

## Supporting Information

### **An Improved Soluble Polynorbornene Support for Peptide Synthesis**

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## General Methods

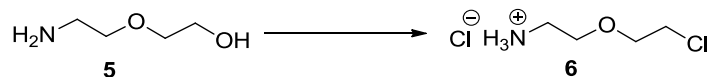
All air-sensitive reactions were performed under an inert atmosphere of nitrogen. Unless stated otherwise, all the reagents for synthesis were purchased from commercially available suppliers and used without further purification. Tetrahydrofuran (THF) was distilled from sodium benzophenoneketyl, *N,N*-Diisopropylethylamine (DIEA), and dichloromethane were distilled from calcium hydride; *N,N*-dimethylformamide (DMF), 20% Piperidine-DMF and *N,N*-Diisopropylcarbodiimide (DIC) were dried over 4 Å molecular sieves. All dry solvents were stored over 4 Å molecular sieves prior to use.

Analytical thin layer chromatography (TLC) was performed on MERCK precoated silica gel 60 F<sub>254</sub>TLC plates. Eluting solvents are reported as volume percents. Compounds were visualized using UV light and KMO<sub>4</sub> stains. Flash column chromatography was performed using silica gel (100-200mesh) from Acme chemicals. All 1D and 2D NMR spectra were recorded on Bruker 400 or Bruker 500 spectrometers using CDCl<sub>3</sub>, CD<sub>3</sub>OD, D<sub>2</sub>O or DMSO-d<sub>6</sub> as solvent. The NMR spectra were referenced using residual solvent peaks as the standard. Chemical shifts are denoted in parts per million ( $\delta$ ) and coupling constants (*J*) are reported in Hertz (Hz). The spin multiplicities are reported as singlet (s), broad singlet (bs), doublet (d), triplet (t), quartet (q), quintet (quint), apparent quintet (app. quint.) and multiplet (m).

High resolution mass spectra (HRMS) were recorded on MICRO-Q-TOF mass spectrometer using the ESI technique. FT-IR spectra were recorded on a JASCO FT/IR-4100 spectrometer. All IR spectra were recorded in the form of a KBr pellet for solids or as thin films in chloroform for liquids. IR spectra peaks are reported in wavenumbers (cm<sup>-1</sup>) as strong (s), medium (m), weak (w), and broad (br).

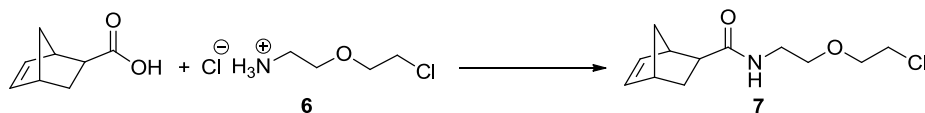
Semi preparative RP-HPLC was carried out on a Waters HPLC system using water (0.1% TFA) and acetonitrile (0.1% TFA) as the mobile phase and a Sunfire prep C 18, 5 $\mu$ m, 10  $\times$  250 mm column as the stationary phase. Peptides were injected at a concentration of 10 mg/mL, and a flow rate of 4.1 mL/min was used for semi preparative RP-HPLC. Peptide elution was monitored at 254 nm with the Waters 2489 UV/visible detector.

## Synthesis and Analytical Data of Compounds



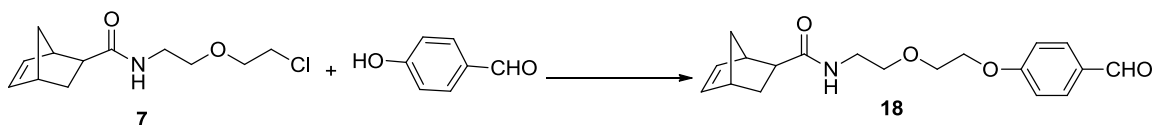
**Preparation of 2-(2-chloroethoxy) ethylamine hydrochloride 6:** To a solution of 2-(2-aminoethoxy)-ethanol **5** (1.0 g, 9.5 mmol, 1 equiv) in dry toluene (10 mL) was added distilled  $\text{SOCl}_2$  (1.0 mL, 11 mmol, 1.2 equiv) at 0 °C. The reaction was allowed to stir at RT for 3 h. After completion of reaction, the solvent was concentrated in *vacuo* to obtain 1.43 g (94%) of product **6** as a brown solid. TLC  $R_f = 0.4$  (2 drops  $\text{Et}_3\text{N}$  in 5 mL of 90% DCM/ MeOH).

$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ , 25 °C):  $\delta = 8.26$  (bs, 3H;  $\text{NH}_3\text{Cl}$ ), 3.87 (t,  $J = 4.8$  Hz, 2H;  $\text{CH}_2$ ), 3.82 (t,  $J = 5.6$  Hz, 2H;  $\text{CH}_2$ ), 3.72 (t,  $J = 5.6$  Hz, 2H;  $\text{CH}_2$ ), 3.33-3.22 (m, 2H;  $\text{CH}_2$ );  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ , 25 °C):  $\delta = 71.3, 66.8, 43.0, 39.8$ ; **IR** (KBr pellet):  $\nu = 3419$  (br), 3025 (br), 1625 (s), 1509 (m), 1302 (w), 1112 (s)  $\text{cm}^{-1}$ ; **HRMS (ESI $^+$ )**: calculated for  $\text{C}_4\text{H}_{11}\text{NOCl}$  ( $\text{MH}^+$ ) 124.0529, found 124.0532.



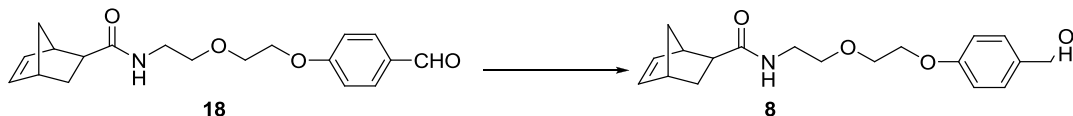
**Compound 7:** To a solution of norbornene-*exo*-acid (0.50 g, 3.7 mmol, 1 equiv) and amine **6** (0.71 g, 4.4 mmol, 1.2 equiv) in  $\text{CH}_2\text{Cl}_2$  (15 mL) at 0 °C, was added HBTU (1.67 g, 4.4 mmol, 1.2 equiv), DIEA (1.2 mL, 7.2 mmol, 2 equiv) and DMAP (0.13 g, 1.0 mmol, 0.3 equiv). The reaction was allowed to warm to RT and stirred for 13 h. Subsequently, the reaction was diluted with  $\text{CH}_2\text{Cl}_2$  (50 mL) and washed with water ( $2 \times 50$  mL). The organic layer was dried over anhydrous sodium sulphate, filtered, and concentrated in *vacuo*. The residue was purified using flash column chromatography (Gradient: 10-40 % ethylacetate/hexane) to afford 0.8 g (92%) of compound **7**. TLC  $R_f = 0.2$  (30 % ethyl acetate/ hexane)

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>, 25 °C): δ = 6.16 - 6.08 (2H; CH=CH), 5.98 (bs, 1H; NH), 3.74 (t, *J* = 4.8 Hz, 2H; CH<sub>2</sub>), 3.64 (t, *J* = 4.8 Hz, 2H; CH<sub>2</sub>), 3.59 (t, *J* = 4.1 Hz, 2H; CH<sub>2</sub>), 3.48 (q, *J* = 4.1 Hz, 2H; CH<sub>2</sub>), 2.94 (bs, 1H; CH<sub>nb</sub>), 2.91 (bs, 1H; CH<sub>nb</sub>), 2.04 -2.00 (m, 1H; CH<sub>nb</sub>), 1.93–1.86 (2H; CH<sub>nb</sub> & solvent), 1.70 (d, *J* = 6.8 Hz, 1H; CH<sub>nb</sub>), 1.38-1.30 (2H; CH<sub>nb</sub>); **<sup>13</sup>C NMR** (100 MHz CDCl<sub>3</sub>, 25 °C): δ = 175.9, 138.3, 136.1, 71.0, 70.0, 47.3, 46.5, 44.8, 43.2, 41.7, 39.3, 30.6; **IR** (thin film): ν = 3312 (br), 2969 (s), 2940 (s), 2871 (s), 1721 (s), 1646 (s), 1542 (s), 1381 (s), 1247 (s), 1129 (s), 724 (m) cm<sup>-1</sup>; **HRMS (ESI<sup>+</sup>)**: calcd. for C<sub>12</sub>H<sub>19</sub>NO<sub>2</sub>Cl (MH<sup>+</sup>) 244.1104, found 244.1111.



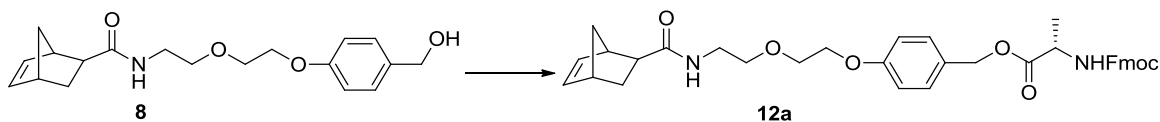
**Aldehyde 18:** To a solution of chloro compound **7** (0.79 g, 0.003 mol, 1 equiv) in DMF (25 mL) was added *p*-hydroxy benzaldehyde (0.47 g, 0.004 mol, 1.2 equiv) and K<sub>2</sub>CO<sub>3</sub> (1.30 g, 0.01 mol, 3 equiv). The reaction was heated to 120 °C and allowed to stir for 12 h. Subsequently, the reaction was cooled to RT and DMF was removed in vacuo. Chloroform (40 mL) was added to the residue and the suspension was filtered over celite. The celite was washed multiple times with CHCl<sub>3</sub>. The combined filtrate was concentrated in vacuo and purified by flash column chromatography (Gradient: 30-50 % ethylacetate/hexane) to give 1g (96%) of Aldehyde **18** as a pale yellow liquid. TLC R<sub>f</sub> = 0.2 (50 % ethylacetate/hexane).

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>, 25 °C): δ = 9.86 (s, 1H; -CHO), 7.80 (d, *J* = 8.5 Hz, 2H; H<sub>Ar</sub>), 7.00 (d, *J* = 8.5 Hz, 2H; H<sub>Ar</sub>), 6.10 (dd, *J* = 5.5 Hz, 3.1 Hz, 1H; CH<sub>nb</sub>), 6.04 (dd, *J* = 5.5 Hz, 3.1 Hz, 1H; CH<sub>nb</sub>), 5.97 (bs, 1H; NH), 4.19 (t, *J* = 4.5 Hz, 2H; CH<sub>2</sub>), 3.84 (t, *J* = 4.5 Hz, 2H; CH<sub>2</sub>), 3.62 (t, *J* = 4.5 Hz, 2H; CH<sub>2</sub>), 3.47 (q, *J* = 5.1 Hz, 2H; CH<sub>2</sub>), 2.87 (s, 2H; CH<sub>nb</sub>), 1.97-1.92 (m, 1H; CH<sub>nb</sub>), 1.86 (dt, *J* = 11.5 Hz, 3.5 Hz, 1H; CH<sub>nb</sub>), 1.67 (d, *J* = 8.5 Hz, 1H; CH<sub>nb</sub>), 1.33-1.22 (2H; CH<sub>nb</sub>); **<sup>13</sup>C NMR** (125 MHz CDCl<sub>3</sub>, 25 °C): δ = 190.9, 176.1, 163.8, 138.4, 136.0, 132.1, 130.3, 115.0, 70.3, 69.3, 67.7, 47.2, 46.5, 44.8, 41.7, 39.4, 30.7; **IR** (thin film): ν = 3301 (br), 2969 (w), 2934 (w), 1659 (s), 1606 (s), 1536 (m), 1511 (w), 1403 (m), 1256 (s), cm<sup>-1</sup>; **HRMS (ESI<sup>+</sup>)**: calcd. for C<sub>19</sub>H<sub>24</sub>NO<sub>4</sub> (MH<sup>+</sup>) 330.1705, found 330.1712.



**Monomer 8:** To a solution of  $\text{NaBH}_4$  (0.45 g, 12.0 mmol, 4 equiv) in MeOH (10 mL) at 0 °C, was slowly added a solution of aldehyde **18** (1.0 g, 3.0 mmol, 1 equiv) in MeOH (15 mL) over a period of 30 min. The reaction mixture was allowed to stir 2 h, following which MeOH was removed in vacuo. DCM (30 mL) was added to the residue and the suspension was filtered over celite. The celite was washed multiple times with DCM and the combined filtrate was concentrated in vacuo. The residue was purified by flash column chromatography (Gradient: 50 % ethyl acetate/hexane) to give 0.9g (90 %) of alcohol **8** as a white solid. TLC  $R_f = 0.2$  (50 % ethylacetate/hexane).

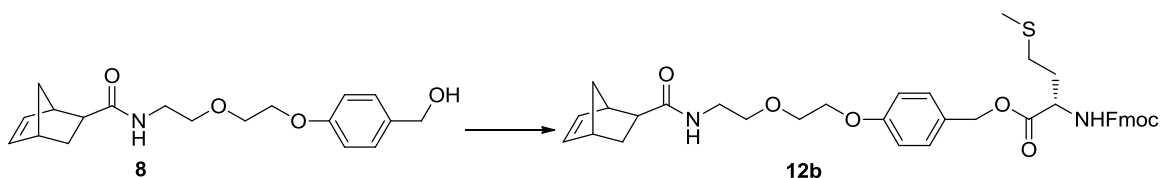
**$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ , 25 °C):  $\delta = 7.28$  (d,  $J = 8.4$  Hz, 2H;  $H_{\text{Ar}}$ ), 6.90 (d,  $J = 8.4$  Hz, 2H;  $H_{\text{Ar}}$ ), 6.12 (dd,  $J = 5.6$  Hz, 2.8 Hz, 1H;  $\text{CH}_{\text{nb}}$ ), 6.06 (dd,  $J = 5.6$  Hz, 2.8 Hz, 1H;  $\text{CH}_{\text{nb}}$ ), 6.01 (bs, 1H;  $\text{NH}$ ), 4.61 (s, 2H;  $\text{CH}_2(\text{Att})$ ), 4.13 (t,  $J = 4.8$  Hz, 2H;  $\text{CH}_2$ ), 3.82 (t,  $J = 4.8$  Hz, 2H;  $\text{CH}_2$ ), 3.63 (t,  $J = 4.8$  Hz, 2H;  $\text{CH}_2$ ), 3.48 (t,  $J = 4.8$  Hz, 2H;  $\text{CH}_2$ ), 2.89 (bs, 2H;  $\text{CH}_{\text{nb}}$ ), 1.97 (dd,  $J = 8.4$  Hz, 4.1 Hz, 1H;  $\text{CH}_{\text{nb}}$ ), 1.88 (dt,  $J = 11.6$  Hz, 4 Hz, 1H;  $\text{CH}_{\text{nb}}$ ), 1.69 (d,  $J = 8$  Hz, 1H;  $\text{CH}_{\text{nb}}$ ), 1.35-1.25 (2H;  $\text{CH}_{\text{nb}}$ );  **$^{13}\text{C}$  NMR** (100 MHz  $\text{CDCl}_3$ , 25 °C):  $\delta = 175.9$ , 158.4, 138.3, 136.1, 133.8, 128.8, 114.8, 70.2, 69.7, 67.6, 65.1, 47.3, 46.5, 44.8, 41.7, 39.4, 30.6; **IR** (KBr pellet):  $\nu = 3309$  (br), 3063 (m), 2975 (m), 2939 (m), 2873 (m), 1638 (s), 1548 (s), 1514 (s), 1246 (s), 1131 (s), 1055 (s), 1012 (w), 722 (m)  $\text{cm}^{-1}$ ; **HRMS (ESI $^+$ )**: calcd. for  $\text{C}_{19}\text{H}_{25}\text{NO}_4\text{Na}$  ( $\text{MNa}^+$ ) 354.1681, found 354.1667.



**Monomer 12a:** (EDCI) N-(3-Dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (0.87 g, 5.00 mmol, 3 equiv) and DMAP (61 mg, 0.50 mmol, 0.3 equiv) were added to a solution of monomer **8** (0.5 g, 1.5 mmol, 1 equiv) and Fmoc-L-Ala-OH (0.56 g, 1.80 mmol, 1.2 equiv) in

CH<sub>2</sub>Cl<sub>2</sub> (15 mL). The reaction was allowed to stir for 1 h at RT, following which DCM (40 mL) was added. The reaction mixture was washed with water (50 mL × 3). The combined organic layers were dried over sodium sulphate, filtered and concentrated in vacuo. The residue was purified by flash column chromatography (Gradient: 30-50 % EtOAc/Hexane) to afford 0.8 g (89 %) of monomer **12a** as a white solid. TLC R<sub>f</sub> = 0.4 (50% EtOAc/Hexane).

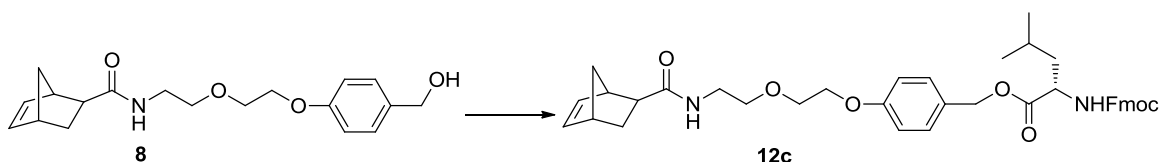
**<sup>1</sup>H NMR** (400 MHz, DMSO-d<sub>6</sub>, 25 °C): δ = 7.94-7.84 (3H; H<sub>Ar(Fmoc)</sub> & NH<sub>nb</sub>), 7.79 (d, J = 7.2 Hz, 1H; NH<sub>Ala</sub>), 7.7 (d, J = 6.8 Hz, 2H; H<sub>Ar(Fmoc)</sub>), 7.42 (t, J = 7.2 Hz, 2H; H<sub>Ar(Fmoc)</sub>), 7.32 (t, J = 7.2 Hz, 2H; H<sub>Ar(Fmoc)</sub>), 7.26 (d, J = 8.4 Hz, 2H; H<sub>Ar</sub>), 6.88 (d, J = 8.8 Hz, 2H; H<sub>Ar</sub>), 6.1 (app. quint, 2H; CH=CH), 5.08-4.99 (m, 2H; ArCH<sub>2</sub>O-), 4.34-4.17 (3H; CH<sub>Fmoc</sub> & CH<sub>2(Fmoc)</sub>), 4.11 (app. quint, 1H; CH<sub>Ala</sub>), 4.04 (t, J = 4.4 Hz, 2H; CH<sub>2</sub>), 3.71 (t, J = 4.8 Hz, 2H; CH<sub>2</sub>), 3.47 (t, J = 6 Hz, 2H; CH<sub>2</sub>), 3.26-3.16 (2H; CH<sub>2</sub>), 2.81 (bs, 1H; CH<sub>nb</sub>), 2.76 (bs, 1H; CH<sub>nb</sub>), 2.03 (dd, J = 10 Hz, 4 Hz, 1H; CH<sub>nb</sub>), 1.75 (dt, J = 11.6 Hz, 4 Hz, 1H; CH<sub>nb</sub>), 1.63 (d, J = 8 Hz, 1H; CH<sub>nb</sub>), 1.28 (d, J = 7.2 Hz, 3H; -CH<sub>3</sub>), 1.17-1.09 (2H; CH<sub>nb</sub>), **<sup>13</sup>C NMR** (125 MHz DMSO-d<sub>6</sub>, 25 °C): δ = 174.8, 172.8, 158.3, 155.9, 143.9, 143.8, 140.7, 137.7, 136.3, 129.7, 128.0, 127.7, 127.1, 125.23, 125.2, 120.1, 114.3, 69.2, 68.6, 67.1, 65.73, 65.66, 49.4, 46.9, 46.6, 45.6, 42.9, 41.0, 38.6, 29.8, 16.9; **IR** (KBr pellet): ν = 3409 (br), 2926 (br), 2877 (br), 1724 (s), 1651 (s), 1520 (s), 1452 (s), 1249 (s), 1111 (s), 736 (s) cm<sup>-1</sup>; **HRMS (ESI<sup>+</sup>)**: calcd. for C<sub>37</sub>H<sub>41</sub>N<sub>2</sub>O<sub>7</sub> (MH<sup>+</sup>) 625.2914, found 625.2923.



**Monomer 12b:** EDCI (0.43 g, 2.30 mmol, 1.5 equiv) and DMAP (54 mg, 0.45 mmol, 0.3 equiv) were added to a solution of monomer **8** (0.5 g, 1.50 mmol, 1 equiv) and Fmoc-L-Met-OH (0.67 g, 1.80 mmol, 1.2 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (15 mL). The reaction was allowed to stir for 2 h at RT, following which reaction mixture was concentrated in vacuo. EtOAc (80 mL) was added and the solution was washed with a saturated aqueous solution of NaHCO<sub>3</sub> (3 × 30 mL). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated in vacuo. Purification of the

residue by flash column chromatography (Gradient: 30-50 % EtOAc/Hexane) afforded 0.8g (80 %) of monomer **12b** as a white solid. TLC  $R_f = 0.2$  (50% EtOAc/Hexane).

**$^1\text{H NMR}$**  (400 MHz,  $\text{CDCl}_3$ , 25 °C):  $\delta = 7.76$  (d,  $J = 7.6$  Hz, 2H;  $H_{\text{Ar(Fmoc)}}$ ), 7.58 (d,  $J = 7.2$  Hz, 2H;  $H_{\text{Ar(Fmoc)}}$ ), 7.40 (t,  $J = 7.2$  Hz, 2H;  $H_{\text{Ar(Fmoc)}}$ ), 7.34-7.23 (4H;  $H_{\text{Ar(Fmoc)}}$ ,  $H_{\text{Ar}}$ ), 6.88 (d,  $J = 8.4$  Hz, 2H;  $H_{\text{Ar}}$ ), 6.14-6.1 (m, 1H;  $\text{CH}=\text{CH}$ ), 6.07-6.03 (m, 1H;  $\text{CH}=\text{CH}$ ), 5.93 (bs, 1H;  $\text{NH}_{\text{nb}}$ ), 5.45 (d,  $J = 8.0$  Hz, 1H;  $\text{NH}_{\text{Met}}$ ), 5.12 (q,  $J = 12$  Hz, 2H;  $\text{ArCH}_2\text{O-}$ ), 4.50 (q,  $J = 7.2$  Hz, 1H;  $\text{CH}_{\text{Fmoc}}$ ), 4.40 (d,  $J = 7.2$  Hz, 2H;  $\text{CH}_{2(\text{Fmoc})}$ ), 4.20 (t,  $J = 6.8$  Hz, 1H;  $\text{CH}_{\text{Met}}$ ), 4.14-4.07 (m, 2H;  $\text{CH}_2$ ), 3.86-3.79 (m, 2H;  $\text{CH}_2$ ), 3.62 (t,  $J = 4.8$  Hz, 2H;  $\text{CH}_2$ ), 3.49 (q,  $J = 5.2$  Hz, 2H;  $\text{NH-CH}_2$ ), 2.93-2.74 (2H;  $\text{CH}_{\text{nb}}$ ), 2.46 (app.q., 2H;  $\text{SCH}_{2(\text{Met})}$ ), 2.18-1.84 (6H;  $\text{CH}_{3(\text{Met})}$ ,  $\text{CH}_{2(\text{Met})}$  &  $\text{CH}_{\text{nb}}$ ), 1.72-1.61 (2H,  $\text{CH}_{\text{nb}}$ ), 1.34-1.23 (2H;  $\text{CH}_{\text{nb}}$ );  **$^{13}\text{C NMR}$**  (100 MHz  $\text{CDCl}_3$ , 25 °C):  $\delta = 175.8$ , 172.0, 159.1, 156.0, 144.0, 143.8, 141.4, 138.3, 136.1, 130.4, 127.9, 127.2, 125.2, 120.1, 114.8, 70.2, 69.5, 67.5, 67.3, 67.2, 53.4, 47.3, 46.5, 44.8, 41.7, 39.4, 32.0, 30.6, 30.0, 15.6; **IR** (KBr pellet):  $\nu = 3394$  (br), 2921 (br), 1719 (s), 1645 (s), 1614 (m), 1513 (s), 1448 (s), 1247 (s), 1170 (s), 1129 (s), 1050 (s), 740 (s)  $\text{cm}^{-1}$ ; **HRMS (ESI $^+$ )**: calcd. for  $\text{C}_{39}\text{H}_{45}\text{N}_2\text{O}_7\text{S}$  ( $\text{MH}^+$ ) 685.2947, found 685.2961.



**Monomer 12c:** EDCI (0.43 g, 2.30 mmol, 1.5 equiv) and DMAP (54 mg, 0.45 mol, 0.3 equiv) were added to a solution of monomer **8** (0.5 g, 1.5 mmol, 1 equiv) and Fmoc-L-Leu-OH (0.64 g, 1.8 mmol, 1.2 equiv) in  $\text{CH}_2\text{Cl}_2$  (15 mL). The reaction was allowed to stir for 2 h at RT, following which the reaction mixture was concentrated in vacuo. EtOAc (80 mL) was added and the solution was washed with a saturated aqueous solution of  $\text{NaHCO}_3$  ( $3 \times 30$  mL). The combined organic layers were dried over  $\text{Na}_2\text{SO}_4$ , filtered and concentrated in vacuo. Purification by flash column chromatography (Gradient: 30-50 % EtOAc/Hexane) afforded 0.82g (82 %) of monomer **12c** as a white solid. TLC  $R_f = 0.4$  (50% EtOAc/Hexane).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>, 25 °C): δ = 7.76 (d, *J* = 7.6 Hz, 2H; *H*<sub>Ar(Fmoc)</sub>), 7.58 (d, *J* = 7.6 Hz, 2H; *H*<sub>Ar(Fmoc)</sub>), 7.40 (t, *J* = 7.6 Hz, 2H; *H*<sub>Ar(Fmoc)</sub>), 7.34-7.21 (5H; *H*<sub>Ar(Fmoc)</sub>, *H*<sub>Ar</sub> & Solvent), 6.88 (d, *J* = 8 Hz, 2H; *H*<sub>Ar</sub>), 6.12 (dd, *J* = 5.6, *J* = 2.8 Hz, 1H; CH=CH), 6.06 (dd, *J* = 5.6, *J* = 2.8 Hz, 1H; CH=CH), 6.04-5.97 (bs, 1H; *NH*<sub>nb</sub>), 5.18 (d, *J* = 8.8 Hz, 1H; *NH*<sub>Leu</sub>), 5.13-5.06 (2H; ArCH<sub>2</sub>O-), 4.47-4.32 (3H; *CH*<sub>Fmoc</sub> & *CH*<sub>2(Fmoc)</sub>), 4.20 (t, *J* = 6.8 Hz, 1H; *CH*<sub>Leu</sub>), 4.14-4.0 (bs, 2H; ArOCH<sub>2</sub>), 3.8 (bs, 2H; CH<sub>2</sub>), 3.54 (bs, 2H; CH<sub>2</sub>), 3.49 (bs, 2H; NH-CH<sub>2</sub>), 2.97-2.85 (2H; *CH*<sub>nb</sub>), 1.98 (dd, *J* = 9.2, *J* = 4.4 Hz, 1H; *CH*<sub>nb</sub>), 1.88 (dt, *J* = 11.2, *J* = 3.6 Hz, 1H; *CH*<sub>nb</sub>), 1.7-1.5 (4H, *CH*<sub>nb</sub>, *CH*<sub>Leu</sub> & *CH*<sub>2(Leu)</sub>), 1.35-1.22 (2H; *CH*<sub>nb</sub>), 0.93 (s, 6H; *CH*<sub>3(Leu)</sub>); **<sup>13</sup>C NMR** (100 MHz CDCl<sub>3</sub>, 25 °C): δ = 176.2, 173.2, 159, 156.1, 143.9, 141.4, 138.4, 136.1, 130.3, 128.1, 127.8, 127.2, 125.2, 120.1, 114.8, 70.2, 69.6, 67.5, 67.1, 67, 52.8, 47.3, 47.2, 46.5, 44.9, 41.8, 41.7, 39.5, 30.7, 24.9, 23, 22; **IR** (KBr pellet): ν = 3395 (br), 3063 (m), 1719 (s), 1645 (s), 1644 (s), 1513 (s), 1449 (s), 1247 (s), 1168 (m), 1123 (m), 1048 (m), 740 (s) cm<sup>-1</sup>; **HRMS (ESI<sup>+</sup>)**: calcd. for C<sub>40</sub>H<sub>47</sub>N<sub>2</sub>O<sub>7</sub> (MH<sup>+</sup>) 667.3383, found 667.3383.

### General Procedure for Polymerization using Grubbs' third generation initiator

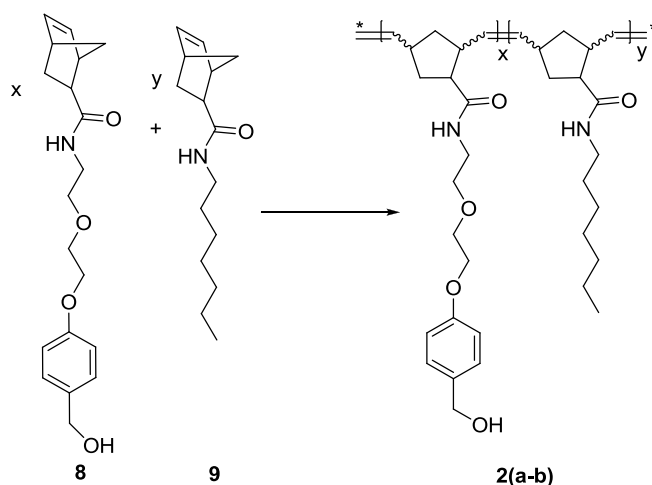
A solution of the requisite monomers in dichloromethane was deoxygenated using a stream of nitrogen for 2 min. A deoxygenated solution of Grubbs' third generation initiator in dichloromethane was added to the solution. The reaction mixture was allowed to stir for 1 h at RT. Ethyl vinyl ether (3 mL) was added and the reaction mixture was allowed to stir for an additional 45 min, following which the mixture was concentrated in vacuo to 4 mL. Diethyl ether (15 mL) was added to obtain the polymer as a precipitate. The precipitate was dissolved in DCM (5 mL) and re-precipitated with ether (15 mL). The process was repeated three times. The precipitate was isolated and dried in vacuo to afford the polymer support as a white solid.

### General procedure for determination of loading and x:y ratio of polymers by <sup>1</sup>H NMR

The number of attachment sites present in the polymer (loading) and x:y ratio of the polymer was determined by recording <sup>1</sup>H NMR spectra of polymer in the presence of a known amount of



1,1,2,2-Tetrachloroethane (TCE). The integration for the peak at  $\delta = 6.9$  ppm corresponding to TCE was compared with the peak at  $\delta = 6.8$  ppm for the aromatic protons of the attachment site in polymer **2** and **3** to determine the number of attachment sites. The x:y ratio of the polymer was determined using  $^1\text{H NMR}$  spectroscopy. The integration values of methyl protons of the alkyl chain ( $\delta=0.8$ ) and the aromatic protons ( $\delta=6.8$ ) were compared to get the x:y ratio of the polymer **2** and **3**.

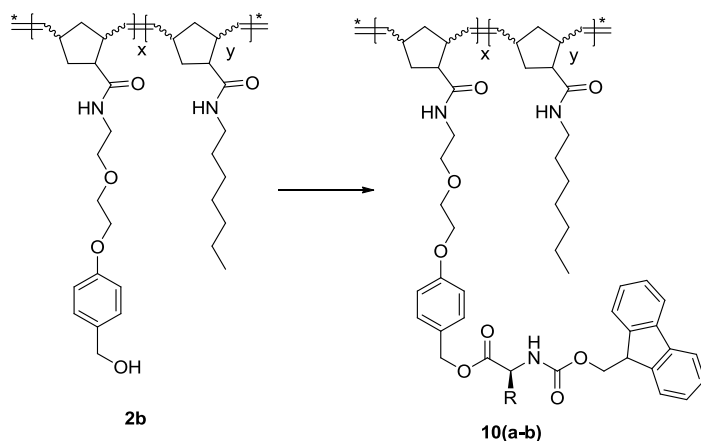


**Polymer 2a:** Grubbs' third generation initiator (15.7 mg, 0.018 mmol, 1 equiv) in  $\text{CH}_2\text{Cl}_2$  (5 mL) was added to monomer **8** (300.0 mg, 0.90 mmol, 50 equiv) and monomer **9** (213.0 mg, 0.9 mmol, 50 equiv) in  $\text{CH}_2\text{Cl}_2$  (10 mL) to afford polymer **2a** (481 mg) in 94% yield. Loading = 1.75 mmol/g, x:y = 1:1.

$^1\text{H NMR}$  (400 MHz,  $\text{DMSO-d}_6$ , 25 °C):  $\delta = 7.9$  (s, DMF solvent peak), 7.7–7.5 (2H; NH), 7.21–7.14 (2H;  $H_{\text{Ar}}$ ), 6.9–6.75 (2H;  $H_{\text{Ar}}$ ), 5.3–5.0 (5H;  $\text{CH}=\text{CH}$  & OH), 4.45–4.35 (2H;  $\text{ArCH}_2\text{OH}$ ), 4.02 (2H;  $\text{ArOCH}_2$ ), 3.67 (2H;  $\text{OCH}_2$ ), 3.5–2.8 (50.5H;  $\text{OCH}_2$ ,  $\text{CH}_{2(\text{alk})}$ ,  $\text{CH}_{(\text{nb})}$  & solvent), 2.7–2.4 (5.7H;  $\text{CH}_{\text{nb}}$  & solvent), 2.4–2.2 (2.5H;  $\text{CH}_{\text{nb}}$ ), 2.0–1.6 (4.4H;  $\text{CH}_{\text{nb}}$ ), 1.6–0.9 (16.2H;  $\text{CH}_{2(\text{alk})}$ , &  $\text{CH}_{(\text{nb})}$ ), 0.83 (3.6H;  $\text{CH}_{3(\text{alk})}$ ).

**Polymer 2b:** Grubbs' third generation initiator (7.80 mg, 0.009 mmol, 1 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (4 mL) was added to monomer **8** (149.0 mg, 0.45 mmol, 50 equiv) and monomer **9** (210.0 mg, 0.9 mmol, 100 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (7 mL) to afford polymer **2b** (343 mg) in 95% yield. Loading = 1.23 mmol/g, x: y = 1:2.

<sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>, 25 °C): δ = 7.8–7.4 (3H; NH), 7.25-7.15 (2.1H; H<sub>Ar</sub>), 6.9-6.75 (2H; H<sub>Ar</sub>), 5.5–5.0 (6.1H; CH=CH & OH), 4.4 (2H; ArCH<sub>2</sub>OH), 4.02 (2.1H; ArOCH<sub>2</sub>), 3.68 (2.1H; OCH<sub>2</sub>), 3.5–2.8 (17.6H; OCH<sub>2</sub>, CH<sub>2(alk)</sub>, CH<sub>(nb)</sub> & solvent), 2.7–2.5 (6.6H; CH<sub>(nb)</sub> & solvent), 2.4–2.2 (3.7H; CH<sub>(nb)</sub>), 2.2–1.7 (7.3H; CH<sub>(nb)</sub>), 1.6–0.9 (30.1H; CH<sub>2(alk)</sub>, & CH<sub>(nb)</sub>), 0.83 (7H; CH<sub>3(alk)</sub>).



### Attachment of first Amino acid on polymer support **2b**

**General procedure:** To a solution of polymer **2b** in THF was added the amino acid (Fmoc-L-AA-OH), DMAP and DIC. The reaction mixture was allowed to stir for the requisite amount of time, following which diethyl ether (5mL) was added. The supernatant solution was decanted, the precipitate was dissolved in a few drops of DMF and re-precipitated with diethyl ether (5 mL × 2) to afford amino acid attached polymer **10 (a and b)**.

**General procedure for determination of amino acid loading:** The loading capacities of polymers **10 (a and b)** were determined by recording their <sup>1</sup>H NMR spectra in the presence of a

known amount of TCE. The integration of the peak at  $\delta = 6.9$  ppm corresponding to TCE was compared with the peak at  $\delta = 6.8$  ppm for the aromatic protons of the polymer.

**Polymer 10a:** Polymer **2b** (50 mg, 0.062 mmol, 1 equiv), Fmoc-L-Phe-OH (28.6 mg, 0.074 mmol, 1.2 equiv), DMAP (2.2 mg, 0.018 mmol, 0.3 equiv) and DIC (38  $\mu$ L, 0.25 mmol, 4 equiv) in 1 mL of THF was used. Reaction was completed in 5 h and 72 mg (97%) of **10a** was obtained. Loading = 0.88 mmol/g.

**<sup>1</sup>H NMR** (400 MHz, DMSO-*d*<sub>6</sub>, 25 °C):  $\delta = 7.9$ – $7.8$  (3.4H;  $NH_{\text{Phe}}$  &  $H_{\text{Ar(Fmoc)}}$ ), 7.75–7.4 (5.8H;  $NH$  &  $H_{\text{Ar(Fmoc)}}$ ), 7.37 (2.5H;  $H_{\text{Ar(Fmoc)}}$ ), 7.32–7.15 (9.8H;  $H_{\text{Ar(Fmoc)}}$  &  $H_{\text{Ar}}$ ), 6.82 (2H;  $H_{\text{Ar}}$ ), 5.4–4.95 (8.4H;  $CH=CH$  &  $\text{Ar}CH_2\text{O}$ ), 4.35–4.1 (4.5H;  $CH_{\text{(Fmoc)}}$ ,  $CH_{2,\text{(Fmoc)}}$ , &  $CH_{\text{Phe}}$ ), 3.98 (2.6H;  $\text{ArO}CH_2$ ), 3.65 (2.6H;  $\text{O}CH_2$ ), 3.5–3.3 (24H;  $\text{O}CH_2$ ,  $CH_{2,\text{(alk)}}$ ,  $CH_{\text{(nb)}}$  & solvent), 3.25–2.7 (13.5H;  $CH_{2,\text{(Phe)}}$  &  $CH_{\text{(nb)}}$ ), 2.65–2.45 (20.5H;  $CH_{\text{nb}}$  & Solvent), 2.4–2.2 (3.9H;  $CH_{\text{nb}}$ ), 2.1–1.6 (6.7H;  $CH_{\text{nb}}$ ), 1.6–0.9 (34.5H;  $CH_{2,\text{(alk)}}$ , &  $CH_{\text{(nb)}}$ ), 0.8 (7.4H;  $CH_{3,\text{(alk)}}$ ).

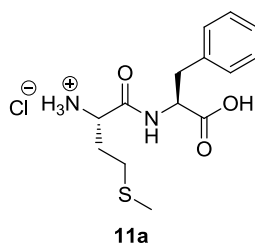
**Polymer 10b:** Polymer **2b** (50 mg, 0.062 mmol, 1 equiv), Fmoc-Gly-OH (22mg, 0.074 mmol, 1.2 equiv), DMAP (2.2 mg, 0.018 mmol, 0.3 equiv) and DIC (38  $\mu$ L, 0.25 mmol, 4 equiv) in 1 mL of THF was used. Reaction was completed in 5 h and 65 mg (96%) of **10b** was obtained. Loading = 0.94 mmol/g.

**<sup>1</sup>H NMR** (400 MHz, DMSO-*d*<sub>6</sub>, 25 °C):  $\delta = 7.9$ – $7.8$  (2.1H;  $H_{\text{Ar(Fmoc)}}$ ), 7.75 (1H;  $NH_{\text{Gly}}$ ), 7.7–7.4 (4.8H;  $NH$  &  $H_{\text{Ar(Fmoc)}}$ ), 7.37 (2H;  $H_{\text{Ar(Fmoc)}}$ ), 7.35–7.2 (4H;  $H_{\text{Ar(Fmoc)}}$  &  $H_{\text{Ar}}$ ), 6.85 (2H;  $H_{\text{Ar}}$ ), 5–4.85 (8.2H;  $CH=CH$  &  $\text{Ar}CH_2\text{O}$ ), 4.35–4.25 (1.6H;  $CH_{2,\text{(Fmoc)}}$ ), 4.19 (1.2H;  $CH_{\text{(Fmoc)}}$ ), 4.15–3.85 (2.3H;  $\text{ArO}CH_2$ ), 3.85–3.7 (2H;  $CH_{2,\text{(Gly)}}$ ), 3.66 (2.2H;  $\text{O}CH_2$ ), 3.5–3.35 (2.6H;  $\text{O}CH_2$ ), 3.25–2.7 (10.8H;  $CH_{\text{(nb)}}$  & solvent), 2.7–2.45 (16H;  $CH_{\text{nb}}$  & Solvent), 2.4–2.2 (3.8H;  $CH_{\text{nb}}$ ), 2.2–2.0 (1.5H;  $CH_{\text{nb}}$ ), 2.0–1.6 (6.1H;  $CH_{\text{nb}}$ ), 1.6–0.9 (30.9H;  $CH_{2,\text{(alk)}}$ , &  $CH_{\text{(nb)}}$ ), 0.8 (6.9H;  $CH_{3,\text{(alk)}}$ ).

## General procedure for peptide synthesis using polymer supports 2

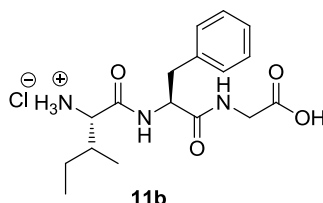
Polymer support **2b** (50 mg) was treated with Fmoc-AA-OH in the presence of DIC (1.5 equiv) and DMAP (0.3 equiv) in THF (1 mL). After completion of reaction, the reaction mixture was concentrated in vacuo to 1 mL. Diethyl ether (5 mL) was added to get amino acid attached polymer as a precipitate. The precipitate was dissolved in a few drops of DMF and re-precipitated with diethyl ether twice to ensure removal of excess reagents and by-products. The precipitate was dried in vacuo and subsequently treated with 20 % piperidine in DMF (0.7 mL). The reaction mixture was allowed to stir for 10 min to deprotect the Fmoc group. The polymer was isolated as a precipitate with diethyl ether and coupled with the second amino acid using HCTU (1.2 equiv) and DIEA (4 equiv) in 1:1 DCM-DMF (2 mL). The dipeptide attached to the support was isolated as a precipitate in diethyl ether as described above (for the attachment of first amino acid). The deprotection and coupling reactions were repeated to obtain tripeptide attached polymer. The final peptide was cleaved from the support using LiOH·H<sub>2</sub>O (3 equiv) in THF. The supernatant solution contained the lithium salt of the peptide, which was treated with aq. HCl to afford the crude peptide **11**. Peptide **11** was obtained after purification using RP-HPLC.

## Characterization of peptides synthesized using supports 2b

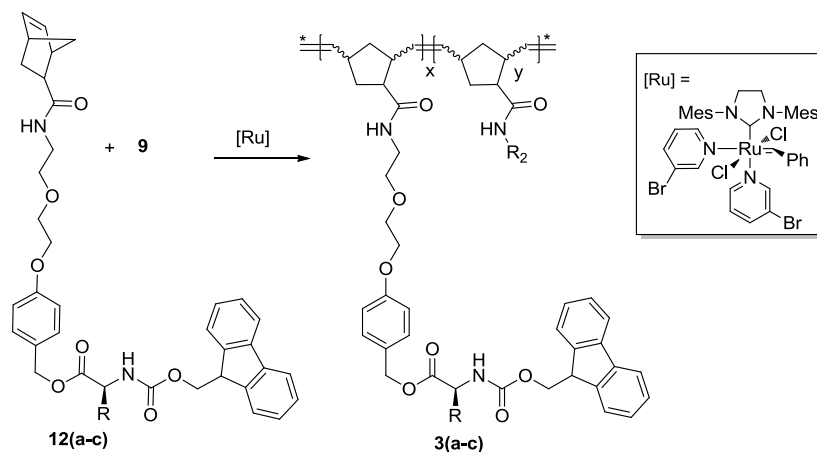


**HCl·H<sub>2</sub>N-Met-Phe-OH 11a:** <sup>1</sup>H NMR (400 MHz, D<sub>2</sub>O, 25 °C): δ = 7.45-7.33 (5H; *H*<sub>Ar</sub>), 4.85-4.75 (1H; *CH*<sub>Phe(merged with solvent)</sub>), 4.09 (t, *J* = 6.8 Hz, 1H; *CH*<sub>Met</sub>), 3.31 (dd, *J* = 14, 6 Hz, 1H; *CH*<sub>aH<sub>b</sub>(Phe)</sub>), 3.16 (dd, *J* = 14, 8.8 Hz, 1H; *CH*<sub>aH<sub>b</sub>(Phe)</sub>), 2.63-2.43 (m, 2H; *SCH*<sub>2(Met)</sub>), 2.2-1.9 (5H; *CH*<sub>3(Met)</sub>, *CH*<sub>2(Met)</sub>); <sup>13</sup>C NMR (100 MHz, D<sub>2</sub>O, 25 °C): δ = 174.3, 169.1, 136.4, 129.2, 128.8,

127.3, 54.4, 52.1, 36.1, 30.0, 27.9, 13.9; **IR** (KBr pellet):  $\nu = 3418$  (br), 3068 (w), 2629 (w), 1675 (s), 1541 (m), 1434 (m), 1200 (s) 1139 (s) 839 (m), 801 (m), 724 (m)  $\text{cm}^{-1}$ ; **HRMS (ESI<sup>+</sup>)**: calcd. for  $\text{C}_{14}\text{H}_{19}\text{N}_2\text{O}_3\text{S}$  ( $\text{MH}^+$ ) 297.1239, found 297.1288.



**HCl·H<sub>2</sub>N-Ile-Phe-Gly-OH 11b**: <sup>1</sup>H NMR (400 MHz, D<sub>2</sub>O, 25 °C):  $\delta = 7.43\text{-}7.3$  (5H;  $H_{\text{Ar}}$ ), 4.85-4.75 (1H;  $CH_{\text{Phe}}$ (merged with solvent)), 4.0-3.83 (3H;  $CH_{\text{Ile}}$  &  $CH_{2(\text{Gly})}$ ), 3.2-3.05 (m, 2H;  $CH_{2(\text{Phe})}$ ), 2.04-1.92 (m, 1H;  $CH_{\text{Ile}}$ ), 1.53-1.42 (m, 1H;  $CH_{\text{a}}H_{\text{b}(\text{Ile})}$ ), 1.25-1.12 (m, 1H;  $CH_{\text{a}}H_{\text{b}(\text{Ile})}$ ), 0.99 (d,  $J = 7.2$  Hz, 3H;  $CH_3(\text{Ile})$ ); 0.92 (t,  $J = 7.2$  Hz, 3H;  $CH_3(\text{Ile})$ ); <sup>13</sup>C NMR (100 MHz, D<sub>2</sub>O, 25 °C):  $\delta = 172.83, 172.77, 169.0, 136.1, 129.2, 128.8, 127.3, 57.6, 55.0, 41.1, 36.9, 36.4, 23.8, 14.0, 10.5$ ; **IR** (KBr pellet):  $\nu = 3406$  (br), 3291 (br), 3073 (w), 2971 (w), 2933 (w), 1667 (s), 1540 (m) 1429 (w), 1200 (s), 1140 (s), 837 (w), 799 (w), 723 (w), 700 (w),  $\text{cm}^{-1}$ ; **HRMS (ESI<sup>+</sup>)**: calcd. for  $\text{C}_{17}\text{H}_{26}\text{N}_3\text{O}_4$  ( $\text{MH}^+$ ) 336.1923, found 336.1929.



**Polymer 3a:** The polymer was synthesized following the general procedure described for synthesis of supports **2**. Grubbs' third generation initiator (9.4 mg, 0.011 mmol, 1 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (3 mL) was added to monomer **12a** (336.0 mg, 0.54 mmol, 50 equiv) and monomer **9** (235.0 mg, 1.1 mmol, 100 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (7 mL) to afford polymer **3a** (518 mg) in 88% yield. Loading = 0.91 mmol/g; x: y = 1:2.

<sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>, 25 °C): δ = 7.9–7.8 (3.5H; NH<sub>Ala</sub> & H<sub>Ar(Fmoc)</sub>), 7.7-7.5 (4H; NH & H<sub>Ar(Fmoc)</sub>), 7.38 (3H; NH & H<sub>Ar(Fmoc)</sub>), 7.32-7.15 (4.1H; H<sub>Ar(Fmoc)</sub> & H<sub>Ar</sub>), 6.82 (2H; H<sub>Ar</sub>), 5.4–4.95 (8.1H; CH=CH & ArCH<sub>2</sub>O), 4.35-3.9 (7H; CH<sub>(Fmoc)</sub>, CH<sub>2,(Fmoc)</sub>, CH<sub>Ala</sub> & ArOCH<sub>2</sub>), 3.64 (2.9H; OCH<sub>2</sub>), 3.5–3.2 (51.2H; OCH<sub>2</sub>, CH<sub>2(alk)</sub>, CH<sub>(nb)</sub> & solvent), 3.2-2.6 (12.5H; CH<sub>(nb)</sub>), 2.4–2.2 (2.3H; CH<sub>(nb)</sub>), 2.1–1.5 (8.2H; CH<sub>(nb)</sub>), 1.4–0.9 (29.7H; CH<sub>2(alk)</sub>, CH<sub>3(Ala)</sub>, & CH<sub>(nb)</sub>), 0.8 (6.7H; CH<sub>3(alk)</sub>).

**Polymer 3b:** The polymer was synthesized following the general procedure described for synthesis of supports **2**. Grubbs' third generation initiator (11.2 mg, 0.013 mmol, 1 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (4 mL) was added to monomer **12b** (435.0 mg, 0.64 mmol, 50 equiv) and monomer **9** (299.0 mg, 1.27 mmol, 100 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (8 mL) to afford polymer **3b** (703 mg) in 96% yield. Loading = 0.87 mmol/g; x: y = 1:2.

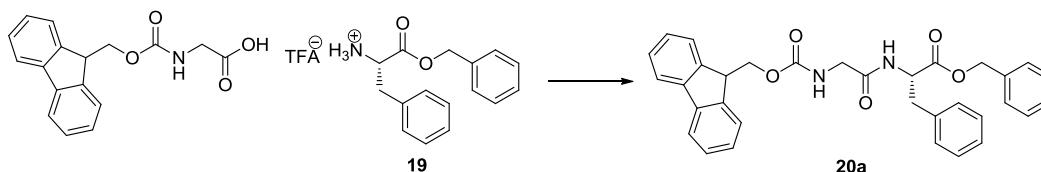
<sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>, 25 °C): δ = 7.9–7.8 (3.4H; H<sub>Ar(Fmoc)</sub> & NH<sub>Met</sub>), 7.78-7.5 (4.3H; NH & H<sub>Ar(Fmoc)</sub>), 7.38 (3H; H<sub>Ar(Fmoc)</sub>), 7.39-7.15 (4.3H; H<sub>Ar(Fmoc)</sub> & H<sub>Ar</sub>), 6.82 (2H; H<sub>Ar</sub>), 5.4–4.9 (8.1H; CH=CH & ArCH<sub>2</sub>O), 4.35-4.1 (4.2H; CH<sub>2,(Fmoc)</sub>, CH<sub>(Fmoc)</sub> & CH<sub>Ala</sub>), 3.98 (2.3H; ArOCH<sub>2</sub>), 3.6 (2.8H; OCH<sub>2</sub>), 3.5–3.02 (206H; OCH<sub>2</sub>, CH<sub>2(deg)</sub>, CH<sub>(nb)</sub> & solvent), 3.15-2.6 (11.7H; CH<sub>(nb)</sub> & CH<sub>2(deg)</sub>), 2.6-2.2 (17.5H; CH<sub>(nb)</sub>, CH<sub>2(Met)</sub> & solvent), 2.1-1.5 (14.8H; CH<sub>(nb)</sub>, CH<sub>2(Met)</sub> & CH<sub>3(Met)</sub>), 1.5-0.9 (30.3H; CH<sub>(nb)</sub> & CH<sub>2(Alk)</sub>), 0.8 (7.2H; CH<sub>3(Alk)</sub>).

**Polymer 3c:** The polymer was synthesized following the general procedure described for synthesis of supports **2**. Grubbs' third generation initiator (6.8 mg, 0.078 mmol, 1 equiv) in

CH<sub>2</sub>Cl<sub>2</sub> (3 mL) was added to monomer **12c** (260.0 mg, 0.39 mmol, 50 equiv) and monomer **9** (183.0 mg, 0.78 mmol, 100 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (5 mL) to afford polymer **3c** (416 mg) in 94% yield. Loading = 0.88 mmol/g; x: y = 1:2.

<sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>, 25 °C): δ = 7.9–7.82 (2.3H; H<sub>Ar(Fmoc)</sub>) 7.8–7.71 (1.1H; NH<sub>Leu</sub>), 7.70–7.5 (5.3H; NH & H<sub>Ar(Fmoc)</sub>), 7.38 (2.1H; H<sub>Ar(Fmoc)</sub>), 7.38–7.15 (4.2H; H<sub>Ar(Fmoc)</sub> & H<sub>Ar</sub>), 6.84 (2H; H<sub>Ar</sub>), 5.4–4.9 (8.2H; CH=CH & ArCH<sub>2</sub>O), 4.35–3.9 (7H; CH<sub>2,(Fmoc)</sub>, CH<sub>(Fmoc)</sub> ArOCH<sub>2</sub> & CH<sub>Leu</sub>), 3.65 (2.1H; OCH<sub>2</sub>), 3.5–3.25 (104.7H; OCH<sub>2</sub>, CH<sub>2(deg)</sub>, CH<sub>(nb)</sub> & solvent), 3.2–2.7 (10H; CH<sub>(nb)</sub> & CH<sub>2(deg)</sub>), 2.7–2.4 (16.9H; CH<sub>nb</sub>, & solvent), 2.4–2.2 (3.9H; CH<sub>(nb)</sub>), 2–1.65 (6.5H; CH<sub>(nb)</sub>), 1.65–0.9 (37.6H; CH<sub>nb</sub> CH<sub>(Leu)</sub> & CH<sub>2(Leu)</sub> & CH<sub>2(Alk)</sub>), 0.9–0.7 (13.3H; CH<sub>3(Alk)</sub> & CH<sub>3(Leu)</sub>).

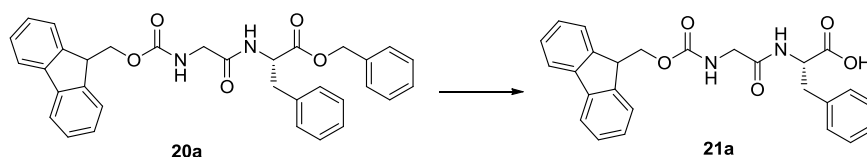
### Dipeptide synthesis in solution for combination approach



**Fmoc-Gly-L-Phe-OBn 20a:** To a solution of Fmoc-Gly-OH (0.48 g, 1.62 mol, 1.2 equiv) in DCM (10 mL) at 0 °C, was added HBTU (0.61 g, 1.62 mmol, 1.2 equiv), TFA salt **19** (0.5 g, 1.35 mmol, 1 equiv) and DIEA (0.9 mL, 5.4 mmol, 4 equiv). The reaction mixture was warmed to RT and allowed to stir 12 h. Subsequently, DCM (30 mL) was added and the mixture was washed with a saturated aqueous solution of NaHCO<sub>3</sub> (2 × 20 mL). The organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated in vacuo. Purification by flash column chromatography (Gradient: 10–50 % EtOAc/Hexane) afforded 0.43 g (60%) of peptide **20a** as a white solid. TLC R<sub>f</sub> = 0.1 (30% ethylacetate/hexane).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, 25 °C): δ = 7.77 (d, *J* = 7.6 Hz, 2H; H<sub>Ar(Fmoc)</sub>), 7.59 (d, *J* = 7.2 Hz, 2H; H<sub>Ar(Fmoc)</sub>), 7.44–7.27 (9H; H<sub>Ar(Fmoc)</sub> & H<sub>Ar</sub>), 7.2–7.14 (3H; H<sub>Ar</sub>), 7.02–6.94 (2H; H<sub>Ar</sub>), 6.47 (d,

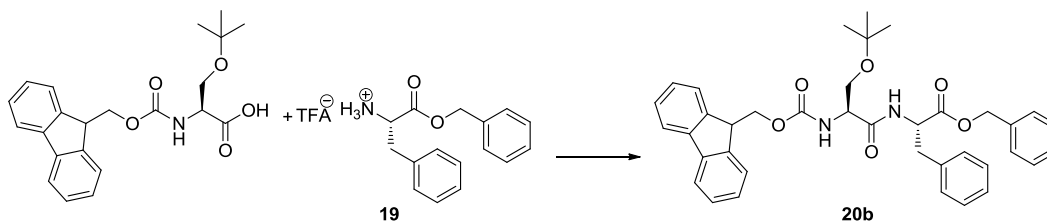
$J = 7.2$  Hz, 1H;  $NH_{\text{Phe}}$ ), 5.45 (bs, 1H;  $NH_{\text{Gly}}$ ), 5.14 (q,  $J = 12$  Hz, 2H;  $CH_2$ ), 4.93 (q,  $J = 6$  Hz, 1H;  $CH_{\text{Phe}}$ ), 4.39 (d,  $J = 7.2$  Hz, 2H;  $CH_{2(\text{Fmoc})}$ ), 4.21 (t,  $J = 7.2$  Hz, 1H;  $CH_{(\text{Fmoc})}$ ), 3.95-3.7 (m, 2H;  $CH_{2(\text{Gly})}$ ), 3.20-3.05 (m, 2H;  $CH_{2(\text{Phe})}$ );  $^{13}\text{C}$  NMR (125 MHz  $\text{CDCl}_3$ , 25 °C):  $\delta = 171.2, 168.6, 156.6, 143.9, 141.5, 135.5, 135.1, 129.4, 128.79, 128.76, 127.9, 127.34, 127.25, 125.2, 120.2, 67.6, 53.3, 47.2, 44.6, 37.9, 29.8$ ; IR (KBr pellet):  $\nu = 3386$  (s), 3252 (s), 1727 (s), 1636 (s), 1557 (s), 1526 (s), 1448 (s), 1243 (s), 1191 (s), 1046 (s), 760 (s), 740 (s), 700 (s)  $\text{cm}^{-1}$ ; HRMS (ESI<sup>+</sup>): calcd. for  $\text{C}_{33}\text{H}_{31}\text{N}_2\text{O}_5$  (MH<sup>+</sup>) 535.2233, found 535.2232.



**Fmoc-Gly-L-Phe-OH 21a:** To a solution of dipeptide **20a** (0.57 g, 1.0 mmol, 1 equiv) in MeOH (22 mL) was added Pd/C (125 mg, 12.5 mmol, 12.5 equiv) at RT. The reaction was allowed to stir in an atmosphere of hydrogen (balloon was used) for 45 min, following which it was filtered over celite. The celite was washed multiple times with MeOH and the combined filtrates were concentrated in vacuo to give 0.46 g (98%) of dipeptide **21a** as a white solid. TLC  $R_f = 0.2$  (5% MeOH/DCM).

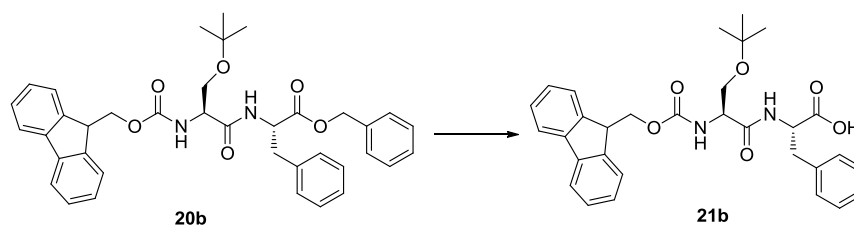
$^1\text{H}$  NMR (500 MHz,  $\text{DMSO}-d_6$ , 25 °C):  $\delta = 8.05$  (d,  $J = 7$  Hz, 1H;  $NH_{\text{Phe}}$ ), 7.89 (d,  $J = 7.5$  Hz, 2H;  $H_{\text{Ar}(\text{Fmoc})}$ ), 7.71 (d,  $J = 7$  Hz, 2H;  $H_{\text{Ar}(\text{Fmoc})}$ ), 7.53-7.46 (m, 1H;  $NH_{\text{Gly}}$ ), 7.41 (t,  $J = 7.5$  Hz, 2H;  $H_{\text{Ar}(\text{Fmoc})}$ ), 7.32 (t,  $J = 7.5$  Hz, 2H;  $H_{\text{Ar}(\text{Fmoc})}$ ), 7.28-7.13 (5H;  $H_{\text{Ar}}$ ), 4.47-4.38 (1H;  $CH_{\text{Phe}}$ ), 4.28-4.12 (3H;  $CH_{2(\text{Fmoc})}$  &  $CH_{(\text{Fmoc})}$ ), 3.64 (dd,  $J = 17$  Hz,  $J = 6$  Hz, 1H;  $CH_aH_b(\text{Gly})$ ), 3.56 (dd,  $J = 16.5$  Hz,  $J = 6$  Hz, 1H;  $CH_aH_b(\text{Gly})$ ), 3.04 (dd,  $J = 13.5$  Hz,  $J = 4.5$  Hz, 1H;  $CH_aH_b(\text{Phe})$ ), 2.89 (dd,  $J = 13.5$  Hz,  $J = 8.5$  Hz, 1H;  $CH_aH_b(\text{Phe})$ );  $^{13}\text{C}$  NMR (125 MHz,  $\text{DMSO}-d_6$ , 25 °C):  $\delta = 172.8, 168.9, 156.4, 143.8, 140.7, 137.5, 129.1, 128.1, 127.6, 127.1, 126.3, 125.2, 120.1, 65.7, 53.6, 46.6, 43.2, 36.9$ ; IR (KBr pellet):  $\nu = 3396$  (br), 3331 (br), 1723 (s), 1640 (m), 1599 (m), 1537 (s), 1449 (m), 1409 (m), 1234 (s), 1158 (m), 741 (s), 700 (w),  $\text{cm}^{-1}$ ; HRMS (ESI<sup>+</sup>): calcd. for  $\text{C}_{26}\text{H}_{25}\text{N}_2\text{O}_5$  (MH<sup>+</sup>) 445.1763, found 445.1751.





**Fmoc-L-Ser(O<sup>t</sup>Bu)-L-Phe-OBn 20b:** To a solution of Fmoc-L-Ser(O<sup>t</sup>Bu)-OH (0.53 g, 1.4 mmol, 1 equiv) in DCM (15 mL) at 0 °C, was added EDCI (0.4 g, 1.7 mmol, 1.2 equiv), TFA salt **19** (0.62 g, 1.7 mmol, 1.2 equiv) and DIEA (0.6 mL, 3.5 mol, 2.5 equiv). The reaction mixture was warmed to RT and allowed to stir 3 h. Subsequently, DCM (30 mL) was added and the mixture was washed with water (2 × 20 mL). The organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated in vacuo. Purification by flash column chromatography (Gradient: 5-20 % EtOAc/Hexane) afforded 0.36g (42%) of peptide **20b** as a white solid. TLC  $R_f$  = 0.5 (20% ethylacetate/hexane).

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>, 25 °C):  $\delta$  = 7.77 (d,  $J$  = 8 Hz, 2H;  $H_{Ar(Fmoc)}$ ), 7.59 (d,  $J$  = 7 Hz, 2H;  $H_{Ar(Fmoc)}$ ), 7.4 (t,  $J$  = 7.5 Hz, 2H;  $H_{Ar(Fmoc)}$ ), 7.38-7.27 (7H;  $H_{Ar(Fmoc)}$ ,  $H_{Ar}$ , &  $NH_{Phe}$ ), 7.24-7.2 (3H;  $H_{Ar}$ ), 7.04 (dd,  $J$  = 7.5 Hz, 3.5 Hz, 2H;  $H_{Ar}$ ), 5.7 (bs, 1H;  $NH_{Ser}$ ), 5.13 (q,  $J$  = 12 Hz, 2H;  $CH_2$ ), 4.94 (q,  $J$  = 6 Hz, 1H;  $CH_{Phe}$ ), 4.23 (d,  $J$  = 7.5 Hz, 2H;  $CH_{2(Fmoc)}$ ), 4.28-4.18 (2H;  $CH_{(Fmoc)}$  &  $CH_{Ser}$ ), 3.81 (dd,  $J$  = 8.5 Hz,  $J$  = 3.5 Hz, 1H;  $CH_aH_b(Ser)$ ), 3.35 (t,  $J$  = 8.5 Hz, 1H;  $CH_aH_b(Ser)$ ), 3.17-3.07 (m, 2H;  $CH_{2(Phe)}$ ), 1.15 (s, 9H;  $CH_{3(tBu)}$ ); **<sup>13</sup>C NMR** (125 MHz CDCl<sub>3</sub>, 25 °C):  $\delta$  = 171.0, 170.1, 156.2, 144.1, 143.9, 141.5, 135.8, 135.2, 129.5, 128.74, 128.70, 127.9, 127.2, 125.3, 120.1, 74.5, 67.3, 61.8, 54.4, 53.6, 47.3, 38.2, 27.4; **IR** (KBr pellet):  $\nu$  = 3286 (s), 3070 (m), 2924 (s), 2856 (s), 1719 (s), 1696 (s), 1648 (s), 1550 (s), 1452 (s), 1355 (s), 1279 (s), 1245 (s), 1188 (s), 1084 (s), 1026 (m), 737 (s), 693 (s) cm<sup>-1</sup>; **HRMS (ESI<sup>+</sup>)**: calcd. for C<sub>38</sub>H<sub>40</sub>N<sub>2</sub>O<sub>6</sub>Na (MNa<sup>+</sup>) 643.2784, found 643.2783.



**Fmoc-L-Ser(O<sup>t</sup>Bu)-L-Phe-OH 21b:** To a solution of dipeptide **20b** (0.32 g, 0.52 mol, 1 equiv) in MeOH (12 mL) was added Pd/C (65 mg, 6.5 mmol, 12.5 equiv) at RT. The reaction was allowed to stir in an atmosphere of hydrogen (balloon was used) for 45 min, following which it was filtered over celite. The celite was washed multiple times with MeOH and the combined filtrates were concentrated in vacuo to give 0.27 g (99%) of dipeptide **21b** as a white solid. TLC  $R_f = 0.2$  (3% MeOH/DCM).

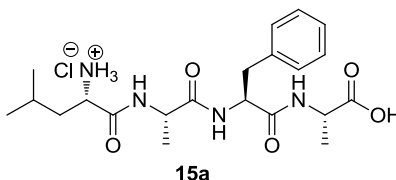
**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>, 25 °C):  $\delta = 8.63$  (bs, 1H; COOH), 7.76 (d,  $J = 7.2$  Hz, 2H;  $H_{Ar(Fmoc)}$ ), 7.58 (d,  $J = 7.2$  Hz, 2H;  $H_{Ar(Fmoc)}$ ), 7.40 (t,  $J = 7.6$  Hz, 2H;  $H_{Ar(Fmoc)}$ ), 7.36-7.21 (5H;  $H_{Ar(Fmoc)}$ ,  $H_{Ar}$ ), 7.2-7.14 (2H;  $H_{Ar}$ ), 5.9 (bs, 1H;  $NH_{Ser}$ ), 4.91 (q,  $J = 6$  Hz, 1H;  $CH_{Phe}$ ), 4.43-4.34 (m, 2H;  $CH_{2(Fmoc)}$ ), 4.27 (bs, 1H;  $CH_{Ser}$ ), 4.2 (t,  $J = 7.2$  Hz, 1H;  $CH_{(Fmoc)}$ ), 3.8-3.7 (m, 1H;  $CH_aH_b(Ser)$ ), 3.39 (t,  $J = 8.4$  Hz, 1H;  $CH_aH_b(Ser)$ ), 3.22 (dd,  $J = 14$  Hz,  $J = 5.2$  Hz, 1H;  $CH_aH_b(Phe)$ ), 3.12 (dd,  $J = 14$  Hz,  $J = 6$  Hz, 1H;  $CH_aH_b(Phe)$ ), 1.14 (s, 9H;  $CH_{3(t-Bu)}$ ); **<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>, 25 °C):  $\delta = 174.9, 170.6, 156.3, 143.8, 141.4, 135.8, 129.5, 128.7, 127.9, 127.3, 127.2, 125.2, 120.1, 74.5, 67.4, 61.7, 54.4, 53.4, 47.2, 37.6, 27.4$ ; **IR** (KBr pellet):  $\nu = 3415$  (w), 3320 (w), 2924 (s), 2855 (s), 1725 (s), 1668 (s), 1527 (m), 1452 (s), 1231 (m), 1190 (m), 1083 (m), 1038 (w), 738 (s), 700 (m) cm<sup>-1</sup>; **HRMS (ESI<sup>+</sup>)**: calcd. for C<sub>31</sub>H<sub>35</sub>N<sub>2</sub>O<sub>6</sub> (MH<sup>+</sup>) 531.2495, found 531.2473.

### General procedure for peptide synthesis using supports 3

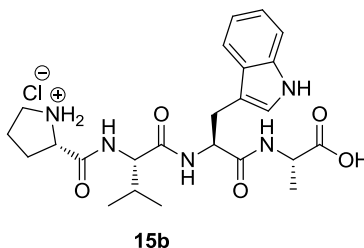
Amino acid attached polymer support **3** (70 mg) was treated with 20 % piperidine in DMF (0.7 mL) and allowed to stir for 10 min to deprotect the Fmoc group. The reaction mixture was washed with hexane (4 × 3 mL). Diethyl ether (8 mL) was added to precipitate the deprotected amino acid attached to the support. The precipitate was dried in vacuo and treated with dipeptide (Fmoc-AA<sub>2</sub>-AA<sub>1</sub>-OH) using HCTU (1.2 equiv) and DIEA (4 equiv) in dichloromethane (3 mL). The reaction mixture was allowed to stir 3 h, following which it was concentrated to 1 mL in vacuo. The crude solution was precipitated with diethyl ether (8 mL) to give the tripeptide attached polymer. The precipitate was dissolved in few drops of DMF and re-precipitated with diethyl ether (8 mL). The process was repeated three times to remove excess coupling reagents

and amino acids. The deprotection and coupling steps described above were repeated to get the desired peptide attached polymer. The peptide was treated with LiOH (3 equiv) in THF (3 mL) and 7-8 drops of water and allowed to stir 45 min. The resulting solution was concentrated in vacuo and diluted with water (5 mL). The supernatant was acidified and treated with dil. HCl to get the crude peptide. The crude peptide was purified by RP-HPLC to afford the pure peptide **15**.

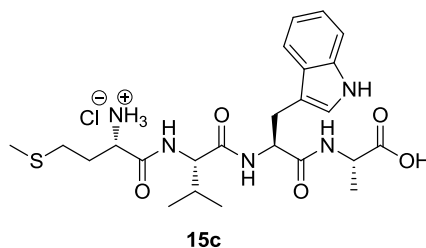
### Characterization of peptides synthesized using supports **3**



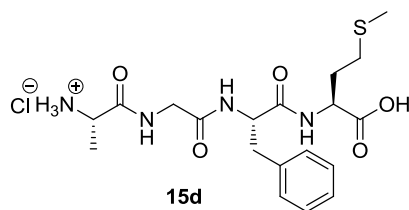
**HCl·H<sub>2</sub>N-Leu-Ala-Phe-Ala-OH 15a:** <sup>1</sup>H NMR (400 MHz, MeOH-*d*<sub>4</sub>, 25 °C): δ = 7.3-7.16 (5H; *H*<sub>Ar</sub>), 4.61 (dd, *J* = 8.4, 5.6 Hz, 1H; *CH*<sub>(Phe)</sub>); 4.44-4.34 (m, 2H; *CH*<sub>(Ala)</sub>), 3.87-3.81 (m, 1H; *CH*<sub>(Leu)</sub>), 3.18 (dd, *J* = 14.4, 4.8 Hz, 1H; *CH*<sub>a</sub>*H*<sub>b(Phe)</sub>), 2.94 (dd, *J* = 14, 8.8 Hz, 1H; *CH*<sub>a</sub>*H*<sub>b(Phe)</sub>), 1.72-1.59 (3H; *CH*<sub>2(Leu)</sub> & *CH*<sub>(Leu)</sub>), 1.40 (d, *J* = 7.2 Hz, 3H; *CH*<sub>3(Ala)</sub>), 1.33 (d, *J* = 7.2 Hz, 3H; *CH*<sub>3(Ala)</sub>), 0.98 (dd, *J* = 8.8, 5.6 Hz, 6H; *CH*<sub>3(Leu)</sub>); <sup>13</sup>C NMR (125 MHz, MeOH-*d*<sub>4</sub>, 25 °C): δ = 175.6, 174.0, 172.9, 170.3, 138.2, 130.5, 129.4, 127.7, 55.6, 52.8, 50.5, 41.6, 38.8, 25.3, 23.2, 21.9, 18.2, 17.7; IR (KBr pellet): ν = 3439 (br), 3283 (w), 2926 (w), 1635 (s), 1544 (w), 1449 (w), 1203 (m) 1141 (m) cm<sup>-1</sup>; HRMS (ESI<sup>+</sup>): calcd. for C<sub>21</sub>H<sub>33</sub>N<sub>4</sub>O<sub>5</sub> (MH<sup>+</sup>) 421.2451, found 421.2435.



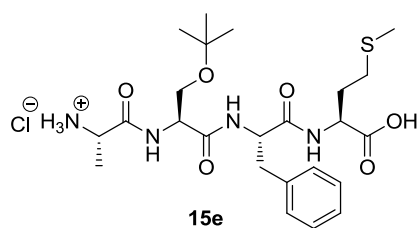
**HCl·H<sub>2</sub>N-Pro-Val-Trp-Ala-OH 15b:** <sup>1</sup>H NMR (400 MHz, D<sub>2</sub>O, 25 °C): δ = 7.74 (d, *J* = 8 Hz, 1H; *H*<sub>Ar(Trp)</sub>), 7.56 (d, *J* = 8 Hz, 1H; *H*<sub>Ar(Trp)</sub>), 7.35-7.28 (2H; *H*<sub>Ar(Trp)</sub>), 7.23 (t, *J* = 7.2 Hz, 1H; *H*<sub>Ar(Trp)</sub>), 4.44-4.32 (2H; *CH*<sub>Pro</sub> & *CH*<sub>Ala</sub>), 4.13 (d, *J* = 7.6 Hz, 1H; *CH*<sub>Val</sub>), 3.48-3.23 (4H; *CH*<sub>2(Pro)</sub> & *CH*<sub>2(Phe)</sub>), 2.39-2.25 (m, 1H; *CH*<sub>Pro</sub>), 2.12-1.98 (2H; *CH*<sub>2(Pro)</sub>), 1.98-1.85 (m, 1H; *CH*<sub>Pro</sub>), 1.71-1.6 (m, 1H; *CH*<sub>Val</sub>), 1.4 (d, *J* = 7.2 Hz, 3H; *CH*<sub>3(Ala)</sub>), 0.96 (dd, *J* = 10.4, 6.8 Hz, 6H; *CH*<sub>3(Val)</sub>); <sup>13</sup>C NMR (125 MHz, D<sub>2</sub>O, 25 °C): δ = 175.9, 172.6, 169.5, 136.2, 126.9, 124.7, 121.9, 119.3, 118.3, 111.8, 108.7, 60, 59.4, 54, 48.7, 46.6, 30.0, 29.8, 27.1, 23.7, 18.2, 17.7, 16.5; **IR** (KBr pellet): ν = 3420 (br), 3283 (w), 1636 (s), 1549 (w), 1455 (w), 1188 (w), 1134 (w), 1040 (w) cm<sup>-1</sup>; **HRMS (ESI<sup>+</sup>):** calcd. for C<sub>24</sub>H<sub>34</sub>N<sub>5</sub>O<sub>5</sub> (MH<sup>+</sup>) 472.2560, found 472.2553.



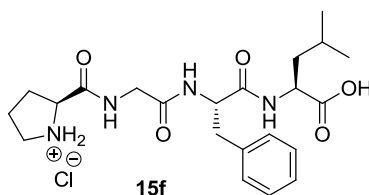
**HCl·H<sub>2</sub>N-Met-Val-Trp-Ala-OH 15c:** <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>CN, 25 °C): δ = 7.55 (d, *J* = 7.6 Hz, 1H; *H*<sub>Ar(Trp)</sub>), 7.36 (d, *J* = 8 Hz, 1H; *H*<sub>Ar(Trp)</sub>), 7.16-7.09 (2H; *H*<sub>Ar(Trp)</sub>), 7.07-7.02 (1H; *H*<sub>Ar(Trp)</sub>), 4.57 (dd, *J* = 8, 6.4 Hz, 1H; *CH*<sub>Trp</sub>), 4.2 (q, *J* = 7.2 Hz, 1H; *CH*<sub>Ala</sub>), 4.05 (d, *J* = 7.6 Hz, 1H; *CH*<sub>Val</sub>), 3.97 (t, *J* = 6.4 Hz, 1H; *CH*<sub>Met</sub>), 3.2 (dd, *J* = 14.8, 6 Hz, 1H; *CH*<sub>aH<sub>b</sub>(Trp)</sub>), 3.04 (dd, *J* = 14.8, 6.8 Hz, 1H; *CH*<sub>aH<sub>b</sub>(Trp)</sub>), 2.35-2.28 (m, 1H; *SCH*<sub>aH<sub>b</sub>(Met)</sub>), 2.25-2.15 (m, 1H; *SCH*<sub>aH<sub>b</sub>(Met)</sub>), 1.97-1.82 (8H; *CH*<sub>3(Met)</sub>, *CH*<sub>2(Met)</sub> & Solvent), 1.24 (d, *J* = 7.2 Hz, 3H; *CH*<sub>3(Ala)</sub>), 0.78 (t, *J* = 6.8 Hz, 6H; *CH*<sub>3(Val)</sub>); <sup>13</sup>C NMR (125 MHz, MeOH-*d*<sub>4</sub>, 25 °C): δ = 173.2, 172.8, 169.8, 138.0, 128.8, 124.8, 122.4, 119.8, 119.4, 112.3, 110.9, 60.7, 55.3, 53.5, 32.1, 31.9, 29.8, 29.0, 19.7, 18.7, 18.1; **IR** (KBr pellet): ν = 3423 (br), 2924 (w), 1671 (s), 1644 (s), 1542 (w), 1455 (w), 1202 (m), 1139 (m), 1024 (w), cm<sup>-1</sup>; **HRMS (ESI<sup>+</sup>):** calcd. for C<sub>24</sub>H<sub>36</sub>N<sub>5</sub>O<sub>5</sub>S (MH<sup>+</sup>) 506.2437, found 506.2414.



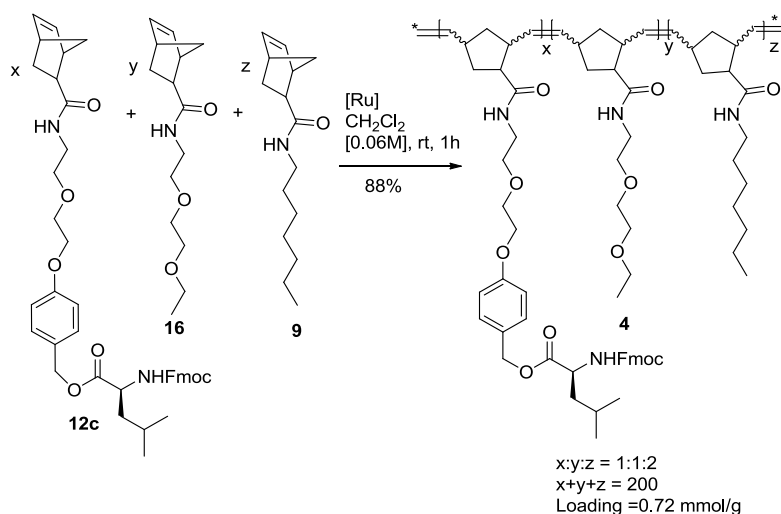
**HCl·H<sub>2</sub>N-Ala-Gly-Phe-Met-OH 15d:** <sup>1</sup>H NMR (500 MHz, D<sub>2</sub>O, 25 °C): δ = 7.32-7.16 (5H; *H*<sub>Ar</sub>), 4.56 (t, *J* = 7.5 Hz, 1H; *CH*<sub>Phe</sub>), 4.41 (dd, *J* = 9.5 Hz, 4.5 Hz, 1H; *CH*<sub>Met</sub>), 4.03 (q, *J* = 7 Hz, 1H; *CH*<sub>Ala</sub>), 3.86 (d, *J* = 3 Hz, 2H; *CH*<sub>Gly</sub>), 3.05 (dd, *J* = 14 Hz, 7 Hz, 1H; *CH*<sub>aH<sub>b</sub>(Phe)</sub>), 2.96 (dd, *J* = 13.5 Hz, 8 Hz, 1H; *CH*<sub>aH<sub>b</sub>(Phe)</sub>), 2.5-2.42 (m, 1H; -*SCH*<sub>aH<sub>b</sub>(Met)</sub>), 2.4-2.32 (m, 1H; -*SCH*<sub>aH<sub>b</sub>(Met)</sub>), 2.09-2.01 (m, 1H; *CH*<sub>aH<sub>b</sub>(Met)</sub>), 2.00 (s, 3H; *CH*<sub>3(Met)</sub>), 1.93-1.84 (1H; *CH*<sub>aH<sub>b</sub>(Met)</sub>), 1.44 (d, *J* = 7.5 Hz, 3H; *CH*<sub>3(Ala)</sub>); <sup>13</sup>C NMR (125 MHz, D<sub>2</sub>O, 25 °C): δ = 174.6, 172.9, 171.2, 170.5, 136.1, 129.2, 128.7, 127.2, 54.9, 51.5, 49.0, 42.0, 37.0, 29.8, 29.2, 16.3, 14.0; **IR** (KBr pellet): ν = 3396 (br), 1640 (s), 1407 (s), 1199 (w), 1136 (w), 635 (w), cm<sup>-1</sup>; **HRMS (ESI<sup>+</sup>):** calcd. for C<sub>19</sub>H<sub>29</sub>N<sub>4</sub>O<sub>5</sub>S (MH<sup>+</sup>) 425.1853, found 425.1847.



**HCl·H<sub>2</sub>N-Ala-Ser(O<sup>t</sup>Bu)-Phe-Met-OH 15e:** <sup>1</sup>H NMR (400 MHz, D<sub>2</sub>O, 25 °C): δ = 7.32-7.17 (5H; *H*<sub>Ar</sub>), 4.61 (t, *J* = 7.2 Hz, 1H; *CH*<sub>Phe</sub>), 4.44-4.36 (2H; *CH*<sub>Met</sub> & *CH*<sub>Ser</sub>), 4.03 (q, *J* = 7.2 Hz, 1H; *CH*<sub>Ala</sub>), 3.55 (d, *J* = 5.6 Hz, 2H; *CH*<sub>2(Ser)</sub>), 3.06 (dd, *J* = 13.6 Hz, 7.2 Hz, 1H; *CH*<sub>aH<sub>b</sub>(Phe)</sub>), 2.97 (dd, *J* = 14 Hz, 7.6 Hz, 1H; *CH*<sub>aH<sub>b</sub>(Phe)</sub>), 2.52-2.32 (2H; -*SCH*<sub>2(Met)</sub>), 2.12-2.01 (4H; *CH*<sub>aH<sub>b</sub>(Met)</sub>, & *CH*<sub>3(Met)</sub>), 1.93-1.84 (m, 1H; *CH*<sub>aH<sub>b</sub>(Met)</sub>), 1.42 (d, *J* = 6.8 Hz, 3H; *CH*<sub>3(Ala)</sub>), 1.09 (s, 9H; *CH*<sub>3(*t*-Bu)</sub>); <sup>13</sup>C NMR (125 MHz, D<sub>2</sub>O, 25 °C): δ = 174.7, 172.2, 170.70, 170.66, 136.0, 129.4, 128.8, 127.2, 75.4, 61.1, 54.6, 54.2, 51.7, 49.0, 37.4, 30.0, 29.3, 26.4, 16.6, 14.0; **IR** (KBr pellet): ν = 3394 (br), 1640 (s), 1407 (s), 1199 (w), 1138 (w), 646 (w), cm<sup>-1</sup>; **HRMS (ESI<sup>+</sup>):** calcd. for C<sub>24</sub>H<sub>39</sub>N<sub>4</sub>O<sub>6</sub>S (MH<sup>+</sup>) 511.2590, found 511.2599.



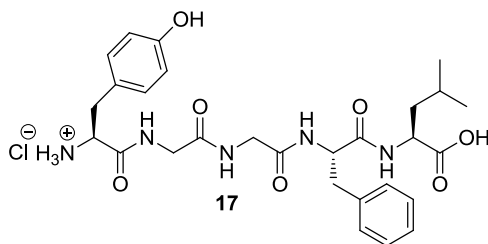
**HCl·H<sub>2</sub>N-Pro-Gly-Phe-Leu-OH 15f:** <sup>1</sup>H NMR (400 MHz, D<sub>2</sub>O, 25 °C): δ = 7.4-7.2 (5H; H<sub>Ar</sub>), 4.62 (t, *J* = 7.2 Hz, 1H; CH<sub>Phe</sub>), 4.37 (t, *J* = 7.6 Hz, 1H; CH<sub>Pro</sub>), 4.32 (t, *J* = 8 Hz, 1H; CH<sub>Leu</sub>), 3.90 (s, 2H; CH<sub>2</sub>(Gly)), 3.43-3.30 (m, 2H; CH<sub>2</sub>(Pro)), 3.11 (dd, *J* = 14 Hz, *J* = 7.2 Hz, 1H; CH<sub>a</sub>H<sub>b</sub>(Phe)), 2.98 (dd, *J* = 13.6 Hz, *J* = 8 Hz, 1H; CH<sub>a</sub>H<sub>b</sub>(Phe)), 2.44-2.35 (m, 1H; CH<sub>Pro</sub>), 2.1-1.9 (m, 3H; CH<sub>Pro</sub> & CH<sub>2</sub>(Pro)), 1.62-1.49 (3H; CH<sub>Leu</sub> & CH<sub>2</sub>(Leu)), 0.87 (d, *J* = 5.6 Hz, 3H; CH<sub>3</sub>(Leu)), 0.82 (d, *J* = 5.6 Hz, 3H; CH<sub>3</sub>(Leu)); <sup>13</sup>C NMR (100 MHz, D<sub>2</sub>O, 25 °C): 176.2, 172.7, 170.4, 170.2, 136.3, 129.3, 128.8, 127.3, 59.8, 54.8, 51.7, 46.6, 42.4, 39.7, 37.2, 29.6, 24.4, 23.8, 22.2, 20.8; IR (KBr pellet): ν = 3392 (br), 1647 (s), 1409 (s), 1021 (w), 653 (w), cm<sup>-1</sup>; HRMS (ESI<sup>+</sup>): calcd. for C<sub>22</sub>H<sub>33</sub>N<sub>4</sub>O<sub>5</sub> (MH<sup>+</sup>) 433.2445, found 433.2462.



**Synthesis of polymer 4:** The polymer was synthesized following the general procedure described for synthesis of supports **2**. Grubbs' third generation initiator (5.4 mg, 0.006 mmol, 1 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (3 mL) was added to monomer **12c** (207.0 mg, 0.31 mmol, 50 equiv), monomer

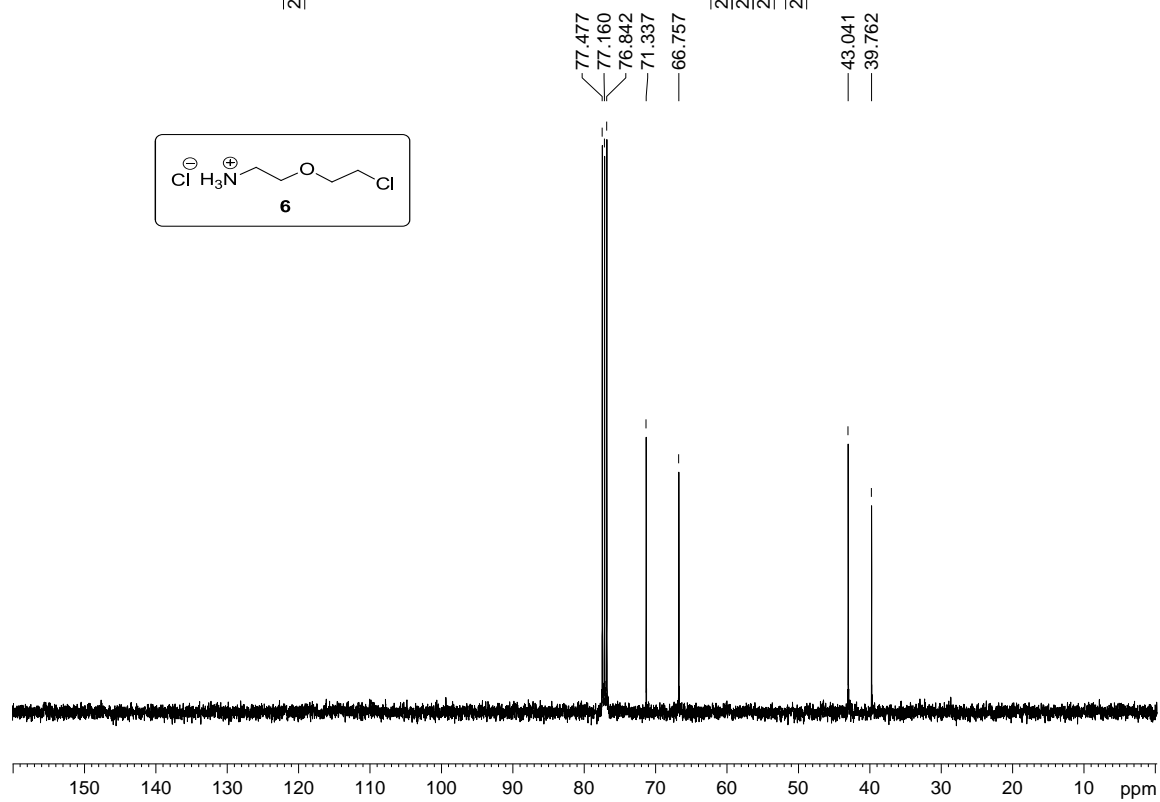
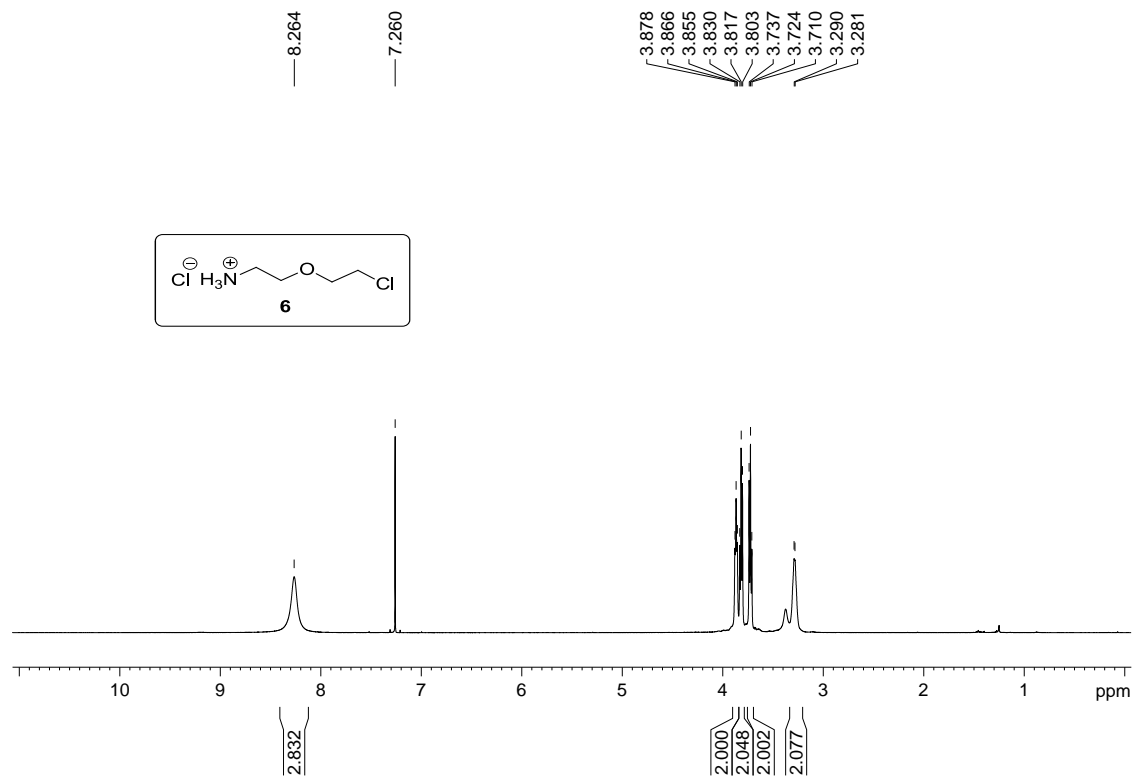
**16** (76.0 mg, 0.31 mmol, 50 equiv) and monomer **9** (146.0 mg, 0.62 mmol, 100 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (6 mL) to afford polymer **4** (380 mg) in 88% yield. Loading = 0.72 mmol/g; x:y:z= 1:1:2.

**<sup>1</sup>H NMR** (400 MHz, DMSO-d<sub>6</sub>, 25 °C): δ = 7.9–7.8 (3.6H; *H*<sub>Ar(Fmoc)</sub>), 7.8–7.5 (5H; *NH*<sub>Leu</sub> & *H*<sub>Ar(Fmoc)</sub>), 7.38 (2.7H; *H*<sub>Ar(Fmoc)</sub>), 7.32–7.15 (4.4H; *H*<sub>Ar(Fmoc)</sub> & *H*<sub>Ar</sub>), 6.83 (2H; *H*<sub>Ar</sub>), 5.4–4.8 (10.4H; *CH=CH*), 4.3–4.1 (3.7H; *CH*<sub>2(Fmoc)</sub>, & *CH*<sub>Ala</sub>), 4.1–3.3 (393H; *CH*<sub>(Fmoc)</sub>, *ArOCH*<sub>2</sub>, *OCH*<sub>2</sub> & solvent), 3.2–2.5. (38.1H; *CH*<sub>2(deg)</sub>, *CH*<sub>(nb)</sub> & solvent), 2.4–2.22 (2.3H; *CH*<sub>(nb)</sub>), 2.0–1.0 (44.2H; *CH*<sub>nb</sub>, *CH*<sub>(Leu)</sub>, *CH*<sub>2(Leu)</sub>, & *CH*<sub>3(deg)</sub>), 0.9–0.7 (12.5H; *CH*<sub>3(Alk)</sub> & *CH*<sub>3(Leu)</sub>).

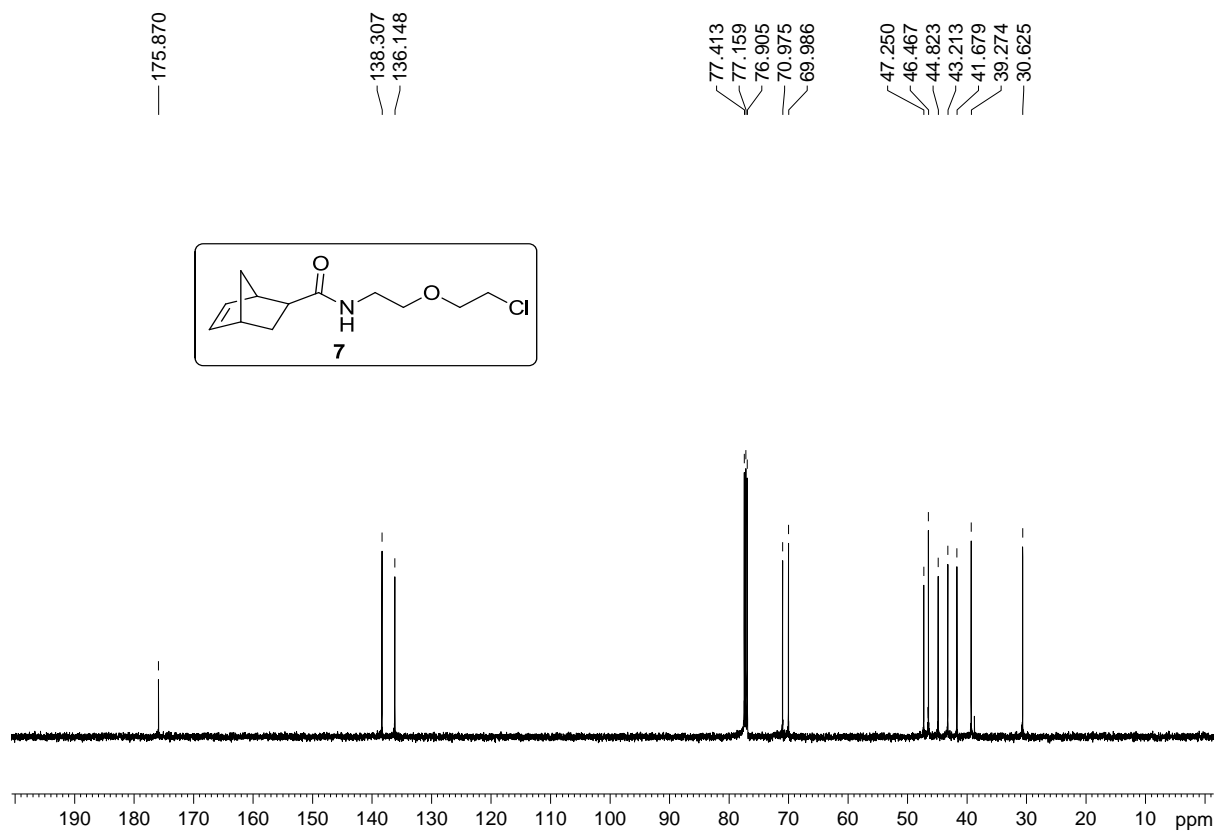
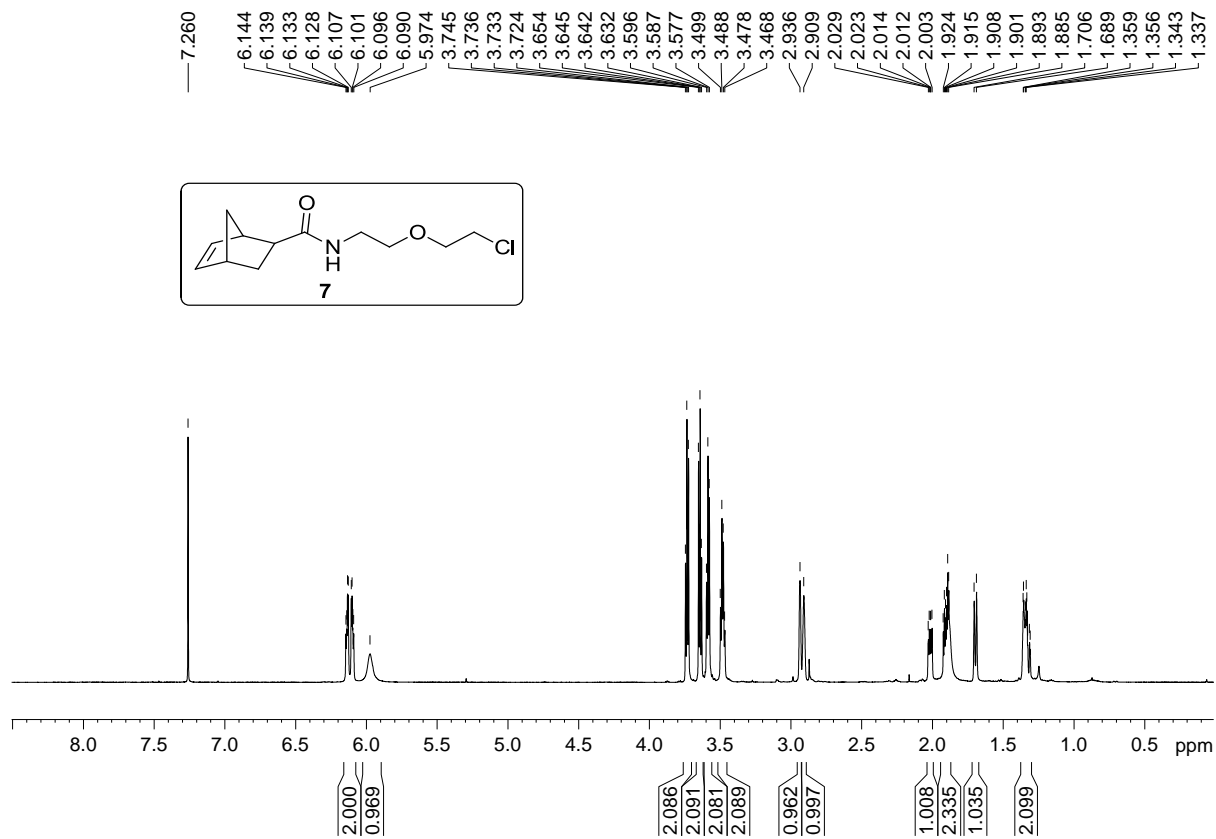


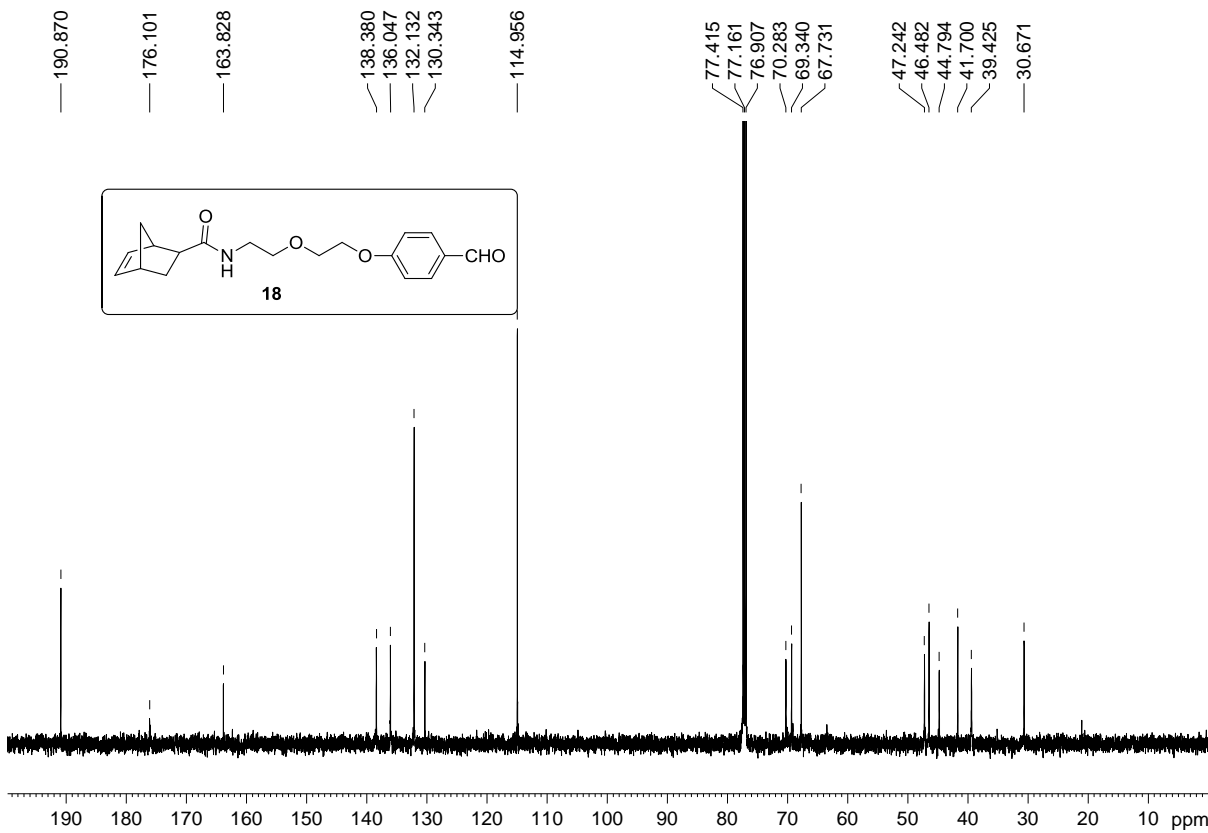
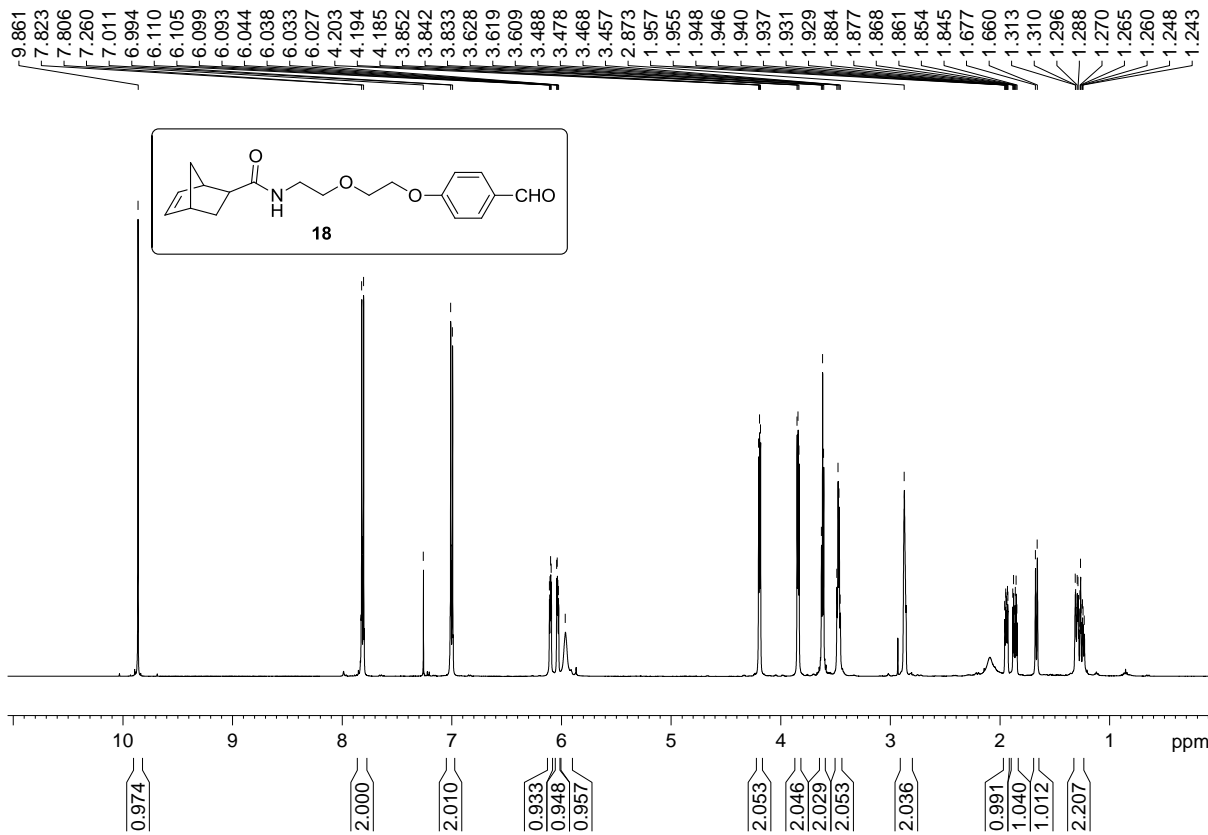
**HCl·H<sub>2</sub>N-Tyr-Gly-Gly-Phe-Leu-OH 17:** The peptide was synthesized following the general procedure described for synthesis of peptides **15** using supports **3**. **<sup>1</sup>H NMR** (400 MHz, D<sub>2</sub>O, 25 °C): δ = 7.35–7.22 (5H; *H*<sub>Ar</sub>), 7.13 (d, *J* = 8.4 Hz, 2H; *H*<sub>Ar(Tyr)</sub>), 6.84 (d, *J* = 8.4 Hz, 2H; *H*<sub>Ar(Tyr)</sub>), 4.61 (t, *J* = 7.2 Hz, 1H; *CH*<sub>Phe</sub>), 4.33–4.27 (m, 1H; *CH*<sub>Leu</sub>), 4.21 (t, *J* = 7.2 Hz, 1H; *CH*<sub>Tyr</sub>), 3.86 (d, *J* = 10 Hz, 2H; *CH*<sub>2(Gly)</sub>), 3.82 (d, *J* = 4.8 Hz, 2H; *CH*<sub>2(Gly)</sub>), 3.15–3.07 (3H; *CH*<sub>aH<sub>b</sub>(Phe)</sub> & *CH*<sub>2(Tyr)</sub>), 3.0–2.9 (2H; *CH*<sub>aH<sub>b</sub>(Phe)</sub> & *OH*), 1.62–1.49 (3H; *CH*<sub>Leu</sub> & *CH*<sub>2(Leu)</sub>), 0.86 (d, *J* = 6 Hz, 3H; *CH*<sub>3(Leu)</sub>), 0.81 (d, *J* = 6 Hz, 3H; *CH*<sub>3(Leu)</sub>); **<sup>13</sup>C NMR** (125 MHz, D<sub>2</sub>O, 25 °C): 176.1, 172.8, 171.2, 170.7, 169.9, 155.3, 136.2, 130.9, 129.3, 128.8, 127.2, 125.5, 115.9, 54.8, 54.6, 51.6, 42.4, 42.2, 39.2, 37.1, 36.0, 24.3, 22.2, 20.7; **[α]<sup>20</sup><sub>D</sub>** = 13.4 (c 0.18 AcOH); **IR** (KBr pellet): ν = 3396 (br), 1641 (s), 1408 (s), 1200 (w), 1137 (w), 640 (w), cm<sup>-1</sup>; **HRMS (ESI<sup>+</sup>)**: calcd. for C<sub>28</sub>H<sub>38</sub>N<sub>5</sub>O<sub>7</sub> (MH<sup>+</sup>) 556.2771, found 556.2774.

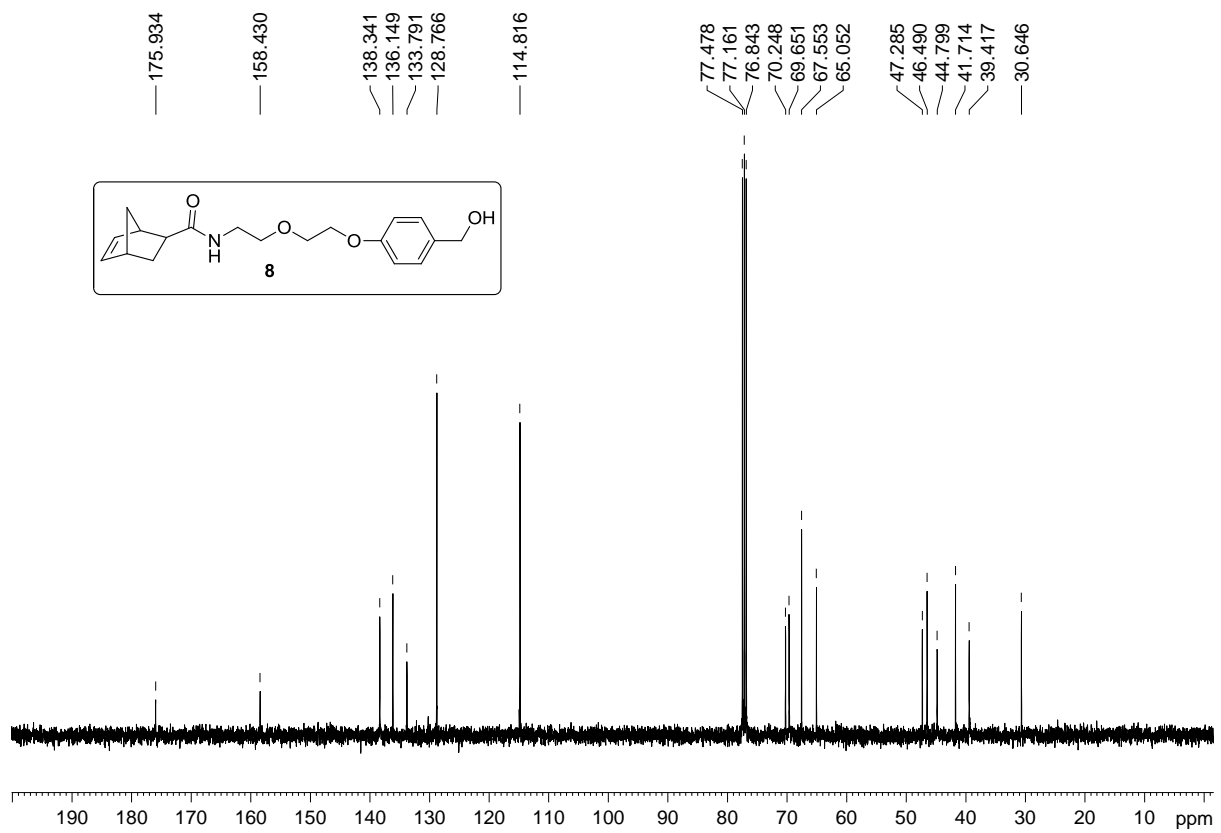
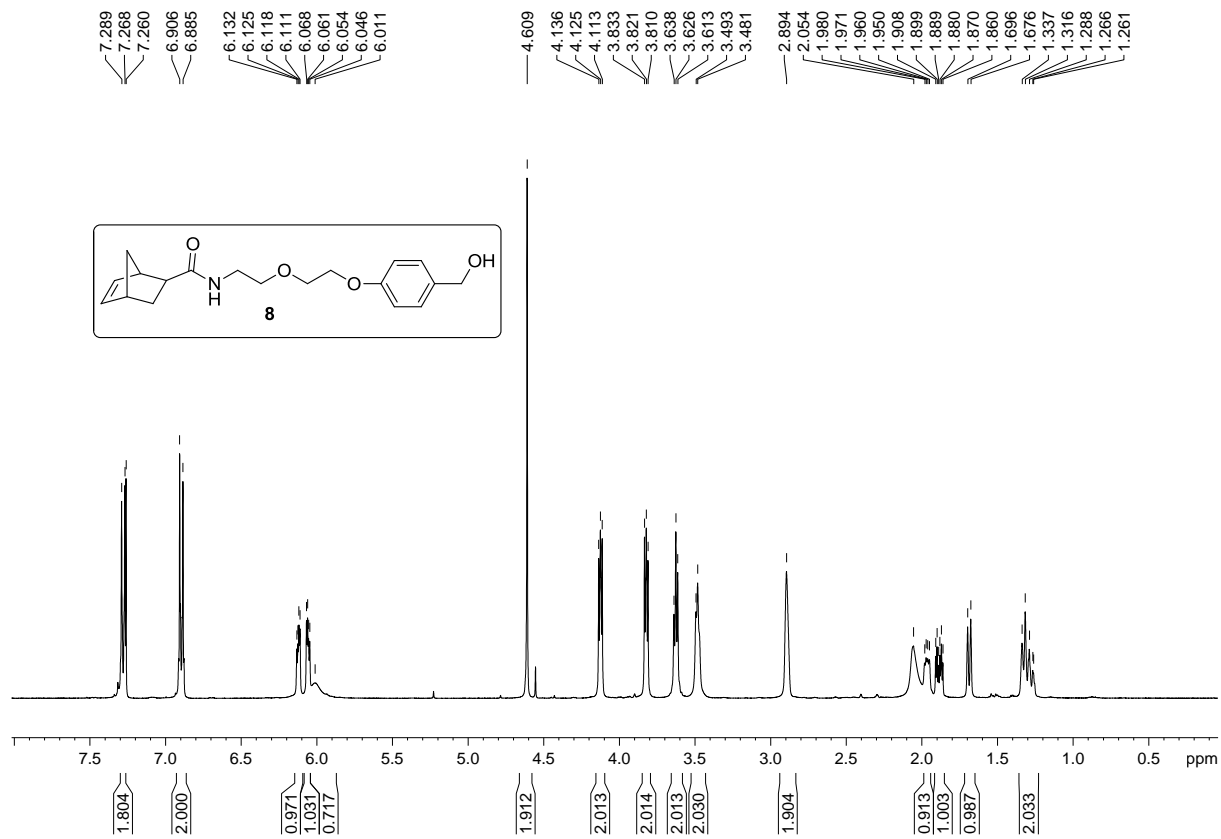
# NMR Spectra of Compounds

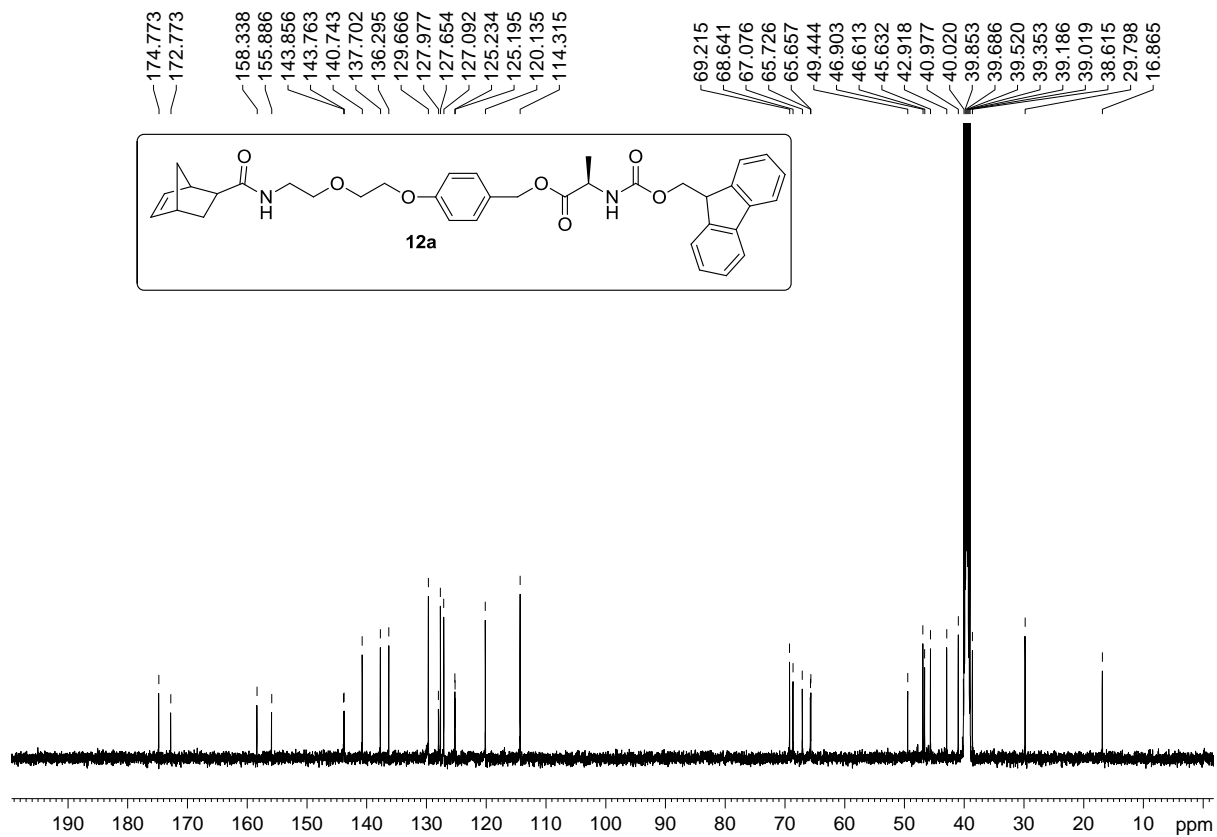
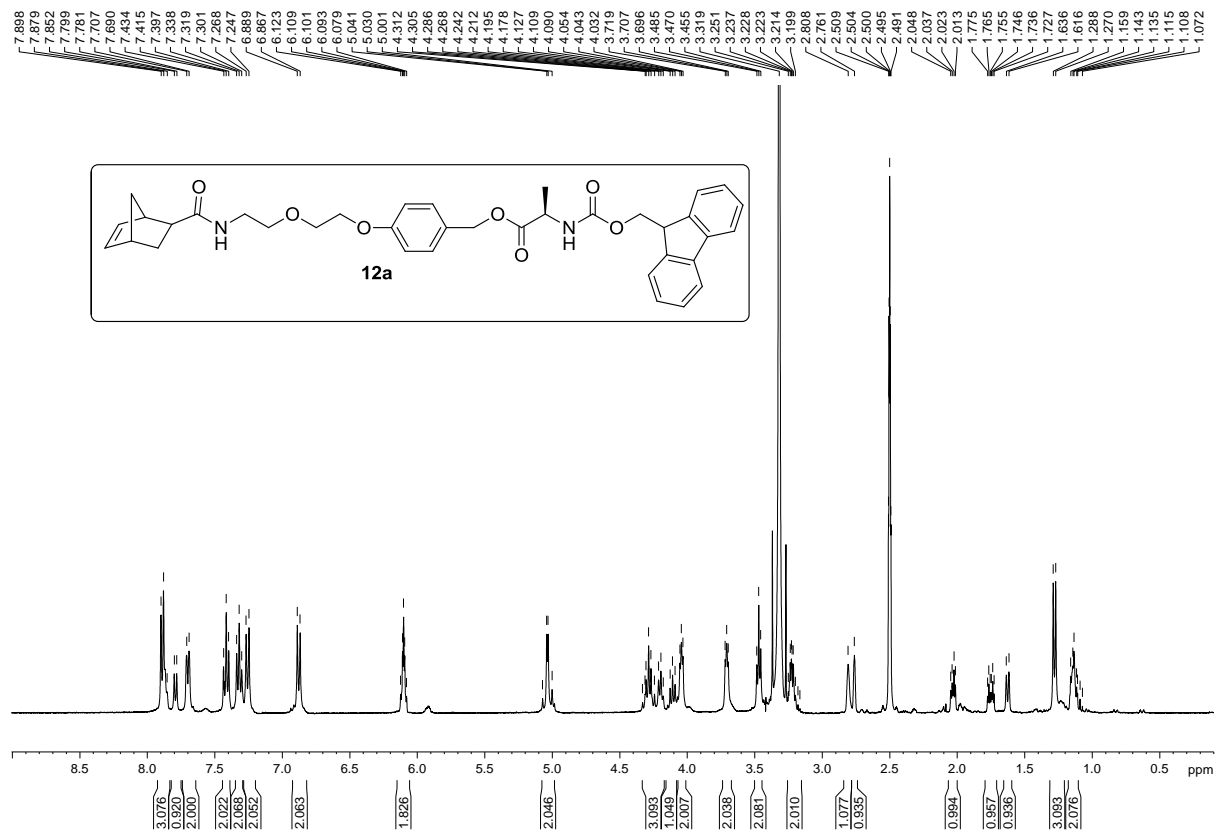




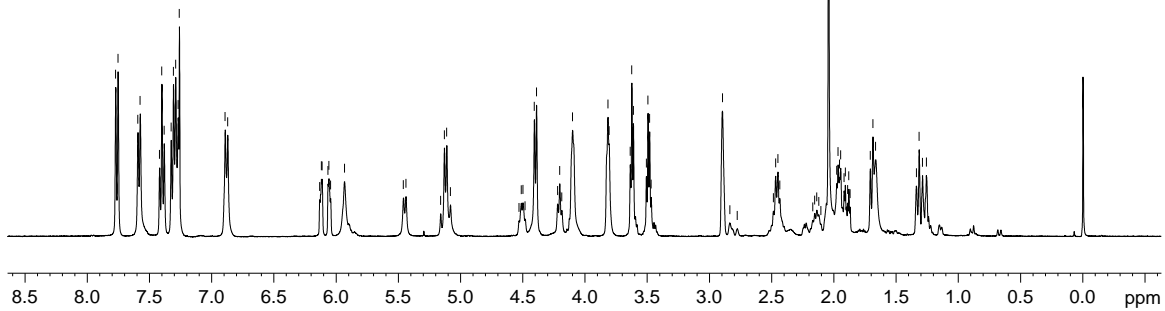
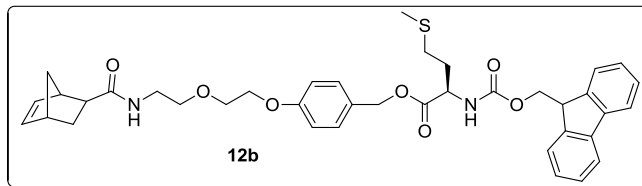








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