Supporting Information

Synthesis of bioactive and stabilized cyclic peptides by macrocyclization using C(sp³)-H activation

Jian Tang, Yadong He, Hongfei Chen, Wangjian Sheng and Huan Wang*
State Key Laboratory of Coordination Chemistry, School of Chemistry and Chemical Engineering, Nanjing University, Nanjing 210093, China
Email: wanghuan@nju.edu.cn

Table of Contents

1. General Information…………………………………………………………………S2
2. Experiment Section…………………………………………………………………..S3
   A. General procedure for the synthesis of linear peptides
   B. General procedure for Pd-catalyzed peptide macrocyclization
   C. Methods for HPLC analysis to assess the purity of peptides
   D. Optimization of reaction conditions for the cyclization of peptides
   E. Synthesis of celogentin C ring A
   F. Cell culture and staining experiments
   G. Experimental figures
   H. Structural characterization of linear and cyclic peptides

References
1. General Information

Solvents were obtained from Sigma-Aldrich, Alfa-Aesar and Acros and used directly without further purification unless indicated. Amino acids and derivatives were obtained from commercial sources. EDCI (N-(3-Dimethylaminopropyl)-N′-ethylcarbodiimide hydrochloride), silver acetate, HFIP (hexafluoro-2-propanol) and aryl iodides were commercially available and used without any purification. Analytical thin layer chromatography was performed on 0.25 mm silica gel 60-F254. Visualization was carried out with UV light. \(^1^H\) NMR spectra were recorded on Bruker AMX-400 instrument (400 MHz) or Bruker DRX-600 instrument (600 MHz). The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Coupling constants, J, were reported in Hertz unit (Hz). \(^{13}C\) NMR spectra were recorded on Bruker AMX-400 instrument (100 MHz) or Bruker DRX-600 instrument (150 MHz), and were fully decoupled by broad band proton decoupling. High-resolution mass spectra (HRMS) were recorded on an Agilent Mass spectrometer using ESI-TOF (electrospray ionization-time of flight). HPLC profiles were obtained on Agilent 1260 HPLC system using commercially available columns.

2. Experimental Section

A. General procedure for linear peptide synthesis

Typically, to a solution of L-amino acid (AA) benzyl ester hydrochloride (15 mmol) and 4-methylmorpholine (NMM, 17 mmol) in DMF was added Phth-Ala-OH (10 mmol) and 1-Hydroxy-7-azabenzotriazole (HOAt, 10 mmol). The mixture was cooled in an ice bath and subsequently 1-ethyl-3-(3- (dimethylamino)propyl)carbodiimide hydrochloride (EDCI, 12 mmol) was added in one portion. After 1.5 h at 0 °C and 6 h at room temperature, the mixture was partitioned between H$_2$O and EtOAc. The aqueous layer was extracted with EtOAc. The organic phase was washed successively with H$_2$O, 0.5 N HCl solution, saturated aqueous NaHCO$_3$ solution and brine, then it was dried over anhydrous Na$_2$SO$_4$, filtered and concentrated to give the ester (Phth-Ala-AA-Obzl) as a white solid. The procedure was repeated to elongate the oligopeptides until the \(^1 m\)-I-Phe was incorporated. (Phth-Ala-OH (>99% ee) was prepared according to literature report.$^1$ \(^1 m\)-I-Phe-OMe was prepared according to literature report$^2$ from \(^1 m\)-I-Phe.)
Scheme S1. Preparation of linear peptides through solution-phase peptide synthesis.
Scheme S2. Procedure for cyclic peptide synthesis through SPPS and on-resin macrocyclization.

B. General procedure for Pd-catalyzed peptide macrocyclization

Typically, the linear peptide (0.2 mmol, 1 eq), Pd(OAc)$_2$ (0.02 mmol, 0.1 eq), AgOAc (0.4 mmol, 2 eq) and DCE (4 ml) was added to a 15 ml sealed reaction tube (a cylinder thick wall pressure-resistance tube purchased from Beijing Synthware Glass Inc.) in air. The reaction mixture was heated and stirred at 100 °C for 12-15 h. Upon completion, the tube was cooled to room temperature and the reaction mixture was diluted by DCM (5 ml), filtered through a Celite pad. The filtrate was concentrated under reduced pressure. The resulting mixture was purified by semi-preparative RP-HPLC, typically using H$_2$O and ACN with 0.1% formic acid as the eluent. The resulting pure cyclized peptide was typically obtained as a white solid.
For on-resin peptide macrocyclization, the resin-bound linear peptide containing $m$-I-Phe (0.05 mmol, 1 eq) was mixed with Pd(OAc)$_2$ (0.02 mmol, 0.1 eq), AgOAc (0.1 mmol, 2 eq) and DCE (2 ml) in a sealed reaction tube. The mixture was first stirred at room temperature for 15 min and then heated at 100 °C for 16 h. The reaction mixture was allowed to cool to room temperature and the resin was filtered and washed by DCE for three times. Finally, the resulting resin-bound cyclic peptide was cleaved from the resin using a solution of TFA/H$_2$O/TIS (95:2.5:2.5) for 2 h. TFA was then removed and the resulting residue was purified by RP-HPLC to yield the cyclic peptide as white solid.

C. Methods for HPLC analysis to assess the purity of peptides

Analytical HPLC analysis was performed using Phenomenex C18 (5 μm, 2.0 × 150 mm) analytical column with mobile phase of water-acetonitrile-(0.1% formic acid) at a flow rate of 1.0 mL/min. Gradient used: isocratic 2% CH$_3$CN for 5 min, then 2% to 85% CH$_3$CN in 15 min, then 85% to 95% CH$_3$CN in 5 min, then isocratic 95% CH$_3$CN for 5 min.

D. Optimization of reaction conditions for the cyclization of peptides

<table>
<thead>
<tr>
<th>Additives</th>
<th>Solvent</th>
<th>Temp (°C)</th>
<th>Yield %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 AgTFA</td>
<td>DMF</td>
<td>120</td>
<td>18</td>
</tr>
<tr>
<td>2 Ag$_2$CO$_3$</td>
<td>DMF</td>
<td>120</td>
<td>n.r</td>
</tr>
<tr>
<td>3 AgOAc</td>
<td>HFIP</td>
<td>100</td>
<td>41</td>
</tr>
<tr>
<td>4 AgOAc</td>
<td>DMF</td>
<td>120</td>
<td>50</td>
</tr>
<tr>
<td>5a AgOAc</td>
<td>DMF</td>
<td>120</td>
<td>trace</td>
</tr>
<tr>
<td>6b AgOAc</td>
<td>DMF</td>
<td>100</td>
<td>n.r</td>
</tr>
<tr>
<td>7 -</td>
<td>DMF</td>
<td>120</td>
<td>n.r</td>
</tr>
<tr>
<td>8 AgOAc</td>
<td>DCE</td>
<td>120</td>
<td>61</td>
</tr>
<tr>
<td>9 AgOAc</td>
<td>DCE</td>
<td>100</td>
<td>76</td>
</tr>
</tbody>
</table>

Table S1. Optimization of reaction conditions for the cyclization of peptides.
Table S2. Peptide sequences attempted for cyclization using para- and ortho-iodophenyl- alanine.

<table>
<thead>
<tr>
<th>Linear peptides</th>
<th>Cyclization</th>
<th>Deiodination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phth-Ala-Gly-Gly-p-I-Phe-OMe</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Phth-Ala-Gly-Val-p-I-Phe-OMe</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Phth-Ala-Gly-Gly-o-I-Phe-OMe</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Phth-Ala-Gly-Val-o-I-Phe-OMe</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

**E. Synthesis of celogentin C ring A**

Under the atmosphere of N\(_2\), Compound 2q (86.7 mg, 0.1 mmol) was suspended in 5 ml of n-butanol at room temperature, followed by the addition of ethylenediamine (0.7 ml, 1 mmol, 10 eq.). The resulting reaction mixture was stirred for 10 h. Upon completion, reaction solvent was removed and the resulting residue was subjected to next reaction without further purification. The residue was mixed with pyroglutamic acid (19.5 mg, 0.15 mmol 1.5 eq) and HOAt (20.4 mg, 0.15 mmol, 1.5 eq), NMM (19 µL, 0.17 mmol, 1.7 eq), EDC (0.12 mmol, 23 mg, 1.2 eq) in anhydrous DMF. The reaction mixture was first stirred at 0°C for 1.5 h and then allowed to proceed at room temperature for additional 6 h. Upon completion, EtOAc and water (1:1, 10 ml) was added and the aqueous layer was extracted with EtOAc (10 ml) for 3 times, The organic phase were combined and dried over anhydrous Na\(_2\)SO\(_4\), concentrated and purified by flash chromatography to yield compound 2r (60% yield over two steps).

**F. Cell culture and staining experiments**

U87MG cell were grown and maintained in DMEM media with 10% FBS and 1% penicillin/streptomycin at 37 °C, 5% CO\(_2\). Before staining experiment with peptides, the cells were seeded on the surface of MatTek glass bottom microwell dishes using 1 mL media. After 1 day, the cells were washed twice with warm DMEM media, incubated at 37 °C with suitable 2 µM peptides for 90 min and fixed. Images were taken using a Leica TCS SP8 confocal fluorescence microscope.
G. Experimental figures

**Figure S1.** HPLC analysis of linear peptide 1a and the resulting cyclic peptide 2a after macrocyclization.

**Figure S2a.** NMR and LC-MS analysis of cyclic peptide 2g generated through macrocyclization of peptide 1g. A). two peaks correspond to the methyl group of Aib residue. B) LC-MS analysis of cyclic peptide 2g indicates a d.r. value of 60:40.
Figure S2b. NMR and LC-MS analysis of cyclic peptide 2h generated through macrocyclization of peptide 1h. A), one doublet peak corresponds to the Hα of Phe1. The coupling vicinal coupling between Hα and Hβ of Phe1 was determined to be 12.0 Hz. B) LC-MS analysis of cyclic peptide 2h indicates a single diastereomer.

Figure S3. HPLC and HRMS analysis of the cyclic peptide 2q. (a) HPLC analysis of cyclic peptide 2q showed a sharp single peak, indicating a single diastereoisomer. (b) HRMS (ESI) Calcd for C47H57N5O9SNa [M+Na]^+: 890.3775 Da; found: 890.3770 Da.
**Figure S4.** HMBC analysis of the cyclic peptide 2q.

**Figure S5.** $^1$H NMR (400M Hz, CDCl$_3$) analysis of the cyclic peptide 2q. Hα of β'-Leu1 showed signal as a double–doublet peak (4.95-4.98 ppm) with a coupling constant of $J_{\alpha\beta}$(Leu1)=12.0 Hz with Hβ of β'-Leu1.
Figure S6. Proposed catalytic intermediates in C-H activations.

Scheme S3. Chemical structures of cyclic peptides in Table 1.

G. Structural characterization of linear and cyclic peptides

**Linear peptide 1a**  
Phth-Ala-Gly-Gly-\textit{m}-I-Phe-OMe

$^1$H NMR (400 MHz, CD$_3$CN) $\delta$ 7.89 – 7.77 (m, 4H), 7.63 – 7.56 (m, 2H), 7.38 (t, $J = 5.3$ Hz, 1H), 7.20
(d, J = 7.8 Hz, 1H), 7.18 – 7.09 (m, 2H), 7.09 – 7.01 (m, 1H), 4.94 (q, J = 7.2 Hz, 1H), 4.53 (td, J = 8.2, 5.9 Hz, 1H), 3.85 – 3.76 (m, 2H), 3.72 (dt, J = 17.1, 5.8 Hz, 2H), 3.63 (d, J = 5.9 Hz, 3H), 3.01 (dd, J = 13.8, 5.8 Hz, 1H), 2.90 (dd, J = 13.8, 8.4 Hz, 1H), 1.62 – 1.58 (m, 3H).

13C NMR (100 MHz, CD3CN) δ 172.0, 171.2, 169.7, 169.6, 168.5, 140.3, 138.7, 136.3, 135.1, 132.6, 130.9, 129.4, 123.8, 117.9, 94.3, 54.3, 52.3, 48.9, 43.9, 42.7, 37.0, 14.9.


1H NMR (400M Hz, CD3CN) (linear peptide 1a):

13C NMR (100M Hz, CD3CN) (linear peptide 1a):
HRMS (ESI) (linear peptide 1a):

\[ [M+Na]^+ \text{ m/z calcd for C}_{25}H_{24}N_4O_7Na 515.1543, \text{ found } 515.1609. \]

**Cyclic peptide 2a**

1H NMR (400 MHz, CD3CN) \( \delta \) 7.83 (s, 4H), 7.52 (s, 1H), 7.13 (s, 2H), 7.07 (t, \( J = 7.6 \text{ Hz}, 1H \)), 6.94 (dd, \( J = 15.4, 7.6 \text{ Hz}, 2H \)), 6.58 (d, \( J = 7.4 \text{ Hz}, 1H \)), 5.15 (dd, \( J = 9.0, 2.5 \text{ Hz}, 1H \)), 4.67 (td, \( J = 7.3, 4.9 \text{ Hz}, 1H \)), 3.80 (d, \( J = 6.6 \text{ Hz}, 2H \)), 3.78 – 3.73 (m, 1H), 3.72 (s, 3H), 3.63 (dd, \( J = 16.6, 5.9 \text{ Hz}, 1H \)), 3.36 (dd, \( J = 13.8, 2.4 \text{ Hz}, 1H \)), 3.29 (dd, \( J = 13.8, 9.0 \text{ Hz}, 1H \)), 3.13 (dd, \( J = 14.2, 7.0 \text{ Hz}, 1H \)), 3.07 (dd, \( J = 14.2, 4.9 \text{ Hz}, 1H \)).

13C NMR (100 MHz, CD3CN) \( \delta \) 172.0, 170.1, 169.9, 169.0, 168.3, 138.5, 136.6, 135.3, 132.4, 132.3, 129.2, 129.0, 127.8, 123.9, 54.3, 53.6, 52.3, 44.2, 42.8, 36.7, 35.0.

HRMS (ESI) [M+Na]^+ m/z calcd for C_{25}H_{23}N_4O_7Na 515.1543, found 515.1609.

1H NMR (400M Hz, CD3CN) (cyclic peptide 2a):
C NMR (100M Hz, CD$_3$CN) (cyclic peptide 2a):

$^{13}$C NMR (100M Hz, CD$_3$CN) (cyclic peptide 2a):
HSQC (100M Hz, CD$_3$CN) (cyclic peptide 2a):

HMBC (100M Hz, CD$_3$CN) (cyclic peptide 2a):
HRMS (ESI) (cyclic peptide 2a):

Linear peptide 1b
Phth-Ala-Leu-Gly-m-I-Phe-OMe

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.81 (dt, $J$ = 6.9, 3.5 Hz, 2H), 7.77 – 7.68 (m, 2H), 7.52 (d, $J$ = 7.9 Hz, 1H), 7.43 (s, 1H), 7.31 – 7.23 (m, 1H), 7.19 (d, $J$ = 7.8 Hz, 1H), 7.07 (d, $J$ = 7.7 Hz, 1H), 6.98 (t, $J$ = 7.7 Hz, 1H), 6.88 (d, $J$ = 7.3 Hz, 1H), 4.94 (q, $J$ = 7.2 Hz, 1H), 4.70 (dd, $J$ = 14.1, 6.6 Hz, 1H), 4.51 – 4.37 (m, 1H), 4.07 (ddd, $J$ = 22.7, 15.5, 6.5 Hz, 1H), 3.85 (dd, $J$ = 16.7, 5.3 Hz, 1H), 3.64 (s, 3H), 2.95 (ddd, $J$ = 34.0, 13.8, 6.5 Hz, 2H), 1.65 (t, $J$ = 8.0 Hz, 3H), 1.62 – 1.51 (m, 2H), 1.26 (t, $J$ = 7.1 Hz, 1H), 0.90 (dd, $J$ = 8.4, 6.2 Hz, 6H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 172.3, 171.6, 169.8, 168.8, 167.8, 138.6, 138.2, 136.1, 134.4, 131.8, 130.2, 128.6, 123.6, 94.3, 77.4, 77.1, 76.7, 60.4, 53.4, 52.6, 52.4, 49.1, 43.2, 40.3, 37.3, 24.8, 23.0, 21.8, 15.4.

HRMS (ESI) [M+Na]$^+$ m/z calcd for C$_{29}$H$_{33}$IN$_4$O$_7$Na 699.1292, found 699.1360.
$^1$H NMR (400 MHz, DMSO-d$_6$) (linear peptide 1b):

$^{13}$C NMR (100 MHz, DMSO-d$_6$) (linear peptide 1b):
HRMS (ESI) (linear peptide 1b):

\[
\text{Cyclic peptide 2b}
\]

\[
\begin{align*}
{^1}H \text{ NMR (400 MHz, DMSO)} & \delta 8.31 (dd, J = 7.1, 5.1 \text{ Hz, 1H}), 8.21 (d, J = 6.9 \text{ Hz, 1H}), 7.96 - 7.84 (m, 4H), 7.37 (s, 1H), 7.25 (t, J = 7.6 \text{ Hz, 1H}), 7.11 (d, J = 7.7 \text{ Hz, 1H}), 7.04 (d, J = 7.6 \text{ Hz, 1H}), 6.80 (d, J = 7.0 \text{ Hz, 1H}), 5.01 (dd, J = 11.8, 2.2 \text{ Hz, 1H}), 4.56 (ddd, J = 9.4, 7.1, 3.8 \text{ Hz, 1H}), 4.22 - 4.06 (m, 1H), 3.88 (dd, J = 16.9, 7.4 \text{ Hz, 1H}), 3.66 (s, 3H), 3.62 (s, 1H), 3.40 (d, J = 4.9 \text{ Hz, 1H}), 3.00 - 2.86 (m, 1H), 2.77 (d, J = 12.1 \text{ Hz, 1H}), 1.44 - 1.37 (m, 1H), 1.33 (dd, J = 10.4, 4.7 \text{ Hz, 2H}), 0.76 - 0.71 (m, 6H). \\
{^{13}}C \text{ NMR (100 MHz, DMSO)} & \delta 172.9, 169.8, 167.9, 167.5, 139.2, 136.3, 135.0, 132.2, 130.6, 129.1, 128.3, 126.9, 123.5, 53.7, 53.3, 52.9, 52.5, 42.9, 40.6, 40.4, 40.2, 39.9, 39.9, 39.5, 39.4, 36.8, 35.4, 24.5, 23.2, 21.5. \\
\text{HRMS (ESI) } [\text{M+H}]^+ \text{ m/z calcd for } C_{29}H_{33}N_7O_7 549.2349, \text{ found } 549.2352.
\end{align*}
\]
$^1$H NMR (400 MHz, DMSO-d$_6$) (cyclic peptide 2b):

$^{13}$C NMR (100 MHz, DMSO-d$_6$) (cyclic peptide 2b):
HRMS (ESI) (cyclic peptide 2b):

[Image]

**Linear peptide 1c**
Phth-Ala-Val-Gly-\textit{m}-I-Phe-OMe

\[\text{Phth-Ala-Val-Gly-}\textit{m}-\text{I-Phe-OMe}\]

\(^1\)H NMR (400 MHz, DMSO-d6) \(\delta\) 8.29 – 8.17 (m, 3H), 7.86 – 7.84 (m, 4H), 7.67 – 7.52 (m, 2H), 7.22 (d, \(J = 7.7\) Hz, 1H), 7.07 (t, \(J = 7.8\) Hz, 1H), 4.75 (q, \(J = 7.1\) Hz, 1H), 4.45 (dd, \(J = 13.7, 7.9\) Hz, 1H), 4.06 (t, \(J = 8.0\) Hz, 1H), 3.69 (d, \(J = 6.1\) Hz, 2H), 3.57 (s, 3H), 2.96 (dd, \(J = 13.5, 5.6\) Hz, 1H), 2.85 (dd, \(J = 13.6, 8.8\) Hz, 1H), 1.87 (dd, \(J = 13.6, 6.8\) Hz, 1H), 1.50 (d, \(J = 7.2\) Hz, 3H), 0.74 (dd, \(J = 19.5, 6.6\) Hz, 6H).

\(^1^3\)C NMR (100 MHz, DMSO-d6) \(\delta\) 171.6, 171.3, 168.8, 168.7, 167.4, 139.7, 137.7, 135.3, 134.3, 131.9, 130.4, 128.5, 122.9, 94.7, 58.9, 53.3, 51.8, 48.0, 41.4, 4.1, 39.9, 39.7, 39.5, 39.3, 39.1, 38.9, 36.1, 29.8, 19.2, 18.6, 15.2, 14.5,

HRMS (ESI) [M+H]+ m/z calcd for C\textsubscript{38}H\textsubscript{32}IN\textsubscript{4}O\textsubscript{7}, 663.1316, found 663.1306.
$^1$H NMR (400 MHz, DMSO-$d_6$) (linear peptide 1c):

$^{13}$C NMR (100 MHz, DMSO-$d_6$) (linear peptide 1c):
HRMS (ESI) (linear peptide 1c):

![HRMS Graph for Linear Peptide 1c]

\[
[M+Na]^+ \quad m/z \text{ calcd for } C_{28}H_{30}N_4O_7Na 557.2012, \text{ found } 557.2011.
\]

**Cyclic peptide 2c**

![Cyclic Peptide 2c Structure]

\(^1\)H NMR (400 MHz, DMSO) \(\delta\) 8.31 (t, \(J = 6.1\) Hz, 1H), 7.98 (d, \(J = 7.8\) Hz, 1H), 7.94 – 7.86 (m, 4H), 7.31 – 7.22 (m, 3H), 7.16 (d, \(J = 7.6\) Hz, 1H), 7.08 (d, \(J = 8.9\) Hz, 1H), 6.92 (d, \(J = 6.9\) Hz, 1H), 4.85 (dd, \(J = 12.0\), 2.3 Hz, 1H), 4.52 (ddd, \(J = 10.4\), 6.4, 3.1 Hz, 1H), 3.94 (t, \(J = 7.7\) Hz, 1H), 3.75 (d, \(J = 12.8\) Hz, 1H), 3.68 (s, 3H), 3.59 (d, \(J = 7.0\) Hz, 1H), 3.55 (d, \(J = 5.7\) Hz, 1H), 3.09 (dd, \(J = 14.1\), 3.5 Hz, 1H), 2.95 – 2.86 (m, 1H), 2.83 (s, 1H), 1.84 (dd, \(J = 14.0\), 6.9 Hz, 1H), 0.70 (t, \(J = 7.2\) Hz, 6H).

\(^1^3\)C NMR (101 MHz, DMSO) \(\delta\) 172.1, 172.0 – 171.5, 169.9, 167.7, 167.6, 138.8, 136.47 (s), 135.0, 132.0, 131.4 – 130.55, 129.3, 128.7 – 127.8, 127.3 – 126.3, 123.6, 59.8, 54.8, 53.8, 52.5, 42.8, 40.0, 36.7, 36.0 – 34.3, 29.5, 19.5, 18.7.

HRMS (ESI) \([M+Na]^+\) m/z calcd for \(C_{28}H_{30}N_4O_7Na\) 557.2012, found 557.2011.

\(^1\)H NMR (400 MHz, DMSO-\(d_6\)) (cyclic peptide 2c):

![Cyclic Peptide 2c NMR Graph]
$^{13}$CNMR (100M Hz, DMSO-$d_6$) (cyclic peptide 2c):
HRMS (ESI) (cyclic peptide 2c):

![Image]

**Linear peptide 1d**

Phth-Ala-Ile-Gly-\textit{m}-I-Phe-OMe

\[
\begin{align*}
\text{Phth} & \quad \text{Ala} & \quad \text{Ile} & \quad \text{Gly} & \quad \text{\textit{m}} & \quad \text{I} & \quad \text{Phe} & \quad \text{OMe} \\
\text{Ph} & \quad \text{NH} & \quad \text{O} & \quad \text{O} & \quad \text{O} & \quad \text{NH} & \quad \text{O} & \quad \text{COOMe}
\end{align*}
\]

\[^1H\text{ NMR (400 MHz, DMSO)} \delta 8.24 (dd, J = 13.4, 6.8 Hz, 2H), 8.17 (d, J = 8.1 Hz, 1H), 7.91 – 7.79 (m, 4H), 7.58 (d, J = 7.4 Hz, 2H), 7.22 (d, J = 7.7 Hz, 1H), 7.08 (t, J = 7.8 Hz, 1H), 4.75 (q, J = 7.2 Hz, 1H), 4.50 – 4.40 (m, 1H), 4.11 (t, J = 8.2 Hz, 1H), 3.70 (ddd, J = 38.0, 16.7, 5.8 Hz, 2H), 3.58 (s, 3H), 3.00 – 2.92 (m, 1H), 2.87 (dd, J = 13.7, 8.7 Hz, 1H), 1.76 – 1.62 (m, 1H), 1.50 (d, J = 7.2 Hz, 3H), 1.33 (ddd, J = 13.4, 7.6, 3.3 Hz, 1H), 1.06 – 0.93 (m, 1H), 0.81 – 0.66 (m, 6H). \\
\[^{13}C\text{ NMR (100 MHz, DMSO)} \delta 172.1, 171.9, 169.3, 169.2, 167.9, 140.2, 138.2, 135.8, 134.8, 132.4, 130.9, 129.0, 123.4, 95.2, 58.1, 53.8, 52.3, 48.5, 41.9, 40.0, 36.0, 24.8, 15.7, 15.7, 11.1.
\]

HRMS (ESI) [M+Na]\(^+ m/z\) calec for C\(_{29}\)H\(_{31}\)IN\(_4\)O\(_7\)Na 699.1292, found 699.1322.
$^1$H NMR (400M Hz, DMSO-d6) (linear peptide 1d):  

$^{13}$C NMR (100M Hz, DMSO-d6) (linear peptide 1d):
HRMS (ESI) (linear peptide 1d):

\[
[M+Na]^+ \\
[M+H]^+
\]

**Cyclic peptide 2d**

\^H NMR (400 MHz, DMSO) \(\delta\) 8.30 (dd, \(J = 7.1, 5.1\) Hz, 1H), 8.21 (d, \(J = 6.9\) Hz, 1H), 7.96 – 7.84 (m, 4H), 7.37 (s, 1H), 7.25 (t, \(J = 7.6\) Hz, 1H), 7.11 (d, \(J = 7.6\) Hz, 1H), 7.04 (d, \(J = 7.6\) Hz, 1H), 6.80 (d, \(J = 7.0\) Hz, 1H), 5.01 (dd, \(J = 11.7, 2.1\) Hz, 1H), 4.62 – 4.50 (m, 1H), 4.13 (d, \(J = 8.2\) Hz, 1H), 3.88 (dd, \(J = 16.9, 7.4\) Hz, 1H), 3.68 (s, 1H), 3.66 (s, 3H), 3.50 (s, 1H), 3.06 (dd, \(J = 14.0, 3.6\) Hz, 1H), 2.93 (dd, \(J = 14.0, 9.2\) Hz, 1H), 2.77 (d, \(J = 12.2\) Hz, 1H), 1.46 – 1.29 (m, 3H), 0.76 – 0.71 (m, 6H).

\[^{13}\text{C} NMR (100 MHz, DMSO) \delta\) 172.9, 171.8, 169.8, 167.9, 167.5, 139.2, 136.3, 135.0, 132.2, 130.6, 129.1, 128.3, 126.9, 123.5, 53.7, 53.3, 52.9, 52.5, 42.9, 40.6, 40.4, 40.2 (s), 39.9, 39.7, 39.5, 39.3, 36.8, 35.42, 24.5, 23.2, 21.5.

HRMS (ESI) [M+H]^+ \(m/z\) calcd for \(\text{C}_{30}\text{H}_{35}\text{N}_{7}\text{O}_{5}\) 549.2349, found 549.2347.
$^1$H NMR (400M Hz, DMSO-$d_6$) (cyclic peptide 2d):

$^{13}$CNMR (100M Hz, DMSO-$d_6$) (cyclic peptide 2d):
HRMS (ESI) (cyclic peptide 2d):

[Image of HRMS spectrum]

Linear peptide 1e
Phth-Ala-Phe-Gly-\(m\)-I-Phe-OMe

\(^1\)H NMR (400 MHz, DMSO) \(\delta\) 8.37 (d, \(J = 7.7\) Hz, 1H), 8.29 (dd, \(J = 9.8, 5.3\) Hz, 2H), 7.85 (s, 4H), 7.65 – 7.53 (m, 2H), 7.23 (d, \(J = 7.7\) Hz, 1H), 7.20 – 7.04 (m, 6H), 4.73 (q, \(J = 7.2\) Hz, 1H), 4.47 (dd, \(J = 14.0, 8.3\) Hz, 1H), 4.40 (ddd, \(J = 10.0, 7.9, 4.4\) Hz, 1H), 3.79 (dd, \(J = 16.8, 6.0\) Hz, 1H), 3.64 (dd, \(J = 9.9, 6.8\) Hz, 1H), 3.59 (s, 3H), 3.03 – 2.94 (m, 1H), 2.93 – 2.81 (m, 2H), 2.81 – 2.73 (m, 1H), 1.45 (d, \(J = 7.2\) Hz, 3H).

\(^1\)C NMR (100 MHz, DMSO) \(\delta\) 172.0, 171.9, 169.4, 169.2, 167.6, 140.2, 138.4, 138.1, 135.9, 134.8, 132.2, 130.9, 129.5, 129.1, 128.4, 126.6, 123.5, 95.2, 55.4, 53.9, 52.4, 48.3, 42.1, 39.9, 37.2, 36.6, 15.3.

HRMS (ESI) [M+Na]^+ m/z calcd for C\(_{32}\)H\(_{31}\)IN\(_4\)O\(_7\)Na 733.1135, found 733.1194.

\(^1\)H NMR (400 MHz, DMSO-\(d_6\)) (linear peptide 1e):
$^{13}$C NMR (100M Hz, DMSO-d$_6$) (linear peptide 1e):

HRMS (ESI) (linear peptide 1e):
Cyclic peptide 2e

\[ \text{\text{\rotatebox{90}{\includegraphics[width=0.5\textwidth]{peptide2e.png}}}} \]

$^1$H NMR (400 MHz, DMSO) $\delta$ 8.28 – 8.10 (m, 2H), 7.89 (s, 4H), 7.25 (dd, $J = 14.6, 7.0$ Hz, 2H), 7.08 (dd, $J = 17.8, 7.7$ Hz, 2H), 7.03 – 6.88 (m, 6H), 4.93 (dd, $J = 11.7, 2.2$ Hz, 1H), 4.52 (ddd, $J = 10.4, 7.0, 3.7$ Hz, 1H), 4.33 (ddd, $J = 10.3, 7.7, 4.5$ Hz, 1H), 3.82 – 3.73 (m, 1H), 3.71 (s, 1H), 3.67 (d, $J = 3.7$ Hz, 3H), 3.53 (dd, $J = 16.6, 5.4$ Hz, 1H), 3.07 (dd, $J = 14.0, 3.5$ Hz, 1H), 2.96 – 2.84 (m, 2H), 2.81 (d, $J = 12.0$ Hz, 1H), 2.71 (dd, $J = 14.1, 10.2$ Hz, 1H).

$^{13}$C NMR (100 MHz, DMSO) $\delta$ 171.9, 171.7, 169.7, 167.6, 167.3, 138.9, 138.11, 136.6, 134.9, 132.0, 130.7, 129.2, 128.3, 127.0, 126.4, 123.6, 55.4, 53.9, 53.8, 52.5, 43.1, 40.0, 36.7, 36.5, 35.0.

MS (ESI) [M+H]$^+$ m/z calcd for C$_{32}$H$_{31}$IN$_4$O$_7$ 583.22, found 583.25.

HRMS (ESI) [M+Na]$^+$ m/z calcd for C$_{32}$H$_{30}$N$_4$O$_7$Na 605.2012, found 605.2008.

$^1$H NMR (400 MHz, DMSO-$d_6$) (cyclic peptide 2e):

![NMR Spectrum](image.png)
$^{13}$C NMR (100M Hz, DMSO-$d_6$) (cyclic peptide 2e):

HRMS (ESI) (cyclic peptide 2e):
**Linear peptide 1f**

Phth-Ala-Gly-Gly-Ala-\(l\)-Phe-OMe

![Peptide Structure](image)

\(^1^H\) NMR (400 MHz, MeOD) \(\delta\) 7.76 (dt, \(J = 6.7, 3.5\) Hz, 2H), 7.74 – 7.69 (m, 2H), 7.50 – 7.43 (m, 2H), 7.12 (d, \(J = 7.7\) Hz, 1H), 6.94 (t, \(J = 7.8\) Hz, 1H), 4.91 (d, \(J = 7.2\) Hz, 1H), 4.50 (dd, \(J = 8.4, 5.8\) Hz, 1H), 4.21 (t, \(J = 7.2\) Hz, 1H), 3.81 – 3.74 (m, 4H), 3.57 (d, \(J = 4.0\) Hz, 3H), 3.00 (dd, \(J = 13.9, 5.8\) Hz, 1H), 2.88 – 2.81 (m, 1H), 1.53 (d, \(J = 7.2\) Hz, 3H), 1.14 (d, \(J = 7.2\) Hz, 3H).

\(^1^C\) NMR (100 MHz, MeOD) \(\delta\) 173.4, 171.5, 171.0, 169.9, 167.9, 139.4, 137.9, 135.7, 134.2, 131.9, 123, 128.5, 123.0, 93.5, 53.6, 51.4, 49.0, 48.6 – 46.3, 43.1, 42.16 (s), 36.3, 16.5, 14.0.

HRMS (ESI) [M+Na]^+ m/z calcd for C\(_{28}\)H\(_{30}\)IN\(_5\)O\(_8\)Na 714.1037, found 714.1051.

\(^1^H\) NMR (400 MHz, MeOH-d\(_4\)) (linear peptide 1f):
$^{13}$C NMR (100M Hz, MeOH-d$_4$) (linear peptide 1f):

HRMS (ESI) (linear peptide 1f):
Cyclic peptide 2f

\[ \begin{array}{c}
\text{MeOOC} \\
\text{N} \\
\text{NH} \\
\text{O} \\
\text{O} \\
\text{NH} \\
\text{N} \\
\text{H} \\
\text{O} \\
\text{HN} \\
\text{O} \\
\end{array} \]

\( ^1H \) NMR (400 MHz, DMSO) \( \delta \) 8.40 – 8.37 (m, 1H), 8.15 (t, \( J = 5.5 \) Hz, 1H), 7.97 (d, \( J = 7.9 \) Hz, 1H), 7.93 – 7.83 (m, 5H), 7.42 (s, 1H), 7.11 (t, \( J = 7.6 \) Hz, 1H), 6.96 (dd, \( J = 16.0, 7.7 \) Hz, 2H), 4.92 (dd, \( J = 9.0, 5.2 \) Hz, 1H), 4.57 (ddd, \( J = 10.9, 8.0, 3.1 \) Hz, 1H), 4.19 (t, \( J = 7.2 \) Hz, 1H), 3.77 (dd, \( J = 15.8, 6.4 \) Hz, 1H), 3.74 – 3.70 (m, 1H), 3.67 (s, 3H), 3.66 – 3.62 (m, 1H), 3.56 (d, \( J = 7.0 \) Hz, 2H), 3.23 – 3.14 (m, 1H), 3.10 (dd, \( J = 14.2, 2.9 \) Hz, 1H), 2.96 (dd, \( J = 14.3, 10.5 \) Hz, 1H), 1.12 (d, \( J = 7.2 \) Hz, 3H).

\( ^13C \) NMR (101 MHz, DMSO) \( \delta \) 172.8, 172.2, 170.3, 169.5, 167.9, 138.1, 135.1, 131.9, 130.5, 128.6, 127.7, 127.3, 123.7, 55.4, 52.5, 44.0, 43.0, 40.6, 40.5, 40.2, 39.9, 39.7, 39.5, 39.3, 36.1, 35.2, 17.5.

HRMS (ESI) [M+Na]\(^+\) m/z calcd for C\(_{28}\)H\(_{29}\)N\(_5\)O\(_8\)Na 586.1914, found 586.1913.

\( ^1H \) NMR (400M Hz, DMSO -d\(_6\)) (cyclic peptide 2f):
$^{13}$C NMR (400M Hz, DMSO -d$_6$) (cyclic peptide 2f):

HRMS (ESI) (cyclic peptide 2f):
**Linear peptide 1g**

Phth-Aib-Gly-Gly-m-I-Phe-OMe

\[ \text{HRMS (ESI) \[M+Na\]^+ m/z} \text{ calcd for } C_{26}H_{27}IN_4O_7\text{Na 657.0744, found 657.0969.} \]

\[ \text{1H NMR (100M Hz, CDCl}_3\text{) \[\delta 173.9, 171.4, 169.6, 169.0, 138.7, 138.2, 136.1, 134.5, 131.7, 130.3, 128.6, 123.4, 94.3, 61.3, 53.4, 52.3, 44.0, 43.2, 37.3, 24.6.} \]

\[ \text{13C NMR (100 MHz, CDCl}_3\text{) \[\delta 173.9, 171.4, 169.6, 169.0, 138.7, 138.2, 136.1, 134.5, 131.7, 130.3, 128.6, 123.4, 94.3, 61.3, 53.4, 52.3, 44.0, 43.2, 37.3, 24.6.} \]

\[ \text{1H NMR (100M Hz, CDCl}_3\text{) (linear peptide 1g):} \]
$^{13}$C NMR (100M Hz, CDCl$_3$) (linear peptide 1g):

HRMS (ESI) (linear peptide 1g):

Cyclic peptide 2g

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.82 – 7.65 (m, 5H), 7.56 (d, $J = 10.1$ Hz, 1H), 7.08 (d, $J = 8.6$ Hz, 1H), 7.00 – 6.85 (m, 1H), 6.82 – 6.73 (m, 1H), 6.72 – 6.63 (m, 1H), 6.51 (dd, $J = 19.0, 7.3$ Hz, 1H), 4.94 (dt, $J = 8.9, 4.5$ Hz, 1H), 4.56 – 4.44 (m, 1H), 4.24 – 4.08 (m, 2H), 3.74 (d, $J = 28.6$ Hz, 3H), 3.70 – 3.48 (m, 2H), 3.36 – 3.15 (m, 2H), 3.00 – 2.77 (m, 2H), 2.13 (d, $J = 10.8$ Hz, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 172.7, 172.0, 171.9, 170.7, 169.5, 169.4, 169.0, 168.9, 136.8, 136.7, 136.0, 135.4, 134.7, 134.5, 133.0, 132.6, 131.2, 131.1, 129.0, 128.4, 128.1, 127.7, 127.6, 123.5, 123.4, 66.2, 66.1, 53.9, 52.6, 52.5, 51.9, 45.1, 44.6, 29.3, 27.3, 27.2, 27.0.
HRMS (ESI) [M+Na]⁺ m/z calcd for C_{26}H_{30}N_{4}O_{7}Na 529.1699, found 529.1690.

^1^H NMR (400 MHz, CDCl₃) (cyclic peptide 2g):

(Note: the peak at 1.26 ppm is due to the “grease” from the solvent)

^1^3^C NMR (100 MHz, CDCl₃) (cyclic peptide 2g):
HRMS (ESI) (cyclic peptide 2g):

![HRMS spectrum](image)

**Linear peptide 1h**

Phth-Phe-Gly-Gly-m-I-Phe-OMe

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 7.73 – 7.62\) (m, 4H), 7.54 – 7.42 (m, 3H), 7.19 (dd, \(J = 15.6, 9.8\) Hz, 1H), 7.15 – 7.06 (m, 7H), 6.98 (t, \(J = 7.7\) Hz, 1H), 5.13 (dd, \(J = 11.2, 5.3\) Hz, 1H), 4.70 (dd, \(J = 13.6, 7.3\) Hz, 1H), 4.00 (dd, \(J = 16.8, 5.4\) Hz, 1H), 3.94 – 3.75 (m, 3H), 3.65 (s, 3H), 3.57 (dd, \(J = 14.1, 5.3\) Hz, 1H), 3.44 (dd, \(J = 14.1, 11.3\) Hz, 1H), 3.02 (dd, \(J = 13.9, 5.8\) Hz, 1H), 2.94 (dd, \(J = 13.6, 7.0\) Hz, 1H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta 171.6, 169.6, 169.3, 168.8, 168.0, 138.6, 138.2, 136.5, 136.1, 134.4, 131.4, 130.3, 129.0, 128.6, 127.0, 123.5, 94.4, 60.4, 55.0, 53.5, 52.5, 43.5, 42.9, 37.2, 34.7, 21.1, 14.2.

HRMS (ESI) [M+Na]\(^+\) m/z calcd for C\(_{31}\)H\(_{29}\)N\(_4\)I\(_3\)O\(_3\)Na 719.0979, found 719.0975.
$^1$H NMR (400 MHz, CDCl$_3$) (linear peptide 1h):

(Note: the peak at 1.26 ppm is due to the “grease” from solvent.)

$^{13}$C NMR (100 MHz, CDCl$_3$) (linear peptide 1h):
HRMS (ESI) (linear peptide 1h):

719.0975
720.1003
721.1038

Cyclic peptide 2h

\[ \text{Cyclic peptide 2h} \]

\[^{1}H\text{ NMR (400 MHz, CDCl}_3) \] \( \delta \) 7.75 (dt, \( J = 7.5, 3.8 \text{ Hz, } 2\text{H} \)), 7.71 – 7.64 (m, 2H), 7.60 (t, \( J = 5.8 \text{ Hz, } 1\text{H} \)), 7.43 (d, \( J = 7.9 \text{ Hz, } 1\text{H} \)), 7.30 (t, \( J = 7.7 \text{ Hz, } 2\text{H} \)), 7.25 (s, 2H), 7.08 (ddd, \( J = 24.5, 14.9, 7.4 \text{ Hz, } 3\text{H} \)), 6.80 – 6.71 (m, 2H), 5.71 (d, \( J = 12.9 \text{ Hz, } 1\text{H} \)), 5.24 (d, \( J = 12.9 \text{ Hz, } 1\text{H} \)), 4.72 (ddd, \( J = 10.0, 7.7, 4.7 \text{ Hz, } 1\text{H} \)), 4.14 (dd, \( J = 16.0, 7.2 \text{ Hz, } 1\text{H} \)), 3.96 (dd, \( J = 15.2, 6.1 \text{ Hz, } 1\text{H} \)), 3.79 (s, 3H), 3.62 (dd, \( J = 15.2, 5.7 \text{ Hz, } 1\text{H} \)), 3.50 (dd, \( J = 15.9, 5.6 \text{ Hz, } 1\text{H} \)), 3.27 (dd, \( J = 14.2, 4.7 \text{ Hz, } 1\text{H} \)), 2.96 (dd, \( J = 14.1, 10.0 \text{ Hz, } 1\text{H} \)).

\[^{13}C\text{ NMR (100 MHz, CDCl}_3) \] \( \delta \) 171.9 – 171.5, 169.8, 169.3, 169.2 – 168.9, 139.7, 139.5, 136.8, 134.5 , 130.0, 129.9 – 129.8, 128.9 , 128.0, 127.5, 126.4, 126.6, 58.8, 53.4, 53.1, 52.6, 50.4, 44.4 – 44.1, 44.0 , 37.0, 3.0, 29.3, 27.2, 22.7

HRMS (ESI) \([\text{M+Na}]^+ \) m/z caled for C\(_{31}\)H\(_{29}\)N\(_4\)O\(_7\)Na 591.1934, found 591.1894.

\[^{1}H\text{ NMR (400 MHz, CDCl}_3) \) (cyclic peptide 2h):
(Note: the peak at 1.26 ppm is due to the “grease” from solvent.)

$^{13}$C NMR (100 MHz, CDCl$_3$) (cyclic peptide 2h):
HRMS (ESI) (cyclic peptide 2h):

![HRMS Graph]

EIC trace of 591.1894 Da:

![EIC Graph]

Linear peptide 1i

![Linear Peptide Structure]

$^{1}$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.84 (dt, $J$ = 6.9, 3.5 Hz, 2H), 7.75 (td, $J$ = 5.1, 2.0 Hz, 2H), 7.54 – 7.45 (m, 2H), 7.40 (d, $J$ = 1.4 Hz, 1H), 7.08 – 7.02 (m, 2H), 6.98 (d, $J$ = 7.7 Hz, 1H), 6.96 – 6.89 (m, 1H), 4.97 (q, $J$ = 7.2 Hz, 1H), 4.70 (q, $J$ = 6.5 Hz, 1H), 4.44 (td, $J$ = 6.3, 4.2 Hz, 1H), 3.98 (d, $J$ = 7.7 Hz, 1H), 3.01 – 2.97 (m, 1H), 2.90 (d, $J$ = 6.4 Hz, 1H), 1.70 (d, $J$ = 7.2 Hz, 3H), 1.16 (s, 9H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 171.3, 170.3, 169.3, 168.6, 167.7, 162.6, 138.5, 138.1, 136.0, 134.4, 131.8, 130.2, 128.5, 123.7, 94.3, 79.7 – 75.2, 74.3, 60.6, 54.0, 53.4, 52.3, 48.8, 43.4 37.4, 27.4, 15.2.

HRMS (ESI) [M+Na]$^+$ m/z calcd for C$_{30}$H$_{36}$IN$_2$NaO$_8$ 729.1397, found 729.1475.

$^{1}$H NMR (400MHz, CDCl$_3$-d) (linear peptide 1i):
$^{13}$C NMR (100M Hz, CDCl$_3$-d) (linear peptide 1i):
HRMS (ESI) (linear peptide 1i):

\[ \text{Cyclic peptide 2i} \]

\(^1\text{H NMR (400 MHz, CDCl}_3\text{)} \delta 7.86 (dt, \ J = 6.9, 3.5 Hz, 2H), 7.80 – 7.73 (m, 2H), 7.31 (t, \ J = 7.6 Hz, 1H), 7.27 (s, 1H), 7.16 (dd, \ J = 19.3, 7.6 Hz, 2H), 6.69 – 6.60 (m, 1H), 6.54 (d, \ J = 6.9 Hz, 1H), 6.47 (d, \ J = 7.2 Hz, 1H), 4.97 (dd, \ J = 11.9, 2.3 Hz, 1H), 4.75 – 4.65 (m, 1H), 4.41 (dd, \ J = 10.5, 5.6 Hz, 1H), 4.17 (d, \ J = 13.0 Hz, 1H), 4.12 – 4.02 (m, 1H), 3.79 (s, 3H), 3.75 (dd, \ J = 8.8, 3.9 Hz, 2H), 3.31 (ddd, \ J = 18.5, 11.5, 5.0 Hz, 2H), 3.07 (dd, \ J = 13.6, 1.9 Hz, 1H), 2.93 (dd, \ J = 14.1, 10.2 Hz, 1H), 1.07 (s, 9H).

\(^{13}\text{C NMR (100 MHz, CDCl}_3\text{)} \delta 171.7, 170.2, 169.2, 167.8, 167.7, 137.4, 136.7, 134.5, 131.6, 129.8, 127.9, 127.4, 123.7, 79.2 – 76.1, 74.0, 60.6, 55.7, 54.1, 53.2, 52.6, 43.5, 36.8, 34.9, 27.3..

HRMS (ESI) \([M+Na]^+ \text{m/z calcd for } C_{30}H_{34}N_4O_8Na 601.2274, \text{ found 601.2299}.

\(^1\text{H NMR (400M Hz, CDCl}_3\text{-d)}\):
$^1$C NMR (100M Hz, CDCl$_3$-d) (cyclic peptide 2i):
HRMS ESI (cyclic peptide 2i):

Linear peptide 1j

Phth-Ala-Lys(Boc)-Gly-\(m\)-I-Phe-OMe

\(^{1}\text{H NMR (400 MHz, DMSO) \delta 8.32 (dd, } J = 17.8, 7.6 \text{ Hz, } 2\text{H), 8.18 (t, } J = 5.8 \text{ Hz, } 1\text{H), 7.91 – 7.79 (m, } 4\text{H), 7.58 (d, } J = 7.5 \text{ Hz, } 2\text{H), 7.23 (d, } J = 7.7 \text{ Hz, } 1\text{H), 7.08 (t, } J = 7.8 \text{ Hz, } 1\text{H), 6.70 (t, } J = 5.4 \text{ Hz, } 1\text{H), 4.78 (q, } J = 7.2 \text{ Hz, } 1\text{H), 4.49 – 4.39 (m, } 1\text{H), 4.17 (dd, } J = 12.8, 8.8 \text{ Hz, } 1\text{H), 3.80 – 3.69 (m, } 1\text{H), 3.63 (dd, } J = 10.7, 6.2 \text{ Hz, } 1\text{H), 3.58 (s, } 3\text{H), 2.97 (dd, } J = 13.7, 5.8 \text{ Hz, } 1\text{H), 2.89 (dd, } J = 9.2, 4.5 \text{ Hz, } 1\text{H), 2.83 (dd, } J = 11.9, 5.9 \text{ Hz, } 2\text{H), 1.57 (td, } J = 15.7, 9.1 \text{ Hz, } 1\text{H), 1.47 (t, } J = 7.1 \text{ Hz, } 3\text{H), 1.41 – 1.33 (m, } 9\text{H), 1.32 – 1.25 (m, } 2\text{H), 1.23 (s, } 1\text{H), 1.21 – 1.08 (m, } 2\text{H).}

\(^{13}\text{C NMR (100 MHz, DMSO) \delta 172.5, 172.1, 169.3, 167.9, 140.3, 138.1, 135.8, 134.8, 132.4, 130.9, 129.1, 123.4, 95.2, 77.8, 53.9, 53.7, 52.3, 48.3, 42.0, 40.6, 40.4, 40.2, 40.0, 39.8, 39.6, 39.4, 36.6, 31.4, 29.4, 28.8, 23.1, 15.6.}

HRMS (ESI) [M+Na]\(^{+}\) \text{m/z calcd for C}_{34}\text{H}_{42}\text{InO}_{9}\text{Na} 814.1925, \text{found 814.1977.}
$^1$H NMR (400M Hz, DMSO-d$_6$) (linear peptide 1j):

$^{13}$C NMR (400M Hz, DMSO-d$_6$) (linear peptide 1j):
HRMS (ESI) (linear peptide 1j):

**Cyclic peptide 2j**

\[ \text{[M+Na]}^+ \]

$^{1}$H NMR (400 MHz, DMSO) $\delta$ 8.27 (dd, $J = 7.1$, 5.2 Hz, 1H), 8.14 (d, $J = 6.6$ Hz, 1H), 7.95 – 7.86 (m, 4H), 7.36 (s, 1H), 7.28 – 7.21 (m, 1H), 7.11 (d, $J = 7.6$ Hz, 1H), 7.03 (d, $J = 7.6$ Hz, 1H), 6.86 – 6.79 (m, 1H), 6.68 (t, $J = 5.4$ Hz, 1H), 5.00 (dd, $J = 11.8$, 2.1 Hz, 1H), 4.64 – 4.47 (m, 1H), 4.02 (dt, $J = 9.1$, 6.1 Hz, 1H), 3.87 (dd, $J = 16.9$, 7.3 Hz, 1H), 3.66 (s, 3H), 3.62 (d, $J = 13.2$ Hz, 1H), 3.44 (d, $J = 4.8$ Hz, 1H), 3.06 (dd, $J = 14.0$, 3.5 Hz, 1H), 2.93 (dd, $J = 14.0$, 9.2 Hz, 1H), 2.83 – 2.76 (m, 2H), 2.74 (d, $J = 6.8$ Hz, 1H), 1.53 (dt, $J = 13.5$, 6.4 Hz, 1H), 1.48 – 1.37 (m, 1H), 1.38 – 1.29 (m, 9H), 1.26 – 1.14 (m, 2H), 1.14 – 0.97 (m, 2H).

$^{13}$C NMR (100 MHz, DMSO) $\delta$ 172.5, 171.8, 169.7, 167.9, 167.5, 155.9, 139.1, 136.3, 135.0, 132.2, 130.6, 129.1, 128.2, 126.9, 123.6, 77.8, 54.6 – 54.1, 53.7, 53.4, 52.5, 42.9, 40.6, 40.4, 40.2, 40.0, 39.8, 39.6, 39.3, 36.8, 35.5, 30.6, 28.7, 23.2.

HRMS (ESI) [M+Na]$^+$ m/z calcd for C$_{34}$H$_{41}$N$_5$O$_9$Na 686.2802, found 686.2837.

$^{1}$H NMR (400M Hz, DMSO-d$_6$) (cyclic peptide 2j):
$\text{C NMR (100M Hz, DMSO-d$_6$) (cyclic peptide 2j):}$
HSQC (cyclic peptide 2j):

HRMS (ESI) (cyclic peptide 2j):
**Linear peptide 1k**
Phth-Ala-Asp(OMe)-Gly-\(m\)-I-Phe-OMe

\[
\begin{align*}
\text{CONH}_2 & \quad \text{CONH}_2 \\
\text{COOMe} & \quad \text{COOMe}
\end{align*}
\]

\(^{1}H\) NMR (400 MHz, DMSO) \(\delta\) 8.47 (d, \(J = 7.9\) Hz, 1H), 8.24 (d, \(J = 7.7\) Hz, 1H), 8.08 (t, \(J = 5.9\) Hz, 1H), 7.90 – 7.82 (m, 4H), 7.58 (dd, \(J = 6.2, 1.2\) Hz, 2H), 7.22 (d, \(J = 7.8\) Hz, 1H), 7.09 (dd, \(J = 9.2, 6.8\) Hz, 1H), 4.81 (d, \(J = 7.2\) Hz, 1H), 4.64 (d, \(J = 6.4\) Hz, 1H), 4.48 – 4.38 (m, 1H), 3.67 (t, \(J = 5.8\) Hz, 1H), 3.65 – 3.60 (m, 1H), 3.58 (s, 3H), 3.56 (s, 3H), 2.97 (dd, \(J = 13.8, 5.9\) Hz, 1H), 2.86 (dd, \(J = 13.7, 8.9\) Hz, 1H), 2.72 (dd, \(J = 16.0, 6.2\) Hz, 1H), 2.44 (dd, \(J = 16.0, 7.9\) Hz, 1H), 1.45 (d, \(J = 7.2\) Hz, 3H).

\(^{13}C\) NMR (100 MHz, DMSO) \(\delta\) 172.0, 171.0, 170.8, 169.4, 169.1, 167.7, 140.2, 138.1, 135.9, 134.8, 132.4, 130.9, 129.4 – 129.3, 123.5, 95.2, 53.9, 52.4, 51.9, 50.3, 48.1, 42.2, 40.6, 40.4, 40.2, 40.0, 39.7, 39.6, 39.4, 36.6, 36.3, 15.4.

HRMS (ESI) \([\text{M+Na}]^+\) m/z calcd for C\(_{28}\)H\(_{29}\)IN\(_{4}\)O\(_9\)Na 715.0877, found 715.0943.

\(^{1}H\) NMR (400M Hz, DMSO-\(d_6\)) (linear peptide 1k):
$^{13}$C NMR (100M Hz, DMSO-d$_6$) (linear peptide 1k):

HRMS (ESI) (linear peptide 1k):

[M+Na]$^+$
Cyclic peptide 2k

1H NMR (400 MHz, DMSO) δ 8.40 (d, J = 7.0 Hz, 1H), 8.16 (t, J = 6.1 Hz, 1H), 7.90 (td, J = 6.1, 3.8, 2.5 Hz, 4H), 7.38 (d, J = 5.7 Hz, 1H), 7.23 (t, J = 7.6 Hz, 1H), 7.12 – 7.00 (m, 3H), 5.05 (dd, J = 11.3, 1.9 Hz, 1H), 4.54 (td, J = 9.0, 3.9 Hz, 1H), 4.48 (dd, J = 14.2, 7.2 Hz, 1H), 3.82 (dd, J = 16.6, 6.7 Hz, 1H), 3.67 (s, 3H), 3.62 (dt, J = 11.9, 4.2 Hz, 2H), 3.59 – 3.56 (m, 1H), 3.46 (s, 4H), 3.06 (dd, J = 13.9, 3.6 Hz, 1H), 2.89 (d, J = 13.0 Hz, 1H), 2.70 (dd, J = 16.2, 5.8 Hz, 1H), 2.46 (d, J = 8.4 Hz, 1H).

13C NMR (100 MHz, DMSO) δ 171.7, 170.8, 169.5, 168.0, 167.4, 138.9, 136.59, 135.0, 132.1, 130.6, 129.1, 128.3, 127.1, 123.6, 53.7, 53.3, 52.5, 51.9, 51.1, 43.1, 40.6, 40.4, 40.2, 40.0, 39.8, 39.5, 39.3, 37.9, 36.7, 35.6, 35.2, 35.0, 21.9.

HRMS (ESI) [M+H]+ m/z calcd for C_{28}H_{29}N_{4}O_{9} 565.1934, found 565.1951.

1H NMR (400M Hz, DMSO-d_6) (cyclic peptide 2k):
$^{13}$C NMR (100M Hz, DMSO-d$_6$) (cyclic peptide 2k):

HSQC(cyclic peptide 2k):
HRMS (ESI) (cyclic peptide 2k):

**Linear peptide 1l**

\[
\begin{align*}
&\text{H NMR (400 MHz, } CD_3\text{OD)} \delta 7.89 - 7.84 (m, 2H), 7.84 - 7.78 (m, 2H), 7.61 (d, J = 1.4 Hz, 1H), 7.53 (d, J = 7.9 Hz, 1H), 7.24 (d, J = 7.8 Hz, 1H), 7.02 (t, J = 7.8 Hz, 1H), 5.02 (t, J = 7.2 Hz, 1H), 4.59 (dd, J = 9.9, 4.8 Hz, 1H), 3.92 (s, 3H), 3.86 - 3.77 (m, 3H), 3.09 (dd, J = 14.1, 4.8 Hz, 1H), 2.86 - 2.80 (m, 1H), 1.65 (d, J = 7.2 Hz, 3H). \\
&\text{C NMR (100 MHz, } CD_3\text{OD)} \delta 173.5, 172.9, 172.6, 172.5, 171.5, 169.3, 141.2, 139.2, 136.9, 135.5, 133.3, 131.2, 129.6, 124.4, 94.9, 56.0, 44.4, 43.5, 41.8, 37.8, 15.3.
\end{align*}
\]

HRMS (ESI) [M+Na]^+ m/z calcd for C_{26}H_{26}IN_{5}NaO_{8} 686.0724, found 686.0720

\[
\begin{align*}
&\text{H NMR (400 MHz, } CD_3\text{OD) (linear peptide 1l)}:
\end{align*}
\]

\[
\begin{align*}
\end{align*}
\]
$\text{C NMR (100 MHz, CD$_3$OD) (linear peptide 11):}$
HRMS (ESI) (linear peptide 1l):

Cyclic peptide 2l

$^1$H NMR (400 MHz, DMSO) $\delta$ 8.50 (t, $J = 5.8$ Hz, 1H), 8.14 (t, $J = 5.6$ Hz, 1H), 7.99 – 7.92 (m, 1H), 7.89 (tdd, $J = 6.2$, 3.8, 2.4 Hz, 2H), 7.46 (s, 1H), 7.41 – 7.29 (m, 3H), 7.20 (dt, $J = 7.6$ Hz, 1H), 7.08 (dd, $J = 15.2$, 7.6 Hz, 1H), 6.89 (d, $J = 7.5$ Hz, 1H), 5.32 (t, $J = 4.7$ Hz, 1H), 5.19 – 5.05 (m, 2H), 4.55 – 4.42 (m, 1H), 4.10 – 3.99 (m, 1H), 3.95 (dd, $J = 15.8$, 5.9 Hz, 1H), 3.74 (t, $J = 16.4$, 5.3 Hz, 1H), 3.62 – 3.55 (m, 1H), 3.55 – 3.41 (m, 2H), 3.03 – 2.93 (m, 1H), 2.93 – 2.83 (m, 1H).

$^{13}$C NMR (100 MHz, DMSO) $\delta$ 174.8, 172.0, 169.6, 168.4, 167.6, 136.4, 135.0, 132.1, 130.1, 128.9, 128.6, 128.4 – 128.3, 123.7, 70.2, 67.3 – 66.5, 66.4, 35.7, 31.8, 29.6, 29.3, 29.1, 27.0, 26.2 – 24.6, 22.6.

HRMS (ESI) [M+Na]$^+$ m/z calcd for C$_{26}$H$_{26}$N$_5$O$_8$ 536.1781 Da, found 536.1789 Da.

$^1$H NMR (400 MHz, DMSO-d$_6$) (cyclic peptide 2l):
$^{13}$C NMR (100 MHz, DMSO-$d_6$) (cyclic peptide 2l):
HRMS (ESI) (cyclic peptide 2l):

**Linear peptide 1m**

\[
\text{H NMR (400 MHz, CDCl}_3\text{) } \delta 7.84 (dd, J = 5.4, 3.1 Hz, 2H), 7.72 (dd, J = 5.5, 3.0 Hz, 2H), 7.54 (d, J = 7.9 Hz, 1H), 7.49 (d, J = 9.5 Hz, 1H), 7.18 (d, J = 7.9 Hz, 1H), 7.49 (d, J = 7.7 Hz, 1H), 7.00 (dd, J = 16.8, 9.0 Hz, 2H), 5.01 (q, J = 7.3 Hz, 1H), 4.78 (td, J = 7.6, 5.5 Hz, 1H), 4.54 – 4.46 (m, 1H), 4.07 (dd, J = 16.5, 3.4 Hz, 1H), 3.93 (dd, J = 17.5, 3.8 Hz, 1H), 3.73 (s, 3H), 3.56 – 3.42 (m, 1H), 3.37 (dd, J = 17.2, 8.6 Hz, 1H), 3.10 (dd, J = 14.0, 5.4 Hz, 1H), 2.95 – 2.86 (m, 1H), 2.29 (dd, J = 11.7, 6.0 Hz, 1H), 2.01 – 1.92 (m, 2H), 1.92 – 1.81 (m, 1H), 1.76 (d, J = 7.3 Hz, 3H).
\]

\[
\text{C NMR (100 MHz, CDCl}_3\text{) } \delta 171.5, 170.4, 169.2, 168.1, 167.8, 138.7, 138.1, 136.0, 134.2, 131.9, 130.1, 128.6, 123.5, 94.3, 77.4, 77.1, 76.8, 60.4, 60.1, 53.1, 52.9, 52.5, 49.0, 46.5, 42.3, 37.2, 27.5, 24.7, 15.4.
\]

HRMS (ESI) [M+Na]^+ m/z calcd for C_{28}H_{29}IN_4O_7Na 683.0979, found 683.1142.

\[
\text{H NMR (400 MHz, CDCl}_3\text{) (linear peptide 1m):}
\]
$	ext{C NMR (100M Hz, CDCl}_3$-$d$) (linear peptide 1m):
HRMS (ESI) (linear peptide 1m):

\[
\text{Cyclic peptide 2m}
\]

\(^{1}H\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.17 (d, \(J = 5.4\) Hz, 1H), 7.91 (dt, \(J = 7.0, 3.5\) Hz, 2H), 7.79 (td, \(J = 5.2, 2.1\) Hz, 2H), 7.62 (dd, \(J = 7.7, 2.5\) Hz, 1H), 7.35 (dd, \(J = 3.9, 1.5\) Hz, 2H), 7.20 (dd, \(J = 5.7, 2.5\) Hz, 1H), 5.32 (dd, \(J = 13.2, 4.8\) Hz, 1H), 4.73 (d, \(J = 7.4\) Hz, 1H), 4.40 – 4.32 (m, 1H), 4.32 – 4.24 (m, 1H), 4.12 (q, \(J = 7.1\) Hz, 1H), 3.93 – 3.83 (m, 1H), 3.80 (s, 3H), 3.59 – 3.47 (m, 1H), 3.45 (dd, \(J = 16.0, 3.0\) Hz, 1H), 3.28 (dd, \(J = 9.5, 7.6\) Hz, 1H), 3.24 – 3.18 (m, 1H), 3.12 (dd, \(J = 14.1, 4.7\) Hz, 1H), 2.56 (dd, \(J = 12.3, 4.8\) Hz, 1H), 2.00 – 1.86 (m, 2H), 1.72 (ddd, \(J = 12.0, 9.9, 6.0\) Hz, 1H).

\(^{13}C\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) 172.3, 170.5, 169.0, 168.0, 167.8, 137.1, 135.5, 134.5, 132.0, 131.6, 129.4, 127.8, 127.1, 123.8, 77.4, 77.1, 76.7, 60.4, 59.4, 56.1, 55.8, 52.5, 47.0, 41.2, 37.5, 36.1, 25.7, 24.6, 21.1, 14.2.

HRMS (ESI) [M+H]\(^{+}\) m/z calcd for C\(_{28}\)H\(_{30}\)N\(_{4}\)O\(_{7}\) 533.2036, found 533.2036; [M+Na]\(^{+}\) m/z calcd for C\(_{28}\)H\(_{30}\)N\(_{4}\)O\(_{7}\)Na 555.1856, found 555.1917.

\(^{1}H\) NMR (400MHz, CDCl\(_3\), d) (cyclic peptide 2m):
$^{13}$C NMR (100M Hz, CDCl$_3$-d) (cyclic peptide 2m):
Linear peptide 1n

\( ^1H \text{ NMR} (400 \text{ MHz, } CDCl_3) \delta 7.84 (dt, J = 6.9, 3.5 \text{ Hz, } 2H), 7.77 – 7.70 (m, 2H), 7.55 (d, J = 7.8 \text{ Hz, } 1H), 7.48 (s, 1H), 7.11 (d, J = 7.6 \text{ Hz, } 1H), 7.01 (dd, J = 9.0, 6.4 \text{ Hz, } 3H), 6.83 (d, J = 7.5 \text{ Hz, } 1H), 4.98 (q, J = 7.3 \text{ Hz, } 1H), 4.75 (dd, J = 13.6, 6.3 \text{ Hz, } 1H), 4.53 – 4.43 (m, 1H), 4.34 (dd, J = 14.3, 7.2 \text{ Hz, } 1H), 4.06 (d, J = 4.0 \text{ Hz, } 2H), 3.71 (s, 3H), 3.62 (dd, J = 12.1, 5.6 \text{ Hz, } 1H), 3.45 (d, J = 8.6 \text{ Hz, } 1H), 3.09 (dd, J = 13.9, 5.9 \text{ Hz, } 1H), 3.04 – 2.94 (m, 1H), 2.27 – 2.17 (m, 1H), 2.15 – 2.06 (m, 1H), 2.05 – 1.96 (m, 2H), 1.73 (d, J = 7.3 \text{ Hz, } 3H), 1.28 (d, J = 7.1 \text{ Hz, } 3H). \)

\( ^{13}C \text{ NMR} (100 \text{ MHz, } CDCl_3) \delta 171.8, 171.6, 170.9, 169.4, 168.3, 167.8, 138.6, 138.3, 136.1, 134.3, 131.9, 130.3, 128.6, 123.6, 94.3, 77.4, 77.0, 76.7, 60.5, 53.3, 52.5, 49.3, 49.0, 46.7, 42.6, 37.2, 28.1, 24.9, 17.2, 15.4. \)

HRMS (ESI) [M+Na]^+ m/z calcd for C_{31}H_{34}IN_5O_8Na 754.1350, found 754.1431.

\( ^1H \text{ NMR} (400 \text{ MHz, } CDCl_3-d) \) (linear peptide 1n):
$^{13}$C NMR (100M Hz, CDCl$_3$-d) (linear peptide 1n):
HRMS (ESI) (linear peptide 1n):

![Linear peptide 1n](image)

**Cyclic peptide 2n**

![Cyclic peptide 2n](image)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.83 (dt, $J = 7.0$, 3.5 Hz, 2H), 7.78 – 7.68 (m, 2H), 7.65 (d, $J = 3.6$ Hz, 1H), 7.35 (s, 1H), 7.25 – 7.15 (m, 2H), 7.11 (dd, $J = 11.1$, 7.9 Hz, 2H), 6.69 (d, $J = 7.5$ Hz, 1H), 4.98 – 4.86 (m, 2H), 4.49 (dd, $J = 8.7$, 2.9 Hz, 1H), 4.20 (t, $J = 7.4$ Hz, 1H), 4.10 – 3.95 (m, 1H), 3.86 (d, $J = 13.6$ Hz, 1H), 3.83 – 3.72 (m, 2H), 3.68 (d, $J = 4.8$ Hz, 3H), 3.42 (dd, $J = 16.5$, 9.2 Hz, 1H), 3.27 (dd, $J = 14.2$, 4.1 Hz, 1H), 2.90 (dddd, $J = 14.1$, 11.0, 8.0 Hz, 2H), 2.19 (dddd, $J = 12.8$, 6.4, 3.2 Hz, 1H), 2.15 – 2.03 (m, 1H), 1.87 (dddd, $J = 29.0$, 12.6, 6.1 Hz, 2H), 1.00 (d, $J = 7.4$ Hz, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 173.1, 172.1 170.2, 169.4, 168.5, 167.9, 137.8, 135.5, 134.7, 131.5, 131.2, 129.5, 127.4, 127.0, 123.8, 78.8 – 75.0, 61.4, 56.5, 52.4, 50.2, 48.0, 43.2, 37.1, 36.7, 29.3, 24.4, 16.8.

HRMS (ESI) [M+H]$^+$ m/z calcld for C$_{31}$H$_{54}$N$_{5}$O$_8$ 604.2407, found 604.2410.

$^1$H NMR (400M Hz, CDCl$_3$ -d) (cyclic peptide 2n):
$^{13}$C NMR (100M Hz, CDCl$_3$-d) (cyclic peptide 2n):
HRMS (ESI) (cyclic peptide 2n):

\[
\begin{align*}
\text{[M+H]}^+ \quad & \text{m/z calcd for C}_{31}\text{H}_{34}\text{IN}_{5}\text{O}_8 \quad 754.1350, \text{ found 754.1412.}
\end{align*}
\]

**Linear peptide 1o**

\[^1\text{H NMR (400 MHz, CDCl}_3)\] \(\delta\) 7.85 (dt, \(J = 7.8, 3.9 \text{ Hz, 2H}\)), 7.75 – 7.70 (m, 2H), 7.57 (t, \(J = 6.9 \text{ Hz, 2H}\)), 7.11 – 7.04 (m, 2H), 6.88 (q, \(J = 5.4 \text{ Hz, 3H}\)), 4.99 (q, \(J = 7.3 \text{ Hz, 1H}\)), 4.75 (dd, \(J = 13.7, 6.2 \text{ Hz, 1H}\)), 4.43 – 4.41 (m, 1H), 4.34 – 4.30 (m, 1H), 4.04 (t, \(J = 4.2 \text{ Hz, 2H}\)), 3.70 (s, 3H), 3.58 (d, \(J = 3.6 \text{ Hz, 1H}\)), 3.45 (dd, \(J = 16.8, 7.7 \text{ Hz, 1H}\)), 3.08 (dt, \(J = 11.4, 5.7 \text{ Hz, 1H}\)), 3.04 – 2.96 (m, 1H), 2.17 (ddd, \(J = 9.0, 6.5, 3.3 \text{ Hz, 1H}\)), 2.08 (dd, \(J = 8.2, 2.5 \text{ Hz, 1H}\)), 2.02 – 1.94 (m, 2H), 1.73 (d, \(J = 7.3 \text{ Hz, 3H}\)), 1.24 (d, \(J = 7.1 \text{ Hz, 3H}\)).

\[^{13}\text{C NMR (100 MHz, CDCl}_3)\] \(\delta\) 171.8, 171.6, 170.9, 169.4, 168.1, 167.8, 137.5, 135.7, 134.2, 131.9, 131.4, 123.5, 92.5, 77.4, 77.1, 76.8, 60.3, 53.1, 52.4, 49.2, 49.0, 46.7, 42.6, 37.2, 28.2, 24.9, 17.2, 15.4.

HRMS (ESI) [M+Na]^+ m/z calcd for C_{31}H_{34}IN_{5}O_8Na 754.1350, found 754.1412.

\[^1\text{H NMR (400M Hz, CDCl}_3)\] (linear peptide 1o) (further purified):
$^{13}$C NMR (100M Hz, CDCl$_3$) (linear peptide 1o) (further purified):

HRMS (ESI) (linear peptide 1o):
Cyclic peptide 2o

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.82 (dd, $J =$ 5.4, 3.0 Hz, 2H), 7.68 (dd, $J =$ 5.4, 3.0 Hz, 2H), 7.33 (d, $J =$ 7.9 Hz, 2H), 7.07 (dd, $J =$ 17.3, 8.2 Hz, 3H), 6.66 (s, 1H), 6.24 (d, $J =$ 7.5 Hz, 1H), 5.31 (dd, $J =$ 12.8, 3.3 Hz, 1H), 4.89 (dt, $J =$ 8.5, 5.2 Hz, 1H), 4.44 – 4.28 (m, 2H), 4.22 (dd, $J =$ 13.2, 6.5 Hz, 1H), 4.10 – 4.00 (m, 1H), 3.78 (d, $J =$ 3.3 Hz, 1H), 3.73 (d, $J =$ 12.2 Hz, 3H), 3.53 – 3.43 (m, 1H), 3.27 (dd, $J =$ 17.2, 7.9 Hz, 1H), 3.17 – 3.08 (m, 2H), 3.03 (dd, $J =$ 13.9, 5.1 Hz, 1H), 2.11 (dd, $J =$ 11.2, 8.1, 3.7 Hz, 2H), 1.88 – 1.79 (m, 2H), 1.28 (d, $J =$ 7.2 Hz, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 170.8, 170.6, 169.2, 167.1, 166.9, 166.7, 134.9, 133.3, 130.9, 129.9, 129.5, 127.8, 122.6, 77.6 – 75.0, 64.5, 60.9, 51.7, 51.5, 51.4, 48.9, 45.9, 42.1, 36.4, 34.33 (s), 29.5, 27.9, 23.6, 18.2, 17.3, 12.7.

HRMS (ESI) [M+Na]$^+$ m/z calcd for C$_{31}$H$_{33}$N$_5$O$_8$Na 626.2227, found 626.2283.

$^1$H NMR (400M Hz, CDCl$_3$-d) (cyclic peptide 2o):
$^{13}$C NMR (100M Hz, CDCl$_3$-d) (cyclic peptide 2o):
HRMS (ESI) (cyclic peptide 2o):

Linear peptide 1p

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.86 (s, 1H), 7.76 (dd, $J = 5.3$, 3.0 Hz, 2H), 7.64 (dd, $J = 5.3$, 3.0 Hz, 2H), 7.57 (d, $J = 8.8$ Hz, 1H), 7.54 – 7.46 (m, 3H), 7.38 (d, $J = 8.1$ Hz, 1H), 7.10 (d, $J = 7.7$ Hz, 1H), 6.99 (dd, $J = 10.0$, 5.9 Hz, 1H), 6.35 (s, 2H), 6.13 (s, 1H), 4.97 (q, $J = 7.0$ Hz, 1H), 4.82 (dd, $J = 13.4$, 5.7 Hz, 1H), 4.65 (dd, $J = 14.1$, 7.2 Hz, 1H), 4.45 (s, 1H), 3.99 – 3.82 (m, 2H), 3.63 – 3.59 (m, 3H), 3.56 (d, $J = 10.9$ Hz, 3H), 3.20 (s, 2H), 2.97 – 2.90 (m, 4H), 2.85 (d, $J = 5.7$ Hz, 1H), 2.72 (dd, $J = 17.0$, 5.8 Hz, 1H), 2.46 (d, $J = 22.2$ Hz, 5H), 2.05 (d, $J = 7.9$ Hz, 4H), 1.89 (dd, $J = 15.4$, 6.7 Hz, 1H), 1.72 (d, $J = 8.5$ Hz, 1H), 1.60 (d, $J = 7.2$ Hz, 3H), 1.56 (s, 2H), 1.45 (s, 6H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 172.8, 171.8, 171.2, 170.5, 170.3, 167.8, 162.6, 158.8, 156.4, 138.9, 138.2, 135.9, 134.2, 132.2, 131.9, 130.2, 128.6, 124.7, 123.4, 117.6, 94.4, 86.5, 78.2 – 76.1, 60.4, 53.6, 52.3, 52.1, 49.6, 48.7, 43.5, 43.2, 37.0, 36.5, 35.3, 28.6, 21.1, 19.3, 18.0, 15.3, 14.2, 12.5.

HRMS (ESI) [M+H]$^+$ m/z calcd C$_{47}$H$_{58}$IN$_8$O$_{13}$S for 1101.2810, found 1101.2875.

$^1$H NMR (400 MHz, CDCl$_3$) (linear peptide 1p):
$^{13}$C NMR (100 MHz, CDCl$_3$) (linear peptide 1p):

HRMS (ESI) (linear peptide 1p):
**Linear peptide 2p**

\[ \begin{align*}
\text{H NMR (400 MHz, DMSO)} & \delta 8.20 (d, J = 7.8 Hz, 1H), 8.19 – 8.09 (m, 1H), 8.03 (d, J = 7.8 Hz, 1H), 7.94 – 7.81 (m, 3H), 7.76 – 7.64 (m, 3H), 7.34 (d, J = 15.0 Hz, 1H), 7.19 (s, 1H), 7.08 (t, J = 7.6 Hz, 1H), 6.92 (d, J = 6.3 Hz, 1H), 6.65 (s, 1H), 6.32 (d, J = 32.6 Hz, 1H), 5.32 (t, J = 4.7 Hz, 1H), 5.05 (dd, J = 8.6, 5.7 Hz, 1H), 4.68 – 4.53 (m, 2H), 4.15 – 4.06 (m, 1H), 3.77 (dd, J = 16.7, 5.2 Hz, 1H), 3.74 – 3.64 (m, 3H), 3.63 – 3.49 (m, 3H), 3.48 – 3.33 (m, 1H), 3.25 – 3.13 (m, 2H), 3.10 (dd, J = 14.0, 3.0 Hz, 1H), 2.96 – 2.85 (m, 4H), 2.44 (s, 3H), 2.39 (s, 2H), 1.98 (s, 3H), 1.63 (dd, J = 14.7, 6.8 Hz, 3H), 1.53 (d, J = 6.6 Hz, 3H), 1.39 (d, J = 5.9 Hz, 6H).
\end{align*} \]

\[ \text{C NMR (100 MHz, DMSO)} \delta 174.8, 170.8, 169.2 – 168.9, 168.1, 167.4, 132.2, 132.0, 130.1, 129.1, 125.3 – 124.6, 123.6, 86.8, 65.5, 40.0, 35.6, 31.8, 30.5, 29.6, 29.5, 29.3, 29.1, 28.8, 27.0, 25.6, 22.6, 19.1, 14.4, 14.0, 12.7. \]

HRMS (ESI) [M+H]^+ m/z calcd for C_{27}H_{37}N_{4}O_{13}S 973.3766, found 973.3761; [M+Na]^+ m/z calcd for C_{27}H_{38}N_{4}O_{13}SNa 995.3585, found 995.3586.

\[ \text{H NMR (400M Hz, DMSO-d}_6) \text{ (cyclic peptide 2p):} \]
$^{13}$C NMR (100M Hz, DMSO-d$_6$) (cyclic peptide 2p):
HRMS (ESI) (cyclic peptide 2p):

**Linear peptide 1q**

\[ \text{HRMS (ESI) [M+Na]}^+ \text{ m/z calcd for C}_{47}\text{H}_{58}\text{IN}_{5}\text{O}_{9}\text{S}_{Na} 1018.2898, \text{found 1018.2886.} \]

\[ ^1\text{H NMR (400 MHz, CDCl}_3\text{-d)} (\text{linear peptide 1q}): \]

\[ ^1\text{C NMR (100 MHz, CDCl}_3\text{-d)} \delta 172.1, 170.6, 169.9, 169.8, 168.2, 145.3, 135.7, 134.9, 134.3, 132.2, 131.6, 130.2, 130.1, 126.9, 124.6, 123.6, 122.4, 121.3 , 117.3, 89.1, 82.7, 77.4, 77.1, 76.7, 58.9, 52.9, 52.7, 52.5, 40.4, 37.5, 30.2, 27.8, 27.3, 25.2, 24.8, 23.2, 23.0, 21.8, 21.6, 21.3, 19.3 , 18.0. \]

\[ \text{HRMS (ESI) [M+Na]}^+ \text{ m/z calcd for C}_{47}\text{H}_{54}\text{N}_3\text{O}_3\text{S}_{Na} 1018.2898, \text{found 1018.2886.} \]

\[ ^1\text{H NMR (400 MHz, CDCl}_3\text{-d)} (\text{linear peptide 1q}): \]

575
$^{13}$C NMR (100M Hz, CDCl$_3$-d) (linear peptide 1q):
HRMS (ESI) (linear peptide 1q):

\[ [M+H]^+ \]

\[ \text{m/z calcd. for C}_{47}\text{H}_{58}\text{N}_{5}\text{O}_{9}\text{S: 890.3775; found: 890.3770.} \]

Cyclic peptide 2q

\[ \text{HRMS (ESI) [M+Na]^+ m/z calcd. for C}_{47}\text{H}_{58}\text{N}_{5}\text{O}_{9}\text{S: 890.3775; found: 890.3770.} \]

\[ \text{1H NMR (400 MHz, CDCl}_3\text{, d) (cyclic peptide 2q):} \]

\[ \delta 7.96 (s, 1H), 7.78 (dd, J = 5.4, 3.0 Hz, 2H), 7.73 (d, J = 8.0 Hz, 1H), 7.68 (d, J = 8.1 Hz, 1H), 7.67 - 7.62 (m, 3H), 7.38 (t, J = 7.6 Hz, 1H), 7.32 (d, J = 8.0 Hz, 1H), 7.27 (d, J = 7.7 Hz, 2H), 6.78 (d, J = 7.5 Hz, 1H), 6.68 (d, J = 8.5 Hz, 1H), 6.62 (d, J = 7.1 Hz, 1H), 4.96 (dd, J = 11.3, 4.9 Hz, 1H), 4.76 (dt, J = 9.8, 6.8 Hz, 1H), 4.47 (dd, J = 14.3, 7.4 Hz, 1H), 4.27 (dd, J = 8.4, 6.0 Hz, 1H), 3.37 (dd, J = 14.3, 5.7 Hz, 1H), 3.15 (dd, J = 14.3, 10.0 Hz, 1H), 2.55 (d, J = 8.4 Hz, 3H), 2.41 - 2.37 (m, 1H), 2.35 (d, J = 4.3 Hz, 1H), 2.30 (dt, J = 13.2, 6.5 Hz, 1H), 1.77 - 1.72 (m, 1H), 1.62 - 1.56 (m, 1H), 1.54 - 1.47 (m, 1H), 1.05 (s, 9H), 0.98 (t, J = 6.4 Hz, 9H), 0.93 (dd, J = 12.2, 6.6 Hz, 9H). \]
\[^1\text{H}]\text{C NMR (100M Hz, CDCl}_3\text{-d) (cyclic peptide 2q):}\]
HSQC (cyclic peptide 2q):

HMBC (cyclic peptide 2q):
NOESY (cyclic peptide 2q):

(Note: No correlation between Hα (4.96 ppm) and Hβ (2.37 ppm) of β-Leu1 was observed, indicating the antiperiplanar arrangement of these two proton)

HRMS (ESI) (cyclic peptide 2q):

Compound 2r (Celogentin C ring A)

\(^1\)H NMR (400 MHz, CD\textsubscript{3}OD) δ 7.86 (dt, \(J = 6.9, 3.5\) Hz, 2H), 7.80 – 7.73 (m, 2H), 7.31 (t, \(J = 7.6\) Hz, 1H), 7.27 (s, 1H), 7.68 (d, \(J = 3.3, 2\)H), 7.64 (s, 1H), 7.50 (d, \(J = 8.1\) Hz, 1H), 7.35 (s, 1H), 7.23 (d, \(J = 8.0, 2\)H), 7.16 (d, \(J = 8.2, 1\)H), 5.30 (dd, \(J = 9.6, 5.5\) Hz, 1H), 4.28 (dd, \(J = 8.5, 3.6\) Hz, 1H), 4.20 (dd, \(J = 10.6, 3.9\) 1H), 3.62 (d, \(J = 7.5, 1\)H), 3.41 (dd, \(J = 15.8, 6.4\) Hz, 1H), 3.21 (dd, \(J = 12.5, 4.0\) Hz, 1H),
2.44 (m, 1H), 2.33 (s, 3H), 2.24 (m, 1H), 1.98 (m, 2H), 1.52 (s, 9H), 1.46-1.28 (m, 3H), 0.92-0.77 (m, 18H).

$^1$C NMR (100 MHz, CD$_3$OD) δ 175.5, 173.9, 172.3, 172.2, 172.0, 147.6, 137.7, 135.4, 131.6, 128.5, 127.0, 124.9, 121.2, 119.9, 118.2, 83.9, 58.3, 54.9, 54.0, 53.3, 51.7, 50.2-49.8, 44.2, 32.8, 31.5, 28.8, 27.4, 26.6, 24.0, 22.6, 22.0, 21.9, 19.5, 19.4, 18.1.

HRMS (ESI) [M+Na]$^+$ m/z calcd for C$_{44}$H$_{60}$N$_2$NaO$_9$S 871.4040, found 871.4043.

$^1$H NMR (400 MHz, CD$_3$OD)

$^1$C NMR (100 MHz, CD$_3$OD)
HRMS (ESI):

- Full scan (8.037 minutes)
- Frag = 135.0 V
- 22-1.d
- Peaks at m/z 871.4043, 1061.4778, 922.0098, 301.1411, 793.3593, 121.0509, 444.1873, 1720.8193