# Robust Carboxylated Polymer Pores from a Cyclic Peptide Template 

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## General Methods

All reagents for synthesis were purchased from commercial suppliers and used without further purification unless stated otherwise. All air-sensitive reactions were performed using oven-dried glassware under an inert atmosphere of nitrogen. Syringe or cannula was used to transfer air-sensitive solvents and solutions. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl; methanol was distilled from magnesium methoxide; $N, N$-diisopropylethylamine (DIEA), dichloromethane $\left(\mathrm{CH}_{2} \mathrm{Cl}_{2}\right)$, chloroform $\left(\mathrm{CH}_{2} \mathrm{Cl}_{2}\right)$ were distilled from calcium hydride and $N, N$-dimethylformamide (DMF) was dried over $4 \AA$ molecular sieves. All dry solvents were stored over $4 \AA$ molecular sieves prior to use. All peptides were synthesized in solution using $O$-(6-Chlorobenzotriazol-1-yl)$N, N, N^{\prime}, N^{\prime \prime}$-teramethyluronium hexafluorophosphate (HCTU) as a coupling reagent. Polymerization reactions were performed by using Grubbs' second generation initiator.

Analytical thin layer chromatography (TLC) was performed on MERCK precoated silica gel $60 \mathrm{~F}_{254}$ TLC plates. Eluting solvents are reported as volume percents. Compounds were visualized using UV light, ninhydrin and/or $\mathrm{KMnO}_{4}$ stains. Flash column chromatography was performed using silica gel (200-400 mesh) from Acme chemicals. All 1D and 2D NMR spectra were recorded on Bruker 400 or Bruker 500 spectrometers using $\mathrm{CDCl}_{3}$ or DMSO- $d_{6}$ as solvent. The NMR spectra were referenced using residual solvent peaks as the standard. Chemical shifts are denoted in parts per million ( $\delta$ ), coupling constants $(J)$ are reported in Hertz $(\mathrm{Hz})$, and spin multiplicities are reported as singlet (s), broad singlet (bs), doublet (d), triplet (t), quartet (q), quintet (quint), apparent triplet (app. t), doublet of doublet (dd), doublet of triplet (dt) or multiplet (m). Mass spectra were recorded on the Bruker Ultraflex extreme or the MICRO-Q-TOF mass spectrometer using the MALDI or ESI technique, respectively. FT-IR spectra were recorded on a JASCO FT/IR-4100 spectrometer. IR spectra were recorded in the form of a KBr pellet for solid samples and as a thin film in $\mathrm{CHCl}_{3}$ for liquid samples. IR peaks are reported in wavenumbers $\left(\mathrm{cm}^{-1}\right)$ as strong (s), medium (m), weak (w), and broad (br).

Dynamic light scattering data was recorded at $25^{\circ} \mathrm{C}$ on a Horiba Zetasizer ZS instrument using 3 mL quartz cells. TEM images were obtained at a voltage of 120 kV on a CM 12 PHILIPS Scanning Transmission Electron Microscope. Carbon coated holey copper grids from Forevision Instruments were used as supports for the TEM studies. AFM images were obtained using a Park-System XE-100 AFM instrument in non-contact mode. AFM silicon tips were purchased from Applied Nanostructures Inc. SEM images were obtained using
quanta 400. Silicon substrates were used for AFM \& SEM analysis. Fluorescence images were recorded by using Olympus 1X51 fluorescence microscope over glass substrate or using Leica DMI 3000 B inverted fluorescence microscope. Thermogravimetric analysis (TGA) was done by using Q500 Hi-Res TGA from TA Instruments.

## Synthesis and analytical data of compounds



Cross-Linker (2): ${ }^{1}$ To a solution of ethylene diamine ( $0.26 \mathrm{~mL}, 3.88 \mathrm{mmol}, 1$ equiv) and norbornene-exo-acid ${ }^{2,3}\left(1.18 \mathrm{~g}, 8.55 \mathrm{mmol}, 2.2\right.$ equiv) in $\mathrm{CH}_{2} \mathrm{Cl}_{2}(16 \mathrm{~mL})$ was added EDC.HCl ( $1.64 \mathrm{~g}, 8.55 \mathrm{mmol}, 2.2$ equiv) and DMAP ( $0.24 \mathrm{~g}, 1.94 \mathrm{mmol}, 0.5$ equiv). The reaction mixture was allowed to stir at RT for 10 h , following which $\mathrm{CH}_{2} \mathrm{Cl}_{2}$ was removed in vacuo. Ethyl acetate ( 200 mL ) was added to the residue and the solution was washed with 0.1 N aqueous $\mathrm{HCl}(3 \times 50 \mathrm{~mL}), 5 \%$ aqueous $\mathrm{NaHCO}_{3}(4 \times 50 \mathrm{~mL})$ and saturated aqueous NaCl $(2 \times 40 \mathrm{~mL})$. The organic layer was dried over anhydrous sodium sulphate, filtered and concentrated in vacuo. The residue was purified by flash column chromatography ( $2.5 \%$ methanol $/ \mathrm{CH}_{2} \mathrm{Cl}_{2}$ ) to afford 1.16 g of compound $2(99 \%)$ as a white fluffy solid. TLC $\mathrm{R}_{f}=$ 0.21 ( $2 \%$ methanol/dichloromethane). ${ }^{1} \mathbf{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}, 25^{\circ} \mathrm{C}$ ): $\delta=6.44$ (bs, 2 H ; 2 NH ), 6.14-6.06 (4H; $2 \mathrm{CH}=\mathrm{CH}), 3.40\left(\mathrm{t}, J=2.4 \mathrm{~Hz}, 4 \mathrm{H} ; 2 \mathrm{CH}_{2}\right), 2.94-2.86(4 \mathrm{H} ; 4 \mathrm{CH})$, 2.04-1.97 (m, 2H; 2 CH ), 1.91-1.82 (m, 2H; CH $\mathrm{CH}_{2}$ ), 1.65 (d, $J=8.0 \mathrm{~Hz}, 2 \mathrm{H} ; \mathrm{CH}_{2}$ ), 1.36-1.24 (4H; $2 \mathrm{CH}_{2}$ ); ${ }^{13} \mathbf{C}$ NMR ( $100 \mathrm{MHz} \mathrm{CDCl} 3,25{ }^{\circ} \mathrm{C}$ ): $\delta=177.2,138.3,136.1,47.3,46.4,44.7$, 41.7, 40.3, 30.6; IR (KBr pellet): $v=3317$ (m), 2982 (m), 1658 (s), 1429 (m), 1266 ( s$), 898$ (m), $744(\mathrm{~s}) \mathrm{cm}^{-1}$; $\mathbf{H R M S}\left(\right.$ ESI $\left.^{+}\right)$: calcd. for $\mathrm{C}_{8} \mathrm{H}_{25} \mathrm{~N}_{2} \mathrm{O}_{2}\left(\mathrm{MH}^{+}\right)$301.1916, found 301.1910.


Boc-L-Ser-OAllyl (3): ${ }^{4}$ To a solution of Boc-L-ser-OH ( $1.24 \mathrm{~g}, 6.05 \mathrm{mmol}, 1$ equiv) in $1: 1$ allylbromide/acetonitrile ( 10 mL ) was added DIEA ( $2.07 \mathrm{~mL}, 12.1 \mathrm{mmol}$, 2 equiv). The reaction mixture was allowed to stir at $75{ }^{\circ} \mathrm{C}$ for 2 h , following which acetonitrile was
removed in vacuo. The reaction mixture was diluted with ethyl acetate ( 150 mL ), washed with 0.1 N aqueous $\mathrm{HCl}(3 \times 50 \mathrm{~mL}), 5 \%$ aqueous $\mathrm{NaHCO}_{3}(3 \times 50 \mathrm{~mL})$ and saturated aqueous $\mathrm{NaCl}(2 \times 30 \mathrm{~mL})$. The organic layer was dried over anhydrous sodium sulphate, filtered and concentrated in vacuo. Purification by flash column chromatography ( $20 \%$ ethyl acetate/hexane) afforded 1.36 g of compound $\mathbf{3}(92 \%)$ as a pale yellow liquid. $\mathrm{TLC}_{f}=0.43$ ( $25 \%$ ethyl acetate/hexane). ${ }^{1} \mathbf{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}, 25^{\circ} \mathrm{C}$ ): $\delta=5.95-5.85(\mathrm{~m}, 1 \mathrm{H}$; $\mathrm{CH}_{\text {allyl }}$ ), 5.49 (bs, $1 \mathrm{H} ; \mathrm{N} H$ ), 5.34 (d, $\left.J=17.2 \mathrm{~Hz}, 1 \mathrm{H} ; \mathrm{HCH}_{\text {allyl }}\right), 5.25$ (d, $J=10.4 \mathrm{~Hz}, 1 \mathrm{H}$; $\left.\mathrm{HCH}_{\text {allyl }}\right), 4.66\left(\mathrm{~d}, \mathrm{~J}=5.6 \mathrm{~Hz}, 2 \mathrm{H} ; \mathrm{CH}_{2(\text { allyl }}\right)$ ), $4.39\left(\mathrm{bs}, 1 \mathrm{H}, \mathrm{CH}_{\text {ser }}\right), 4.0-3.88\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2(\text { ser) }}\right)$, $2.42\left(\mathrm{bs}, 1 \mathrm{H}, \mathrm{O} H_{\text {ser }}\right), 1.4\left(\mathrm{~s}, 9 \mathrm{H}, 3 \mathrm{CH}_{3(\mathrm{Boc})}\right){ }^{13} \mathbf{C}$ NMR ( $100 \mathrm{MHz}, \mathrm{CDCl}_{3}, 25^{\circ} \mathrm{C}$ ): $\delta=170.7$, 155.9, 131.6, 118.9, 80.4, 66.3, 63.6, 55.9, 28.4; IR $\left(\mathrm{CHCl}_{3}\right): v=3457$ (m), 1736 (s), 1377 (m), 1248 ( s ), 1050 ( s$), 922(\mathrm{~m}), 735(\mathrm{~s}) \mathrm{cm}^{-1}$; HRMS (ESI ${ }^{+}$): calcd. for $\mathrm{C}_{11} \mathrm{H}_{19} \mathrm{NO}_{5} \mathrm{Na}$ $\left(\mathrm{MNa}^{+}\right) 268.1161$, found 268.1150 .


TFA- L-ser-(O-NB)-O-Allyl (4): To a solution of Boc- L-ser-O-allyl 3 ( $0.93 \mathrm{~g}, 3.80 \mathrm{mmol}, 1$ equiv) and norbornene-exo-acid ( $0.5 \mathrm{~g}, 3.8 \mathrm{mmol}$, 1 equiv) in $\mathrm{CH}_{2} \mathrm{Cl}_{2}(10 \mathrm{~mL})$ was added EDC.HCl ( $1.094 \mathrm{~g}, 5.7 \mathrm{mmol}, 1.5$ equiv) and DMAP ( $0.139 \mathrm{~g}, 1.14 \mathrm{mmol}, 0.3 \mathrm{equiv})$.The reaction mixture was allowed to stir at RT for 4 h , following which $\mathrm{CH}_{2} \mathrm{Cl}_{2}$ was removed in vacuo. The residue was diluted with ethyl acetate ( 150 mL ) and sequentially washed with 0.1 N aqueous $\mathrm{HCl}(3 \times 50 \mathrm{~mL}), 5 \%$ aqueous $\mathrm{NaHCO}_{3}(3 \times 50 \mathrm{~mL})$ and saturated aqueous $\mathrm{NaCl}(2 \times 30 \mathrm{~mL})$. The organic layer was dried over anhydrous sodium sulphate, filtered and concentrated in vacuo. The residue was purified by flash column chromatography ( $12 \%$ ethyl acetate/Hexane) to afford 1.219 g of norbornene coupled product $\mathbf{1 5}$ (88\%) as a pale yellow liquid. $\mathrm{TLC}_{\mathrm{f}}=0.31$ ( $12 \%$ ethyl acetate/hexane). ${ }^{\mathbf{1}} \mathbf{H} \mathbf{N M R}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}, 25^{\circ} \mathrm{C}\right): \delta=$ 6.15-6.06 ( $2 \mathrm{H} ; \mathrm{CH}=\mathrm{CH}_{\mathrm{nb}}$ ), $5.95-5.84\left(\mathrm{~m}, 1 \mathrm{H} ; \mathrm{CH}_{\text {allyl }}\right), 5.36-5.22\left(3 \mathrm{H} ; \mathrm{CH}_{2 \text { (allyl) }} \& \mathrm{~N} H\right), 4.7-$ $4.57\left(3 \mathrm{H} ; \mathrm{CH}_{2 \text { (allyl) }} \& \mathrm{CH}_{\text {ser }}\right.$ ), 4.56-4.46 (m, $1 \mathrm{H} ; \mathrm{CHH}_{\text {ser }}$ ), 4.37-4.28 (m, $1 \mathrm{H} ; \mathrm{CHH}_{\text {ser }}$ ), 3.04$2.95\left(1 \mathrm{H} ; \mathrm{CH} H_{\mathrm{nb}}\right), 2.91\left(\mathrm{bs}, 1 \mathrm{H} ; \mathrm{CH}_{\mathrm{nb}}\right), 2.24-2.16\left(\mathrm{~m}, 1 \mathrm{H} ; \mathrm{CH} \mathrm{nb}_{\mathrm{b}}\right), 1.94-1.82\left(\mathrm{~m}, 1 \mathrm{H} ; \mathrm{HCH}_{\mathrm{nb}}\right)$, $1.63\left(\mathrm{~d}, J=1.6 \mathrm{~Hz}, 1 \mathrm{H} ; \mathrm{HCH}_{\mathrm{nb}}\right), 1.45\left(\mathrm{~s}, 9 \mathrm{H} ; \mathrm{CH}_{3(\mathrm{Boc})}\right), 1.4-1.30\left(2 \mathrm{H} ; \mathrm{HCH}_{\mathrm{nb}}, \mathrm{HCH}_{\mathrm{nb}}\right) ;{ }^{13} \mathbf{C}$ NMR ( $100 \mathrm{MHz}, \mathrm{CDCl}_{3}, 25^{\circ} \mathrm{C}$ ): $\delta=175.9,169.7,155.3,138.3,135.7,131.5,119.1,80.5$,
66.5, 64.3, 53.3, 46.9, 46.5, 43.1, 41.7, 30.6, 28.4; IR $\left(\mathrm{CHCl}_{3}\right): v=3439(\mathrm{~m}), 1724(\mathrm{~s}), 1506$ (m), 1317 (m), 1166 (s), $930(\mathrm{~m}), 765(\mathrm{~s}) \mathrm{cm}^{-1}$; HRMS (ESI ${ }^{+}$): calcd. for $\mathrm{C}_{19} \mathrm{H}_{27} \mathrm{NO}_{6} \mathrm{Na}$ $\left(\mathrm{MNa}^{+}\right) 388.1736$, found 388.1735 .

To a solution of Boc-L-ser(O-NB)-O-allyl 15 ( $1.12 \mathrm{~g}, 3.07 \mathrm{mmol}, 1$ equiv) in $\mathrm{CH}_{2} \mathrm{Cl}_{2}$ $(6 \mathrm{~mL})$ at $0^{\circ} \mathrm{C}$ was added TFA ( $3.54 \mathrm{~mL}, 46.03 \mathrm{mmol}, 15$ equiv) over a period of 5 min . The reaction mixture was allowed to stir at RT for 3 h , following which $\mathrm{CH}_{2} \mathrm{Cl}_{2}$ was removed in vacuo. Excess TFA was removed as an azeotrope with water. The product was dissolved in water ( 5 mL ) and lyophilized to give 1.14 g trifluoroacetate salt $\mathbf{4}(99 \%)$ as a pale yellow gummy solid. $\mathrm{R}_{f}=0.17$ ( $3 \%$ methanol/dichloromethane and 2 drops of TEA for 3 mL ).
${ }^{1} \mathbf{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}, 25^{\circ} \mathrm{C}$ ): $\delta=8.35\left(\mathrm{bs}, 3 \mathrm{H} ; \mathrm{NH}_{3}\right), 6.17-6.03\left(2 \mathrm{H} ; \mathrm{CH}=\mathrm{CH} H_{\mathrm{nb}}\right)$, $5.95-$ $5.81\left(\mathrm{~m}, 1 \mathrm{H} ; \mathrm{CH}_{\text {allyl }}\right), 5.35\left(\mathrm{~d}, J=17.6 \mathrm{~Hz}, 1 \mathrm{H} ; \mathrm{HCH}_{\text {allyl }}\right), 5.30\left(\mathrm{~d}, J=10.4 \mathrm{~Hz}, 1 \mathrm{H} ; \mathrm{HCH}_{\text {allyl }}\right)$, 4.72-4.3 (5H; $\mathrm{OCH}_{2 \text { (allyl) }}, \mathrm{CH}_{2(\text { ser) }}, \mathrm{CH}_{\text {ala }}$ ), 3.0-2.85 ( $2 \mathrm{H} ; \mathrm{CH}_{\mathrm{nb}}$ ), 2.23-2.2 (m, $1 \mathrm{H} ; \mathrm{CH}_{\mathrm{nb}}$ ), 1.9$1.75\left(\mathrm{~m}, 1 \mathrm{H} ; \mathrm{HCH}_{\mathrm{nb}}\right), 1.43-1.3\left(3 \mathrm{H} ; \mathrm{CH}_{2(\mathrm{nb})} \& \mathrm{HCH}_{\mathrm{nb}}\right) ;{ }^{13} \mathbf{C}$ NMR ( $100 \mathrm{MHz}, \mathrm{CDCl}_{3}, 25^{\circ} \mathrm{C}$ ): $\delta=176.1,166.7,138.2,135.5,130.4,120.5,68.0,61.6,53.1,46.8,46.4,42.7,41.7,30.7$; IR ( $\mathrm{CHCl}_{3}$ ): 3438 ( s , 2976 ( s$), 1710$ ( s$), 1504$ ( s$), 1345$ (m), 1211 (s), 1045 (m), 932 (m), 674 (s) $v=\mathrm{cm}^{-1} ;$ HRMS (ESI ${ }^{+}$): calcd. for $\mathrm{C}_{16} \mathrm{H}_{21} \mathrm{NO}_{6} \mathrm{~F}_{3}\left(\mathrm{MH}^{+}\right)$380.1321, found 380.1310.


Boc-d-ala- L-ser(O-NB)-O-allyl (5): To a solution of Boc-D-ala-OH ( $0.499 \mathrm{~g}, 2.64 \mathrm{mmol}, 1$ equiv) and TFA-L-ser-(O-NB)-O-allyl $4\left(1.0 \mathrm{~g}, 2.64 \mathrm{mmol}, 1\right.$ equiv) in $\mathrm{CH}_{2} \mathrm{Cl}_{2}(12 \mathrm{~mL})$ was added HCTU ( $1.31 \mathrm{~g}, 3.17 \mathrm{mmol}, 1.2$ equiv) and DIEA ( $1.6 \mathrm{~mL}, 9.2 \mathrm{mmol}, 3.5$ equiv). The reaction mixture was allowed to stir at RT for 7 h , following which $\mathrm{CH}_{2} \mathrm{Cl}_{2}$ removed in vacuo. The reaction mixture was diluted with ethyl acetate $(150 \mathrm{~mL})$ and sequentially washed with 0.1 N aqueous $\mathrm{HCl}(3 \times 50 \mathrm{~mL}), 5 \%$ aqueous $\mathrm{NaHCO}_{3}(3 \times 50 \mathrm{~mL})$ and saturated aqueous $\mathrm{NaCl}(2 \times 30 \mathrm{~mL})$. The organic layer was dried over anhydrous sodium sulphate, filtered and concentrated in vacuo. The residue was purified by flash column chromatography ( $26 \%$ ethyl acetate/Hexane) to afford 1.06 g of dipeptide $5(92 \%)$ as a dense pale yellow liquid. $\mathrm{TLC}_{f}=$ 0.38 ( $30 \%$ ethyl acetate/hexane). ${ }^{\mathbf{1}} \mathbf{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}, 25^{\circ} \mathrm{C}$ ): $\delta=7.03(\mathrm{bs}, 1 \mathrm{H} ; \mathrm{NH})$,
6.15-6.05 ( $2 \mathrm{H} ; \mathrm{CH}=\mathrm{CH}_{\mathrm{nb}}$ ), 5.95-5.83 (m, $\left.1 \mathrm{H} ; \mathrm{CH}_{\text {allyl }}\right), 5.35-5.22\left(2 \mathrm{H} ; \mathrm{CH}_{\text {allyl }}\right), 4.95$ (bs, 1 H ; NH ), 4.89-4.8 (m, $1 \mathrm{H} ; \mathrm{CH}_{\text {ser }}$ ), 4.66-4.62 (m, $\left.2 \mathrm{H} ; \mathrm{OCH}_{2(\text { (allyl }}\right), 4.57-4.47\left(\mathrm{~m}, 1 \mathrm{H} ; \mathrm{HCH}_{\text {ser }}\right)$, 4.42-4.32 (m, 1H; $\mathrm{HCH}_{\text {ser }}$ ), 4.3-4.25 (m, 1H; $\mathrm{CH}_{\text {ala }}$ ), 3.03-2.89 ( $2 \mathrm{H} ; 2 \mathrm{CH} H_{\mathrm{nb}}$ ), 2.23-2.16 (m, $\left.1 \mathrm{H} ; \mathrm{CH}_{\mathrm{nb}}\right), 1.92-1.82\left(\mathrm{~m}, 1 \mathrm{H} ; \mathrm{HCH}_{\mathrm{nb}}\right), 1.7-1.66\left(\mathrm{~m}, 1 \mathrm{H} ; \mathrm{HCH}_{\mathrm{nb}}\right), 1.45\left(\mathrm{~s}, 9 \mathrm{H} ; 3 \mathrm{CH}_{3(\mathrm{Boc})}\right)$, 1.38-1.32 ( $5 \mathrm{H} ; \mathrm{CH}_{3 \mathrm{ala}}, \mathrm{HCH}_{\mathrm{nb}}, \mathrm{HCH}_{\mathrm{nb}}$ ); ${ }^{13} \mathbf{C}$ NMR ( $100 \mathrm{MHz}, \mathrm{CDCl}_{3}, 25^{\circ} \mathrm{C}$ ): $\delta=175.8$, 172.7, 169.1, 155.7, 138.3, 135.7, 131.4, 119.2, 80.4, 66.5, 63.8, 52.1,50.0, 46.7, 46.5, 43.1, 41.7, 30.4, 28.4, 18.1; IR (KBr pellet): $v=3427(\mathrm{~m}), 3020(\mathrm{~s}), 1722(\mathrm{~s}), 1512(\mathrm{~m}), 1216$ (s), $1039(\mathrm{~m}), 761(\mathrm{~s}) \mathrm{cm}^{-1}$; HRMS (ESI ${ }^{+}$): calcd. for $\mathrm{C}_{22} \mathrm{H}_{32} \mathrm{~N}_{2} \mathrm{O}_{7} \mathrm{Na}\left(\mathrm{MNa}^{+}\right)$459.2107, found 459.2115.


Boc-d-ala-L-ser(O-NB)-OH (6): To a solution of Boc-D-ala-L-ser(O-NB)-O-allyl 5 ( 0.51 g , 1.17 mmol , 1 equiv) in $\mathrm{CH}_{2} \mathrm{Cl}_{2}(8 \mathrm{~mL})$ at $0{ }^{\circ} \mathrm{C}$ was added $\mathrm{Pd}\left(\mathrm{PPh}_{3}\right)_{4}(0.068 \mathrm{~g}, 0.059 \mathrm{mmol}$, 0.05 equiv), $\mathrm{PPh}_{3}(0.062 \mathrm{~g}, 0.235 \mathrm{mmol}, 0.2$ equiv) and pyrrolidine $(0.12 \mathrm{~mL}, 1.41 \mathrm{mmol}, 1.2$ equiv). The reaction mixture was allowed to stir at $0^{\circ} \mathrm{C}$ for 15 min ., following which $\mathrm{CH}_{2} \mathrm{Cl}_{2}$ was removed in vacuo. The reaction mixture was acidified with $0.1 \mathrm{~N} \mathrm{HCl}(50 \mathrm{~mL})$ and extracted with ethyl acetate ( $3 \times 75 \mathrm{~mL}$ ). The combined organic layers were dried over anhydrous sodium sulphate, filtered and concentrated in vacuo. The product was purified by flash column chromatography ( $4 \% \mathrm{MeOH} / \mathrm{CH}_{2} \mathrm{Cl}_{2}$ ) to afford 0.403 g of compound $\mathbf{8}(87 \%)$ as a pale yellow gummy solid. $\mathrm{R}_{f}=0.13(30 \%$ ethyl acetate/hexane and 2 drops of AcOH for 3 mL ). ${ }^{1} \mathbf{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}, 25^{\circ} \mathrm{C}$ ): $\delta=8.61(\mathrm{bs}, 1 \mathrm{H} ; \mathrm{COOH}), 7.34(\mathrm{bs}, 1 \mathrm{H} ; \mathrm{NH})$, 6.13-6.02 2H; CH=CH $H_{\mathrm{nb}}$ ), $5.57\left(\mathrm{~d}, J=7.2 \mathrm{~Hz}, 1 \mathrm{H} ; \mathrm{NH}\right.$ ), 4.85-4.75 (m, $1 \mathrm{H} ; \mathrm{CH}_{\text {ser }}$ ), 4.55-4.10 ( $3 \mathrm{H} ; \mathrm{CH}_{2(\text { ser })} \& \mathrm{CH}_{\text {ala }}$ ), 3.06-2.85 ( $2 \mathrm{H} ; 2 \mathrm{CH}_{\mathrm{nb}}$ ), 2.22-2.15 (m, $1 \mathrm{H} ; \mathrm{CH}_{\mathrm{nb}}$ ), 1.92-1.82 (m, 1 H ; $\left.\mathrm{HCH}_{\mathrm{nb}}\right), 1.52-1.39\left(10 \mathrm{H} ; 3 \mathrm{CH}_{3(\mathrm{Boc})} \& \mathrm{HCH}_{\mathrm{nb}}\right), 1.38-1.28\left(5 \mathrm{H} ; \mathrm{CH}_{3(\mathrm{ala})}, \mathrm{HCH}_{\mathrm{nb}} \& \mathrm{HCH}_{\mathrm{nb}}\right)$; IR ( KBr pellet): $v=3419$ ( s ), 3058 (m), 2980 ( s ), 1721 ( s , 1513 ( s$), 1374$ (m), 1262 ( s$), 1167$ (s),1039 (m), $738(\mathrm{~s}) \mathrm{cm}^{-1} ;$ HRMS (ESI ${ }^{+}$): calcd. for $\mathrm{C}_{19} \mathrm{H}_{28} \mathrm{~N}_{2} \mathrm{O}_{7} \mathrm{Na}\left(\mathrm{MNa}^{+}\right) 419.4316$, found 419.4303 .


TFA-d-ala-L-ser(O-NB)-O-allyl (7): To a solution of Boc-D-ala-L-ser(O-NB)-O-allyl 5 ( $0.39 \mathrm{~g}, 0.88 \mathrm{mmol}, 1$ equiv) in $\mathrm{CH}_{2} \mathrm{Cl}_{2}(6 \mathrm{~mL})$ at $0{ }^{\circ} \mathrm{C}$ was added TFA ( $1.02 \mathrm{~mL}, 13.24$ mmol, 15 equiv) over a period of 3 min . The reaction mixture was allowed to stir at RT for 3h, following which $\mathrm{CH}_{2} \mathrm{Cl}_{2}$ was removed in vacuo. Excess TFA was removed as an azeotrope with water. The product was dissolved in water ( 3 mL ) and lyophilized to give 0.393 g of $7(99 \%)$ as a pale yellow gummy solid. $\mathrm{R}_{f}=0.12(30 \%$ ethyl acetate/hexane and 2 drops of TEA for 3 mL ). ${ }^{1} \mathbf{H}$ NMR ( 400 MHz , DMSO- $d_{6}, 25^{\circ} \mathrm{C}$ ): $\delta=9.08(\mathrm{~d}, J=8 \mathrm{~Hz}, 1 \mathrm{H}$; $\left.\mathrm{N} H), 8.21(\mathrm{~s}, 3 \mathrm{H} ; \mathrm{NH})_{3}\right), 6.2-6.1\left(2 \mathrm{H} ; \mathrm{CH}=\mathrm{CH}_{\mathrm{nb}}\right), 5.96-5.85\left(\mathrm{~m}, 1 \mathrm{H} ; \mathrm{CH}_{\text {ally }}\right), 5.33(\mathrm{~d}, J=17.6$ $\left.\mathrm{Hz}, 1 \mathrm{H} ; \mathrm{HCH}_{\text {ally }}\right), 5.23\left(\mathrm{~d}, J=10.4 \mathrm{~Hz}, 1 \mathrm{H} ; \mathrm{HCH}_{\text {ally }}\right), 4.8-4.72\left(\mathrm{~m}, 1 \mathrm{H} ; \mathrm{CH}_{\text {ser }}\right), 4.63(\mathrm{~d}, J=$ $4.8 \mathrm{~Hz}, 2 \mathrm{H} ; \mathrm{CH}_{2 \text { (allyl) }}$ ), 4.45-4.25 (m, $2 \mathrm{H} ; \mathrm{CH}_{2(\text { (ser) })}$ ), 3.95 (app. s, $1 \mathrm{H} ; \mathrm{CH}_{\text {ala }}$ ), 3.0-2.87 ( $2 \mathrm{H} ; 2$ $\left.\mathrm{CH}_{\mathrm{nb}}\right), 2.2-2.13\left(\mathrm{~m}, 1 \mathrm{H} ; \mathrm{CH}_{\mathrm{nb}}\right), 1.85-1.76\left(\mathrm{~m}, 1 \mathrm{H} ; \mathrm{HCH}_{\mathrm{nb}}\right), 1.4-1.2\left(6 \mathrm{H} ; \mathrm{CH}_{3(\text { ala })}, \mathrm{CH}_{2(\mathrm{nb}}\right)$, $\mathrm{HCH}_{\mathrm{nb}}$ ); ${ }^{13} \mathbf{C}$ NMR ( 100 MHz, DMSO- $d_{6}, 25^{\circ} \mathrm{C}$ ): $\delta=174.8,170.0,168.5,138.0,135.5,132.0$, 118.1, 65.5, 62.8, 51.4, 48.1, 46.0, 45.9, 42.4, 41.1, 29.8, 17.3; IR (KBr pellet): $v=3449$ (s), 2992 ( s , 2362 (m), 1683 ( s$), 1192$ ( s ), 1022 (m), 763 ( s$) \mathrm{cm}^{-1}$; HRMS (ESI ${ }^{+}$): calcd. for $\mathrm{C}_{17} \mathrm{H}_{25} \mathrm{~N}_{2} \mathrm{O}_{5}\left(\mathrm{MH}^{+}\right)$337.1763, found 337.1778.


Boc-[D-ala-L-ser(O-NB)] $]_{2}$-O-allyl (8): To a solution of Boc-D-ala-L-ser(O-NB)-OH 6 (0.349 $\mathrm{g}, 0.88 \mathrm{mmol}, 1$ equiv) and TFA-D-ala-L-ser-(O-NB)-O-allyl 7 ( $0.397 \mathrm{~g}, 0.88 \mathrm{mmol}, 1$ equiv) in $\mathrm{CH}_{2} \mathrm{Cl}_{2}(10 \mathrm{~mL})$ was added $\mathrm{HCTU}(0.437 \mathrm{~g}, 1.057 \mathrm{mmol}, 1.2$ equiv) and DIEA ( 0.53 mL , $3.08 \mathrm{mmol}, 3.5$ equiv). The reaction mixture was allowed to stir at RT for 9 h , following
which $\mathrm{CH}_{2} \mathrm{Cl}_{2}$ removed in vacuo. The reaction mixture was diluted with ethyl acetate (150 mL ), washed with 0.1 N aqueous $\mathrm{HCl}(3 \times 50 \mathrm{~mL}), 5 \%$ aqueous $\mathrm{NaHCO}_{3}(3 \times 50 \mathrm{~mL})$ and saturated aqueous $\mathrm{NaCl}(2 \times 30 \mathrm{~mL})$. The organic layer was dried over anhydrous sodium sulphate, filtered and concentrated in vacuo. The residue was purified by flash column chromatography ( $40 \%$ ethyl acetate/Hexane) to afford 0.466 g of tetrapeptide 8 ( $74 \%$ ) as a pale yellow dense liquid. TLC $\mathrm{R}_{f}=0.34$ ( $40 \%$ ethyl acetate/hexane). ${ }^{1} \mathbf{H}$ NMR ( 500 MHz , $\mathrm{CDCl}_{3}, 25^{\circ} \mathrm{C}$ ): $\delta=7.48$ (bs, 2H; 2 NH ), 7.37 (bs, $1 \mathrm{H} ; \mathrm{NH}$ ), 6.13-6.04 ( $4 \mathrm{H} ; 2 \mathrm{CH}=\mathrm{CH}_{\mathrm{nb}}$ ), 5.92-5.83 (m, 1H; CH allyl ), $5.38(\mathrm{bs}, 1 \mathrm{H} ; \mathrm{NH}), 5.32\left(\mathrm{~d}, J=17.0 \mathrm{~Hz}, 1 \mathrm{H} ; \mathrm{HCH}_{\text {allyl }}\right), 5.24(\mathrm{~d}, J=$ $\left.10.5 \mathrm{~Hz}, 1 \mathrm{H} ; \mathrm{HCH}_{\text {ally }}\right), 4.89-4.77\left(2 \mathrm{H} ; 2 \mathrm{CH}_{\text {ser }}\right), 4.68-4.6\left(2 \mathrm{H}, \mathrm{OCH}_{2 \text { (allyl }}\right), 4.5-4.38(4 \mathrm{H} ; 2$ $\left.\mathrm{CH}_{2(\text { ser })}\right), 4.36-4.3\left(\mathrm{~m}, 1 \mathrm{H} ; \mathrm{CH}_{\mathrm{ala}}\right), 4.22-4.12\left(1 \mathrm{H} ; \mathrm{CH}_{\text {ala }}\right), 3.04-2.96\left(2 \mathrm{H} ; 2 \mathrm{C} H_{\mathrm{nb}}\right), 2.89(\mathrm{bs}$, $2 \mathrm{H} ; 2 \mathrm{CH}_{\mathrm{nb}}$ ), 2.23-2.17 $\left(2 \mathrm{H} ; 2 \mathrm{CH}_{\mathrm{nb}}\right), 1.90-1.83\left(2 \mathrm{H} ; 2 \mathrm{HCH}_{\mathrm{nb}}\right), 1.5-1.40\left(11 \mathrm{H} ; 2 \mathrm{HCH}_{\mathrm{nb}}, 3\right.$ $\left.\mathrm{CH}_{3(\mathrm{Boc})}\right), 1.4-1.3\left(10 \mathrm{H} ; 2 \mathrm{CH}_{3(\text { (ala })}, 2 \mathrm{HCH}_{\mathrm{nb}}, 2 \mathrm{HCH}_{\mathrm{nb}}\right) ;{ }^{13} \mathbf{C}$ NMR ( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}, 25^{\circ} \mathrm{C}$ ): $\delta=176.1,176.0,173.7,172.3,169.4,169.0,155.8,138.2,138.1,135.60,135.55,131.2$, $119.1,80.4,66.6,63.5,63.3,52.3,52.1,50.5,49.0,46.6,46.5,46.4,43.0,42.96,42.93,41.6$, $30.4,30.3,28.3,17.9,17.7$; IR $\left(\mathrm{CHCl}_{3}\right): v=3323(\mathrm{~m}), 3022(\mathrm{~s}), 1723(\mathrm{~s}), 1520(\mathrm{~m}), 1217(\mathrm{~s})$, $766(\mathrm{~s}) \mathrm{cm}^{-1}$; HRMS (ESI' ${ }^{+}$: calcd. for $\mathrm{C}_{36} \mathrm{H}_{51} \mathrm{~N}_{4} \mathrm{O}_{11}\left(\mathrm{MH}^{+}\right) 715.3554$, found 715.3542.


Boc-[D-ala-L-ser(O-NB)] $2_{2}$ OH (9): To a solution of Boc-[D-ala-L-ser(O-NB)] $2_{2}$-O-allyl $\mathbf{8}$ ( $0.46 \mathrm{~g}, 0.64 \mathrm{mmol}, 1$ equiv) in $\mathrm{CH}_{2} \mathrm{Cl}_{2}(7 \mathrm{~mL})$ at $0{ }^{\circ} \mathrm{C}$ was added $\left.\mathrm{Pd}^{\left(\mathrm{PPh}_{3}\right)}\right)_{4}(0.037 \mathrm{~g}, 3.22 \times$ $10^{-2} \mathrm{mmol}, 0.05$ equiv $), \mathrm{PPh}_{3}\left(0.034 \mathrm{~g}, 12.9 \times 10^{-2} \mathrm{mmol}, 0.2\right.$ equiv $)$ and pyrrolidine ( 0.064 $\mathrm{mL}, 0.77 \mathrm{mmol}, 1.2$ equiv). The reaction mixture allowed to stir at $0{ }^{\circ} \mathrm{C}$ for 15 min ., following which $\mathrm{CH}_{2} \mathrm{Cl}_{2}$ was removed in vacuo. The reaction mixture acidified with 0.1 N $\mathrm{HCl}(50 \mathrm{~mL})$ and extracted with ethyl acetate $(3 \times 75 \mathrm{~mL})$. The combined organic layers were dried over anhydrous sodium sulphate, filtered and concentrated in vacuo. The product was purified by flash column chromatography ( $6 \% \mathrm{MeOH} / \mathrm{CH}_{2} \mathrm{Cl}_{2}$ ) to afford 0.351 g of compound $9(81 \%)$ as a pale yellow solid. $\mathrm{R}_{f}=0.14$ ( $4 \%$ methanol/ $\mathrm{CH}_{2} \mathrm{Cl}_{2}$ and 2 drops of AcOH for 3 mL ). ${ }^{1} \mathbf{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{DMSO}-d_{6}, 25^{\circ} \mathrm{C}$ ): $\delta=8.24$ (bs, $1 \mathrm{H} ; \mathrm{NH}$ ), 8.08 (app. bs, $2 \mathrm{H} ; 2 \mathrm{~N} H$ ), $7.06(\mathrm{bs}, 1 \mathrm{H} ; \mathrm{NH}), 6.2-6.09\left(2 \mathrm{H} ; \mathrm{CH}=\mathrm{CH}_{\mathrm{nb}}\right), 4.63-4.55\left(\mathrm{~m}, 1 \mathrm{H} ; \mathrm{CH}_{\text {ser }}\right), 4.45-$
$4.07\left(6 \mathrm{H} ; \mathrm{CH}_{\text {ser }}, \mathrm{CH}_{\text {ala }} \& 2 \mathrm{CH}_{2 \text { (ser) }}\right)$, 4.0 (app. quint, $\left.1 \mathrm{H} ; \mathrm{CH}_{\text {ala }}\right), 3.0-2.93\left(2 \mathrm{H} ; 2 \mathrm{CH}_{\mathrm{nb}}\right), 2.86$ (bs, $2 \mathrm{H} ; 2 \mathrm{CH}_{\mathrm{nb}}$ ), 2.15-2.08 ( $2 \mathrm{H} ; 2 \mathrm{CH}_{\mathrm{nb}}$ ), 1.84-1.76 (m, $2 \mathrm{H} ; 2 \mathrm{HCH}_{\mathrm{nb}}$ ), 1.41-1.3 (11H; 2 $\left.\mathrm{HCH}_{\mathrm{nb}}, 3 \mathrm{CH}_{3(\mathrm{Boc})}\right), 1.28-1.1\left(10 \mathrm{H} ; 2 \mathrm{CH}_{3(\mathrm{ala})}, 2 \mathrm{HCH}_{\mathrm{nb}}, 2 \mathrm{HCH}_{\mathrm{nb}}\right) ;{ }^{13} \mathbf{C} \mathbf{N M R}(125 \mathrm{MHz}$, DMSO- $d_{6}, 25^{\circ} \mathrm{C}$ ): (some overlapping signals) $\delta=174.96,174.7,172.9,171.6,170.4,167.8$, 155.1, 137.9, 135.7, 135.6, 78.1, 63.97, 63.5, 52.0, 51.6, 49.8, 48.1, 46.0, 45.97, 45.8, 42.5, 42.5, 41.1, 29.8, 29.79, 29.0, 28.2, 18.4, 17.9; IR (KBr pellet): $v=3316$ (m), 3058 (m), 2980 (s), 1724 (s), 1663 (s), 1263 (s), 1166 (s), 735 (s) $\mathrm{cm}^{-1}$; HRMS (ESI ${ }^{+}$): calcd. for $\mathrm{C}_{33} \mathrm{H}_{46} \mathrm{~N}_{4} \mathrm{O}_{11} \mathrm{Na}\left(\mathrm{MNa}^{+}\right) 697.3061$, found 697.3060 .


TFA-[D-ala-L-ser(O-NB)] $]_{2}$-O-allyl (10): To a solution of Boc-[D-ala-L-ser(O-NB)] $]_{2}-\mathrm{O}-$ allyl $8\left(0.312 \mathrm{~g}, 0.437 \mathrm{mmol}, 1\right.$ equiv) in $\mathrm{CH}_{2} \mathrm{Cl}_{2}(5 \mathrm{~mL})$ at $0{ }^{\circ} \mathrm{C}$ was added TFA $(0.505 \mathrm{~mL}, 6.55$ $\mathrm{mmol}, 15$ equiv) over a period of 3 min . The reaction mixture allowed to stir at RT for 3 h , following which $\mathrm{CH}_{2} \mathrm{Cl}_{2}$ was removed in vacuo. Excess TFA was removed as an azeotrope with water. The product was dissolved in water ( 3 mL ) and lyophilized to give 0.313 g of $\mathbf{1 0}$ $(99 \%)$ as a pale yellow gummy solid. $\mathrm{R}_{f}=0.14$ ( $4 \%$ methanol/dichloromethane and 2 drops of TEA for 3 mL ). ${ }^{1} \mathbf{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{DMSO}-d_{6}, 25^{\circ} \mathrm{C}$ ): $\delta=8.77(\mathrm{dd}, J=10,6.5 \mathrm{~Hz}, 1 \mathrm{H}$; $\mathrm{N} H), 8.67(\mathrm{~d}, J=9.5 \mathrm{~Hz}, 1 \mathrm{H} ; \mathrm{N} H), 8.51(\mathrm{~d}, J=10 \mathrm{~Hz}, 1 \mathrm{H} ; \mathrm{N} H), 8.10\left(\mathrm{bs}, 3 \mathrm{H} ; \mathrm{N} H_{3}\right), 6.10-$ $6.09\left(4 \mathrm{H} ; 2 \mathrm{CH}=\mathrm{C} H_{\mathrm{nb}}\right), 5.95-5.83\left(\mathrm{~m}, 1 \mathrm{H} ; \mathrm{CH}_{\text {allyl }}\right), 5.32\left(\mathrm{dt}, J=21.5,2 \mathrm{~Hz}, 1 \mathrm{H} ; \mathrm{HCH}_{\text {allyl }}\right)$, $5.22\left(\mathrm{dt}, J=13,1.5 \mathrm{~Hz}, 1 \mathrm{H} ; \mathrm{HCH}_{\text {allyl }}\right), 4.82-4.75\left(\mathrm{~m}, 1 \mathrm{H} ; \mathrm{CH}_{\text {ser }}\right), 4.72-4.65\left(\mathrm{~m}, 1 \mathrm{H} ; \mathrm{CH}_{\text {ser }}\right)$, $4.60\left(\mathrm{~d}, J=6.5 \mathrm{~Hz}, 2 \mathrm{H} ; \mathrm{CH}_{2 \text { (allyl) }}\right), 4.47$ (app. quint, $1 \mathrm{H} ; \mathrm{CH}_{\text {ala }}$ ), 4.4-4.12 ( $4 \mathrm{H} ; 2 \mathrm{CH}_{2(\text { ser) })}$ ), 4$3.3\left(\mathrm{~m}, 1 \mathrm{H} ; \mathrm{CH}_{\mathrm{ala}}\right), 3.1-2.9\left(2 \mathrm{H} ; 2 \mathrm{CH} \mathrm{nb}_{\mathrm{b}}\right), 2.88\left(\mathrm{bs} ; 2 \mathrm{CH}_{\mathrm{nb}}\right), 2.2-2.1\left(2 \mathrm{H} ; 2 \mathrm{CH}_{\mathrm{nb}}\right), 1.85-1.76$ $\left(2 \mathrm{H} ; 2 \mathrm{HCH}_{\mathrm{nb}}\right), 1.40-1.10\left(12 \mathrm{H} ; 2 \mathrm{HCH}_{\mathrm{nb}}, 2 \mathrm{CH}_{3(\text { ala })} \& 2 \mathrm{CH}_{2(\mathrm{nb})}\right),{ }^{13} \mathbf{C}$ NMR ( 125 MHz , DMSO- $d_{6}, 25{ }^{\circ} \mathrm{C}$ ): (some overlapping signals) $\delta=174.9,174.7,172.3,169.7,168.9,167.4$, $138.0,135.5,132.1,117.9,65.3,63.6,63.0,51.6,51.2,48.1,47.9,46.0,45.9,42.5,41.1,29.9$, 29.8, 18.7, 17.3 ; IR $\left(\mathrm{CHCl}_{3}\right): v=3417(\mathrm{~m}), 1729(\mathrm{~s}), 1525(\mathrm{~m}), 1429(\mathrm{~m}), 1216(\mathrm{~s}), 930(\mathrm{~m})$, $755(\mathrm{~s}) \mathrm{cm}^{-1} ; \mathbf{H R M S}\left(\mathbf{E S I}{ }^{+}\right)$: calcd. for $\mathrm{C}_{31} \mathrm{H}_{43} \mathrm{~N}_{4} \mathrm{O} 9\left(\mathrm{MH}^{+}\right)$615.3030, found 615.2158 .


Boc-[D-ala-L-ser(O-NB)] ${ }_{4}$-O-allyl (11): To a solution of Boc-[D-ala-L-ser(O-NB)] 2 -OH 9 $(0.161 \mathrm{~g}, 0.239 \mathrm{mmol}, 1$ equiv) and TFA-[D-ala-L-ser-(O-NB)]2-O-allyl 10 ( $0.174 \mathrm{~g}, 0.239$ mmol, 1 equiv) in $\mathrm{CH}_{2} \mathrm{Cl}_{2}(5 \mathrm{~mL})$ was added $\mathrm{HCTU}(0.119 \mathrm{~g}, 0.287 \mathrm{mmol}, 1.2$ equiv) and DIEA ( $0.143 \mathrm{~mL}, 0.836 \mathrm{mmol}, 3.5$ equiv). The reaction mixture was allowed to stir at RT for 14 h , following which $\mathrm{CH}_{2} \mathrm{Cl}_{2}$ removed in vacuo. The reaction mixture was diluted with ethyl acetate ( 200 mL ), washed with 0.1 N aqueous $\mathrm{HCl}(3 \times 50 \mathrm{~mL})$ and $5 \%$ aqueous $\mathrm{NaHCO}_{3}(3 \times$ 50 mL ). The organic layer was dried over anhydrous sodium sulphate, filtered and concentrated in vacuo. The residue was purified by flash column chromatography ( $3 \%$ methanol $/ \mathrm{CH}_{2} \mathrm{Cl}_{2}$ ) to afford 0.195 g of compound $\mathbf{1 1}(64 \%)$ as a pale yellow solid. TLC $\mathrm{R}_{f}=$ 0.39 ( $4 \%$ methanol/ $\mathrm{CH}_{2} \mathrm{Cl}_{2}$ ). ${ }^{1} \mathbf{H}$ NMR ( 500 MHz , DMSO- $d_{6}, 25^{\circ} \mathrm{C}$ ): $\delta=8.56-8.54(\mathrm{~m}, 1 \mathrm{H}$; $\mathrm{N} H$ ), 8.38-8.3 ( $2 \mathrm{H} ; 2 \mathrm{~N} H$ ), 8.27-8.19 ( $3 \mathrm{H} ; 3 \mathrm{NH}$ ), 8.07 (d, $J=7 \mathrm{~Hz}, 1 \mathrm{H} ; \mathrm{N} H$ ), 7.06-7.01 (m, $1 \mathrm{H} ; \mathrm{NH}$ ), 6.18-6.08 ( $8 \mathrm{H} ; 4 \mathrm{CH}=\mathrm{CH}_{\mathrm{nb}}$ ), $5.93-5.85\left(\mathrm{~m}, 1 \mathrm{H} ; \mathrm{CH}_{\text {allyl }}\right), 5.33$ (dt, $J=22,2 \mathrm{~Hz}, 1 \mathrm{H}$; $\left.\mathrm{HCH}_{\text {allyl }}\right), 5.21\left(\mathrm{dt}, J=10.5,1.5 \mathrm{~Hz}, 1 \mathrm{H} ; \mathrm{HCH}_{\text {allyl }}\right), 4.72-4.58\left(6 \mathrm{H} ; 4 \mathrm{CH}_{\text {ser }}, \mathrm{OCH}_{2(\text { allyl }}\right), 4.45-$ $4.12\left(11 \mathrm{H} ; 4 \mathrm{CH}_{2 \text { (ser) }}, 3 \mathrm{CH}_{\text {ala }}\right.$ ), 4.0 (app. quint, $1 \mathrm{H} ; \mathrm{CH}_{\text {ala }}$ ), $3.0-2.94$ ( $4 \mathrm{H} ; 4 \mathrm{CH}_{\mathrm{nb}}$ ), 2.87 (bs, $4 \mathrm{H} ; 4 \mathrm{CH}_{\mathrm{nb}}$ ), 2.18-2.1 ( $4 \mathrm{H} ; 4 \mathrm{CH}_{\mathrm{nb}}$ ), 1.85-1.77 ( $4 \mathrm{H} ; 4 \mathrm{HCH}_{\mathrm{nb}}$ ), 1.41-1.32 ( $13 \mathrm{H} ; 4 \mathrm{HCH}_{\mathrm{nb}}, 3$ $\left.\mathrm{CH}_{3(\mathrm{Boc})}\right), 1.3-1.18\left(17 \mathrm{H} ; 3 \mathrm{CH}_{3(\text { (ala })}, 4 \mathrm{HCH}_{\mathrm{nb}}, 4 \mathrm{HCH}_{\mathrm{nb}}\right), 1.15\left(\mathrm{~d}, J=7.5 \mathrm{~Hz}, 3 \mathrm{H} ; \mathrm{CH}_{3(\text { (ala })}\right) ;$ ${ }^{13} \mathbf{C}$ NMR ( 125 MHz, DMSO- $d_{6}, 25^{\circ} \mathrm{C}$ ): (some overlapping signals) $\delta=174.9,174.85,174.8$, $173.0,172.3,168.9,168.3,168.2,168.0,155.2,138.0,137.97,135.6,135.5,132.1,118.0$, $78.2,65.3,63.6,63.0,51.6,51.5,51.2,59.9,48.6,48.0,46.0,45.9,42.54,42.5,42.4,41.1$, 29.9, 29.86, 29.82, 29.8, 29.0, 28.2, 18.5, 18.1, 18.0, 17.8; IR (KBr pellet): $v=3316$ (s), 2977 ( s), 1734 ( s), 1666 (m), 1525 (s), 1246 (m), 1167 (s), 1040 (m), 852 (s) cm ${ }^{-1}$; HRMS (ESI' ${ }^{+}$: calcd. for $\mathrm{C}_{64} \mathrm{H}_{86} \mathrm{~N}_{8} \mathrm{O}_{19} \mathrm{Na}\left(\mathrm{MNa}^{+}\right)$1293.5907, found 1293.5908 .


Cyclo-[D-ala-L-ser(O-NB)] (1): To a solution of Boc-[D-ala-L-ser(O-NB)]4 -O-allyl 11 $\left(0.072 \mathrm{~g}, 5.66 \times 10^{-2} \mathrm{mmol}, 1\right.$ equiv) in $\mathrm{CH}_{2} \mathrm{Cl}_{2}(3 \mathrm{~mL})$ at $0{ }^{\circ} \mathrm{C}$ was added $\mathrm{Pd}\left(\mathrm{PPh}_{3}\right)_{4}(0.0032$ $\mathrm{g}, 2.8 \times 10^{-3} \mathrm{mmol}, 0.05$ equiv), $\mathrm{PPh}_{3}\left(0.003 \mathrm{~g}, 1.13 \times 10^{-2} \mathrm{mmol}, 0.2\right.$ equiv $)$ and pyrrolidine ( $0.006 \mathrm{~mL}, 6.79 \times 10^{-2} \mathrm{mmol}, 1.2$ equiv). The reaction mixture allowed to stir at $0{ }^{\circ} \mathrm{C}$ temperature for 20 min ., following which $\mathrm{CH}_{2} \mathrm{Cl}_{2}$ was removed in vacuo. The reaction mixture was acidified with $0.1 \mathrm{~N} \mathrm{HCl}(10 \mathrm{~mL})$ and extracted with ethyl acetate $(3 \times 50 \mathrm{~mL})$. The combined organic layers were dried over anhydrous sodium sulphate, filtered and concentrated in vacuo. The product was purified by flash column chromatography ( $15 \%$ methanol $/ \mathrm{CH}_{2} \mathrm{Cl}_{2}$ ) to afford 0.067 g of alloc deprotected linear octapeptide $\mathbf{1 6}(95 \%)$ as a pale yellow solid. $\mathrm{R}_{f}=0.17$ ( $12 \%$ methanol/ $\mathrm{CH}_{2} \mathrm{Cl}_{2}$ and 1 drop of AcOH for 3 mL ). ${ }^{\mathbf{1}} \mathbf{H}$ NMR ( 500 $\mathrm{MHz}, \mathrm{DMSO}-d_{6}, 25^{\circ} \mathrm{C}$ ): $\delta=9.09$ (bs, $1 \mathrm{H} ; \mathrm{N} H$ ), 8.74 (bs, $1 \mathrm{H} ; \mathrm{N} H$ ), 8.55-8.3 ( $4 \mathrm{H} ; 4 \mathrm{~N} H$ ), 7.63-7.52 (m, 1H; NH), $7.05(\mathrm{~d}, J=6 \mathrm{~Hz}, 1 \mathrm{H} ; \mathrm{N} H), 6.16-6.06\left(8 \mathrm{H} ; 4 \mathrm{CH}=\mathrm{CH}_{\mathrm{nb}}\right), 4.65-4.52$
$\left(3 \mathrm{H} ; 3 \mathrm{CH}_{\text {ser }}\right), 4.47-4.38\left(\mathrm{~m}, 1 \mathrm{H} ; \mathrm{CH}_{\text {ser }}\right), 4.36-3.95\left(12 \mathrm{H} ; 4 \mathrm{CH}_{2(\mathrm{ser})}, 4 \mathrm{CH}_{\mathrm{ala}}\right), 3.0-2.91(4 \mathrm{H} ; 4$ $\left.\mathrm{CH}_{\mathrm{nb}}\right), 2.88-2.8\left(4 \mathrm{H} ; 4 \mathrm{CH} H_{\mathrm{nb}}\right), 2.16-2.04\left(4 \mathrm{H} ; 4 \mathrm{C} H_{\mathrm{nb}}\right), 1.84-1.74\left(4 \mathrm{H} ; 4 \mathrm{HCH}_{\mathrm{nb}}\right), 1.4-1.3$ ( $\left.13 \mathrm{H} ; 4 \mathrm{HCH}_{\mathrm{nb}}, 3 \mathrm{CH}_{3(\mathrm{Boc})}\right), 1.28-1.12\left(20 \mathrm{H} ; 4 \mathrm{CH}_{3(\text { ala })}, 4 \mathrm{HCH}_{\mathrm{nb}}, 4 \mathrm{HCH}_{\mathrm{nb}}\right)$; IR ( KBr pellet): $v=3332$ (m), 3024 (s), 2403 (m), 1727 (s), 1664 (s), 1522 (s), 1217 (s), 929 (m), 767 (s), $\mathrm{cm}^{-}$ ${ }^{1}$; HRMS (ESI ${ }^{+}$): calcd. for $\mathrm{C}_{61} \mathrm{H}_{82} \mathrm{~N}_{8} \mathrm{O}_{19} \mathrm{Na}\left(\mathrm{MNa}^{+}\right)$1253.5594, found 1253.5602.

To a solution of alloc deprotected linear octapeptide $16\left(0.060 \mathrm{~g}, 4.87 \times 10^{-2} \mathrm{mmol}, 1\right.$ equiv) in $\mathrm{CH}_{2} \mathrm{Cl}_{2}(3 \mathrm{~mL})$ at $0{ }^{\circ} \mathrm{C}$ was added TFA ( 2 mL ) over a period of 3 min . The reaction mixture was allowed to stir at RT for 3 h , following which $\mathrm{CH}_{2} \mathrm{Cl}_{2}$ was removed in vacuo. Excess TFA was removed as an azeotrope with water. The product was dissolved in water (2 mL ) and lyophilized to give 0.060 g of deprotected linear octapeptide $\mathbf{1 7}$ ( $99 \%$ ) as a pale yellow solid liquid. $\mathrm{R}_{f}=0.17$ ( $20 \%$ methanol/dichloromethane). ${ }^{1} \mathbf{H} \mathbf{N M R}$ ( 500 MHz , DMSO- $d_{6}, 25^{\circ} \mathrm{C}$ ): $\delta=8.75$ (bs, $\left.1 \mathrm{H} ; \mathrm{NH}\right), 8.53-8.22(8 \mathrm{H} ; 5 \mathrm{NH} \& \mathrm{NH} 3$ ), 7.7-7.5 (m, $1 \mathrm{H} ; \mathrm{NH}$ ), 4.8-4.5 (4H; $4 \mathrm{CH}_{\text {ser }}$ ), 4.44-4.25 (11H; $\mathrm{CH}_{2(\text { ser })} \& 3 \mathrm{CH}_{\text {ala }}$ ), 3.93 (app. bs, $1 \mathrm{H} ; \mathrm{CH}_{\text {ala }}$ ), 2.98 (bs, $4 \mathrm{H} ; 4 \mathrm{CH} H_{\mathrm{nb}}$ ), 2.87 (bs, $4 \mathrm{H} ; 4 \mathrm{CH}_{\mathrm{nb}}$ ), 2.18-2.11 ( $4 \mathrm{H} ; 4 \mathrm{CH} \mathrm{nb}$ ), 1.85-1.78 ( $4 \mathrm{H} ; 4 \mathrm{HCH}_{\mathrm{nb}}$ ), 1.4-1.15 (24H; $\left.4 \mathrm{HCH}_{\mathrm{nb}}, 4 \mathrm{CH}_{2(\mathrm{nb})} \& 3 \mathrm{CH}_{3(\mathrm{Boc})}\right) ;$ IR (KBr pellet): $v=3290(\mathrm{~s}), 2970(\mathrm{~m})$, 2354 ( s), 1730 (s), 1642 (s), 1536 (s), 1166 (s), 712 (m), cm ${ }^{-1}$; HRMS (ESI ${ }^{+}$): calcd. for $\mathrm{C}_{56} \mathrm{H}_{75} \mathrm{~N}_{8} \mathrm{O}_{17}\left(\mathrm{MH}^{+}\right) 1131.5250$, found 1131.5293.

To a solution of deprotected peptide $17\left(0.052 \mathrm{~g}, 4.2 \times 10^{-2} \mathrm{mmol}, 1\right.$ equiv) in DMF $(14 \mathrm{~mL},[0.003] \mathrm{mM})$ at $0{ }^{\circ} \mathrm{C}$ was added HCTU ( $0.035 \mathrm{~g}, 8.35 \times 10^{-2} \mathrm{mmol}, 2$ equiv) and DIEA ( $0.029 \mathrm{~mL}, 16.7 \times 10^{-2} \mathrm{mmol}, 4$ equiv). The reaction mixture allowed to stir at $0^{\circ} \mathrm{C}$ for 2 h , then warmed to RT. The reaction mixture was stirred at RT for 48 h , following which the solvent was removed in vacuo. The residue was precipitated with water to obtaine the crude cyclic peptide 1. The Crude cyclic peptide residue was washed sequentially with water ( $5 \times$ $10 \mathrm{~mL})$ and methanol $(4 \times 10 \mathrm{~mL})$ to afford 0.034 g of cyclic peptide $\mathbf{1}(72 \%)$ as a pale yellow solid. ${ }^{1} \mathbf{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{DMSO}-d_{6}, 25^{\circ} \mathrm{C}$ ): $\delta=8.7-8.0(8 \mathrm{H} ; 8 \mathrm{NH}), 6.2-6(8 \mathrm{H} ; 4$ $\left.\mathrm{CH}=\mathrm{CH}_{\mathrm{nb}}\right), 4.8-4.0\left(16 \mathrm{H} ; 4 \mathrm{CH}_{\mathrm{ser}}, 4 \mathrm{CH}_{2(\text { ser })} \& 4 \mathrm{CH}_{\mathrm{ala}}\right), 2.9-2.7\left(8 \mathrm{H} ; 8 \mathrm{CH} H_{\mathrm{nb}}\right), 2.12(\mathrm{bs}, 4 \mathrm{H} ; 4$ $\left.\mathrm{CH}_{\mathrm{nb}}\right), 1.80\left(4 \mathrm{H} ; 4 \mathrm{HCH}_{\mathrm{nb}}\right), 1.4-1.1\left(24 \mathrm{H} ; 4 \mathrm{HCH}_{\mathrm{nb}}, 4 \mathrm{CH}_{2(\mathrm{nb})} \& 4 \mathrm{CH}_{3(\mathrm{ala})}\right) ;$ IR ( KBr pellet): $v=3285$ ( s , 2975 ( s , 2354 ( s ), 1733 ( s$), 1641$ ( s$), 1535$ ( s$), 1339$ (m), 1165 ( s$), 1035$ (m), $715(\mathrm{~m}) \mathrm{cm}^{-1}$; MS (MALDI ${ }^{+}$) for $\mathrm{C}_{56} \mathrm{H}_{72} \mathrm{~N}_{8} \mathrm{O}_{16} \mathrm{Na}\left(\mathrm{MNa}^{+}\right)$1135.496, found 1135.731.

## General procedure for synthesis of PPC 12

A solution of cyclic peptide 1 in 1:4 DMF-THF was allowed to stand for 5 days at RT. The solution was subsequently deoxygenated using stream of nitrogen gas. Deoxygenated solutions of Grubbs' second generation initiator and cross-linker 2 in 1:4 DMF-THF were added to this solution over a period of 15 min using a syringe pump. The reaction mixture was allowed to stir at room temperature. After completion of polymerization, ethyl vinyl ether ( 1 mL ) was added to the reaction mixture and it was stirred for an additional 30 min , following which it was concentrated in vacuo to a minimum volume. Methanol ( 10 mL ) was added to precipitate the PPC 12. The precipitate was washed sequentially with methanol $(4 \times 10 \mathrm{~mL})$ followed by water $(4 \times 10 \mathrm{~mL})$ to afford PPC $\mathbf{1 2}$ as a solid.

Table S1. Reaction conditions used to obtain PPC 12

| No. | 1 $\text { (equiv) }{ }^{[a]}$ | $\begin{aligned} & \mathbf{2} \\ & \text { (equiv) }^{[\mathrm{a}]} \end{aligned}$ | Conc. $(\mathrm{mM})$ | Time <br> (h) | $\begin{aligned} & \hline \text { PPC } \\ & \mathbf{1 2} \end{aligned}$ | Yield ${ }^{[b]}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 1. | 80 | 160 | 0.8 | 8 | 12a | 68\% |
| 2. | 100 | 0 | 0.6 | 4 | 12b | 79\% |
| 3. | 100 | 0 | 0.6 | 6 | 12c | 76\% |
| 4. | 100 | 0 | 0.6 | 8 | 12d | 82\% |
| 5. | 100 | 200 | 0.6 | 4 | 12e | 77\% |
| 6. | 100 | 200 | 0.4 | 4 | 12 f | 87\% |
| 7. | 200 | 0 | 0.2 | 2 | 12g | 88\% |
| 8. | 200 | 400 | 0.2 | 2 | 12h | 87\% |

${ }^{[a]}$ Equiv with respect to Ru. ${ }^{[b]}$ Based on weight of isolated polymer.

## PPC 12a:

Grubbs second generation initiator ( $0.05 \mathrm{mg}, 5.9 \times 10^{-5} \mathrm{mmol}$, 1 equiv) in 1:4 DMF-THF ( 0.5 $\mathrm{mL})$ and cross-linker $2\left(2.8 \mathrm{mg}, 9.4 \times 10^{-3} \mathrm{mmol}, 160\right.$ equiv $)$ in 1:4 DMF-THF ( 0.5 mL ) were added to a solution of self-assembled cyclic peptide $\mathbf{1}\left(5.2 \mathrm{mg}, 4.7 \times 10^{-3} \mathrm{mmol}, 80\right.$ equiv) in 1:4 DMF-THF ( 5 mL ) to afford PPC 12a in $68 \%$ yield ( 5.44 mg ).

## PPC 12b:

Grubbs second generation initiator ( $0.03 \mathrm{mg}, 3.5 \times 10^{-5} \mathrm{mmol}, 1$ equiv) in 1:4 DMF-THF ( 2 $\mathrm{mL})$ was added to a solution of self-assembled cyclic peptide $1\left(3.9 \mathrm{mg}, 3.5 \times 10^{-3} \mathrm{mmol}, 100\right.$ equiv) in 1:4 DMF-THF ( 4 mL ) to afford PPC 12b in $79 \%$ yield $(3.08 \mathrm{mg})$.

## PPC 12c:

Grubbs second generation initiator ( $0.04 \mathrm{mg}, 4.7 \times 10^{-5} \mathrm{mmol}$, 1 equiv) in 1:4 DMF-THF ( 2 $\mathrm{mL})$ was added to a solution of self-assembled cyclic peptide $\mathbf{1}\left(5.2 \mathrm{mg}, 4.7 \times 10^{-3} \mathrm{mmol}, 100\right.$ equiv) in 1:4 DMF-THF ( 6 mL ) to afford PPC 12c in $76 \%$ yield ( 3.95 mg ).

## PPC 12d:

Grubbs second generation initiator ( $0.04 \mathrm{mg}, 4.7 \times 10^{-5} \mathrm{mmol}$, 1 equiv) in 1:4 DMF-THF ( 2 $\mathrm{mL})$ was added to a solution of self-assembled cyclic peptide $\mathbf{1}\left(5.2 \mathrm{mg}, 4.7 \times 10^{-3} \mathrm{mmol}, 100\right.$ equiv) in 1:4 DMF-THF ( 6 mL ) to afford PPC 12d in $82 \%$ yield ( 4.26 mg ).

## PPC 12e:

Grubbs second generation initiator ( $0.05 \mathrm{mg}, 5.9 \times 10^{-5} \mathrm{mmol}$, 1 equiv) in 1:4 DMF-THF ( 2 mL ) and cross-linker $2\left(3.6 \mathrm{mg}, 11.8 \times 10^{-3} \mathrm{mmol}\right.$, 200 equiv) in 1:4 DMF-THF ( 1 mL ) were added to a solution of self-assembled cyclic peptide $\mathbf{1}\left(6.6 \mathrm{mg}, 5.9 \times 10^{-3} \mathrm{mmol}, 100\right.$ equiv) in 1:4 DMF-THF ( 12 mL ) to afford PPC 12e in $77 \%$ yield $(7.85 \mathrm{mg})$.

## PPC 12f:

Grubbs second generation initiator ( $0.04 \mathrm{mg}, 4.3 \times 10^{-5} \mathrm{mmol}$, 1 equiv) in 1:4 DMF-THF ( 2 $\mathrm{mL})$ and cross-linker $2\left(2.6 \mathrm{mg}, 8.6 \times 10^{-3} \mathrm{mmol}\right.$, 200 equiv) in 1:4 DMF-THF ( 1 mL ) were added to a solution of self-assembled cyclic peptide $\mathbf{1}\left(4.8 \mathrm{mg}, 4.3 \times 10^{-3} \mathrm{mmol}, 100\right.$ equiv $)$ in 1:4 DMF-THF ( 8 mL ) to afford PPC 12f in $87 \%$ yield ( 6.44 mg ).

## PPC 12g:

Grubbs second generation initiator ( $0.03 \mathrm{mg}, 3.5 \times 10^{-5} \mathrm{mmol}$, 1 equiv) in 1:4 DMF-THF ( 2 mL ) was added to a solution of self-assembled cyclic peptide $\mathbf{1}\left(7.9 \mathrm{mg}, 7.0 \times 10^{-3} \mathrm{mmol}, 200\right.$ equiv) in 1:4 DMF-THF ( 34 mL ) to afford PPC 12g in $88 \%$ yield ( 6.95 mg ). IR ( KBr pellet): $v=3389(\mathrm{~b}), 2962(\mathrm{~m}), 1729(\mathrm{~s}), 1652(\mathrm{~s}), 1530(\mathrm{~m}), 1163(\mathrm{~s}), 714(\mathrm{~m}) \mathrm{cm}^{-1}$.

## PPC 12h:

Grubbs second generation initiator ( $0.03 \mathrm{mg}, 3.5 \times 10^{-5} \mathrm{mmol}, 1$ equiv) in 1:4 DMF-THF ( 2 mL ) and cross-linker $2\left(2.8 \mathrm{mg}, 14.1 \times 10^{-3} \mathrm{mmol}, 400\right.$ equiv) in 1:4 DMF-THF ( 2 mL ) were added to a solution of self-assembled cyclic peptide $\mathbf{1}\left(7.9 \mathrm{mg}, 7.0 \times 10^{-3} \mathrm{mmol}, 200\right.$ equiv) in 1:4 DMF-THF ( 32 mL ) to afford PPC 12h in $87 \%$ yield ( 9.31 mg ). IR ( KBr pellet): $v=$ 3398 (b), 3286 (s), 2926 (m), 1732 (s), 1639 (s), 1538 (m), 1018 (b), 709 (m) cm ${ }^{-1}$.

FP 13: To a solution of PPC $\mathbf{1 2 h}(5 \mathrm{mg})$ in $1: 1 \mathrm{MeOH} / \mathrm{H}_{2} \mathrm{O}(16 \mathrm{~mL})$ was added $\mathrm{LiOH} . \mathrm{H}_{2} \mathrm{O}$ (10mg). The reaction mixture was sonicated for 30 min , following which the mixture was allowed to stir at RT. After 48 h , the solvent was removed in vacuo and the residue was washed with methanol to obtained crude FP 13. The crude FP residue was sequentially washed with 1:1 TFA/water $(3 \times 5 \mathrm{~mL})$ and 1:1 TFA/methanol $(3 \times 5 \mathrm{~mL})$ to afford 0.8 mg of FP 13 in $16 \%$ yield $(0.8 \mathrm{mg})$ with respect to the weight of PPC 12h. IR (KBr pellet): $v=$ 3406 (b), 2924 (m), 1636 (m), 1535 (s), 1441 ( $), 1074$ (m), 863 (s) $\mathrm{cm}^{-1}$.

NAcid-CL Polymer 14: A solution of norbornene acid ( $6.5 \mathrm{mg}, 4.7 \times 10^{-2} \mathrm{mmol}, 400$ equiv) in 1:4 DMF/THF ( 40 mL ) was deoxygenated using a stream of nitrogen gas. Deoxygenated solutions of Grubbs second generation initiator ( $0.1 \mathrm{mg}, 1.16 \times 10^{-4} \mathrm{mmol}, 1$ equiv) in $1: 4$ DMF/THF ( 10 mL ) and cross-linker $2\left(7 \mathrm{mg}, 2.36 \times 10^{-2} \mathrm{mmol}\right.$, 200 equiv) in 1:4 DMF/THF $(10 \mathrm{~mL})$ were added over a period of 15 min . The reaction mixture was allowed to stir at RT for 2 h , following which ethyl vinyl ether ( 1 mL ) was added and the mixture was stirred for an additional 30 min . The mixture was concentrated in vacuo to a minimum volume. Methanol $(10 \mathrm{~mL})$ was added to precipitate the polymer residue. The residue was washed sequentially with methanol $(4 \times 10 \mathrm{~mL})$ and water $(4 \times 10 \mathrm{~mL})$ to afford NAcid-CL polymer $\mathbf{1 4}$ in $96 \%$
yield (12.9 mg). IR (KBr pellet): $v=3269$ (b), 2924 (m), 1644 (s), 1637 (s), 1240 (m), 971 (m), 734 (m) $\mathrm{cm}^{-1}$.

## Self-assembly studies with cyclic peptide 1

## Sample preparation for TEM

A solution of cyclic peptide $\mathbf{1}$ in $1: 4$ DMF -THF $(0.1 \mathrm{mg} / \mathrm{mL})$ was allowed to stand at room temperature for 5 days. The solution was drop-casted onto a copper grid and dried in vacuo for TEM analysis.


Figure S1. TEM image of peptide 1.

## Characterization of PPC 12a-g by microscopy

## Sample preparation for SEM

A solution of the PPC 12 in 1:4 DMF-THF $(0.1 \mathrm{mg} / 5 \mathrm{~mL})$ was drop-casted onto a silicon grid and dried in vacuo for SEM analysis.


Figure S2. SEM images of PPC12a-f, TEM image of 12g.

## Dynamic Light Scattering (DLS) studies

## Sample preparation for DLS studies

A solution of cyclic peptide 1, PPC 12 or FP $13(0.1 \mathrm{mg} / 10 \mathrm{~mL})$ in 5\% DMF-THF ( $\mathrm{v} / \mathrm{v}$ ) was allowed to self-assemble for 3 days and the DLS data was obtained for the solution. The solution was concentrated to a minimum volume (approximately 0.5 mL ) in vacuo and re-dispersed in 10 mL DMF/TFA ( $3: 1 \mathrm{v} / \mathrm{v}$ ) and the DLS data was obtained.


Figure S3. DLS data to indicate stability of PPC 12g in the presence of TFA.

## TGA data



Figure S4. TGA data under nitrogen for a) cyclic peptide 1; b) polymer 14; c) PPC 12g; d) PPC 12h.

## IR Data



Figure S5. Stacked IR plots of a) PPC 12g, PPC 12h \& peptide 1; b) FP 13 and PPC 12h; c) FP 13 and polymer 14.

## Characterization of FP 13 by microscopy

## Sample preparation for SEM \& TEM

A solution of functionalized pores $\mathbf{1 3}$ in 1:4 DMF -THF ( $0.1 \mathrm{mg} / 5 \mathrm{~mL}$ ) was dropcasted onto a silicon grid and dried in vacuo for SEM analysis. The remaining solution was concentrated in vacuo and redispersed in 5 mL DMF/TFA ( $3: 1 \mathrm{v} / \mathrm{v}$ ). This solution was dropcasted over copper grid for TEM analysis.


Figure S6. SEM image of FP 13.

## Procedure for incorporation of lucigenin dye into FP 13 and PPC 12h.

FP $13(0.2 \mathrm{mg}) /$ PPC 12h $(0.2 \mathrm{mg})$ was dissolved in DMF $(0.5 \mathrm{~mL})$ and the resultant solution was treated with 0.1 mL of an aqueous solution of lucigenin dye ( 1 mM ). This solution was further diluted with deionized water $(4 \mathrm{~mL})$ and allowed to stir at RT for 14 h . The solution was concentrated in vacuo to half of its original volume and methanol was added. This precipitate was washed with water $(10 \times 5 \mathrm{~mL})$ to remove unreacted dye and analysed using fluorescence microscopy.

## Fluorescence microscopy with dye incorporated FP 13/ PPC 12h

## Sample preparation for studies with Leica inverted fluorescence microscope

A solution of dye treated PPC 12h or FP 13 in 1:4 DMF-THF $(0.2 \mathrm{mg} / 5 \mathrm{~mL})$ was coated over a glass slide. Fluorescence images were acquired without drying the solution.


Figure S7. Bright field image after dye encapsulation experiment with PPC 12h.

## Sample preparation and images using Olympus 1X51 fluorescence microscope

A solution of dye incorporated functionalized pore in 1:4 DMF - THF $(0.1 \mathrm{mg} / 5 \mathrm{~mL})$ was coated over a glass slide. Fluorescence images were acquired without drying the solution.


Figure S8. Fluorescent and bright field images of lucigenin incorporated FP 13.

## Sample preparation to determine Zeta potential

To a solution of functional pores $\mathbf{1 3}(0.3 \mathrm{mg})$ in DMF ( 0.5 mL ) was added 3 mL of 0.001 m NaNO 3 . The pH of the suspension was maintained at 7.2 by adding $\mathrm{HNO}_{3} / \mathrm{NaOH}$ 0.01 m . This suspension was sonicated for 10 min . and then zeta potential was measured.

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Spectra of compounds








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