Supporting Information:

General Methods and Materials. ^{1}H and ^{13}C NMR spectra were recorded at 300 MHz and 75.5 MHz, respectively. The azido acids (**1**, **2**, and **4**) and final crude peptide products (**11a**–**11c**) were analyzed by automated LC/MS as follows. All mass spectra were acquired using a Waters (Micromass) ZMD single quadrupole mass spectrometer equipped with a Z-spray electrospray interface and probe. The LC instrument used was a Waters Alliance 2690 equipped with a 5-carousel, 120 vial position autosampler, and a model 996 PDA (photodiode array) detector. The PDA is scanned from 210 to 400 nm with a 2.4 nm resolution at a scan rate of 1 spectrum/second. The HPLC column used was a Waters, Inc. XTerra MS C18, 2.1 x 50 mm, 5µm. The mobile phases used are 0.1% formic acid in water (A) and 0.1% formic acid in acetonitrile (B). Purity was determined for the peptide products (**11a**–**11c**) by integration of the UV peak for the product as a percent of total area. Samples were run at 0.8 mL per min with a gradient of 10%B to 95% B over 2 min. All azido acid products (**1**, **2**, and **4**) were analyzed by IR and gave a spectral band in the range of 2160–2095 cm^{-1}, consistent with the presence of the azido functionality.

Triflyl anhydride and Cu(II)SO_4 pentahydrate 99.999% were obtained from Aldrich. ε-N-Fmoc-L-lysine (**5**) and L-Glu-OtButylester (**3**) were obtained from Bachem. Fmoc-Phe-Wang-resin (1 mmol/g, 100 mesh) and Fmoc-Val-OSu were obtained from Advanced Chem Tech. Preparation of many common α-azidoacid building blocks was described earlier.[13] The azidoacids (azido-Val, azido-Ile, and azido-Ala) incorporated into the cyclic peptide products were synthesized by the same method.

Synthesis of (4S)-4-azido-5-tert-butoxy-5-oxo pentanoic acid (4). The diazo transfer reactions utilize the method of Wong[14] for carbohydrates with a modified work-up to accommodate the free acid products.[13] Triflyl azide preparation: A solution of sodium azide (2.25 g, 34.7 mmol) was dissolved in deionized H_2O (5.7 mL) with CH_2Cl_2 (9.5 mL) and cooled in an ice bath. Triflyl anhydride (1.18 mL, 7.04 mmol) was added slowly over 5 min while stirring continued for 2 h. The mixture was placed in a separatory funnel and the CH_2Cl_2 phase removed. The aqueous portion was extracted with CH_2Cl_2 (2 × 4.75 mL). The organic fractions, containing the triflyl azide, were combined and washed once with saturated Na_2CO_3 and used without further purification. L-Glu-OtButylester (**3**) (715 mg, 3.52 mmol) was combined with K_2CO_3 (731 mg, 5.3 mmol), Cu(II)SO_4 pentahydrate (8.8 mg, 35.2 µmol), distilled H_2O (11.4 mL) and CH_3OH (22.7 mL). The triflyl azide in CH_2Cl_2 (19 mL) was added and the mixture was stirred at ambient temperature overnight. Subsequently, the organic solvents were removed under reduced pressure and the aqueous slurry was diluted with H_2O (75 mL). This was acidified to pH 2 with 6 N HCl. The product was isolated by CH_2Cl_2 extractions (3 × 50 mL). The organic extracts were combined, washed with H_2O (1×), dried ($MgSO_4$), and evaporated to dryness giving 807 mg of the pale oil (**4**) in 82% yield with no need for further purification. $[\alpha]^{22}_D$ = –60.5 (*c* = 1.0 in CH_3OH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.85 (dd, *J* = 5.2, 8.7 Hz, 1H), 2.49 (t, *J* = 7.6 Hz, 2H) 2.25–2.10 (m, 1H), 2.10–1.95 (m, 1H), 1.49 (s, 9H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 177.8, 168.9, 83.3, 61.4, 29.8, 28.0, 26.1; LC/MS retention time 1.30 min, $[M - H]^-$ 228.

Synthesis of α-azido-γ-9-fluorenylmethylester-L-glutamic acid (1). Compound **4** (370 mg, 1.61 mmol), dimethylaminopyridine (39.3 mg, 0.322 mmol), and 9-fluorenylmethanol (348 mg, 1.78 mmol) were dissolved in CH_2Cl_2 (6.6 mL) and cooled to 0 °C. Next, EDC (340 mg, 1.78 mmol) was added and the reaction was stirred for 1 h at 0 °C and then allowed to warm to room temperature. The crude reaction was concentrated under reduced pressure and treated with 50% TFA in CH_2Cl_2 for 30 min at room temperature. After concentration the reaction mixture was partitioned between EtOAc (75 mL) and brine (75 mL). The organic phase was washed with brine, H_2O (2×), and dried ($MgSO_4$). After concentration, flash chromatography eluting with 5% CH_3OH in CH_2Cl_2 gave 566 mg of a pale oil (**1**) in 65% yield. Lyophilization gave the product as a white solid. mp 56–58°C; R_f 0.30 (5% CH_3OH in CH_2Cl_2); $[\alpha]^{22}_D$ = –27.8 (*c* = 1.0 in CH_3OH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80–7.20 (m, 8H), 4.41 (d, *J* = 6.8 Hz, 2H), 4.18 (t, *J* = 6.8 Hz, 1H), 3.99 (dd, *J* = 5.1, 8.2 Hz, 1H), 2.53 (t, *J* = 7.2 Hz, 2H), 2.30–2.15 (m, 1H), 2.10–1.95 (m, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 175.5, 172.5, 143.6, 141.3, 127.8, 127.1, 124.9, 120.0, 66.6, 61.8, 46.7, 30.0, 26.5; LC/MS retention time 1.76 min, $[M - H]^-$ 350, $[M + H]^+$ 352.

Synthesis of α-azido-ε-N-Fmoc-L-lysine (2). A 15 mL alloquot of triflyl azide (5.58 mmol, 2 equiv.) prepared as described above, was added to ε-N-Fmoc-L-lysine (**5**) (1.03 gm, 2.79 mmol) and Cu(II)SO_4 pentahydrate (7.00 mg, 27.9 µmol) in distilled H_2O (9 mL) and CH_3OH (18 mL). Next, DIPEA (971 µL, 5.58 mmol) was added with stirring and the reaction continued overnight. The organic solvents were removed under vacuum and H_2O (100 mL) was added. The pH was adjusted to 2.5 with 6 N HCl. After extraction with EtOAc (3 × 100mL), the organic fractions were combined, washed with H_2O and dried ($MgSO_4$). Concentration afforded the crude product, **2** as a yellow oil. Flash chromatography eluting with 5% CH_3OH in CH_2Cl_2 gave 638 mg of the white solid (**2**) in 58% yield. mp 76–78°C; R_f 0.30 (5% CH_3OH in CH_2Cl_2); $[\alpha]^{24}_D$ = +7.9 (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, CD_3OD) δ 7.90–7.35 (m, 8H), 4.46 (d, *J* = 6.8 Hz, 2H), 4.32 (t, *J* = 7.0 Hz, 1H), 3.95 (dd, *J* = 4.9, 8.2 Hz, 1H), 3.23 (t, *J* = 6.6 Hz, 2H), 2.10–1.50 (m, 6H); ^{13}C NMR (75.5 MHz, CD_3OD) δ 176.0, 159.4, 145.9, 143.1, 129.3, 128.7, 126.7, 121.5, 68.1, 64.7, 49.0, 42.0, 32.9, 30.9, 24.7;

LC/MS retention time 1.77 min, $[M - H]^-$ 393, $[M + H]^+$ 395.

Peptide Synthesis. The common peptide intermediate (**6**) was synthesized using Wang resin solid phase methodology.[15] Resin bound methodology was carried out on a 25 μmol scale using 3 mL filtration tubes equipped with stopcocks in combination with a Burdick and Jackson multiport vacuum manifold system for resin washing. Each filtration tube was fitted with a cap for horizontal agitation on an orbital shaker during coupling reactions. Fmoc-Phenylalanine on Wang-resin was deprotected with 20% piperidine in DMF for 2 min and 8 min consecutively. The resin was washed with DMF (5×), CH_2Cl_2 (5×), and CH_3OH (3×) and dried by aspiration. Synthesis of the amide bond to produce **6** was carried out by activating α-azido-ε-N-Fmoc-L-lysine (**2**) (39.4 mg, 100 μmol) with 100 μmol each of HOBt (13.5 mg) and DCC (100 μL of a 1M solution in CH_2Cl_2) in 1.0 mL DMF. The condensation reactions was carried out for at least 1h while monitoring with the Kaiser test[16] and repeated if necessary after washing with the above protocol.

Synthesis of azido peptides (7a–7c) utilizing the reduction-hydrolysis-coupling protocol. The resin-bound azido dipeptide intermediate (**6**) (25 μmol) was suspended in a mixture of dioxane (400 μL) and H_2O (100 μL) to promote hydrolysis of the iminophosphorane intermediate to the amine. Trimethylphosphine (1M in toluene) was added (150 μL, 150 μmol, 6.0 equiv.), capped, and shaken for 40 min. This was washed with anhydrous dioxane (5×) to remove excess trimethylphosphine. Azido-Val (14.3 mg, 100 μmol) to be coupled was dissolved in 1.0 mL dioxane with *N*-hydroxysuccinimide (11.5 mg, 100 μmol). While stirring on an ice bath DCC 1M (100 μL, 100 μmol) was added. After 5 min the reaction was removed from the ice bath stirred for an additional 45 min. This was added to the resin bound amine (reduced **6**), with the resulting mixture capped and agitated for at least 2h with some couplings allowed to proceed overnight. The resin bound azido tripeptide was then washed with DMF (5×), CH_2Cl_2 (5×), and CH_3OH (3×) and dried by aspiration. All condensations were monitored with the Kaiser test[16] and recoupled if needed. The reduction and coupling procedure was repeated to add α-azido-γ-9-fluorenylmethylester-L-glutamic acid (**1**) in the fourth position to form **7a**. An azido-Ile (for **7b**) or an azido-Ile followed by azido-Ala (for **7c**), were incorporated between the Val residue in position 3 and the α-azido-γ-9-fluorenylmethylester-L-glutamic acid (**1**).

Synthesis of cyclized peptides (11a–11c). The protected peptide intermediates (**7a–7c**), were deprotected on the side chains of the Lys and Glu residues by two 10 min treatments with 20% piperidine in DMF. The peptides (**8a–8c**) were washed with DMF (5×) and CH_2Cl_2 (5×). Cyclization to **9a–9c** was performed under acid activating conditions[10g] with HOBt (8.5 mg, 2.5 equiv.) and DCC (62.5 μL of a 1M solution in CH_2Cl_2, 2.5 equiv.) in 1.3 mL DMF for 24 h. The amine was monitored with the Kaiser test after washing with DMF (5 ×) and CH_2Cl_2 (5×). Re-treatment with HOBt and DCC was routinely performed until the resin was ninhydrin negative, indicating the formation of **9a–9c** was complete.

After washing with DMF (5×), CH_2Cl_2 (5×), and CH_3OH (3×) the resins were dried under vacuum. The N-terminal azides (**9a–9c**), were suspended in a mixture of dioxane (400 μL) and H_2O (100 μL). Trimethylphosphine (1M in toluene) was added (150 μL, 150 μmol, 6.0 equiv.), capped, and shaken for 40 min, followed by washing with anhydrous dioxane (5×). The resins were then treated with Fmoc-Val-OSu (43.7 mg, 100 μM, 4 equiv.) in 1.5 mL dioxane for 1 h. The resin bound targets (**10a–10c**) were washed with DMF (5×), CH_2Cl_2 (5×), and CH_3OH (3×) and dried under vacuum. Treatment with 2 mL TFA:CH_2Cl_2 (50:50) for 1 h and collection of the cleavage solution followed by washing with the same solution (1×) provided crude **11a–11c** which were concentrated under reduced pressure and analyzed. Analytical data for **11a**. LC/MS retention time 1.60 min, $[M - H]^-$ 824, purity > 90%; **11b**. LC/MS retention time 1.80 min, $[M - H]^-$ 937, $[M + H]^+$ 939, purity > 90%; HRMS *m*/*e* calcd for $C_{51}H_{67}N_7O_{10}$ $(M + H)^+$ 938.4952, found 938.50156; **11c**. LC/MS retention time 1.86 min, $[M - H]^-$ 1008, $[M + H]^+$ 1010, purity > 90%; HRMS *m*/*e* calcd for $C_{54}H_{72}N_8O_{11}$ $(M + H)^+$ 1009.53233, found 1009.53836.