flask was sequentially added (S)-5-tert-butyl 1-propyl 2-(((benzyloxy)carbonyl)amino)pentanedioate (0.409 g, 1.079 mmol), EtOAc (19.6 mL) and Pd/C (0.052 g, 0.049 mmol). The reaction mixture was then stirred for 1 hour under an H₂ atmosphere. After completion of the reaction was confirmed by TLC, the reaction mixture was filtered through celite and concentrated in vacuo to afford a crude residue which was used in the next step without further purification. The residue was dissolved in DMSO (4.9 mL) and 3-(nitromethylene)oxetane (0.113 g, 0.981 mmol) was added in one portion. The reaction was then stirred for 2 hours at room temperature, at which point it was diluted with a mixture of ether/EtOAc (ca. 3/1, 100 mL) and washed successively with 50% brine, water, and brine, (50 mL each) dried over Na₂SO₄, filtered and concentrated in vacuo. The resulting residue was purified with silica gel chromatography (20-33% EtOAc/hexane) to afford nitro alkane 9 as a colorless oil (275 mg, 78% yield).

Data for (S)-5-tert-butyl 1-propyl 2-((3-(nitromethyl)oxetan-3-yl)amino)pentanedioate (9): Colorless oil; ¹H NMR (300 MHz, CDCl₃) δ 4.83-4.69 (m, 2H), 4.59-4.48 (m, 2H), 4.42 (d, J = 7.2 Hz, 1H), 4.36 (d, J = 7.0 Hz, 1H), 4.00 (d, J = 6.8 Hz, 2H), 3.48 (s (br), 1H), 2.34-2.20 (m, 3H), 1.99-1.81 (m, 1H), 1.73-1.52 (m, 3H), 1.37 (s, 9H), 0.88 (t, J = 7.4 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 175.0, 172.0, 80.4, 78.8, 78.5, 78.2, 67.0, 59.3, 54.9, 31.3, 29.3, 28.0, 21.9, 10.4; IR (thin film, NaCl) 2970, 2881, 1722, 1555, 1150, 979, 733 cm⁻¹; HRMS (ESI, H) m/z calc’d for C₁₆H₂₉N₂O₇ (M + H)⁺ 361.1969, found 361.1974; [α]D²³ -11.9 (c 0.50, CHCl₃).

Data for (S)-propyl 3-((4-tert-butoxy)phenyl)-2-((3-(nitromethyl)oxetan-3-yl)amino) propanoate (7): (colorless oil, 15-18% EtOAc/hexanes, 71% yield); ¹H NMR (300 MHz,
CDCl₃ δ 7.03 (d, J = 8.4 Hz, 2H), 6.88 (d, J = 8.4 Hz, 2H), 4.94-4.62 (m, 2H), 4.48 (d, J = 7.1 Hz, 1H), 4.35-4.31 (m, 3H), 4.10-3.86 (m, 2H), 3.63 (t, J = 6.3 Hz, 1H), 2.91 (d, J = 13.3, 6.2 Hz, 1H), 2.77 (dd, J = 13.3, 7.5 Hz, 1H), 2.38 (s (br), 1H), 1.73-1.48 (m, 2H), 1.30 (s, 9H), 0.86 (t, J = 7.4 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 174.3, 153.9, 131.4, 129.6, 124.0, 78.6, 78.51, 78.48, 78.4, 67.0, 59.4, 57.7, 40.2, 28.9, 22.0, 10.5; IR (thin film, NaCl) 2973, 2879, 1728, 1555, 1505, 1159, 982, 894 cm⁻¹; HRMS (ESI, H) m/z calc’d for C₂₀H₃₁N₂O₆ (M + H)⁺ 395.2177, found 395.2183; [α]₂⁵ D −2.37 (c 0.50, CHCl₃).

Data for (S)-propyl 3-(tert-butoxy)-2-((3-(nitromethyl)oxetan-3-yl)amino)propanoate (8):
(Pale yellow oil, 33-50% EtOAc/hexanes, 81% yield); ¹H NMR (300 MHz, CDCl₃) δ 4.81 (s, 2H), 4.60 (d, J = 7.0 Hz, 1H), 4.52 (s, 2H), 4.44 (d, J = 7.0 Hz, 1H), 4.03 (td, J = 6.7, 1.8 Hz, 2H), 3.64-3.54 (m, 1H), 3.52-3.43 (m, 2H), 2.58 (s (br), 1H), 1.71-1.49 (m, 2H), 1.09 (s, 9H), 0.90 (d, J = 7.4 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 172.9, 79.2, 79.0, 78.2, 73.4, 66.9, 64.0, 59.4, 56.7, 27.4, 22.1, 10.6; IR (thin film, NaCl) 2972, 2879, 1732, 1554, 1190, 978, 749 cm⁻¹; HRMS (ESI, H) m/z calc’d for C₁₄H₂₇N₂O₆ (M + H)⁺ 319.1864, found 319.1863; [α]₂⁴ D −12.5 (c 0.50, CHCl₃).

Data for (S)-propyl 2-((3-(nitromethyl)oxetan-3-yl)amino)-4-oxo-4-(tritylamino)butanoate (10):
(White solid, 25% acetone/hexanes, 73% yield); ¹H NMR (300 MHz, CDCl₃) δ 7.47-7.12 (m, 15H), 7.08 (s, 1H), 4.75 (s, 2H), 4.63 (d, J = 7.1 Hz, 1H), 4.51 (d, J = 7.2 Hz, 1H), 4.43 (d, J = 7.2 Hz, 1H), 4.34 (d, J = 7.1 Hz, 1H), 4.04 (t, J = 6.7 Hz, 2H), 3.90 (s (br), 1H), 2.79 (d, J = 6.2 Hz, 1H), 2.69 (dd, J = 15.0, 3.9 Hz, 1H), 2.55 (dd, J = 15.0, 8.3 Hz, 1H), 1.73-1.54 (m, 2H), 0.92 (t, J = 7.4 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 173.9, 168.0, 144.1, 128.5, 127.8, 126.9, 78.7, 77.7, 70.8, 67.5, 59.3, 53.0, 41.9, 22.0, 10.6; IR (thin film, NaCl) 2966, 2360, 1730, 1668, 1552, 1275, 1180, 750 cm⁻¹; HRMS (ESI, H) m/z calc’d for C₃₀H₃₄N₃O₆ (M + H)⁺ 532.2442, found 532.2440; [α]₂⁶ D −21.9 (c 0.50, CHCl₃).
Data for (S)-propyl 6-((tert-butoxycarbonyl)amino)-2-((3-(nitromethyl)oxetan-3-yl)amino)hexanoate (11): (colorless oil, 25-35% EtOAc/hexanes, 66% yield); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 4.89–4.72 (m, 2H), 4.61 (dd, $J = 15.1, 7.1$ Hz, 2H), 4.57-4.49 (m, 2H), 4.41 (d, $J = 7.0$ Hz, 1H), 4.06 (t, $J = 6.8$ Hz, 2H), 3.43 (dd, $J = 7.5, 5.6$ Hz, 1H), 3.12-3.03 (m, 2H), 2.33 (s (br), 1H), 1.71-1.61 (m, 2H), 1.59–1.23 (m, 15H), 0.94 (t, $J = 7.4$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 175.6, 156.2, 79.3, 79.2, 79.0, 78.6, 67.3, 59.8, 56.0, 40.4, 34.2, 30.0, 28.6, 23.0, 22.1, 10.5; IR (thin film, NaCl) 3344, 2970, 2935, 1703, 1555, 1365, 1247, 1172, 982 cm$^{-1}$; HRMS (ESI, TOF-MS) m/z calcd for: C$_{18}$H$_{34}$N$_3$O$_7$ (M+H)$^+$ 404.2391; found (M+H)$^+$ 404.2381; $\alpha$$_D$$^{20}$ −6.3 (c 1.00, CHCl$_3$).

General Procedure (B): Conjugate addition of free based amino acids to 3-(nitromethylene)oxetane. The synthesis of (S)-propyl 4-(methylthio)-2-((3-(nitromethyl)oxetan-3-yl)amino)butanoate (12): To a solution of (S)-propyl 2-amino-4-(methylthio)butanoate (0.150 g, 0.782 mmol) in DMSO (4 mL) was added 3-(nitromethylene)oxetane (0.075 g, 0.652 mmol). The reaction was then allowed to stir at room temperature for 90 minutes. The solution was then diluted with ETOAc (100 mL) and washed with brine (2x, 50 mL), the organic layer was dried over Na$_2$SO$_4$ and concentrated in vacuo to afford a residue. The residue was purified by flash column chromatography (20-30% ETOAc/hexanes) to afford nitro alkane 14 as a colorless oil (195 mg, 98% yield).

Data for (S)-propyl 4-(methylthio)-2-((3-(nitromethyl)oxetan-3-yl)amino)butanoate (12): $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 4.87–4.76 (m, 2H), 4.66 (d, $J = 7.1$ Hz, 1H), 4.59 (d, $J = 7.2$ Hz, 1H), 4.53 (d, $J = 7.2$ Hz, 1H), 4.46 (d, $J = 7.1$ Hz, 1H), 4.08 (t, $J = 6.8$ Hz, 2H), 3.73-3.61 (m, 1H), 2.59 (dd, $J = 8.0, 8.0$ Hz, 2H), 2.37 (d, $J = 10.5$ Hz, 1H), 2.09 (s, 3H), 2.02-1.89 (m 1H), 1.82-1.61 (m, 3H), 0.95 (t, $J = 7.4$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 175.7, 79.0, 78.9, 78.7, 67.5, 59.7, 54.5, 33.5, 30.4, 22.1, 15.3, 10.5; IR (thin film, NaCl) 3330, 2967, 2918, 2879, 1726, 1559, 1554, 1378, 1276, 1178, 980, 896 cm$^{-1}$; HRMS (ESI, TOF-MS) m/z calcd for: C$_{12}$H$_{23}$N$_2$O$_5$S (M+H)$^+$ 307.1322; found (M+H)$^+$ 307.1327; $\alpha$$_D$$^{20}$ −36.0 (c 1.00, CHCl$_3$).
Data for (S)-propyl 2-((3-(nitromethyl)oxetan-3-yl)amino)-3-(1-trityl-1H-imidazol-4-yl)propanoate (13): (colorless oil, 25-33% acetone/hexanes, 60% yield); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.48-7.22 (m, 10H), 7.19-7.02 (m, 6H), 6.59 (d, \(J = 1.0\) Hz, 1H), 4.83-4.72 (m, 2H), 4.51 (t, \(J = 7.7\) Hz, 1H), 4.42 (dd, \(J = 14.0, 8.0\) Hz, 3H), 4.13-3.87 (m, 2H), 3.79 (dd, \(J = 12.3, 7.4\) Hz, 1H), 2.95 (dd, \(J = 14.3, 4.9\) Hz, 1H), 2.77 (dd, \(J = 14.3, 8.1\) Hz, 1H), 2.62 (d, \(J = 7.8\) Hz, 1H), 1.70-1.42 (m, 2H), 0.88 (t, \(J = 7.4\) Hz, 3H); \(^13\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 174.5, 142.2, 138.6, 136.3, 129.6, 127.9, 119.7, 79.1, 78.5, 78.2, 75.2, 66.9, 59.3, 56.1, 33.0, 21.9, 10.5; IR (thin film, NaCl) 2967, 2878, 2355, 1729, 1553, 748, 700 cm\(^{-1}\); HRMS (ESI, H) m/z calc’d for C\(_{32}\)H\(_{35}\)N\(_4\)O\(_5\) (M + H\(^+\)) 555.2602, found 555.2592; \([\alpha]_D^{26}\) –14.6 (c 0.40, CHCl\(_3\)).

Data for (S)-tert-butyl 3-2-((3-(nitromethyl)oxetan-3-yl)amino)-3-oxo-3-propoxypropyl)-1H-indole-1-carboxylate (14): (colorless oil, 20% EtOAc/hexanes, 76% yield); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 8.12 (d, \(J = 7.9\) Hz, 1H), 7.54 (d, \(J = 7.1\) Hz, 1H), 7.39 (s, 1H), 7.27 (dd, \(J = 19.9, 7.3\) Hz, 2H), 4.91-4.68 (m, 2H), 4.56 (d, \(J = 7.1\) Hz, 1H), 4.44 (t, \(J = 7.8\) Hz, 2H), 4.35 (d, \(J = 7.1\) Hz, 1H), 3.99 (t, \(J = 6.7\) Hz, 2H), 3.81 (s (br), 1H), 3.04 (qd, \(J = 14.2, 6.5\) Hz, 2H), 2.50 (d, \(J = 5.7\) Hz, 1H), 1.66 (s, 9H), 1.61-1.48 (m, 2H), 0.84 (t, \(J = 7.4\) Hz, 3H); \(^13\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 174.5, 149.4, 135.3, 130.1, 124.4, 124.2, 122.4, 118.8, 115.20, 115.18, 83.6, 78.7, 78.4, 67.2, 59.5, 56.1, 30.3, 28.3, 21.8, 10.4; IR (thin film, NaCl) 2972, 2879, 1726, 1554, 1452, 1368, 1255, 1154, 1083, 747 cm\(^{-1}\); HRMS (ESI, H) m/z calc’d for C\(_{23}\)H\(_{32}\)N\(_3\)O\(_7\) (M + H\(^+\)) 462.2235, found 462.2236; \([\alpha]_D^{25}\) +1.47 (c 0.50, CHCl\(_3\)).
Data for (S)-propyl 2-((S)-4-methyl-2-((3-(nitromethyl)oxetan-3-yl)amino)pentanamido)-3-phenylpropanoate (16): (colorless oil, 20-50% EtOAc/hexanes, 80%); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.33-7.18 (m, 4H), 7.12-7.07 (m, 2H), 4.80-4.57 (m 4H), 4.50 (d, \(J = 7.6\) Hz, 1H), 4.32 (dd, \(J = 14.7, 7.4\) Hz, 2H), 4.05 (td, \(J = 6.7, 1.5\) Hz, 2H), 3.50-3.36 (m, 1H), 2.98 (dd, \(J = 13.9, 7.7\) Hz, 1H), 2.03 (d, \(J = 2.4\) Hz, 1H), 1.65-1.54 (m, 3H), 1.46-1.35 (m, 1H), 1.26-1.17 (m, 1H), 0.96-0.80 (m, 9H); \(^1^3\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 174.3, 171.3, 135.8, 129.0, 128.4, 127.0, 79.5, 77.3, 76.7, 67.1, 59.0, 55.7, 52.6, 43.7, 37.9, 24.7, 23.2, 22.0, 21.9, 10.4; IR (thin film, NaCl) 3319, 2958, 2878, 1734, 1656, 1552, cm\(^{-1}\); HRMS (ESI, H) \(m/z\) calc’d for C\(_{22}\)H\(_{34}\)N\(_3\)O\(_6\) (M + H\(^+\)) 436.2442, found 436.2436; \([\alpha]\)_D\(^{28}\) \(-8.79\) (c 0.66, CHCl\(_3\)).

Data for Propyl 2-((3-(nitromethyl)oxetan-3-yl)amino)acetate (2): (colorless oil, 50-100% EtOAc/cyclohexane, 59% yield); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 4.82 (s, 2H), 4.62 (d, \(J = 7.3\) Hz, 2H), 4.56 (d, \(J = 7.3\) Hz, 2H), 4.09 (t, \(J = 6.8\) Hz, 2H), 3.52 (s, 2H), 2.35 (s (br), 1H), 1.65 (q, \(J = 7.2\) Hz, 2H), 0.93 (t, \(J = 7.5\) Hz, 3H); \(^1^3\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 174.3, 171.3, 135.8, 129.0, 128.4, 127.0, 79.5, 77.3, 76.7, 67.1, 59.5, 44.9, 22.1, 10.5; IR (thin film) 3338, 1735, 1554, 1382, 1206, 981 cm\(^{-1}\); (ESI, H) \(m/z\) calcd for C\(_9\)H\(_{17}\)N\(_2\)O\(_5\) (M+H\(^+\)) 233.1132, found (M+H\(^+\)) 233.1136.

Data for (S)-Propyl 2-((3-(nitromethyl)oxetan-3-yl)amino)propanoate (3): (colorless oil, 50-100% EtOAc/cyclohexane, 74% yield); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 4.85 (d, \(J = 12.9\) Hz, 1H), 4.80 (d, \(J = 12.9\) Hz, 1H), 4.64-4.57 (m, 2H), 4.51 (d, \(J = 7.2\) Hz, 1H), 4.41 (d, \(J = 6.9\) Hz, 1H), 4.04 (t, \(J = 6.7\) Hz, 2H), 3.56 (q, \(J = 7.0\) Hz, 1H), 2.37 (s (br), 1H), 1.71-1.57 (m, 2H), 1.28 (d, \(J = 6.9\) Hz, 3H), 0.92 (t, \(J = 7.4\) Hz, 3H); \(^1^3\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 175.6, 79.1, 79.0, 78.3, 67.1, 59.7, 51.4, 22.0, 20.6, 10.5; IR (thin film) 2963, 2874, 2360, 1727, 1554, 1450, 1377, 1285, 1193,
976 cm\(^{-1}\); HRMS (ESI, H) \(m/z\) calcd for C\(_{15}\)H\(_{19}\)N\(_2\)O\(_5\) (M+H): 247.1288, found (M+H): 247.1281; \([\alpha]_D^{27}\) –14.3 (c 0.24, CHCl\(_3\)).

Data for (S)-Propyl 3-methyl-2-((3-(nitromethyl)oxetan-3-yl)amino)butanoate (4): (colorless oil, 25-50% EtOAc/cyclohexane, 72% yield); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 4.87-4.72 (m, 2H), 4.66–4.53 (m, 2H), 4.52-4.40 (m, 2H), 4.05 (t, \(J = 6.8\) Hz, 2H), 3.20 (s (br), 1H), 2.29 (s (br), 1H), 1.98-1.82 (m, 1H), 1.73-1.56 (m, 2H), 0.98-0.81 (m, 9H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 175.3, 78.9, 78.6, 78.6, 67.0, 61.4, 59.5, 32.2, 22.1, 19.4, 18.1, 10.6; IR (thin film) 2964, 2878, 1721, 1558, 1463, 1377, 1265, 1188, 981 cm\(^{-1}\); HRMS (ESI, H) \(m/z\) calcd for: C\(_{12}\)H\(_{23}\)N\(_2\)O\(_5\) (M+H): 275.1601, found (M+H): 275.1603; \([\alpha]_D^{25}\) –12.2 (c 0.18, CHCl\(_3\)).

Data for (S)-Propyl 4-methyl-2-((3-(nitromethyl)oxetan-3-yl)amino)pentanoate (5): (colorless oil, 25-50% EtOAc/cyclohexane, 52% yield); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 4.87 (d, \(J = 12.8\) Hz, 1H), 4.79 (d, \(J = 12.8\) Hz, 1H), 4.65-4.57 (m, 2H), 4.51 (d, \(J = 7.1\) Hz, 1H), 4.40 (d, \(J = 6.9\) Hz, 1H), 4.04 (t, \(J = 6.7\) Hz, 2H), 3.56–3.36 (m, 1H), 2.23 (br. s, 1H), 1.74-1.58 (m, 3H), 1.54-1.33 (m, 2H), 0.98-0.86 (m, 9H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 176.0, 79.1, 78.9, 78.4, 67.0, 59.7, 54.5, 43.8, 24.8, 22.9, 22.4, 22.1, 10.6; IR (thin film) 2955, 2878, 1729, 1557, 1467, 1433, 1381, 1269, 1183, 981 cm\(^{-1}\); HRMS (ESI, H) \(m/z\) calcd for: C\(_{13}\)H\(_{25}\)N\(_2\)O\(_5\) (M+H): 289.1758, found (M+H): 289.1752; \([\alpha]_D^{27}\) –17.5 (c 0.77 CHCl\(_3\)).

Data for (S)-Propyl 2-((3-(nitromethyl)oxetan-3-yl)amino)-3-phenylpropanoate (6): (colorless oil, 25-50% EtOAc/cyclohexane, 95% yield); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.42-7.12 (m, 5H), 4.90-4.68 (m, 2H), 4.55 (d, \(J = 7.2\) Hz, 1H), 4.47-4.25 (m, 3H), 4.04 (t, \(J = 6.7\) Hz, 2H), 3.77-3.67 (m, 1H), 3.00 (dd, \(J = 13.3, 6.2\) Hz, 1H), 2.89 (dd, \(J = 13.3, 7.3\) Hz, 1H), 2.42 (d, \(J = 7.5\) Hz, 1H), 1.69-1.55 (m, 2H), 0.91 (t, \(J = 7.4\) Hz, 3H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 174.6, 136.6, 129.4,
General Procedure C: Conjugate addition of glycine propyl ester. The synthesis of propyl 2-[(3-(2-(2-(3-(2-(4-(tert-butoxy)phenyl)-1-nitroethyl)oxetan-3-yl)amino)acetate (47): To a solution of 1-(tert-butoxy)-4-(2-nitroethyl)benzene (0.335 g, 1.50 mmol) in oxetan-3-one (0.147 mL, 2.250 mmol) was added Et₃N (0.052 mL, 0.375 mmol). After stirring for 1 hour at room temperature, the reaction mixture was diluted with CH₂Cl₂ (7 mL) and cooled to −78 °C and then treated with MsCl (0.129 mL, 1.650 mmol) and Et₃N (0.272 mL, 1.950 mmol). The resulting mixture was stirred for 30 min at −78 °C and then allowed to warm to 0 °C over 60 minutes. After stirring for an additional 1 hour at 0 °C, the reaction mixture was diluted with EtOAc, washed with water, dried over Na₂SO₄, filtered and concentrated in vacuo. In a separate flask Et₃N (0.63 mL, 4.50 mmol) was added to a solution of propyl 2-aminoacetate hydrochloride (0.691 g, 4.50 mmol), and in DMSO (4 mL), and the mixture stirred 10 minutes at room temperature. The resulting residue of the nitro compound was dissolved in DMSO (4 mL) and then added to the flask of propyl 2-aminoacetate in a dropwise manner via cannula. The flask of nitro compound was rinsed with 4 mL of DMSO. After stirring for 2 hours at room temperature the mixture was diluted with EtOAc (150 mL), and washed with water and brine, (75 mL each) the combined aqueous layers were then back-extracted with ether/Et₂O ca. 3:1, the combined organics were then dried over Na₂SO₄, filtered and concentrated in vacuo. The resulting residue was purified by silica gel chromatography (17-22% EtOAc/hexanes) to afford nitro alkane 39 as a pale yellow solid (432 mg, 71% yield).

Data for propyl 2-[(3-(2-(2-(3-(2-(4-(tert-butoxy)phenyl)-1-nitroethyl)oxetan-3-yl)amino)acetate (47): ¹H NMR (300 MHz, CDCl₃) δ 7.08 (d, J = 8.4 Hz, 2H), 6.89 (d, J = 8.4 Hz, 2H), 5.07 (dd, J = 9.5, 4.7 Hz, 1H), 4.73-4.53 (m, 2H), 4.41 (s, 2H), 4.09 (t, J = 6.7 Hz, 2H), 3.61 (q, J = 17.3 Hz, 2H), 3.34 (dd, J = 14.6, 9.5 Hz, 1H), 3.23 (dd, J = 14.6, 4.7 Hz, 1H), 2.46 (s, 1H), 1.68-1.61 (m, 2H), 1.29 (s, 9H), 0.92 (t, J = 7.4 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 171.8, 154.6, 129.9, 129.2, 124.4, 92.7, 78.5, 77.6, 77.1, 66.9, 62.0, 44.5, 33.9, 28.9, 22.0, 10.4; IR (thin film, NaCl) 3338, 2977, 2884, 1731, 1555 cm⁻¹; HRMS (ESI, H) m/z calc'd for C₂₀H₃₁N₂O₅ (M + H)⁺ 395.2177, found 395.2178.
Data for propyl 2-((3-(3-methyl-1-nitrobutyl)oxetan-3-yl)amino)acetate (46): (pale yellow oil, 25-50% EtOAc/cyclohexane, 62% yield); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 4.89 (d, \(J = 11.2\) Hz, 1H), 4.67-4.43 (m, 4H), 4.08 (t, \(J = 6.7\) Hz, 2H), 3.64 (dd, \(J = 17.3, 6.2\) Hz, 1H), 3.50 (dd, \(J = 17.3, 5.6\) Hz, 1H), 2.47-2.22 (m, 2H), 1.74-1.46 (m, 4H), 1.06-0.83 (m, 9H); \(^1^3\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 171.9, 89.4, 77.0, 67.0, 62.4, 44.7, 37.0, 25.7, 23.2, 21.4, 10.5; IR (thin film, NaCl) 3342, 2964, 2878, 1738, 1557, 1463, 1372, 1205, 1132, 985, 852 cm\(^{-1}\); HRMS (ESI, H) \(m/z\) calcd for C\(_{13}\)H\(_{25}\)N\(_2\)O\(_5\) (M+H)\(^+\) 289.1758, found (M+H)\(^+\) 289.1759.

Data for tert-butyl 4-nitro-4-((2-oxo-2-propoxyethyl)amino)oxetan-3-yl)butanoate (48): (colorless oil, 20% EtOAc/hex, 63% yield); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 5.06-4.91 (m, 1H), 4.71 (d, \(J = 7.6\) Hz, 1H), 4.68-4.49 (m, 3H), 4.11 (t, \(J = 6.7\) Hz, 2H), 3.73-3.44 (m, 2H), 2.54-2.13 (m, 5H), 1.71-1.59 (m, 2H), 1.45 (s, 9H), 0.94-0.83 (t, \(J = 7.4\) Hz, 3H); \(^1^3\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 172.2, 171.4, 90.4, 81.6, 77.3, 77.2, 67.2, 62.4, 44.8, 31.4, 28.3, 23.9, 22.1, 10.5; IR (thin film, NaCl) 3338, 2972, 2884, 1731, 1555, 1368, 1210, 1155, 985, 845 cm\(^{-1}\); HRMS (ESI, TOF-MS) \(m/z\) calcd for: C\(_{16}\)H\(_{29}\)N\(_2\)O\(_7\) (M+H)\(^+\) 361.1969; found (M+H)\(^+\) 361.1976.

propyl 2-((3-(5-((tert-butoxycarbonyl)amino)-1-nitropentyl)oxetan-3-yl)amino)acetate (49): (light yellow oil, 35% EtOAc/hexanes, 89% yield); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 4.81 (dd, \(J = 11.1, 2.9\) Hz, 1H), 4.70-4.47 (m, 5H), 4.11 (t, \(J = 6.7\) Hz, 2H), 3.74-3.46 (m, 2H), 3.24-3.01 (m, 2H), 2.40-2.23 (m, 2H), 1.99-1.87 (m, 1H), 1.75-1.32 (m, 15H), 0.95 (t, \(J = 7.4\) Hz, 3H); \(^1^3\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 172.3, 156.2, 91.6, 79.5, 67.3, 62.4, 44.8, 40.1, 29.7, 28.6, 28.1, 23.8, 22.1,
10.6; IR (thin film, NaCl) 3340, 2971, 1736, 1701, 1552, 1520, 1364, 1249, 1171, 980 896 cm$^{-1}$; HRMS (ESI, TOF-MS) m/z calcd for: C$_{18}$H$_{34}$N$_3$O$_7$ (M+H)$^+$ 404.2391; found (M+H)$^+$ 404.2397.

**Data for propyl 2-((3-(1-nitro-2-(1-tosyl-1H-indol-3-yl)ethyl)oxetan-3-yl)amino)acetate (50):** (pale brown solid, 25% EtOAc/hexanes, 63% yield); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.96 (d, J = 8.4 Hz, 1H), 7.68 (d, J = 8.4 Hz, 2H), 7.47-7.45 (m, 2H), 7.31-7.11 (m, 4H), 5.18 (dd, J = 10.0, 4.2 Hz, 1H), 4.63 (s, 2H), 4.47 (q, J = 7.8 Hz, 2H), 4.14-3.39 (m, 3H), 3.67-3.59 (m, 2H), 3.37 (dd, J = 15.4, 4.1Hz, 1H), 2.50 (s (br), 1H), 2.28 (s, 3H), 1.70-1.61 (m, 2H), 0.94 (t, J = 7.3 Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 171.9, 145.0, 135.0, 134.7, 129.8, 129.7, 126.6, 125.1, 124.7, 123.4, 118.7, 116.3, 113.9, 90.5, 77.6, 77.1, 67.0, 62.2, 44.6, 24.3, 22.0, 21.6, 10.4; IR (thin film, NaCl) 3329, 2975, 2879, 1738, 1552, 1167 cm$^{-1}$; HRMS (ESI, H) m/z calc'd for C$_{25}$H$_{30}$N$_3$O$_7$S (M + H)$^+$ 516.1799, found 516.1799.

![Propyl 2-((3-(1-nitro-2-(1-tosyl-1H-indol-3-yl)ethyl)oxetan-3-yl)amino)acetate](image)

**Data for (2S)-propyl 6-((tert-butoxycarbonyl)amino)-2-((3-((tert-butoxycarbonyl)amino)-1-nitropentyl)oxetan-3-yl)amino)hexanoate (51):** (pale yellow oil, 40% EtOAc/hexanes, 81% yield); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 4.86-4.74 (m, 2H), 4.73-4.65 (m, 1H), 4.65-4.38 (m, 11H), 4.10-4.02 (m, 4H), 3.72-3.61 (m, 1H), 3.56-3.48 (m, 1H), 3.20-3.00 (m, 8H), 2.52-2.46 (m, 1H), 2.39-2.21 (m, 2H), 2.20-2.12 (m, 1H), 2.00-1.81 (m, 2H), 1.72-1.23 (m, 60H), 0.99-0.88 (m, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 176.0, 156.2, 92.9, 90.6, 79.5, 79.3, 78.3, 78.2, 77.7, 77.4, 67.3, 67.2, 62.5, 62.4, 55.6, 40.5, 40.4, 40.1, 34.8, 34.3, 30.0, 29.7, 28.6, 28.2, 27.8, 24.0, 23.8, 23.2, 22.9, 22.1, 10.6, 10.5; IR (thin film, NaCl) 3349, 2970, 2875, 1699, 1551, 1519, 1365, 1248, 1173, 983 cm$^{-1}$; HRMS (ESI, H) m/z calc'd for: C$_{27}$H$_{53}$N$_4$O$_9$ (M+H)$^+$ 575.3651, found (M+H)$^+$ 575.3650.
General Procedure D: Nitro group reduction and Cbz protection. The synthesis of (S)-5-tert-butyl 1-propyl 2-((3-(((benzyloxy)carbonyl)amino)methyl)oxetan-3-yl)amino)pentanedioate (24): To a solution of (S)-5-tert-butyl 1-propyl 2-((3-(nitromethyl)oxetan-3-yl)amino)pentanedioate (0.210 g, 0.583 mmol), benzyl (2,5-dioxopyrrolidin-1-yl) carbonate (0.218 g, 0.874 mmol) and NaHCO₃ (0.146 g, 1.75 mmol) in THF (5.8 mL) was added Raney-Nickel (500 mg, 50% slurry in water, ca. 1.0 mL) at room temperature. The reaction was then stirred for 2 hours under a H₂ atmosphere. After completion was confirmed by TLC, the catalyst was removed by filtration through celite and washed with EtOAc (100 mL). The filtrate was then diluted with water (75 mL) and extracted with EtOAc (3x 75 mL), the combined organics were then dried over Na₂SO₄, filtered and concentrated in vacuo. The resulting residue was purified by silica gel chromatography (50% EtOAc/hexanes) to afford protected amine 24 as a colorless oil (170 mg, 63%).

Data for (S)-5-tert-butyl 1-propyl 2-((3-(((benzyloxy)carbonyl)amino)methyl)oxetan-3-yl)amino)pentanedioate (24): ¹H NMR (300 MHz, C₆D₆) δ 7.28 (d, J = 7.1 Hz, 2H), 7.19-7.10 (m, 3H), 5.52 (t, J = 5.5 Hz, 1H), 5.12 (s, 2H), 4.35 (d, J = 6.2 Hz, 1H), 4.21 (s, 3H), 3.77 (td, J = 6.7, 2.2 Hz, 2H), 3.60 (dd, J = 14.0, 6.0 Hz, 1H), 3.42 (dd, J = 13.9, 5.6 Hz, 1H), 3.31 (dd, J = 8.7, 4.6 Hz, 1H), 2.25-2.19 (m, 2H), 2.03-1.80 (m, 2H), 1.76-1.58 (m, 1H), 1.34 (s, 9H), 1.31-1.24 (m, 2H), 0.65 (d, J = 7.4 Hz, 3H); ¹³C NMR (75 MHz, C₆D₆) δ 175.8, 172.0, 157.0, 137.2, 128.4, 128.3, 127.9, 79.9, 79.3, 79.0, 66.7, 66.6, 59.9, 54.8, 45.6, 31.8, 29.7, 28.0, 22.1, 10.3; IR (thin film, NaCl) 3331, 2970, 2878, 1721, 1257, 1148, 976, 750 cm⁻¹; HRMS (ESI, H) m/z calc’d for C₂₄H₃₇N₂O₇ (M + H)⁺ 465.2595, found 465.2583; [α]₂³⁻1.70 (c 0.50, CHCl₃).

Data for (S)-propyl 2-((3-(((benzyloxy)carbonyl)amino)methyl)oxetan-3-yl)amino)-3-(4-(tert-butoxy)phenyl)propanoate (22): (colorless oil, 17% acetone/hexanes, 82% yield); ¹H NMR (300 MHz, CDCl₃) δ 7.40-7.26 (m, 5H), 7.07 (d, J = 8.4 Hz, 2H), 6.90 (d, J = 8.4 Hz, 2H), 5.13-5.03 (m, 3H), 4.29-4.21 (m, 2H), 4.20-4.12 (m, 2H), 4.01 (td, J = 6.7, 1.5 Hz, 2H), 3.56-3.37 (m, 3H), 2.94 (dd, J = 13.4, 5.5 Hz, 1H), 2.85-2.57 (m, 1H), 2.05 (s (br), 1H), 1.87-
1.47 (m, 2H), 1.30 (s, 9H), 0.80 (t, J = 7.4 Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 175.1, 156.4, 154.0, 149.2, 136.3, 131.7, 129.5, 128.3, 127.9, 124.1, 79.6, 79.3, 78.4, 67.0, 66.8, 59.4, 57.6, 45.1, 40.2, 29.0, 22.0, 10.6; IR (thin film, NaCl) 3331, 2973, 2877, 1721, 1505, 1159, 976, 895, 750 cm$^{-1}$; HRMS (ESI, H) m/z calc’d for C$_{28}$H$_{39}$N$_2$O$_6$ (M + H)$^+$ 499.2803, found 499.2813; [α]$_D^{25}$ -6.23 (c 0.50, CHCl$_3$).

Data for (S)-propyl 2-((3-((((benzyloxy)carbonyl)amino)methyl)oxetan-3-yl)amino)-3-(tert-butoxy)propanoate (23): (colorless oil, 9-33% acetone/hexanes, 76% yield); $^1$H NMR (300 MHz, CDCl$_3$) δ 7.29 (m, 5H), 5.64 (t, J = 5.2 Hz, 1H), 5.09 (s, 2H), 4.45-4.39 (m, 4H), 4.06 (t, J = 6.7 Hz, 2H), 3.59 (d, J = 5.6 Hz, 2H), 3.53-3.36 (m, 3H), 2.31 (s (br), 1H), 1.79-1.52 (m, 2H), 1.14 (s, 9H), 0.92 (t, J = 7.4 Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 173.5, 156.6, 136.4, 128.3, 128.0, 127.9, 80.4, 80.0, 73.7, 67.0, 66.7, 63.8, 59.3, 56.5, 44.7, 27.4, 22.0, 10.5; IR (thin film, NaCl) 3339, 2971, 2876, 1715, 1259, 764, 750 cm$^{-1}$; HRMS (ESI, H) m/z calc’d for C$_{22}$H$_{35}$N$_2$O$_6$ (M + H)$^+$ 423.2490, found 423.2492; [α]$_D^{24}$ -4.98 (c 0.50, CHCl$_3$).

Data for (S)-propyl 2-((3-((((benzyloxy)carbonyl)amino)methyl)oxetan-3-yl)amino)-4-oxo-4-(tritylamino)butanoate (25): (white solid, 20% acetone/hexanes, 72% yield); $^1$H NMR (300 MHz, CDCl$_3$) δ 7.45 (s, 1H), 7.28-7.19 (m, 19H), 5.65 (t, J = 5.4 Hz, 1H), 5.01 (q, J = 12.3 Hz, 2H), 4.41 (m, 3H), 4.11 (d, J = 6.6 Hz, 1H), 4.03 (qt, J = 10.7, 5.3 Hz, 2H), 3.87 (d, J = 6.9 Hz, 1H), 3.62 (qd, J = 14.2, 5.9 Hz, 2H), 2.63 (dd, J = 14.9, 3.5 Hz, 1H), 2.49 (dd, J = 14.8, 9.7 Hz, 2H), 1.86 (s (br), 1H), 1.71-1.48 (m, 2H), 0.92 (t, J = 7.4 Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 174.7, 168.6, 157.1, 144.2, 136.3, 128.6, 128.3, 127.9, 127.8, 126.9, 79.8, 79.4, 70.8, 67.3, 66.7, 59.7, 52.6, 45.0, 41.1, 21.9, 10.5; IR (thin film, NaCl) 3317, 2966, 2868, 2361, 1718, 1667, 1519, 1259, 764, 750 cm$^{-1}$; HRMS (ESI, H) m/z calc’d for C$_{38}$H$_{42}$N$_3$O$_6$ (M + H)$^+$ 636.3068, found 636.3067; [α]$_D^{27}$ -22.8 (c 0.50, CHCl$_3$).
Data for (S)-propyl 2-(((3-(((benzoyloxy)carbonyl)amino)methyl)oxetan-3-yl)amino)-3-(1-trityl-1H-imidazol-4-yl)propanoate (28): (colorless oil, 17-50% acetone/hexanes, 49% yield); \(^1\)H NMR (300 MHz, CDCl\textsubscript{3}) \(\delta\) 7.40 (s, 1H), 7.35-7.21 (m, 14H), 7.11-7.08 (m, 6H), 6.59 (s, 1H), 6.27 (t, \(J = 5.4\) Hz, 1H), 5.02 (s, 2H), 4.35-4.31 (m, 2H), 4.27 (d, \(J = 6.4\) Hz, 1H), 4.21 (d, \(J = 6.4\) Hz, 1H), 4.00 (td, \(J = 6.7, 1.5\) Hz, 2H), 3.69-3.51 (m, 3H), 2.95 (dd, \(J = 14.5, 3.8\) Hz, 1H), 2.72 (dd, \(J = 14.5, 9.2\) Hz, 1H), 2.17 (s (br), 1H), 1.75-1.46 (m, 2H), 0.89 (t, \(J = 7.4\) Hz, 3H); \(^{13}\)C NMR (75 MHz, CDCl\textsubscript{3}) \(\delta\) 175.0, 156.9, 142.1, 138.7, 136.6, 129.6, 128.3, 127.9, 127.7, 119.6, 80.3, 80.0, 75.3, 66.9, 66.4, 59.5, 55.6, 32.3, 21.9, 10.5; IR (thin film, NaCl) 3322, 2965, 2875, 1715, 1493, 1445, 1235, 748, 699 cm\(^{-1}\); HRMS (ESI, H) \(m/z\) calc'd for C\(_{40}\)H\(_{43}\)N\(_4\)O\(_5\) (M + H\(^+\)) 659.3228, found 659.3210; \([\alpha]_D^{26}\) +8.28 (c 0.10, CHCl\(_3\)).

Data for (S)-tert-butyl 3-(((3-(((benzoyloxy)carbonyl)amino)methyl)oxetan-3-yl)amino)-3-oxo-3-propoxypropyl)-1H-indole-1-carboxylate (29): (colorless oil, 25-33% EtOAc/hexanes, 69%); \(^1\)H NMR (300 MHz, C\(_6\)D\(_6\)) \(\delta\) 8.45 (s, 1H), 7.77-7.47 (m, 2H), 7.33-6.99 (m, 7H), 5.15-5.00 (m, 3H), 4.26 (d, \(J = 6.4\) Hz, 1H), 4.10 (d, \(J = 5.2\) Hz, 2H), 4.02 (d, \(J = 6.5\) Hz, 1H), 3.82-3.61 (m, 3H), 3.54 (dd, \(J = 13.9, 6.3\) Hz, 1H), 3.25 (dd, \(J = 13.9, 5.2\) Hz, 1H), 2.96 (dd, \(J = 14.3, 6.2\) Hz, 1H), 2.81 (d, \(J = 14.1, 7.2\) Hz, 1H), 2.09 (s (br), 1H), 1.36 (s, 9H), 1.24 (dq, \(J = 14.1, 7.1\) Hz, 2H), 0.57 (t, \(J = 7.4\) Hz, 3H); \(^{13}\)C NMR (75 MHz, C\(_6\)D\(_6\)) \(\delta\) 175.4, 156.7, 149.5, 137.2, 135.9, 130.7, 128.4, 128.3, 127.9, 124.7, 124.3, 122.8, 119.2, 116.4, 115.7, 83.0, 79.1, 79.0, 66.7, 59.8, 56.1, 45.5, 30.6, 27.9, 22.0, 10.3; IR (thin film, NaCl) 3331, 2968, 2868, 2360, 1723, 1154, 747 cm\(^{-1}\); HRMS (ESI, H) \(m/z\) calc'd for C\(_{31}\)H\(_{40}\)N\(_3\)O\(_7\) (M + H\(^+\)) 566.2861, found 566.2857; \([\alpha]_D^{26}\) +4.00 (c 0.25, CHCl\(_3\)).
Data for (S)-propyl 2-((3-(((benzyloxy)carbonyl)amino)methyl)oxetan-3-yl)amino)-6-((tert-butoxy carbonyl) am-ino)hexanoate (26): (colorless oil, 40-45-50% EtOAc/hexanes, 57% yield); \(^1\)H NMR (400 MHz, C\(_6\)D\(_6\)) \(\delta\) 7.40–7.20 (m, 1H), 7.20–6.97 (m, 4H), 5.24 (s, (br) 1H), 5.13 (s, 2H), 4.35 (d, \(J = 6.3\) Hz, 1H), 4.30–4.04 (m, 4H), 3.85-3.74 (m, 2H), 3.66 (dd, \(J = 13.8, 6.4\) Hz, 1H), 3.32 (dd, \(J = 13.8, 5.1\) Hz, 1H), 3.14 (s (br) 1H), 2.90 (s (br) 2H), 1.89 (s (br), 1H), 1.53–1.23 (m, 13H), 1.22–0.98 (m, 4H), 0.68 (t, \(J = 7.4\) Hz, 3H); \(^13\)C NMR (100 MHz, C\(_6\)D\(_6\)) \(\delta\) 177.6, 176.9, 157.7, 156.5, 138.0, 80.1, 79.7, 79.1, 67.5, 67.2, 60.5, 56.2, 46.4, 40.9, 34.8, 30.6, 29.9, 29.1, 23.6, 22.7, 11.0; IR (thin film, NaCl) 3336, 2968, 2935, 1713, 1522, 1248, 1173, 978 cm\(^{-1}\); HRMS (ESI, TOF-MS) m/z calc'd for: C\(_{26}\)H\(_{42}\)N\(_3\)O\(_7\) (M+H)\(^+\) 508.3017; found (M+H)\(^+\) 508.3012; 
\([\alpha]_D^{20}\) 0.584 (c 1.00, CHCl\(_3\)).

Data for propyl 2-((3-(1-(((benzyloxy)carbonyl)amino)-2-(4-(tert-butoxy)phenyl)ethyl) oxetan-3-yl)amino)acetate (53): (colorless oil, 40% EtOAc/Hex, 43% yield); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.37-7.26 (m, 5H), 7.13 (d, \(J = 8.2\) Hz, 2H), 6.89 (d, \(J = 8.3\) Hz, 2H), 5.28 (d, \(J = 9.2\) Hz, 1H), 5.04 (s, 2H), 4.49-4.38 (m, 3H), 4.22-4.05 (m, 4H), 3.70 (q, \(J = 17.5\) Hz, 2H), 2.79 (d, \(J = 6.8\) Hz, 2H), 2.03 (s (br), 1H), 1.69 (dd, \(J = 14.2, 6.9\) Hz, 2H), 1.31 (s, 9H), 0.96 (t, \(J = 7.4\) Hz, 3H); \(^13\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 172.6, 156.1, 154.0, 136.2, 129.4, 128.4, 128.0, 127.8, 124.3, 78.4, 78.3, 77.6, 67.0, 66.8, 62.6, 57.4, 44.7, 35.6, 28.9, 22.0, 10.5; IR (thin film, NaCl) 3351, 2973, 2935, 1713, 1522, 1248, 1173, 978 cm\(^{-1}\); HRMS (ESI, H) m/z calc’d for: C\(_{28}\)H\(_{39}\)N\(_2\)O\(_6\) (M + H)\(^+\) 499.2803, found 499.2805.

tert-butyl 4-(((benzyloxy)carbonyl)amino)-4-(3-(2-oxo-2-propoxyethyl)amino)oxetan-3-
butanoate (54): (colorless oil, 25-35% EtOAc/hexanes, 55% yield); \(^1\)H NMR (400 MHz, C\(_6\)D\(_6\)) \(\delta\) 7.31-7.18 (m, 2H), 7.17-6.97 (m, 3H), 5.18-4.92 (m, 3H), 4.50-4.10 (m, 5H), 3.86 (t, \(J = 6.7\) Hz, 2H), 3.42-3.19 (m, 2H), 2.32-2.12 (m, 2H), 1.77-1.59 (m, 2H), 1.47-1.14 (m, 12H), 0.69 (t, \(J = 7.4\) Hz, 3H); \(^13\)C NMR (100 MHz, C\(_6\)D\(_6\)) \(\delta\) 172.9, 172.6, 157.3, 137.6, 128.9, 128.7, 80.3, 77.9, 77.3, 67.1, 66.7, 63.4, 55.7, 45.1, 32.4, 28.4, 25.0, 22.4, 10.6; IR (thin film, NaCl) 3324, 2973, 2879, 1826, 1533, 1365, 1250, 1154, 742 cm\(^{-1}\); HRMS (ESI, TOF-MS) m/z calcd for: C\(_{24}\)H\(_{37}\)N\(_2\)O\(_7\) (M+H)\(^+\) 465.2595; found (M+H)\(^+\) 465.2589.

Data for propyl 2-((3-(13,13-dimethyl-3,11-dioxo-1-phenyl-2,12-dioxa-4,10-diazatetradecan-5-yl)oxetan-3-yl)amino)acetate (55): (colorless oil, 20-30-40% EtOAc/hexanes, 64% yield) \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.26 (d, \(J = 7.0\) Hz, 2H), 7.22-7.00 (m, 3H), 5.25-4.97 (m, 3H), 4.50 (d, \(J = 7.1\) Hz, 1H), 4.32-4.07 (m, 5H), 3.89 (t, \(J = 6.7\) Hz, 2H), 3.36 (dd, \(J = 32.4, 8.4\) Hz, 2H), 2.91 (s (br), 2H), 1.71 (m, 1H), 1.55-1.27 (m, 11H), 1.28-0.83 (m, 6H), 0.70 (t, \(J = 7.4\) Hz, 3H); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 173.4, 157.7, 156.6, 138.1, 129.8, 79.0, 78.4, 77.6, 67.5, 67.2, 63.8, 56.6, 45.5, 40.1, 30.4, 29.6, 29.2, 24.2, 22.8, 11.0; IR (thin film, NaCl) 3340, 2864, 2934, 2875, 1711, 1527, 1245, 1168, 979, 737, 698 cm\(^{-1}\); C\(_{26}\)H\(_{42}\)N\(_3\)O\(_7\) (M+H)\(^+\) 508.3017; found (M+H)\(^+\) 508.3008.

(2S)-propyl 6-((tert-butoxycarbonyl)amino)-2-((3-(13,13-dimethyl-3,11-dioxo-1-phenyl-2,12-dioxa-4,10-diazatetradecan-5-yl)oxetan-3-yl)amino)hexanoate (57): (colorless gum, 25-30-35-40% EtOAc/hexanes, 55% yield); \(^1\)H NMR (400 MHz, C\(_6\)D\(_6\)) \(\delta\) 7.32-7.21 (m, 4H), 7.19-7.04 (m, 6H), 5.52-5.35 (m, 1H), 5.25-5.01 (m, 5H), 4.70-4.57 (m, 2H), 4.53-4.18 (10H), 3.93-3.84 (m, 4H), 3.73-3.53 (m, 2H), 3.03-2.80 (m, 8H), 1.62-1.01 (m, 6H), 0.78-0.63 (m, 6H); \(^13\)C NMR (100 MHz, C\(_6\)D\(_6\)) \(\delta\) 177.1, 158.0, 157.8, 156.7, 156.6, 156.5, 138.2, 138.1, 129.3,
General Procedure E: Nitro group reduction and Boc protection. The synthesis of (S)-Propyl 2-(((S)-2-(((S)-2-(((tert-butoxycarbonyl)amino)methyl)oxetan-3-yl)amino)-4-methylpentanoate (20): To a solution of (S)-propyl 1-(3-(nitromethyl)oxetan-3-yl)pyrrolidine-2-carboxylate (0.250 g, 0.918 mmol), and (Boc)$_2$O (0.256 mL, 1.102 mmol) in THF (10 mL) was added NaHCO$_3$ (0.154 g, 1.836 mmol) and Raney Nickel (500 mg, 50% slurry in water, ca. 1 mL). The reaction was then stirred at room temperature for 3 hours under an atmosphere of H$_2$. After completion was confirmed by TLC, the catalyst was removed by filtration through celite and washing with EtOAc (100 mL). The filtrate was then diluted with water (75 mL) and extracted with EtOAc (3x 75 mL), the combined organics were then dried over Na$_2$SO$_4$, filtered and concentrated in vacuo. The residue was purified by silica gel chromatography (5-20% EtOAc/hexanes) to afford protected amine 20 as a colorless oil (256 mg, 78%).

Data for (S)-Propyl 2-(((S)-2-(((tert-butoxycarbonyl)amino)methyl)oxetan-3-yl)amino)-4-methylpentanoate (20): $^1$H NMR (300 MHz, CDCl$_3$) δ 4.76 (s (br), 1H), 4.56-4.31 (m, 5H), 4.16-4.06 (m, 3H), 3.59 (d, $J = 17.6$ Hz, 1H), 1.90 (s (br), 1H), 1.75-1.60 (m, 3H), 1.47 (s (br), 1H), 1.42 (s, 9H), 1.30-0.84 (m, 9H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 176.7, 156.2, 79.9, 79.5, 66.9, 59.6, 54.1, 44.9, 43.9, 28.5, 24.9, 23.0, 22.3, 22.1, 10.6; IR (thin film, NaCl) 2964, 2878, 1716, 1506, 1390, 1368, 1248, 1175, 977 cm$^{-1}$; HRMS (ESI, H) m/z calcd for: calculated for C$_{18}$H$_{35}$N$_2$O$_5$ (M+H)$^+$ 359.2540, found (M+H)$^+$ 359.2539; $[\alpha]_D^{27}$ –3.8 ($c = 1.30$, CHCl$_3$).

(S)-propyl 2-(((S)-2-(((S)-2-(((tert-butoxycarbonyl)amino)methyl)oxetan-3-yl)amino)-4-methyl pentanamido)-3-phenylpropanoate (32): (colorless oil, 33-50% EtOAc/hexanes, 78% yield); $^1$H NMR (300 MHz, CDCl$_3$) δ 7.38 (d, $J = 8.3$ Hz, 1H), 7.30-7.18 (m, 3H), 7.15-7.08 (m,
2H), 5.36 (s (br), 1H), 4.84 (td, J = 8.1, 5.7 Hz, 1H), 4.40 (d, J = 6.6 Hz, 1H), 4.32 (d, J = 6.9 Hz, 1H), 4.28 (d, J = 6.7 Hz, 1H), 4.23 (d, J = 6.9 Hz, 1H), 4.07 (t, J = 6.7 Hz, 2H), 3.53 (dd, J = 14.2, 7.3 Hz, 1H), 3.34-3.21 (m, 2H), 3.17 (dd, J = 13.9, 5.6 Hz, 1H), 2.97 (dd, J = 13.9, 7.8 Hz, 1H), 1.76 (s (br), 1H), 1.70-1.53 (m, 3H), 1.43 (s, 9H), 1.40-1.31 (m, 1H), 1.25-1.13 (m, 1H), 0.92-0.85 (m, 9H); 

$^{13}$C NMR (75 MHz, CDCl$_3$) δ 174.9, 171.9, 156.6, 135.8, 129.0, 128.4, 126.9, 79.4, 78.8, 78.7, 67.2, 60.5, 55.7, 52.4, 45.8, 44.0, 38.2, 28.4, 24.8, 23.2, 22.1, 21.9, 10.4; IR (thin film, NaCl) 3319, 2959, 2873, 2361, 1658, 1512, 1167 cm$^{-1}$; HRMS (ESI, H) m/z calcd for C$_{27}$H$_{44}$N$_3$O$_6$ (M + H)$^+$ 506.3225, found 506.3219; $[\alpha]_D^{28}$ +10.6 (c 0.40, CHCl$_3$).

Data for Propyl 2-((3-(((tert-butoxycarbonyl)amino)methyl)oxetan-3-yl)amino)acetate (17): (colorless oil, 9-25% MTBE/CH$_2$Cl$_2$, 62% yield); $^1$H NMR (300 MHz, CDCl$_3$) δ 5.07 (s (br), 1H), 4.46 (d, J = 6.7 Hz, 2H), 4.37 (d, J = 6.7 Hz, 2H), 4.09 (t, J = 6.7 Hz, 2H), 3.48 (d, J = 5.6 Hz, 2H), 3.30 (s, 2H), 2.04 (s (br), 1H), 1.72-1.58 (m, 2H), 1.43 (s, 9H), 0.93 (t, J = 7.4 Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 174.9, 171.9, 156.6, 135.8, 129.0, 128.4, 126.9, 79.4, 78.8, 78.7, 67.2, 60.5, 55.7, 52.4, 45.8, 44.0, 38.2, 28.4, 24.8, 23.2, 22.1, 21.9, 10.4; IR (thin film, NaCl) 3319, 2959, 2873, 2361, 1658, 1512, 1167 cm$^{-1}$; HRMS (ESI, H) m/z calcd for: C$_{27}$H$_{44}$N$_3$O$_6$ (M + H)$^+$ 506.3225, found 506.3219; $[\alpha]_D^{28}$ +10.6 (c 0.40, CHCl$_3$).

Data for (S)-Propyl 2-((3-(((tert-butoxycarbonyl)amino)methyl)oxetan-3-yl)amino)propanoate (18): (colorless oil, 9-25% MTBE/CH$_2$Cl$_2$, 76% yield); $^1$H NMR (300 MHz, CDCl$_3$) δ 4.99 (s (br), 1H), 4.47-4.26 (m, 4H), 4.05 (t, J = 6.8 Hz, 2H), 3.67-3.55 (m, 1H), 3.49-3.32 (m, 2H), 2.08 (s (br), 1H), 1.72-1.57 (m, 2H), 1.54 (s, 9H), 1.30 (d, J = 7.0 Hz, 3H), 0.93 (t, J = 7.4 Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 176.3, 156.3, 80.1, 80.0, 79.6, 79.3, 67.0, 59.7, 51.2, 44.7, 28.5, 22.1, 21.0, 10.6; IR (thin film, NaCl) 3325, 2964, 2930, 2878, 1712, 1514, 1391, 1364, 1245, 1175, 977 cm$^{-1}$; HRMS (ESI, H) m/z calcd for: C$_{15}$H$_{29}$N$_2$O$_5$ (M+H)$^+$ 317.2071, found (M+H)$^+$ 317.2074; $[\alpha]_D^{24}$ $-$$6.8$ (c 0.43, CHCl$_3$).
Data for (S)-Propyl 2-((3-(((tert-butoxycarbonyl)amino)methyl)oxetan-3-yl)amino)-3-methyl butanoate (19): (colorless oil, 5-18% MTBE/CH₂Cl₂, 85% yield); ⁱH NMR (300 MHz, CDCl₃) δ 4.95 (s (br), 1H), 4.43 (d, J = 6.4 Hz, 1H), 4.39-4.20 (m, 2H), 4.05 (t, J = 6.7 Hz, 2H), 3.58 (dd, J = 13.8, 6.0 Hz, 1H), 3.38 (dd, J = 13.8, 5.3 Hz, 1H), 3.11 (s (br), 1H), 1.99 (s), 1.97-1.58 (m, 2H), 1.43 (s, 9H), 1.02-0.82 (m, 9H); ¹³C NMR (75 MHz, CDCl₃) δ 176.0, 156.3, 79.7, 79.6, 66.9, 61.0, 59.7, 45.2, 32.2, 28.6, 22.1, 19.6, 18.2, 10.7; IR (thin film, NaCl) 2964, 2924, 2874, 1719, 1509, 1468, 1391, 1367, 1245, 1172, 981 cm⁻¹; HRMS (ESI, H) m/z calcd for: C₁₇H₃₃N₂O₅ (M+H)⁺ 345.2384, found (M+H)⁺ 345.2388; [α]D₂⁶ −0.1 (c 0.59, CHCl₃).

Data for (S)-Propyl 2-((3-(((tert-butoxycarbonyl)amino)methyl)oxetan-3-yl)amino)-3-phenyl propanoate (21): (colorless oil, 5-18% MTBE/CH₂Cl₂, 81% yield); ¹H NMR (300 MHz, CDCl₃) δ 7.37-7.14 (m, 5H), 4.58 (s (br), 1H), 4.30-4.10 (m, 4H), 4.10-3.96 (m, 2H), 3.49 (dd, J = 8.7, 5.3 Hz, 1H), 3.41-3.35 (m, 2H), 2.98 (dd, J = 13.3, 5.3 Hz, 1H), 2.75 (dd, J = 13.4, 8.7 Hz, 1H), 2.06 (s (br), 1H), 1.67-1.53 (m, 2H), 1.42 (s, 9H), 0.89 (t, J = 7.4 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 175.4, 156.1, 137.2, 129.3, 128.6, 127.0, 80.0, 79.5, 79.3, 67.1, 59.5, 57.5, 44.4, 40.9, 28.5, 22.0, 10.5; IR (thin film, NaCl) 3402, 3325, 2964, 2886, 1712, 1492, 1450, 1390, 1248, 1170, 977, 758, 697 cm⁻¹; HRMS (ESI, H) m/z calcd for: C₂₁H₃₃N₂O₅ (M+H)⁺ 393.2384, found (M+H)⁺ 393.2379; [α]D₂⁷ −6.9 (CHCl₃, c 1.61).

Data for Propyl 2-((3-(1-((tert-butoxycarbonyl)amino)-3-methylbutyl)oxetan-3-yl)amino)acetate (52): (pale yellow wax, 5-18% MTBE/CH₂Cl₂, 65% yield); ¹H NMR (300 MHz, CDCl₃) δ 4.76 (d, J = 9.7 Hz, 1H), 4.62-4.26 (m, 4H), 4.15-4.07 (m, 3H), 3.85-3.43 (m, 2H), 1.90 (s (br), 1H), 1.76-1.60 (m, 3H), 1.42 (s, 9H), 1.34-1.04 (m, 2H), 1.04-0.85 (m, 9H); ¹³C NMR (75
MHz, CDCl₃) δ 172.8, 156.1, 79.4, 78.2, 77.5, 67.0, 63.4, 53.2, 45.0, 39.0, 28.6, 25.2, 24.0, 22.2, 21.9, 10.6; IR (thin film, NaCl) 3338, 2959, 2879, 1739, 1713, 1519, 1391, 1364, 1356, 1250, 1206, 1166, 981 cm⁻¹; HRMS (ESI, H) m/z calc'd for C₁₈H₃₅N₂O₅ (M+H)⁺ 359.2540, found (M+H)⁺ 359.2550.

Data for propyl 2-((3-(1-((tert-butoxycarbonyl)amino)-2-(1-tosyl-1H-indol-3-yl)ethyl)oxetan-3-yl)amino)acetate (56): (pale yellow solid, 20-33% EtOAc/hexanes, 28% yield); ¹H NMR (300 MHz, C₆D₆) δ 8.26 (d, J = 8.3 Hz, 1H), 7.74 (d, J = 8.3 Hz, 2H), 7.67 (s, 1H), 7.52 (d, J = 7.6 Hz, 1H), 7.17-7.12 (m, 1H), 7.04 (t, J = 7.2 Hz, 1H), 6.56 (d, J = 7.8 Hz, 2H), 4.86 (d, J = 9.3 Hz, 1H), 4.55 (dd, J = 14.8, 7.0 Hz, 1H), 4.37 (d, J = 7.1 Hz, 1H), 4.15 (d, J = 7.3 Hz, 1H), 4.01-3.87 (m, 4H), 3.37 (q, J = 17.5 Hz, 2H), 2.61-2.58 (m, 2H), 1.67 (s, 4H), 1.45-1.34 (m, 11H), 0.72 (t, J = 7.4 Hz, 3H); ¹³C NMR (75 MHz, C₆D₆) δ 172.6, 144.2, 136.0, 135.7, 135.3, 131.3, 129.6, 126.8, 124.9, 124.3, 123.4, 119.8, 119.4, 114.2, 79.3, 77.7, 77.2, 66.6, 63.0, 55.0, 44.8, 28.4, 25.4, 22.2, 21.0, 10.4; IR (thin film, NaCl) 2878, 1702, 1171 cm⁻¹; HRMS (ESI, H) m/z calc'd for C₃₀H₄₀N₃O₇S (M + H)⁺ 586.2581, found 586.2583.

The synthesis of (S)-propyl 2-((3-(((tert-butoxycarbonyl)amino)methyl)oxetan-3-yl)amino)-4-(methylthio) butanoate (27): To a solution of (S)-propyl 4-(methylthio)-2-((3-(nitromethyl)oxetan-3-yl)amino)butanoate (0.049 g, 0.160 mmol) in n-PrOH (1.6 mL) was added ZnO (0.031 g, 0.480 mmol) (zinc powder used) and 1.0 M HCl (aq.) (0.8 mL, 0.800 mmol). The reaction was then stirred 1.5 hours at room temperature before being directly cannulated into a solution of (Boc)₂O (0.048 mL, 0.208 mmol) in THF (1.0 mL) and 1.0 mL of saturated aqueous NaHCO₃ in a dropwise manner. The flask and cannula were washed with 1 mL THF. This milky white solution was stirred rapidly at room temperature for 1 hour. The reaction was then diluted with brine (60 mL) and extracted with EtOAc (3x 50 mL), dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by flash column chromatography (10-15% acetone/hexanes) to afford protected amine 29 as a colorless oil.
(21 mg, 35%).

Data for (S)-propyl 2-((3-(((tert-butoxycarbonyl)amino)methyl)oxetan-3-yl)amino)-4-(methylthio) butanoate (27): $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.05 (s (br), 1H), 4.48 (d, $J = 6.5$ Hz, 1H), 4.41-4.24 (m, 3H), 4.08 (t, $J = 6.7$ Hz, 2H), 3.66-3.52 (m, 2H), 3.45 (dd, $J = 13.9$, 5.6 Hz, 1H), 2.71-2.55 (m, 2H), 2.15-2.03 (m, 4H), 1.98-1.88 (m, 1H), 1.84-1.59 (m, 3H), 1.45 (s, 9H), 0.95 (t, $J = 7.4$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 176.4, 156.6, 79.9, 79.8, 79.7, 67.3, 59.9, 54.2, 45.1, 33.5, 30.6, 28.6, 22.1, 15.4, 10.6; IR (thin film, NaCl) 3335, 2969, 2935, 2874, 1717, 1507, 1364, 1247, 1170, 974 cm$^{-1}$; HRMS (ESI, TOF-MS) m/z calcd for: C$_{17}$H$_{33}$N$_2$O$_5$S (M+H)$^+$ 377.2105; found (M+H)$^+$ 377.2109; [$\alpha$]$_D^{20}$ $-15.0$ (c 1.00, CHCl$_3$).

The synthesis of (S)-propyl 1-(3-(((tert-butoxycarbonyl)amino)methyl)oxetan-3-yl)pyrrolidine-2-carboxylate (30): To a solution of (S)-propyl pyrrolidine-2-carboxylate (0.148 g, 0.938 mmol) in DMSO (4 mL) was added 3-(nitromethylene)oxetane (0.090 g, 0.782 mmol). The reaction was then allowed to stir at room temperature for 4 hours. The solution was then diluted with EtOAc (100 mL) and washed with brine (2x, 50 mL), the organic layer was dried over Na$_2$SO$_4$ and concentrated in vacuo to afford a residue. The residue was purified by flash column chromatography (20-30% EtOAc/hexanes) to afford a compound that had a $^1$H NMR consistent with the structure of the nitro alkane 15, although contaminated with a minor inseparable impurity (ca. 0.184 g, ca. 86% yield). This material was carried on without any further purification.

To a solution of (S)-propyl 1-(3-(nitromethyl)oxetan-3-yl)pyrrolidine-2-carboxylate (0.184 g, 0.676 mmol), and (Boc)$_2$O (0.204 mL, 0.878 mmol) in THF (6 mL) was added NaHCO$_3$ (0.170 g, 2.027 mmol) and Raney Nickel (500 mg, 50% slurry in water, ca. 1 mL). The reaction was then stirred at room temperature for 3 hours under an atmosphere of H$_2$. After completion was confirmed by TLC, the catalyst was removed by filtration through celite and washing with EtOAc (100 mL). The filtrate was then diluted with water (75 mL) and extracted with EtOAc (3x 75 mL), the combined organics were then dried over Na$_2$SO$_4$, filtered and concentrated in vacuo. The residue was purified by silica gel chromatography (5-20% EtOAc/hexanes) to afford protected amine 30 as a colorless oil (176 mg, 65% over two steps).

Data for (S)-propyl 1-(3-(((tert-butoxycarbonyl)amino)methyl)oxetan-3-yl)pyrrolidine-2-carboxylate (30): (colorless oil, 4-8-10% acetone/hexanes, 76% yield) $^1$H NMR (400 MHz, C$_6$D$_6$) $\delta$ 5.62 (s, 1H), 4.46-4.37 (m, 2H), 4.23-4.15 (m, 2H), 3.81 (t, $J = 6.7$ Hz, 2H), 3.64 (dd, $J = 13.5$, 5.6 Hz, 2H), 3.05 (dd, $J = 13.9$, 5.6 Hz, 1H), 2.71-2.55 (m, 2H), 2.15-2.03 (m, 4H), 1.98-1.88 (m, 1H), 1.84-1.59 (m, 3H), 1.45 (s, 9H), 0.95 (t, $J = 7.4$ Hz, 3H); $^{13}$C NMR (100 MHz, C$_6$D$_6$) $\delta$ 176.4, 156.6, 79.9, 79.8, 79.7, 67.3, 59.9, 54.2, 45.1, 33.5, 30.6, 28.6, 22.1, 15.4, 10.6; IR (thin film, NaCl) 3335, 2969, 2935, 2874, 1717, 1507, 1364, 1247, 1170, 974 cm$^{-1}$; HRMS (ESI, TOF-MS) m/z calcd for: C$_{17}$H$_{33}$N$_2$O$_5$S (M+H)$^+$ 377.2105; found (M+H)$^+$ 377.2109; [$\alpha$]$_D^{20}$ $-15.0$ (c 1.00, CHCl$_3$).
The synthesis of Tripeptide 58 through \(n\)-propyl ester saponification: To a solution of (S)-tert-butyl 2-((3-(((benzyloxy)carbonyl)amino)methyl)oxetan-3-yl)amino)-3-oxo-3-proxypropyl-1H indole-1-carboxylate (0.061 g, 0.107 mmol) in MeOH (2.7 mL) at room temperature was added 1M aqueous NaOH (0.75 mL, 0.752 mmol) and the resulting mixture was stirred for 2 hours. After 2 hours, the reaction mixture was diluted with EtOAc and 1M NaHSO\(_4\) (50 mL) and extracted with EtOAc (3x 50 mL). The organic layers were collected, dried over Na\(_2\)SO\(_4\), filtered, and concentrated in vacuo to afford a residue which was used without further purification. To the residue was sequentially added DMF (0.22 mL), (S)-propyl 2-amino-3-phenylpropanoate hydrochloride (0.031 g, 0.129 mmol), and DIEA (0.056 mL, 0.322 mmol). After stirring 1 hour at 0 °C, the ice bath was removed and stirring was continued for 24 hours at room temperature. Then the reaction was concentrated in vacuo and the resulting residue was purified by silica gel chromatography (40-50% EtOAc/hexanes) to afford tripeptide 58 as a pale yellow solid (58 mg, 76% yield).

Data for tert-butyl 3-((S)-2-(((benzyloxy)carbonyl)amino)methyl)oxetan-3-yl)amino)-3-oxo-3-(((S)-1-oxo-3-phenyl-1-propoxypropan-2-yl)amino)propyl)-1H-indole-1-carboxylate (58): \(^1\)H NMR (300 MHz, C\(_6\)D\(_6\)) \(\delta\) 8.42 (s, 1H), 7.71 (d, \(J = 7.7\) Hz, 1H), 7.60 (s, 1H), 7.53 (d, \(J = 8.3\) Hz, 1H), 7.34-6.94 (m, 9H), 6.88 (d, \(J = 7.2\) Hz, 2H), 5.48 (t, \(J = 5.4\) Hz, 1H), 5.09 (m, 2H), 4.98 (dd, \(J = 14.2, 6.6\) Hz, 1H), 4.12 (d, \(J = 6.1\) Hz, 2H), 4.04 (t, \(J = 6.2\) Hz, 2H), 3.90-3.74 (m, 2H), 3.57-3.49 (m, 1H), 3.41 (dd, \(J = 14.3, 7.0\) Hz, 1H), 3.14-3.00 (m, 2H), 2.98-2.80 (m, 3H), 1.95 (s (br), 1H), 1.37 (s, 9H), 1.33-1.22 (m, 3H), 0.62 (d, \(J = 7.5\) Hz, 3H); \(^{13}\)C NMR (75 MHz, C\(_6\)D\(_6\)) \(\delta\) 173.6, 172.0, 157.2, 149.5, 137.2, 136.3, 135.9, 130.6, 129.5, 129.3, 128.4, 127.0, 126.6, 124.9, 124.6, 123.1, 119.5, 116.2, 115.7, 83.3, 78.5,
67.0, 66.8, 66.1, 60.6, 57.2, 53.1, 46.1, 38.2, 30.1, 27.9, 22.0, 10.3; IR (thin film, NaCl) 3320, 2964, 1723, 1513, 1452, 1155 cm\(^{-1}\); HRMS (ESI, H) \(m/z\) calc'd for C\(_{40}\)H\(_{49}\)N\(_4\)O\(_8\) (M + H\(^+\)) 713.3545, found 713.3550; \([\alpha]_D^{26}\) \(-5.90\) (c 0.50, CHCl\(_3\)).

**Synthesis of tripeptide 59 through deprotection of N-Boc group:** A 0 °C solution of 20% TFA in CH\(_2\)Cl\(_2\) (1.7 mL) was added to (S)-propyl 1-(3-(((S)2-((tert-butoxycarbonyl)amino)-3-methylbutanamido)methyl)oxetan-3-yl)pyrrolidine-2-carboxylate (0.059 g, 0.172 mmol) at 0 °C, via cannula. After stirring for 30 minutes at 0 °C the ice bath was removed and the reaction was allowed to stir 1 hour at room temperature. Then toluene (ca. 1 mL) was added and the solution was evaporated in vacuo. The addition of 1 mL of toluene and evaporation was repeated two more times to afford a crude TFA salt which was used without further purification. To the crude TFA salt was sequentially added DMF (0.35 mL), (S)-2-((tert-butoxycarbonyl)amino)-3-methylbutanoic acid (0.045 g, 0.207 mmol), DIEA (0.090 mL, 0.517 mmol), the reaction was then cooled to 0 °C and 2-(1H-benzo[d][1,2,3]triazol-1-yl)-1,1,3,3-tetramethylisouronium hexafluorophosphate(V) (0.078 g, 0.207 mmol) in one portion. After stirring for 1 hour stirring at 0 °C, the ice bath was removed and the reaction stirred for 24 hours at room temperature. The reaction was then concentrated in vacuo. The resulting crude residue was purified by silica gel chromatography (33-66% EtOAc/hexanes) to afford tripeptide 59 as a pale yellow oil (51 mg, 67% yield).

**Data for (S)-propyl 1-(3-(((S)-2-((tert-butoxycarbonyl)amino)-3-methylbutanamido)methyl)oxetan-3-yl)pyrrolidine-2-carboxylate (59):**

\(^1\)H NMR (300 MHz, C\(_6\)D\(_6\)) \(\delta\) 7.10 (t, \(J = 4.5\) Hz, 1H), 5.61 (d, \(J = 8.8\) Hz, 1H), 4.43 (t, \(J = 7.0\) Hz, 2H), 4.34-4.29 (m, 1H), 4.26 (d, \(J = 6.8\) Hz, 1H), 4.18 (d, \(J = 6.6\) Hz, 1H), 3.82 (t, \(J = 6.6\) Hz, 2H), 3.76-3.62 (m, 1H), 3.62-3.53 (m, 1H), 2.74-2.69 (m, 1H), 2.25-2.17 (m, 2H), 1.74-1.49 (m, 3H), 1.42 (s, 9H), 1.38-1.26 (m, 3H), 1.02 (d, \(J = 6.7\) Hz, 3H), 0.90 (d, \(J = 6.8\) Hz, 3H), 0.69 (d, \(J = 7.4\) Hz, 3H); \(^{13}\)C NMR (75 MHz, C\(_6\)D\(_6\)) \(\delta\) 175.5, 171.9, 155.9, 78.8, 77.2, 76.4, 66.4, 62.2, 60.4, 59.8, 47.7, 45.2, 31.7, 31.0, 28.4, 24.6, 22.2, 19.6, 18.0, 10.4; IR (thin film, NaCl) 3313, 2964, 2877, 1660, 1515, 1163 cm\(^{-1}\); HRMS (ESI, H) \(m/z\) calc'd for C\(_{22}\)H\(_{40}\)N\(_2\)O\(_6\) (M + H\(^+\)) 442.2912, found 442.2904; \([\alpha]_D^{28}\) \(+11.6\) (c 0.44, CHCl\(_3\)).
Synthesis of tripeptide 60 through deprotection of N-Cbz group: To a solution of (S)-5-tert-butyl 1-propyl 2-((3-(((benzyloxy)carboxyl)amino)methyl)oxetan-3-yl)amino)pentanedioate (0.120 g, 0.257 mmol) in EtOAc (5.1 mL) was added 10% Pd/C (0.014 g, 0.013 mmol) and the reaction mixture was stirred under H2 for one hour. Then the reaction was then filtered through celite and the filtrate was concentrated to afford a residue which was used without further purification. To the residue was sequentially added DMF (0.26 mL), (S)-2-(((benzyloxy)carboxyl)amino)-4-methylpentanoic acid (0.082 g, 0.309 mmol), and DIEA (0.090 mL, 0.515 mmol), the solution was then cooled to 0 °C and 2-(1H-benzo[d][1,2,3]triazol-1-yl)-1,1,3,3-tetramethylisouronium hexafluorophosphate(V) (HBTU) (0.117 g, 0.309 mmol) was added in one portion. After stirring for 1 hour at 0 °C, the ice bath was removed, and the reaction was further stirred for 24 hours at room temperature. The reaction was then concentrated in vacuo and the resulting crude residue was purified by silica gel chromatography (33-50% EtOAc/hexanes) to afford tripeptide 60 as a colorless oil (92 mg, 62% yield).

Data for (S)-5-tert-butyl 1-propyl 2-((3-(((benzyloxy)carboxyl)amino)-4-methylpentanamido)methyl)oxetan-3-yl)amino)pentanedioate (60): 1H NMR (300 MHz, C6D6) δ 7.25 (d, J = 7.0 Hz, 3H), 7.18-7.01 (m, 2H), 6.17 (d, J = 8.3 Hz, 1H), 5.10 (s, 2H), 4.59 (dd, J = 13.5, 8.6 Hz, 1H), 4.46 (d, J = 6.3 Hz, 1H), 4.35 (d, J = 6.4 Hz, 1H), 4.30 (d, J = 5.2 Hz, 2H), 3.84-3.61 (m, 4H), 3.39 (dd, J = 8.7, 4.4 Hz, 1H), 2.37-2.19 (m, 3H), 2.04-1.59 (m, 5H), 1.44-1.26 (m, 12H), 0.96 (d, J = 5.9 Hz, 3H), 0.92 (d, J = 6.2 Hz, 3H), 0.67 (d, J = 7.4 Hz, 3H); 13C NMR (75 MHz, C6D6) δ 175.8, 173.4, 172.5, 156.5, 137.1, 128.4, 127.9, 80.2, 79.6, 79.3, 66.8, 66.7, 60.1, 54.9, 54.2, 43.8, 41.9, 32.2, 29.9, 28.0, 25.1, 23.2, 22.1, 22.0, 10.4; IR (thin film, NaCl) 3316, 2959, 2874, 1723, 1550, 1150 cm⁻¹; HRMS (ESI, H) m/z calc’d for C30H48N3O8 (M + H)⁺ 578.3436, found 578.3427; [α]D²⁶ −11.3 (c 0.50, CHCl₃).

General Procedure (F): Conjugate addition of free-based amino acids to 3-(nitromethylene)oxetane.
A solution of 3-(nitromethylene)oxetane (1 mmol) in THF was added to a solution of the desired amino acid (1 mmol) and NaHCO$_3$ (3 mmol) in a mixture of water and THF. The reaction mixture was stirred at room temperature until disappearance of the nitro-olefin. To the reaction mixture was then added Ra-Ni (commercial suspension in water, 1 mL) and the reaction mixture was stirred at room temperature under H$_2$ (1 atm) until disappearance of the intermediate nitro-acid. The reaction mixture was filtered through Celite® and washed with THF. The filtrate was evaporated to a minimal amount of solvent and treated with either CbzCl or FmocOSu (1.1 eq) and reacted until disappearance of the aminoacid dimer. The crude mixtures were acidified to pH 2 and extracted with ethyl acetate. The combined organic extracts were concentrated and the residues purified by chromatography (SiO$_2$, CH$_2$Cl$_2$, MeOH) to afford the desired products.

Data for (S)-2-(((3-(((benzyloxy)carbonyl)amino)methyl)oxetan-3-yl)amino)-3-(tert-butoxy)propanoic acid (37): $^1$H NMR (400 MHz, CD$_3$OD) δ 7.43-7.26 (m, 5H), 5.10 (s, 2H), 4.61 (dd, $J = 6.4$, 6.4 Hz, 2H), 4.45 (dd, $J = 6.4$, 6.4 Hz, 2H), 3.77-3.50 (m, 5H), 1.20 (s, 9H); $^{13}$C-NMR (100 MHz, CD$_3$OD) δ 176.8, 159.4, 138.1, 129.5, 129.1, 128.9, 79.7, 79.3, 74.9, 67.9, 64.1, 62.0, 59.9, 45.3, 27.7; IR (thin film, NaCl) 3317, 2972, 1713, 1635, 1455, 1410, 1391, 1364, 1236, 1190, 1080, 1023, 979, 863, 775, 738, 697, 665, 555, 459 cm$^{-1}$; HRMS (Dual (MALDI/ESI)) m/z calcd for C$_{19}$H$_{29}$N$_2$O$_6$ (M + H)$^+$ 381.2020, found 381.2019; [α]$_D^{23}$ -1.084 (c 0.50, MeOH).

Data for (S)-2-(((3-(((benzyloxy)carbonyl)amino)methyl)oxetan-3-yl)amino)-3-(4-(tert-butoxy)phenyl)propanoic acid (38): $^1$H NMR (400 MHz, CD$_3$OD) δ 7.40-7.23 (m, 6H), 7.19 (d, $J = 8.2$ Hz, 2H), 6.89 (d, $J = 8.3$ Hz, 2H), 5.07 (s, 2H), 4.31-4.14 (m, 4H), 3.45-3.33 (m, 3H), 3.06 (dd, $J = 13.4$, 4.5 Hz, 1H), 2.64 (dd, $J = 13.0$, 9.0 Hz, 1H), 1.28 (s, 9H); $^{13}$C-NMR
(100 MHz, CD$_3$OD) δ 183.1, 159.3, 155.2, 139.2, 135.4, 131.1, 131.0, 129.5, 129.0, 128.9, 125.2, 80.5, 80.1, 79.4, 67.7, 61.4, 61.1, 46.2, 41.2, 29.2; IR (thin film, NaCl) 3319, 2928, 1694, 1569, 1506, 1411, 1365, 1236, 1160, 1017, 974, 924, 896, 847, 774, 736, 697, 544, 474 cm$^{-1}$; HRMS (Dual (MALDI/ESI)) $m/z$ calcd for C$_{25}$H$_{33}$N$_2$O$_6$ (M + H)$^+$ 457.2333, found 457.2331; [α]$_D^{23}$ -33.74 (c 0.45, MeOH).
Data for (S)-2-(((3-(((benzyloxy)carbonyl)amino)methyl)oxetan-3-yl)amino)-3-(1-(tert-butoxycarbonyl)-1H-indol-3-yl)propanoic acid (39): $^1$H NMR (400 MHz, d$_6$-DMSO) $\delta$ 8.00 (d, $J =$ 7.4 Hz, 1H), 7.66 (d, $J =$ 7.4 Hz, 1H), 7.50 (s, 1H), 7.40-7.14 (m, 7H), 5.00 (d, $J =$ 12.6 Hz, 1H), 4.98 (d, $J =$ 12.6 Hz, 1H), 4.19 (d, $J =$ 5.2 Hz, 1H), 4.17 (s, 2H), 4.10 (d, $J =$ 6.0 Hz, 1H), 3.54-3.26 (m, 3H), 3.22 (dd, $J =$ 13.9, 5.5 Hz, 1H), 3.03 (d (br), $J =$11.3 Hz, 1H), 2.72 (dd, $J =$ 14.1, 7.8 Hz, 1H), 1.60 (s, 9H); $^{13}$C-NMR (100 MHz, d$_6$-DMSO) $\delta$ 178.7, 157.1, 149.6, 137.6, 135.0, 131.2, 128.8, 128.2, 128.1, 124.5, 124.0, 122.7, 120.1, 115.0, 83.8, 78.7, 65.8, 60.2, 57.8, 45.6, 30.8, 28.2; IR (thin film, NaCl) 3406, 2936, 2244, 1727, 1574, 1452, 1367, 1309, 1255, 1227, 1155, 1085, 1018, 976, 855, 836, 766, 745, 697, 651, 573, 473, 423 cm$^{-1}$; HRMS (Dual (MALDI/ESI)) m/z calcd for C$_{28}$H$_{34}$N$_3$O$_7$ (M + H)$^+$ 524.2391, found 524.2391.

Data for (3-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)methyl)oxetan-3-yl)-L-valine (40):

$^1$H-NMR (400 MHz, Methanol-d$_4$) $\delta$ 7.79 (d, $J =$ 7.5 Hz, 2H), 7.65 (d, $J =$ 7.1 Hz, 2H), 7.38 (t, $J =$ 7.5 Hz, 2H), 7.30 (t, $J =$ 7.4 Hz, 2H), 4.59 (d, $J =$ 6.8 Hz, 1H), 4.52 (d, $J =$ 7.0 Hz, 1H), 4.47-4.32 (m, 4H), 4.21 (t, $J =$ 6.9 Hz, 1H), 3.62 (d, $J =$ 14.3 Hz, 1H), 3.51 (d, $J =$ 14.4 Hz, 1H), 3.32 (m, 1H), 2.02 (ddd, $J =$ 13.1, 9.1, 5.5 Hz, 1H), 0.99 (d, $J =$ 10.0, 3H), 0.98 (d, $J =$ 10.0 Hz, 3H). $^{13}$C- NMR (100 MHz, CD$_3$OD) $\delta$ 178.7, 159.5, 145.3, 145.3, 142.6, 128.8, 128.1, 126.2, 126.2, 120.9, 79.5, 79.4, 68.0, 63.3, 62.0, 49.6, 49.5, 49.4, 49.3, 49.2, 49.1, 49.0, 48.8, 48.6, 48.5, 48.4, 46.2, 32.7, 19.5, 18.6. IR (thin film, NaCl) 2962, 1697, 1623, 1536, 1449, 1389, 1248, 1149, 982, 908, 758, 730, 647, 621, 560, 542, 425 cm$^{-1}$; HRMS (Dual (MALDI/ESI)) m/z calcd for C$_{24}$H$_{29}$N$_3$O$_5$ (M + H)$^+$ 425.2071, found 425.2070; $[^{[a]D}]$ 4.314 (c 0.60, CHCl$_3$).
General Procedure G: Synthesis of n-propyl ester amino acids through CDI mediated coupling with n-PrOH. The synthesis of (S)-5-tert-butyl 1-propyl 2-(((benzyloxy)carbonyl)amino)pentanedioate (S-9): To a solution of (S)-3-(4-(tert-butoxy)phenyl)-2-(((tert-butoxycarbonyl)amino)propanoic acid (0.500 g, 1.482 mmol) in CH₂Cl₂ (3 ml) at room temperature was added CDI (0.240 g, 1.482 mmol) in a portion wise manner (evolution of CO₂(g)). The reaction mixture was stirred for 1 h at room temperature, then n-propanol (0.55 mL, 7.41 mmol) was added and stirring was continued overnight at the same temperature. The reaction was then quenched with 1M aqueous citric acid, extracted with CH₂Cl₂, dried over Na₂SO₄, filtered and concentrated in vacuo. The resulting residue was purified by silica gel chromatography (50% EtOAc/hexane) to afford ester S-9 as colorless oil (564 mg, 98% yield).

Data for (S)-5-tert-butyl 1-propyl 2-(((benzyloxy)carbonyl)amino)pentanedioate (S-9):

\[^1\text{H} \text{NMR (300 MHz, CDCl\textsubscript{3})} \delta \text{7.33-7.23 (m, 5H), 5.54 (d, J = 8.2 Hz, 1H), 5.07 (s, 2H), 4.36 (td, J = 8.3, 5.0 Hz, 1H), 4.06 (t, J = 6.7 Hz, 2H), 2.42-2.20 (m, 2H), 2.16-2.20 (m, 1H), 1.98-1.85 (m, 1H), 1.62 (dt, J = 13.9, 7.0 Hz, 2H), 1.41 (s, 9H), 0.91 (t, J = 7.4 Hz, 3H); \[^{13}\text{C} \text{NMR (75 MHz, CDCl\textsubscript{3})} \delta \text{171.7, 171.6, 155.6, 155.6, 136.0, 128.2, 127.9, 127.8, 80.6, 67.1, 66.9, 53.6, 31.6, 28.2, 27.8, 22.1, 10.5; IR (thin film, NaCl) 3353, 2972, 1723, 1520, 1148, 1055, 896, 736, 697 cm\textsuperscript{-1}; HRMS (ESI, H) m/z calc'd for C\textsubscript{20}H\textsubscript{30}NO\textsubscript{6} (M + H)\textsuperscript{+} 380.2068, found 380.2072; [\alpha]\text{D}\textsuperscript{25} +4.82 (c 0.50, CHCl\textsubscript{3}). \]
Data for (S)-propyl 2-(((benzylloxy)carbonyl)amino)-3-(tert-butoxy)propanoate (S-8): (colorless oil, 50% EtOAc/hexanes, 94% yield); $^1$H NMR (300 MHz, CDCl$_3$) δ 7.37-7.21 (m, 5H), 5.68 (d, J = 8.9 Hz, 1H), 5.09 (s, 2H), 4.43 (dt, J = 8.8, 2.9 Hz, 1H), 4.09-4.02 (m, 2H), 3.78 (dd, J = 8.9, 2.8 Hz, 1H), 3.54 (dd, J = 8.9, 3.2 Hz, 1H), 1.70-1.52 (m, 2H), 1.09 (s, 9H), 0.90 (t, J = 7.4 Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 170.5, 156.0, 136.3, 128.3, 127.9, 73.1, 66.7, 61.9, 27.1, 21.8, 10.2; IR (thin film, NaCl) 3446, 3343, 2971, 1724, 1503, 1194, 1062, 737, 697 cm$^{-1}$; HRMS (ESI, H) m/z calc’d for C$_{18}$H$_{28}$NO$_5$ (M + H)$^+$ 338.1962, found 338.1962; [$\alpha$]$_D^{25}$ +6.85 (c 0.50, CHCl$_3$).

Data for (S)-propyl 2-(((benzylloxy)carbonyl)amino)-4-oxo-4-(tritylamino)butanoate (S-10): (white solid, 33-50%, EtOAc/hexanes, 83%); $^1$H NMR (300 MHz, CDCl$_3$) δ 7.33-7.14 (m, 20H), 6.72 (s, 1H), 6.06 (d, J = 8.1 Hz, 1H), 5.10 (s, 2H), 4.54 (dt, J = 8.5, 4.2 Hz, 1H), 4.03 (t, J = 6.7 Hz, 2H), 3.06 (dd, J = 15.6, 4.2 Hz, 1H), 2.81 (dd, J = 15.7, 3.8 Hz, 1H), 1.84-1.46 (m, 2H), 0.87 (t, J = 7.4 Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 170.8, 169.0, 156.1, 144.1, 136.2, 128.5, 128.4, 127.9, 127.7, 127.0, 70.9, 67.3, 66.8, 51.1, 38.6, 21.9, 10.4; IR (thin film, NaCl) 3302, 1967, 1702, 1651, 1523, 1255, 1056, 698 cm$^{-1}$; HRMS (ESI, H) m/z calc’d for C$_{34}$H$_{35}$N$_2$O$_5$ (M + H)$^+$ 551.2540, found 551.2543; [$\alpha$]$_D^{25}$ +4.41 (c 0.50, CHCl$_3$).

Synthesis of (S)-propyl 2-(((benzylloxy)carbonyl)amino)-3-(1-trityl-1H-imidazol-4-yl) propanoate (S-11): To n-PrOH (4.1 mL) at 0 °C was added SOCl$_2$ (0.298 mL, 4.08 mmol) followed by (S)-2-(((benzylloxy)carbonyl)amino)-3-(1H-imidazol-4-yl)propanoic acid (0.590 g, 2.039 mmol). The reaction mixture was stirred for 30 minutes at the same temperature and then the ice bath was removed. The resultant mixture was then stirred for 3 days at room
temperature. The reaction mixture was then concentrated *in vacuo* to afford a blue oil, which was then diluted with CH$_2$Cl$_2$ (200 mL) and washed with saturated aqueous NaHCO$_3$, and brine (100 mL each), dried over Na$_2$SO$_4$, filtered and concentrated *in vacuo*. The resulting crude residue was carried on without further purification.

The residue was dissolved in CH$_2$Cl$_2$ (10.2 mL) and treated with Et$_3$N (0.341 mL, 2.448 mmol), and (chloromethanetriyl)tribenzene (0.682 g, 2.448 mmol). After stirring for 6 hours at room temperature, the reaction mixture was diluted with EtOAc (150 mL) and washed with water, and brine (75 mL each); dried over Na$_2$SO$_4$, filtered and concentrated *in vacuo*. The residue was purified by silica gel chromatography (20-33% EtOAc/hexane) to afford protected amino acid S-11 as a white solid (1.05 g, 90% yield over two steps).

**Data for (S)-propyl 2-(((benzylxoy)carbonyl)amino)-3-(1-trityl-1H-imidazol-4-yl)propanoate (S-11):** $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.48-7.23 (m, 15H), 7.16-7.01 (m, 6H), 6.53 (s, 1H), 6.45 (d, $J$ = 8.4 Hz, 1H), 5.10 (s, 2H), 4.77-4.39 (m, 1H), 3.97 (dd, $J$ = 11.2, 6.2 Hz, 2H), 3.05 (t, $J$ = 4.6 Hz, 2H), 1.54 (dd, $J$ = 14.1, 7.0 Hz, 2H), 0.84 (t, $J$ = 7.3 Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 171.4, 156.0, 142.1, 138.7, 136.4, 136.2, 129.6, 128.3, 127.9, 127.8, 119.4, 75.2, 66.71, 66.66, 54.2, 30.2, 22.0, 10.5; IR (thin film, NaCl) 3330, 2966, 2359, 1721, 1494, 1185, 749, 700 cm$^{-1}$; HRMS (ESI, H) m/z calc'd for C$_{36}$H$_{36}$N$_3$O$_4$ (M + H)$^+$ 574.2700, found 574.2689; $[\alpha]_{D}^{26}$ +10.8 (c 0.50, CHCl$_3$).

**Synthesis of (S)-tert-butyl 3-(2-(((benzylxoy)carbonyl)amino)-3-oxo-3-propoxypropyl)-1H-indole-1-carboxylate (S-12):** To a solution of (S)-2-(((benzylxoy)carbonyl)amino)-3-(1H-indol-3-yl)propanoic acid (1.7 g, 5.02 mmol) in CH$_2$Cl$_2$ (10 mL) at room temperature was added CDI (0.896 g, 5.53 mmol) in a portion wise manner. The reaction mixture was stirred for 1 hour at room temperature, and then propan-1-ol (1.90 mL, 25.1 mmol) was added. After stirring overnight at room temperature, reaction was quenched with 1M aqueous citric acid, extracted with CH$_2$Cl$_2$ (3x 150 mL) then dried over Na$_2$SO$_4$, filtered and concentrated *in vacuo*. The resulting residue was purified by silica gel chromatography (20% EtOAc/hexanes) to afford a compound with which exhibited a $^1$H NMR spectrum which was consistent with the propyl ester, although contaminated with some minor impurities (ca. 1.4
This mixture was carried on without further purification.

To a solution of the propyl ester in dry CH$_2$Cl$_2$ (35.9 mL) were sequentially added tetrabutylammonium hydrogen sulfate (0.122 g, 0.359 mmol) and freshly powdered NaOH (0.718 g, 17.95 mmol). The resulting solution was stirred for 15 min, and a solution of (Boc)$_2$O (2.50 mL, 10.77 mmol) in CH$_2$Cl$_2$ (10 mL) was added in drop wise manner over 5 minutes. The resulting white suspension was vigorously stirred for 1.5 hours at room temperature. Water (150 mL) was then added to the reaction, layers separated, and the aqueous layer was extracted with CH$_2$Cl$_2$ (4x, 150 mL), the combined organics were then dried over Na$_2$SO$_4$, filtered and concentrated in vacuo. The resulting residue was purified by silica gel chromatography (10% EtOAc/hexane) to afford protected amino acid S-12 as a colorless oil (948 mg, 39% yield in two steps).

Data for (S)-tert-butyl 3-((benzyloxy)carbonyl)amino)-3-oxo-3-propoxypropyl)-1H-indole-1-carboxylate (S-12): $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.14 (d, $J = 7.9$ Hz, 1H), 7.72-7.05 (m, 9H), 5.51 (d, $J = 8.0$ Hz, 1H), 5.24-4.96 (m, 2H), 4.75 (dd, $J = 13.5$, 5.7 Hz, 1H), 4.05 (td, $J = 6.5$, 2.3 Hz, 2H), 3.26 (t, $J = 5.0$ Hz, 2H), 1.67 (s, 9H), 1.65-1.37 (m, 2H), 0.87 (d, $J = 7.4$ Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 171.3, 155.4, 149.2, 136.0, 135.1, 130.3, 128.3, 128.0, 127.9, 124.4, 123.9, 122.4, 118.7, 115.1, 114.8, 83.6, 67.2, 67.0, 54.3, 28.4, 28.1, 22.0, 10.5; IR (thin film, NaCl) 3351, 2973, 1725, 1153, 747 cm$^{-1}$; HRMS (ESI, H) m/z calc'd for C$_{27}$H$_{33}$N$_2$O$_6$ (M + H)$^+$ 481.2333, found 481.2327; [$\alpha$]$_D^{25}$ +23.8 (c 0.50, CHCl$_3$).

Data for (S)-propyl 2-((benzyloxy)carbonyl)amino)-6-((tert-butoxycarbonyl)amino)hexanoate (S-13): (colorless oil, 33-50%, EtOAc/hexanes, 83% yield); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.39-7.27 (m, 5H), 5.45-5.31 (m, 1H), 5.09 (s, 2H), 4.65-4.48 (m, 1H), 4.40-4.28 (m, 1H), 4.16-3.99 (m, 2H), 3.14-2.97 (m, 2H), 1.90-1.78 (m, 1H), 1.74-1.57 (m, 3H), 1.52-1.25 (m, 12H), 0.93 (t, $J = 7.4$ Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 172.7, 156.2, 136.5, 128.7, 128.4, 128.3, 79.3, 67.2, 67.1, 54.0, 40.2, 32.5, 29.8, 28.6, 22.5, 22.1, 10.5; IR (thin film, NaCl) 3349, 2966, 2931, 1712, 1524, 1249, 1169, 1055, 739 cm$^{-1}$; HRMS (ESI, H) m/z calc’d for C$_{22}$H$_{34}$N$_2$Na (M + Na)$^+$ 445.2309, found 445.2313; [$\alpha$]$_D^{29}$ +3.02 (c 2.00, CHCl$_3$).
General Procedure G: the synthesis of propyl esters through Fisher esterification. The synthesis of (S)-propyl pyrrolidine-2-carboxylate hydrochloric acid salt (S-15): To n-PrOH (50 mL) at 0 °C was added SOCl₂ (9.51 mL, 130 mmol) in a dropwise manner via addition funnel over 20 minutes. Upon completion of addition (S)-proline (5.00 g, 43.4 mmol) was added in one portion and the reaction was allowed to warm to room temperature and stir overnight. The reaction was then concentrated in vacuo, ether (150 mL) was then added to the residue, and the mixture stirred rapidly for 30 minutes. The ether was then decanted, and the residue dried on the high vacuum to afford HCl salt S-15 as a green gum (3.45 g, 51% yield).

Data for (S)-propyl pyrrolidine-2-carboxylate hydrochloric acid salt (S-15): light green gum; ¹H NMR (400 MHz, MeOD) δ 4.54-4.49 (m, 1; ¹³C NMR (100 MHz, MeOD) δ 170.9, 70.1, 61.6, 48.0, 30.2, 25.4, 23.7, 11.4; IR (thin film, NaCl) 3393, 2880, 2723, 1741, 1398, 1243, 1058 cm⁻¹; HRMS (ESI, Na) m/z calc’d for C₈H₁₆NO₂ (M + H)⁺ 158.1176, found 158.1174; [α]D²⁵ +33.0 (c 2.0, MeOH).

Synthesis of (S)-propyl 2-amino-4-(methylthio)butanoate (S-14): To n-PrOH (50 mL) at 0 °C was added H₂SO₄ (8.93 mL, 168 mmol) in a drop wise manner, the solution was allowed to stir 10 minutes at 0 °C. Then (S)-methionine (5.00 g, 33.50 mmol) was added in one portion, the reaction was then allowed to warm to room temperature and stir overnight. The reaction was then diluted with water (200 mL) and basified to pH 10 with solid K₂CO₃. The organic layer was then extracted to EtOAc (3x 150 mL), dried over Na₂SO₄, filtered and concentrated in vacuo. The resulting residue was purified by silica gel chromatography (3% MeOH/CH₂Cl₂) to afford ester S-12 as a colorless oil (2.50 g, 39%).

Data for (S)-propyl 2-amino-4-(methylthio)butanoate (S-14): ¹H NMR (400 MHz, CDCl₃) δ 4.12-3.99 (m, 2H), 3.60-3.52 (m, 1H), 2.65-2.55 (m, 2H), 2.13-1.95 (m, 4H), 2.85-1.70 (m, 1H), 1.70-1.57 (m, 2H), 1.48 (s (br), 2H), 0.99-0.88 (m, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 176.0, 66.8, 53.6, 34.2, 30.7, 22.2, 15.6, 10.6; IR (thin film, NaCl) 3379, 2966, 1731, 1438, 1182, 969, 838 cm⁻¹; HRMS (ESI, Na) m/z calc’d for C₈H₁₆NO₂S (M + H)⁺ 192.1053, found 192.1049; [α]D°⁻³⁰ −0.384 (c 1.0, CHCl₃).
The synthesis of 1-(tert-butoxy)-4-(2-nitroethyl)benzene (42): A 50 mL flask equipped reflux condenser was charged with 4-(tert-butoxy)benzaldehyde (1.15 g, 6.45 mmol), NH₄OAc (1.24 g, 16.13 mmol) and AcOH (12.90 mL). To the solution at room temperature was added MeNO₂ (1.08 mL, 20.00 mmol) and the reaction mixture was then heated at 60 °C for 30 minutes (TLC suggested that Rᵣ value of desired product was the same as aldehyde). The reaction was then heated at 80 °C overnight (completion of the reaction was confirmed by LCMS). The reaction was concentrated in vacuo, and the resulting residue was diluted with EtOAc (200 mL) and washed with saturate aqueous NaHCO₃ and brine (75 mL each), the organic layer was dried over Na₂SO₄, filtered, and concentrated in vacuo. The resulting residue was purified by silica gel chromatography (5-10% EtOAc/hexane) to afford a mixture of the nitro olefin, contaminated with some aldehyde and an unidentified by-product (ca. 1 g). This mixture was used for next step without further purification.

To a solution of the nitro olefin and silica gel (2.085 g, 34.7 mmol) in CHCl₃/2-propanol (12 mL, 3/1) was added NaBH₄ (0.673 g, 17.79 mmol) in a portion wise manner. After stirring for 2 hours at room temperature the reaction mixture was filtered through celite and concentrated in vacuo. The resulting residue was dissolved in EtOAc (150 mL) and washed with water and brine (75 mL each), dried over Na₂SO₄, filtered, and concentrated in vacuo. The resulting residue was purified by silica gel chromatography (20-50% EtOAC/hexanes) to afford nitro alkane title compound as a pale yellow solid (627 mg, 44% yield over 2 steps).

Data for 1-(tert-butoxy)-4-(2-nitroethyl)benzene (42): ¹H NMR (300 MHz, CDCl₃) δ 7.09-7.07 (m, 2H), 7.00-6.91 (m, 2H), 4.58-4.55 (m, 2H), 3.26 (t, J = 7.4 Hz, 2H), 1.33 (s, 9H); ¹³C NMR (75 MHz, CDCl₃) δ 154.4, 130.1, 128.8, 124.3, 78.5, 76.4, 33.0, 29.0; IR (thin film, NaCl) 2975, 2939, 1543, 1506 cm⁻¹; HRMS (ESI, Na) m/z calc’d for C₁₂H₁₇NO₃Na (M + H)⁺ 246.1101, found 246.1101.

Synthesis of tert-butyl (5-nitropentyl)carbamate (44): To a solution of 5-aminopentan-1-ol (7.37 mL, 67.9 mmol) in dioxane (260 mL) and MeOH (180 mL) at 0 °C was added (Boc)₂O (15.75 mL, 67.9 mmol). The reaction was then allowed to warm to room temperature and stir overnight. The following morning the reaction was diluted with water
(300 mL), brine (100 mL) and ether (300 mL) layers separated, and the aqueous layer extracted with ether (2x 300 mL). The combined organics were washed with 0.1 M aqueous HCl dried over MgSO4 and concentrated in vacuo to afford a colorless residue which was carried on without further purification.

The residue was then taken up in benzene (50 mL) and concentrated (2x) to remove residual MeOH. The material was then taken up in CH2Cl2 (400 mL), cooled to 0 °C and CBr4 (28.1 g, 85 mmol) was added in one portion. Upon its dissolution PPh3 (30.3 g, 115 mmol) was added in a portionwise manner over 20 min, until the reaction had a persistent yellow/orange color. Then 700 mL hexanes was added (a milky suspension forms) and the reaction was filtered through a plug of SiO2. The plug was then washed with 400 mL of 2:1 hexanes:CH2Cl2. The filtrate was then concentrated to afford an oil which was carried on without any further purification.

The oil was then taken up in dry DMF (20 mL) and added to a stirring solution of phloroglucinol dihydrate (7.38 g, 58.6 mmol), urea (6.42 g, 107 mmol), and NaNO2 (6.07 g, 88 mmol) in DMF (100 mL) at 0 °C, the solution had a slightly rose tint. The reaction was allowed to warm to room temperature and stir overnight. The reaction was then diluted with 500 mL water and extracted to ether (3x 350 mL) the combined organics were then washed with brine, dried over MgSO4 and concentrated in vacuo. The resulting residue was purified by silica gel chromatography (20-25-30% EtOAc/hexanes) to afford the title compound as a colorless oil which solidified upon standing (46% yield over three steps).

**Data for tert-butyl (5-nitropentyl)carbamate (44):** 1H NMR (400 MHz, CDCl3) δ 4.56 (s (br), 1H), 4.37 (t, J = 6.9 Hz, 2H), 3.20-3.02 (m, 2H), 2.09-1.96 (m, 2H), 1.61-1.34 (m, 13H); 13C NMR (100 MHz, CDCl3) δ 156.2, 79.4, 75.7, 40.2, 29.6, 28.6, 27.2, 23.7; IR (thin film, NaCl) 3372, 2984, 2970, 2949, 2867, 1688, 1565, 1524, 1482, 1467, 1388, 1364, 1263, 1249, 1174, 992, 870, 651 cm⁻¹; HRMS (ESI, Na) m/z calc'd for C10H20N2O4Na (M + Na)⁺ 255.1315, found 255.1317.

![Image](image.png)

**The synthesis of 3-(2-nitroethyl)-1-tosyl-1H-indole (45):** To a solution of (E)-3-(2-nitrovinyl)-1-tosyl-1H-indole (0.750 g, 2.191 mmol) and silica gel (3.42 g, 57.0 mmol) in CHCl3/2-propanol (22 mL, 3/1) was added NaBH₄ (0.166 g, 4.38 mmol) in a portion wise manner. After stirring for 2 hours, the reaction mixture was filtered through celite and filtrate was concentrated in vacuo. The resulting residue was dissolved in EtOAc (150 mL), and washed with water and brine (75 mL each), dried over Na₂SO₄, filtered and concentrated in vacuo. The resulting residue was purified by silica gel chromatography (20-25%
EtOAc/hexanes) to afford the title compound as a pale brown solid (515 mg, 68% yield).

**Data for 3-(2-nitroethyl)-1-tosyl-1H-indole (45):**  
$^{1}$H NMR (300 MHz, CDCl$_3$) δ 7.97 (d, $J$ = 8.2 Hz, 1H), 7.72 (d, $J$ = 8.4 Hz, 2H), 7.48-7.18 (m, 6H), 4.64 (t, $J$ = 7.1 Hz, 2H), 3.30 (t, $J$ = 7.1 Hz, 2H), 2.33 (s, 3H);  
$^{13}$C NMR (75 MHz, CDCl$_3$) δ 144.8, 134.9, 134.7, 129.7, 129.5, 126.6, 125.0, 124.0, 123.3, 118.6, 116.4, 113.8, 74.4, 23.3, 21.8; IR (neat) 2991, 1724, 1553, 1370 cm$^{-1}$; HRMS (ESI, Na) m/z calc’d for C$_{17}$H$_{16}$N$_2$NaO$_4$S (M + Na)$^+$ 367.0723, found 367.733.

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