Supporting Information

for

UV resonance Raman spectroscopy of the supramolecular ligand guanidiniocarbonyl indole (GCI) with 244 nm laser excitation

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DFT calculation results and detailed synthesis routes
Table S1 contains the theoretical vibrational spectrum of GCI ethyl amide in the single protonated form calculated at the B3LYP-D3/6-311++G(d,p) and B2PLYP-D3/G-311++G(d,p) level of theory employing the Gaussian 16 program package. All normal modes together with their wavenumber values and Raman activities are listed.

**Table S1:** Calculated Raman spectrum of GCI ethyl amide in the single protonated form. Level of theory: B3LYP-D3/6-311++G(d,p) and B2PLYP-D3/G-311++G(d,p).

| Mode | Mode | B3LYP-D3 | B2PLYP-D3 |
|------|------|----------|-----------|
|      | Wavenumber [cm⁻¹] | Raman activity | Wavenumber [cm⁻¹] | Raman activity |
| 1    | 19.48 | 1.650 | 22.56 | 1.857 |
| 2    | 36.23 | 2.199 | 37.39 | 2.455 |
| 3    | 41.13 | 2.368 | 42.92 | 2.573 |
| 4    | 46.44 | 3.180 | 46.89 | 2.895 |
| 5    | 60.56 | 1.389 | 60.66 | 1.324 |
| 6    | 73.76 | 1.081 | 70.48 | 0.948 |
| 7    | 86.71 | 1.478 | 87.15 | 1.367 |
| 8    | 119.78 | 0.187 | 111.99 | 0.926 |
| 9    | 140.21 | 2.560 | 131.24 | 2.393 |
| 10   | 169.97 | 1.194 | 168.00 | 0.993 |
| 11   | 203.40 | 0.577 | 196.19 | 0.736 |
| 12   | 218.96 | 4.264 | 217.09 | 6.302 |
| 13   | 254.10 | 6.136 | 229.33 | 8.079 |
| 14   | 257.77 | 0.205 | 250.85 | 2.605 |
| 15   | 272.11 | 2.126 | 253.84 | 0.567 |
| 16   | 276.35 | 0.812 | 272.22 | 0.647 |
| 17   | 297.11 | 2.149 | 290.47 | 4.896 |
| 18   | 312.57 | 6.133 | 293.77 | 6.009 |
| 19   | 328.64 | 1.071 | 324.94 | 0.981 |
| 20   | 362.50 | 1.251 | 354.45 | 0.818 |
| 21   | 387.30 | 2.255 | 380.69 | 2.587 |
| 22   | 407.20 | 4.323 | 401.72 | 7.257 |
| 23   | 421.46 | 2.672 | 406.81 | 2.777 |
| 24   | 459.21 | 2.524 | 434.76 | 1.154 |
| 25   | 471.14 | 1.205 | 456.26 | 1.678 |
| 26   | 481.28 | 11.412 | 465.27 | 1.040 |
| 27   | 484.08 | 9.582 | 483.51 | 21.404 |
| 28   | 502.38 | 5.236 | 493.68 | 5.021 |
| 29   | 533.87 | 2.244 | 522.52 | 1.435 |
| 30   | 584.91 | 2.130 | 572.50 | 3.959 |
| 31   | 589.17 | 4.033 | 585.82 | 4.151 |
| 32   | 603.06 | 7.906 | 596.31 | 7.477 |
| 33   | 614.22 | 4.644 | 611.77 | 4.061 |

S1
|   |       |       |       |       |
|---|-------|-------|-------|-------|
| 34| 666.93| 29.087| 655.34| 5.020 |
| 35| 689.16| 6.086 | 663.70| 21.355|
| 36| 705.35| 8.833 | 671.54| 12.714|
| 37| 723.32| 1.879 | 693.78| 8.293 |
| 38| 739.28| 0.573 | 723.94| 0.789 |
| 39| 746.57| 2.597 | 725.57| 3.438 |
| 40| 774.83| 16.557| 769.92| 13.046|
| 41| 784.71| 4.784 | 780.33| 3.424 |
| 42| 817.87| 11.777| 801.62| 5.651 |
| 43| 819.32| 15.825| 814.89| 24.967|
| 44| 846.48| 7.412 | 829.19| 8.057 |
| 45| 855.83| 2.907 | 838.54| 0.944 |
| 46| 866.71| 1.123 | 844.94| 3.677 |
| 47| 887.68| 6.525 | 885.87| 6.720 |
| 48| 898.35| 45.927| 896.60| 69.450|
| 49| 931.17| 15.989| 926.07| 2.193 |
| 50| 962.74| 0.969 | 927.82| 21.909|
| 51| 970.20| 22.033| 967.93| 24.435|
| 52| 1013.84| 30.355| 1019.52| 23.145|
| 53| 1036.03| 100.442| 1034.13| 72.298|
| 54| 1048.10| 16.370| 1047.45| 11.570|
| 55| 1076.98| 9.311 | 1076.81| 9.791 |
| 56| 1081.14| 18.446| 1082.25| 12.124|
| 57| 1103.62| 69.065| 1106.82| 113.040|
| 58| 1119.63| 83.512| 1113.93| 27.110|
| 59| 1123.71| 9.408 | 1127.13| 6.597 |
| 60| 1140.56| 4.772 | 1138.65| 30.739|
| 61| 1187.80| 9.951 | 1183.44| 9.895 |
| 62| 1213.58| 2.904 | 1205.34| 2.310 |
| 63| 1232.10| 51.645| 1229.34| 30.302|
| 64| 1257.45| 39.564| 1256.48| 40.743|
| 65| 1274.30| 512.863| 1274.30| 282.310|
| 66| 1296.71| 340.337| 1295.87| 429.881|
| 67| 1337.18| 15.908| 1342.55| 69.137|
| 68| 1340.76| 37.363| 1344.11| 18.332|
| 69| 1349.29| 17.612| 1352.06| 95.731|
| 70| 1358.90| 317.856| 1358.26| 236.080|
| 71| 1372.96| 0.635 | 1376.22| 0.552 |
| 72| 1406.46| 70.380| 1405.92| 142.007|
| 73| 1442.67| 11.561| 1448.84| 11.242|
| 74| 1445.31| 7.473 | 1452.04| 7.271 |
| 75| 1458.79| 62.794| 1458.73| 29.875|
| 76| 1465.77| 4.625 | 1462.90| 127.130|
| 77| 1469.42| 85.093| 1473.34| 11.261|
| 78| 1479.42| 60.892| 1474.55| 75.608|
| 79| 1503.22| 516.891| 1501.26| 629.622|
|     | Absorbance [OD] | Wavelength [nm] |
|-----|----------------|-----------------|
| 80  | 1542.27        | 49.245          |
| 81  | 1554.53        | 6.601           |
| 82  | 1595.78        | 1213.020        |
| 83  | 1619.38        | 58.509          |
| 84  | 1649.87        | 3.792           |
| 85  | 1669.50        | 140.290         |
| 86  | 1699.06        | 755.304         |
| 87  | 2913.48        | 276.720         |
| 88  | 2914.39        | 112.570         |
| 89  | 2969.10        | 62.663          |
| 90  | 2995.96        | 149.947         |
| 91  | 2997.05        | 45.912          |
| 92  | 3063.23        | 50.762          |
| 93  | 3073.02        | 90.382          |
| 94  | 3092.48        | 151.471         |
| 95  | 3129.27        | 72.422          |
| 96  | 3263.04        | 91.461          |
| 97  | 3445.49        | 32.851          |
| 98  | 3460.42        | 44.814          |
| 99  | 3463.26        | 134.171         |
| 100 | 3485.90        | 65.572          |
| 101 | 3525.30        | 81.355          |
| 102 | 3570.94        | 63.089          |

**Figure S1:** UV–vis absorption spectra of GCI, RGD, BisTrisBuffer and a 1:1 GCI–RGD mixture.
Figure S2: DFT calculated Raman spectrum of GCI ethyl amide plotted in the region 800–1800 cm$^{-1}$ using the density functional B3LYP-D3 with three different basis sets: Pople & aug-cc-pVTZ & SNSD.

General information

All solvents were distilled before use. Millipore water was obtained with a TKA MicroPure ultrapure water system. All other commercially available reagents were used as obtained unless otherwise specified. The reactions were monitored by TLC on silica gel plates (Macherey-Nagel POLYGRAM SIL G/UV254) and spots were visualized by UV light (254 nm and 366 nm). Reversed phase column chromatography was performed with an Armen Instrument Spot Flash Liquid Chromatography MPLC apparatus with RediSep C-18 Reversed Phase columns. Lyophilisation was done with a Christ Alpha 1-4 LD plus freeze dryer. The melting points were obtained with a Büchi Melting-Point B-540 apparatus with open end glass capillary tubes. The melting points are not corrected. The IR spectra were measured on a Varian 3100 FT-IR Excalibur Series. The low resolution ESI mass spectra were recorded with a Bruker amaZon SL and the high resolution ESI mass spectra with a Bruker maXis 4G UHR-TOF. Analytical HPLC was performed on a Dionex HPLC apparatus that consisted of a P680 pump, an ASI-100 automated sample injector and an UVD 340U photodiode array detector with a YMC ODS-AQ column (column size: 150 × 3.0 mm, particle size: 5 μm, pore size: 12 nm). The NMR spectra were measured with Bruker DMX 300, AV NEO 400, DRX 500 or AVHD 600 spectrometers. All measurements were recorded at room temperature using DMSO-d$_6$ as solvent. The chemical shifts are relative to the signals of DMSO-d$_6$ (δ $^1$H = 2.50 ppm and δ $^{13}$C = 39.5 ppm). The apparent coupling constants are given in hertz (Hz). The description of the fine structure means: s = singlet, br. s = broad singlet, d = doublet, t = triplet, m = multiplet.
Synthesis

The GCI building block I was synthesized starting from commercially available methyl 3-amino-4-iodobenzoate (A) following a synthesis strategy inspired and adjusted from a previous work. The building block I was further functionalized with ethyl amine to achieve GCI ethyl amide 2.

Scheme S1: Synthesis of the GCI ethyl amide 2.

The GCP ethyl amide 1 was synthesized starting from literature-known GCP building block K.

Scheme S2: Synthesis of the GCP ethyl amide 1.
6-(Methoxycarbonyl)-1H-indole-2-carboxylic (C)

To freshly sublimed DABCO (6.074 g, 54.15 mmol, 3 equiv), sodium pyruvate (B, 5.959 g, 54.15 mmol, 3 equiv) and methyl 3-amino-4-iodobenzoate (A, 5 g, 18.05 mmol, 1 equiv), 260 mL degassed dry DMF was added under an argon atmosphere. Then, palladium(II) acetate (0.33 g, 1.47 mmol, 0.08 equiv) was added and the mixture was heated to 105 °C for 19 h. After cooling to room temperature, 150 mL water was added, the solution was acidified with 1 M HCl to pH 2 and extracted with ethyl acetate (5 × 150 mL). The combined organic layers were washed with brine (2 × 150 mL), dried (MgSO₄), and the solvent was evaporated in vacuo to obtain a brown solid. The crude product was purified by column chromatography (SiO₂, ethyl acetate/cyclohexane 2:1 + 1% acetic acid) to give compound C (3.321 g, 15.15 mmol, 84%) as yellow solid.

Molecular Formula: C₁₁H₉NO₄.

Molecular Mass: 219.193 g/mol.

¹H NMR (300 MHz, DMSO-d₆): δ [ppm] = 13.14 (s, 1H, COOH), 12.17 (s, 1H, NH), 8.11 (s, 1H, H-7), 7.75 (d, J = 8.5 Hz, 1H, H-5), 7.65 (dd, J = 8.5, 1.5 Hz, 1H, H-4), 7.16 (dd, J = 2.0, 0.8 Hz, 1H, H-3), 3.87 (s, 3H, CH₃).

¹³C NMR (75 MHz, DMSO-d₆): δ [ppm] = 166.79, 162.39, 131.61, 130.19, 125.07, 121.94, 120.94, 120.08, 114.51, 107.03, 51.93.

HR-MS: (pos. ESI, MeOH) m/z = 220.0616 ([M+H]+, calc.: 220.0604).

FT-IR (ATR) ν [cm⁻¹] = 3648.66 (s), 2534.01 (w), 2159.88 (w), 2032.6 (w), 1683.55 (m), 1506.13 (m), 1438.64 (s), 1240 (m), 827.312 (s), 771.387 (s), 732.817 (s).

mp: 230 °C (decomposition).

N-tert-Boc-guanidine (F)

The reaction was performed as described in the literature. A solution of t-Boc₂O (E, 12.0 g, 55.0 mmol, 1 equiv) in acetonitrile (100 mL) was added very slowly over 8 h at 0 °C under vigorous stirring to a mixture of guanidinium chloride (D, 26.3 g, 275 mmol, 5 equiv) in an aqueous sodium hydroxide solution (12.0 g, 0.3 mol NaOH in 50 mL water). The resulting suspension was stirred at room temperature for additional 20 h. The acetonitrile was evaporated in vacuo and then 100 mL water was added. The aqueous suspension was extracted with ethyl acetate (3 times with 100 mL). The combined organic phases were washed with brine (3 times with 100 mL), dried (MgSO₄), and evaporated in vacuo. The resulting white crystals were dried to yield 7.66 g (87%) of analytically pure guanidine F.

Molecular Formula: C₆H₁₃N₃O₂.
Molecular Mass: 159.186 g/mol.

$^1$H NMR (300 MHz, DMSO-d$_6$): δ [ppm] = 6.88 (br.s 4H, NH), 1.33 (s, 9H, Boc-H).

$^{13}$C NMR (75 MHz, DMSO-d$_6$): δ [ppm] = 28.19, 75.49, 162.62, 163.25.

HR-MS: (pos. ESI, MeOH) m/z = 160.1081 ([M+H]$^+$, calc.: 160.1081).

FT-IR (ATR) $\tilde{\nu}$ [cm$^{-1}$] = 3408 (s), 1650 (s), 1540 (s), 1450 (m), 1311 (s), 1253 (m), 1142 (s), 1066 (s), 950 (w), 806 (m).

mp: 165 °C (decomposition).

6-((Benzyloxy)carbonyl)-1H-indole-2-carboxylic acid (G)

A sodium benzylate solution, prepared from sodium (0.603 g, 26.33 mmol, 5 equiv) in dry benzyl alcohol (300 mL), was added to a solution of carboxylic acid C (1.071 g 4.88 mmol, 1 equiv) in dry benzyl alcohol (48 mL) and dry toluene (42 mL) under argon. The resulting dark brown solution was stirred at 95 °C for 4 h. After cooling to room temperature, 1 M hydrochloric acid (26 mL) and water (60 mL) was added. The solution was extracted with chloroform (3 × 100 mL) and the solvent evaporated in vacuo. The crude product was purified by flash chromatography (RP-18 MeOH/H$_2$O, 40% MeOH to 100% MeOH, gradient) to give product G (0.589 g, 2.03 mmol, 40%) as yellow solid.

Molecular Formula: C$_{17}$H$_{13}$NO$_4$.

Molecular Mass: 295.289 g/mol.

$^1$H NMR (300 MHz, DMSO-d$_6$): δ [ppm] = 13.23 (s, 1H, COOH), 12.13 (s, 1H, NH), 8.15 (s, 1H, H-7), 7.76 (d, $J$ = 8.5 Hz, 1H, H-5), 7.68 (dd, $J$ = 8.5, 1.4 Hz, 1H, H-4), 7.52 – 7.33 (m, 5H, Cbz-Ar-H), 7.19 – 7.11 (m, 1H, H-3), 5.37 (s, 2H, Cbz-CH$_2$).

$^{13}$C NMR (75 MHz, DMSO-d$_6$): δ [ppm] = 166.15, 162.33, 136.27, 131.71, 130.31, 128.49, 128.05, 127.95, 124.99, 122.02, 120.14, 114.64, 107.03, 65.99.

HR-MS: (pos. ESI, MeOH) m/z = 296.0920 ([M+H]$^+$, calc.: 296.0917).

FT-IR (ATR) $\tilde{\nu}$ [cm$^{-1}$] = 3853.08 (s), 3748.94 (s), 3675.66 (s), 3648.66 (s), 3253.32 (w), 2528.22 (w), 2159.88 (w), 2034.53 (w), 1673.91 (m), 1324.86 (m), 1241.93 (m), 1207.22 (m).

mp: 209 °C (decomposition).
Benzyl 2-((N-(tert-butoxycarbonyl)carbamimidoyl)carbamoyl)-1H-indole-6-carboxylate (H)

A mixture of the benzyl ester G (0.358 g, 1.256 mmol, 1 equiv), HCTU (1.0392 g, 2.512 mmol, 2 equiv), and NMM (0.5082 g, 5.024 mmol, 4 equiv) was stirred in DMF abs. (15 mL) at room temperature for 15 min. Then, t-Boc-guanidine F (0.299 g, 1.884 mmol, 1.5 equiv) was added and the resulting solution stirred at 40 °C. After 19 h the solution was poured into vigorously stirred water (150 mL) at 0 °C. A slightly yellow solid precipitated. The product was filtered, washed with cold water, and dried in vacuo, yielding the product H as slightly yellow solid (0.528 g, 1.21 mmol, 96%).

**Molecular Formula:** C_{23}H_{24}N_{4}O_{5}.

**Molecular Mass:** 436.47 g/mol.

**{^1}H NMR** (400 MHz, DMSO-d_6): δ [ppm] = 11.82 (s, 1H, NH), 10.99 (s, 1H, NH), 9.48 (s, 1H, NH), 8.63 (s, 1H, NH), 8.17 (s, 1H, H-7), 7.73 (d, J = 8.5 Hz, 1H, H-5), 7.65 (dd, J = 8.5, 1.4 Hz, 1H, H-4), 7.51 – 7.33 (m, 5H, Cbz-Ar-H), 7.18 (s, 1H, H-3), 5.36 (s, 2H, Cbz-CH₂), 1.48 (s, 9H, Boc-CH₃).

**{^{13}}C NMR** (101 MHz, DMSO-d_6): δ [ppm] = 166.33, 158.64, 136.42, 136.16, 130.72, 128.55, 128.09, 128.00, 121.88, 119.96, 114.62, 105.64, 65.96, 27.73.

**HR-MS:** (pos. ESI, MeOH) m/z = 437.1815 ([M+H]^+ , calc.: 437.1819).

**FT-IR:** (ATR) ν [cm⁻¹] = 3853.08 (s), 3748.94 (s), 3675.66 (s), 3648.66 (s), 2524.36 (w), 2159.88 (w), 2030.68 (w), 1700.91 (m), 1617.98 (m), 1558.2 (m), 1540.85 (m), 1496.49 (m), 1191.79 (m), 1145.51 (m), 1085.73 (m).

**mp:** 270 °C.

GCI building block (I)

A mixture of the benzyl ester H (0.528 g, 1.21 mmol, 1 equiv), 10% Pd/C (30 mg) in 150 mL methanol, and 5 mL triethylamine was vigorously stirred under a hydrogen atmosphere for 16 h. The resulting solution was filtered through a folded filter and washed with methanol/triethylamine. The solvent was removed under reduced pressure yielding the GCI building block I as off-white solid (0.516 g, 1.15 mmol, 95%).

**Molecular Formula:** C_{22}H_{33}N_{5}O_{5}.

**Molecular Mass:** 447.528 g/mol.
$^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ [ppm] = 11.76 (s, 1H, NH), 9.46 (s, 1H, NH), 8.63 (s, 1H, NH), 8.09 (d, J = 0.8 Hz, 1H, H-7), 7.68 – 7.59 (m, 2H, H-5, H-4), 7.17 (s, 1H, H-3), 2.65 (q, J = 7.2 Hz, 6H, NEt$_3$-CH$_2$), 1.48 (s, 9H, Boc-CH$_3$), 1.02 (t, J = 7.2 Hz, 9H, NEt$_3$-CH$_3$).

$^{13}$C NMR (101 MHz, DMSO-$d_6$): $\delta$ [ppm] = 168.79, 158.59, 136.43, 129.77, 121.21, 120.51, 114.37, 105.70, 81.50, 45.37, 27.75, 10.48.

HR-MS: (pos. ESI, MeOH) m/z = 347.1351 ([M+H]$^+$, calc.: 347.1350).

FT-IR (ATR) $\tilde{\nu}$ [cm$^{-1}$] = 3648.66 (s), 2979.48 (w), 2159.88 (w), 1718.26 (s), 1540.85 (m), 1496.49 (m), 1365.35 (m), 1321 (w), 1238.08 (w), 1147.44 (s), 746.317 (s).

mp: 138 °C.

Boc-GCI ethyl amide J

The GCI building block I (79 mg, 0.223 mmol, 1 equiv) and HCTU (184.2 mg, 0.446 mmol, 2 equiv) was dissolved in DMF abs. (10 mL) and NMM (90.23 mg, 0.892 mmol, 4 equiv) was added. After stirring the solution for 20 min at room temperature ethylamine (15 mg, 0.335 mmol, 1.5 equiv) was added and the resulting solution was stirred at room temperature for 17 h. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (RP-18 MeOH/H$_2$O, 20% MeOH to 100% MeOH, gradient) to give amide J (60.1 mg, 0.161 mmol, 72%) as white solid.

Molecular Formula: C$_{18}$H$_{23}$N$_5$O$_4$.

Molecular Mass: 373.406 g/mol.

$^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ [ppm] = 11.73 (s, 1H, NH), 10.96 (s, 1H, NH), 9.43 (s, 1H, NH), 8.61 (s, 1H, NH), 8.41 (t, J = 5.5 Hz, 1H, H-7), 7.95 (s, 1H, H-3), 7.65 (d, J = 8.4 Hz, 1H, H-5), 7.52 (dd, J = 8.5 Hz, 1H, H-4), 7.17 (s, 1H, NH), 3.35 – 3.24 (m, 2H, CH$_2$), 1.47 (s, 9H, Boc-CH$_3$), 1.13 (t, J = 7.2 Hz, 3H, CH$_3$).

$^{13}$C NMR (300 MHz, DMSO-$d_6$): $\delta$ [ppm] = 159.58, 158.79, 155.42, 132.97, 125.22, 115.90, 112.17, 33.62, 14.58.

HR-MS: (pos. ESI, MeOH) m/z = 374.1826 ([M+H]$^+$, calc.: 374.1823).

FT-IR (ATR) $\tilde{\nu}$ [cm$^{-1}$]: 3357.46 (w), 2979.48 (w), 1725.98 (w), 1625.7 (m), 1546.63 (m), 1511.92 (m), 1369.21 (w), 1326.79 (m), 1241.93 (s), 1147.44 (s), 844.669 (m), 752.102 (w), 632.537 (m), 609.396 (m).

mp: 124 °C (decomposition).
GCl ethyl amide 2

To a solution of Boc-GCI ethyl amide J (221 mg, 0.592 mmol, 1 equiv) in DCM/TFA (15 mL each), was added and the solution was stirred at room temperature for 3 h. The solvent was evaporated in vacuo to receive the off-white crude product, which was purified by flash chromatography (RP 18 MeOH/H₂O + 0.1% TFA, 10% MeOH + 0.1% TFA to 100% MeOH + 0.1% TFA, gradient) and treated several times with 1 M HCl with respective solvent removal to give the chloride salt 2 (103 mg, 0.333 mmol, 56%) as white solid with a purity of 97% (HPLC).

Molecular Formular: C₁₃H₁₆ClN₅O₂.

Molecular Mass: 309.751 g/mol.

¹H NMR (600 MHz, DMSO-d₆): δ [ppm] = 12.36 (m, 2H, indole-NH, amide-NH), 8.76 (s, 2H, guanidine-NH), 8.54 (m, 3H, guanidine-NH), 7.99 (s, 1H, H-7), 7.95 (d, 1H, J = 1.4 Hz, H-3), 7.76 (d, 1H, J = 8.5 Hz, H-5), 7.59 (dd, J = 8.5, 1.3 Hz, 1H, H-4), 3.33 – 3.27 (m, 2H, C₅H₂), 1.13 (t, 3H, J = 7.2 Hz, CH₃).

¹³C NMR (151 MHz, DMSO-d₆): δ [ppm] = 166.32, 161.06, 155.46, 137.37, 132.07, 130.24, 128.25, 122.17, 119.40, 112.44, 108.00, 34.14, 14.87.

HR-MS: (pos. ESI, MeOH) m/z = 274.1318 ([M+H]+, calc.: 274.1299)

FT-IR (ATR) ν [cm⁻¹] = 3097.12 (w), 2159.88 (w), 2032.6 (w), 1683.55 (m), 1635.34 (m), 1606.41 (m), 1560.13 (m), 1498.42 (s), 1448.28 (s), 1413.57 (s), 1375 (s), 1322.93 (m), 1216.86 (w), 1081.87 (s), 836.955 (s), 727.032 (m), 632.537 (w).

mp: 189 °C.

Boc-GCP-ethyl amide L

GCP building block K (5 g, 12.6 mmol, 1 equiv), HCTU (10.42 g, 25.2 mmol, 2 equiv) and NMM (5.10 g, 50.4 mmol, 4 equiv) were dissolved in dry DMF (200 mL). After 15 min ethylamine [2 M in THF] (9.5 mL, 18.9 mmol, 1.5 equiv) was added and the reaction mixture was stirred at room temperature for 16 h, extracted with chloroform (5 × 100 mL) and dried in vacuo. The crude product was purified by flash chromatography (RP-18 MeOH/H₂O, 10% MeOH to 100% MeOH, gradient) to give the product L (2.62 g, 8.11 mmol, 64%) as off-white solid.

Molecular Formula: C₁₄H₂₁N₅O₄.

Molecular Mass: 323.348 g/mol.
$^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ [ppm] = 11.24 (s, 1H, NH), 10.85 (s, 1H, NH), 9.32 (s, 1H, NH), 8.57 (s, 1H, NH), 8.33 (s, 1H, pyrrole-CH), 6.81 (s, 1H, pyrrole-CH), 6.75 (d, $J = 3.8$ Hz, 1H, pyrrole-CH), 3.25 (q, $J = 7.1$, 5.6 Hz, 2H, CH$_2$), 1.45 (s, 9H, Boc-CH$_3$), 1.11 (t, $J = 7.2$ Hz, 3H, CH$_3$).

$^{13}$C NMR (151 MHz, DMSO-$d_6$): $\delta$ [ppm] = 159.37, 158.43, 111.50, 48.60, 33.54, 27.77, 14.78.

HR-MS: (pos. ESI, MeOH) m/z = 324.1666 ([M+H]$^+$, calc.: 324.1666).

FT-IR (ATR) $\tilde{\nu}$ [cm$^{-1}$]: 3748.94 (s), 3648.66 (s), 3318.89 94. (w), 2977.55 (w), 2159.88 (w), 2030.68 (w), 1718.26 (s), 1621.84 (m), 1540.85 (m), 1455.99 (s), 1367.28 (s), 1286.29 (m), 1238.08 (w), 1141.65 (w), 842.74 (s), 748.245 (m);

mp: 138 °C.

GCP ethyl amide 1

Boc-GCP-ethyl amide L (101 mg, 0.308 mmol, 1 equiv) was dissolved in dichloromethane (2 mL). TFA (2 mL) was added and the reaction mixture was stirred at room temperature for 3 h. The solvent was removed under reduced pressure and the crude product was treated with 1 M HCl. The solvent was removed to receive GCP ethyl amide 1 as white solid (90 mg, 0.267 mmol, 87%) with a purity of 95% (HPLC).

Molecular Formula: C$_9$H$_{14}$ClN$_5$O$_2$.

Molecular Mass: 259.693 g/mol.

$^1$H NMR (600 MHz, DMSO-$d_6$): $\delta$ [ppm] = 12.32 (s, 1H, pyrrole-NH), 11.32 (s, 1H, amide-NH), 8.55 – 8.12 (m, $J = 11.2$, 5.1 Hz, 5H, guanidine-NH), 7.16 (dd, $J = 3.9$, 2.3 Hz, 1H, pyrrole-CH), 6.85 (dd, $J = 3.8$, 2.4 Hz, 1H, pyrrole-CH), 3.33 – 3.21 (m, 2H, CH$_2$), 1.12 (t, $J = 7.2$ Hz, 3H, CH$_3$).

$^{13}$C NMR (151 MHz, DMSO-$d_6$): $\delta$ [ppm] = 158.81, 155.03, 132.89, 125.22, 115.50, 112.09, 33.63, 14.58.

HR-MS: (pos. ESI, MeOH) m/z = 224.1148 ([M+H]$^+$, calc.: 224.1142).

FT-IR: (ATR) $\tilde{\nu}$ [cm$^{-1}$] = 3309.21 (w), 2159.88 (s), 1685.48 (w), 1633.41 (m), 1558.2 (m), 1473.35 (s), 1292.07 (s), 1203.36 (s), 1064.51 (s), 804.171 (s), 746.317 (m), 698.105 (m), 609.396 (m).

mp: 234 °C (decomposition).
NMR Spectra

Figure S3: $^1$H NMR spectrum of C (300 MHz, DMSO-$_d$6).

Figure S4: $^{13}$C NMR spectrum of C (75 MHz, DMSO-$_d$6).
Figure S5: $^{1}$H NMR spectrum of F (300 MHz, DMSO-$d_6$).

Figure S6: $^{13}$C NMR spectrum of F (75 MHz, DMSO-$d_6$).
Figure S7: $^1$H NMR spectrum of G (300 MHz, DMSO-$d_6$).

Figure S8: $^{13}$C NMR spectrum of G (75 MHz, DMSO-$d_6$).
Figure S9: $^1$H NMR spectrum of H (400 MHz, DMSO-$d_6$).

Figure S10: $^{13}$C NMR spectrum of H (101 MHz, DMSO-$d_6$).
Figure S11: $^1$H NMR spectrum of I (400 MHz, DMSO-$d_6$).

Figure S12: $^{13}$C NMR spectrum of I (101 MHz, DMSO-$d_6$).
Figure S13: $^1$H NMR spectrum of J (300 MHz, DMSO-$d_6$).

Figure S14: $^{13}$C NMR spectrum of J (75 MHz, DMSO-$d_6$).
Figure S15: $^{1}$H NMR spectrum of 2 (600 MHz, DMSO-$d_6$).

Figure S16: $^{13}$C NMR spectrum of 2 (151 MHz, DMSO-$d_6$).
Figure S17: $^1$H NMR spectrum of $L$ (300 MHz, DMSO-$d_6$).

Figure S18: $^{13}$C NMR spectrum of $L$ (101 MHz, DMSO-$d_6$).
Figure S19: $^1$H NMR spectrum of 1 (600 MHz, DMSO-$d_6$).

Figure S20: $^{13}$C NMR spectrum of 1 (151 MHz, DMSO-$d_6$).
Mass spectra

**Figure S21**: HR-ESI mass spectrum of C (positive ion mode, MeOH) and predicted mass spectrum of peaks which belongs to C.

**Figure S22**: HR-ESI mass spectrum of F (positive ion mode, MeOH) and predicted mass spectrum of peaks which belongs to F.
Figure S23: HR-ESI mass spectrum of G (positive ion mode, MeOH) and predicted mass spectrum of peaks which belongs to G.

Figure S24: HR-ESI mass spectrum of H (positive ion mode, MeOH) and predicted mass spectrum of peaks which belongs to H.
Figure S25: HR-ESI mass spectrum of I (positive ion mode, MeOH) and predicted mass spectrum of peaks which belongs to I.

Figure S26: HR-ESI mass spectrum of J (positive ion mode, MeOH) and predicted mass spectrum of peaks which belongs to J.
Figure S27: HR-ESI mass spectrum of 2 (positive ion mode, MeOH) and predicted mass spectrum of peaks which belongs to 2.

Figure S28: HR-ESI mass spectrum of L (positive ion mode, MeOH) and predicted mass spectrum of peaks which belongs to L.
**Figure S29:** HR-ESI mass spectrum of 1 (positive ion mode, MeOH) and predicted mass spectrum of peaks which belongs to 1.
Analytical HPLC

**Figure S30:** Analytical HPLC (RP 18 MeOH/H$_2$O + 0.1% TFA, 10% MeOH + 0.1% TFA to 100% MeOH + 0.1% TFA, gradient) 2.

**Figure S31:** Analytical HPLC (RP 18 MeOH/H$_2$O + 0.1% TFA, 10% MeOH + 0.1% TFA to 100% MeOH + 0.1% TFA, gradient) 1.

**References**

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