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1. General methods

All reactions were carried out in oven dried glassware under an atmosphere of nitrogen, unless for the oxidative decarboxylation and if stated otherwise. For flash chromatography, distilled technical grade solvents were used. THF, CH$_3$CN, toluene and CH$_2$Cl$_2$ were dried by passage over activated alumina under nitrogen atmosphere (H$_2$O content < 10 ppm, Karl-Fischer titration). All chemicals were purchased from Acros, Aldrich, Fluka, VWR, TCI, Merck or Bachem and used as such unless stated otherwise. All dipeptides starting materials were commercially available and used as received. Chromatographic purification was performed as flash chromatography using Macherey-Nagel silica 40-63, 60 Å, using the solvents indicated as eluent with 0.1-0.5 bar pressure. TLC was performed on Merck silica gel 60 F254 TLC aluminum or glass plates and visualized with UV light and KMnO$_4$ stain. $^1$H-NMR spectra were recorded on a Brucker DPX-400 400 MHz spectrometer in chloroform-d, DMSO-d$_6$ or acetonitrile-d$_3$, all signals are reported in ppm with the internal chloroform signal at 7.26 ppm, the internal DMSO signal at 2.50 ppm or the internal acetonitrile signal at 1.94 ppm as standard. The data is being reported as (s = singlet, d = doublet, t= triplet, q = quadruplet, q$_i$ = quintet, m = multiplet or unresolved, br = broad signal, app = apparent, coupling constant(s) in Hz, integration, interpretation).$^{13}$C-NMR spectra were recorded with $^1$H-decoupling on a Brucker DPX-400 100 MHz spectrometer in chloroform-d, DMSO-d$_6$ or acetonitrile-d$_3$, all signals are reported in ppm with the internal chloroform signal at 77.0 ppm, the internal DMSO signal at 39.5 ppm or the internal acetonitrile signals at 1.32 and 118.26 ppm as standard. Infrared spectra were recorded on a JASCO FT-IR B4100 spectrophotometer with an ATR PRO410-S and a ZnSe prism and are reported as cm$^{-1}$ (w = weak, m = medium, s = strong, br = broad).

High resolution mass spectrometric measurements were performed by the mass spectrometry service of ISIC at the EPFL on a MICROMASS (ESI) Q-TOF Ultima API. MS-MS analyses were performed on a LTQ Orbitrap FTMS instrument (LTQ Orbitrap Elite FTMS, Thermo Scientific, Bremen, Germany) operated in the positive mode coupled with a robotic chip-based nano-ESI source (TriVersa Nanomate, Advion Biosciences, Ithaca, NY, U.S.A.). A standard data acquisition and instrument control system was utilized (Thermo Scientific) whereas the ion source was controlled by Chipsoft 8.3.1 software (Advion BioScience). Samples were loaded onto a 96-well plate (Eppendorf, Hamburg, Germany) within an injection volume of 5µl. The experimental conditions for the ionization voltage was +1.4kV and the gas pressure was set at 0.30 psi. The temperature of ion transfer capillary was 275 °C, tube voltages. FTMS spectra were obtained in the 80-1000 m/z range in the reduce profile mode with a resolution set to 120,000. In all spectra one microscan was acquired with a maximum injection time value of 1000ms. Typical CID experiments were carried out using Normalized collision energy values of 26-28 and 5 Da of isolation width.

Photoredox catalyzed reactions were performed in test tubes (5 and 10 mL), which were held using a rack for test tubes placed at the center of a crystallization flask. On this flask were attached the blue LEDs (RUBAN LED 5MÈTRES - 60LED/M - 3528 BLEU - IP65 with Transformateur pour Ruban LED 24W/2A/12V, bought directly on RubanLED.com). The distance between the LEDs and the test tubes was approximatively 2 cm for the test tubes
and 5 cm for the Schlenk flasks. Long irradiation resulted in temperature increasing up to 37°C during overnight reactions.

Tetramers peptides were synthesized by solid phase peptide synthesis using a Multipep RSi Intavis. Crude products were purified by preparative RP-HPLC on an Agilent 1260 HPLC system with a G2260A 1260 Prep ALS Autosampler, a G1361a 1260 Prep Pump, a G1365C 1260 MWD detector and a G1364B 1260 FC-PS collector, coupled with a Waters XBridge semi-preparative C18 column (19 x 150 mm, 5 µm). Water (solvent A) and water:acetonitrile 5:95 (solvent B), each containing 0.1% TFA, were used as the mobile phase at a flow rate of 20 mL.min⁻¹. The following method was used: 100% A to 100% B in 20 minutes.

RP-HPLC-MS measurements were performed on an Agilent 1290 Infinity HPLC system with a G4226a 1290 Autosampler, a G4220A 1290 Bin Pump and a G4212A 1290 DAD detector, connected to a 6130 Quadrupole LC/MS MS, coupled with a Waters XBridge C18 column (250 x 4.6 mm, 5 µm). Water:acetonitrile 95:5 (solvent A) and water:acetonitrile 5:95 (solvent B), each containing 0.1% formic acid, were used as the mobile phase at a flow rate of 0.6 mL/min⁻¹. The gradient was programmed as follows: 100% A to 100% B in 20 minutes then isocratic for 5 minutes. The column temperature was set up to 25 °C. Low resolution mass spectrometric measurements were acquired using the following parameters: positive electrospray electrospray ionization (ESI), temperature of drying gas = 350 °C, flow rate of drying gas = 12 L. min⁻¹, pressure of nebulizer gas = 60 psi, capillary voltage = 2500 V and fragmentor voltage = 70 V.
2. Preparation of reagents and catalysts

1-Hydroxy-1,2-benziodoxol-3-(1H)-one (10)

Following a reported procedure,[1] NaIO₄ (40.5 g, 189 mmol, 1.05 equiv) and 2-iodobenzoic acid (9) (44.8 g, 180 mmol, 1.0 equiv) were suspended in 30% (v:v) aq. AcOH (350 mL). The mixture was vigorously stirred and refluxed for 5 h. The reaction mixture was then diluted with cold water (250 mL) and allowed to cool to rt, protecting it from light. After 1 h, the crude product was collected by filtration, washed on the filter with ice water (3 x 150 mL) and acetone (3 x 150 mL), and air-dried in the dark overnight to afford 1-Hydroxy-1,2-benziodoxol-3-(1H)-one (10) (44.3 g, 168 mmol, 93%) as a white solid.

1H NMR (400 MHz, DMSO-d₆) δ 8.02 (dd, J = 7.7, 1.4 Hz, 1H, ArH), 7.97 (m, 1H, ArH), 7.85 (dd, J = 8.2, 0.7 Hz, 1H, ArH), 7.71 (td, J = 7.6, 1.2 Hz, 1H, ArH). 13C NMR (100 MHz, DMSO-d₆) δ 167.7, 134.5, 131.5, 131.1, 130.4, 126.3, 120.4. The values of the NMR spectra are in accordance with reported literature data.[1]

1-Acetoxy-1,2-benziodoxol-3-(1H)-one (BI-OAc, 2)

Following a reported procedure,[2] 1-hydroxy-1,2-benziodoxol-3-(1H)-one (10, 10.3 g, 39.1 mmol, 1.00 equiv) was suspended in acetic anhydride (35 mL) and heated to reflux for 30 minutes. The resulting clear, slightly yellow solution was slowly let to warm up to room temperature and then cooled to 0 °C for 30 minutes. The white suspension was filtered and the filtrate was again cooled to 0 °C for 30 minutes. The suspension was once again filtered and the combined two batches of solid product were washed with hexane (2 x 20 mL) and dried in vacuo affording 2 (10.8 g, 35.3 mmol, 90%) as a white solid.

1H NMR (400 MHz, Chloroform-d) δ 8.24 (dd, J = 7.6, 1.6 Hz, ArH), 8.00 (dd, 1H, J = 8.3, 1.0 Hz, ArH), 7.92 (ddd, 1H, J = 8.4, 7.2, 1.6 Hz, ArH), 7.71 (td, 1H, J = 7.3, 1.1 Hz, ArH), 2.25 (s, 3H, COCH₃). 13C NMR (100 MHz, Chloroform-d) δ 176.5, 168.2, 136.2, 133.3, 131.4, 129.4, 129.1, 118.4, 20.4. The values of the NMR spectra are in accordance with reported literature data.[2]

1-Methoxy-1,2-benziodoxol-3(1H)-one (BI-OME, 2b)
Following a reported procedure,[3] BI-OAc (2a, 1.0 g, 3.3 mmol, 1.0 equiv) was refluxed in MeOH (10 mL) for 15 min until a clear, colorless solution was obtained. The mixture was cooled to room temperature and then to -20°C. The precipitate was filtered, washed with a minimal amount of MeOH, and dried under vacuum. BI-OMe 2b (0.69 g, 2.5 mmol, 76%) was obtained as white crystals.

1H NMR (400 MHz, Chloroform-d) δ 8.27 (dd, J = 7.6, 1.6 Hz, 1H, ArH), 7.90 (dd, J = 8.5, 7.2, 1.6 Hz, 1H, ArH), 7.76 (dd, J = 8.3, 1.0 Hz, 1H, ArH), 7.69 (td, J = 7.4, 1.0 Hz, 1H, ArH), 4.27 (s, 3H, OMe). 13C NMR (101 MHz, Chloroform-d) δ 168.1, 135.2, 133.0, 131.1, 130.7, 126.0, 118.6, 62.4. The values of the NMR spectra are in accordance with reported literature data.[3]

Preparation of catalysts

General procedure 1:
Sodium hydride (60% suspension in mineral oil, 8.0 equiv) was added slowly to a stirred solution of substituted-carbazole (5.0 equiv) in dry THF (0.05 M) under a nitrogen atmosphere at RT. After 30 min, 2,4,5,6-tetrafluoroisophthalonitrile (1.0 mmol, 1.0 equiv) was added. After stirring at RT for 15 h, 2 mL water was added to the reaction mixture to quench the excess of NaH. The resulting mixture was then concentrated under reduced pressure. The crude product was purified by recrystallization from hexane/CH2Cl2 then filtered. The brown liquid filtrate was concentrated and recrystallized as before. The combined solids were then purified by column chromatography on silica gel with DCM/Hexane.

General procedure 2:
Sodium hydride (60% suspension in mineral oil, 8.0 equiv) was added slowly to a stirred solution of substituted-diphenylamine (6.0 equiv) in dry DMF (0.1 M) under a nitrogen atmosphere at RT. After 45 min - 1 h, 2,4,5,6-tetrafluoroisophthalonitrile (1.0 equiv) was added. After stirring at RT for 15 h, water and ice were added to the reaction mixture to quench the excess of NaH. The precipitate was filtered and purified by recrystallization from pentane/CH2Cl2 then filtered. The brown liquid filtrate was concentrated and recrystallized as before. The combined solids were then purified by column chromatography on silica gel with DCM/Hexane.

2,4,5,6-Tetra(9H-carbazol-9-yl)isophthalonitrile (4CzIPN, 3a)
Following the general procedure 1 and starting from 9H-carbazole 12 (1.67 g, 10.0 mmol, 5.00 equiv), sodium hydride (0.60 g, 15 mmol, 7.5 equiv) and 2,4,5,6-tetrafluoroisophthalonitrile 13 (0.40 g, 2.0 mmol) in 40 mL of THF. Recrystallization (Hexanes/CH₂Cl₂ (1:1, 90 mL)) afforded the crude product as a yellow powder. Column chromatography afforded 2,4,5,6-tetra(9H-carbazol-9-yl)isophthalonitrile (3a) as a bright yellow crystalline solid (1.14 g, 1.45 mmol, 73% yield).

Rf (Hexane/DCM 1/1) = 0.29. (yellow spot on TLC). ¹H NMR (400 MHz, Chloroform-d) δ 8.2 (d, J = 7.7 Hz, 2H, ArH), 7.8 – 7.6 (m, 8H, ArH), 7.5 (ddd, J = 8.0, 6.6, 1.6 Hz, 2H, ArH), 7.3 (d, J = 7.5 Hz, 2H, ArH), 7.2 (ddd, J = 8.4, 1.5 Hz, 4H, ArH), 7.2 – 7.0 (m, 8H, ArH), 6.8 (t, J = 7.8 Hz, 4H, ArH), 6.6 (td, J = 7.6, 1.2 Hz, 2H, ArH). ¹³C NMR (101 MHz, Chloroform-d) δ 145.2, 144.6, 140.0, 138.2, 136.9, 134.7, 127.0, 125.8, 124.9, 124.7, 124.5, 123.8, 122.4, 121.9, 121.4, 121.0, 120.4, 119.6, 116.3, 111.6, 109.9, 109.5, 109.4. The values of the NMR spectra are in accordance with reported literature data. [4]

2,4,5,6-Tetrakis(diphenylamino)isophthalonitrile (4DPAIPN, 3b)

Following the general procedure 2 and starting from diphenylamine 14 (1.01 g, 6.00 mmol, 6.0 equiv), sodium hydride (320 mg, 8.00 mmol, 8.0 equiv) and 2,4,5,6-tetrafluoroisophthalonitrile 13 (200 mg, 1.00 mmol) in 10 mL of DMF. The deprotonation was performed at 50°C for 1 h, followed by stirring at the same temperature for 4 h. Recrystallization (CH₂Cl₂/pentane (1:2)) gave 2,4,5,6-tetrakis(diphenylamino)isophthalonitrile (3b) as a yellow-orange crystalline solid (400 mg, 0.502 mmol, 50 % yield).

Rf (pentane/DCM 1:1): 0.3. (yellow spot on TLC). ¹H NMR (400 MHz, Chloroform-d) δ 7.32 – 7.22 (m, 4H, ArH), 7.12 – 7.05 (m, 12H, ArH), 7.07 – 6.98 (m, 2H, ArH), 6.96 – 6.84 (m, 8H, ArH), 6.73 – 6.63 (m, 10H, ArH), 6.56 (d, J = 7.4 Hz, 4H, ArH). ¹³C NMR (101 MHz, Chloroform-d) δ 154.2, 151.7, 145.5, 144.6, 143.1, 140.3, 129.4, 128.6, 127.5, 124.2, 123.9, 122.9, 122.6, 122.6, 121.1, 113.1, 113.0. IR (νmax, cm⁻¹) 3065 (w), 3040 (w), 2361 (w), 1586 (m), 1535 (m), 1497 (s), 1415 (s), 1275 (m), 1244 (m), 1028 (w), 907 (m), 742 (s), 698 (s). HRMS (ESI/QTOF) m/z: [M + H]+ Calcd for C₅₆H₄₁N₆⁺ 797.3387; Found 797.3375. The values of the NMR spectra are in accordance with reported literature data. [5]
3. Peptide synthesis

The used dipeptides were commercially available. All peptide tetramers were synthesized by solid phase peptide synthesis using a 2-chlorotrityl chloride resin (1.0-1.6 mmol/g, 100-200 mesh). The first amino acid was loaded on the resin by incubation of the Fmoc-protected monomer (3 equiv of the number of active sites on the resin), DIPEA (4 equiv) in dichloromethane for 2 h. A cycle consisted first of the deprotection, achieved by stirring for 20 min with a 20% solution of piperidine in DMF, twice. Then the resin was washed with DMF (7x). Double couplings were performed by adding the Fmoc-protected monomer (4 equiv), HBTU (4 equiv), HOBt (4 equiv), NMM (4 equiv) and stirring for 45 min. Capping was carried out at the end of each cycle, followed by a DMF wash (7x). Acetylation of the N-terminal was achieved by incubating the resin with an Acetic Anhydride/DIPEA/DMF 10/15/75 solution for 30 min, twice. Cleavage of peptides with no protecting groups on the side-chains was performed by stirring the resin in a 20% solution of HFIP in dichloromethane for 30 min. In the presence of protecting groups, a TFA/water/triisopropylsilane 95/2.5/2.5 was used instead and the stirring time increased to 2 h. The cleavage mixture was poured into cold diethyl ether and precipitated peptides were recovered. The crude peptides were purified by preparative RP-HPLC using a gradient water-95% acetonitrile in 20 min. Pure peptides were analyzed by RP-HPLC and HRMS.
4. Optimization

4.1. Optimization of the oxidative decarboxylation

Degassed solvent was added in a 10 mL test tube containing a teflon coated stirring bar, Z-Gly-Pro (1a) (31 mg, 0.10 mmol, 1.0 equiv), R-BX (2) (0.15 mmol, 1.5 equiv), the base and the catalyst under a nitrogen atmosphere. The reaction mixture was irradiated using blue light LEDs at RT.

Procedure for HPLC yields:
The reaction was monitored by dilution of 50 μL of the crude with 950 μL of acetonitrile. The yield was estimated by the absorbance of product in comparison to the overall absorbance of product, unreacted starting material and side-products if any.

Procedure for isolated yields:
The crude mixture was diluted with 10 mL of sat. NaHCO₃ and extracted with diethyl ether (3 x 50 mL). The combined organic layers were washed with brine (3 x 20 mL), dried over MgSO₄, filtered and concentrated under vacuum. The crude product was purified by preparative TLC (DCM/ethyl acetate 7:3).

Table S1. Optimization of the oxidative decarboxylation on dipeptides

| Entry | Solvent | Concentration (mM) | Catalyst | Base (equiv) | Alcohol (equiv) | HPLC yield (%) |[a] |
|-------|---------|--------------------|----------|-------------|----------------|----------------|----|
| 1     | DMF     | 10                 | 4CzIPN (3a) | K₂HPO₄ (2)  | MeOH (50)      | 46             |    |
| 2     | DMF     | 10                 | Ru(bpyp)Cl₂·6H₂O | K₂HPO₄ (2)   | MeOH (50)      | 59             |    |
| 3     | DMF     | 10                 | Ru(bpyp)Cl₂·6H₂O | K₂HPO₄ (2)   | MeOH (10)      | 78             |    |
| 4     | DMF     | 50                 | Ru(bpyp)Cl₂·6H₂O | K₂HPO₄ (2)   | MeOH (10)      | 82             |    |
| 5     | DMF     | 50                 | Ru(bpyp)Cl₂·6H₂O | K₂HPO₄ (2)   | MeOH (5)       | >95            |    |
| 6     | DMF     | 50                 | Ru(bpyp)Cl₂·6H₂O | K₂HPO₄ (2)   | MeOH (2)       | >95            |    |
| 7     | DMF     | 50                 | Eosin Y    | K₂HPO₄ (2)   | MeOH (5)       | 17             |    |
| 8[b]  | DMF     | 50                 | Rhodamine B | K₂HPO₄ (2)   | MeOH (5)       | 27             |    |
| 9[b]  | DMF     | 50                 | Rose Bengal | K₂HPO₄ (2)   | MeOH (5)       | 35             |    |
| 10[b] | DMF     | 50                 | 4DPAIPN (3b) | K₂HPO₄ (2)   | MeOH (5)       | 45             |    |
| 11    | MeCN    | 50                 | Ru(bpyp)Cl₂·6H₂O | K₂HPO₄ (2)   | MeOH (5)       | >95            |    |
| 12    | MeCN    | 50                 | Ru(bpyp)Cl₂·6H₂O | -            | MeOH (5)       | >95 (68)[c]    |    |
| 13    | DCE     | 50                 | Ru(bpyp)Cl₂·6H₂O | -            | MeOH (5)       | >95            |    |

[a] Ratio of integration at 214 nm by RP-HPLC. [b] green LEDs. [c] isolated yield.
Control experiments were carried out and only traces of the desired product were observed in the absence of light or catalyst.

4.2. Robustness experiments

Degassed MeCN (2 mL) was added in a 5 mL test tube containing Cbz-Gly-Pro (1a) (31 mg, 0.10 mmol, 1.0 equiv), the protected amino acid (0.1 mmol, 1 equiv), BI-OMe (2b) (42 mg, 0.45 mmol, 1.5 equiv) and Ru(bpy)₃Cl₂·6H₂O (2.3 mg, 3.00 μmol, 3 mol%) under a nitrogen atmosphere. The reaction mixture was irradiated using blue light LEDs for 15 h at RT.

The reaction was monitored by dilution of 50 μL of the crude with 950 μL of acetonitrile. The yield was estimated by the absorbance of product in comparison to the overall absorbance of product, unreacted starting material and side-products if any.

Table S2. Robustness experiments

| Entry | Amino acid (1 equiv) | HPLC yield (%) |
|-------|----------------------|----------------|
| 1     | Cbz-Met-OMe          | 15             |
| 2     | Cbz-Ser-OMe          | 90⁺           |
| 3     | Cbz-His-OMe          | 25             |
| 4     | Cbz-Arg-OMe          | >95            |
| 5     | Cbz-Tyr-OMe          | <5             |
| 6     | Cbz-Trp-OMe          | <5             |
| 7     | Cbz-Gln-OMe          | 36             |
| 8     | Cbz-Lys-OMe          | <5             |
| 9     | Cbz-Asp-OMe          | >95            |
| 10    | Cbz-Cys-OMe          | 62             |

⁺ + 10% of Serine addition on Z-Gly-Pro (x).
5. Scope on dipeptides

General procedure 1 for the oxidative decarboxylation of dipeptides

Degassed MeCN (6 mL) was added in a 10 mL test tube containing the corresponding dipeptide (0.30 mmol, 1.0 equiv), BI-OMe (2b) (125 mg, 0.450 mmol, 1.50 equiv) and Ru(bpy)_3Cl_2·6H_2O (6.8 mg, 9.0 μmol, 3 mol%) under a nitrogen atmosphere. The reaction mixture was irradiated using blue light LEDs for 15 h at RT.

A solution obtained by dilution of 50 μL of the crude with 950 μL of acetonitrile was injected into the HPLC to monitor the conversion of the starting material.

The crude mixture was diluted with 10 mL of sat. NaHCO_3 and extracted with diethyl ether (3 x 30 mL). The combined organic layers were washed with brine (10 mL), dried over MgSO_4, filtered and concentrated under vacuum. The crude product was purified by column chromatography DCM to DCM/ethyl acetate on triethylamine deactivated silica (5 vol% in DCM).

General procedure 2 for the oxidative decarboxylation of dipeptides

Degassed MeCN (6 mL) was added in a 10 mL test tube containing the corresponding dipeptide (0.30 mmol, 1.0 equiv), BI-OAc (2a) (138 mg, 0.450 mmol, 1.50 equiv), the alcohol (0.60 mmol, 2.0 equiv) and Ru(bpy)_3Cl_2·6H_2O (6.8 mg, 9.0 μmol, 3 mol%) under a nitrogen atmosphere. The reaction mixture was irradiated using blue light LEDs for 15 h at RT.

A solution obtained by dilution of 50 μL of the crude with 950 μL of acetonitrile was injected into the HPLC to monitor the conversion of the starting material.

The crude mixture was diluted with 10 mL of sat. NaHCO_3 and extracted with diethyl ether (3 x 30 mL). The combined organic layers were washed with brine (10 mL), dried over MgSO_4, filtered and concentrated under vacuum. The crude product was purified by column chromatography DCM to DCM/ethyl acetate on triethylamine deactivated silica (5 vol% in DCM).

General procedure 3 for the decarboxylative arylation of dipeptides

Degassed DCE (6 mL) was added in a 10 mL test tube containing the corresponding dipeptide (0.30 mmol, 1.0 equiv), BI-OAc (2a) (138 mg, 0.450 mmol, 1.50 equiv) and Ru(bpy)_3Cl_2·6H_2O (6.8 mg, 9.0 μmol, 3 mol%) under a nitrogen atmosphere. The reaction mixture was irradiated using blue light LEDs for 15 h at RT.

A solution obtained by dilution of 50 μL of the crude with 950 μL of acetonitrile was injected into the HPLC to monitor the conversion of the starting material.

The phenol (0.45 mmol, 1.5 equiv) was added and the reaction mixture degassed by Ar bubbling before cooling at 0 °C. BF_3·OEt_2 (158 μL, 0.600 mmol, 2.00 equiv) was added dropwise and the mixture stirred for 2 h at 0 °C.
The crude mixture was diluted with 10 mL of sat. NaHCO₃ and extracted with diethyl ether (3 x 30 mL). The combined organic layers were washed with brine (10 mL), dried over MgSO₄, filtered and concentrated under vacuum. The crude product was purified by column chromatography DCM to DCM/ethyl acetate on triethylamine deactivated silica (5 vol% in DCM).

**General procedure 4 for the decarboxylative arylation of dipeptides**

Degassed MeCN (6 mL) was added in a 10 mL test tube containing the corresponding dipeptide (0.30 mmol, 1.0 equiv), Bi-OAc (2a) (138 mg, 0.450 mmol, 1.50 equiv) and Ru(bpy)₃Cl₂·6H₂O (6.8 mg, 9.0 μmol, 3 mol%) under a nitrogen atmosphere. The reaction mixture was irradiated using blue light LEDs for 15 h at RT.

A solution obtained by dilution of 50 μL of the crude with 950 μL of acetonitrile was injected into the HPLC to monitor the conversion of the starting material.

The mixture was diluted with 10 mL of sat. NaHCO₃ and extracted with diethyl ether (3 x 30 mL). The combined organic layers were washed with brine (10 mL), dried over MgSO₄, filtered and concentrated under vacuum. The crude product was purified by column chromatography DCM to DCM/ethyl acetate on triethylamine deactivated silica (5 vol% in DCM).

**Benzyl (2-(2-methoxypyrrolidin-1-yl)-2-oxoethyl)carbamate (4a)**

Following General Procedure 1 and starting with Cbz-Gly-Pro (1a) (92 mg, 0.30 mmol, 1.0 equiv), 4a was obtained after column chromatography DCM to DCM/ethyl acetate 8:2 as a pale yellow oil (66 mg, 0.23 mmol, 75%).

Rf (DCM/ethyl acetate 7:3): 0.3. ¹H NMR (400 MHz, Chloroform-d, 1:1 mixture of rotamers (R¹/R²)) δ 7.40-7.26 (m, 5H, ArH (R¹+R²)), 5.70 (s, 1H, NH (R¹+R²)), 5.43 (d, J = 4.9 Hz, 0.5H, NCHCOMe (R¹)), 5.12 (s, 2H, OCH₂Ph (R¹+R²)), 4.96 (d, J = 4.5 Hz, 0.5H, NCHCOMe (R²)), 4.18-4.05 (m, 1H, NC(O)CH₂NH(Cbz (R¹))), 4.05-3.91 (m, 1H, NC(O)CH₂NH(Cbz (R²))), 3.67 (ddd, J = 11.3, 8.4, 2.3 Hz, 0.5H, C(O)NCH₂ (R¹)), 3.58-3.48 (m, 0.5H, C(O)NCH₂ (R²)), 3.38 (s, 1.5H, OCH₃ (R¹)), 3.43-3.32 (m, 1H, C(O)NCH₂ (R¹+R²)), 3.31 (s, 1.5H, OCH₃ (R²)), 2.24-1.66 (m, 4H, NCH₂CH₂CH₂CH₂ (R¹+R²)). ¹³C NMR (101 MHz, Chloroform-d, mixture of rotamers, signals not fully resolved) δ 168.3, 168.2, 156.2, 156.2, 136.4, 136.3, 128.4, 128.0, 127.9, 88.2, 87.5, 66.8, 66.8, 56.6, 54.2, 45.8, 44.8, 43.4, 42.9, 31.2, 30.7, 22.7, 20.7. IR (νmax, cm⁻¹) 3324 (m), 2980 (m), 2886 (m), 2339 (w), 1718 (s), 1655 (s), 1520 (m), 1451 (m), 1246 (s), 1170 (m), 1055 (s), 914 (m), 826 (w), 741 (m), 699 (m). HRMS (ESI/QTOF) m/z: [M + Na]⁺ Calcd for C₁₅H₂₀N₂NaO₄⁺ 315.1315; Found 315.1315.

**Benzyl (2-(2-(allyloxy)pyrrolidin-1-yl)-2-oxoethyl)carbamate (4b)**
Following General Procedure 2 and starting with Cbz-Gly-Pro (1a) (92 mg, 0.30 mmol, 1.0 equiv) and allyl alcohol (41 µL, 0.60 mmol, 2.0 equiv), 4b was obtained after column chromatography DCM to DCM/ethyl acetate 9:1 as a pale yellow oil (73 mg, 0.23 mmol, 76%).

Rf (DCM/ethyl acetate 7:3): 0.35. 1H NMR (400 MHz, Chloroform-d, 6:4 mixture of rotamers (major/minor) δ 7.42-7.27 (m, 5H, ArH (major+minor)), 5.97-5.81 (m, 1H, CH₂CH=CH₂ (major+minor)), 5.72 (br s, 1H, NH (major+minor)), 5.56 (d, J = 4.9 Hz, 0.6H, C(O)NCH (major)), 5.37-5.20 (m, 1.2H, CH₂CH=CH₂ (major)), 5.17-5.06 (m, 3.2H, CH₂CH=CH₂ (minor), OCH₂Ph (major+minor) and C(O)NCH (minor)), 4.22-3.86 (m, 4H, CH₂CH=CH₂ and C(O)CH₂NHCCbz (major+minor)), 3.68 (ddd, J = 11.3, 8.6, 2.0 Hz, 0.4H, C(O)NCH₂ (minor)), 3.57-3.48 (m, 0.6H, C(O)NCH₂ (major)), 3.44-3.25 (m, 1H, C(O)NCH₂ (major+minor)), 2.30-1.64 (m, 4H, NCH₂CH₂CH₂CH₂ (major+minor)). 13C NMR (101 MHz, Chloroform-d, mixture of rotamers, signals not fully resolved) δ 168.2, 168.1, 156.2, 156.2, 156.4, 156.4, 156.3, 156.3, 134.7, 133.5, 128.4, 128.0, 127.9, 117.9, 116.6, 86.8, 86.1, 70.2, 68.0, 66.9, 66.8, 45.9, 44.9, 43.4, 43.1, 31.7, 31.5, 22.8, 20.7. IR (νmax, cm⁻¹) 3331 (m), 2982 (m), 2898 (m), 1720 (s), 1657 (s), 1538 (m), 1451 (m), 1247 (s), 1171 (m), 1052 (s), 915 (m), 740 (m). HRMS (ESI/QTOF) m/z: [M + Na]+ Calcd for C₁₇H₂₃N₂NaO₄ + 341.1472; Found 341.1476.

Benzyl (2-oxo-2-(2-prop-2-yn-1-yl)pyrrolidin-1-yl)carbamate (4c)

Following General Procedure 2 and starting with Cbz-Gly-Pro (1a) (92 mg, 0.30 mmol, 1.0 equiv) and propargyl alcohol (36 µL, 0.60 mmol, 2.0 equiv), 4c was obtained after column chromatography DCM to DCM/ethyl acetate 10:1 as a pale yellow oil (61 mg, 0.19 mmol, 64%).

Rf (DCM/ethyl acetate 7:3): 0.33. 1H NMR (400 MHz, Chloroform-d, 6:4 mixture of rotamers (major/minor) δ 7.39-7.28 (m, 5H, ArH (major+minor)), 5.69 (br s, 1H, NH (major+minor)), 5.66 (d, J = 4.9 Hz, 0.6H, C(O)NCH (major)), 5.31 (d, J = 4.1 Hz, 0.4H, C(O)NCHO (minor)), 5.12 (s, 2H, OCH₂Ph (major+minor)), 4.30 (qd, J = 15.7, 2.4 Hz, 1.2H, OCH₂CCH (major)), 4.23-4.07 (m, 1.4H, OCH₂CCH (minor) and C(O)CH₂NHCbz (major+minor)), 4.05-3.90 (m, 1.4H, C(O)CH₂NHCbz (major+minor)), 3.71-3.63 (m, 0.4H, C(O)NCH₂ (minor)), 3.53 (t, J = 8.8 Hz, 0.6H, C(O)NCH₂ (major)), 3.36 (dq, J = 27.4, 9.7, 8.7 Hz, 1H, C(O)NCH₂ (major+minor)), 2.58 (m, 0.4H, OCH₂CCH (minor)), 2.42 (t, J = 2.36 Hz, 0.6H, OCH₂CCH (major)), 2.30-1.70 (m, 4H, NCH₂CH₂CCH₂ (major+minor)). 13C NMR (101 MHz, Chloroform-d, mixture of rotamers, signals not fully resolved) δ 168.7, 168.3, 156.4, 136.6, 136.5, 128.6, 128.2, 128.1, 86.3, 86.1, 80.3, 78.7, 75.9, 73.9, 67.1, 57.1, 54.5, 46.1, 45.1, 43.6, 43.5, 32.0, 31.5, 22.9, 20.8. IR (νmax, cm⁻¹) 3416 (w), 3299 (m), 2973 (w), 2889 (w), 2116 (w), 1720 (s), 1662 (s), 1524 (m), 1430 (s), 1254 (s), 1172 (m), 1058 (s), 911 (m), 737 (s), 700 (m). HRMS (ESI/QTOF) m/z: [M + Na]+ Calcd for C₁₇H₂₃N₂NaO₄: 339.1315; Found 339.1315.

Benzyl (2-(2-(benzyloxy)pyrrolidin-1-yl)-2-oxoethyl)carbamate (4d)
Following General Procedure 2 and starting with Cbz-Gly-Pro (1a) (92 mg, 0.30 mmol, 1.0 equiv) and benzyl alcohol (65 µL, 0.60 mmol, 2.0 equiv), 4d was obtained after column chromatography DCM to DCM/ethyl acetate 20:1 as a pale yellow oil (108 mg, 0.293 mmol, 98%).

Rf (DCM/ethyl acetate 7:3): 0.41. 1H NMR (400 MHz, Chloroform-d, 6:4 mixture of rotamers (major/minor)) δ 7.40-7.27 (m, 10H, ArH (major+minor)), 5.74-5.63 (m, 1.6H, NH (major+minor) and C(O)NCH (major)), 5.20 (d, J = 4.1 Hz, 0.4H, C(O)NCH (minor)), 5.13 (d, J = 2.5 Hz, 2H, C(O)OCH2Ph (major+minor)), 4.70 (br s, 0.6H, NCHOCH2Ph (major)), 4.67 (d, J = 3.0 Hz, 0.6H, NCHOCH2Ph (major)), 4.56-4.46 (m, 0.8H, NCHOCH2Ph (minor)), 4.09 (qd, J = 17.0, 4.6 Hz, 0.8H, C(O)CH2NHCbz (minor)), 3.91 (m, 1.2H, C(O)CH2NHCbz (major)), 3.74-3.65 (m, 0.4H, C(O)NCH2 (minor)), 3.49 (t, J = 8.9 Hz, 0.6H, C(O)NCH2 (major)), 3.41 (td, J = 11.2, 10.5, 7.0 Hz, 0.4H, C(O)NCH2 (minor)), 3.31 (q, J = 9.6 Hz, 0.6H, C(O)NCH2 (major)), 2.34-1.67 (m, 4H, NCH2CH2CH2CH (major+minor)). 13C NMR (101 MHz, Chloroform-d, mixture of rotamers, signals not fully resolved) δ 168.4, 168.3, 156.4, 156.3, 149.3, 141.0, 138.7, 137.0, 136.6, 136.5, 128.8, 128.7, 128.6, 128.4, 128.3, 128.2, 128.1, 128.0, 127.8, 127.6, 127.1, 87.2, 86.5, 71.3, 69.5, 67.1, 67.0, 65.5, 46.1, 45.0, 43.6, 43.3, 32.0, 31.7, 23.0, 21.0. IR (νmax, cm⁻¹) 3418 (w), 3329 (w), 2979 (w), 2881 (w), 1721 (s), 1659 (s), 1524 (m), 1452 (m), 1347 (w), 1253 (m), 1172 (m), 1107 (m), 1054 (s), 914 (m), 740 (s). HRMS (ESI/QTOF) m/z: [M + Na]+ Calcd for C24H24N4NaO4 391.1628; Found 391.1633.

Benzyi (2-(2-(2-cyanoethoxy)pyrrolidin-1-yl)-2-oxoethyl)carbamate (4e)

Following General Procedure 2 and starting with Cbz-Gly-Pro (1a) (92 mg, 0.30 mmol, 1.0 equiv) and 3-hydroxypropionitrile (41 µL, 0.60 mmol, 2.0 equiv), 4e was obtained after column chromatography DCM to DCM/ethyl acetate 10:1 as a pale yellow oil (47 mg, 0.14 mmol, 47%).

Rf (DCM/ethyl acetate 7:3): 0.24. 1H NMR (400 MHz, Chloroform-d, 8:2 mixture of rotamers (major/minor)) δ 7.39-7.28 (m, 5H, ArH (major+minor)), 5.63 (br s, 1H (major+minor)), 5.55 (d, J = 4.9 Hz, 0.8H, C(O)NCH (major)), 5.12 (m, 2.2H, OCH2Ph (major+minor) and C(O)NCH (minor)), 4.10 (qd, J = 16.9, 4.8 Hz, 0.4H, C(O)CH2NHCbz (minor)), 4.01-3.91 (m, 1.6H, C(O)CH2NHCbz (major)), 3.83 (tq, J = 7.4, 4.0 Hz, 1.6H, OCH=CH:CN (major)), 3.69 (dq, J = 12.9, 5.3, 3.9 Hz, 0.4H, OCH=CH:CN (minor)), 3.65-3.61 (m, 0.2H, C(O)NCH2 (minor)), 3.56 (t, J = 9.0 Hz, 0.8H, C(O)NCH2 (major)), 3.45-3.38 (m, 0.2H, C(O)NCH2 (minor)), 3.34 (q, J = 9.8 Hz, 0.8H, C(O)NCH2 (major)), 2.63 (t, J = 6.4 Hz, 0.4H, OCH=CH:CN (minor)), 2.55 (m, 1.6H, OCH=CH:CN (major)), 2.31-1.68 (m, 4H, NCH2CH2CH2CHO (major+minor)). 13C NMR (101 MHz, Chloroform-d, mixture of rotamers, signals not fully resolved) δ 169.0, 168.3, 156.5, 156.4, 136.5, 128.7, 128.3, 128.2, 118.1, 117.5, 87.5, 86.7, 67.1, 63.9, 61.5, 46.1, 45.9, 45.3, 43.6, 43.2, 32.0, 31.7, 23.0, 20.9, 19.3, 19.2. IR (νmax, cm⁻¹) 3407 (w), 3329 (w), 2959 (w),
2887 (w), 2251 (w), 1720 (s), 1660 (s), 1525 (m), 1429 (s), 1336 (m), 1254 (s), 1172 (m), 1085 (s), 1060 (s), 914 (m), 739 (s). HRMS (ESI/QTOF) m/z: [M + Na]+ Calcd for C₁₇H₂₁N₃NaO₇ 354.1424; Found 354.1422.

Benzyl (2-(2-(3-chloropropoxy)pyrrolidin-1-yl)-2-oxoethyl)carbamate (4f)

Following General Procedure 2 and starting with Cbz-Gly-Pro (1a) (92 mg, 0.30 mmol, 1.0 equiv) and 3-chloropropan-1-ol (25 μL, 0.60 mmol, 2.0 equiv), 4f was obtained after column chromatography DCM to DCM/ethyl acetate 10:1 as a pale yellow oil (74 mg, 0.21 mmol, 70%).

Rf (DCM/ethyl acetate 7:3): 0.29. ¹H NMR (400 MHz, Chloroform-d, 6:4 mixture of rotamers (major/minor) δ 7.38-7.28 (m, 5H, ArH (major-minor)), 5.75-5.63 (m, 1H, NH (major-minor)), 5.51 (d, J = 4.86 Hz, 0.6H, C(O)NCH₃ (major)), 5.12 (s, 2H, OCH₂Ph (major-minor)), 5.07 (d, J = 4.2 Hz, 0.4H C(O)NCH₃ (minor)), 4.18-4.01 (m, 1H, C(O)CH₂NHCbz (major-minor)), 3.96 (dt, J = 17.4, 4.5 Hz, 1H, C(O)CH₂NHCbz (major-minor)), 3.72-3.49 (m, 5H, OCH₂CH₂CH=Cl, OCH=CH₂CH=Cl and C(O)NCH₂, (major+minor)), 3.34 (dq, J = 26.5, 9.7, 8.6 Hz, 1H, C(O)NCH₂ (major-minor)), 2.33-1.55 (m, 6H, NCH₂CH₂CH₂CH and OCH=CH₂CH=Cl (major-minor)). ¹³CNMR (101 MHz, Chloroform-d, mixture of rotamers, signals not fully resolved) δ 168.4, 168.3, 156.4, 136.5, 128.6, 128.2, 128.1, 87.2, 86.5, 67.0, 65.2, 62.9, 46.1, 45.1, 43.6, 43.2, 42.0, 41.7, 32.7, 32.3, 31.7, 31.6, 23.0, 21.0. IR (νmax, cm⁻¹) 3415 (w), 3319 (w), 2959 (m), 2882 (w), 1720 (s), 1660 (s), 1525 (m), 1430 (s), 1246 (m), 1171 (m), 1059 (s), 996 (m), 911 (m), 738 (s), 701 (m). HRMS (ESI/QTOF) m/z: [M + Na]+ Calcd for C₁₇H₂₃ClN₂NaO₇ 377.1239; Found 377.1232.

Benzyl (2-(2-(3-azidopropoxy)pyrrolidin-1-yl)-2-oxoethyl)carbamate (4g)

Following General Procedure 2 and starting with Cbz-Gly-Pro (1a) (92 mg, 0.30 mmol, 1.0 equiv) and 3-azidopropan-1-ol (600 μL, 1M in DCM, 0.60 mmol, 2.0 equiv), 4g was obtained after column chromatography DCM to DCM/ethyl acetate 10:1 as a pale yellow oil (99 mg, 0.27 mmol, 91%).

Rf (DCM/ethyl acetate 7:3): 0.38. ¹H NMR (400 MHz, Chloroform-d, 6:4 mixture of rotamers (major/minor) δ 7.38-7.28 (m, 5H, ArH (major-minor)), 5.75-5.63 (m, 1H, NH (major-minor)), 5.50 (d, J = 4.9 Hz, 0.6H, C(O)NCH₃ (major)), 5.12 (s, 2H, OCH₂Ph (major-minor)), 5.05 (d, J = 4.2 Hz, 0.4H C(O)NCH₃ (minor)), 4.16-4.01 (m, 0.8H, C(O)CH₂NHCbz (minor)), 4.01-3.91 (m, 1.2H, C(O)CH₂NHCbz (major)), 3.76 (t, J = 4.7 Hz, 0.8H, OCH=CH₂CH=N₃ (minor)), 3.65 (qd, J = 6.1, 5.1, 1.8 Hz, 1.2H, OCH=CH₂CH=N₃ (major)), 3.56-3.26 (m, 4H, OCH₂CH₂CH=N₃ and (CO)NCH₂ (major-minor)), 2.24-1.66 (m, 6H, NCH₂CH₂CH=CHO and OCH=CH₂CH=CH=N₃ (major-minor)). ¹³C NMR (101 MHz, Chloroform-d, mixture of rotamers, signals not fully resolved) δ 168.4, 168.2, 156.4, 136.5, 128.6, 128.2, 128.1, 87.3, 86.6, 67.0, 65.7, 63.4, 60.1,
IR (νmax, cm⁻¹) 3418 (w), 3318 (w), 2952 (m), 2881 (m), 2097 (s), 1721 (s), 1661 (s), 1523 (m), 1452 (s), 1256 (s), 1172 (m), 1056 (s), 912 (m), 739 (s). HRMS (ESI/QTOF) m/z: [M + Na]+ Calcd for C₁₇H₂₃N₅NaO₄⁺ 384.1642; Found 384.1646.

Benzyl (2-((1R,2S,5R)-2-isopropyl-5-methylcyclohexyl)oxy)pyrrolidin-1-yl)-2-oxoethyl)carbamate (4h)

Following General Procedure 2 and starting with Cbz-Gly-Pro (1a) (92 mg, 0.30 mmol, 1.0 equiv) and (1R,2S,5R)-(-)-menthol (94 mg, 0.60 mmol, 2.0 equiv), 4h was obtained after column chromatography DCM to DCM/ethyl acetate 15:1 as a pale yellow oil as an unresolved mixture of diastereoisomers (44 mg, 0.11 mmol, 35%).

Rf (DCM/ethyl acetate 7:3): 0.63. ¹H NMR (400 MHz, Chloroform-d, unresolved mixture of diastereoisomers and rotamers) δ 7.39-7.28 (m, 5H, ArH), 5.79-5.71 (m, 0.7H, NH and C(O)NC₅H₄), 5.66 (br s, 0.4H, NHH and C(O)NC₅H₄), 5.58 (m, 0.5H, NH and C(O)NC₅H₄), 5.26 (d, J = 4.16 Hz, 0.4H, C(O)NC₅H₄), 5.19-5.07 (m, 2H, OC₅H₅Ph), 4.22-3.82 (m, 2H, C(O)C₅H₅NHCbz), 3.69 (t, J = 9.3 Hz, 0.3H, C(O)NC₅H₄), 3.54 (t, J = 9.3 Hz, C(O)NC₅H₄), 5.31-3.19 (m, 2H, C(O)NC₅H₄ and NCHOCH₅), 3.12 (tt, J = 11.5, 5.7 Hz, 0.3H, C(O)NC₅H₄), 2.32-1.83 (m, 6H, NCH₂CH₂CH₂CH and Hmenthol), 1.79-1.61 (m, 4H, NCH₂CH₂CH₂CH and Hmenthol), 1.43-1.07 (m, 3H, Hmenthol), 1.06-0.61 (m, 13H, Hmenthol). ¹³C NMR (101 MHz, Chloroform-d, mixture of diastereoisomers and rotamers, signals not fully resolved) δ 168.3, 168.0, 167.7, 156.5, 156.4, 156.3, 136.6, 136.5, 128.6, 128.2, 128.1, 128.0, 85.7, 83.2, 82.8, 77.8, 75.7, 74.9, 67.0, 66.9, 48.8, 48.3, 48.1, 46.0, 45.0, 44.7, 43.7, 43.5, 43.4, 41.8, 41.7, 40.8, 39.7, 34.7, 34.6, 34.4, 32.5, 31.8, 31.7, 31.6, 31.5, 31.4, 25.7, 25.5, 25.2, 25.1, 23.3, 23.2, 23.1, 22.9, 22.5, 22.4, 21.4, 21.3, 21.1, 20.8, 16.2, 16.1, 15.9. IR (νmax, cm⁻¹) 3417 (w), 3315 (w), 2954 (m), 2871 (m), 1724 (s), 1661 (s), 1523 (m), 1452 (s), 1242 (s), 1173 (m), 1095 (m), 1049 (s), 912 (m), 739 (s). HRMS (ESI/QTOF) m/z: [M + Na]+ Calcd for C₂₄H₄₃N₂NaO₄⁺ 439.2567; Found 439.2567.

(2S)-Methyl 2-(((benzoxoyacetyl)amino)-3-((1-((benzoxoyacetyl)amino)acetyl)pyrrolidin-2-yl)oxy)propanoate (4i)

Following General Procedure 2 and starting with Cbz-Gly-Pro (1a) (92 mg, 0.30 mmol, 1.0 equiv) and Cbz-Ser-OMe (114 mg, 0.450 mmol, 1.50 equiv), 4i was obtained after column chromatography DCM to DCM/ethyl acetate 1:1 as a pale yellow oil and a mixture of diastereoisomers (65 mg, 0.13 mmol, 42%).
Rf (DCM/ethyl acetate 7:3): 0.3. 1H NMR (400 MHz, Chloroform-\(d\), mixture of rotamers of diastereoisomers)  δ 7.40-7.25 (m, 10H, ArH), 6.05 (d, 0.3H, NH Ser), 5.93 (d, J = 8.4 Hz, 0.1H, NH Ser), 5.72 (br s, 1H, NH Gly), 5.65 (s, 0.4H, NH Ser), 5.47 (d, J = 4.8 Hz, 0.3H, C(O)NCH Pro), 5.41 (d, J = 4.9 Hz, 0.4H, C(O)NCH Pro), 5.12 (s, 4H, OCH\(_2\)Ph Gly νSer), 5.09-5.05 (m, 0.3H, C(O)NCH Pro), 4.59-4.49 (m, 0.3H, NHCH Ser), 4.51-4.41 (m, 0.7H, NHCH Ser), 4.12-3.78 (m, 4H, OCH\(_2\) Ser and C(O)CH\(_2\)NHCbz Gly), 3.77-3.62 (m, 3H, CO\(_2\)CH\(_2\) Ser), 3.59-3.51 (m, 2H, C(O)NCH\(_2\) Pro), 2.19-1.61 (m, 4H, NCH\(_2\)CH\(_2\)CH Pro). 13C NMR (101 MHz, Chloroform-\(d\), mixture of rotamers of diastereoisomers, signals not fully resolved) δ 170.8, 170.7, 170.2, 168.5, 168.2, 156.2, 155.9, 136.3, 136.3, 136.2, 128.5, 128.4, 128.2, 128.1, 128.1, 128.0, 128.0, 127.9, 87.6, 87.2, 87.0, 86.7, 86.9, 86.8, 68.9, 67.1, 67.0, 66.9, 66.3, 66.2, 54.6, 54.4, 54.3, 54.0, 52.8, 52.7, 52.5, 52.4, 45.9, 45.1, 44.9, 43.4, 43.4, 42.9, 42.8, 33.7, 31.5, 31.4, 31.1, 31.1, 22.7, 22.7, 20.7, 20.6, 20.4. IR (ν_{max}, cm\(^{-1}\)) 3324 (m), 2979 (m), 2885 (w), 1718 (s), 1658 (s), 1518 (m), 1436 (m), 1242 (m), 1054 (s), 914 (m), 738 (s), 699 (m). HRMS (ESI/QTOF) m/z: [M + Na]\(^+\) Calcd for C\(_{28}\)H\(_{31}\)N\(_3\)NaO\(_6\)\(^+\) 536.2003; Found 536.2014.

(2S,3R)-methyl 2-(((benzoxyl)carbonyl)amino)-3-((1-(2-(((benzoxyl)carbonyl)amino) acetyl)pyrrolidin-2-yl)oxy)butanoate (4j)

Following General Procedure 2 and starting with Cbz-Gly-Pro (1a) (92 mg, 0.30 mmol, 1.0 equiv) and Cbz-Thr-OMe (160 mg, 0.450 mmol, 1.50 equiv), 4j was obtained after column chromatography DCM to DCM/ethyl acetate 1:1 as a pale yellow oil and a mixture of diastereoisomers (60 mg, 0.11 mmol, 38%).

Rf (DCM/ethyl acetate 7:3): 0.36. 1H NMR (400 MHz, Chloroform-\(d\), mixture of rotamers of diastereoisomers)  δ 7.40-7.28 (m, 10H, ArH), 5.67 (d, J = 14.7 Hz, 1H, NH Gly), 5.60 (d, J = 9.4 Hz, 0.5H, NH Thr), 5.55 (d, J = 4.7 Hz, 0.6H, C(O)NCH Pro), 5.54-5.48 (m, 0.25H, NH Thr), 5.43 (d, J = 9.7 Hz, 0.25H, NH Thr), 5.40 (d, J = 4.7 Hz, 0.4H, C(O)NCH Pro), 5.17-5.06 (m, 4H, OCH\(_2\)Ph Gly and Ser), 4.54-4.37 (m, 0.5H, OCH and NHCH Thr), 4.37-4.22 (m, 1.2H, OCH and NHCH Thr), 4.22-4.11 (m, 0.3H, OCH and NHCH Thr), 3.96 (m, 2H, C(O)CH\(_2\)NHCbz Gly), 3.78-3.58 (m, 3H, OCH\(_2\) Thr), 3.47 (dq, J = 16.4, 5.9, 8.5 Hz, 0.5H, C(O)NCH Pro), 3.40-3.19 (m, 1.5H, C(O)NCH Pro), 2.15-1.68 (m, 4H, NCH\(_2\)CH\(_2\)CH\(_2\)CH Pro), 1.39-1.16 (m, 3H, 3H, OCH\(_2\)CH\(_2\) Pro). 13C NMR (101 MHz, Chloroform-\(d\), mixture of diastereoisomers and rotamers, signals not fully resolved) δ 171.6, 171.4, 168.7, 168.0, 156.8, 156.7, 156.3, 136.5, 136.4, 136.3, 128.7, 128.6, 128.3, 128.2, 128.1, 86.7, 84.4, 83.9, 74.7, 72.3, 71.3, 67.4, 67.3, 67.2, 67.1, 59.1, 59.0, 52.7, 52.5, 52.4, 46.1, 45.7, 45.0, 44.8, 43.6, 43.5, 43.2, 32.2, 31.7, 31.3, 22.9, 22.8, 20.5, 20.4, 17.8, 16.9, 16.0. IR (ν_{max}, cm\(^{-1}\)) 3365 (w), 2979 (w), 2890 (w), 2099 (w), 1719 (s), 1663 (m), 1523 (m), 1436 (m), 1318 (m), 1256 (m), 1173 (m), 1065 (s), 1002 (m), 911 (m), 739 (s). HRMS (ESI/QTOF) m/z: [M + Na]\(^+\) Calcd for C\(_{27}\)H\(_{33}\)N\(_3\)NaO\(_6\)\(^+\) 550.2160; Found 550.2161;

Benzyl ((2S)-1-((1-methoxyethyl)amino)-1-oxopropan-2-yl)carbamate (4k)

\(^1\) Due to the complexity of the mixture, signals were not attributed to each rotamer and diastereoisomer.
Following General Procedure 1 and starting with Cbz-Ala-Ala (1b) (88 mg, 0.30 mmol, 1.0 equiv), 4k was obtained after column chromatography DCM to DCM/ethyl acetate 8:2 as a white amorphous solid (57 mg, 0.20 mmol, 68%) and as a mixture of unresolved diastereoisomers.

Rf (DCM/ethyl acetate 7:3): 0.25. ¹H NMR (400 MHz, Chloroform-d, mixture of diastereomers and rotamers) δ 1H NMR (400 MHz, CDCl₃) δ 7.40-7.28 (m, 5H, ArH), 6.30 (br s, 1H, NH), 5.33 (s, 1H, NHCBz), 5.24 (dq, J = 9.2, 5.9, 3.3 Hz, 1H, C(O)NCHCOMe), 5.12 (s, 2H, OCH₂Ph), 4.22 (q, J = 6.8 Hz, 1H, CbzNCHMe), 3.30 (s, 1H, OCH₃), 3.27 (s, 2H, OCH₂), 1.40 (t, J = 7.3 Hz, 3H, CbzNCH₂), 1.30 (d, J = 5.9 Hz, 3H, C(O)NHCH₂C₆H₅). δ¹³C NMR (101 MHz, Chloroform-d, mixture of rotamers, signals not fully resolved) δ 172.3, 156.0, 136.0, 128.6, 128.3, 128.1, 78.4, 67.2, 55.6, 50.7, 28.9, 21.5, 18.7, 18.3. IR (νmax, cm⁻¹) 3286 (m), 2981 (w), 1688 (s), 1651 (s), 1540 (s), 1453 (m), 1382 (w), 1324 (m), 1261 (s), 1135 (m), 1070 (m), 914 (m), 738 (s), 699 (s). HRMS (ESI/QTOF) m/z: [M + Na]^+ Calcd for C₁₄H₂₁N₂O₄ Na⁺ 303.1315; Found 303.1315.

**Benzyl (2-((1-(3-azidopropoxy)-2-phenylethyl)amino)-2-oxoethyl)carbamate (4l)**

Following General Procedure 2 and starting with Cbz-Gly-Phe (1c) (107 mg, 0.30 mmol, 1.0 equiv) and 3-azidopropan-1-ol (600 µL, 1M in DCM, 0.60 mmol, 2.0 equiv), 4l was obtained after column chromatography DCM to DCM/ethyl acetate 10:1 as a colourless oil (57 mg, 0.14 mmol, 46%).

Rf (DCM/ethyl acetate 7:3): 0.52. ¹H NMR (400 MHz, Acetonitrile-d₆, 75:25 mixture of rotamers (major/minor)) δ 7.41-7.21 (m, 10H, ArH (major+minor)), 6.88 (d, J = 5.4 Hz, 1H, NH Phe (major+minor)), 6.02 (m, 0.25H, NH Gly (major)), 5.90 (m, 0.75H, NH Gly (major)), 5.28 (dt, J = 9.6, 6.3 Hz, 1H, NHCH₂Phe (major+minor)), 5.09 (d, J = 9.8 Hz, 2H, OCH₂Ph (major+minor)), 3.81 (d, J = 6.1 Hz, 0.5H, NHCH₂ Gly (minor)), 3.66 (dd, J = 6.1, 2.8 Hz, 1.5H, NHCH₂ Gly (major)), 3.60-3.51 (m, 1H, OCH₂CH₂CH₂N₃ (major+minor)), 3.42-3.35 (m, 1.5H, OCH₂CH₂CH₂N₃ (major+minor) and OCH₂CH₂CH₂N₃ (minor)), 3.23 (t, J = 6.7 Hz, 1.5H, OCH₂CH₂CH₂N₃ (major)), 2.94 (dd, J = 13.8, 6.2 Hz, 1H, NHCH₂H₂ Phe (major+minor)), 2.83 (dd, J = 13.7, 6.3 Hz, 1H, NHCH₂H₂ Phe (major+minor)), 1.77-1.63 (m, 2H, OCH₂CH₂CH₂N₃ (major+minor)). ¹³C NMR (101 MHz, Acetonitrile-d₆, mixture of rotamers, signals not fully resolved) δ 170.5, 168.2, 157.6, 138.1, 138.0, 137.5, 130.6, 129.6, 129.5, 129.2, 128.9, 128.8, 127.4, 126.4, 123.6, 113.5, 81.1, 67.4, 67.3, 65.2, 59.4, 49.1, 44.8, 41.9, 32.4, 29.6. IR (νmax, cm⁻¹) 3347 (m), 3064 (m), 2935 (m), 2880 (m), 2097 (s), 1708 (s), 1644 (s), 1517 (s), 1455 (m), 1257 (s), 1155 (m), 1050 (s), 909 (m), 738 (s), 699 (s). HRMS (ESI/QTOF) m/z: [M + Na]^+ Calcd for C₂₁H₂₅N₄O₄ Na⁺ 434.1799; Found 434.1801.

**Benzyl (2S)-2-((1-(benzyloxy)-2-methylpropyl)carbamoyl)pyrrolidine-1-carboxylate (4m)**
Following General Procedure 2 and starting with Cbz-Pro-Val (1d) (105 mg, 0.30 mmol, 1.0 equiv) and benzyl alcohol (65 μL, 0.60 mmol, 2.0 equiv), 4m was obtained after column chromatography DCM to DCM/ethyl acetate 15:1 as a colourless oil (63 mg, 0.15 mmol, 51%).

Rf (DCM/ethyl acetate 7:3): 0.71. 1H NMR (400 MHz, Acetonitrile-d$_5$, mixture of rotamers of diastereoisomers) δ 7.45-7.16 (m, 10H, ArH), 6.97-6.70 (m, 1H, NH$_i$), 5.18-5.05 (m, 1.5H, OCH$_2$Ph Cbz), 4.99 (d, J = 13.3 Hz, 0.5H, OCH$_2$Ph Cbz), 4.91 (m, 1H, NHCH Val), 4.54 (m, 0.5H, OCH$_2$Ph Val), 4.49-4.33 (m, 1H, OCH$_2$Ph Val), 4.26 (m, 1.5H, OCH$_2$Ph Val and CbzNCH Pro), 3.59-3.40 (m, 2H, CbzNCH$_2$ Pro), 2.33-2.19 (m, 1H, CbzNCH$_2$CH$_2$CH$_2$CH$_2$ Pro), 2.05-1.95 (m, 1H, CbzNCH$_2$CH$_2$CH$_2$CH$_2$ Pro), 1.92-1.73 (m, 3H, CbzNCH$_2$CH$_2$CH$_2$CH$_2$ Pro and NHCHCH Val), 0.98-0.72 (m, 6H, CH$_2$ Val). 13C NMR (101 MHz, Acetonitrile-d$_5$, mixture of rotamers of diastereoisomers, signals not fully resolved) δ 174.1, 173.8, 173.7, 156.2, 155.5, 139.8, 139.7, 138.1, 129.4, 129.3, 129.2, 128.9, 128.7, 128.6, 128.4, 128.3, 84.5, 84.3, 70.1, 67.5, 67.4, 62.1, 62.0, 61.6, 61.4, 48.3, 47.8, 33.7, 32.5, 30.8, 25.3, 24.3, 18.6, 18.0, 17.9, 17.8. IR (ν$_{max}$, cm$^{-1}$) 3338 (m), 3063 (m), 2929 (m), 1672 (s), 1529 (s), 1417 (s), 1356 (s), 1231 (m), 1119 (s), 1089 (m), 1039 (m), 912 (m), 737 (s), 697 (s). HRMS (ESI/QTOF) m/z: [M + Na]$^+$ Calcd for C$_{32}$H$_{30}$N$_2$NaO$_4$+ 433.2098; Found 433.2090.

Benzyl (2-(2-(2-hydroxy-5-methylphenyl)pyrrolidin-1-yl)-2-oxoethyl)carbamate (5a)

Following General Procedure 3 and starting with Cbz-Gly-Pro (1a) (92 mg, 0.30 mmol, 1.0 equiv) and p-cresol (49 mg, 0.45 mmol, 1.5 equiv), 5a was obtained after column chromatography DCM to DCM/ethyl acetate 7:3 as a pale yellow amorphous solid (68 mg, 0.19 mmol, 62%).

Rf (DCM/ethyl acetate 7:3): 0.4. 1H NMR (400 MHz, Chloroform-d, 7:3 mixture of rotamers (major+minor)) δ 8.94 (s, 1H, OH (major+minor)), 7.33 (dt, J = 9.1, 4.6 Hz, 5H, ArH (major+minor)), 6.94 (d, J = 8.1 Hz, 0.7H, ArH (major)), 6.89 (s, 0.7H, ArH (major)), 6.82 (d, J = 7.6 Hz, 0.3H, ArH (minor)), 6.76 (d, J = 8.1 Hz, 0.7H, ArH (major)), 6.66 (s, 0.3H, ArH (minor)), 6.51 (d, J = 8.0 Hz, 0.3H, ArH (minor)), 5.79 (br s, 0.3H, NH (minor)), 5.67 (br s, 0.7H, NH (major)), 5.39 (dd, J = 7.5, 3.0 Hz, 0.7H, C(O)NCH (major)), 5.17 (d, J = 7.7 Hz, 0.3H, C(O)NCH (minor)), 5.11 (s, 1.4H, OCH$_2$Ph (major)), 5.07 (s, 0.6H, OCH$_2$Ph (minor)), 4.07 (td, J = 20.3, 18.9, 4.6 Hz, 1H, C(O)CH$_2$NHBz (major+minor)), 3.92 (dd, J = 17.4, 4.0 Hz, 0.7H, C(O)CH$_2$NHBz (major)), 3.79 (d, J = 6.0 Hz, 0.3H, C(O)NCH$_2$ (minor)), 3.73 (d, J = 8.1 Hz, 0.3H, C(O)NCH$_2$ (minor)), 3.67-3.51 (m, 1.4H, C(O)NCH$_2$ (major)), 3.43 (dd, J = 17.2, 3.3 Hz, 0.3H, C(O)CH$_2$NHBz (minor)), 2.43-2.14 (m, 6H, NCH$_2$CH$_2$CH$_2$CH and CH$_3$ (major+minor)), 1.98-1.82 (m, 1H, NCH$_2$CH$_2$CH$_2$CH (major+minor)). 13C NMR (101 MHz, Chloroform-d, mixture of rotamers, signals not fully resolved) δ 167.4, 156.6, 156.4, 153.1, 150.7, 136.4, 129.9, 129.6, 129.0, 128.6, 128.3, 128.1, 127.8, 127.4, 126.5, 125.9, 118.4, 115.6, 67.1, 55.9, 55.2, 47.5, 46.2, 43.6, 43.3, 34.4, 31.2, 30.5, 25.2, 21.8, 21.0, 20.9. IR (ν$_{max}$, cm$^{-1}$) 3313 (w), 2978 (m), 2899 (w), 2360 (w), 1714 (s), 1640 (s), 1510 (m), 1436 (m), 1269 (m), 1055 (m), 738 (m), 699 (m). HRMS (ESI/QTOF) m/z: [M + Na]$^+$ Calcd for C$_{21}$H$_{23}$N$_2$NaO$_4$+ 389.1472; Found 389.1472.

Benzyl (2-(2-(2-hydroxy-5-methoxyphenyl)pyrrolidin-1-yl)-2-oxoethyl)carbamate (5b)
Following General Procedure 3 and starting with Cbz-Gly-Pro (1a) (92 mg, 0.30 mmol, 1.0 equiv) and 4-methoxyphenol (56 mg, 0.45 mmol, 1.5 equiv), 5b was obtained after column chromatography DCM to DCM/ethyl acetate 7:3 as a pale yellow oil (90 mg, 0.23 mmol, 78%).

Rf (DCM/ethyl acetate 7:3): 0.35. 1H NMR (400 MHz, Chloroform-d, 7:3 mixture of rotamers (major + minor)) δ 8.73 (s, 1H, OH (major + minor)), 7.38-7.28 (m, 5H, ArH (major + minor)), 6.78 (d, J = 8.7 Hz, 0.7H, ArH (major)), 6.68 (dd, J = 8.7, 2.9 Hz, 0.7H, ArH (major)), 6.65 (d, J = 2.8 Hz, 0.7H ArH (major)), 6.57-6.50 (m, 0.6H, ArH (minor)), 6.45 (d, J = 2.1 Hz, 0.3H, ArH (minor)), 5.81 (s, 0.3H, NH (minor)), 5.66 (s, 0.7H, NH (major)), 5.41-5.35 (m, 0.7H, C(O)NCH (major)), 5.16 (d, J = 7.1 Hz, 0.3H, C(O)NCH (minor)), 5.11 (s, 1.4H, OCH3Ph (major)), 5.08 (s, 0.6H, OCH2Ph (minor)), 4.16-4.00 (m, 1H, C(O)CH2NHCbz (major + minor)), 3.93 (dd, J = 17.4, 4.2 Hz, 0.7H, C(O)CH2NHCbz (major)), 3.74 (s, 2.1H, OCH3H (major)), 3.70 (s, 0.9H, OCH3H (minor)), 3.62 (dd, J = 11.1, 7.1 Hz, 1H, C(O)NCH (major + minor)), 3.59-3.53 (m, 1H, C(O)NCH (major + minor)), 3.46 (dd, J = 17.1, 3.6 Hz, 0.3H, C(O)CH2NHCbz (minor)), 2.40-2.11 (m, 3H, NCH2CH2CH2CH (major + minor)), 1.99-1.82 (m, 1H, NCH2CH2CH2CH (major + minor)). 13C NMR (101 MHz, Chloroform-d, mixture of rotamers, signals not fully resolved) δ 168.0, 167.2, 156.5, 156.3, 153.5, 153.4, 149.2, 147.0, 136.4, 129.2, 128.7, 128.6, 128.3, 128.1, 118.9, 116.3, 113.4, 112.7, 112.6, 111.8, 111.8, 67.1, 56.0, 55.9, 55.4, 47.5, 46.5, 43.6, 43.3, 34.3, 31.2, 25.1, 21.7. IR (νmax, cm⁻¹) 3671 (m), 3320 (m), 2987 (s), 2899 (m), 1717 (s), 1638 (s), 1507 (s), 1453 (s), 1434 (s), 1350 (m), 1286 (s), 1207 (s), 1045 (s), 815 (m), 740 (m). HRMS (ESI/QTOF) m/z: [M + H]+ Calcd for C21H25N2O5+ 385.1758; Found 385.1747.

and Benzyl (2-(2-((8S,9R,13R,14R)-3-hydroxy-13-methyl-17-oxo-7,8,9,11,12,13,14,15, 16,17-decahydro-6H-cyclopenta[a]phenanthren-2-yl)pyrrolidin-1-yl)-2-oxoethyl) carbamate and Benzyl (2-(2-((8S,9R,13R,14R)-3-hydroxy-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-4-yl)pyrrolidin-1- yl)-2-oxoethyl)carbamate (5c)

Following General Procedure 3 and starting with Cbz-Pro-Gly (1a) (92 mg, 0.30 mmol, 1.0 equiv) and estrone (122 mg, 0.450 mmol, 1.50 equiv), 5c was obtained after column chromatography DCM to DCM/ethyl acetate 7:3 as a pale yellow amorphous solid (100 mg, 0.188 mmol, 63%, ratio major/minor 7:3).

Rf (DCM/ethyl acetate 7:3): 0.32.

Major: 1H NMR (400 MHz, Acetonitrile-d6, unresolved mixture of rotamers of diastereoisomers) δ 7.31 (m, 5H, ArH), 7.23-7.10 (m, 0.4H, OH), 7.10-6.95 (m, 1H, ArH), 6.89-6.73 (m, 0.6H, OH), 6.68-6.48 (m, 1H, ArH), 5.89-5.59 (m, 1H, NH Gly), 5.17 (m, 1H, C(O)NCH), 5.01 (m, 2H, OCH2Ph), 4.00-3.40 (m, 4H, C(O)CH2NHCbz and C(O)NCH2), 3.29-2.97 (m, 1H, ArCH2 estrone), 2.90-2.60 (m, 1H ArCH2 estrone), 2.48-2.26 (m, 3H), 2.04 (m, 5H), 1.90-1.73 (m, 2H), 1.67-1.25 (m, 7H), 0.86 (m, 3H, CH3). 13C NMR (101 MHz, Acetonitrile-d6, mixture of
rotamers of diastereoisomers, signals not fully resolved) δ 166.8, 157.1, 153.2, 153.0, 138.2, 136.5, 132.5, 129.4, 128.8, 128.7, 127.3, 126.4, 125.7, 125.5, 114.8, 114.6, 79.3, 78.6, 67.1, 67.0, 56.8, 56.5, 51.2, 48.7, 48.5, 48.1, 47.3, 47.1, 45.3, 45.1, 44.9, 43.9, 43.8, 43.2, 39.4, 38.3, 36.4, 34.0, 32.6, 32.4, 31.4, 30.4, 29.8, 27.6, 27.4, 27.2, 27.1, 26.8, 26.6, 25.0, 24.8, 22.1, 14.3, 14.2. IR (νmax, cm⁻¹) 3305 (m), 2929 (m), 2867 (m), 1726 (s), 1633 (s), 1509 (s), 1451 (s), 1372 (m), 1281 (s), 1257 (s), 1056 (s), 831 (m), 741 (m), 698 (s). HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: [M + H]^+ Calcd for C_{32}H_{38}N_{2}O_{5}; Found 531.2840

Minor: ¹H NMR (400 MHz, Acetonitrile-d₅, unresolved mixture of rotamers of diastereoisomers) δ 8.26-8.17 (m, 0.2H, OH), 8.04-7.93 (m, 0.4H, OH), 7.32 (m, 5H ArH), 6.99-6.90 (m, 0.6H, ArH), 6.82 (s, 0.4H, ArH), 6.58-6.45 (m, 1H, ArH), 5.89-5.59 (m, 1H, NH Gly), 5.27-5.09 (m, 1H, C(O)NCH₂), 5.03 (m, 2H, OCH₂Ph), 4.00-3.85 (m, 1.6H, C(O)CH₂NHCbz), 3.84-3.74 (m, 0.4H, C(O)CH₂NHCbz), 3.73-3.46 (m, 2H, C(O)NCH₂), 2.88-2.66 (m, 2H, ArCH₂ estrone), 2.47-2.25 (m, 3H), 2.13-1.97 (m, 5H), 1.87-1.72 (m, 2H), 1.67-1.33 (m, 7H), 0.88 (m, 3H, CH₂). ¹³C NMR (101 MHz, Acetonitrile-d₅, mixture of rotamers of diastereoisomers, signals not fully resolved) δ 174.0, 168.6, 153.0, 152.0, 138.3, 137.8, 132.2, 129.4, 129.3, 128.8, 128.7, 127.3, 127.1, 124.1, 123.8, 116.3, 67.1, 56.4, 51.1, 48.7, 47.9, 47.0, 44.9, 44.8, 44.0, 43.8, 39.7, 39.4, 39.2, 36.3, 35.0, 34.5, 32.6, 32.3, 32.1, 31.1, 29.8, 29.6, 27.3, 26.9, 26.6, 26.1, 25.5, 24.5, 23.7, 22.3, 22.2, 14.3, 14.2, 11.3. IR (νmax, cm⁻¹) 3307 (m), 2951 (s), 2872 (m), 1733 (s), 1638 (s), 1509 (s), 1454 (s), 1426 (s), 1284 (s), 1254 (s), 1055 (s), 775 (m), 699 (m). HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: [M + Na]^+ Calcd for C_{32}H_{39}N_{2}O_{5}+Na; Found 531.2835

Benzyl (2S)-2-((1-(2-hydroxy-5-methoxyphenyl)-2-phenylethyl)amino)-2-oxoethyl carbamate (5d)

Following General Procedure 3 and starting with Cbz-Gly-Phe (1c) (107 mg, 0.300 mmol, 1.00 equiv) and 4-methoxyphenol (56 mg, 0.45 mmol, 1.50 equiv), 5d was obtained after column chromatography DCM to DCM/ethyl acetate 10:1 as a colorless oil (81 mg, 0.19 mmol, 62%).

Rf (DCM/ethyl acetate 7:3): 0.31. ¹H NMR (400 MHz, Chloroform-d, unresolved mixture of rotamers) δ 7.98-7.49 (br s, 1H, OH), 7.34 (m, 5H, ArH), 7.19 (dq, J = 14.2, 7.0 Hz, 4H, ArH), 7.10 (d, J = 6.7 Hz, 2H, ArH), 6.78 (d, J = 8.7 Hz, 1H, ArH), 6.68 (dd, J = 8.7, 2.9 Hz, 1H, ArH), 6.64 (s, 1H, NH Phe), 5.40 (s, 1H, NH Gly), 5.28 (q, J = 8.48 Hz, 1H, NHCHAr), 5.09 (s, 2H, OCH₂Ph), 3.69 (d, J = 7.47 Hz, 5H, OCH₃ and NHCH₂), 3.20-3.05 (m, 2H, NHCH₂Ph). ¹³C NMR (101 MHz, Chloroform-d, mixture of rotamers, signals not fully resolved) δ 169.8, 156.8, 153.5, 148.4, 137.7, 136.1, 129.2, 128.8, 128.6, 128.5, 128.3, 128.1, 126.8, 118.4, 114.0, 113.4, 67.5, 55.9, 51.1, 44.6. 40.1. IR (νmax, cm⁻¹) 3402 (m), 3065 (m), 2935 (m), 2836 (w), 1707 (s), 1655 (s), 1524 (s), 1455 (m), 1350 (m), 1260 (s), 1211 (s), 1154 (s), 1032 (m), 910 (s), 735 (s). HRMS (ESI/QTOF) m/z: [M + Na]^+ Calcd for C_{25}H_{26}N_{2}O_{5}+Na; Found 457.1734

Benzyl (2S)-2-((1-(2-hydroxy-5-methoxyphenyl)-2-methylpropyl)carbamoyl)pyrrolidine-1-carboxylate (5e)
Following General Procedure 3 and starting with Cbz-Pro-Val (1d) (105 mg, 0.300 mmol, 1.00 equiv) and 4-methoxyphenol (56 mg, 0.45 mmol, 1.50 equiv), 5e was obtained after column chromatography DCM to DCM/ethyl acetate 10:1 as a colorless oil (63 mg, 0.15 mmol, 49%).

Rf (DCM/ethyl acetate 7:3): 0.32. 1H NMR (400 MHz, Chloroform-d, mixture of rotamers and diastereomers) δ 8.08-7.51 (m, 1H, OH), 7.33 (m, 4H, ArH), 7.22 (m, 1H, ArH), 7.09-6.90 (m, 1H, NH), 6.78 (d, J = 3.7 Hz, 1H, ArH), 6.72-6.59 (m, 2H, ArH), 5.31-4.88 (m, 2H, OCH2Ph), 4.60 (t, J = 8.8 Hz, 1H, NHCAr), 4.34 (m, 1H, NCH(O)), 3.74 (m, 3H, OCH3), 3.63-3.32 (m, 2H, CH2NCbz), 2.38-1.55 (m, 5H, NCH2CH2CH3 and NHCHCH3), 1.09-0.69 (m, 6H, CH(CH3)2). 13C NMR (101 MHz, Chloroform-d, mixture of diastereomers and rotamers, signals not fully resolved) δ 172.7, 172.6, 156.4, 155.6, 153.7, 153.5, 149.9, 148.9, 128.7, 128.4, 128.0, 116.2, 114.9, 113.7, 113.4, 67.7, 60.6, 55.9, 55.8, 47.6, 31.1, 24.7, 24.6, 20.4, 20.0. IR (νmax, cm⁻¹) 3330 (m), 2958 (m), 2873 (m), 1685 (s), 1530 (s), 1508 (s), 1432 (s), 1356 (s), 1207 (s), 1119 (s), 1040 (m), 911 (s), 735 (s). HRMS (ESI/QTOF) m/z: [M + H]+ Calcd for C24H31N2O5+ 427.2227; Found 427.2229.

Benzyl ((2S)-1-((1-((2-hydroxy-5-methoxyphenyl)ethyl)amino)-1-oxopropan-2-yl) carbamate (5f)

Following General Procedure 3 and starting with Cbz-Ala-Ala (1b) (88 mg, 0.30 mmol, 1.0 equiv) and 4-methoxyphenol (56 mg, 0.45 mmol, 1.50 equiv), 5f was obtained after column chromatography DCM to DCM/ethyl acetate 10:1 as a colorless oil (71 mg, 0.19 mmol, 64%).

Rf (DCM/ethyl acetate 7:3): 0.34. 1H NMR (400 MHz, Chloroform-d, mixture of rotamers and diastereomers) δ 8.23 (br s, 1H, OH), 7.41-7.27 (m, 5H, ArH), 7.07-6.90 (br s, 1H, ArCHNH), 6.82 (dd, J = 8.7, 4.7 Hz, 1H, ArH), 6.71 (ddd, J = 11.6, 6.2, 3.2 Hz, 2H, ArH), 5.50-5.28 (m, 1H, CbzNH), 5.17 (dt, J = 15.0, 7.2 Hz, 1H, ArCHNH), 5.08 (m, 2H, OCH2Ph), 4.17 (m, 1H, CbzNHC), 3.73 (m, 3H, OCH3), 1.49 (dd, J = 16.9, 6.2 Hz, 3H, ArCHCH2), 1.37-1.27 (m, 3H, CbzNHCHCH3). 13C NMR (101 MHz, Chloroform-d, mixture of diastereomers and rotamers, signals not fully resolved) δ 173.0, 172.9, 156.2, 156.0, 153.4, 148.5, 135.9, 129.4, 128.6, 128.3, 128.1, 118.6, 118.5, 113.7, 112.3, 111.2, 67.2, 55.8, 50.4, 50.3, 44.1, 19.6, 18.6, 18.0. IR (νmax, cm⁻¹) 3327 (m), 3079 (m), 2936 (m), 2834 (m), 1705 (s), 1651 (s), 1508 (s), 1453 (s), 1258 (s), 1207 (s), 1030 (m), 910 (m), 734 (s), 699 (m). HRMS (ESI/QTOF) m/z: [M + Na]+ Calcd for C20H26N2NaO5+ 395.1577; Found 395.1582.

Benzyl (S)-2-((5-bromo-2-hydroxybenzyl)carbamoyl)pyrrolidine-1-carboxylate (5g)
Following General Procedure 3 and starting with Cbz-Pro-Gly (1e) (92 mg, 0.30 mmol, 1.0 equiv) and 4-bromophenol (78 mg, 0.45 mmol, 1.5 equiv), 5g was obtained after column chromatography DCM to DCM/ethyl acetate 10:1 as a white amorphous solid (61 mg, 0.14 mmol, 47%).

Rf (DCM/ethyl acetate 7:3): 0.5. 1H NMR (400 MHz, Chloroform-d, 7:3 mixture of rotamers (major/minor)) δ 9.33 (br s, 1H, OH (major+minor)), 7.83 (br m, 0.7H, NH (major)), 7.44-7.27 (br m, 5H, ArH (major+minor)), 7.19 (br m, 2H, ArH (major+minor)), 7.04-6.91 (br m, 0.3H, NH (minor)), 6.80 (d, J = 8.6 Hz, 1H, ArH (major+minor)), 5.09 (br m, 2H, OCH2Ph (major+minor)), 4.44-4.05 (br m, 3H, NCH2O), NHCH2Ar (major+minor)), 3.46 (br m, 2H, CH2NCbz (major+minor)), 2.13 (br m, 4H, NCH2CH2CH2CH (major+minor)). 13C NMR (101 MHz, Chloroform-d, mixture of rotamers, signals not fully resolved) δ 175.0, 174.4, 156.7, 155.2, 136.1, 133.4, 132.8, 128.8, 128.5, 128.1, 126.3, 120.0, 111.5, 67.8, 60.7, 60.2, 47.7, 47.4, 40.2, 28.1, 24.7, 23.9. IR (νmax, cm⁻¹) 3291 (m), 3055 (m), 2933 (w), 1682 (s), 1542 (s), 1481 (s), 1419 (s), 1355 (s), 1275 (s), 1173 (s), 1092 (m), 909 (s), 732 (s). HRMS (ESI/QTOF) m/z: [M + Na]+ Calcd for C20H17BrN2NaO4 455.0577; Found 455.0579.

Benzy1 (S)-2-((5-fluoro-2-hydroxybenzyl)carbamoyl)pyrroolidine-1-carboxylate (5h)

Following General Procedure 3 and starting with Cbz-Pro-Gly (1e) (92 mg, 0.30 mmol, 1.0 equiv) and 4-fluorophenol (50 mg, 0.45 mmol, 1.5 equiv), 5h was obtained after column chromatography DCM to DCM/ethyl acetate 10:1 as a pale yellow oil (64 mg, 0.17 mmol, 57%).

Rf (DCM/ethyl acetate 7:3): 0.48. 1H NMR (400 MHz, Chloroform-d, 1:1 mixture of rotamers (R¹/R²)) δ 9.02 (br s, 1H, OH (R¹ + R²)), 7.82 (br m, 0.5H, NH (R¹)), 7.30 (br m, 5H, ArH (R¹ + R²)), 7.18 (br m, 0.5H, NH (R²)), 6.87 (qd, J = 8.8, 5.5 Hz, 2H, ArH (R¹ + R²)), 6.72 (br m, 1H, ArH (R¹ + R²)), 5.23-4.91 (br s, 2H, OCH2Ph (R¹ + R²)), 4.44-4.08 (br m, 3H, NCH2O), NHCH2Ar (R¹ + R²)), 3.46 (br m, 2H, CH2NCbz (R¹ + R²)), 2.47-1.79 (br m, 4H, NCH2CH2CH (R¹ + R²)). 13C NMR (101 MHz, Chloroform-d, mixture of rotamers, signals not fully resolved) δ 174.3, 156.7, 156.3 (d, J = 236.7 Hz), 151.9 (d, J = 2.0 Hz), 136.2, 128.8, 128.5, 128.1, 125.2, 119.0 (d, J = 7.9 Hz), 116.8 (d, J = 23.1 Hz), 116.4 (d, J = 23.2 Hz), 67.8, 60.2, 59.5, 47.3, 47.0, 40.3, 28.0, 24.7, 23.9, 22.8. 19F NMR (376 MHz, Chloroform-d) δ -124.92, -125.08. IR (νmax, cm⁻¹) 3314 (m), 2925 (m), 2853 (m), 1684 (s), 1536 (m), 1508 (s), 1444 (s), 1356 (s), 1256 (s), 1188 (s), 1122 (s), 909 (s), 733 (s). HRMS (ESI/QTOF) m/z: [M + Na]+ Calcd for C20H12BrN2NaO4 455.0577; Found 455.0579.

Benzy1(S)-2-((5-((S)-2-(((benzyloxy)carbonyl)amino)-3-methoxy-3-oxopropyl)-2-hydroxy benzyl)carbamoyl)pyrroolidine-1-carboxylate (5i)
Following General Procedure 3 and starting with Cbz-Pro-Gly (1e) (92 mg, 0.30 mmol, 1.0 equiv) and Cbz-Tyr-OMe (148 mg, 0.450 mmol, 1.50 equiv), 5i was obtained after column chromatography DCM to DCM/ethyl acetate 10:1 as a white amorphous solid (65 mg, 0.11 mmol, 37%).

Rf (DCM/ethyl acetate 7:3): 0.32. 1H NMR (400 MHz, Chloroform-d, complex mixture of rotamers) δ 9.05 (br s, 1H, OH), 7.68 (br m, 0.5H, NH Gly), 7.43-7.27 (m, 10H, ArH), 7.19 (br m, 0.5H, NH Gly), 6.91 (dd, J = 8.3, 2.2 Hz, 1H, ArH), 6.81 (d, J = 8.2 Hz, 2H, ArH), 5.10 (m, 5H, OCH2Ph Pro+Tyr and NH Tyr), 4.59 (q, J = 5.9 Hz, 0.8H, NHCH Tyr), 4.46 (br s, 0.2H, NHCH Tyr), 4.33 (br m, 1H, NCHC(O) Pro), 4.25 (br m, 0.5H, NHCH2Ar Gly), 4.14 (dt, J = 12.1, 6.1 Hz, 1.5H, NHCH2Ar Gly), 3.71 (s, 3H, OCH3 Tyr), 3.44 (br m, 2H, CH2NCbz Pro), 2.99 (qd, J = 14.0, 5.9 Hz, 2H, NHCHCH2 Tyr), 2.44-1.73 (br m, 4H, NCH2CH2CH2CH Pro). 13C NMR (101 MHz, Chloroform-d, mixture of rotamers, signals not fully resolved) δ 174.1, 172.2, 156.6, 155.8, 155.1, 136.4, 136.2, 131.8, 130.8, 128.7, 128.6, 128.4, 128.3, 128.2, 128.1, 127.0, 124.2, 118.2, 67.7, 67.1, 60.3, 55.1, 52.5, 47.3, 40.5, 37.4, 28.1, 24.7. IR (νmax, cm⁻¹) 3317 (m), 3065 (m), 2949 (m), 1693 (s), 1533 (s), 1436 (s), 1355 (s), 1262 (s), 1213 (s), 1121 (m), 911 (s), 732 (s). HRMS (ESI/QTOF) m/z: [M + H]+ Calcd for C32H36N3O5s 590.2497; Found 590.2490.

Benzyl (S)-2-((5-((S)-2-((((benzyloxy)carbonylamino)propanamido)-3-methoxy-3-oxopropyl)-2-hydroxybenzyl)carbamoyl)pyrrolidine-1-carboxylate (5j)

Following General Procedure 3 and starting with Cbz-Pro-Gly (1e) (92 mg, 0.30 mmol, 1.0 equiv) and Cbz-Ala-Tyr-OMe (180 mg, 0.450 mmol, 1.50 equiv), 5j was obtained after column chromatography DCM to DCM/ethyl acetate 7:3 as a white amorphous solid (80 mg, 0.12 mmol, 40%).

Rf (DCM/ethyl acetate 7:3): 0.16. 1H NMR (400 MHz, Acetonitrile-d8, complex mixture of rotamers) δ 9.07 (s, 0.3H, OH), 8.54 (s, 0.4H, OH), 7.74 (s, 1H, NH Gly), 7.42-7.23 (m, 9H, ArH), 7.16 (d, J = 5.8 Hz, 1H, ArH), 6.99-6.83 (m, 3H, ArH and NH Tyr), 6.71 (d, J = 8.1 Hz, 1H, ArH), 6.18-6.06 (m, 0.7H, NH Ala), 5.89 (s, 0.3H, NH Ala), 5.19-4.87 (m, 4H, OCH2Ph Pro+Ala), 4.57 (ddt, J = 10.3, 7.9, 4.0 Hz, 1H, NHCH Tyr), 4.31-4.01 (m, 4H, NCHPro, NHCH2 Gly and NHCH Ala), 3.66 (d, J = 3.3 Hz, 3H, OCH3 Tyr), 3.46 (m, 2H, NCH2 Pro), 3.07-2.96 (m, 1H, NCHCH2 Tyr), 2.85 (m, 1H, NCHCH2 Tyr), 2.15-2.01 (m, 1H, NCH2CH2CH2CH Pro), 1.91-1.72 (m, 3H, NCH2CH2CH2CH Pro), 1.20 (dd, J = 16.9, 7.1 Hz, 3H, CH2 Ala). 13C NMR (101 MHz, Acetonitrile-d8, mixture of rotamers, signals not fully resolved) δ 176.2, 175.5,
173.4, 173.3, 172.8, 172.7, 172.6, 157.1, 156.9, 156.2, 155.6, 155.5, 155.0, 152.2, 138.1, 138.0, 137.9, 133.0, 132.4, 131.5, 131.1, 130.5, 130.4, 130.1, 129.5, 129.4, 128.9, 128.7, 128.6, 128.4, 125.7, 120.6, 117.4, 117.3, 67.7, 67.5, 67.3, 67.1, 61.9, 61.4, 54.6, 54.4, 52.8, 51.5, 48.2, 47.8, 40.2, 39.6, 37.0, 36.9, 32.1, 30.9, 25.1, 24.3, 18.5, 18.3. IR (νmax, cm⁻¹) 3317 (s), 2954 (m), 1661 (s), 1535 (s), 1448 (s), 1358 (s), 1256 (s), 1213 (s), 1120 (m), 1059 (m), 910 (s), 773 (m), 735 (s), 698 (s). HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: [M + H]^+ Calcd for C_{35}H_{41}N_{4}O_{5}^+ 661.2868; Found 661.2883. MS-MS (nanochip-ESI/LTQ-Orbitrap): selected ion 661.2883. Measured c and z ions are reported in the table below.

|     | G   | Y   | A   |
|-----|-----|-----|-----|
| N-terminal | 1   | 2   | 3   |
| c     | 249.12 | -   | -   |
| C-terminal | 3   | 2   | 1   |
| z     | 413.17 | -   | 510.22 |

Benzyl (2-(2-(1H-indol-3-yl)pyrrolidin-1-yl)-2-oxoethyl)carbamate (6a)

Following General Procedure 4 and starting with Cbz-Gly-Pro (1a) (92 mg, 0.30 mmol, 1.0 equiv) and 1H-indole (36 mg, 0.31 mmol, 1.02 equiv), 6a was obtained after column chromatography DCM to DCM/ethyl acetate 10:1 as a pale yellow amorphous solid (75 mg, 0.20 mmol, 66%).

Rf (DCM/ethyl acetate 7:3): 0.25. ¹H NMR (400 MHz, Chloroform-d, 7:3 mixture of rotamers(major/minor)) δ 8.42 (s, 0.3H, NH indole (minor)), 8.35 (s, 0.7H, NH indole (major)), 7.58 (d, J = 7.9 Hz, 0.3H, ArH (minor)), 7.50 (d, J = 7.9 Hz, 0.7H, ArH (major)), 7.39-7.27 (m, 6H, ArH (major+minor)), 7.24-7.17 (m, 1H, ArH (major+minor)), 7.17-7.09 (m, 1H, ArH (major+minor)), 6.88-6.80 (m, 1H, ArH (major+minor)), 5.80 (s, 0.3H, NH Gly (minor)), 5.66 (s, 0.7H, NH Gly (major)), 5.59 (dd, J = 7.1, 2.7 Hz, 0.3H, C(O)NCH (minor)), 5.23-5.14 (m, 0.7H, C(O)NCH (major)), 5.11 (s, 0.6H, OCH₂Ph (minor)), 5.04 (s, 1.4H, OCH₂Ph (major)), 4.04 (dd, J = 15.8, 4.6 Hz, 1.3H, C(O)CH₂NHGlb (major+minor)), 3.81 (dt, J = 12.0, 5.8 Hz, 0.7H, C(O)NCH₂ (major)), 3.69 (m, 1.7H, C(O)CH₂NHGlb (major) and C(O)NCH₂ (major+minor)), 3.53 (q, J = 8.1 Hz, 0.3H, C(O)NCH₂ (minor)), 2.36-1.85 (m, 4H, NCH₂CH₂CH₂CH (major+minor)).¹³C NMR (101 MHz, Chloroform-d, mixture of rotamers, signals not fully resolved) δ 167.7, 166.7, 156.5, 156.3, 137.0, 136.6, 128.6, 128.2, 128.1, 125.3, 124.8, 122.7, 122.2, 121.4, 121.3, 120.0, 119.6, 119.0, 118.7, 116.8, 116.7, 116.7, 111.8, 111.6, 67.0, 66.9, 55.0, 54.9, 46.9, 46.0, 45.9, 43.7, 43.4, 34.5, 32.1, 24.2, 22.2. IR (νmax, cm⁻¹) 3311 (m), 3046 (w), 2977 (m), 2876 (w), 1710 (s), 1638 (s), 1521 (m), 1455 (s), 1252 (s), 1165 (m), 1055 (m), 910 (m), 737 (s) HRMS (ESI/QTOF) m/z: [M + Na]^+ Calcd for C_{22}H_{23}N_{3}NaO_{5}^+ 400.1632; Found 400.1629.

Benzyl (2-(2-(5-chloro-1H-indol-3-yl)pyrrolidin-1-yl)-2-oxoethyl)carbamate (6b)
Following General Procedure 4 and starting with Cbz-Gly-Pro (1a) (92 mg, 0.30 mmol, 1.0 equiv) and 5-Chloro-1H-indole (46 mg, 0.31 mmol, 1.02 equiv), 6b was obtained after column chromatography DCM to DCM/ethyl acetate 10:1 as a pale yellow oil (82 mg, 0.20 mmol, 66%).

Rf (DCM/ethyl acetate 7:3): 0.36. ¹H NMR (400 MHz, Chloroform-­d, 6:4 mixture of rotamers(major/minor)) δ 8.72 (s, 0.4H, NH indole (minor)), 8.59 (s, 0.6H, NH indole (major)), 7.51 (d,  J = 1.7 Hz, 0.4H, ArH (minor)), 7.47-7.41 (m, 0.6H, ArH (major)), 7.36-7.27 (m, 5H, ArH (major+minor)), 7.22 (dd,  J = 14.1, 8.7 Hz, 1H, ArH (major+minor)), 7.11 (td,  J = 8.7, 8.0, 1.7 Hz, 1H, ArH (major+minor)), 6.82 (d,  J = 1.9 Hz, 0.4H, ArH (minor)), 6.73 (d,  J = 2.4 Hz, 0.6H, ArH (minor)), 5.75 (s, 0.4H, NH Gly (minor)), 5.68 (s, 0.6H, NH Gly (major)), 5.53-5.47 (m, 0.4H, C(O)NCH₂ (minor)), 5.15-4.99 (m, 2.6H, C(O)NCH₂ (major) and OCH₂Ph (major+minor)), 4.13-3.93 (m, 1.4H, C(O)CH₃ NHCbz (major+minor)), 3.81-3.68 (m, 1.6H, C(O)NCH₂ (major+minor)), 3.64 (dd,  J = 17.4, 4.5 Hz, 0.6H, C(O)CH₃ NHCbz (major)), 3.53 (q,  J = 7.8 Hz, 0.4H, C(O)NCH₂ (minor)), 2.35-2.16 (m, 1H, NCH₂CH₂CH₂CH (major+minor)), 2.06 (ddt,  J = 17.1, 8.2, 3.7 Hz, 2H, NCH₂CH₂CH₂CH (major+minor)), 1.96-1.84 (m, 1H, NCH₂CH₂CH₂CH (major+minor)). ¹³C NMR (101 MHz, Chloroform-­d, mixture of rotamers, signals not fully resolved) δ 167.6, 166.9, 156.4, 156.3, 136.4, 135.3, 135.2, 128.5, 128.4, 128.1, 128.1, 128.0, 127.9, 126.1, 125.6, 125.5, 125.1, 122.9, 122.7, 122.3, 118.2, 118.0, 116.3, 116.2, 112.8, 112.6, 67.0, 66.9, 54.8, 54.6, 46.8, 46.0, 43.6, 43.3, 34.4, 32.1, 24.0, 22.1. IR (νmax cm⁻¹) 3308 (m), 2927 (m), 1710 (s), 1638 (s), 1520 (m), 1454 (s), 1254 (s), 1173 (m), 1055 (m), 909 (s), 733 (s). HRMS (ESI/QTOF) m/z: [M + Na]⁺ Calcd for C₂₂H₂₂ClN₃NaO₃⁺ 434.1242; Found 434.1253.

Benzyl (2-oxo-2-(2-(6-(trifluoromethyl)-1H-indol-3-yl)pyrroolidin-1-yl)ethyl)carbamate (6c)

Following General Procedure 4 and starting with Cbz-Gly-Pro (1a) (92 mg, 0.30 mmol, 1.0 equiv) and 6-trifluoromethyl-1H-indole (57 mg, 0.31 mmol, 1.02 equiv), 6c was obtained after column chromatography DCM to DCM/ethyl acetate 7:3 as a pale yellow oil (67 mg, 0.15 mmol, 50%).

Rf (DCM/ethyl acetate 7:3): 0.35. ¹H NMR (400 MHz, Acetonitrile-­d₃, 1:1 mixture of rotamers, (R¹/R²) δ 9.69 (s, 0.5H, NH indole (R¹)), 9.52 (s, 0.5H, NH indole (R²)), 7.79-7.73 (m, 1H, ArH (R¹+R²)), 7.73-7.66 (m, 1H, ArH (R¹+R²)), 7.39-7.26 (m, 5H, ArH (R¹+R²)), 7.26-7.21 (m, 1H, ArH (R¹+R²)), 7.19-7.09 (m, 1H, ArH (R¹+R²)), 5.84 (s, 0.5H, NH Gly (R¹)), 5.72 (s, 0.5H, NH Gly (R²)), 5.47-5.39 (m, 0.5H, C(O)NCH₂ (R¹)), 5.29 (d,  J = 5.4 Hz, 0.5H, C(O)NCH₂ (R²)), 5.05 (s, 1H, OCH₂Ph (R¹)), 4.98 (s, 1H, OCH₂Ph (R²)), 3.96 (d,  J = 5.3 Hz, 1H, C(O)CH₂NHCbz (R¹+R²)), 3.89 (dd,  J = 17.2, 5.3 Hz, 0.5H, NC(O)CH₂NHCbz (R¹)), 3.72 (dt,  J = 11.7, 6.3 Hz, 1H, C(O)NCH₂ (R¹+R²)), 3.57 (m, 1H, C(O)NCH₂ (R¹+R²)), 3.44 (dd,  J = 17.0, 5.5 Hz, 0.5H,
C(O)CH₂NHCbz (R²), 2.39-2.13 (m, 2H, NCH₂CH₂CH₂CH₃ (R¹+R²)), 2.03-1.97 (m, 1H, NCH₂CH₂CH₂CH₂CH₂CH₃ (R¹+R²)), 1.91-1.82 (m, 1H, NCH₂CH₂CH₂CH₂CH₂CH₂CH₃ (R¹+R²)).¹³C NMR (101 MHz, Acetonitrile-d₃, mixture of rotamers, signals not fully resolved) δ 168.5, 167.8, 157.3 (d, J = 12.25 Hz), 138.2, 136.7, 136.4, 129.4, 129.3, 128.8, 128.7, 128.3, 127.8, 126.3, 125.9, 125.1, 124.3, 124.0, 123.8, 123.5, 120.28 (d, J = 13.93 Hz), 118.8, 116.4 (dd, J = 36.31, 3.45 Hz), 110.12 (dd, J = 28.22, 4.43 Hz), 67.1, 67.0, 55.0, 54.8, 47.4, 46.6, 44.1, 43.8, 35.5, 33.0, 30.3, 24.7, 22.8. IR (νmax, cm⁻¹) 3365 (s), 3032 (m), 2930 (m), 1710 (s), 1642 (s), 1509 (s), 1454 (s), 1336 (s), 1257 (s), 1157 (s), 1111 (s), 1053 (s), 961 (m), 878 (m), 816 (s), 698 (s). HRMS (ESI/QTOF) m/z: [M + Na]⁺ Calcd for C₂₃H₂₂F₃N₃NaO₂⁺ 468.1505; Found 468.1513.

**Benzyl (2-(2-(2-methyl-1H-indol-3-yl)pyrrolidin-1-yl)-2-oxoethyl)carbamate (6d)**

Following General Procedure 4 and starting with Cbz-Gly-Pro (1a) (92 mg, 0.30 mmol, 1.0 equiv) and 2-Methyl-1H-indole (40 mg, 0.31 mmol, 1.02 equiv), 6d was obtained after column chromatography DCM to DCM/ethyl acetate 10:1 as a brown amorphous solid (58 mg, 0.15 mmol, 49%).

Rf (DCM/ethyl acetate 7:3): 0.36. ¹H NMR (400 MHz, Chloroform-d, 7:3 mixture of rotamers (major/minor) δ 8.25 (s, 0.3H, NH indole (minor)), 8.18 (s, 0.7H, NH indole (major)), 7.34-7.22 (m, 7H, ArH (major+minor)), 7.16-7.08 (m, 1H, ArH (major+minor)), 7.04 (dd, J = 9.3, 6.6 Hz, 1H, ArH (major+minor)), 5.65 (s, 1H, NH Gly (major+minor)), 5.32 (t, J = 6.9 Hz, 0.3H, C(O)NCH (minor)), 5.10-4.98 (m, 2.7H, C(O)NCH (major) and OCH₂Ph (major+minor)), 4.10 (dd, J = 17.0, 4.5 Hz, 0.3H, C(O)CH₂NHCbz (minor)), 4.00-3.90 (m, 1.7H, C(O)CH₂NHCbz (major+minor) and C(O)NCH₂ (major)), 3.79 (dt, J = 12.8, 7.2 Hz, 1H, C(O)NCH₂ (major+minor)), 3.69 (td, J = 10.1, 8.0, 5.6 Hz, 0.3H, C(O)NCH₂ (minor)), 3.30 (dd, J = 17.3, 3.2 Hz, 0.7H, C(O)CH₂NHCbz (major)), 2.40-2.28 (m, 4H, CH₃ and NCH₂CH₂CH₂CH₂CH₃ (major+minor)), 2.22-1.84 (m, 3H, NCH₂CH₂CH₂CH₂CH₃ (major+minor)).¹³C NMR (101 MHz, Chloroform-d, mixture of rotamers, signals not fully resolved) δ 167.8, 166.4, 156.3, 156.2, 136.6, 135.5, 131.9, 131.3, 128.6, 128.1, 128.0, 126.2, 125.7, 121.6, 120.9, 119.9, 119.4, 118.1, 117.7, 111.6, 111.1, 110.9, 66.9, 66.8, 55.1, 54.8, 47.8, 47.1, 43.7, 43.3, 35.6, 32.7, 25.4, 23.7, 12.0, 11.8. IR (νmax, cm⁻¹) 3393 (m), 3299 (m), 3060 (m), 2965 (m), 2875 (m), 1710 (s), 1637 (s), 1510 (m), 1459 (s), 1237 (m), 910 (m), 737 (s). HRMS (ESI/QTOF) m/z: [M + H]⁺ Calcd for C₂₃H₂₃N₂O₂⁺ 392.1969; Found 392.1977.

**Benzyl (2-(2-(3-methyl-1H-indol-1-yl)pyrrolidin-1-yl)-2-oxoethyl)carbamate (6e)**

Following General Procedure 4 and starting with Cbz-Gly-Pro (1a) (92 mg, 0.30 mmol, 1.0 equiv) and 3-Methyl-1H-indole (40 mg, 0.31 mmol, 1.02 equiv), 6e was obtained after column chromatography DCM to DCM/ethyl acetate 10:1 as a white amorphous solid (50 mg, 0.13 mmol, 43%).

Rf (DCM/ethyl acetate 7:3): 0.58. ¹H NMR (400 MHz, Chloroform-d, 6:4 mixture of rotamers (major/minor) δ 7.55 (dd, J = 17.6, 7.8 Hz, 1H, ArH (major+minor)), 7.43 (d, J = 8.2 Hz, 0.4H,
Benzyl (2-((2(2-acetamidoethyl)-5-methoxy-1H-indol-1-yl)pyrrolidin-1-yl)-2-oxoethyl) carbamate (6f)

Following General Procedure 4 and starting with Cbz-Gly-Pro (1a) (92 mg, 0.30 mmol, 1.0 equiv) and melatonin (71 mg, 0.31 mmol, 1.02 equiv), 6f was obtained after column chromatography DCM to ethyl acetate as a colorless oil (95 mg, 0.19 mmol, 64% yield).

Rf (DCM/ethyl acetate 7:3): 0.13. 1H NMR (400 MHz, Chloroform-d, 7:3 mixture of rotamers (major/minor) δ 7.38-7.27 (m, 5.3H, ArH (major+minor)), 7.19 (d, J = 8.9 Hz, 0.7H, ArH (major)), 7.03 (d, J = 2.3 Hz, 0.7H, ArH (major)), 6.98 (d, J = 2.3 Hz, 0.3H, ArH (minor)), 6.90 (dt, J = 8.8, 2.9 Hz, 1H, ArH (major+minor)), 6.86 (s, 0.3H, ArH (minor)), 6.82 (s, 0.7H, ArH (major)), 6.40 (d, J = 5.3 Hz, 0.3H, C(O)NCH (minor)), 6.28 (s, 0.7H, AcNH (major)), 6.08 (dd, J = 6.0, 2.8 Hz, 0.7H, C(O)NCH (major)), 5.65 (s, 0.6H, AcNH and CbzNH (minor)), 5.48 (s, 0.7H, CbzNH (major)), 5.09 (s, 0.6H, OCH2Ph (minor)), 5.00 (d, J = 2.8 Hz, 1.4H, OCH2Ph (major)), 4.15-3.89 (m, 1.7H, C(O)CH2NHCbz (major+minor) and C(O)NCH2 (major)), 3.89-3.70 (m, 4.3H, OCH2 (major), C(O)CH2NHCbz (minor) and C(O)NCH2 (major+minor)), 3.54 (m, 2.3H, C(O)NCH2 (minor) and CH2NHAc (major+minor)), 3.17 (dd, J = 17.4, 5.6 Hz, 0.7H, C(O)CH2NHCbz (major)), 2.90 (dt, J = 13.9, 7.0 Hz, 2H, CH2CH2NHAc (major+minor), 2.47-1.97 (m, 4H, NCH2CH2CH2CH (major+minor)), 1.88 (d, J = 14.7 Hz, 3H, NHC(O)CH2 (major+minor)). 13C NMR (101 MHz, Chloroform-d, mixture of rotamers, signals not fully resolved) δ 170.7, 170.3, 168.6, 168.0, 156.5, 154.6, 154.3, 136.4, 136.2, 130.9, 129.8, 129.6, 128.8, 128.6, 128.3, 128.2, 128.1, 122.9, 122.6, 114.1, 113.0, 112.3, 112.2, 110.8, 110.2, 101.4, 101.1, 69.2, 68.5, 67.1, 56.0, 47.2, 46.1, 43.8, 43.0, 40.2, 39.5, 34.7, 32.2, 25.5, 25.0, 23.9, 23.5, 23.3, 21.8. IR (νmax, cm⁻¹): 3330 (m), 3033 (m), 2946 (m), 2833 (m), 1715 (s), 1654 (s), 1542 (s), 1484 (s), 1453 (s), 1220 (s), 1050 (m), 909 (s), 733 (s). HRMS (ESI/QTOF) m/z: [M + Na]+ Calcd for C27H52N4O5 515.2265; Found 515.2276

Benzyl (2-((1H-indol-3-yl)-2-phenylethyl)amino)-2-oxoethyl)carbamate (6g)
Following General Procedure 4 and starting with Cbz-Gly-Phe (1c) (107 mg, 0.30 mmol, 1.0 equiv) and 1H-indole (36 mg, 0.31 mmol, 1.02 equiv), 6g was obtained after column chromatography DCM to DCM/ethyl acetate 10:1 as a red amorphous solid (74 mg, 0.17 mmol, 58%).

Rf (DCM/ethyl acetate 7:3): 0.32. \( ^1 \text{H NMR} \ (400 \text{ MHz, Chloroform}-d) \delta 8.12-7.93 \ (m, 1H, NH indole), 7.64 \ (d, J = 7.9 \text{ Hz}, 1H, ArH), 7.34 \ (d, J = 7.9 \text{ Hz}, 6H, ArH), 7.24-7.06 \ (m, 7H, ArH), 6.93-6.88 \ (m, 1H, ArH), 6.45-6.19 \ (m, 1H, NH Phe), 5.59 \ (q, J = 7.2 \text{ Hz}, 1H, NHCH Phe), 5.45-5.28 \ (m, 1H, NH Gly), 5.08 \ (s, 2H, OCH\text{Ph}), 3.74 \ (t, J = 6.9 \text{ Hz}, 2H, NHCH\text{Gly}), 3.26 \ (tt, J = 13.6, 6.7 \text{ Hz}, 2H, NHCH\text{CH}_2\text{Phe}). \)

\( ^{13}\text{C NMR} \ (101 \text{ MHz, Chloroform-d}) \delta 168.1, 156.7, 138.0, 136.6, 136.2, 129.4, 128.7, 128.4, 128.3, 128.2, 126.8, 125.9, 122.6, 122.1, 120.1, 119.3, 116.0, 111.6, 67.3, 48.1, 44.8, 41.1. \)

IR (\( \nu_{\text{max}} \text{ cm}^{-1} \)) 3344 (m), 2962 (m), 2946 (m), 1712 (s), 1691 (s), 1661 (s), 1521 (s), 1455 (m), 1339 (m), 1259 (m), 1155 (m), 1075 (m), 910 (s), 740 (s), 699 (s). HRMS (ESI/QTOF) m/z: [M + Na]^+ Calcd for C_{29}H_{26}N_{3}NaO_{5}^+ 450.1788; Found 450.1792.

**Benzyl (2S)-2-((1-(1H-indol-3-yl)-2-methylpropyl)carbamoyl)pyrrolidine-1-carboxylate (6h)**

Following General Procedure 4 and starting with Cbz-Pro-Val (1d) (105 mg, 0.30 mmol, 1.0 equiv) and 1H-indole (x) (36 mg, 0.31 mmol, 1.02 equiv), 6h was obtained after column chromatography DCM to DCM/ethyl acetate 10:1 as a red amorphous solid (81 mg, 0.19 mmol, 64%).

Rf (DCM/ethyl acetate 7:3): 0.29. \( ^1 \text{H NMR} \ (400 \text{ MHz, Chloroform-d}, \text{complex mixture of diastereomers and rotamers}) \delta 8.22-7.85 \ (m, 1H, NH indole), 7.62-7.41 \ (m, 1H, ArH), 7.26 \ (m, 5H, ArH), 7.14-6.74 \ (m, 4H, ArH), 6.24 \ (m, 0.4H, NH Val not fully resolved), 5.21-4.86 \ (m, 3H, OCH\text{Ph} and NHCH Val), 4.47-4.19 \ (m, 1H, CbzNCH Pro), 3.56-3.18 \ (m, 2H, CbzNCH Pro), 2.42-1.94 \ (m, 3H, NHCHCH Val and NCH_2CH\text{CH}_2CH\text{Pro}), 1.89-1.63 \ (m, 2H, NCH_2CH\text{CH}_2CH\text{Pro}), 0.97-0.69 \ (m, 6H, CH\_3 Val). \)

\( ^{13}\text{C NMR} \ (101 \text{ MHz, Chloroform-d}, \text{mixture of diastereomers and rotamers, signals not fully resolved}) \delta 171.2, 170.7, 156.4, 155.7, 136.6, 136.5, 128.7, 128.3, 126.3, 122.1, 121.9, 119.5, 116.7, 116.2, 111.4, 67.4, 61.4, 60.8, 52.5, 47.8, 47.1, 32.8, 31.2, 28.1, 24.7, 23.6, 20.2, 19.0, 18.7. \)

IR (\( \nu_{\text{max}} \text{ cm}^{-1} \)) 3314 (m), 2962 (m), 2910 (m), 1690 (s), 1660 (s), 1520 (m), 1418 (s), 1356 (s), 1210 (m), 1118 (m), 909 (s), 735 (s), 698 (m). HRMS (ESI/QTOF) m/z: [M + Na]^+ Calcd for C_{29}H_{26}N_{3}NaO_{5}^+ 442.2101; Found 442.2107.

**Methyl N\text{a}-(((benzylloxy)carbonyl)-1-1-(((benzylloxy)carbonyl)glycyl)pyrrolidin-2-yl)-L-tryptophanate (6i)**
Following General Procedure 4 and starting with Cbz-Gly-Pro (1a) (92 mg, 0.30 mmol, 1.0 equiv) and Z-Trp-OMe (108 mg, 0.306 mmol, 1.02 equiv), 6i was obtained after column chromatography DCM to DCM/ethyl acetate 10:1 as a white amorphous solid (105 mg, 0.171 mmol, 57% yield).

Rf (DCM/ethyl acetate 7:3): 0.58. ¹H NMR (400 MHz, Chloroform-δ, complex mixture of diastereomers and rotamers) δ 7.57-7.39 (m, 2H, ArH), 7.38-7.27 (m, 10H, ArH), 7.21-7.06 (m, 2H, ArH), 6.83-6.66 (m, 1H, ArH), 6.45 (d, J = 6.2 Hz, 0.4H, C(O)NCH Pro), 6.17 (t, J = 5.5 Hz, 0.6H, C(O)NCH Pro), 5.66-5.22 (m, 2H, NH Gly+Trp), 5.05 (m, 4H, OCH₃Ph Gly+Trp), 4.76-4.64 (m, 1H, NHCH Trp), 4.18-3.86 (m, 2H, C(O)NCH₂ Pro and NHCH₃ Gly), 3.79-3.50 (m, 4H, OCH₃ Trp and C(O)NCH₂ Pro), 3.41-2.96 (m, 3H, NHCH₂ Gly and NHCH₂CH₂ Trp), 2.46-1.88 (m, 4H, NCH₂CH₂CH₂CH₂ Pro). ¹³C NMR (101 MHz, Chloroform-δ, mixture of diastereomers and rotamers, signals not fully resolved) δ 172.5, 172.4, 172.2, 168.9, 168.8, 167.8, 156.5, 156.4, 155.9, 155.8, 136.5, 136.2, 135.5, 134.7, 129.2, 128.6, 128.5, 128.2, 128.1, 122.9, 122.8, 122.4, 122.2, 120.6, 119.9, 119.8, 119.6, 119.1, 118.8, 111.3, 110.9, 110.1, 109.8, 109.4, 68.7, 68.3, 67.0, 67.0, 55.1, 54.8, 54.6, 52.6, 52.5, 47.2, 46.1, 43.8, 43.0, 34.8, 32.2, 28.3, 28.1, 23.8, 21.5. IR (νmax, cm⁻¹) 3411 (m), 3280 (m), 3061 (m), 2937 (m), 1716 (s), 1677 (s), 1517 (m), 1347 (m), 1344 (m), 1211 (s), 1060 (m), 911 (m), 738 (s). HRMS (ESI/QTOF) m/z: [M + Na]⁺ Calcd for C₃₉H₃₆N₄NaO₇⁺ 635.2476; Found 635.2491.

Methyl No-(((benzylloxy)carbonyl)-L-valyl)-1-(1-(((benzylloxy)carbonyl)glycyl)pyrrolidin-2-yl)-L-tryptophanate (6j)

Following General Procedure 4 and starting with Cbz-Gly-Pro (1a) (92 mg, 0.30 mmol, 1.0 equiv) and Z-Val-Trp-OMe (138 mg, 0.306 mmol, 1.02 equiv), 6j was obtained after column chromatography DCM to DCM/ethyl acetate 10:1 as a white amorphous solid (106 mg, 0.149 mmol, 50% yield).

Rf (DCM/ethyl acetate 7:3): 0.48. ¹H NMR (400 MHz, Acetonitrile-δ₆, complex mixture of diastereomers and rotamers) δ 7.57-7.42 (m, 2H, ArH), 7.38-7.25 (m, 10H, ArH), 7.18 (dt, J = 8.1, 4.9 Hz, 1H, ArH), 7.09 (dt, J = 15.1, 7.5 Hz, 2H, ArH), 7.04-6.98 (m, 0.5H, NH Trp), 6.82 (dd, J = 16.7, 7.4 Hz, 0.5H, NH Trp), 6.40-6.25 (m, 1H, C(O)NCH Pro), 5.91 (d, J = 9.0 Hz, 2H, NH Gly+Val), 5.12-4.95 (m, 4H, OCH₃Ph Gly+Val), 4.77-4.64 (m, 1H, NHCH Trp), 4.10-3.79 (m, 4H, NHCH₂ Gly, NHCH₂ Val and 1H C(O)NCH₂ Pro), 3.68-3.50 (m, 4H, OCH₃ Trp and 1H C(O)NCH₂ Pro), 3.35-2.77 (m, 2H, NHCH₂CH₂ Trp), 2.48-2.19 (m, 2H, NCH₂CH₂CH₂CH₂ Pro), 2.13-2.01 (m, 3H, NCH₂CH₂CH₂CH₂ Pro and NHCH₂CH₂ Val), 0.94-0.72 (m, 6H, CH₂ Val). ¹³C NMR (101 MHz, Acetonitrile-δ₆, mixture of diastereomers and rotamers, signals not fully resolved) δ 173.1, 173.0, 172.9, 172.8, 172.3, 172.1, 169.6, 169.4, 169.2, 157.6, 157.4, 157.3, 157.0, 138.2, 138.0, 136.2, 135.8, 129.4, 129.3, 129.0, 128.8, 128.7,
128.6, 128.5, 125.1, 124.9, 124.7, 124.4, 123.2, 123.1, 122.8, 122.6, 122.5, 120.8, 120.7, 120.2, 120.1, 120.0, 119.7, 119.6, 119.1, 112.1, 111.8, 111.6, 111.1, 111.0, 110.7, 110.5, 110.0, 109.8, 109.0, 106.9, 69.5, 69.3, 69.1, 67.2, 67.1, 66.9, 61.4, 61.1, 60.9, 60.3, 56.1, 54.6, 54.2, 53.9, 53.8, 53.5, 53.4, 52.7, 47.7, 47.6, 46.9, 46.8, 44.2, 43.5, 43.4, 35.4, 35.2, 33.4, 33.1, 33.0, 32.6, 32.2, 31.8, 31.7, 28.1, 28.0, 27.9, 27.8, 26.6, 25.7, 25.2, 24.3, 22.3, 22.2, 19.6, 19.5, 19.4, 19.2, 18.3, 18.1, 18.0, 17.8. IR (ν_{max}, cm\(^{-1}\)) 3307 (m), 2963 (m), 2892 (m), 1714 (s), 1660 (s), 1524 (s), 1438 (s), 1324 (m), 1236 (s), 1055 (m), 910 (m), 735 (s). HRMS (ESI/QTOF) m/z: [M + Na]\(^+\) Calcd for C\(_{39}\)H\(_{45}\)N\(_5\)NaO\(_8\)\(^+\) 734.3160; Found 734.3167. MS-MS (nanochip-ESI/LTQ-Orbitrap): selected ion 734.3167. Measured b and y ions are reported in the table below

|         | P       | W       |
|---------|---------|---------|
| N-terminal | 1       | 2       |
| b        | -       | -       |
| C-terminal | 2       | 1       |
| y        | 521.28  | 479.23  |
6. Scope on Tetrapeptides

General procedure 5 for the decarboxylative arylation of Tetrapeptides

A 5 mL test tube was charged under Ar with tetrapeptide (5.0 μmol, 1.0 equiv), BIOAc (4.6 mg, 15 μmol, 3.0 equiv), Ru(bpy)₃Cl₂ (1.1 mg, 1.5 μmol, 0.30 equiv) and 1.0 mL of degased MeCN. The solution was degased by argon sparging for 5 min. 0.20 mL of the solution were placed into a sealed vial under argon. The reaction mixture was irradiated using blue light LEDs at rt overnight. Then a 41 mM solution of 1H-indole in MeCN (50 μL, 2.0 μmol, 2.0 equiv) and 2,2,2-trifluoroacetic acid (1.2 μL, 15 μmol, 15 equiv) were added. The reaction was let stirring for 1 h. At the end of the reaction, the crude was diluted with 3x the volume of MeCN and injected in RP-HPLC. The yields were determined as the ratio of Aprod/Atotal where Aprod = area in mAU of the product peak (blue arrow in HPLC traces) and Atotal = area in mAU of all peptides products (product, starting material, and side-products if present (red arrow in HPLC traces)). Reported result is an average of 3 independent trials.

(2S)-N-(2-((1H-indol-3-yl)ethyl)amino)-2-oxoethyl)-2-((S)-2-acetamidopropanamido)-3-phenylpropanamide (8a)

Following general procedure 5, Ac-Ala-Phe-Gly-Ala-OH (7a) afforded 8a in more than 95% HPLC ratio (66% yield with calibration curve) as a mixture of diastereoisomers (retention time 11.299 min).

Reaction performed on 20 μmol scale afforded 8a after purification by preparative RP-HPLC (gradient water-95% acetonitrile in 20 min) as a brown fluffy solid (1.7 mg, 3.6 μmol, 18%).

1H NMR (400 MHz, Acetonitrile-d₅, complex mixture of diastereomers and rotamers) δ 9.21-9.01 (m, 1H, NH indole), 7.66-7.56 (m, 1H, ArH), 7.42-7.35 (m, 1H, ArH), 7.34-7.16 (m, 7H, ArH+NH Gly), 7.13 (dddd, J = 8.2, 7.1, 4.7, 1.1 Hz, 1H, ArH), 7.08-6.91 (m, 3H, ArH+NH Ala+Phe), 6.80-6.64 (m, 1H, NH Ala), 5.41-5.29 (m, 1H, NHCHIndole), 4.33 (dddt, J = 9.2, 7.1, 5.0, 2.2 Hz, 1H, NHCH Phe), 4.10-4.02 (m, 0.5H, AcNHCH Ala), 4.01-3.93 (m, 0.5H, AcNHCH Ala), 3.77-3.68 (m, 2H, NHCH₂ Gly), 3.17 (dt, J = 14.1, 5.0 Hz, 1H, NHCHCH₂Ph Phe), 2.94 (dt, J = 10.3, 5.3 Hz, 1H, NHCHCH₂Ph Phe), 1.84 (s, 1.5H C(O)CH₃ Ac-Ala), 1.77 (s, 1.5H C(O)CH₃ Ac-Ala), 1.55 (dd, J = 6.9, 4.8 Hz, 3H, CH₃ Ala-indole), 1.15 (dd, J = 7.2, 1.5 Hz, 1.5H, CH₃ Ac-Ala), 1.08 (d, J = 7.2 Hz, 1.5H, CH₃ Ac-Ala). 19C NMR (101 MHz, Acetonitrile-d₅, mixture of diastereomers and rotamers, signals not fully resolved) δ 174.3, 174.2, 172.2, 172.2, 168.8, 168.7, 138.6, 138.5, 137.7, 137.6, 130.2, 129.3, 127.6, 122.7, 122.6, 122.6, 120.1, 120.1, 120.0, 120.0, 112.3, 56.2, 56.1, 50.9, 50.9, 43.7, 43.6, 42.6, 42.4, 37.2, 37.1, 22.9, 22.7, 21.6, 21.5, 17.1, 17.0.

HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: [M + H]⁺ Calcd for C_{28}H_{38}N_{5}O_{7}⁺ 478.2449; Found 478.2467. MS-MS (nanochip-ESI/LTQ-Orbitrap): selected ion 478.2467. Measured c and z ions are reported in the table below
Calibration with arylated 8a was achieved through the preparation of several samples of different concentrations and their analysis on RP HPLC. The following linear regression was obtained $y = 0.0001x - 0.0147$ and $R^2 = 0.998$, where $Y$ is the concentration in $\mu$mol/mL of 8a and $X$ the absorbance area of the peak at 214 nm.

![Graph showing linear regression](image)

**Ac-Ala-Phe-Gly-Ala-OH (7a)**

HRMS of 7a (ESI/QTOF) m/z: [M + Na]$^+$ Calcd for C$_{19}$H$_{20}$N$_4$NaO$_6$ 429.1745; Found 429.1736.

HPLC-UV chromatogram at 214 nm

Control experiment without peptide: Iodobenzoic acid (9) (12.713 min) and degradation of Ru(bpy)$_3$Cl$_2$6H$_2$O (5.945, 14.321, 16.218 min) are observed.
Crude reaction mixture:

(2S)-2-((S)-2-acetamidopropanamido)-N-(2-((2-hydroxy-1-(1H-indol-3-yl)ethyl)amino)-2-oxoethyl)-3-phenylpropanamide (8b)

Following general procedure 5, Ac-Ala-Phe-Gly-Ser-OH (7b) afforded 8b in more than 95% HPLC ratio as a mixture of diastereomers (retention time 10.186 min)

HRMS (ESI/QTOF) m/z: [M + Na]^+ Calcd for C_{26}H_{31}N_{5}NaO_{5}^+ 516.2217; Found 516.2220

Ac-Ala-Phe-Gly-Ser-OH (7b)

HRMS of 7b (ESI/QTOF) m/z: [M + Na]^+ Calcd for C_{19}H_{26}N_{4}NaO_{7}^+ 445.1694; Found 445.1688.

HPLC-UV chromatogram at 214 nm of the crude reaction mixture
(2S)-N-(2-((1-(1H-indol-3-yl)-3-oxo-3-(tritylamino)propyl)amino)-2-oxoethyl)-2-((S)-2-acetamidopropanamido)-3-phenylpropanamide (8c)

Following general procedure 5, Ac-Ala-Phe-Gly-Asn(Trt)-OH (7c) afforded 8c in 43% HPLC ratio as a mixture of diastereomers (retention time 16.064 min), which could not be fully separated from a side product.

HRMS (ESI/QTOF) m/z: [M + H]^+ Calcd for C_{46}H_{47}N_{6}O_{5}^+ 763.3602; Found 763.3605.

Ac-Ala-Phe-Gly-Asn(Trt)-OH (7c)

HRMS of 7c (nanochip-ESI/LTQ-Orbitrap) m/z: [M + H]^+ Calcd for C_{39}H_{42}N_{5}O_{7}^+ 692.3079; Found 692.3075.

HPLC-UV chromatogram at 214 nm of the crude reaction mixture

Tert-butyl ((4S,7S)-7-benzyl-13-(1H-indol-3-yl)-4-methyl-2,5,8,11-tetraoxo-3,6,9,12-tetraazaheptadecan-17-yl)carbamate (8d)
Following general procedure 5, Ac-Ala-Phe-Gly-Lys(Boc)-OH (7d) afforded 8d in 35% HPLC ratio as a mixture of diastereomers (retention time 11.683 min).

HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: [M + H]^+ Calcd for C_{34}H_{67}N_{6}O_{6}^+ 635.3552; Found 635.3564.

Ac-Ala-Phe-Gly-Lys(Boc)-OH (7d)

HRMS of 7d (nanochip-ESI/LTQ-Orbitrap) m/z: [M + H]^+ Calcd for C_{27}H_{42}N_{5}O_{8}^+ 564.3028; Found 564.3027.

HPLC-UV chromatogram at 214 nm of the crude reaction mixture.

Methyl1-(1-(2-((S)-2-(2-acetamidopropanamido)-3-phenylpropanamido)acetamido)ethyl)-Nα-((benzyloxy)carbonyl)-L-tryptophanate (8e)

Following general procedure 5, Ac-Ala-Phe-Gly-Ala-OH (7a) afforded 8e in 48% HPLC ratio as a mixture of isomers (retention time 13.873 min + 14.992 min).

HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: [M + H]^+ Calcd for C_{39}H_{65}N_{5}O_{8}^+ 713.3293; Found 713.3287. MS-MS (nanochip-ESI/LTQ-Orbitrap): selected ion 713.3287. Measured b and y ions are reported in the table below.
Methyl1-{1-{2-((S)-2-{2-acetamidopropanamido)-3-phenylpropanamido)acetamido)ethyl}-Na-{{(benzyloxy)carbonyl)-L-valyl}-L-tryptophanate (8f)}

Following general procedure 5, Ac-Ala-Phe-Gly-Ala-OH (7a) afforded 8f in 76% HPLC ratio as a mixture of isomers (retention time 15.302 min + 15.965 min)

HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: [M + H]^+ Calcd for C_{43}H_{54}N_{7}O_{9}^+ 812.3978; Found 812.3973. MS-MS (nanochip-ESI/LTQ-Orbitrap): selected ion 812.3973. Measured b and y ions are reported in the table below

|     | A   | F   | G   | A*  | W*  | V   |
|-----|-----|-----|-----|-----|-----|-----|
| N-terminal b | 1   | 2   | 3   | -   | 4   | -   |
| C-terminal y   | 3   | 2   | 1   | -   | 1   | -   |

HPLC-UV chromatogram at 214 nm of the crude reaction mixture
Tert-butyl (4S,7S)-7-benzyl-13-(1H-indol-3-yl)-4-methyl-2,5,8,11-tetraoxo-3,6,9,12-tetraazapentadecan-15-oate (8g)

Following general procedure 5, Ac-Ala-Phe-Gly-Asp(OtBu)-OH (7e) afforded 8g in 26% HPLC ratio as a mixture of diastereomers (retention time 13.457 min)

HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: [M + H]⁺ Calcd for C₃₁H₄₀N₅O₆⁺ 578.2973; Found 578.2982. MS-MS (nanochip-ESI/LTQ-Orbitrap); selected ion 578.2982. Measured c and z ions are reported in the table below

|        | A      | F      | G      | A*     |
|--------|--------|--------|--------|--------|
| N-terminal | 1  | 2  | 3  | 4  |
| c      | - | - | 278.15 | 335.17 |
| C-terminal | 4  | 3  | 2  | 1  |
| z      | 519.26 | - | - | 244.13 |

Ac-Ala-Phe-Gly-Asp(OtBu)-OH (7e)

HRMS of 7e (nanochip-ESI/LTQ-Orbitrap) m/z: [M + H]⁺ Calcd for C₂₄H₃₅N₄O₆⁺ 507.2449; Found 507.2448.

HPLC-UV chromatogram at 214 nm of the crude reaction mixture
(2S)-N-(2-((1H-indol-3-yl)-2-((1-trityl-1H-imidazol-4-yl)ethyl)amino)-2-oxoethyl)-2-((S)-2-acetamidopropanamido)-3-phenylpropanamide (8h)

Following general procedure 5, Ac-Ala-Phe-Gly-His(Trt)-OH (7f) afforded 8h in 13% HPLC ratio as a mixture of diastereomers (retention time 13.098 min)

HRMS (ESI/QTOF) m/z: [M + H]^+ Calcd for C_{48}H_{48}N_{7}O_{4}^+ 786.3762; Found 786.3744.

Ac-Ala-Phe-Gly-His(Trt)-OH (7f)

HRMS of 7f (nanochip-ESI/LTQ-Orbitrap) m/z: [M + H]^+ Calcd for C_{41}H_{42}N_{6}O_{6}^+ 715.3239; Found 715.3237.

HPLC-UV chromatogram at 214 nm of the crude reaction mixture

(2S)-N-(2-((1H-indol-3-yl)-4-((2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-yl)sulfonyl)guanidino)butyl)amino)-2-oxoethyl)-2-((S)-2-acetamidopropanamido)-3-phenylpropanamide (8i)
Following general procedure 5, Ac-Ala-Phe-Gly-Arg(Pbf)-OH (7g) afforded 8i in 11% HPLC ratio as a mixture of diastereomers (retention time 16.150 min)

HRMS (ESI/QTOF) m/z: [M + H+] Calcd for C_{42}H_{53}N_{8}O_{7}S· 813.3763; Found 813.3754.

Ac-Ala-Phe-Gly-Arg(Pbf)-OH (7g)

HRMS of 7g (nanochip-ESI/LTQ-Orbitrap) m/z: [M + H]+ Calcd for C_{35}H_{50}N_{7}O_{9}S+ 744.3385; Found 744.3383.

HPLC-UV chromatogram at 214 nm of the crude reaction mixture.
7. References

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8. NMR spectra

$^1$H-NMR (400 MHz, Chloroform-$d$) (4a)

$^{13}$C-NMR (101 MHz, Chloroform-$d$) (4a)
$^1$H-NMR (400 MHz, Chloroform-$d$) (4b)

$^{13}$C-NMR (101 MHz, Chloroform-$d$) (4b)
$^1$H-NMR (400 MHz, Chloroform-$d$) (4c)

$^{13}$C-NMR (101 MHz, Chloroform-$d$) (4c)
$^{1}H$-NMR (400 MHz, Chloroform-$d$) (4d)

$^{13}C$-NMR (101 MHz, Chloroform-$d$) (4d)
$^1$H-NMR (400 MHz, Chloroform-$d$) (4e)

$^{13}$C-NMR (101 MHz, Chloroform-$d$) (4e)
$^1$H-NMR (400 MHz, Chloroform-$d$) (4f)

$^{13}$C-NMR (101 MHz, Chloroform-$d$) (4f)
$^1$H-NMR (400 MHz, Chloroform-$d$) (4g)

$^{13}$C-NMR (101 MHz, Chloroform-$d$) (4g)
$^1$H-NMR (400 MHz, Chloroform-$d$) (4h)

$^{13}$C-NMR (101 MHz, Chloroform-$d$) (4h)
$^1$H-NMR (400 MHz, Chloroform-$d$) (4i)

$^{13}$C-NMR (101 MHz, Chloroform-$d$) (4i)
$^1$H-NMR (400 MHz, Chloroform-$d$) (4j)

$^{13}$C-NMR (101 MHz, Chloroform-$d$) (4j)
$^{1}$H-NMR (400 MHz, Chloroform-$d$) (4k)

$^{13}$C-NMR (101 MHz, Chloroform-$d$) (4k)
$^1$H-NMR (400 MHz, Acetonitrile-$d_3$) (4l)

$^{13}$C-NMR (101 MHz, Acetonitrile-$d_3$) (4l)
$^1$H-NMR (400 MHz, Acetonitrile-$d_3$) (4m)

$^{13}$C-NMR (101 MHz, Acetonitrile-$d_3$) (4m)
$^1$H-NMR (400 MHz, Chloroform-$d$) (5a)

$^{13}$C-NMR (101 MHz, Chloroform-$d$) (5a)
$^1$H-NMR (400 MHz, Chloroform-$d$) (5b)

$^{13}$C-NMR (101 MHz, Chloroform-$d$) (5b)
$^1$H-NMR (400 MHz, Acetonitrile-$d_3$) (5c major)

$^{13}$C-NMR (101 MHz, Acetonitrile-$d_3$) (5c major)
$^1\text{H-NMR}$ (400 MHz, Acetonitrile-$d_3$) (5c minor)

$^{13}\text{C-NMR}$ (101 MHz, Acetonitrile-$d_3$) (5c minor)
$^1$H-NMR (400 MHz, Chloroform-$d$) (5d)

$^{13}$C-NMR (101 MHz, Chloroform-$d$) (5d)
$^1$H-NMR (400 MHz, Chloroform-$d$) (5e)

$^{13}$C-NMR (101 MHz, Chloroform-$d$) (5e)
$^1$H-NMR (400 MHz, Chloroform-$d$) (5f)

$^{13}$C-NMR (101 MHz, Chloroform-$d$) (5f)
$^1$H-NMR (400 MHz, Chloroform-$d$) (5g)

$^{13}$C-NMR (101 MHz, Chloroform-$d$) (5g)
$^1$H-NMR (400 MHz, Chloroform-$d$) (5h)

$^{13}$C-NMR (101 MHz, Chloroform-$d$) (5h)
$^{19}$F-NMR (376 MHz, Chloroform-$d$) (5h)
$^1$H-NMR (400 MHz, Chloroform-$d$) (5i)

$^{13}$C-NMR (101 MHz, Chloroform-$d$) (5i)
$^1$H-NMR (400 MHz, Acetonitrile-$d_3$) (5j)

$^{13}$C-NMR (101 MHz, Acetonitrile-$d_3$) (5j)
$^1$H-NMR (400 MHz, Chloroform-$d$) (6a)

$^{13}$C-NMR (101 MHz, Chloroform-$d$) (6a)
$^{1}H$-NMR (400 MHz, Acetonitrile-$d_3$) (6c)

$^{13}C$-NMR (101 MHz, Acetonitrile-$d_3$) (6c)
$^{19}$F-NMR (376 MHz, Acetonitrile-$d_3$) (6c)
$^1$H-NMR (400 MHz, Chloroform-$d$) (6d)

$^{13}$C-NMR (101 MHz, Chloroform-$d$) (6d)
$^1$H-NMR (400 MHz, Chloroform-$d$) (6e)

$^{13}$C-NMR (101 MHz, Chloroform-$d$) (6e)
$^1$H-NMR (400 MHz, Chloroform-$d$) (6f)

$^{13}$C-NMR (101 MHz, Chloroform-$d$) (6f)
$^1$H-NMR (400 MHz, Chloroform-d) (6g)

$^{13}$C-NMR (101 MHz, Chloroform-d) (6g)
$^1$H-NMR (400 MHz, Chloroform-$d$) (6h)

$^{13}$C-NMR (101 MHz, Chloroform-$d$) (6h)
$^1$H-NMR (400 MHz, Chloroform-$d$) (6i)

$^{13}$C-NMR (101 MHz, Chloroform-$d$) (6i)
$^1$H-NMR (400 MHz, Acetonitrile-$d_3$) (6j)

$^{13}$C-NMR (101 MHz, Acetonitrile-$d_3$) (6j)
$^1$H-NMR (400 MHz, Acetonitrile-$d_3$) (8a)

$^{13}$C-NMR (101 MHz, Acetonitrile-$d_3$) (8a)