

Supporting information

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1-General information

Chemicals: Rink amine resin (0.62mmol/g loading) was obtained from Novabiochem, piperidine and dichloromethane from Carlo Erba; 3-chloromethylbenzoylchloride, TFA, DIPEA, isopropyl, and propargyl amines from TCI; *N*-methylpyrrolidone from Alfa Aesar and DMSO from Acros. Benzyl azide (**1a**)¹, (azidomethyl)cyclohexane (**1b**)², *tert*-butyl azido acetate (**1c**)³, *tert*-butyl (2-azidoethyl)carbamate (**1d**)⁴ and 3-azido propane-1-ol (**1e**)⁵ were synthesized according to literature procedures. 10 mL jacketed reactors were purchased from Kamush and thermo-regulated using a Lauda thermostat. NMR was recorded on Bruker advance 400 spectrometer. Purification was performed on a Buchi Pure Chromatography system.

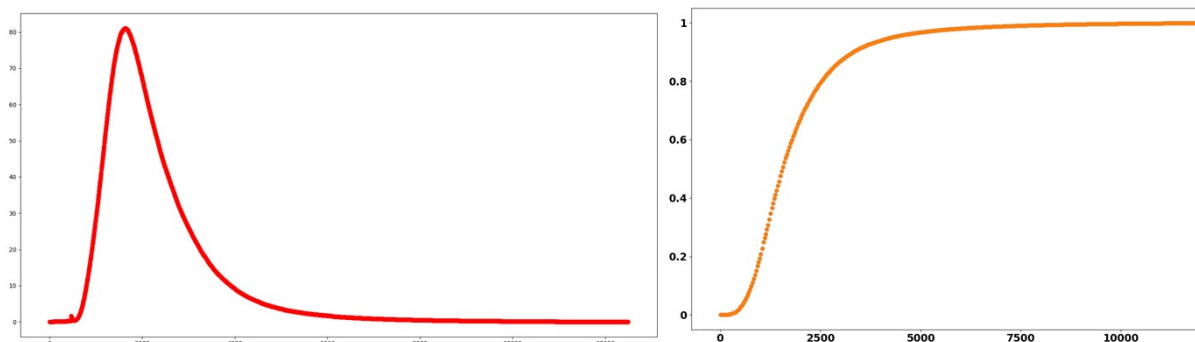
Analytical HPLC was recorded on an Hitachi liquid chromatograph (Oven 5310, 30°C; Pump 5160; DAD detector 5430) equipped with a C18 Acclaim column (4.6mm×250mm, 5µm, 120Å). Detection wavelength was 240nm or 280nm and flow rate 0.5mL/min. Gradient elution used (A) water/0.1% TFA; (B) methanol according Method A: (Solvents A/B: 0 to 5 minutes isocratic at 95/5; 5 to 25 minutes gradient to 5/95; 25 to 35 minutes isocratic at 5/95; 35 to 45 minutes gradient to 95/5; 45 to 50 minutes 95/5) or Method B (Solvents A/B: 0 to 5 minutes isocratic at 95/5; 5 to 10 minutes gradient to 75/25; 10 to 50 minutes gradient to 40/60; 50 to 65 minutes gradient to 5/95; 65 to 70 minutes isocratic at 5/95; 70 to 80 minutes gradient to 95/5).

Reactions kinetics were carried out in a THT Micro Reaction Calorimeter, which allows continuous monitoring of the instantaneous enthalpy exchanged by the reactor. The sample vessel consists in a 1.5 ml septum-cap vial equipped with a magnetic stirrer. The system operates by comparing the heat exchanged (*q*) in the reaction sample vessel compared with that from a reference compartment.

Fraction conversion is given by the:

$$\% (t) = \frac{\int_0^t q \cdot dt}{\int_0^{\infty} q \cdot dt}$$

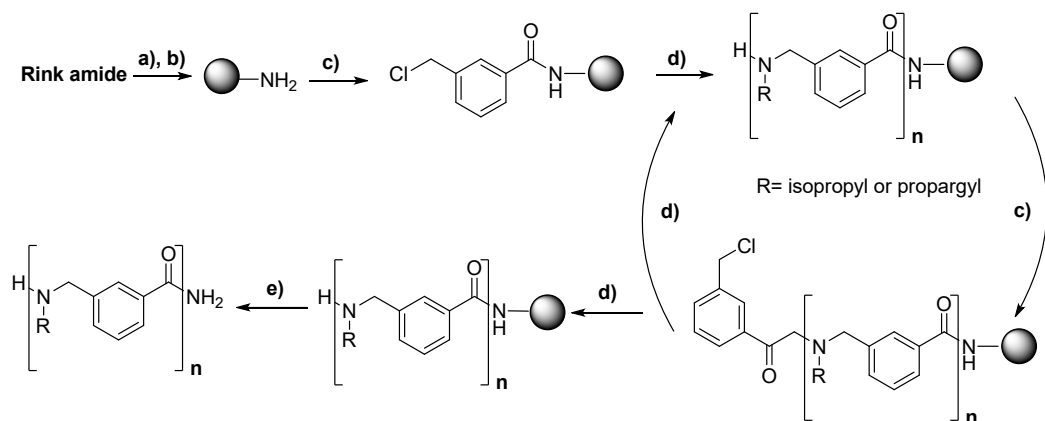
Integrations were determined using a house build python programme using the trapezoid method. Time constant of the system was measured to 50s⁻¹ and was not used for correction. A typical example for heat flow (mW) versus time is given below (figure left) (*C*_{propargyl alcohol} = 0.5M, *C*_{benzyl azide} = 0.5M Catalyst: 1mol-%). The integration method affords the following conversion versus time curve (Figure right). Conversion determined from the heat flow integration method was compared to conversions measured by NMR.



2-General procedures

2.1- Synthesis of alkyne substituted peptoids (General procedure A)

The synthesis of the *meta*-arylopeptoid hexamer was performed according to the submonomer synthesis using Rink amide resin (100-200 mesh, loading 0.54 mmol/g, novabiochem, 8.55001.0005, Batch no. S7816901016).⁶



Scheme S1. Solid-phase submonomer synthesis on Rink amide resin

1-For 100mg of resin, swelling: 2 ml of CH₂Cl₂ at RT for 10 min

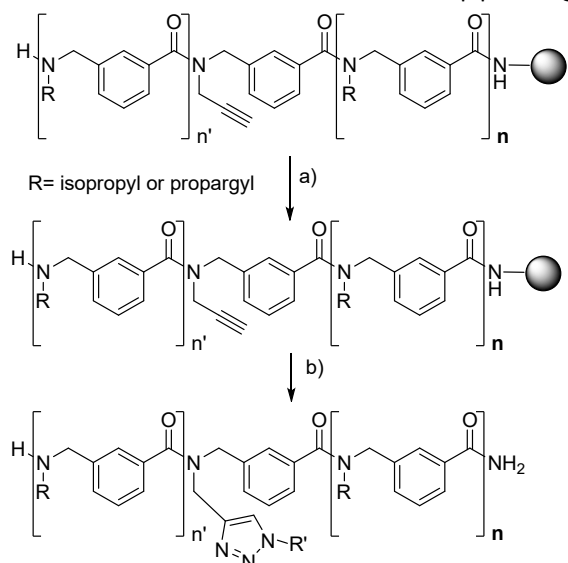
2- Fmoc Deprotection: resin was washed with NMP (N-Methyl-2-pyrrolidone) (5x2ml), then piperidine/NMP 1:4 (1ml) was added and agitated for 2 min and then drained. Further piperidine/NMP 1:4 (1.0 mL) was added and the resin was agitated for 15 min, drained and washed with NMP (5x2 mL) and CH₂Cl₂ (5x2 mL)

3- 3-chloromethylbenzoylchloride (3 equiv. per mmol loading) and DIPEA (6 equiv. per mmol loading) dissolved in 1 mL CH₂Cl₂ were added at RT, shaken 10 minutes, then washed with CH₂Cl₂ (5x2ml), then with DMSO (5x2ml).

4- Isopropyl or propargyl amine (20 equiv per mmol loading) dissolved in 0.5 mL of DMSO was added. The temperature was raised to 50°C for 1h then the resin was washed with DMSO (5x2ml), then with CH₂Cl₂ (5x2ml).

Steps 2 and 3 were repeated to grow the targeted arylopeptoid oligomer until the expected sequence length.

2.2- Click reaction on support: general procedure B.



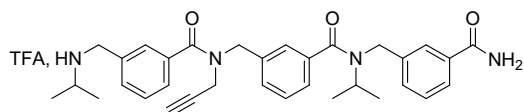
a) Azide, catalyst (5mol-% per alkyne), CH_2Cl_2 / MeOH; b) Cleavage: TFA/TIS/ H_2O (95:2.5:2.5).

Figure S1 General procedure B

Resin-bound arylopeptoid obtained from 100 mg of resin were introduced in a reactor containing 1 mL of CH_2Cl_2 /MeOH mixture (v/v = 8:2). Azides (4.0 equiv. per alkyne) and 5 mol-% of catalyst per alkyne were added. The reactor is gently shaken for 3h at 50°C. The resin was washed with MeOH (5x2ml) at 50°C and then with CH_2Cl_2 (5x2ml) at room temperature. Cleavage was performed by gently shaking in a 1 mL solution of TFA/TIS/ H_2O (95:2.5:2.5) for 10 min at RT. The solution was drained out and evaporated to dryness under reduced pressure. The foam was dissolved in a minimum amount of CH_2Cl_2 (≈ 0.4 mL), then 30 volumes (≈ 12 mL) of diethyl ether were added. The white precipitate formed was isolated after centrifugation.

3-Synthesis and Characterization data of arylopeptoid trimers

3.1-meta-arylopeptoid trimer III-3(Alk₂).



Trimer III-3(Alk₂) was synthesised according general procedure A using 50 mg of RA resin (0.027mmol).

$m_{\text{crude}} = 30 \text{ mg}$ (purity 85%), crude yield 170%

$m_{\text{pure}} = 17 \text{ mg}$ (purity 100%), isolated yield 98%

HRMS (TOF MS ES⁺): m/z calcd for C₃₃H₃₉N₄O₃ [M+H]⁺: 539.30167; found: 539.3013 (-0.74 ppm).

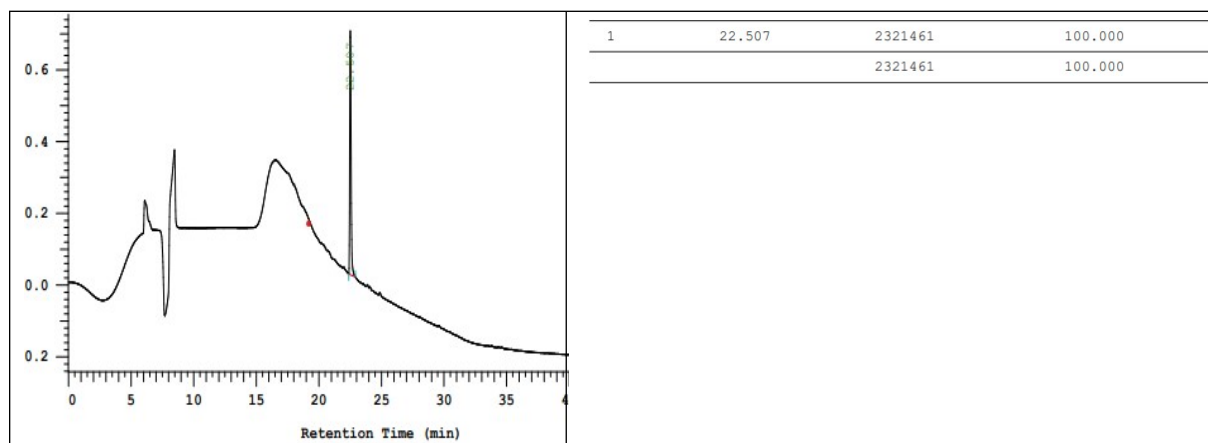


Figure S2 HPLC chromatogram of purified III-3(Alk₂).

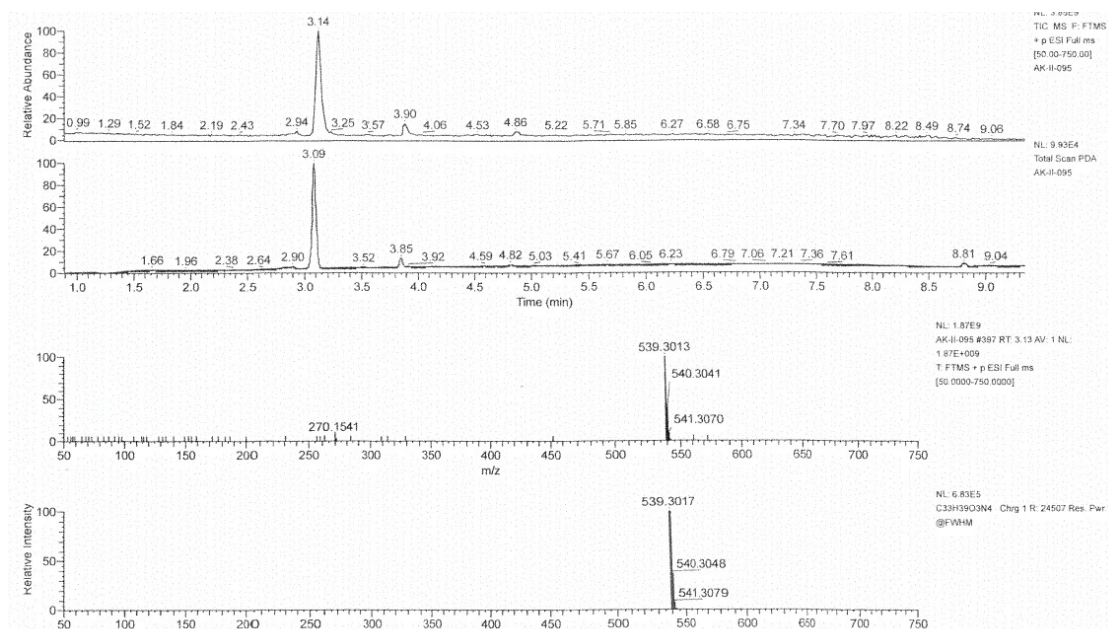


Figure S3 LCMS spectra of III-3(Alk₂).

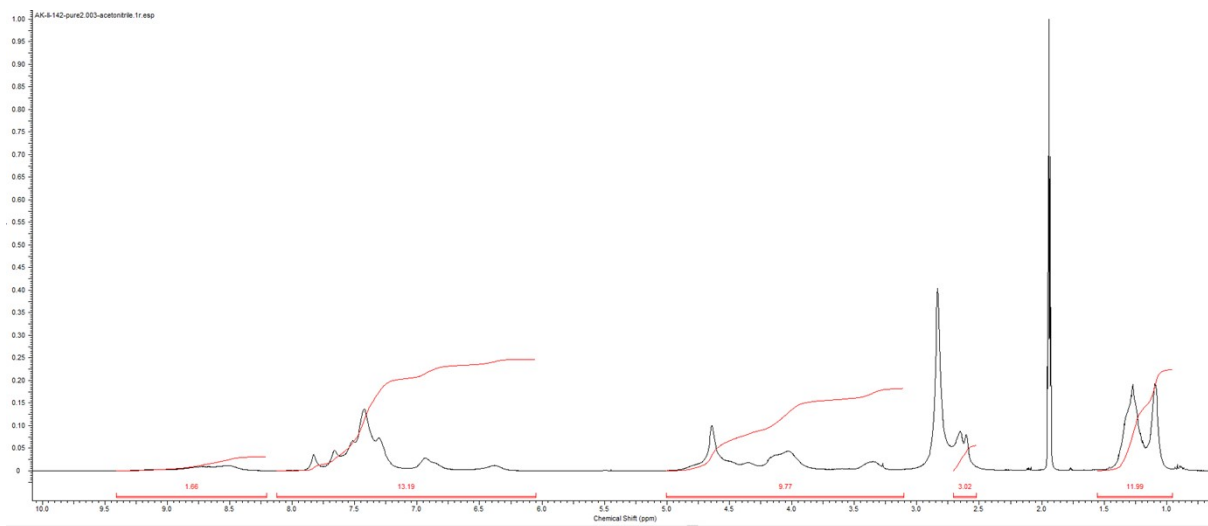


Figure S4 $^1\text{H-NMR}$ spectra in CD_3CN of **III-3(Alk₂)**.

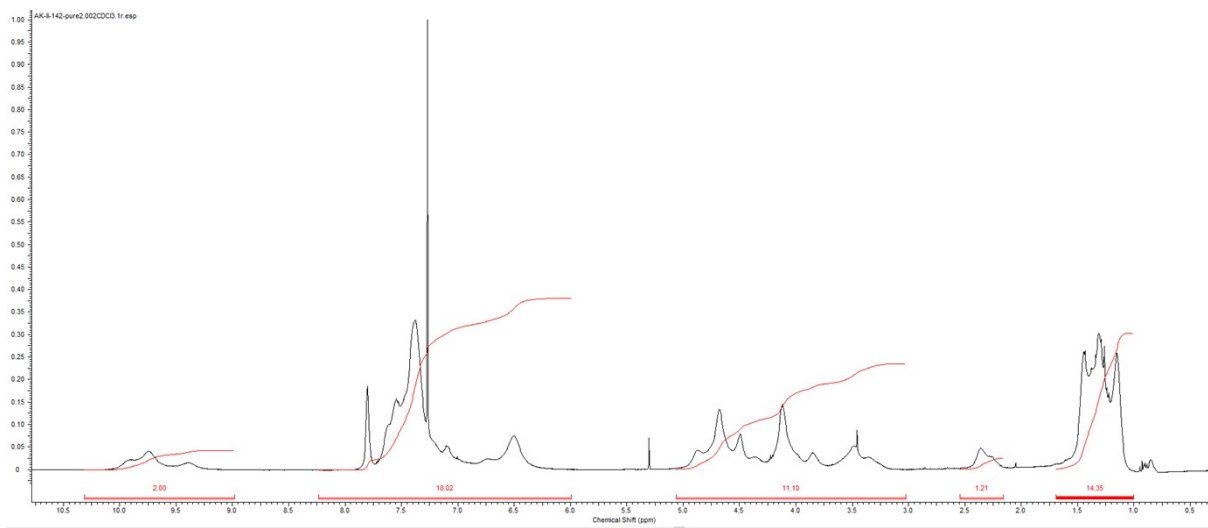
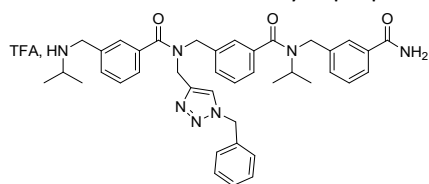


Figure S5 $^1\text{H-NMR}$ spectra in CDCl_3 of **III-3(Alk₂)**.

3.2- meta-arylopeptoid trimer III-3(a₂).



Trimer **III-3(a₂)** was synthesised according general procedure A then general procedure B using 50 mg of RA resin (0.027mmol).

m_{crude} = 33 mg (purity 85%), 155% crude yield

m_{pure} = 20.8 mg (purity 98%), 98% isolated yield

HRMS (TOF MS ES⁺): m/z calcd for C₄₀H₄₆N₇O₃ [M+H]⁺: 672.36566; found: 672.3645 (-1.73 ppm).

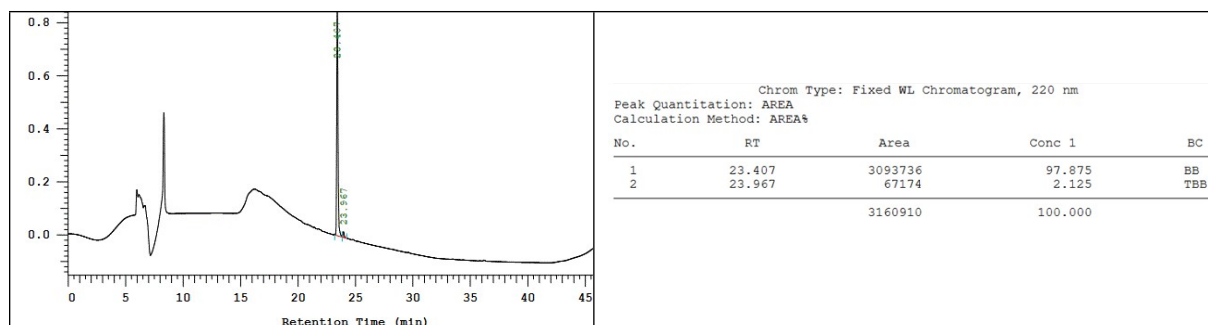


Figure S6 HPLC chromatogram of purified **III-3(a₂)**.

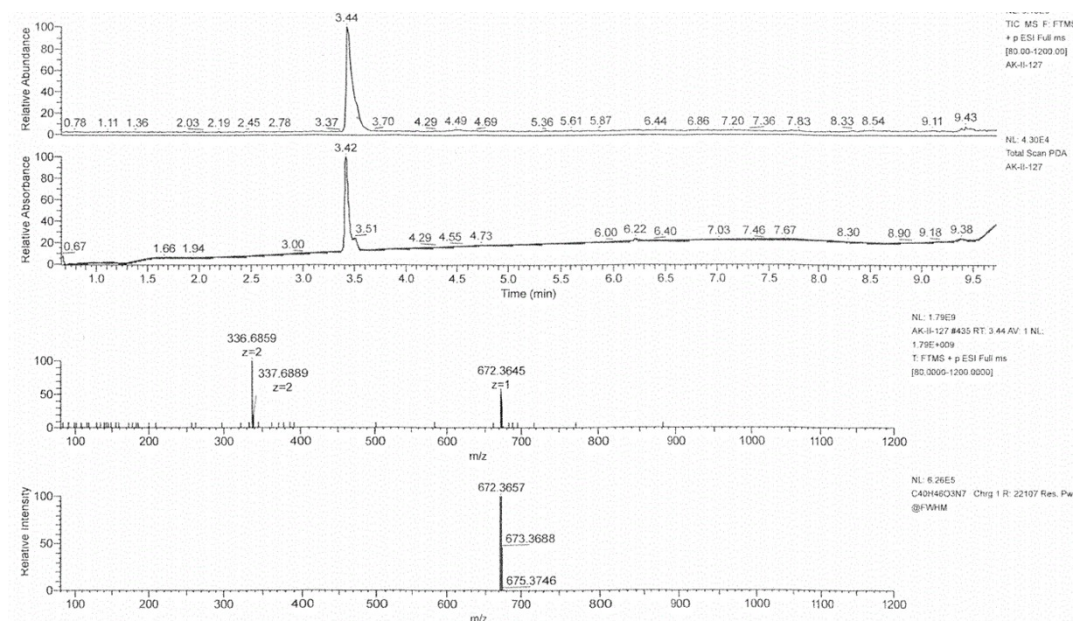


Figure S7 LCMS spectra of **III-3(a₂)**.

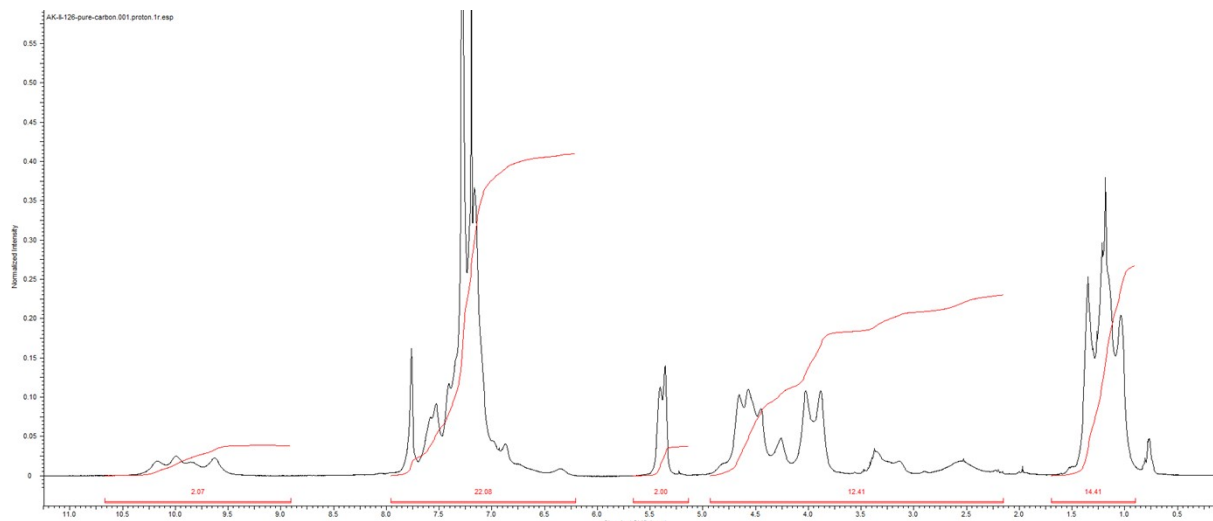
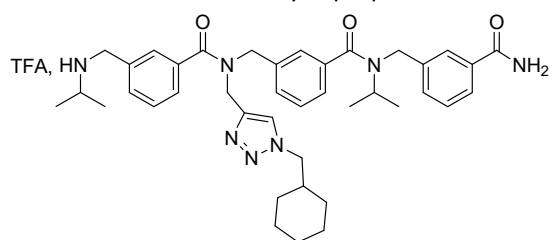


Figure S8 $^1\text{H-NMR}$ spectra in CDCl_3 of **III-3(a₂)**.

3.3- meta-arylopeptoid trimer, III-3(b₂).



Trimer **III-3(b₂)** was synthesised according general procedure A then general procedure B using 100 mg of RA resin (0.054 mmol).

m_{crude} = 46.2 mg (purity 83%), crude yield 112%

m_{pure} = 30 mg (purity 85%), isolated yield 85%

HRMS (TOF MS ES⁺): m/z calcd for C₄₀H₅₂N₇O₃ [M+H]⁺: 678.41261; found: 678.4128 (0.24 ppm).

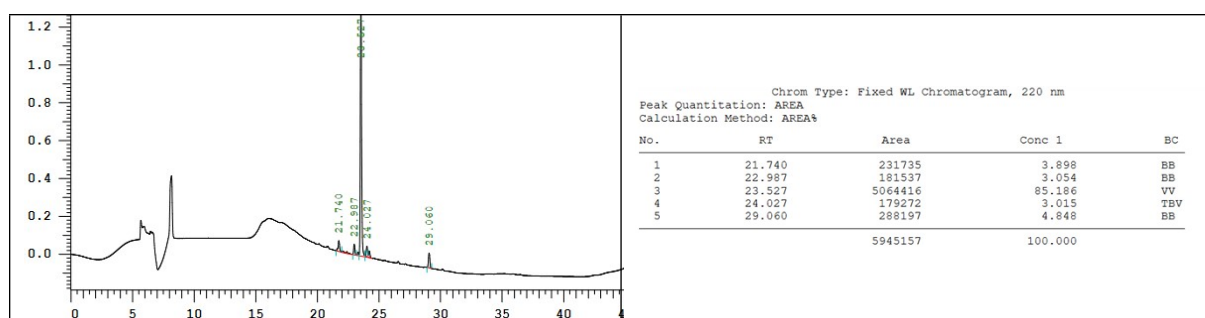


Figure S9 HPLC chromatogram of purified **III-3(b₂)**

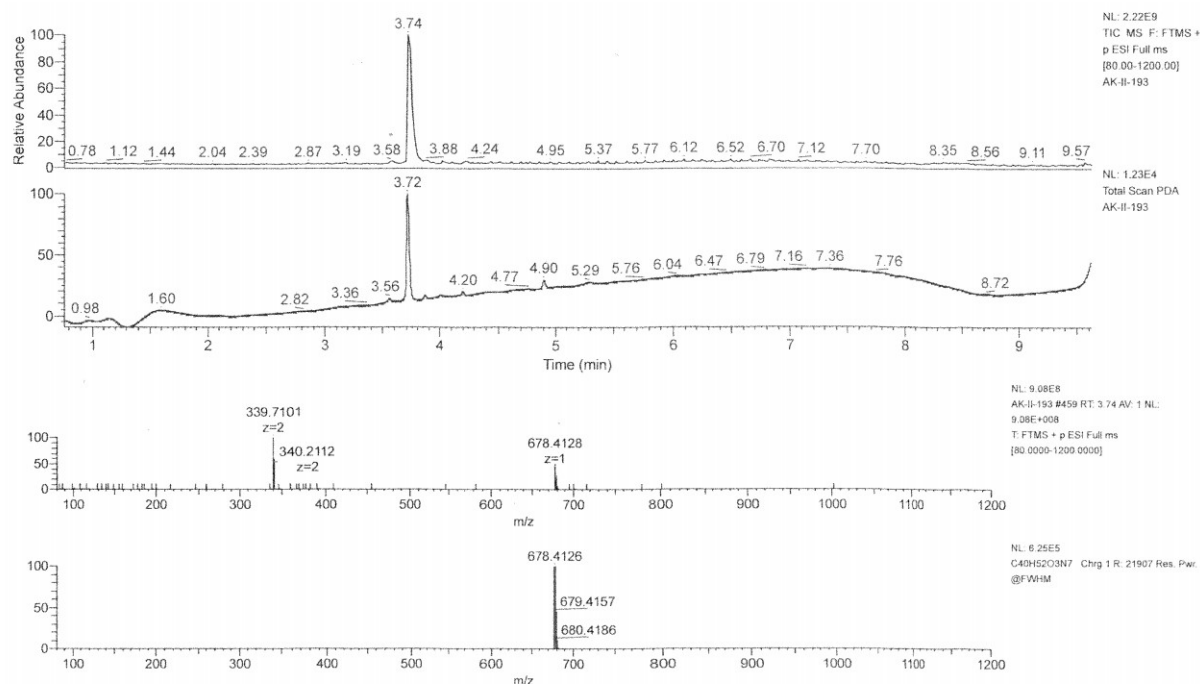


Figure S10 LCMS spectra of **III-3(b₂)**

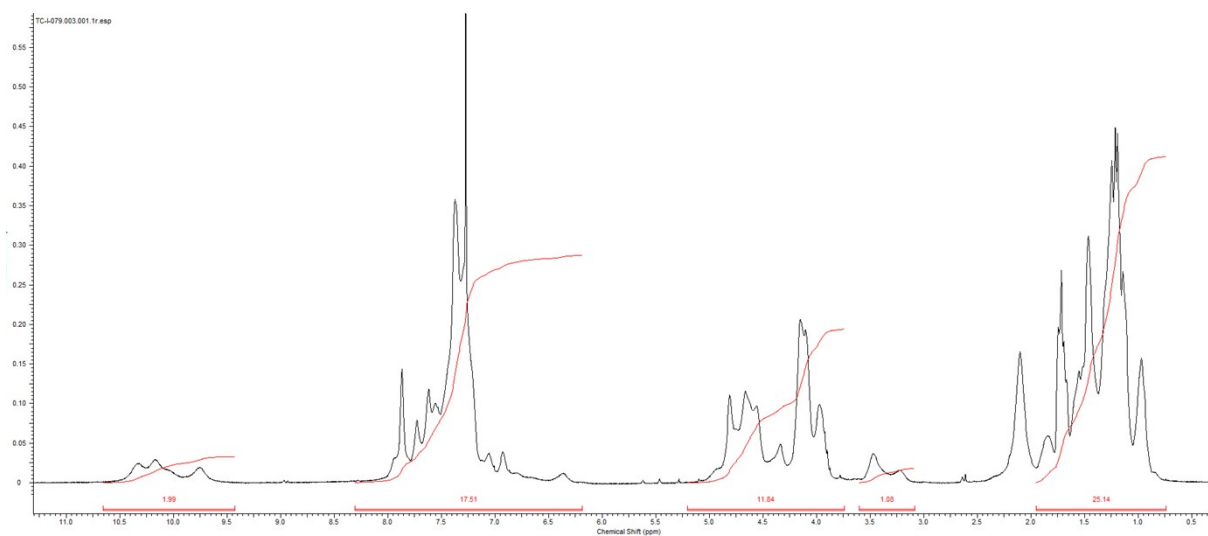
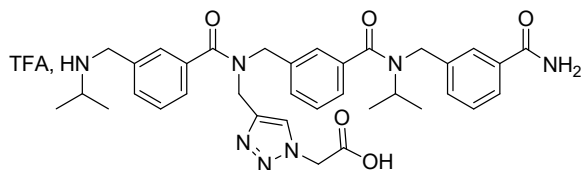


Figure S11 $^1\text{H-NMR}$ spectra in CDCl_3 of **III-3(b₂)**.

3.4-meta-arylopeptoid trimer III-3(c₂).



Trimer **III-3(c₂)** was synthesised according to general procedure A then general procedure B using 50 mg of RA resin (0.027mmol). After cleavage from the resin, the acid group was deprotected by treatment in 3ml TFA/CH₂Cl₂ (2/8) solution at room temperature overnight.

m_{crude} = 30mg (purity 85%), crude yield 147%

m_{pure} = 20 mg (purity 96%), isolated yield 97%

HRMS (TOF MS ES+): m/z calcd for C₃₅H₄₂N₇O₅ [M+H]⁺: 640.32419; found: 640.3235 (-1.1 ppm).

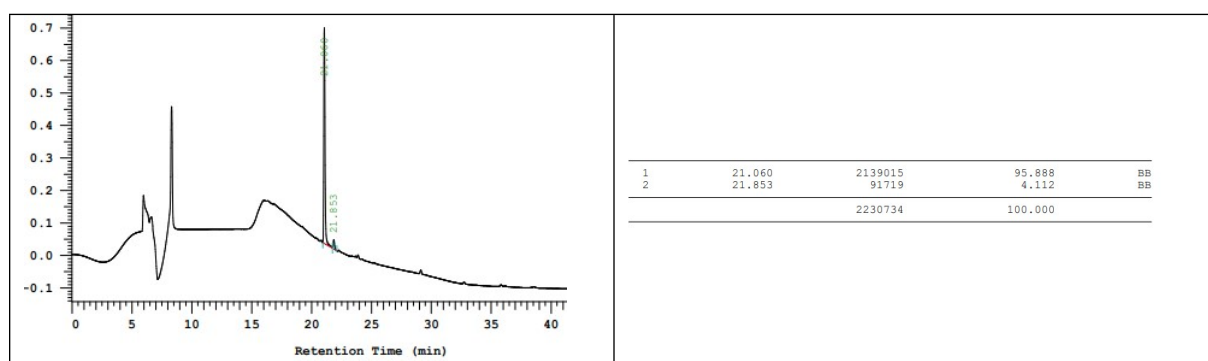


Figure S12 HPLC chromatogram of purified **III-3(c₂)**

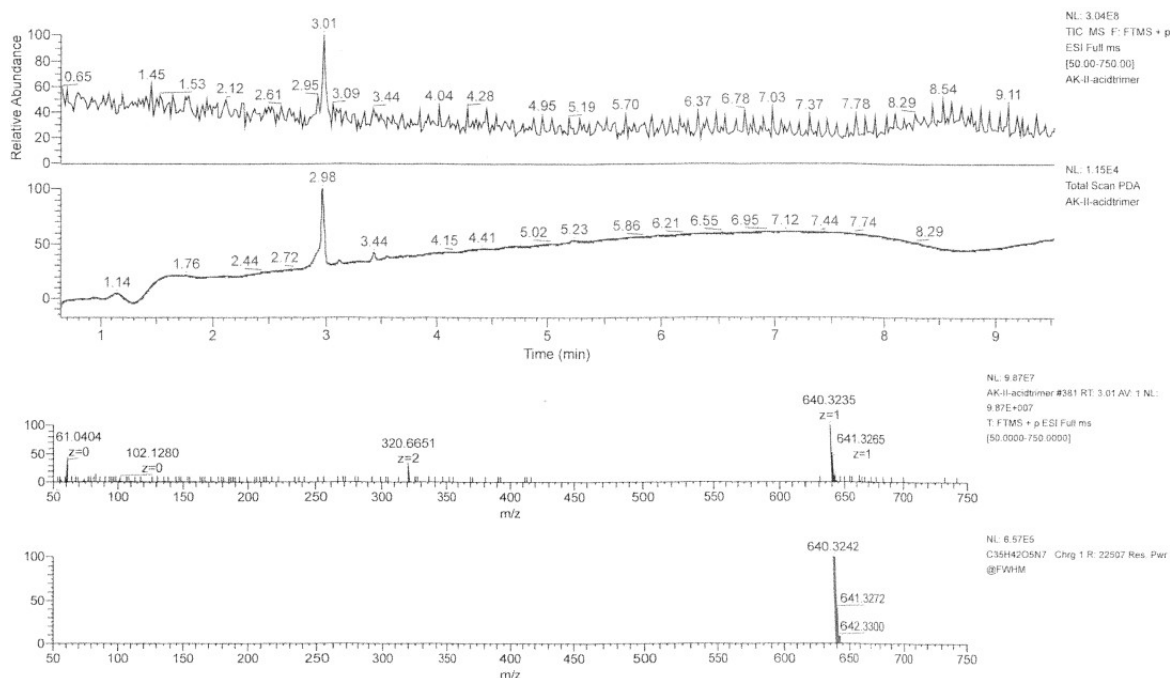


Figure S13 LCMS spectra of **III-3(c₂)**

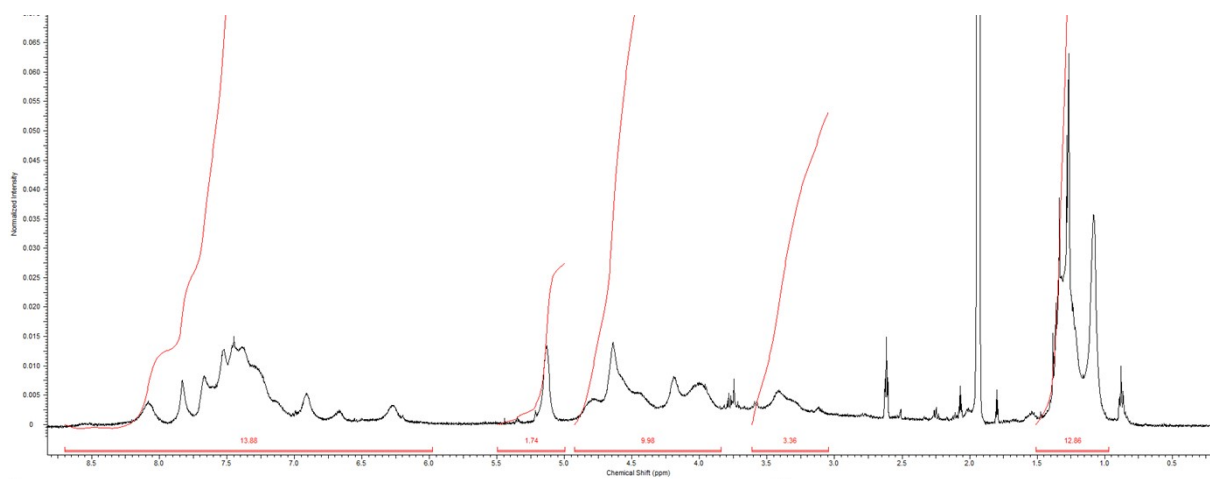
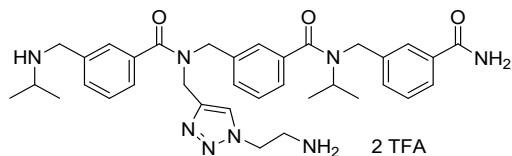


Figure S14 $^1\text{H-NMR}$ spectra in CD_3CN of III-3(c2).

3.5- meta-arylopeptoid trimer III-3(d₂).



Trimer **III-3(d₂)** was synthesised according general procedure A then general procedure B using 250 mg of RA resin (0.135mmol).

m_{crude} = 139 mg (purity 87%), crude yield 120%

m_{pure} = 98 mg (purity 97%), isolated yield 85%

HRMS (TOF MS ES⁺): m/z calcd for C₃₅H₄₅N₈O₃ [M+H]⁺: 625.36091; found: 625.3611 (0.27 ppm).

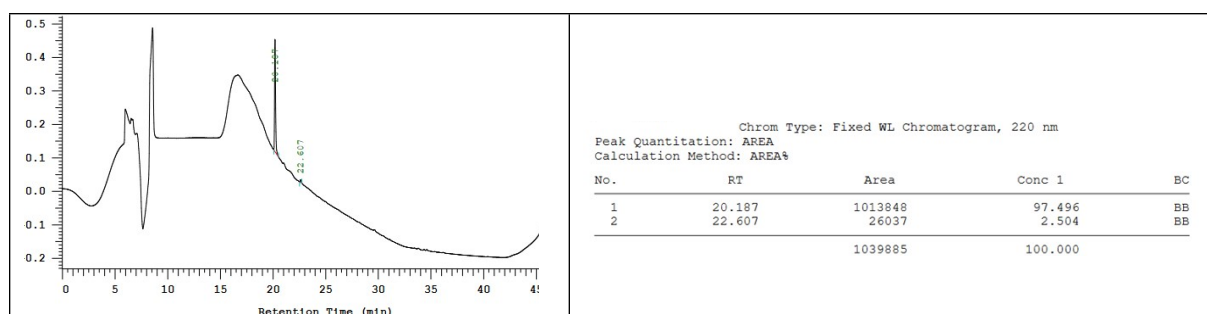


Figure S15 HPLC chromatogram of purified **III-3(d₂)**.

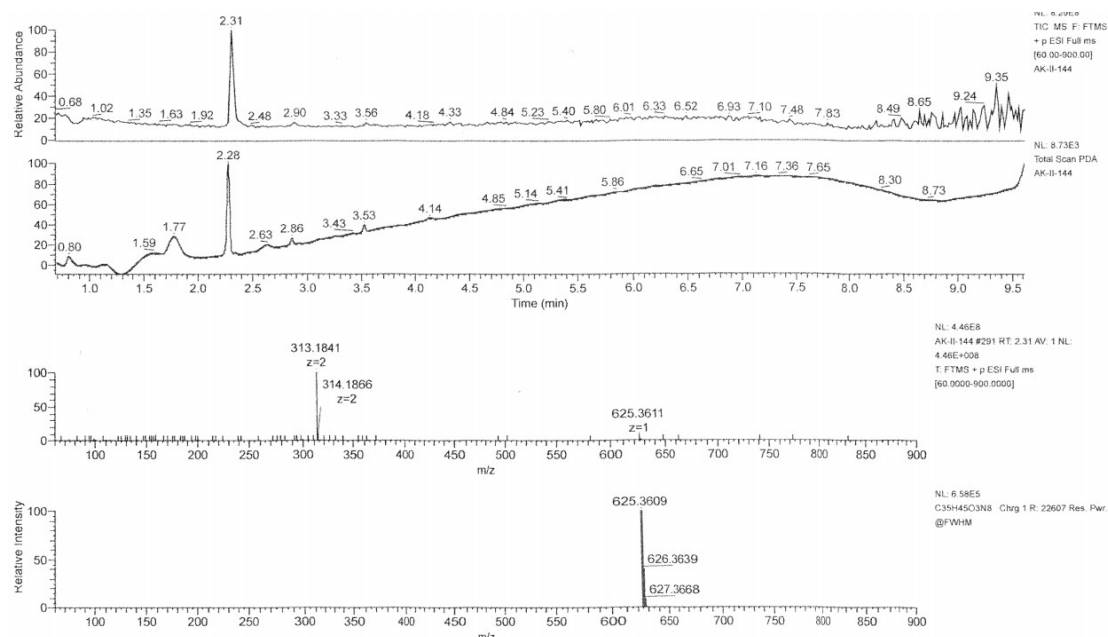


Figure S16 LCMS spectra of **III-3(d₂)**.

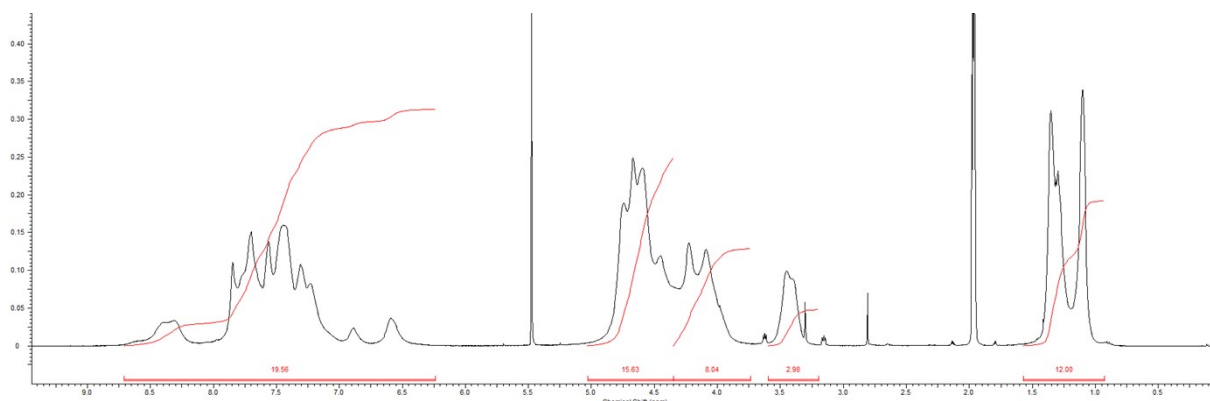
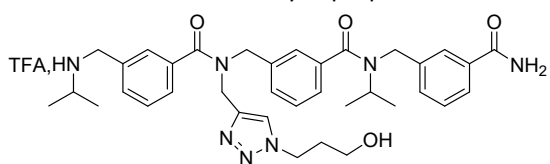


Figure S17 $^1\text{H-NMR}$ spectra in CD_3CN of **III-3(d₂)**.

3.6- meta-arylopeptoid trimer, III-3(e₂).



Trimer **III-3(e₂)** was synthesised according general procedure A then general procedure B using 100 mg of RA resin (0.054 mmol).

m_{crude} = 42 mg (purity 80%), crude yield 120%

m_{pure} = 30 mg (purity 99%), isolated yield 90%

HRMS (TOF MS ES+): m/z calcd for C₃₆H₄₆N₇O₄ [M+H]⁺: 640.36058; found: 640.3593 (-1.98 ppm).

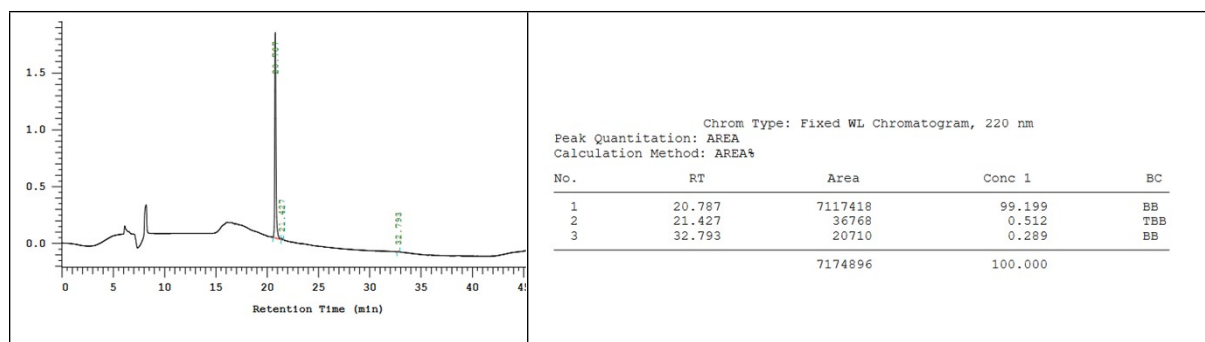


Figure S18 HPLC chromatogram of purified **III-3(e₂)**.

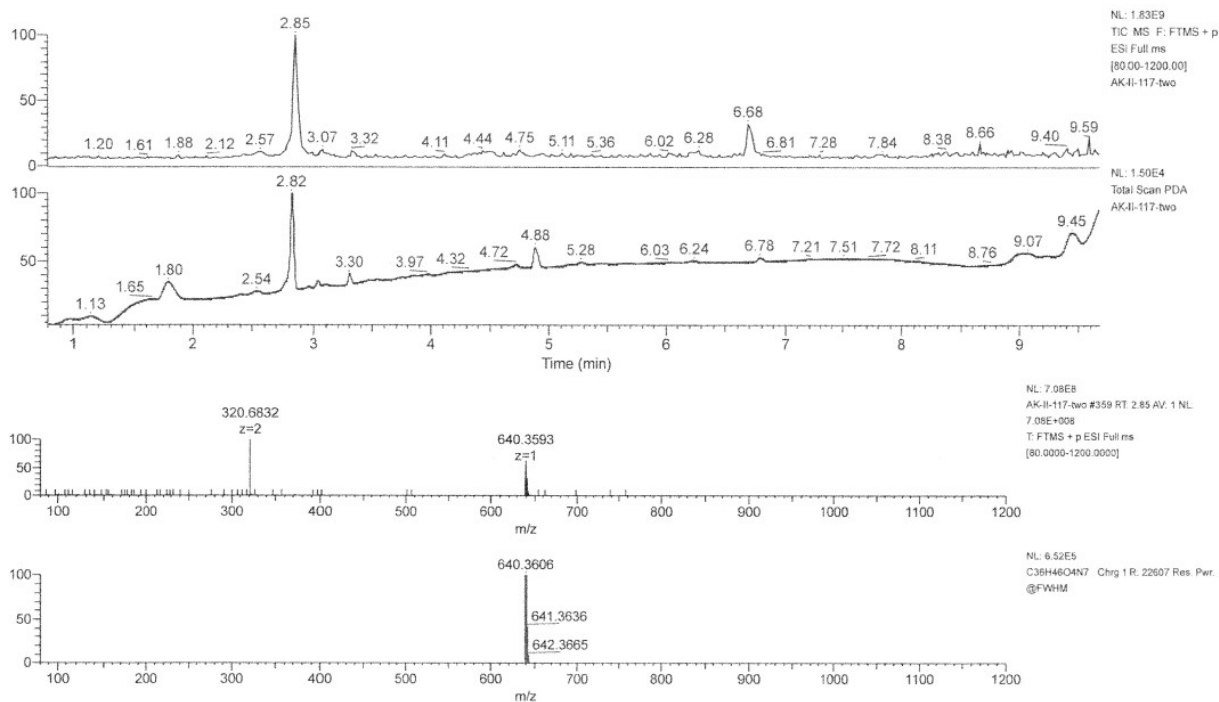


Figure S19 LCMS spectra of **III-3(e₂)**.

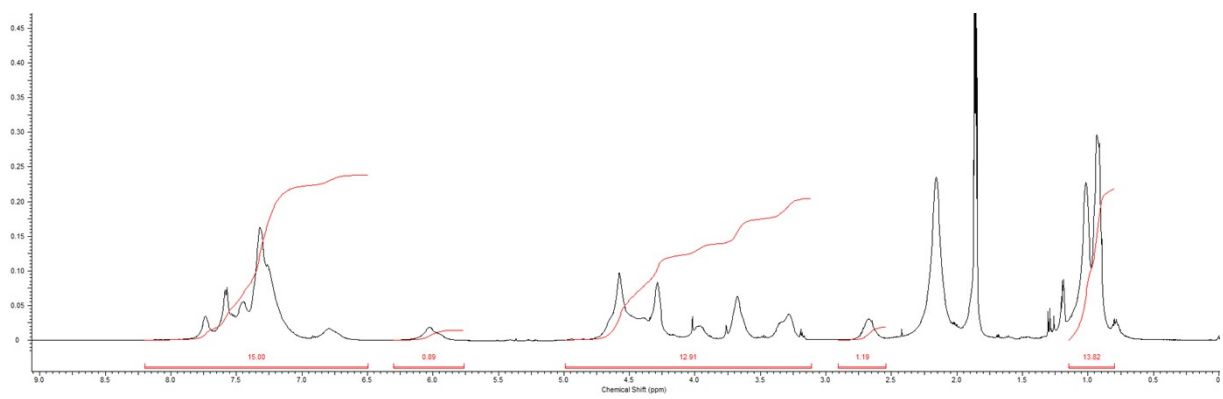
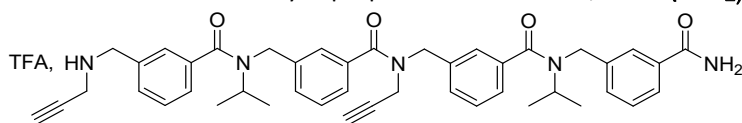


Figure S20 $^1\text{H-NMR}$ spectra in CD_3CN of **III-3(e₂)**.

4- Synthesis and Characterization data of arylopeptoid tetramers.

4.1- meta-arylopeptoid tetramer, **II-4-(Alk_{2,4})**.



Tetramer **II-4-(Alk_{2,4})** was synthesised according to general procedure A using 100 mg of RA resin (0.054 mmol), then cleavage by gently shaking a solution of TFA/TIS/H₂O (95:2.5:2.5, 1mL) for 10 min at RT.

m_{crude} = 50mg (purity 80%), crude yield 112%

m_{pure} = 32 mg (purity 96%), isolated yield 72%

HRMS (TOF MS ES⁺): m/z calcd for C₄₄H₄₈N₅O₄ [M+H]⁺: 710.37008; found: 710.3702 (0.14 ppm).

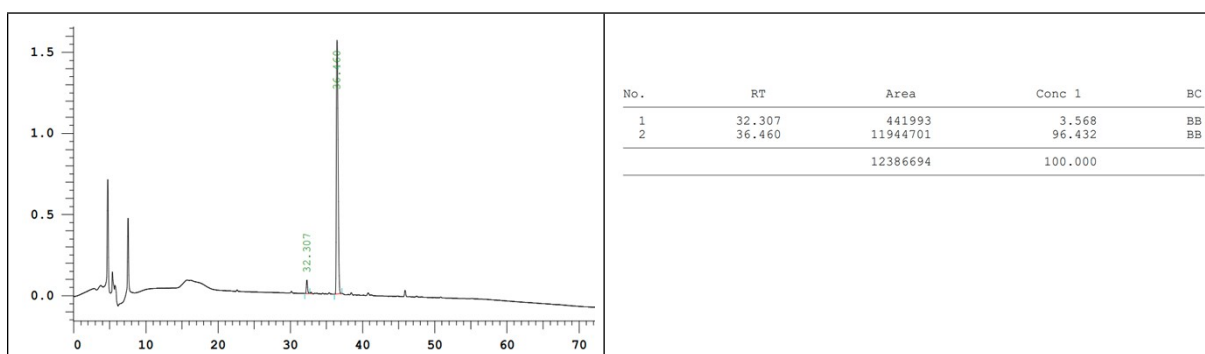


Figure S21 HPLC chromatogram of purified **II-4-(Alk_{2,4})**.

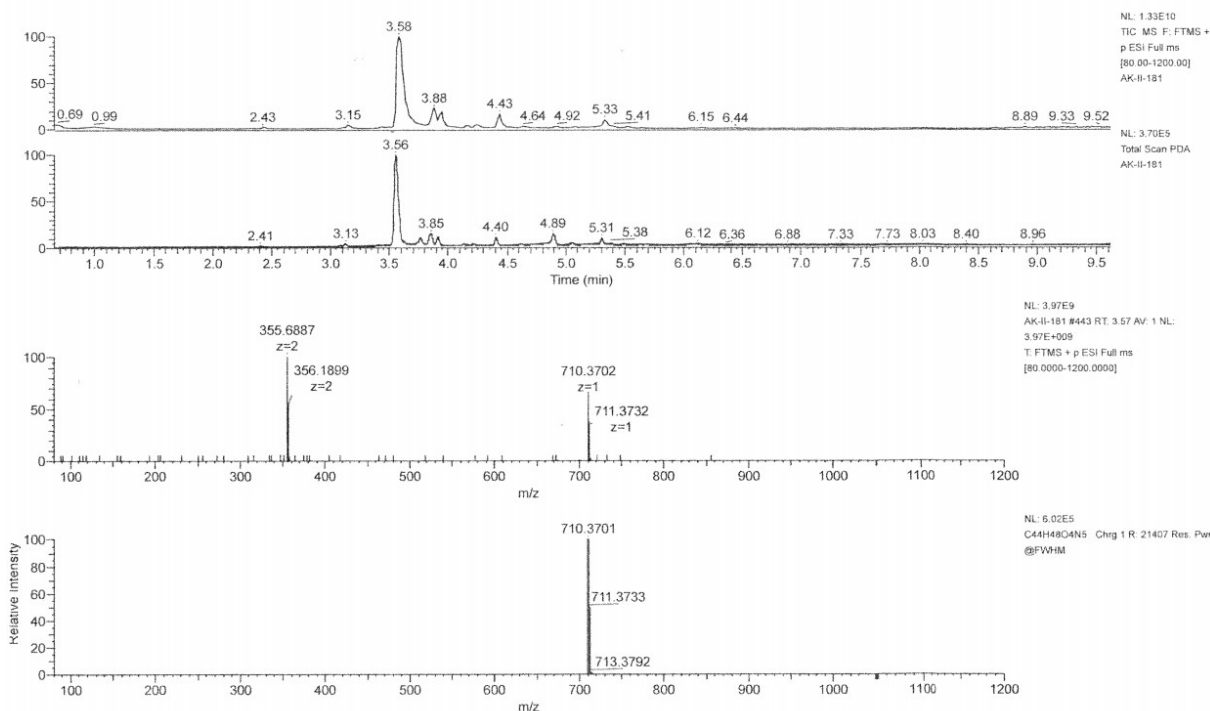


Figure S22 LCMS spectra of **II-4-(Alk_{2,4})**.

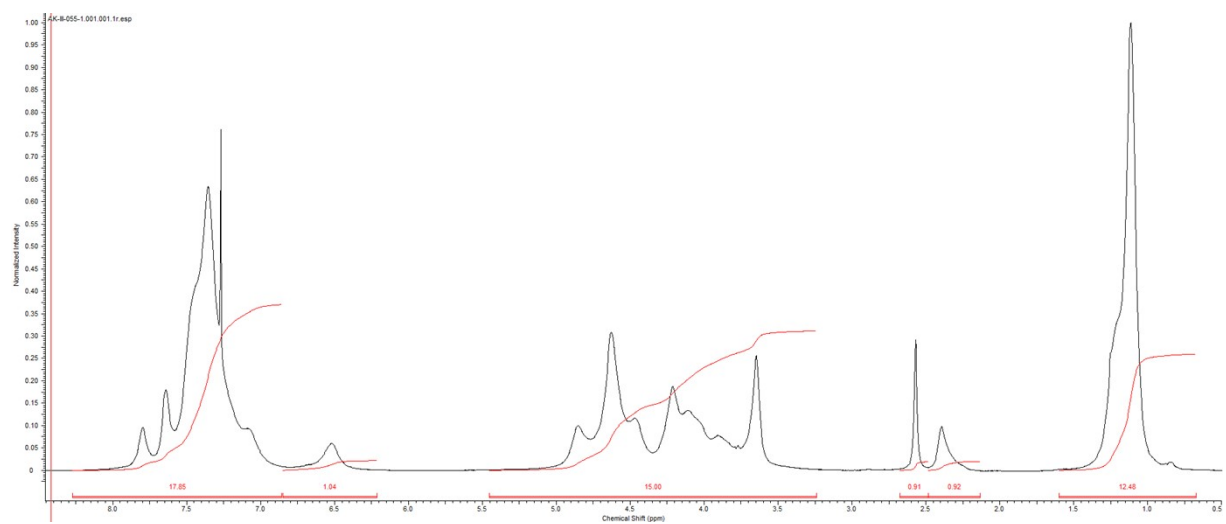
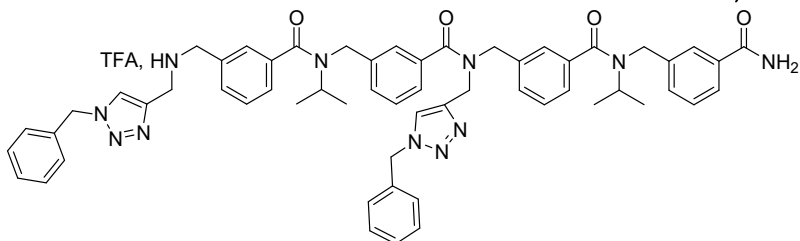


Figure S23 ¹H-NMR spectra in CD₃Cl₃ of II-4-(Alk_{2,4}).

4.2- Homo clicked arylopeptoids

4.2.1- meta-arylopeptoid tetramer, III-4(a_{2,4}).



Tetramer III-4(a_{2,4}) was synthesised according general procedure A then general procedure B using 100 mg of RA resin (0.054 mmol)

m_{crude} = 68 mg (purity 82%), crude yield 115%

m_{pure} = 44 mg (purity 87%), isolated yield 85%

HRMS (TOF MS ES+): *m/z* calcd for C₅₈H₆₂N₁₁O₄ [M+H]⁺: 976.49808; found: 976.4974 (-0.72 ppm).

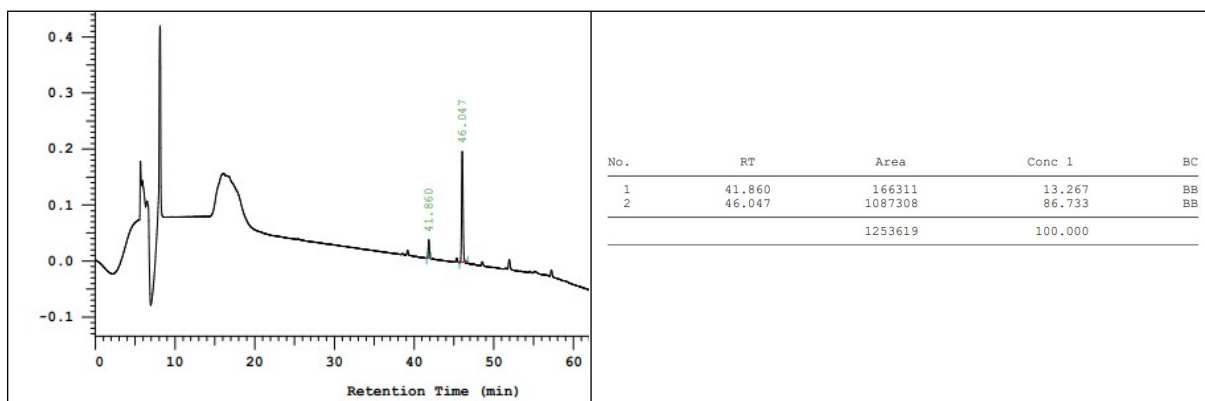
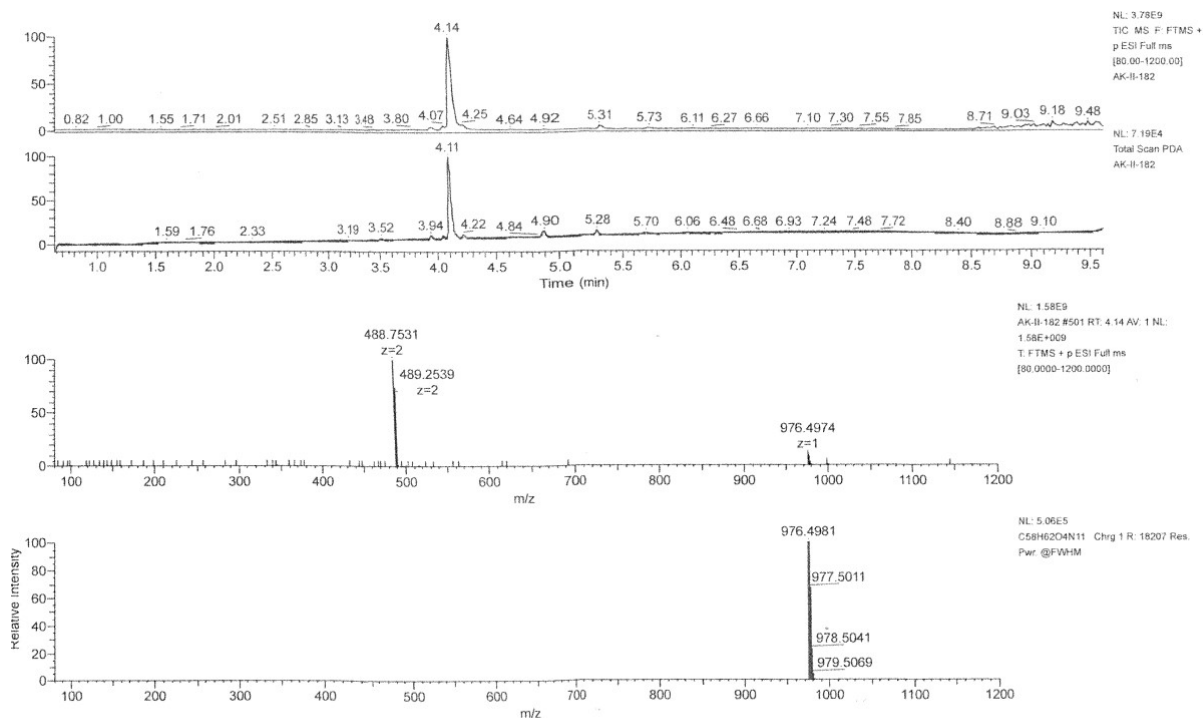
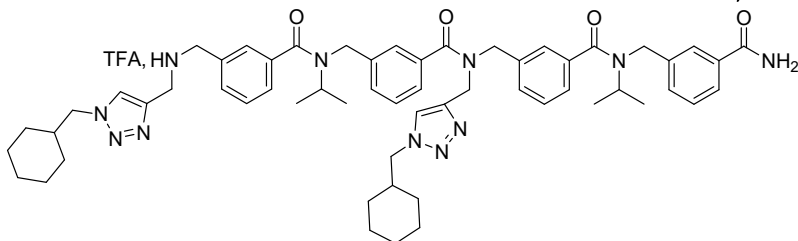


Figure S24 HPLC chromatogram of purified III-4(a_{2,4}).



4.2.2- meta-arylopeptoid tetramer, III-4(b_{2,4})



Tetramer III-4(b_{2,4}) was synthesised according general procedure A then general procedure B using 100 mg of RA resin (0.054 mmol)

m_{crude} = 73 mg (purity 85%), crude yield 124%

m_{pure} = 40 mg (purity 95%), isolated yield 75%

HRMS (TOF MS ES⁺): m/z calcd for C₅₈H₇₄N₁₁O₄ [M+H]⁺: 988.59198; found: 988.5907 (-1.29 ppm).

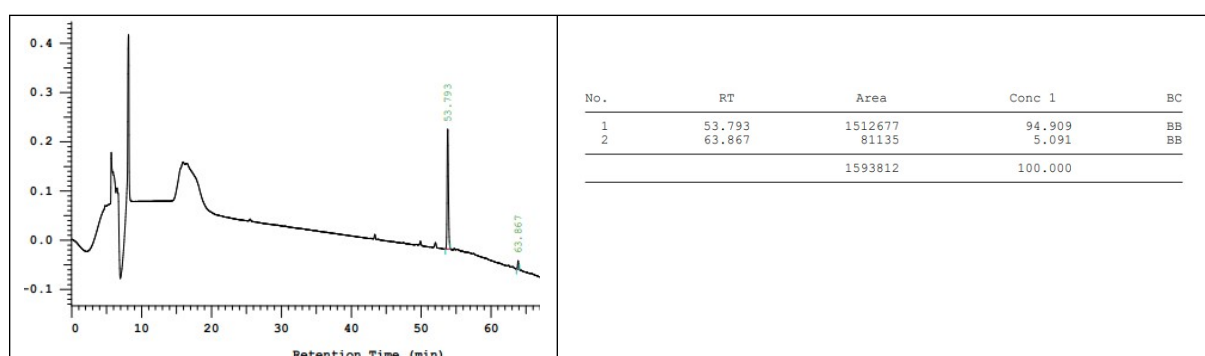


Figure S26 HPLC chromatogram of purified III-4(b_{2,4}).

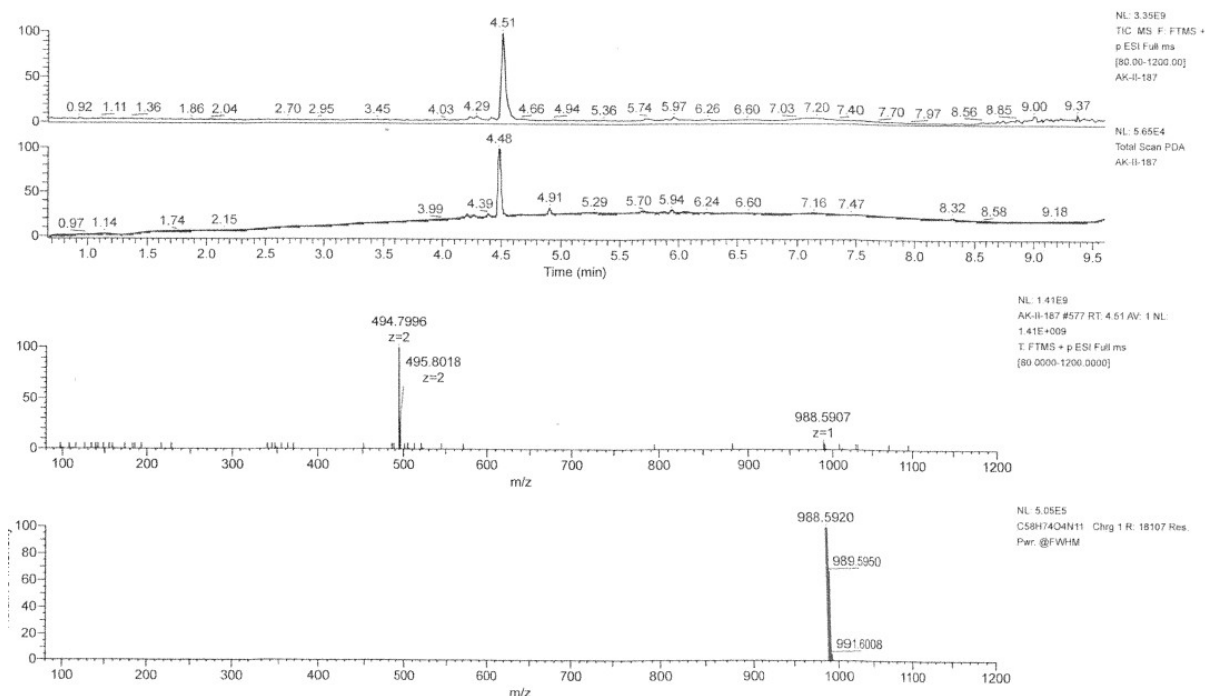
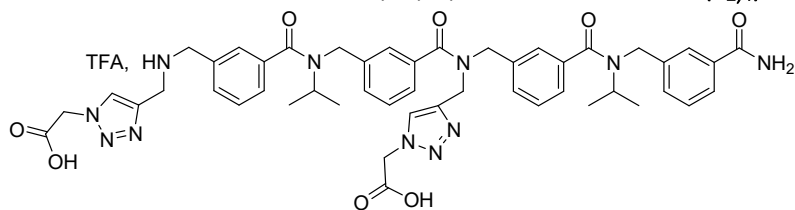


Figure S27 LCMS spectra of III-4(b_{2,4}).

4.2.3- meta-arylopeptoid tetramer, III-4(c_{2,4}).



Tetramer III-4(c_{2,4}) was synthesised according general procedure A then general procedure B using 100 mg of RA resin (0.054 mmol).

m_{crude} = 73mg (purity 78%), 131% crude yield

m_{pure} = 44mg (purity 81%), 85% isolated yield

HRMS (TOF MS ES+): *m/z* calcd for C₄₈H₅₅N₁₁O₈ [M+2H]²⁺: 456.71121; found: 456.7113 (0.22 ppm).

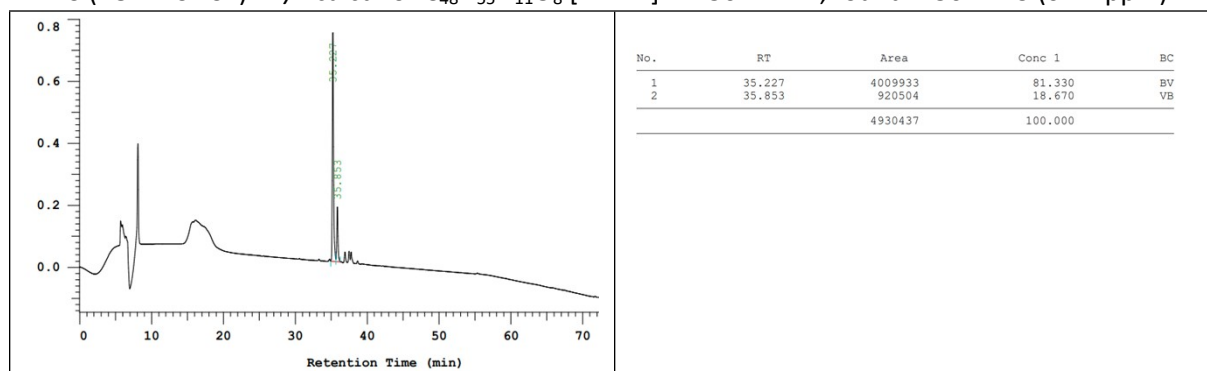


Figure S28 HPLC chromatogram of purified III-4(c_{2,4}).

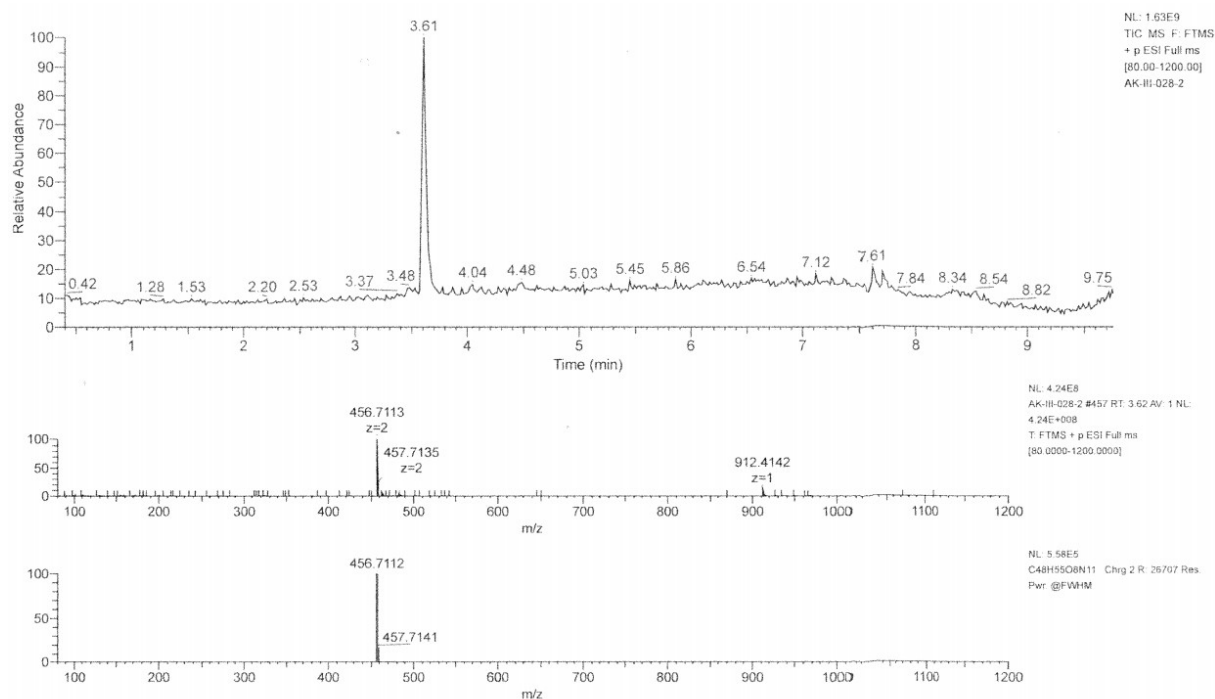
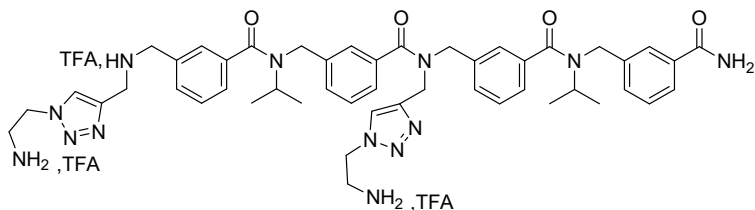


Figure S29 LCMS spectra of III-4(c_{2,4}).

4.2.4- meta-arylopeptoid tetramer, III-4(d_{2,4}).



Tetramer III-4(d_{2,4}) was synthesised according general procedure A then general procedure B using 100 mg of RA resin (0.054 mmol)

$m_{\text{crude}} = 73\text{mg}$ (purity 80%), crude yield 110%

$m_{\text{pure}} = 36\text{mg}$ (purity 95%), isolated yield 77%

HRMS (TOF MS ES⁺): m/z calcd for C₄₈H₆₂N₁₃O₄ [M+3H]³⁺: 294.83438; found: 294.8345 (0.33 ppm).

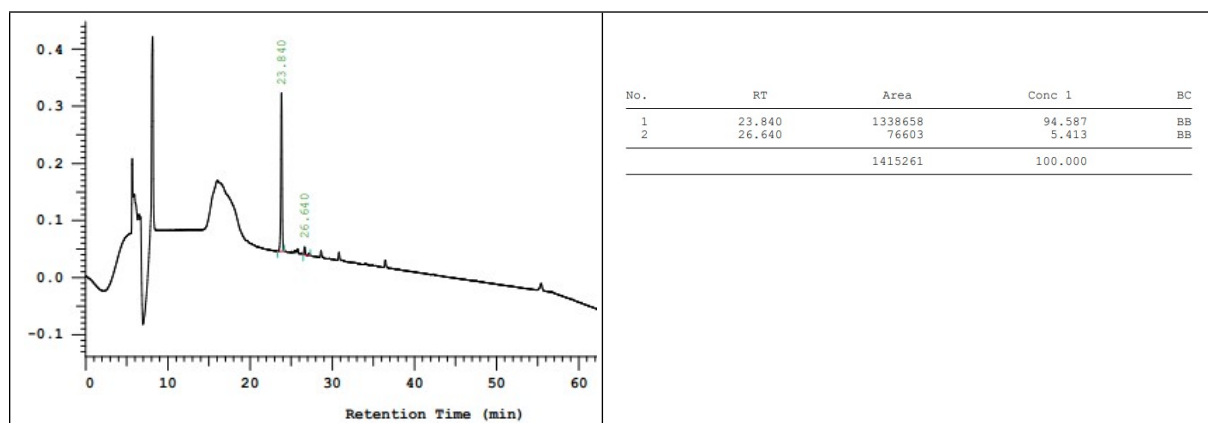


Figure S30 HPLC chromatogram of purified III-4(d_{2,4}).

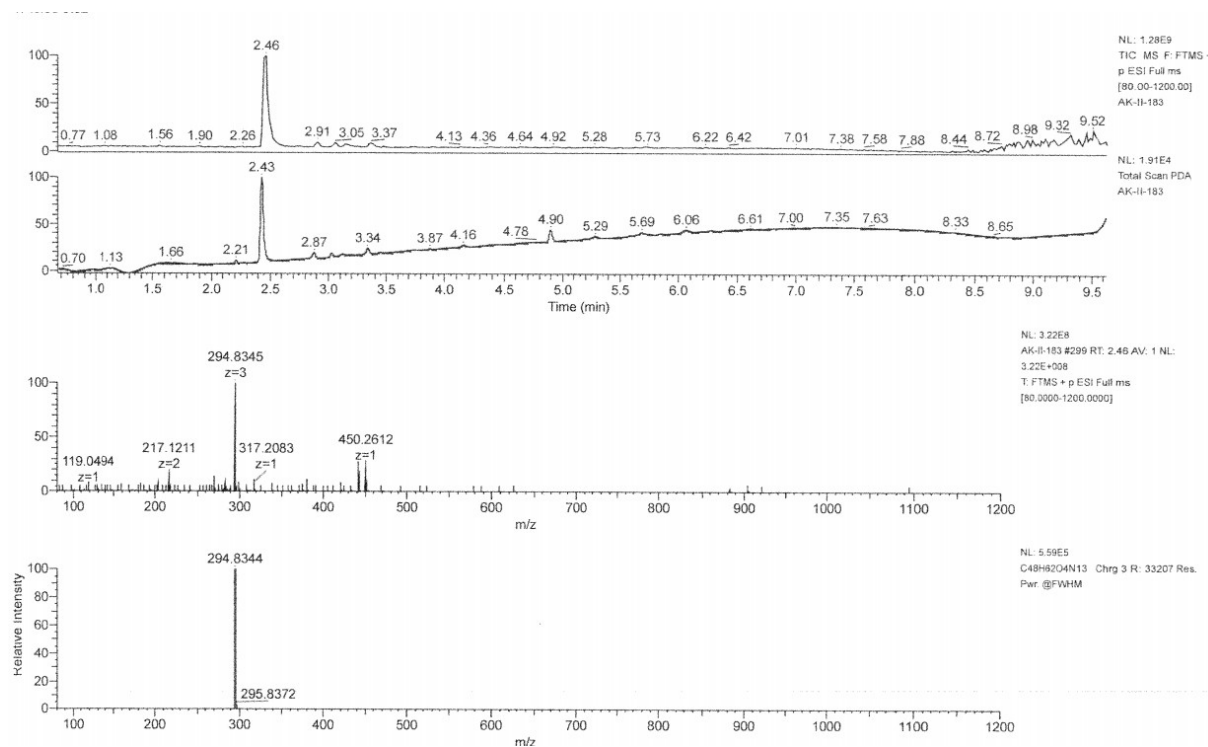
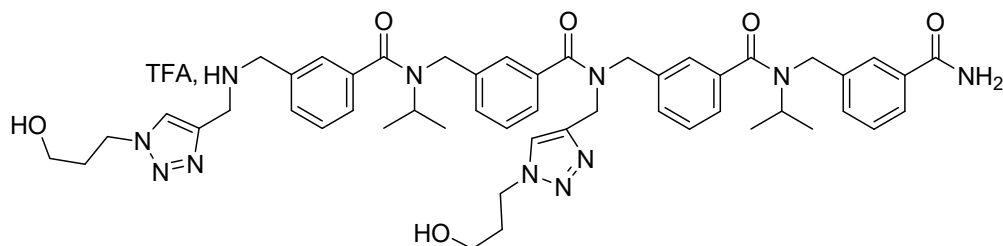


Figure S31 LCMS spectra of III-4(d_{2,4}).

4.2.5- meta-arylopeptoid tetramer, III-4(e_{2,4}).



Tetramer III-4(e_{2,4}) was synthesised according general procedure A then general procedure B using 125 mg of RA resin (0.0775 mmol)

m_{crude} = 101 mg (purity 85%), crude yield 148%

m_{pure} = 70 mg (purity 97 %), isolated yield 98%

HRMS (TOF MS ES+): *m/z* calcd for C₅₀H₆₂N₁₁O₆ [M+H]⁺: 912.48791; found: 912.4866 (-1.46 ppm).

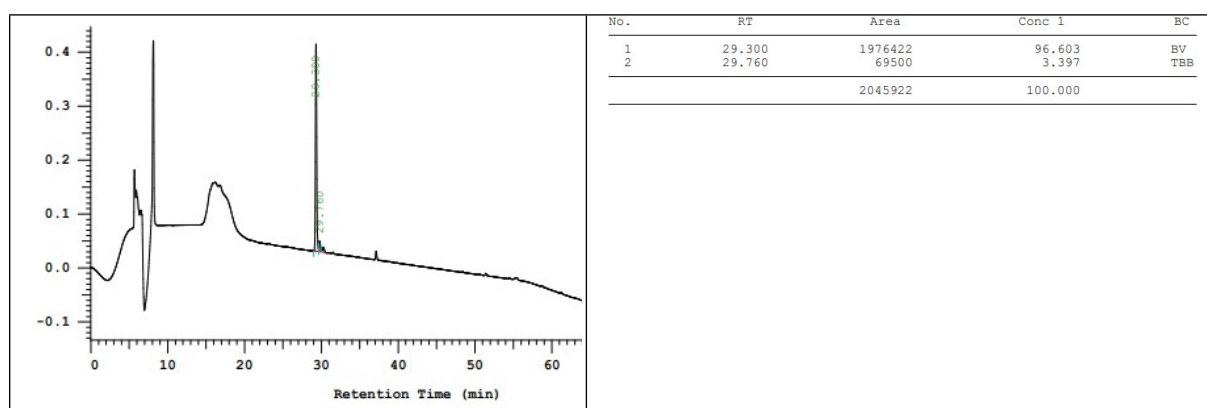


Figure S32 HPLC chromatogram of purified III-4(e_{2,4})

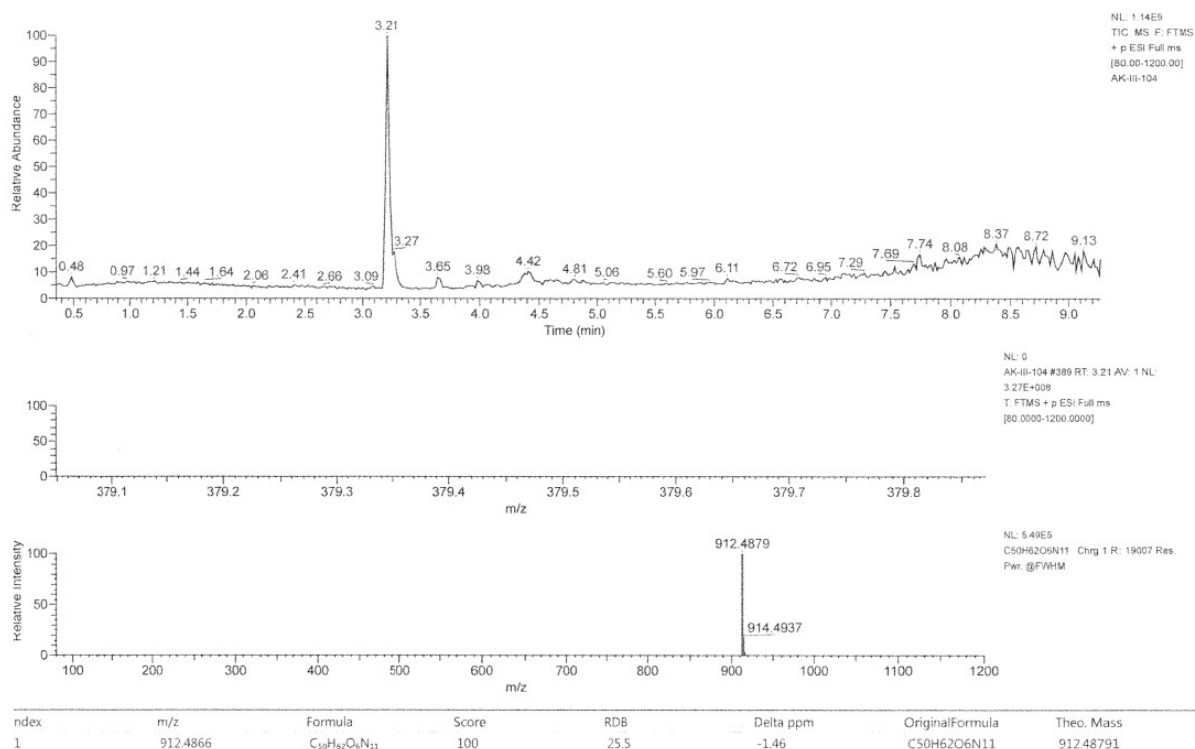
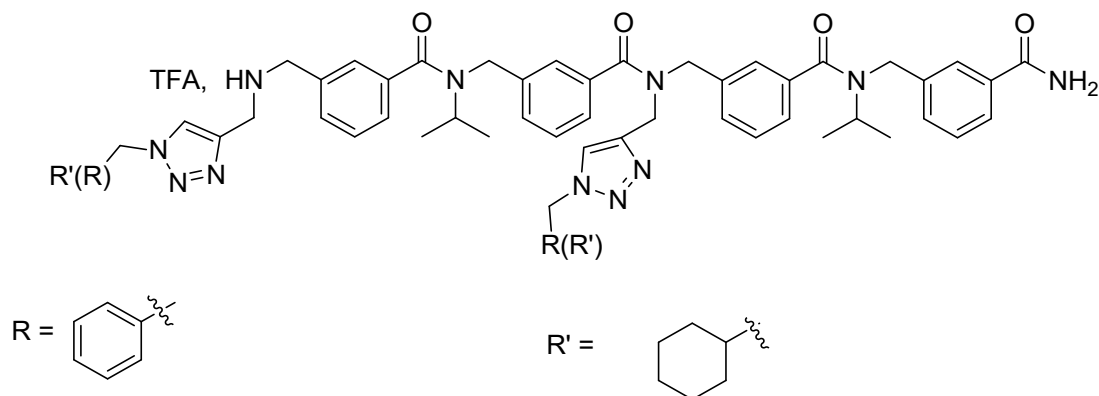


Figure S33 LCMS spectra of III-4(e_{2,4})

4.3- Combinatorial on arylopeptoid tetramers

4.3.4- meta-arylopeptoid tetramer, III-4(a,b)(2,4).



Tetramer III-4(a,b)(2,4) was synthesised according general procedure A then general procedure B using 100 mg of RA resin (0.054 mmol)

$m_{\text{crude}} = 74$ mg (purity 81%), crude yield 121%

$m_{\text{pure}} = 50$ mg (purity 97 %), isolated yield 82%

LCMS pic at 4.16 min: HRMS (TOF MS ES+): m/z calcd for $C_{58}H_{62}N_{11}O_4$ [M+H]⁺: 976.49808 found: 976.4979 (-0.15 ppm).

LCMS pic at 4.33 min: HRMS (TOF MS ES+): m/z calcd for $C_{58}H_{68}N_{11}O_4$ [M+H]⁺: 982.54503; found: 982.545 (0.02 ppm).

LCMS pic at 4.52 min: HRMS (TOF MS ES+): m/z calcd for $C_{58}H_{75}N_{11}O_4$ [M+2H]²⁺: 494.79963; found: 494.8005 (1.84 ppm).

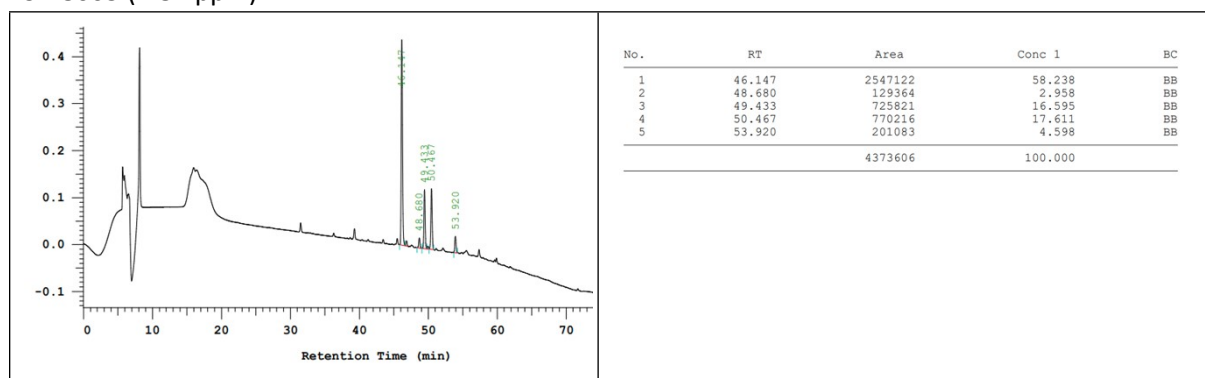


Figure S34 HPLC chromatogram of purified III-4(a,b)(2,4).

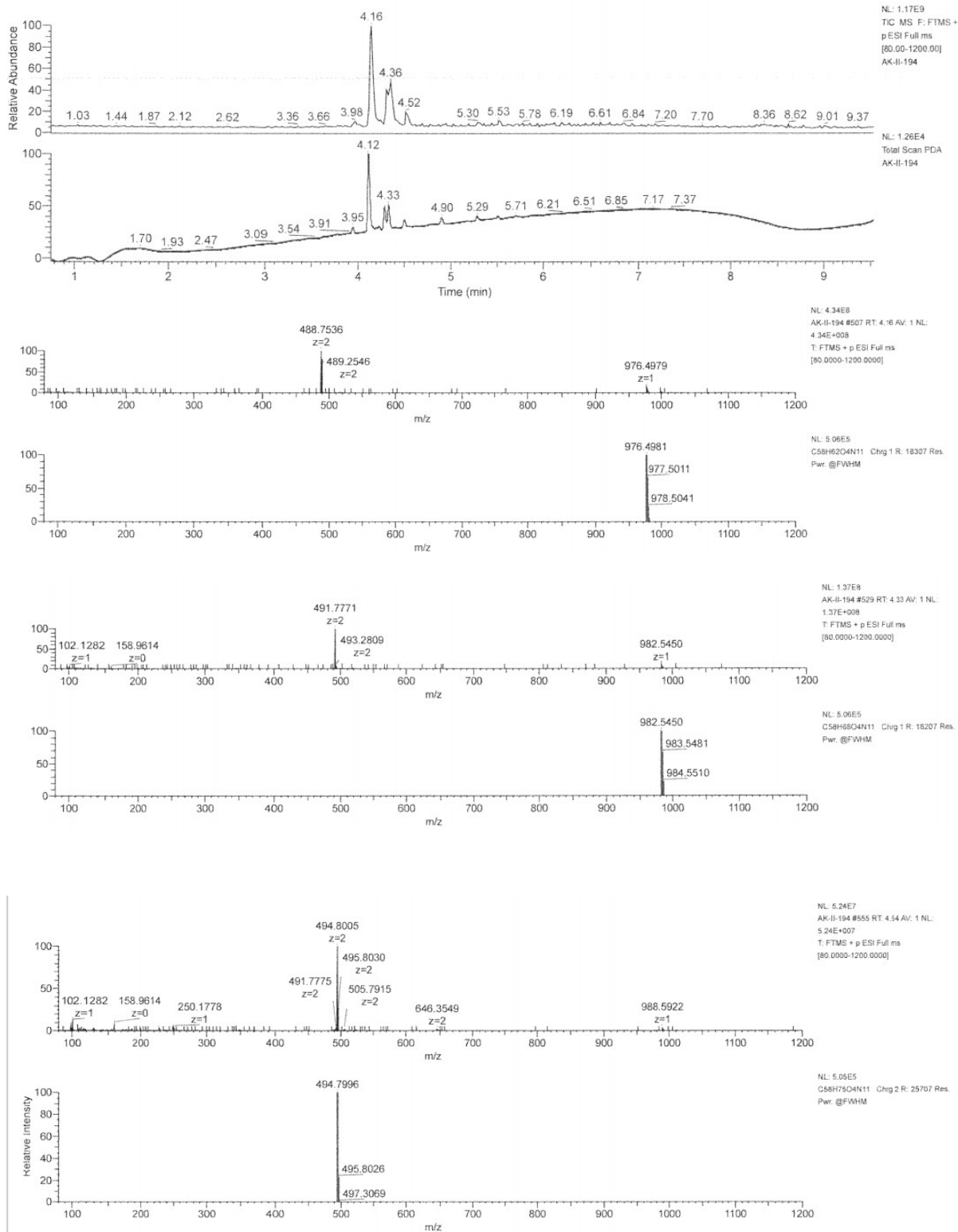
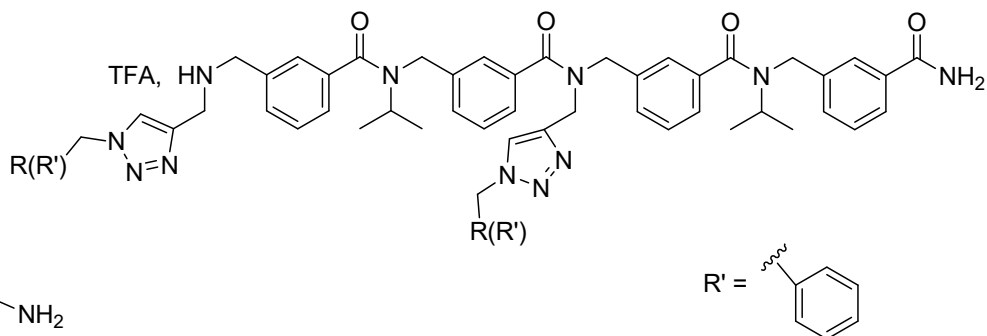


Figure S35 LCMS spectra of III-4(a,b)(2,4).

4.3.2- meta-arylopeptoid tetramer III-4(a,d)(2,4).



Tetramer III-4(a,d)(2,4) was synthesised according general procedure A then general procedure B using 100 mg of RA resin (0.054 mmol)

$m_{\text{crude}} = 71 \text{ mg}$ (purity 79%), crude yield 116%

$m_{\text{pure}} = 46 \text{ mg}$ (purity 93%), isolated yield 91%

LCMS pic at 4.12 min: HRMS (TOF MS ES+): m/z calcd for $\text{C}_{58}\text{H}_{63}\text{N}_{11}\text{O}_4$ $[\text{M}+2\text{H}]^{2+}$: 488.75268; found: 488.753 (0.58 ppm).

LCMS pic at 3.14 min: HRMS (TOF MS ES+): m/z calcd for $\text{C}_{53}\text{H}_{62}\text{N}_{12}\text{O}_4$ $[\text{M}+2\text{H}]^{2+}$: 465.2503; found: 465.2506 (0.67 ppm).

LCMS pic at 3.27 min: HRMS (TOF MS ES+): m/z calcd for $\text{C}_{53}\text{H}_{62}\text{N}_{12}\text{O}_4$ $[\text{M}+2\text{H}]^{2+}$: 465.2503; found: 465.2505 (0.4 ppm).

LCMS pic at 2.46 min: HRMS (TOF MS ES+): m/z calcd for $\text{C}_{48}\text{H}_{61}\text{N}_{13}\text{O}_4$ $[\text{M}+2\text{H}]^{2+}$: 441.74793 found: 441.748 (0.21 ppm).

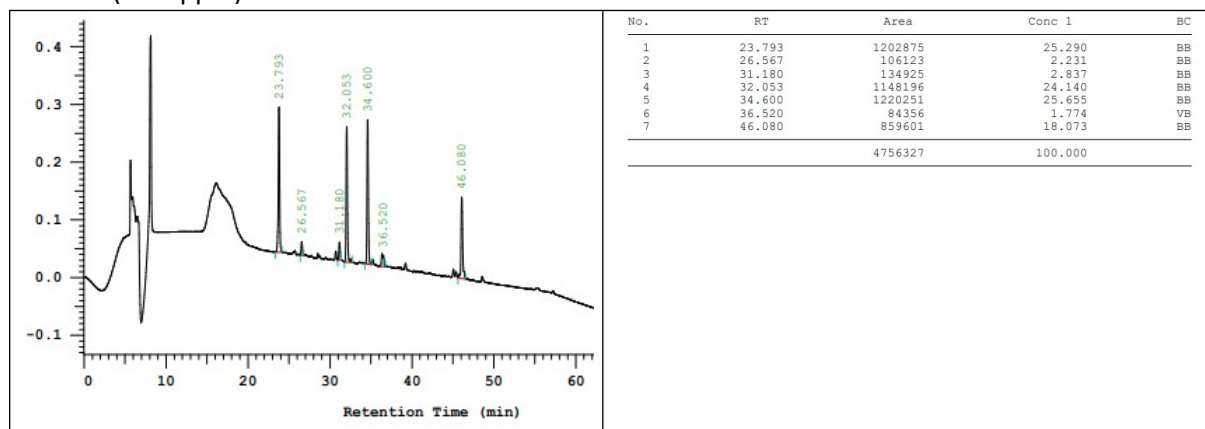
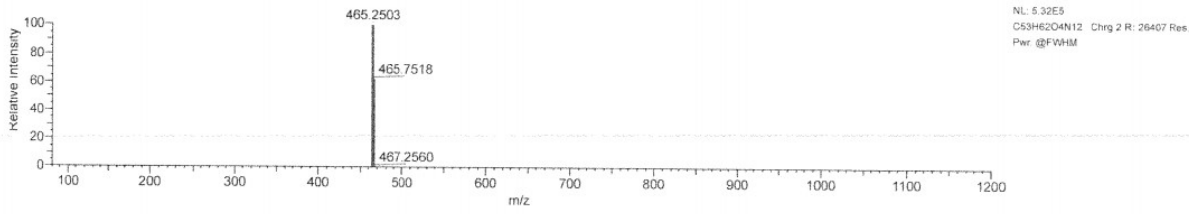
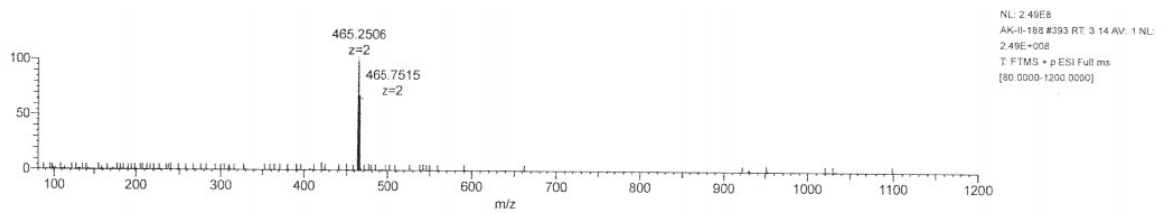
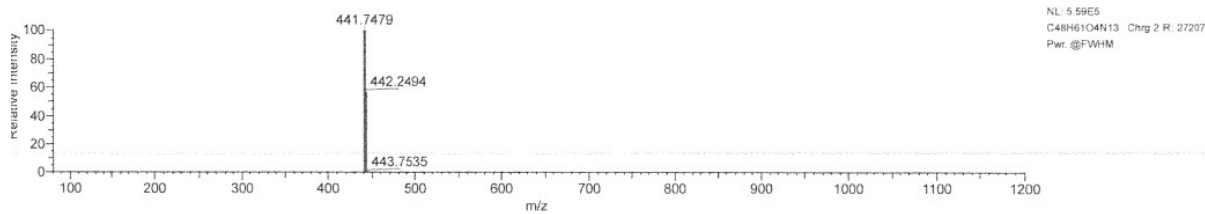
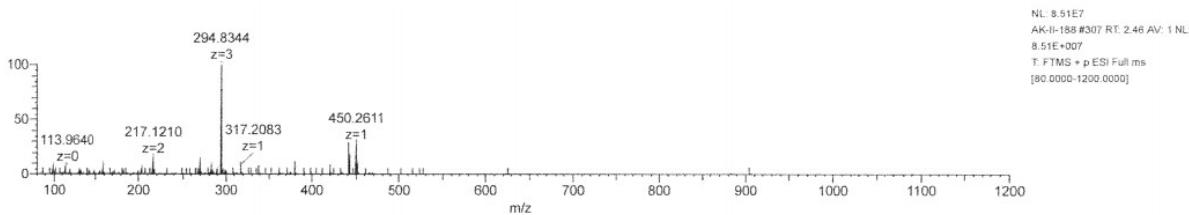
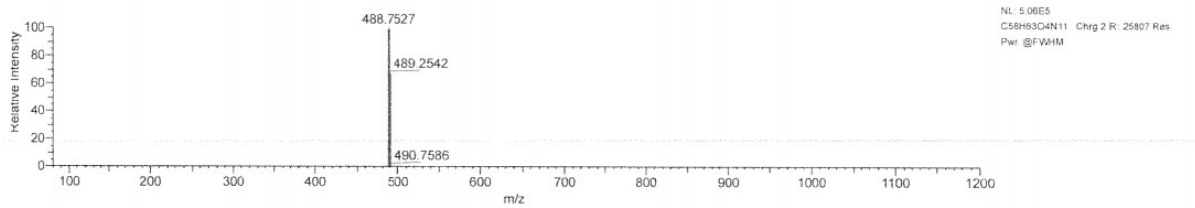
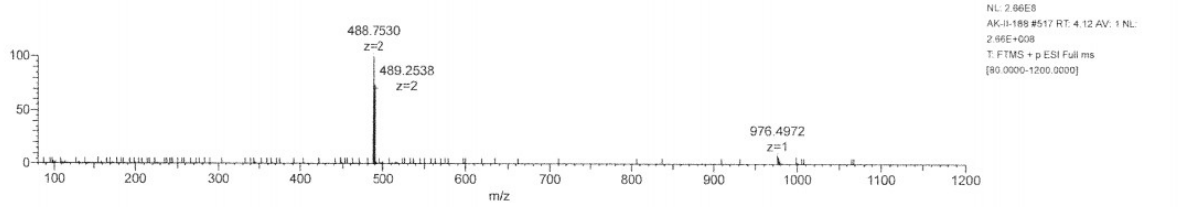
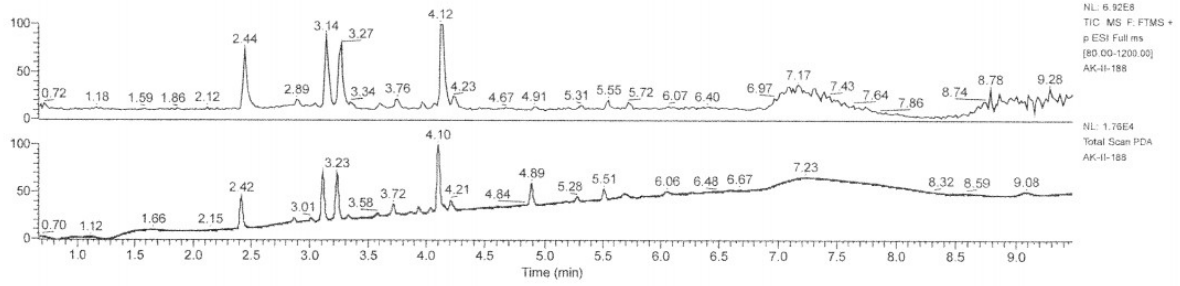


Figure S36 HPLC chromatogram of purified III-4(a,d)(2,4).



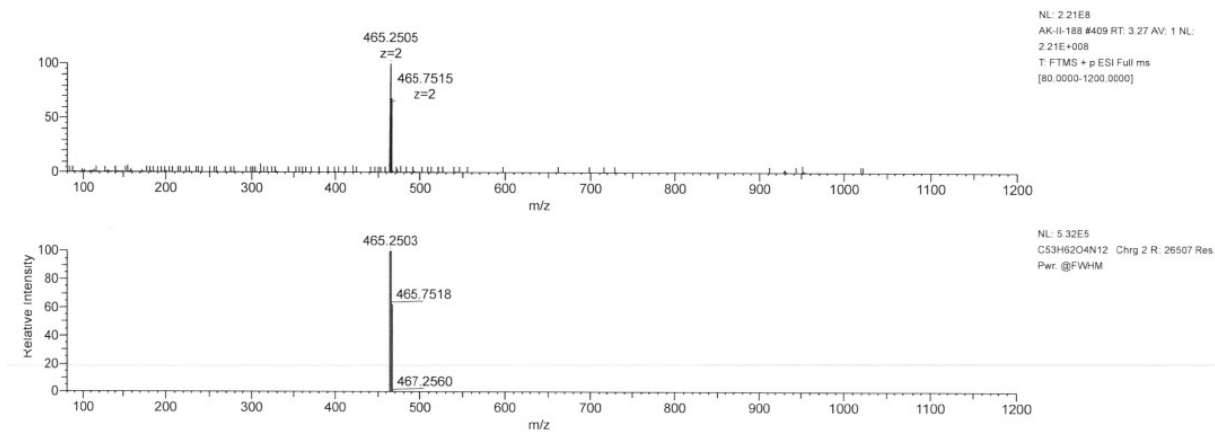
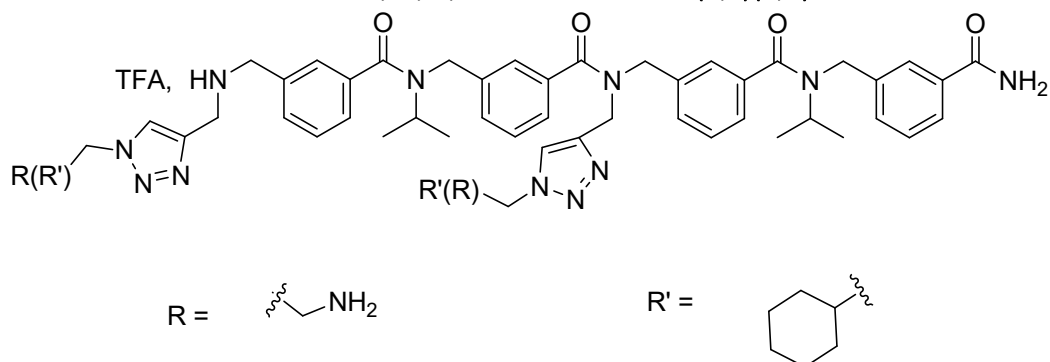


Figure 37 LCMS spectra of III-4(a,d)(2,4)

4.3.3- meta-arylopeptoid tetramer III-4(b,c)(2,4).



Tetramer III-4(b,c)(2,4) was synthesised according general procedure A then general procedure B using 100 mg of RA resin (0.054 mmol)

$m_{\text{crude}} = 74\text{ mg}$ (purity 81%), crude yield 121%

$m_{\text{pure}} = 46\text{ mg}$ (purity 92%), isolated yield 82%

LCMS pic at 2.45 min: HRMS (TOF MS ES+): m/z calcd for $\text{C}_{48}\text{H}_{62}\text{N}_{13}\text{O}_4$ $[\text{M}+3\text{H}]^{3+}$: 294.83438 found: 294.8346 (0.64 ppm)

LCMS pic at 3.30 min: HRMS (TOF MS ES+): m/z calcd for $\text{C}_{53}\text{H}_{68}\text{N}_{12}\text{O}_4$ $[\text{M}+2\text{H}]^{2+}$: 468.27378; found: 468.274 (0.52 ppm).

LCMS pic at 3.45 min: HRMS (TOF MS ES+): m/z calcd for $\text{C}_{53}\text{H}_{68}\text{N}_{12}\text{O}_4$ $[\text{M}+2\text{H}]^{2+}$: 468.27378; found: 468.274 (0.58 ppm).

LCMS pic at 4.51 min: HRMS (TOF MS ES+): m/z calcd for $\text{C}_{58}\text{H}_{75}\text{N}_{11}\text{O}_4$ $[\text{M}+2\text{H}]^{2+}$: 494.79963; found: 494.7999 (0.48 ppm)

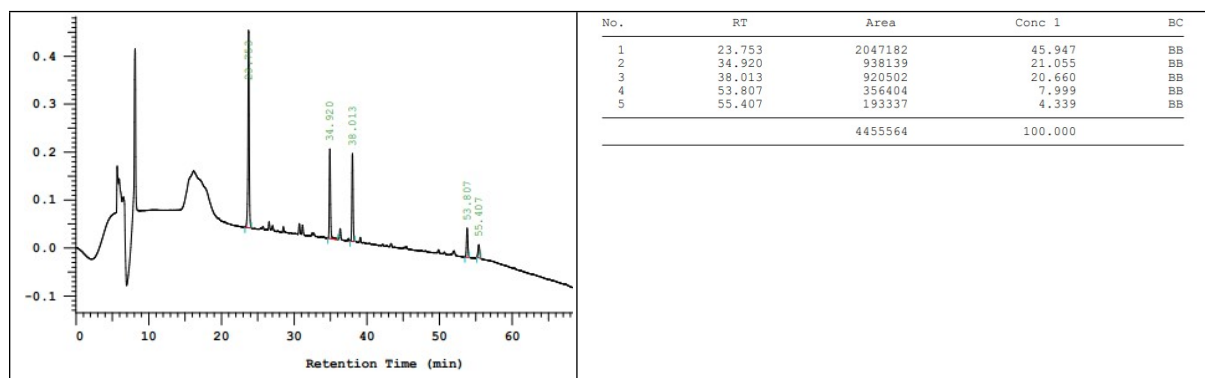
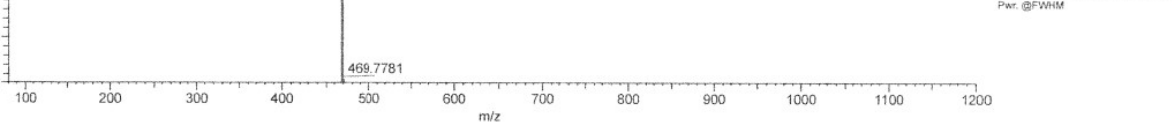
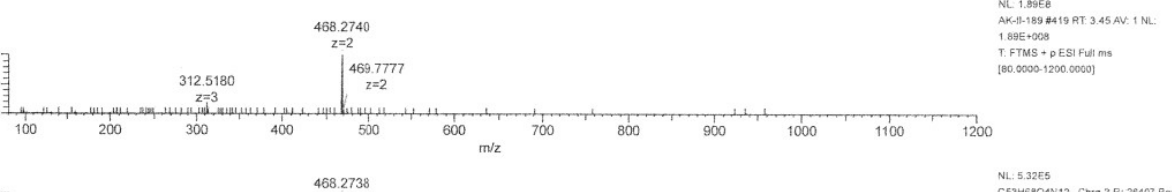
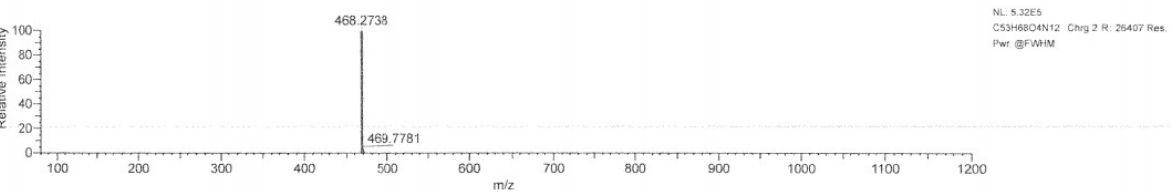
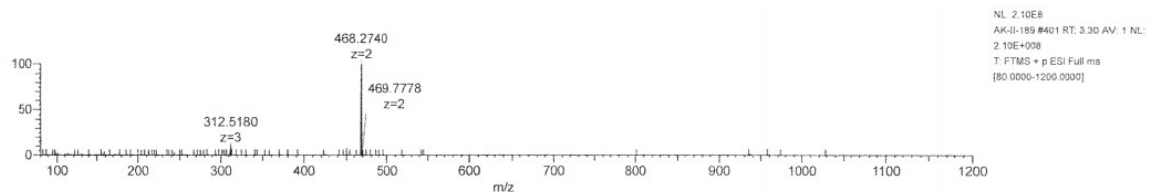
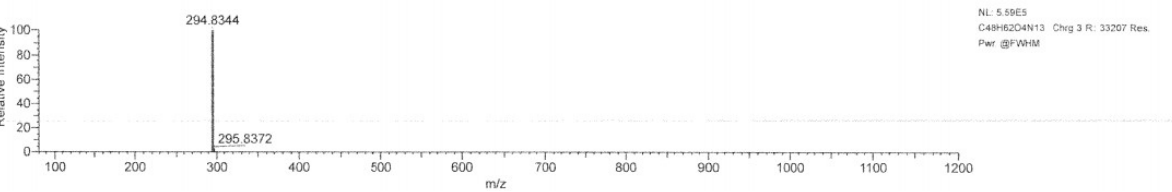
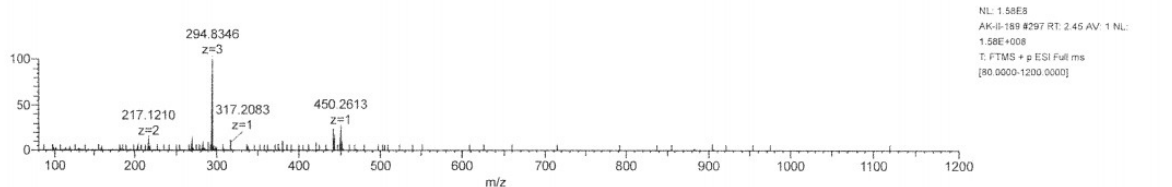
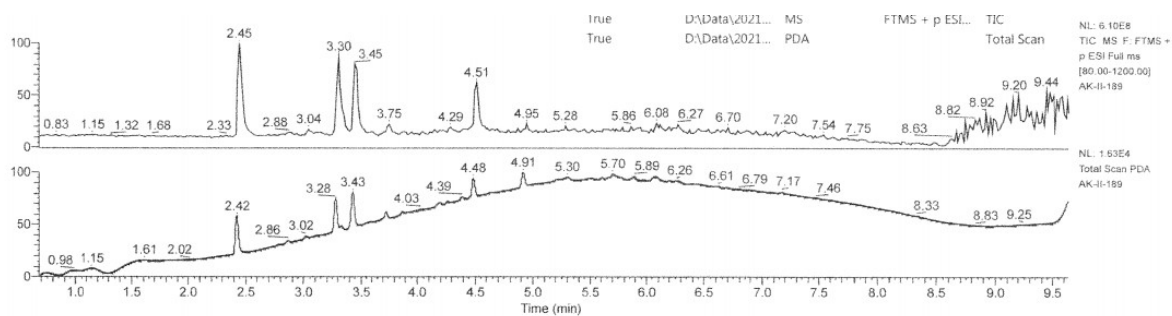


Figure S38 HPLC chromatogram of purified III-4(b,c)(2,4)



Index	m/z	Formula	Score	RDB	Delta ppm	OriginalFormula	Theo. Mass
	468.2740	C ₅₃ H ₆₈ O ₄ N ₁₂	100	26	0.58	C ₅₃ H ₆₈ O ₄ N ₁₂	468.27378

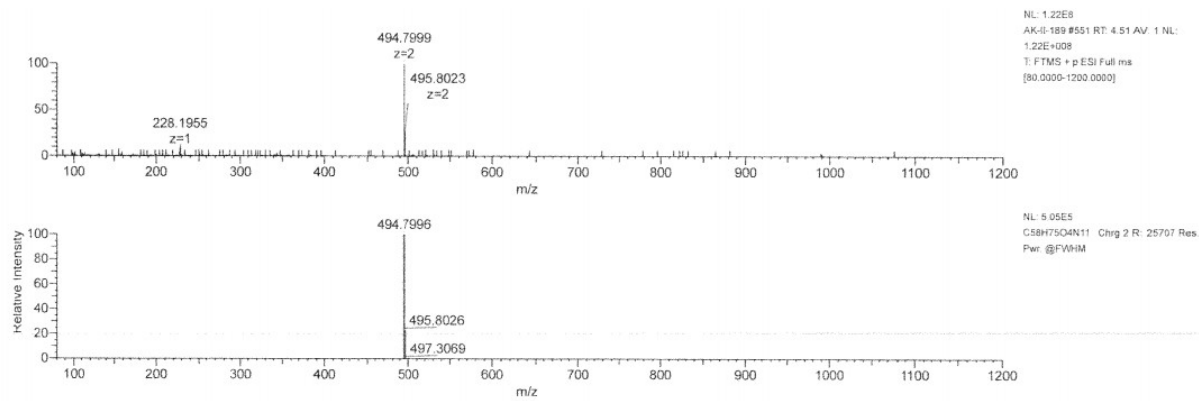
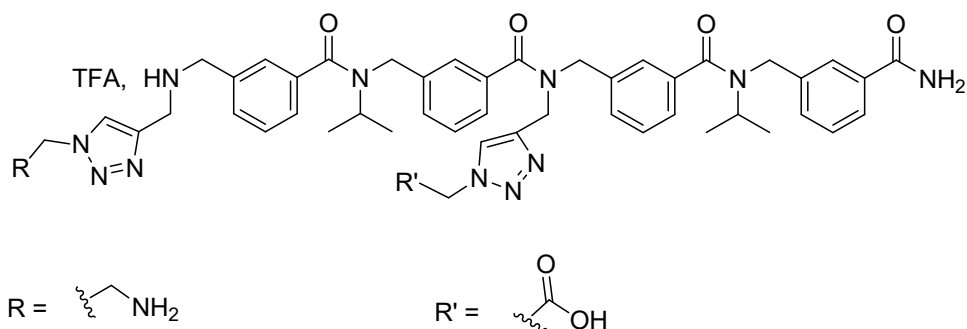


Figure S39 LCMS spectra of III-4(b,c)(2,4).

4.3.1- meta-arylopeptoid tetramer III-4(c,d)(2,4).



Tetramer III-4(c,d)(2,4) was synthesised according general procedure A then general procedure B using 100 mg of RA resin (0.054 mmol)

$m_{\text{crude}} = 78\text{mg}$ (purity 87%), crude yield 119%

$m_{\text{pure}} = 50\text{mg}$ (purity 91%), isolated yield 68%

LCMS pic at 2.42 min: HRMS (TOF MS ES+): m/z calcd for $\text{C}_{48}\text{H}_{62}\text{N}_{13}\text{O}_4$ $[\text{M}+3\text{H}]^{3+}$: 294.8343 found: 294.8342 (-0.71 ppm).

LCMS pic at 2.96 min: HRMS (TOF MS ES+): m/z calcd for $\text{C}_{48}\text{H}_{58}\text{N}_{12}\text{O}_6$ $[\text{M}+2\text{H}]^{2+}$: 449.2296; found: 449.22957 (0.18 ppm).

LCMS pic at 3.02 min: HRMS (TOF MS ES+): m/z calcd for $\text{C}_{48}\text{H}_{58}\text{N}_{12}\text{O}_6$ $[\text{M}+2\text{H}]^{2+}$: 449.2296; found: 449.22957 (-0.03 ppm).

LCMS pic at 3.60 min: HRMS (TOF MS ES+): m/z calcd for $\text{C}_{48}\text{H}_{55}\text{N}_{11}\text{O}_8$ $[\text{M}+2\text{H}]^{2+}$: 456.7112; found: 456.71121 (0.01 ppm).

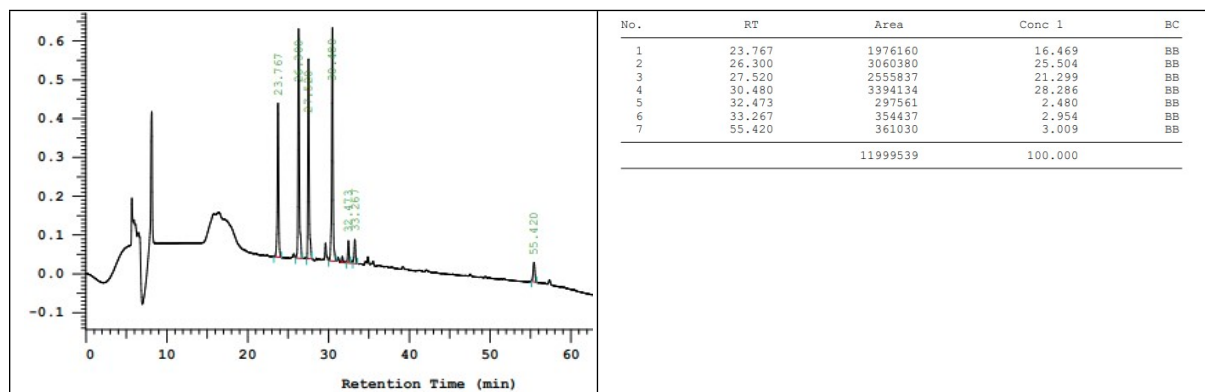


Figure S40 HPLC chromatogram of purified III-4(c,d)(2,4).

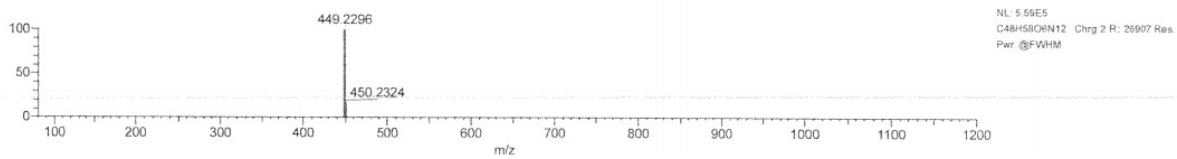
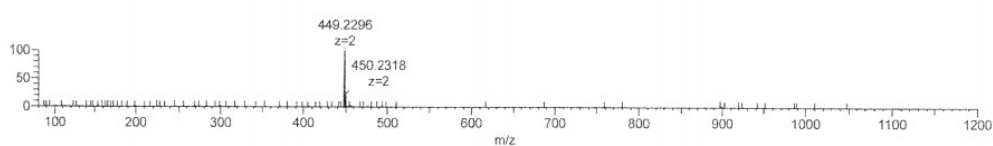
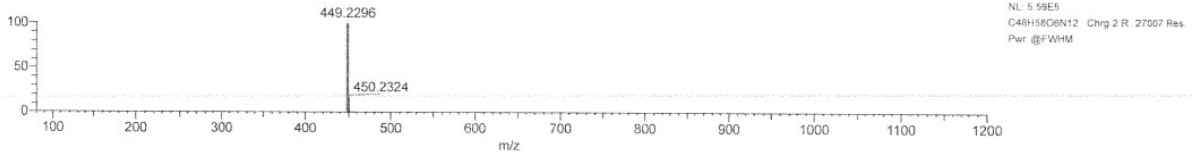
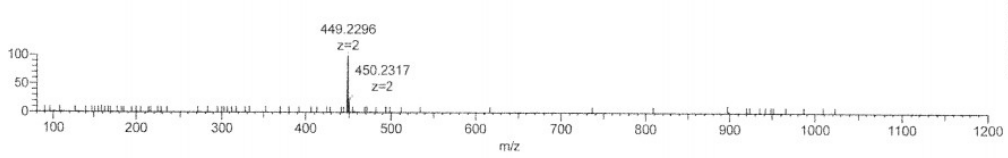
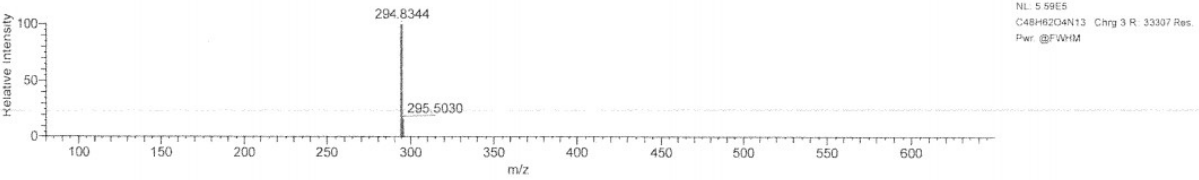
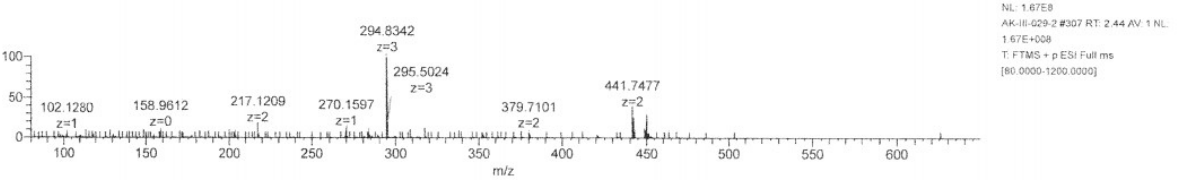
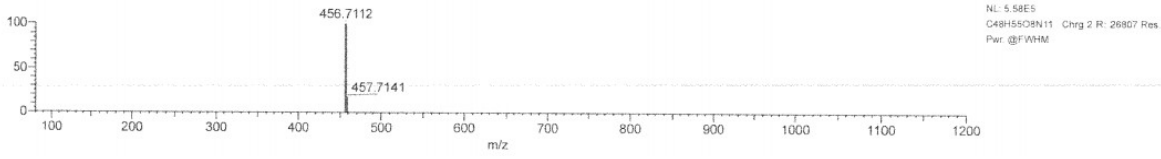
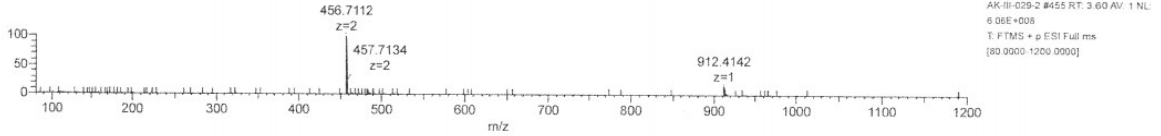
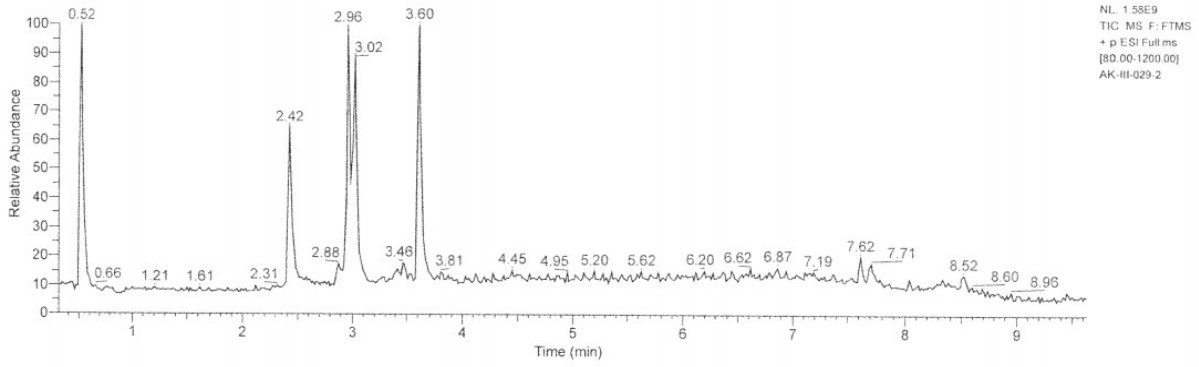
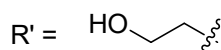
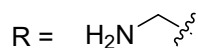
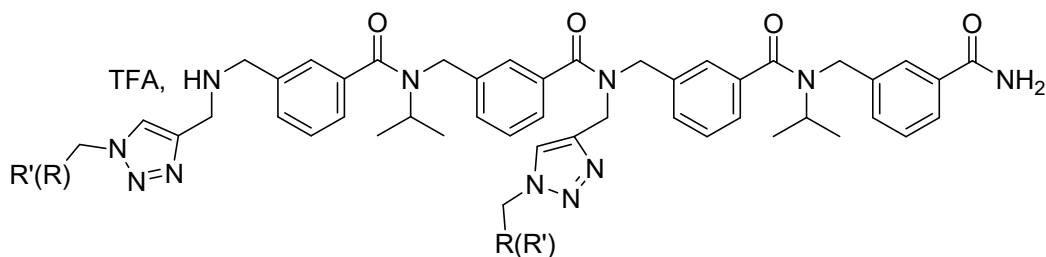


Figure S41 LCMS spectra of III-4(c,d)(2,4).

4.3.4- meta-arylopeptoid tetramer, III-4(d,e)(2,4).



Tetramer III-4(d,e)(2,4) was synthesised according general procedure A then general procedure B using 25 mg of RA resin (0.0155 mmol)

$m_{\text{crude}} = 25 \text{ mg}$ (purity 81%), crude yield 118%

$m_{\text{pure}} = 17.8 \text{ mg}$ (purity 97%), isolated yield 84%

LCMS pic at 3.2 min: HRMS (TOF MS ES+): m/z calcd for $\text{C}_{50}\text{H}_{63}\text{N}_{11}\text{O}_6$ $[\text{M}+2\text{H}]^{2+}$: 456.74759; found: 456.747 (-1.21 ppm).

LCMS pic at 2.76 min: HRMS (TOF MS ES+): m/z calcd for $\text{C}_{49}\text{H}_{62}\text{N}_{12}\text{O}_4$ $[\text{M}+2\text{H}]^{2+}$: 449.24776; found: 449.2473 (-0.99 ppm).

LCMS pic at 2.74 min: HRMS (TOF MS ES+): m/z calcd $\text{C}_{49}\text{H}_{61}\text{N}_{12}\text{O}_5$ $[\text{M}+2\text{H}]^{2+}$: 897.48824; found: 897.4871 (-1.31 ppm).

LCMS pic at 2.44 min: HRMS (TOF MS ES+): m/z $\text{C}_{48}\text{H}_{61}\text{N}_{13}\text{O}_4$ $[\text{M}+2\text{H}]^{2+}$: 441.74793; found: 441.7474 (-1.11 ppm).

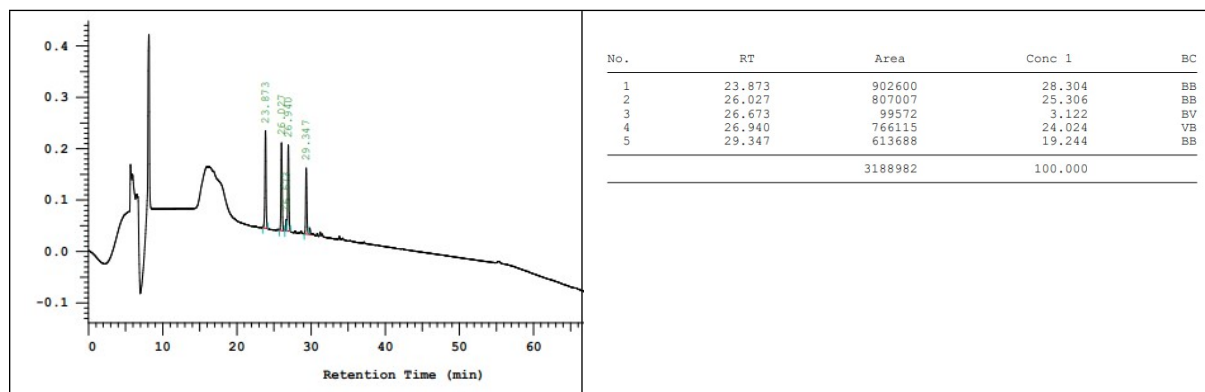


Figure S42 HPLC chromatogram of purified III-4(d,e)(2,4).

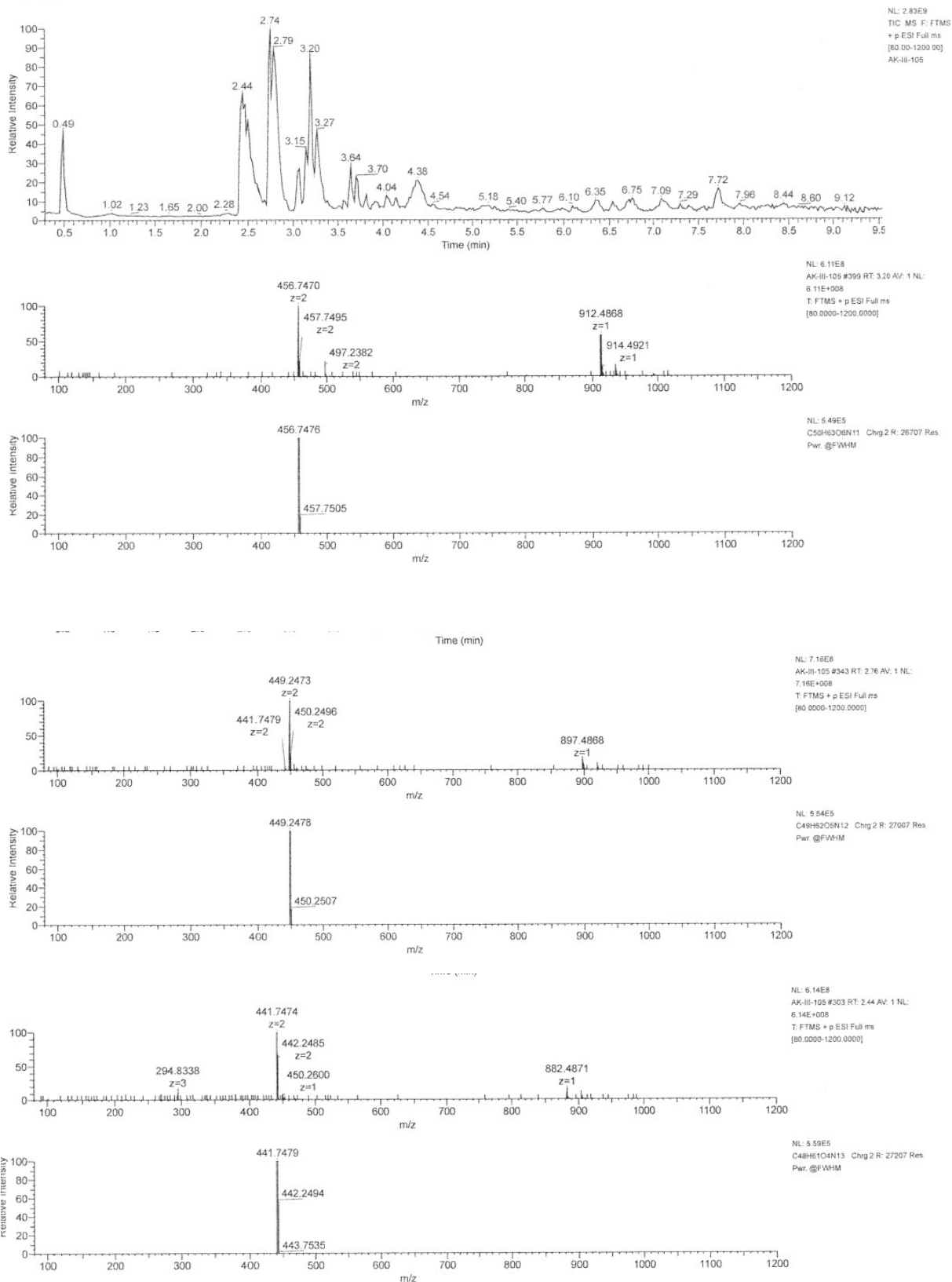
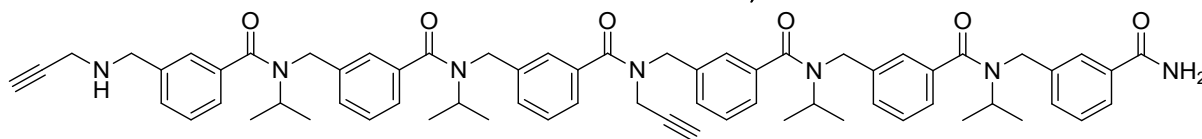


Figure S43 LCMS spectra of III-4(d,e)(2,4).

5- Synthesis and Characterization data of arylopeptoid hexamers

5.1.1-meta-arylopeptoid hexamer, III-6(Alk_{3,6}).



Hexamer III-6(Alk_{3,6}) was synthesised according to general procedure A using 50 mg of RA resin (0.027 mmol), then cleavage by gently shaking a solution of TFA/TIS/H₂O (95:2.5:2.5, 1mL) for 10 min at RT.

m_{crude} = 33 mg, crude yield 118%

m_{pure} = 24 mg (purity 94%), isolated yield 84%

HRMS (TOF MS ES+): *m/z* calcd for C₆₆H₇₄N₇O₆ [M+H]⁺: 1060.56951; found: 1060.5684 (-1.08 ppm).

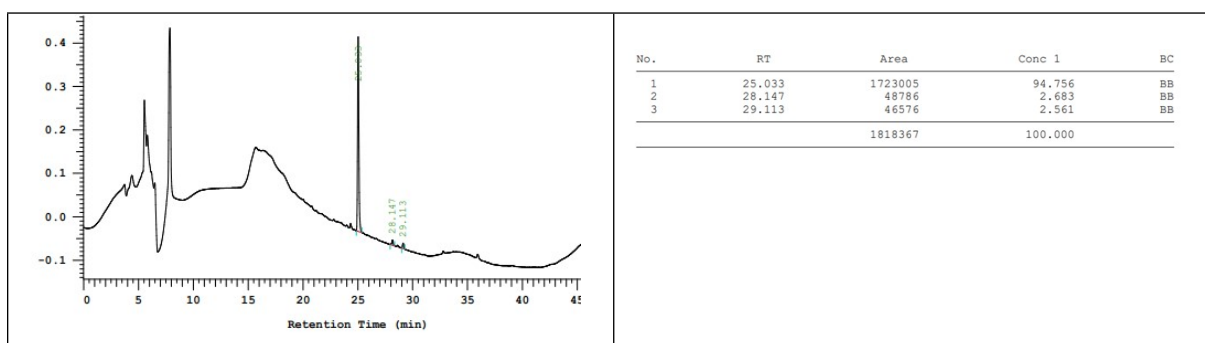


Figure S44 HPLC chromatogram of purified III-6(Alk_{3,6}).

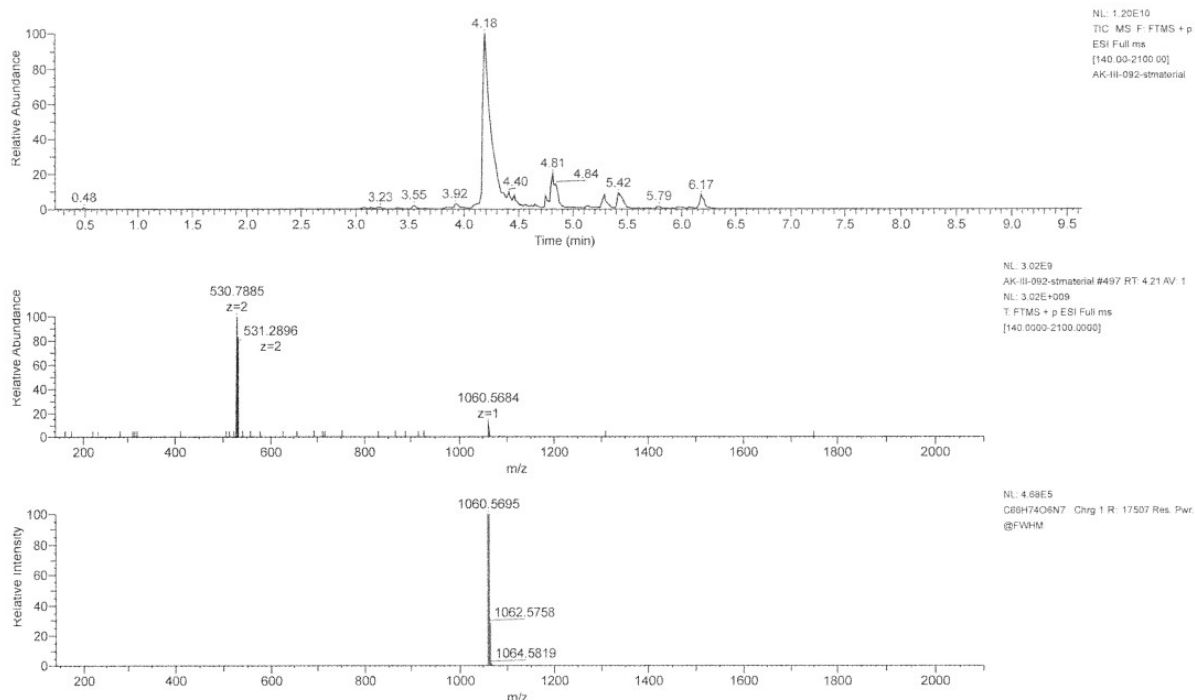


Figure S45 LCMS spectra of III-6(Alk_{3,6}).

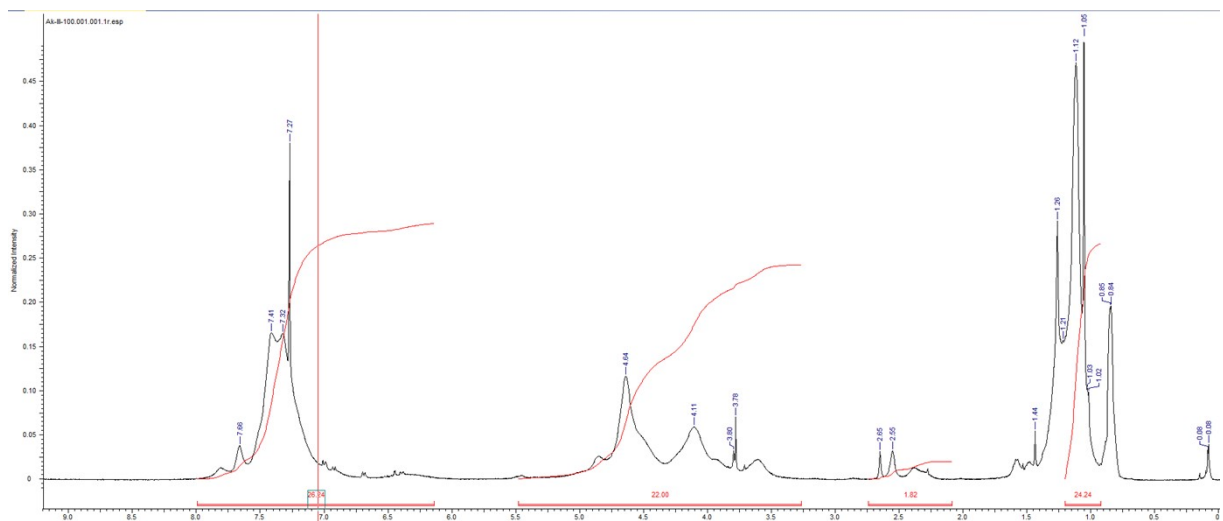
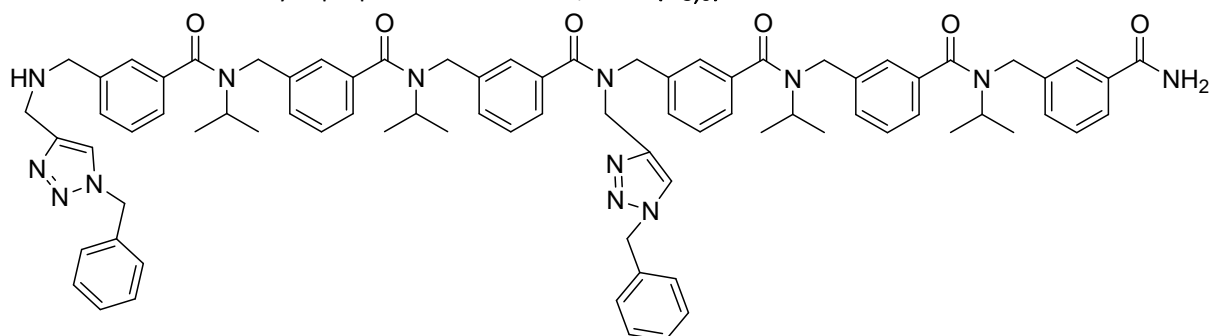


Figure 46 $^1\text{H-NMR}$ in CDCl_3 of III-6(Alk3,6)

5.2-meta-arylopeptoid hexamer, **III-6(a_{3,6})**.



Hexamer **III-6(a_{3,6})** was synthesised according general procedure A then general procedure B using 50 mg of RA resin (0.027 mmol)

$m_{\text{crude}} = 42$ mg (purity 84%), crude yield 117%

$m_{\text{pure}} = 28.2$ mg (purity 94%), isolated yield 85%

HRMS (TOF MS ES⁺): m/z calcd for C₈₀H₈₈N₁₃O₆ [M+H]⁺: 1326.6975; found: 1326.6975 (0 ppm).

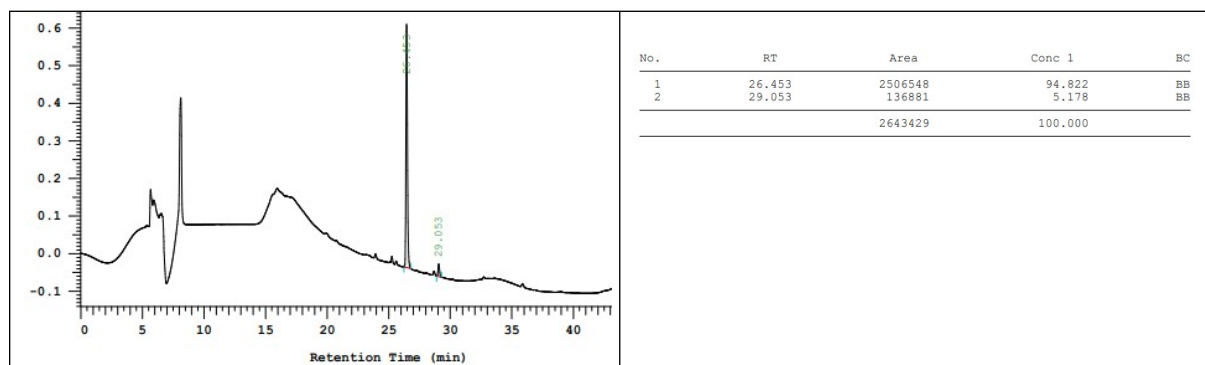


Figure S47 HPLC chromatogram of purified **III-6(a_{3,6})**.

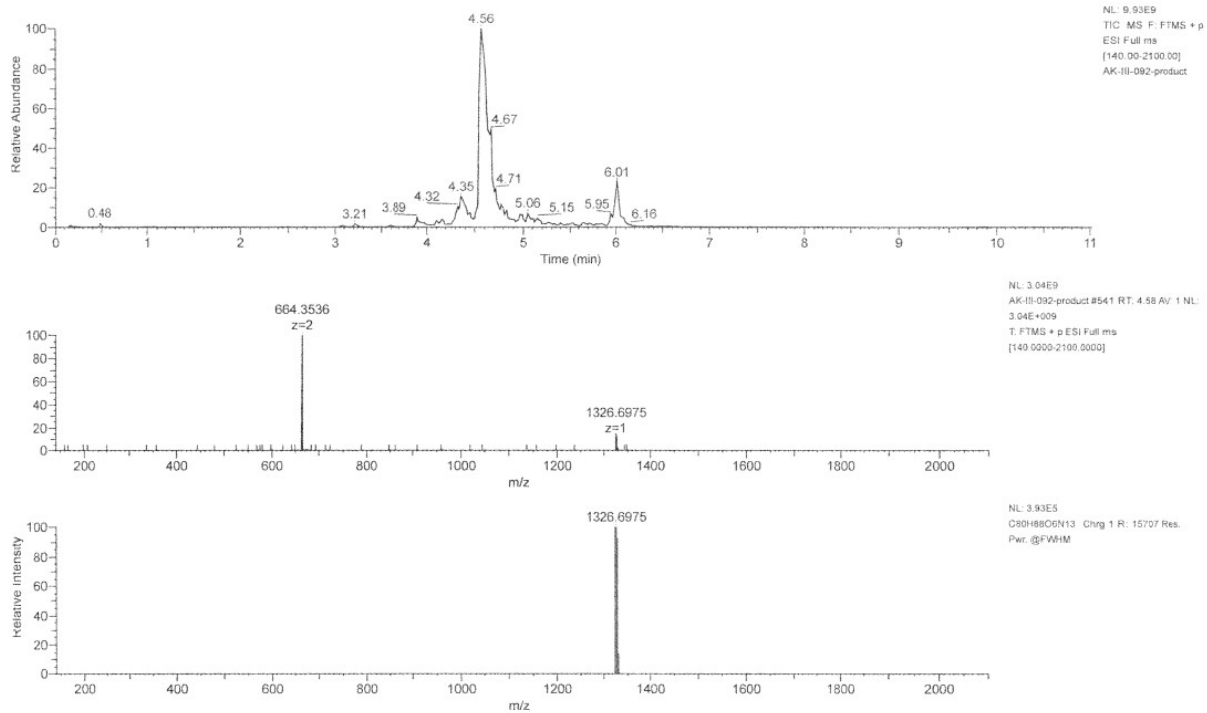
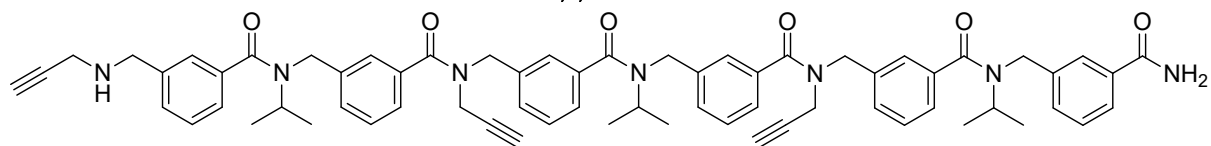


Figure S48 LCMS spectra of III-6(a_{3,6}).

5.2- Starting material, III-6(Alk_{2,4,6}).



Hexamer III-6(Alk_{2,4,6}) was synthesised according to general procedure A using 100 mg of RA resin (0.054 mmol), then cleavage by gently shaking a solution of TFA/TIS/H₂O (95:2.5:2.5, 1mL) for 10 min at RT.

$m_{\text{crude}} = 77\text{mg}$ (purity 85%), crude yield 121%

$m_{\text{pure}} = 50.2\text{mg}$ (purity 97%), isolated yield 87%

HRMS (TOF MS ES+): m/z calcd for C₈₀H₈₈N₁₃O₆ [M+H]⁺: 1056.53821; found: 1056.5367 (-1.39ppm).

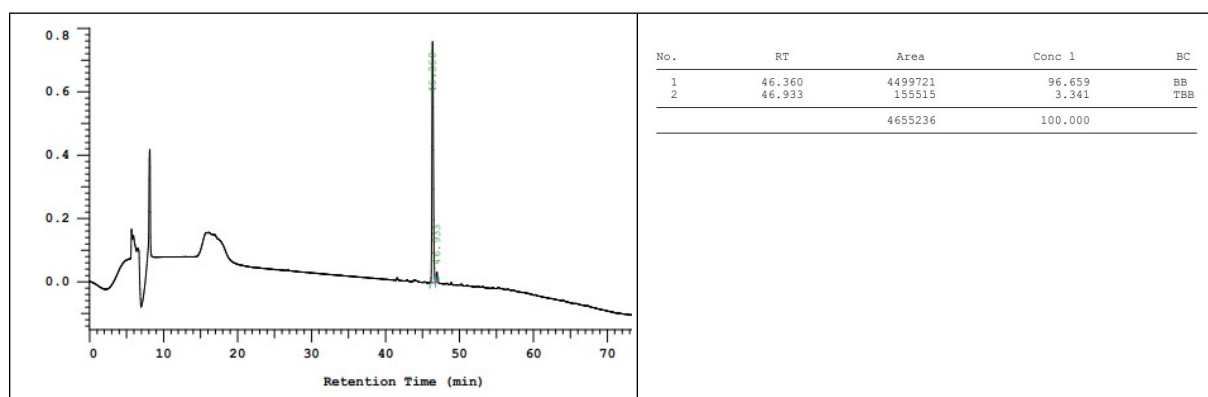


Figure S49 HPLC chromatogram of purified III-6(Alk_{2,4,6})

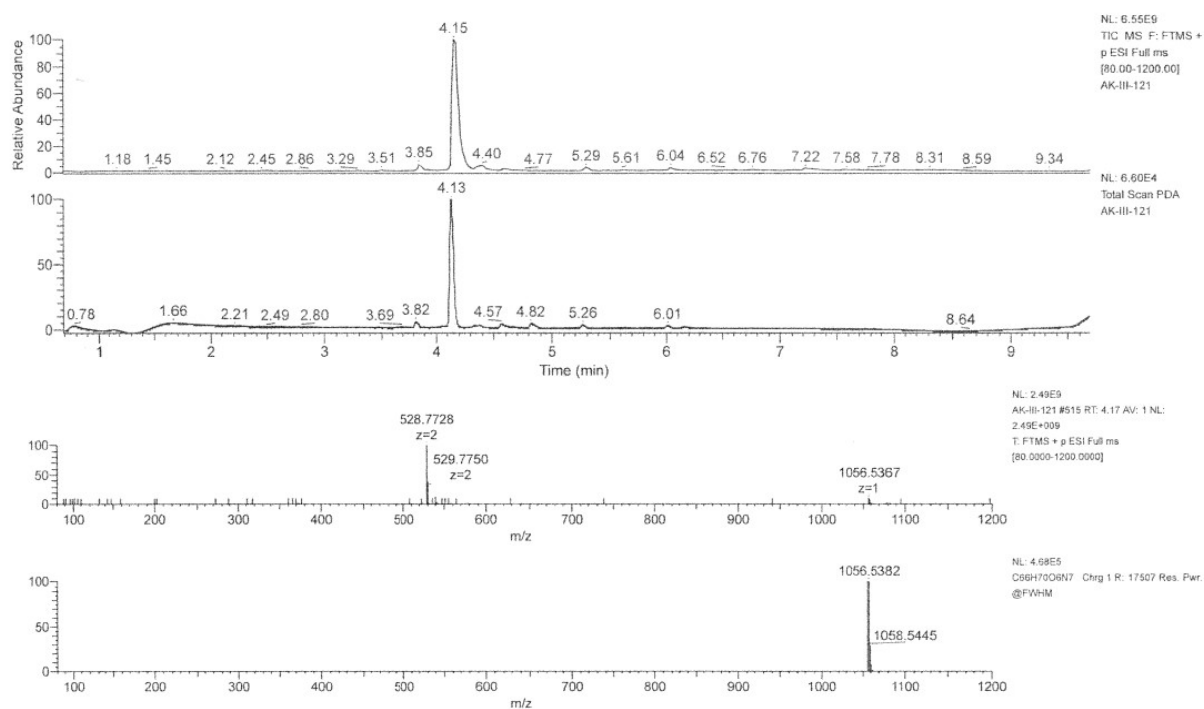


Figure S50 LCMS spectra of III-6(Alk_{2,4,6}).

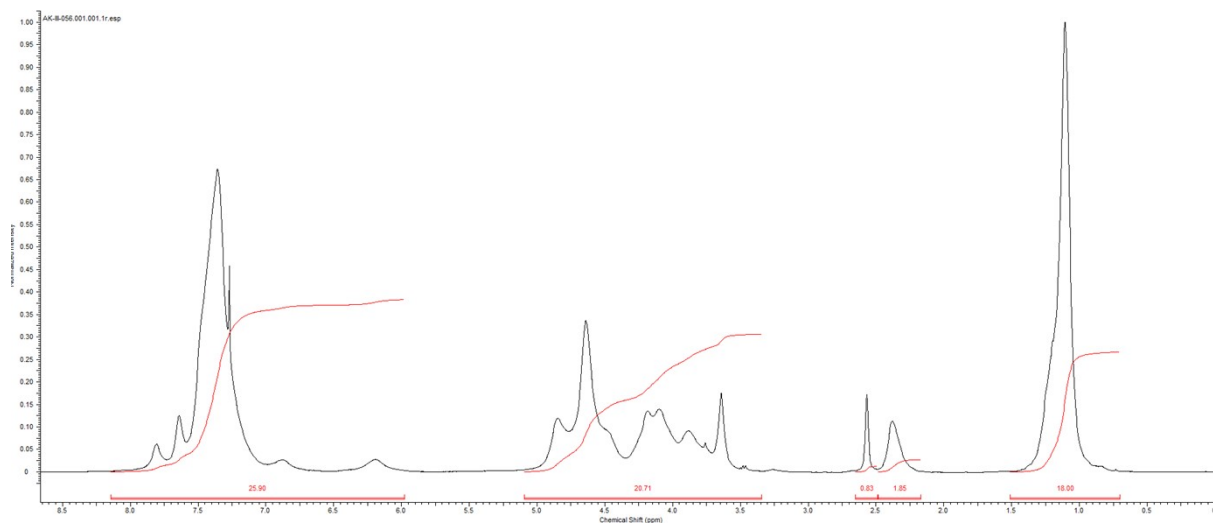
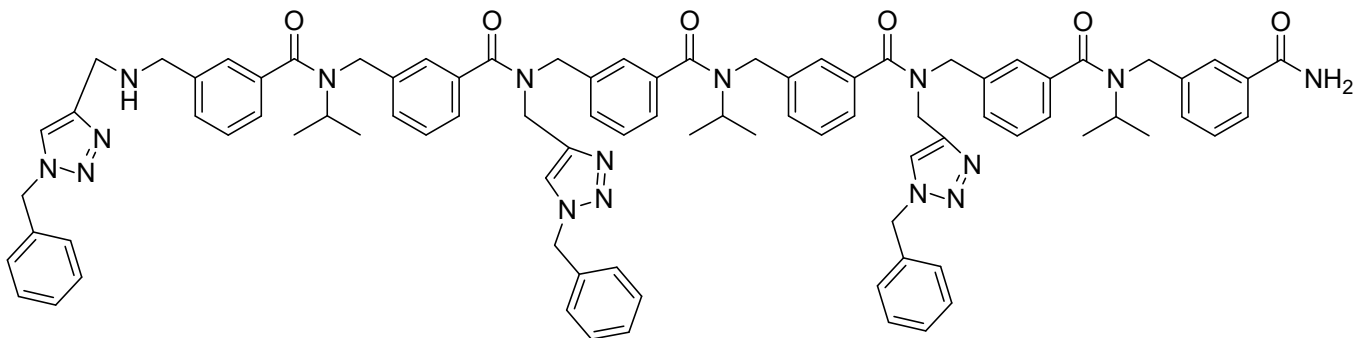


Figure S51 $^1\text{H-NMR}$ spectra in CDCl_3 of **III-6(Alk_{2,4,6})**

5.2- Homo-clicked arylopeptoids

5.2.1- meta-arylopeptoid hexamer, III-6(a_{2,4,6}).



Hexamer III-6(a_{2,4,6}) was synthesised according general procedure A then general procedure B using 100 mg of RA resin (0.054 mmol)

m_{crude} = 116 mg (purity 87%), crude yield 137%

m_{pure} = 64 mg (purity 88%), isolated yield 78%

HRMS (TOF MS ES⁺): *m/z* calcd for C₈₇H₉₁N₁₆O₆ [M+H]⁺: 1455.7302; found: 1455.7341 (2.7 ppm).

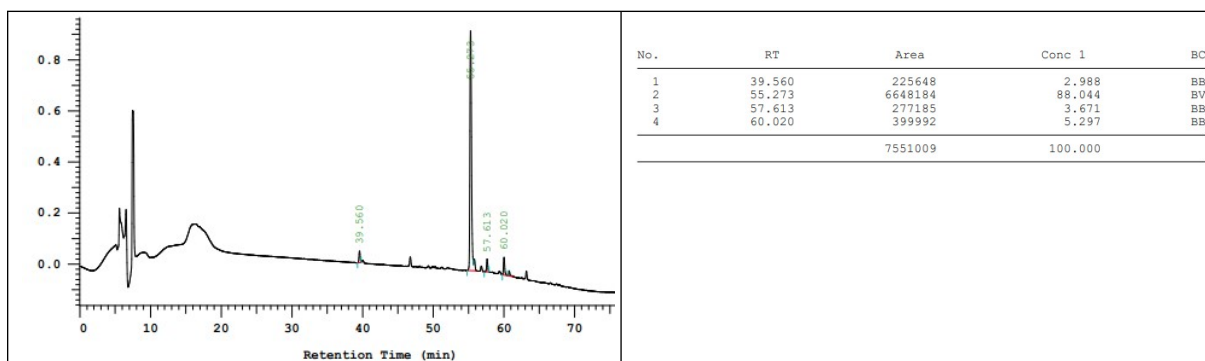


Figure S52 HPLC chromatogram of purified III-6(a_{2,4,6}).

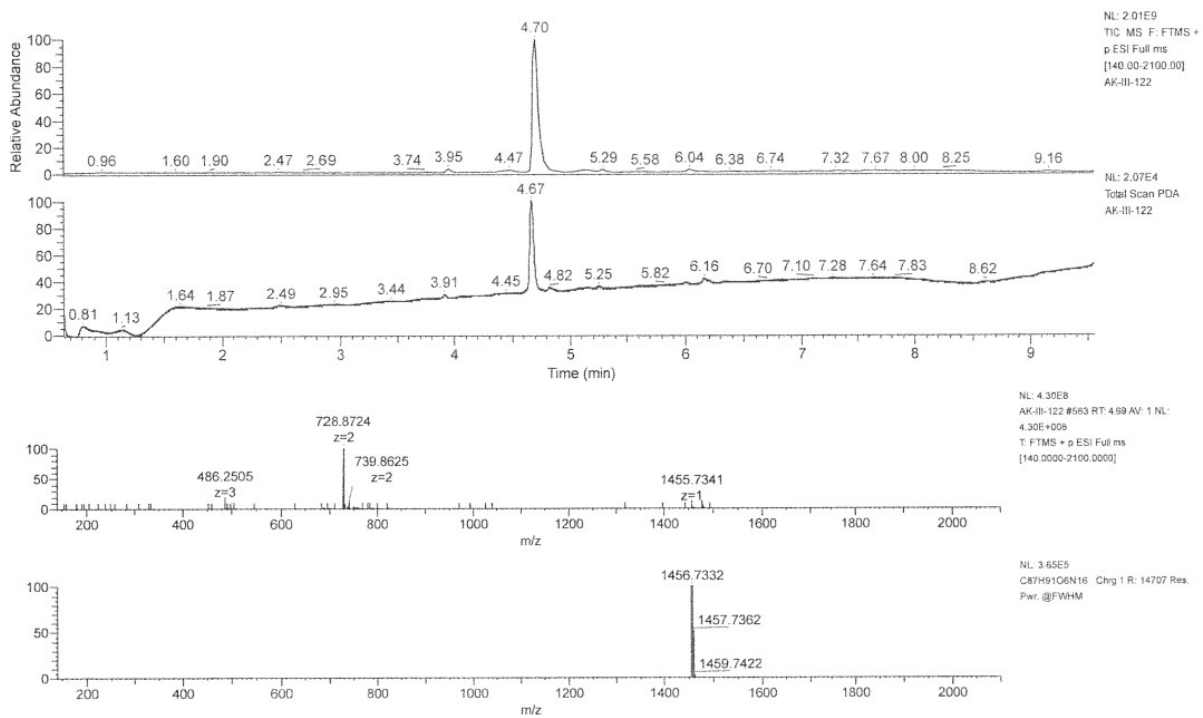
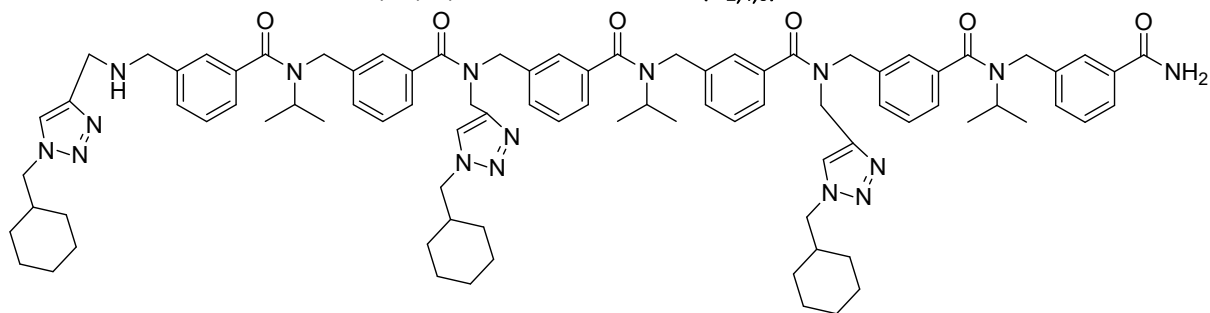


Figure S53 LCMS spectra of III-6($\alpha_{2,4,6}$).

5.2.2- meta-arylopeptoid hexamer, **III-6(b_{2,4,6})**.



Hexamer **III-6(b_{2,4,6})** was synthesised according general procedure A then general procedure B using 50 mg of RA resin (0.027 mmol)

$m_{\text{crude}} = 38 \text{ mg}$ (purity 86%), crude yield 96%

$m_{\text{pure}} = 30 \text{ mg}$ (purity 91%), isolated yield 76%

HRMS (TOF MS ES⁺): m/z calcd for $\text{C}_{87}\text{H}_{110}\text{N}_{16}\text{O}_6$ $[\text{M}+\text{H}]^{2+}$: 737.43916; found: 737.4398 (0.81 ppm).

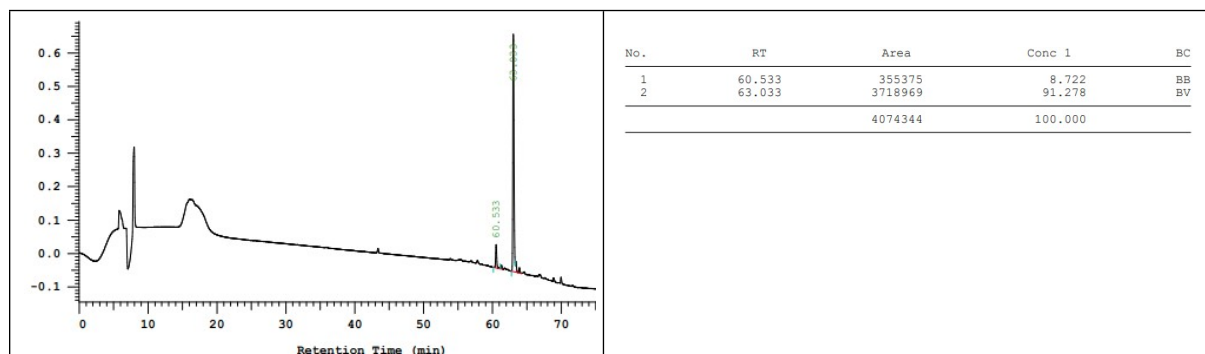


Figure S54 HPLC chromatogram of purified **III-6(b_{2,4,6})**.

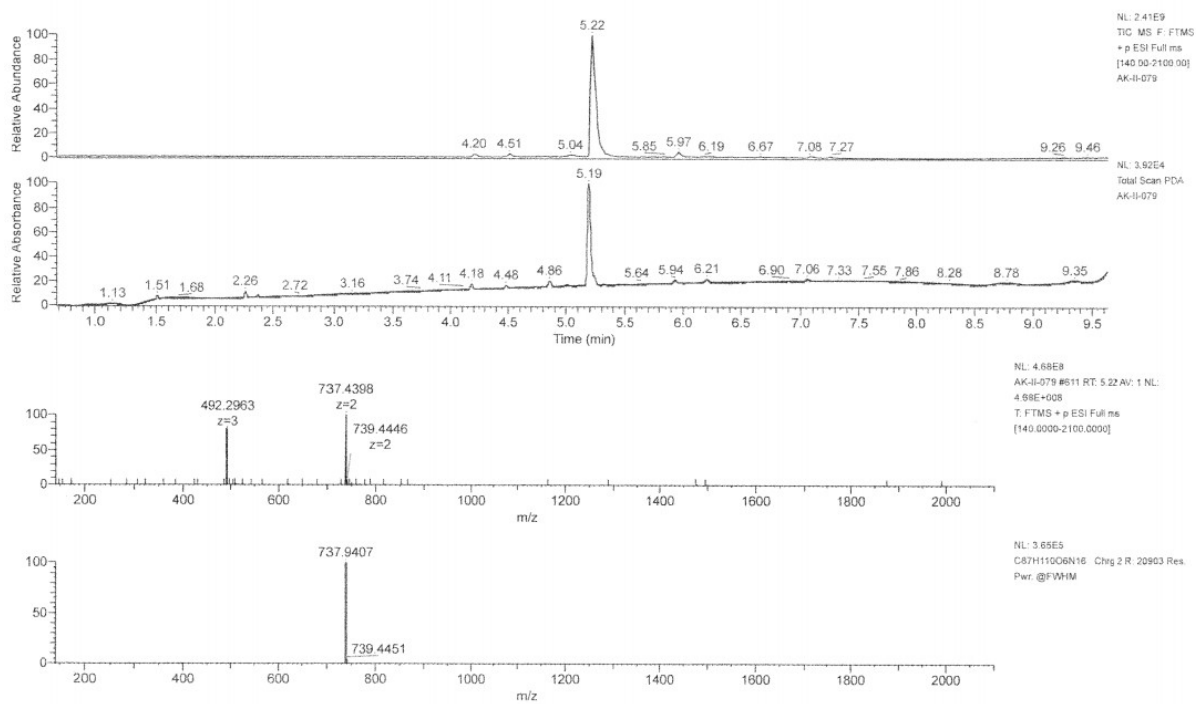
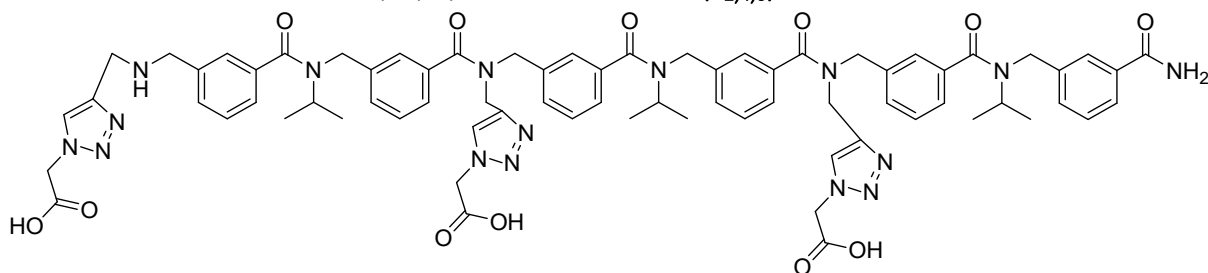


Figure S55 LCMS spectra of III-6(b_{2,4,6}).

5.2.3- meta-arylopeptoid hexamer, III-6(C_{2,4,6}).



Hexamer III-6(C_{2,4,6}) was synthesised according general procedure A then general procedure B using 100 mg of RA resin (0.054 mmol)

m_{crude} = 90 mg (purity 85%), crude yield 113%

m_{pure} = 49 mg (purity 94%), isolated yield 68%

HRMS (TOF MS ES+): *m/z* calcd for C₇₂H₈₀N₁₆O₁₂ [M+2H]²⁺: 680.30653; found: 680.3074 (1.33 ppm).

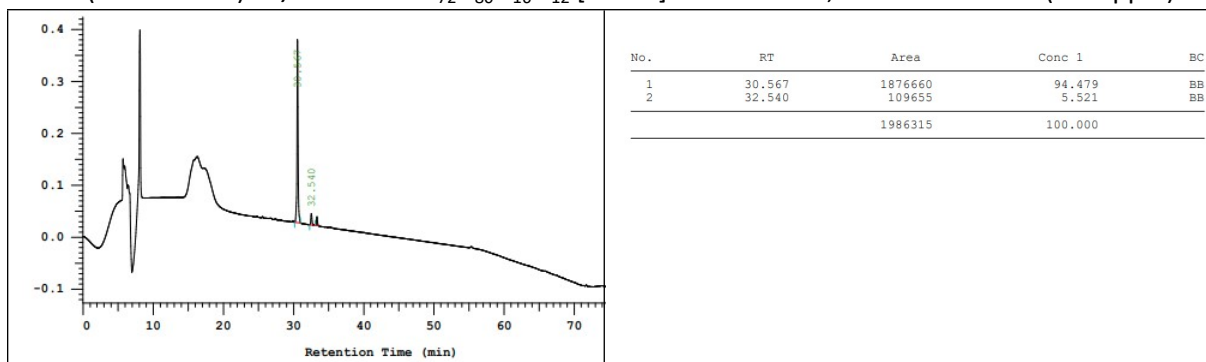


Figure 56 HPLC chromatogram of purified III-6(C_{2,4,6}).

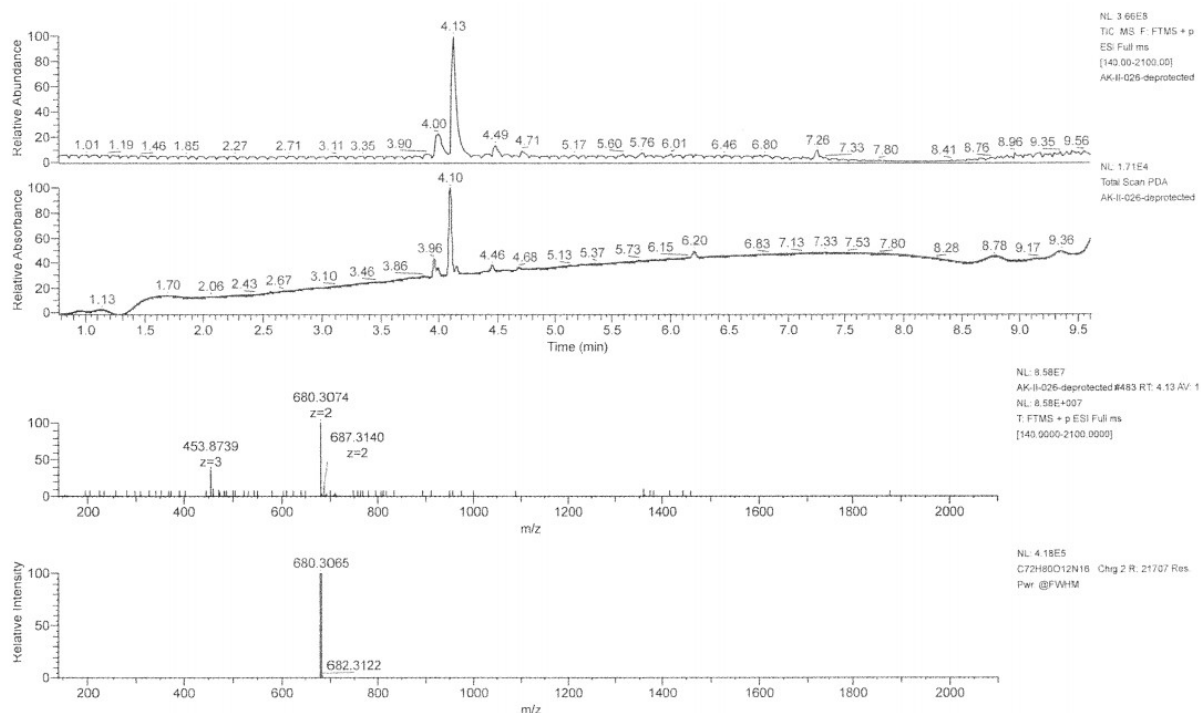
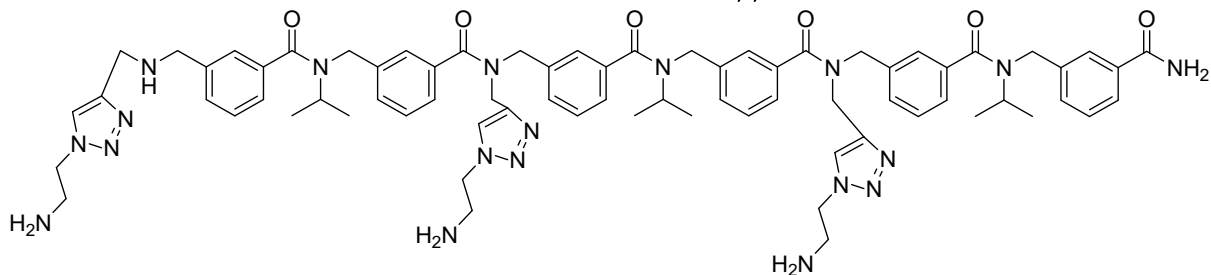


Figure 57 LCMS spectra of III-6(C_{2,4,6}).

5.2.4- meta-arylopeptoid hexamer, III-6(d_{2,4,6}).



Hexamer III-6(d_{2,4,6}) was synthesised according general procedure A then general procedure B using 100 mg of RA resin (0.054 mmol)

m_{crude} = 116 mg (purity 86%), crude yield 98%

m_{pure} = 64 mg (purity 93%), isolated yield 70%

HRMS (TOF MS ES+): *m/z* calcd for C₇₂H₉₀N₁₉O₁₂ [M+3H]³⁺: 438.91017; found: 438.9101 (-0.09ppm).

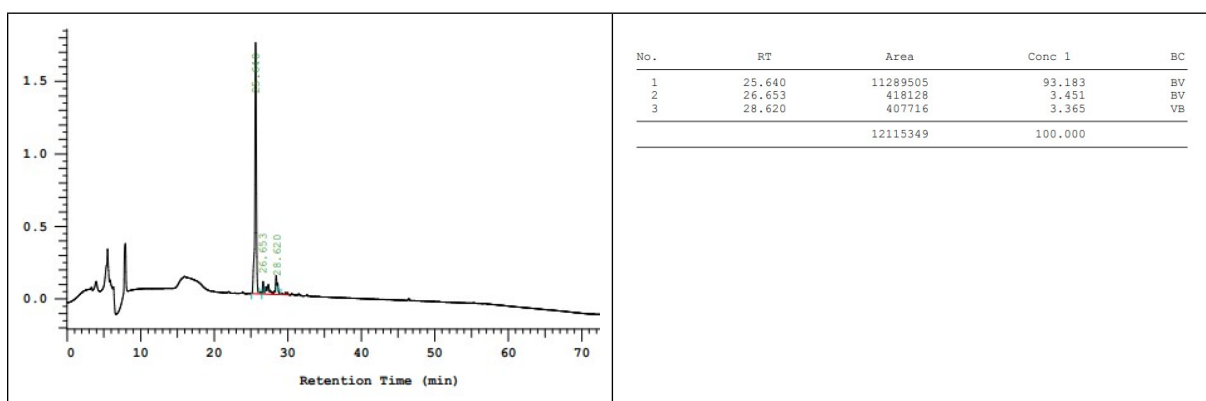


Figure 58 HPLC chromatogram of purified III-6(d_{2,4,6}).

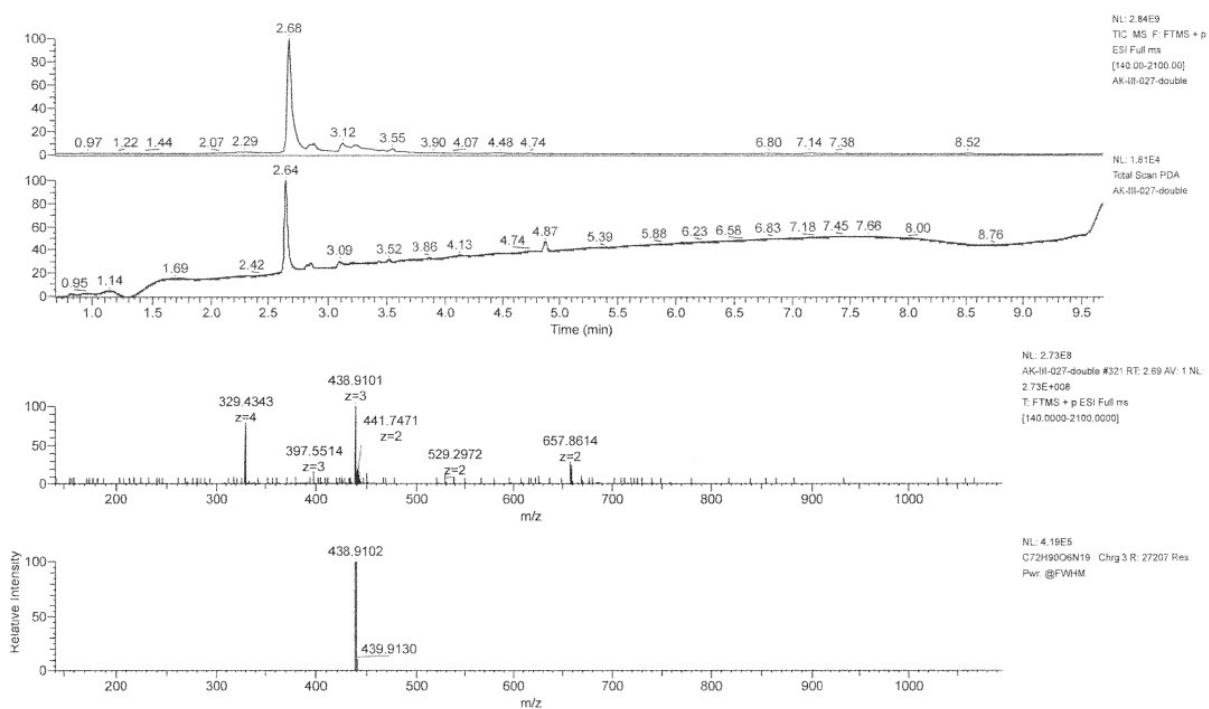
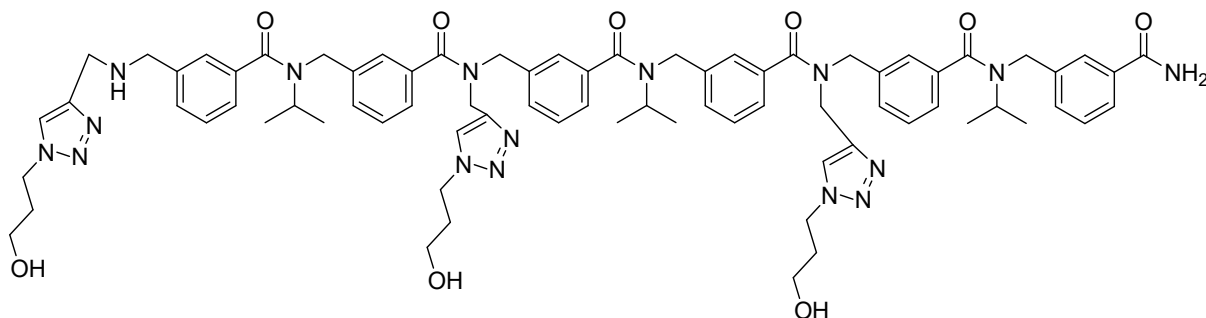


Figure 59 LCMS spectra of III-6(d_{2,4,6}).

5.2.5- meta-arylopeptoid hexamer, III-6(e_{2,4,6}).



Hexamer III-6(e_{2,4,6}) was synthesised according general procedure A then general procedure B using 50 mg of RA resin (0.027 mmol)

m_{crude} = 46 mg (purity 86%), crude yield 116%

m_{pure} = 33.80 mg (purity 100%), isolated yield 82%

HRMS (TOF MS ES+): *m/z* calcd for C₇₅H₉₂N₁₆O₉ [M+2H]²⁺: 680.36111; found: 680.3602 (-1.38 ppm).

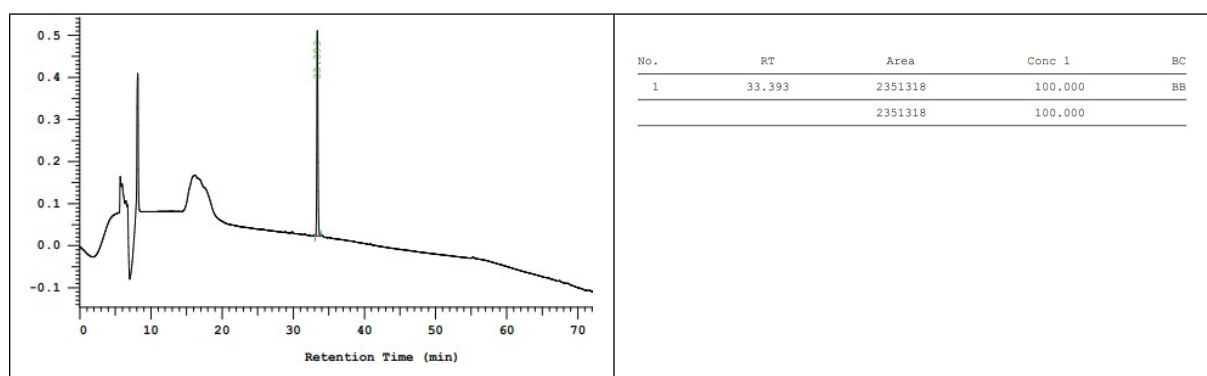


Figure 60 HPLC chromatogram of purified III-6(e_{2,4,6}).

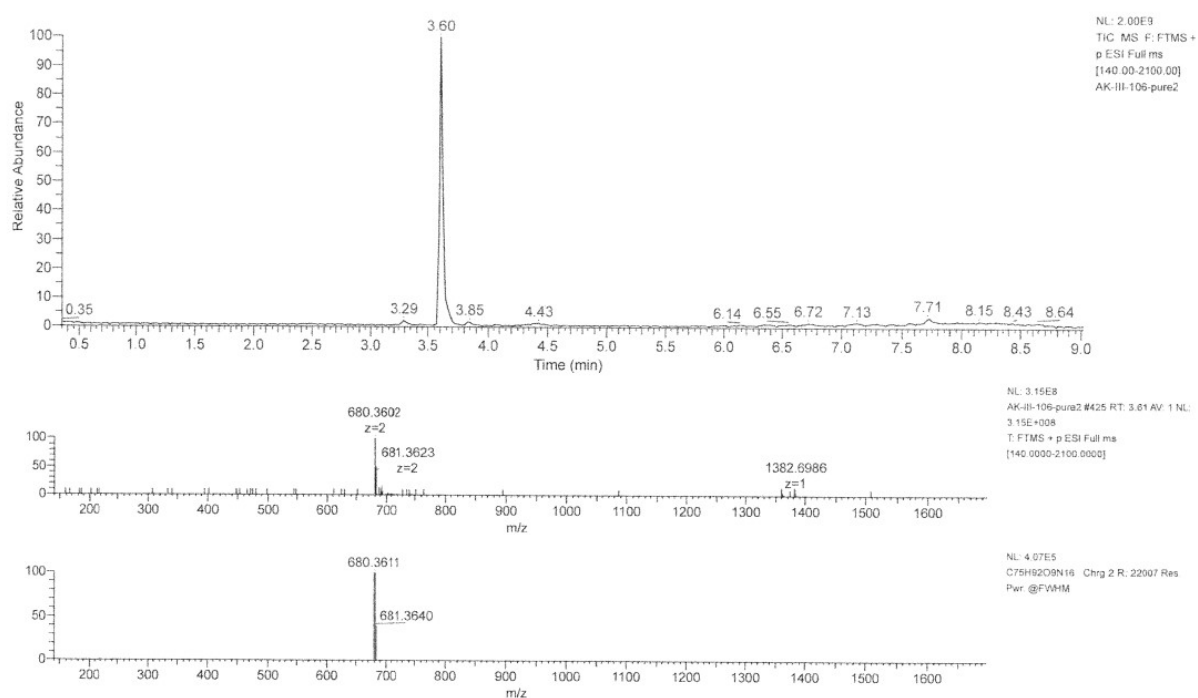
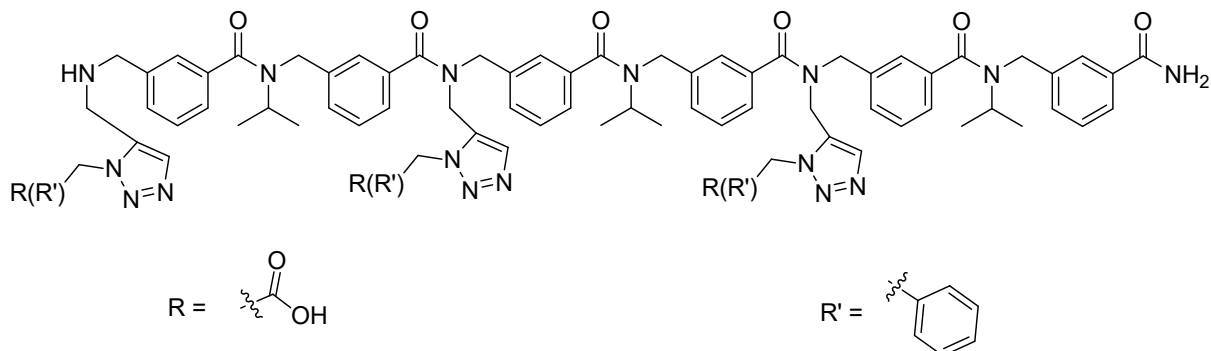


Figure S61 LCMS spectra of III-6(e_{2,4,6}).

5.3- Combinatorial on hexamer

5.3.1- Meta-arylopeptoid hexamer III-6(a,c)(2,4,6).



Hexamer III-6(a,c)(2,4,6) was synthesised according general procedure A then general procedure B using 100 mg of RA resin (0.054 mmol)

$m_{\text{crude}} = 122$ mg (purity 89%), crude yield 159%

$m_{\text{pure}} = 51$ mg (purity 98%), isolated yield 67%

LCMS pic at 4.12 min: HRMS (TOF MS ES+): m/z calcd for $C_{72}H_{80}N_{16}O_{12}$ [M+2H]²⁺: 680.30653 found: 680.3069 (0.52 ppm)

LCMS pic at 4.27 min: HRMS (TOF MS ES+): m/z calcd for $C_{77}H_{84}N_{16}O_{10}$ [M+2H]²⁺: 696.32727 found: 696.3272 (-0.08 ppm)

LCMS pic at 4.42 min: HRMS (TOF MS ES+): m/z calcd for $C_{77}H_{84}N_{16}O_{10}$ [M+2H]²⁺: 696.32727 found: 696.3273 (0.09 ppm)

LCMS pic at 4.73 min: HRMS (TOF MS ES+): m/z calcd for $C_{77}H_{90}N_{16}O_{10}$ [M+2H]²⁺: 699.35074 found: 699.3508 (0.05 ppm)

LCMS pic at 4.5 min: HRMS (TOF MS ES+): m/z calcd for $C_{77}H_{84}N_{16}O_{10}$ [M+2H]²⁺: 696.32727 found: 696.3275 (0.27 ppm)

LCMS pic at 4.5 min: HRMS (TOF MS ES+): m/z calcd for $C_{82}H_{88}N_{16}O_8$ [M+2H]²⁺: 712.348 found: 712.3472 (-1.09 ppm)

LCMS pic at 4.59 min: HRMS (TOF MS ES+): m/z calcd for $C_{82}H_{88}N_{16}O_8$ [M+2H]²⁺: 712.348 found: 712.3477 (-0.4 ppm)

LCMS pic at 4.72 min: HRMS (TOF MS ES+): m/z calcd for $C_{82}H_{88}N_{16}O_8$ [M+2H]²⁺: 712.348 found: 712.3477 (-0.4 ppm)

LCMS pic at 4.72 min: HRMS (TOF MS ES+): m/z calcd for $C_{87}H_{92}N_{16}O_6$ [M+2H]²⁺: 728.36874 found: 728.368 (-1.04 ppm)

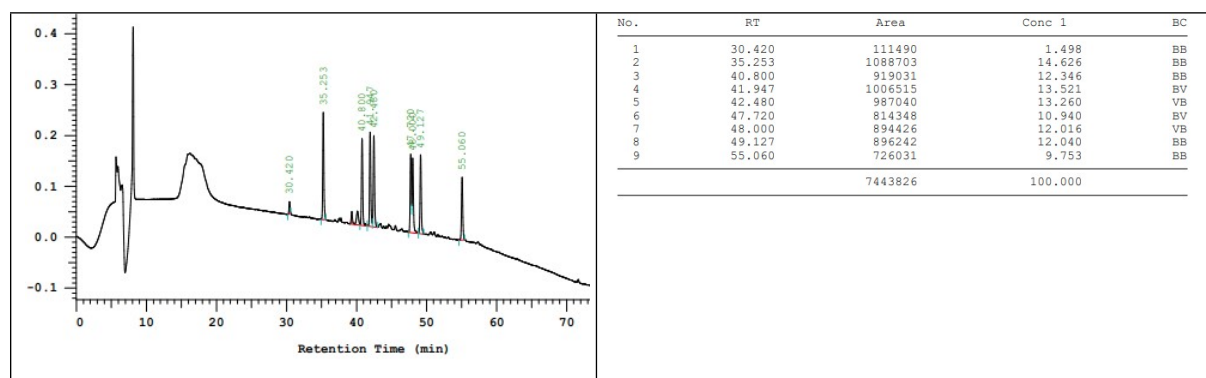
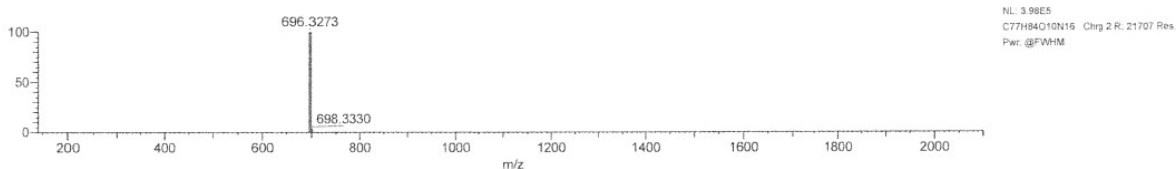
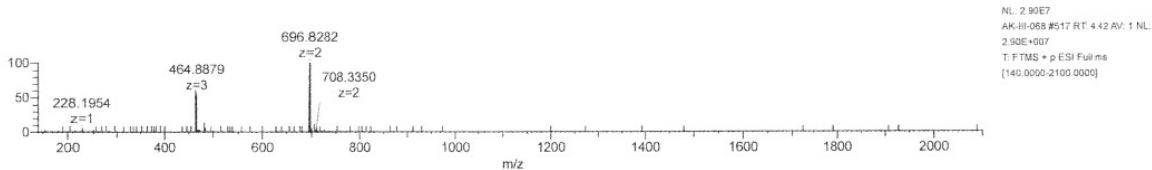
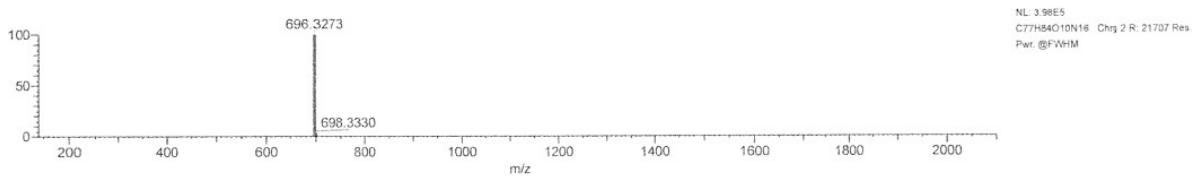
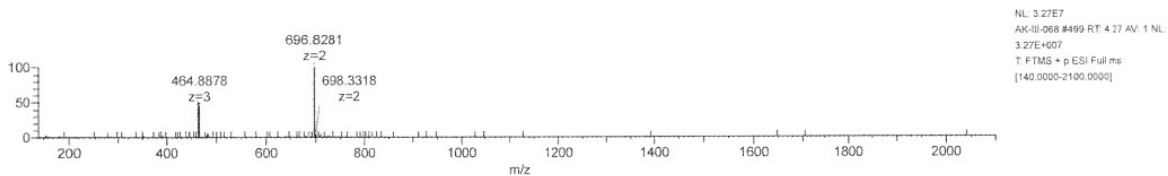
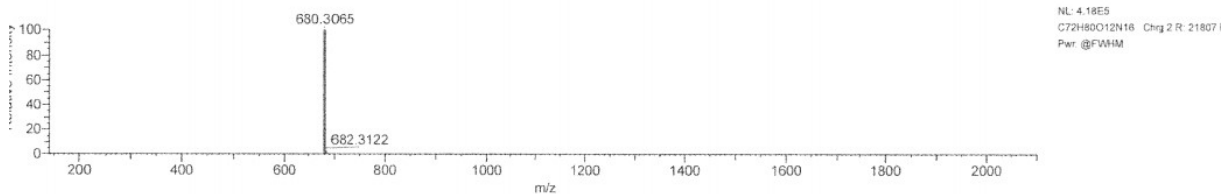
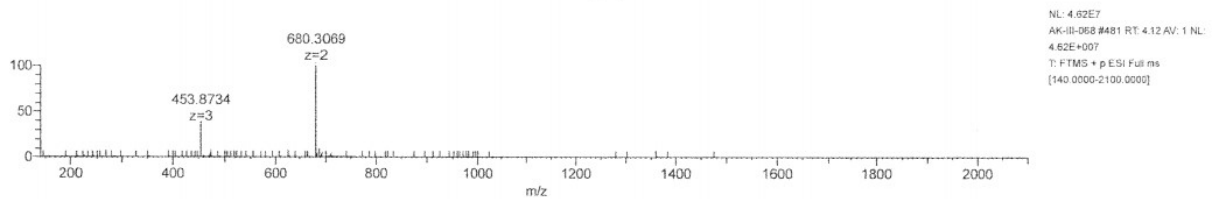
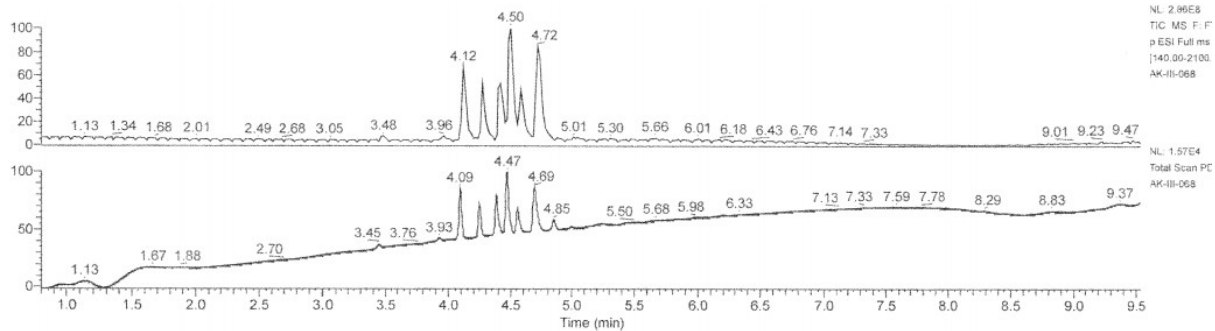


Figure S62 HPLC chromatogram of purified III-6(a,c)(2,4,6)



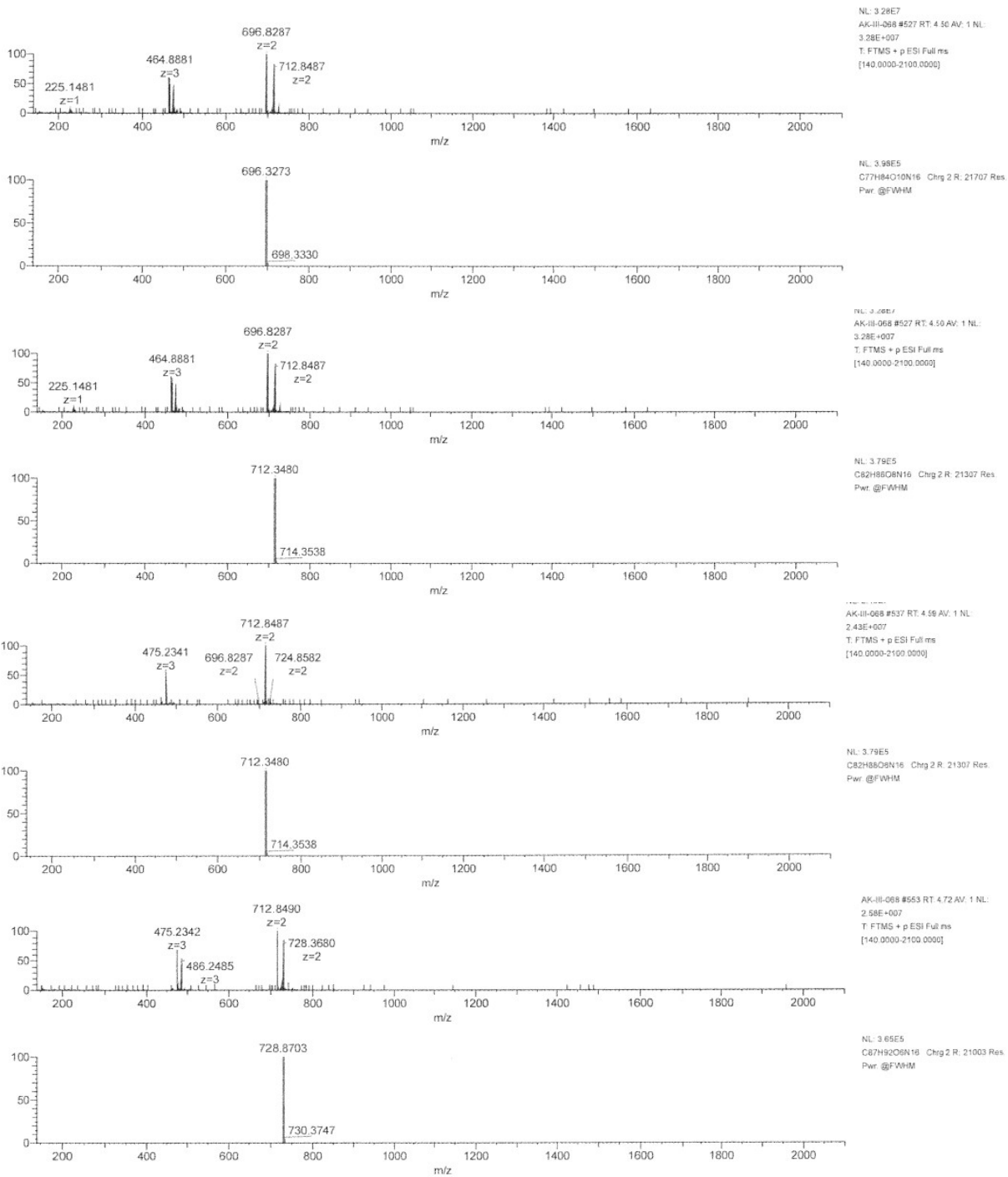
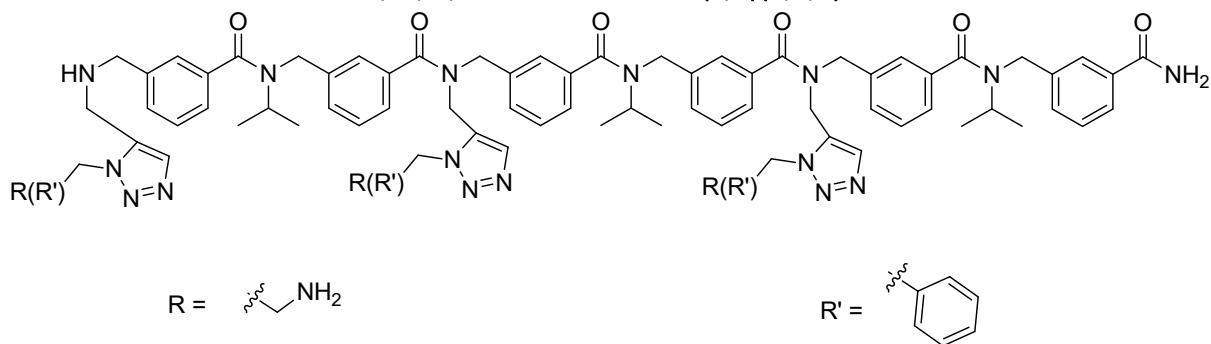


Figure S63 LCMS spectra of III-6(a,c)(2,4,6).

5.3.2- meta-arylopeptoid hexamer, III-6(a,d)(2,4,6).



Hexamer III-6(a,d)(2,4,6) was synthesised according general procedure A then general procedure B using 50 mg of RA resin (0.031 mmol)

$m_{\text{crude}} = 58 \text{ mg}$ (purity 89%), crude yield 150%

$m_{\text{pure}} = 30 \text{ mg}$ (purity 95%), isolated yield 80%

LCMS pic at 3.13 min: HRMS (TOF MS ES+): m/z calcd for $C_{72}H_{89}N_{19}O_6$ $[M+2H]^{2+}$: 657.86161 found: 657.8621 (0.68 ppm).

LCMS pic at 3.29 min: HRMS (TOF MS ES+): m/z calcd for $C_{77}H_{90}N_{18}O_6$ $[M+2H]^{2+}$: 681.36399 found: 681.3641 (0.22 ppm).

LCMS pic at 3.76 min: HRMS (TOF MS ES+): m/z calcd for $C_{82}H_{91}N_{17}O_6$ $[M+2H]^{2+}$: 704.86636 found: 704.8671 (1 ppm)

LCMS pic at 3.76 min: HRMS (TOF MS ES+): m/z calcd for $C_{82}H_{91}N_{17}O_6$ $[M+2H]^{2+}$: 704.86636 found: 704.8671 (1 ppm)

LCMS pic at 4.09 min: HRMS (TOF MS ES+): m/z calcd for $C_{82}H_{91}N_{17}O_6$ $[M+2H]^{2+}$: 704.86636 found: 704.8668 (0.56 ppm)

LCMS pic at 4.66 min: HRMS (TOF MS ES+): m/z $C_{87}H_{92}N_{16}O_6$ $[M+2H]^{2+}$: 728.36874 found: 728.3690 (0.3 ppm)

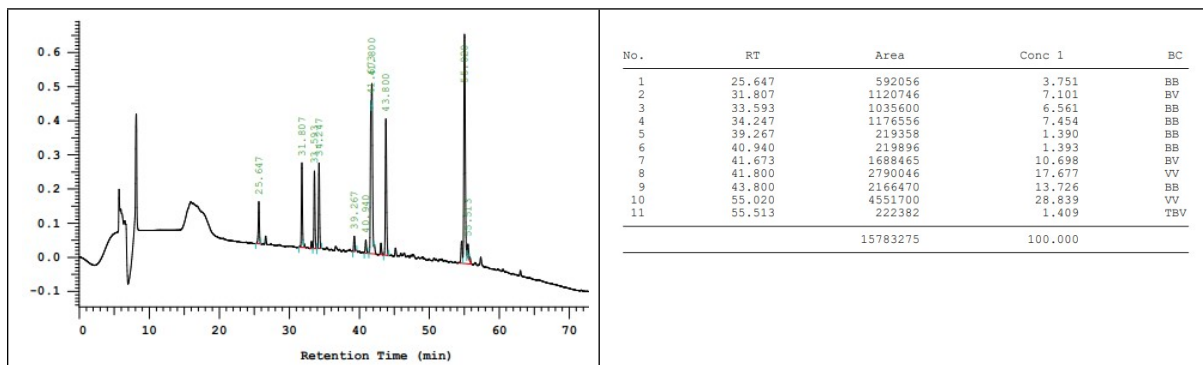
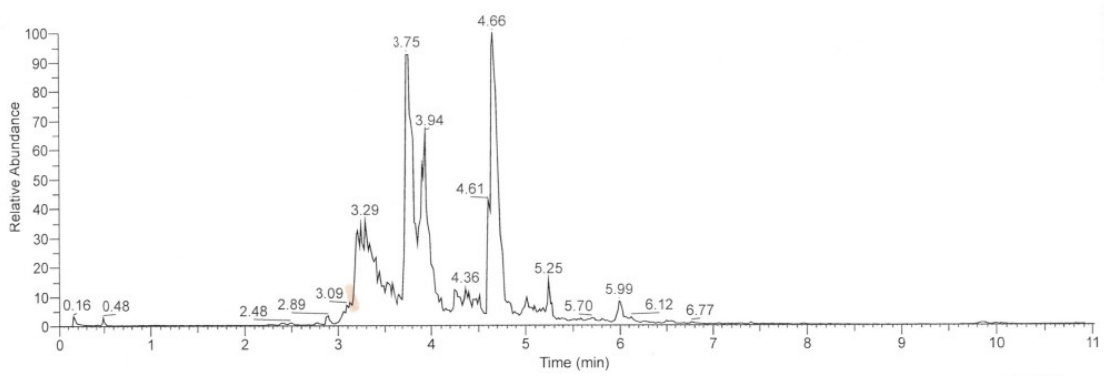
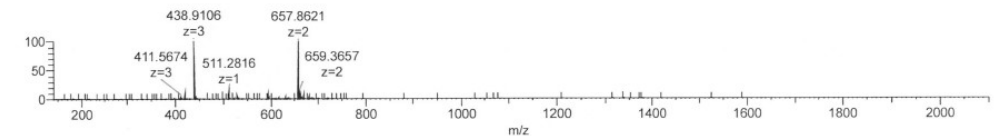


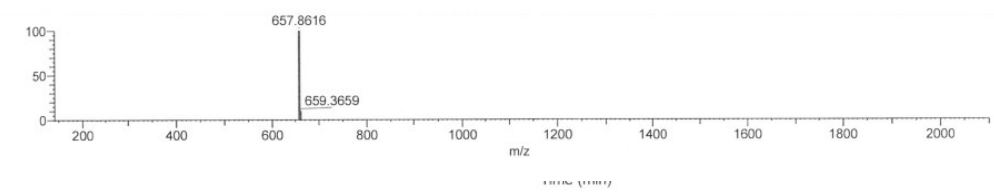
Figure S64 HPLC chromatogram of purified III-6(a,d)(2,4,6).



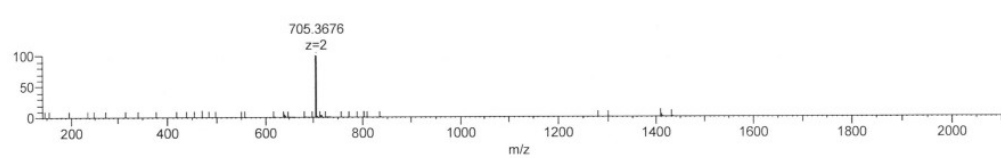
NL: 2.80E9
 TIC MS F: FTMS
 + p ESI Full ms
 [140.00-2100.00]
 AK-III-095



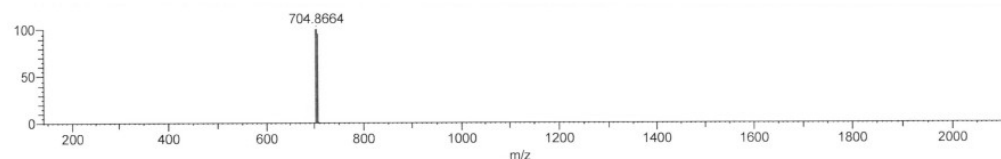
NL: 2.74E7
 AK-III-095 #367 RT: 3.13 AV: 1 NL:
 2.74E+007
 T: FTMS + p ESI Full ms
 [140.0000-2100.0000]



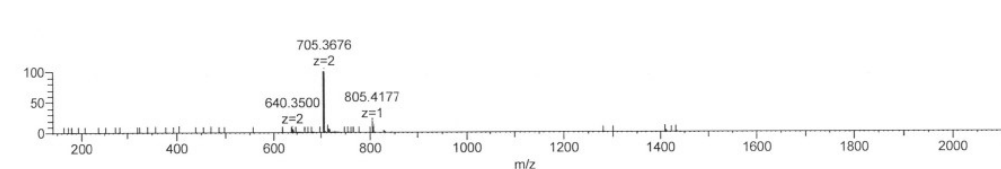
NL: 4.19E5
 C72H89O6N19 Chrg 2 R: 22207 Res.
 Pwr: @FWHM



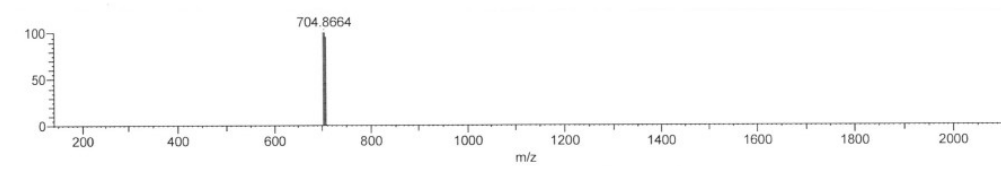
NL: 8.07E8
 AK-III-095 #445 RT: 3.76 AV: 1 NL:
 8.07E+008
 T: FTMS + p ESI Full ms
 [140.0000-2100.0000]



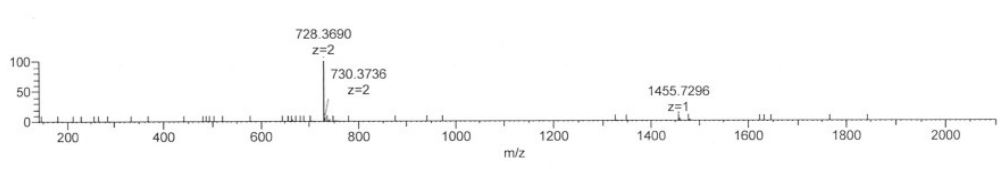
NL: 3.79E5
 C82H91O6N17 Chrg 2 R: 21507 Res.
 Pwr: @FWHM



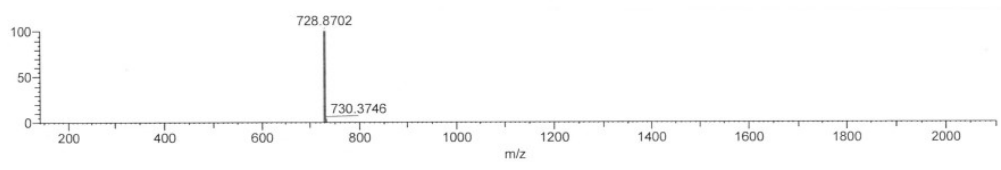
NL: 3.80E8
 AK-III-095 #465 RT: 3.92 AV: 1 NL:
 3.80E+008
 T: FTMS + p ESI Full ms
 [140.0000-2100.0000]



NL: 3.79E5
 C82H91O6N17 Chrg 2 R: 21507 Res.
 Pwr: @FWHM



NL: 8.83E8
 AK-III-095 #555 RT: 4.66 AV: 1 NL:
 8.83E+008
 T: FTMS + p ESI Full ms
 [140.0000-2100.0000]



NL: 3.65E5
 C87H92O6N16 Chrg 2 R: 21107 Res.
 Pwr: @FWHM

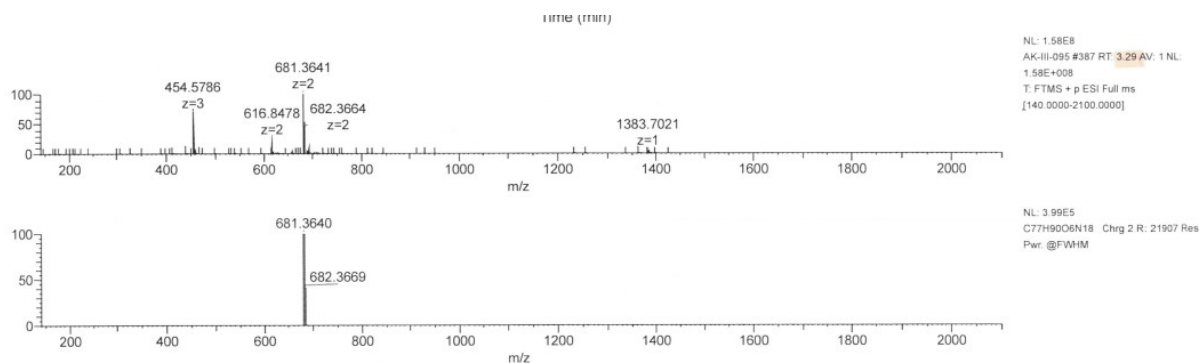
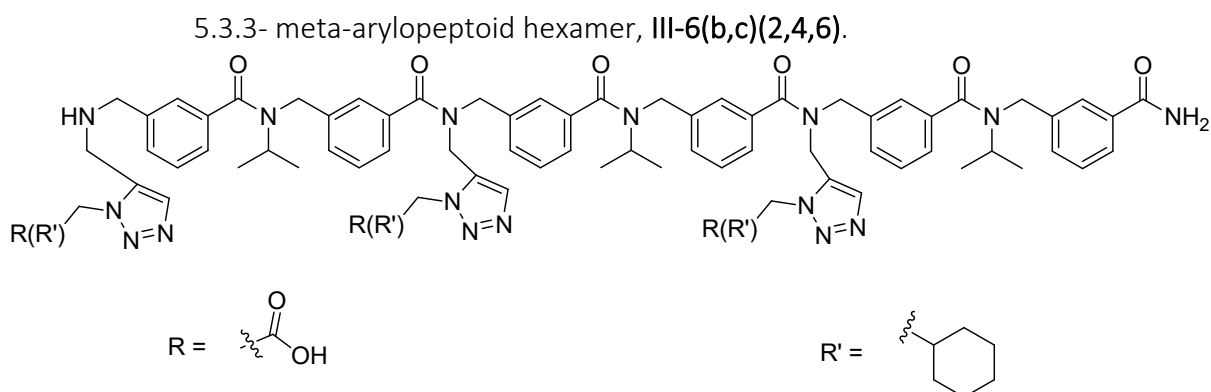


Figure S65 LCMS spectra of **III-6(a,d)(2,4,6)**.



Hexamer **III-6(b,c)(2,4,6)** was synthesised according general procedure A then general procedure B using 100 mg of RA resin (0.054 mmol)

$m_{\text{crude}} = 112$ mg (purity 80%), crude yield 137%

$m_{\text{pure}} = 62$ mg (purity 88%) isolated yield 82%

LCMS pic at 4.12 min: HRMS (TOF MS ES+): m/z calcd for $C_{72}H_{80}N_{16}O_{12}$ $[M+2H]^{2+}$: 680.30653 found: 680.3065 (-0.11 ppm).

LCMS pic at 4.46 min: HRMS (TOF MS ES+): m/z calcd for $C_{77}H_{90}N_{16}O_{10}$ $[M+2H]^{2+}$: 699.35074 found: 699.3507 (-0.05 ppm)

LCMS pic at 4.63 min: HRMS (TOF MS ES+): m/z calcd for $C_{77}H_{90}N_{16}O_{10}$ $[M+2H]^{2+}$: 699.35074 found: 699.3507 (-0.05 ppm)

LCMS pic at 4.73 min: HRMS (TOF MS ES+): m/z calcd for $C_{77}H_{90}N_{16}O_{10}$ $[M+2H]^{2+}$: 699.35074 found: 699.3508 (0.05 ppm)

LCMS pic at 4.85 min: HRMS (TOF MS ES+): m/z calcd for $C_{82}H_{100}N_{16}O_8$ $[M+2H]^{2+}$: 718.39495 found: 718.3951 (0.18 ppm)

LCMS pic at 4.94 min: HRMS (TOF MS ES+): m/z calcd for $C_{82}H_{100}N_{16}O_8$ $[M+2H]^{2+}$: 718.39495 found: 718.395 (0.01 ppm)

LCMS pic at 5.12 min: HRMS (TOF MS ES+): m/z calcd for $C_{82}H_{100}N_{16}O_8$ $[M+2H]^{2+}$: 718.39495 found: 718.395 (0.09 ppm)

LCMS pic at 5.24 min: HRMS (TOF MS ES+): m/z calcd for $C_{87}H_{110}N_{16}O_6$ $[M+2H]^{2+}$: 737.43916 found: 737.4392 (0.06 ppm)

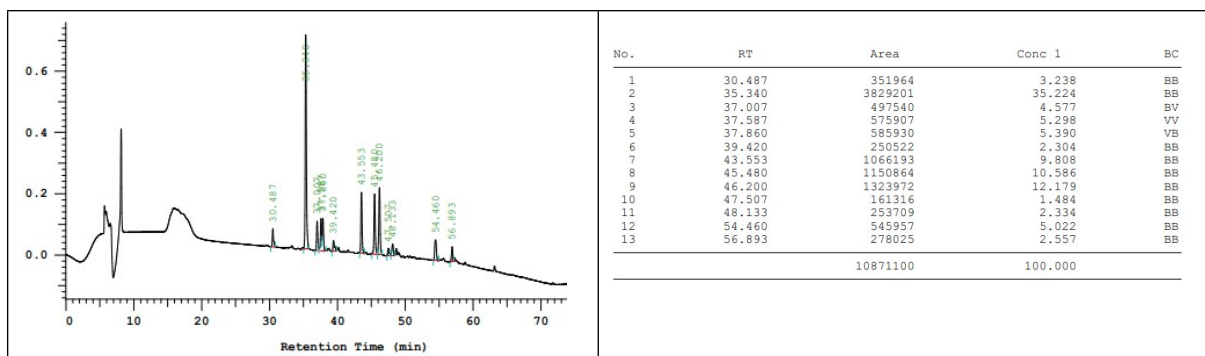
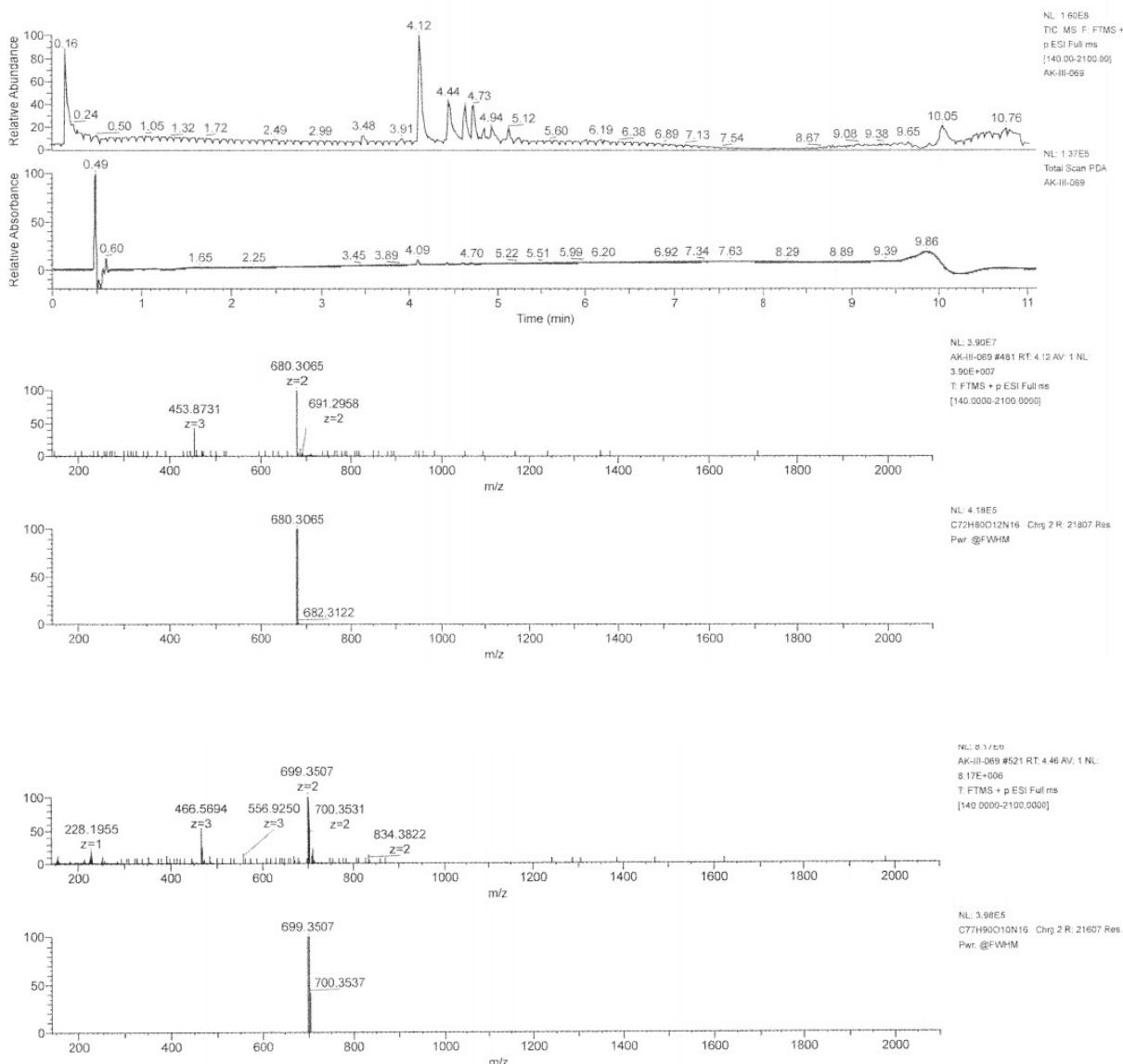
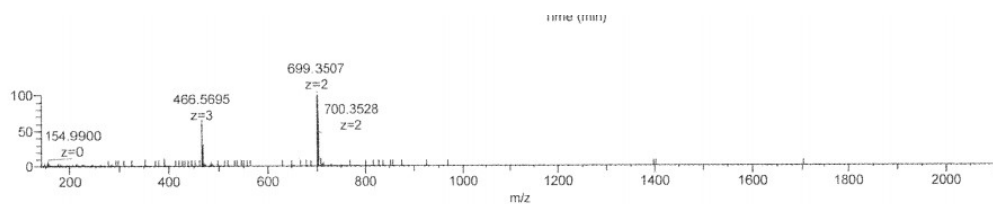
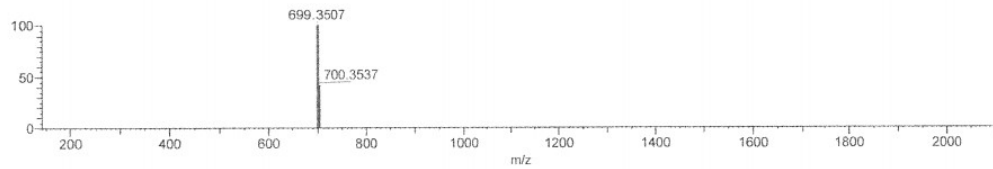


Figure S66 HPLC chromatogram of purified III-6(b,c)(2,4,6).

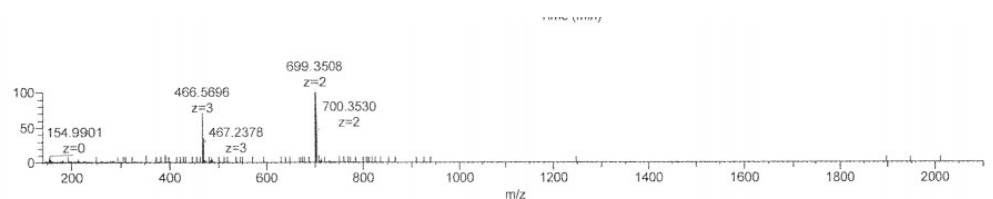




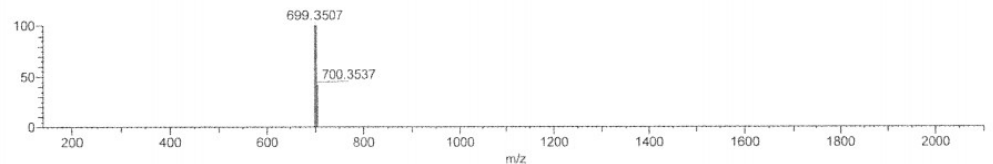
NL: 1.05E7
AK-III-069 #541 RT: 4.63 AV: 1 NL:
1.05E+007
T: FTMS + p ESI Full ms
[140.0000-2100.0000]



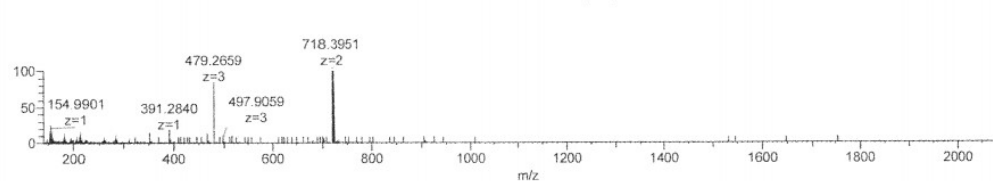
NL: 3.98E5
C77H90O10N16 Chg 2 R: 21707 Res.
Pwr: @FWHM



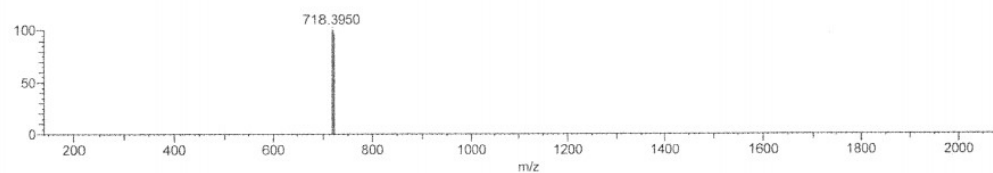
NL: 1.02E7
AK-III-069 #553 RT: 4.73 AV: 1 NL:
1.02E+007
T: FTMS + p ESI Full ms
[140.0000-2100.0000]



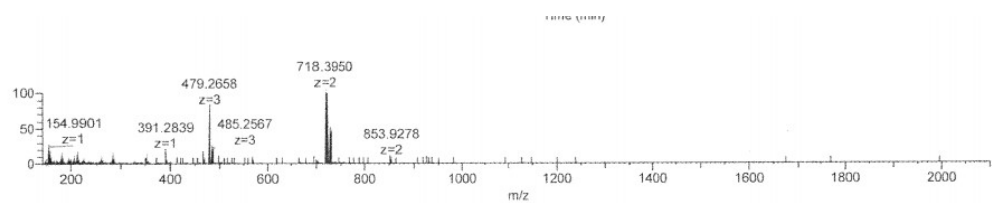
NL: 3.98E5
C77H90O10N16 Chg 2 R: 21907 Res.
Pwr: @FWHM



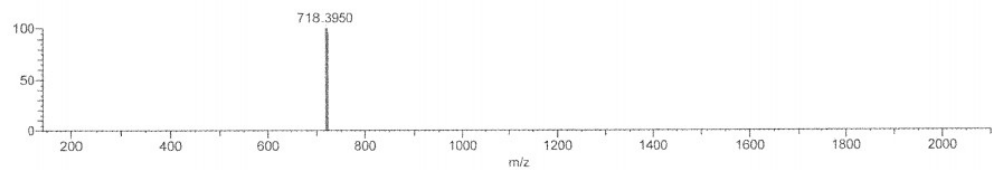
NL: 3.11E6
AK-III-069 #567 RT: 4.85 AV: 1 NL:
3.11E+006
T: FTMS + p ESI Full ms
[140.0000-2100.0000]



NL: 3.78E5
C82H100O8N16 Chg 2 R: 21307 Res.
Pwr: @FWHM



NL: 2.58E6
AK-III-069 #577 RT: 4.94 AV: 1 NL:
2.58E+006
T: FTMS + p ESI Full ms
[140.0000-2100.0000]



NL: 3.78E5
C82H100O8N16 Chg 2 R: 21307 Res.
Pwr: @FWHM

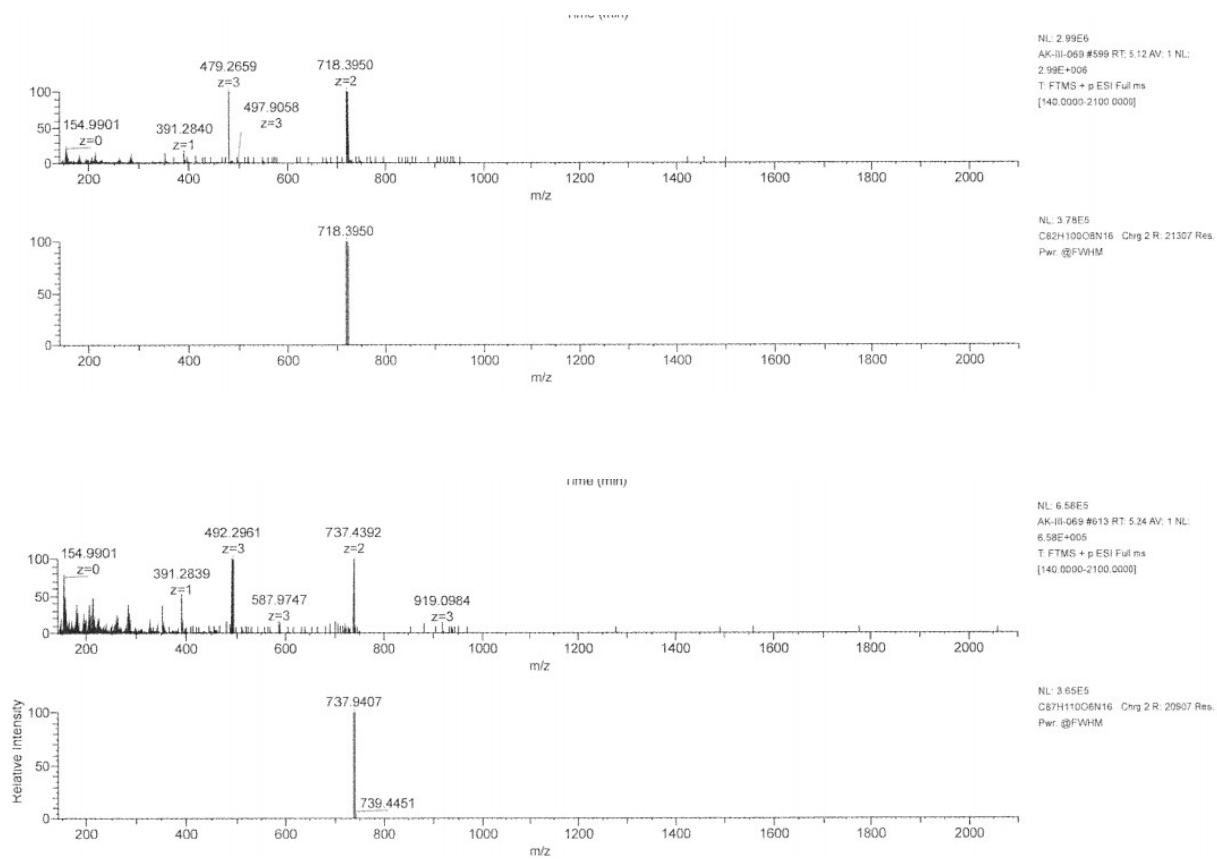
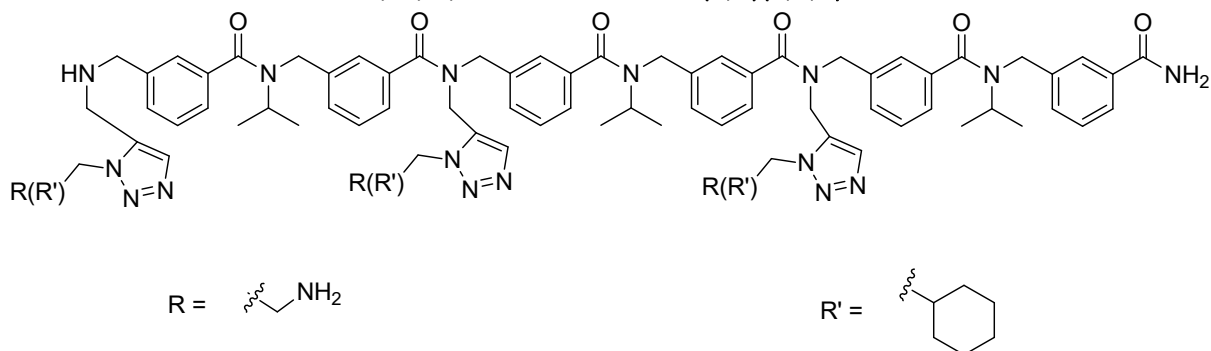


Figure S67 LCMS spectra of III-6(b,c)(2,4,6).

5.3.3- meta-arylopeptoid hexamer, III-6(b,d)(2,4,6).



Hexamer III-6(b,d)(2,4,6) was synthesised according general procedure A then general procedure B using 100 mg of RA resin (0.054 mmol)

$m_{\text{crude}} = 74$ mg (purity 81%), crude yield 88%

$m_{\text{pure}} = 62$ mg (purity 96%), isolated yield 82%

LCMS pic at 3.64 min: HRMS (TOF MS ES+): m/z calcd for $C_{72}H_{90}N_{19}O_6$ $[M+3H]^{3+}$: 438.91017 found: 438.9103 (0.39 ppm)

LCMS pic at 3.8 min: HRMS (TOF MS ES+): m/z calcd for $C_{77}H_{97}N_{18}O_6$ $[M+3H]^{3+}$: 456.59407 found: 456.5945 (1.04 ppm)

LCMS pic at 4.26 min: HRMS (TOF MS ES+): m/z calcd for $C_{82}H_{103}N_{17}O_6$ $[M+2H]^{2+}$: 710.91331 found: 710.9135 (0.2 ppm)

LCMS pic at 4.51 min: HRMS (TOF MS ES+): m/z calcd for $C_{82}H_{103}N_{17}O_6$ $[M+2H]^{2+}$: 710.91331 found: 710.9135 (0.2 ppm)

LCMS pic at 4.09 min: HRMS (TOF MS ES+): m/z calcd for $C_{82}H_{91}N_{17}O_6$ $[M+2H]^{2+}$: 704.86636 found: 704.8668 (0.56 ppm)

LCMS pic at 4.66 min: HRMS (TOF MS ES+): m/z calcd for $C_{87}H_{110}N_{16}O_6$ $[M+2H]^{2+}$: 737.43916 found: 737.4396 (0.64 ppm)

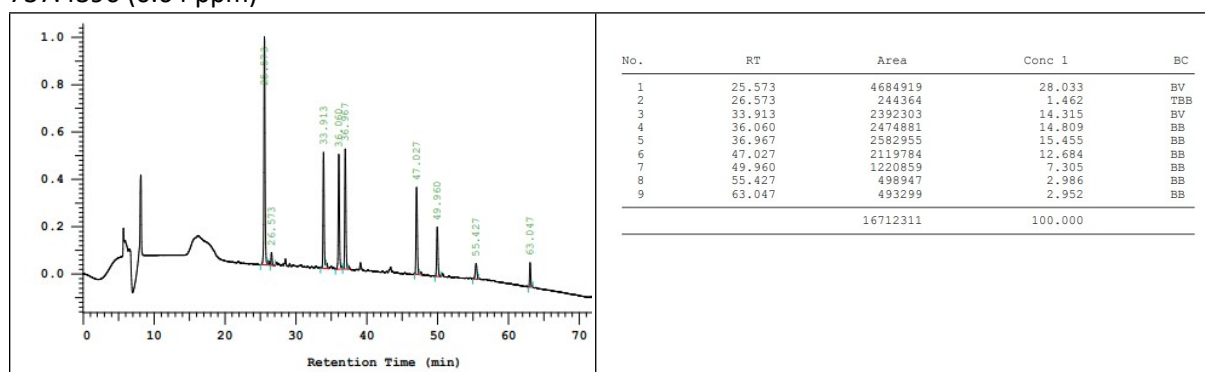
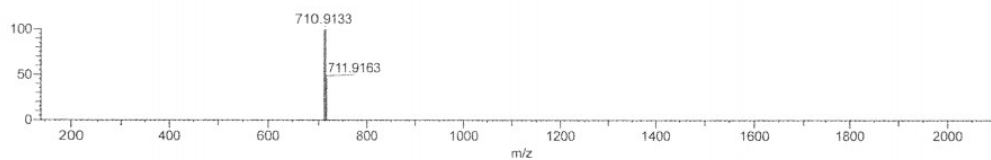
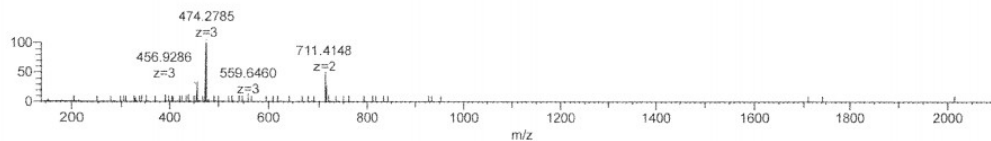
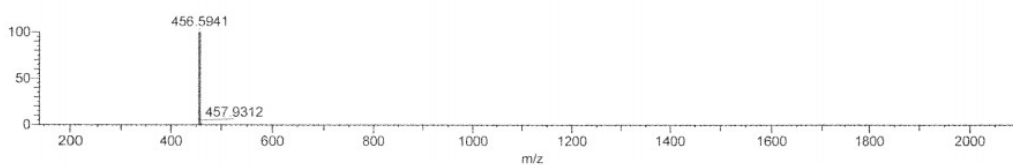
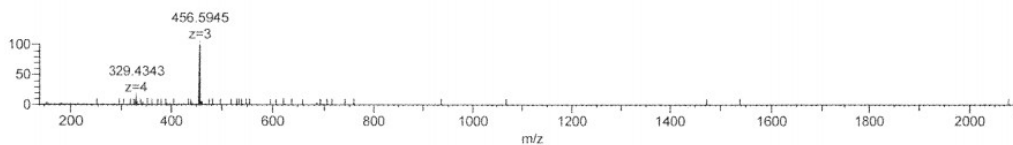
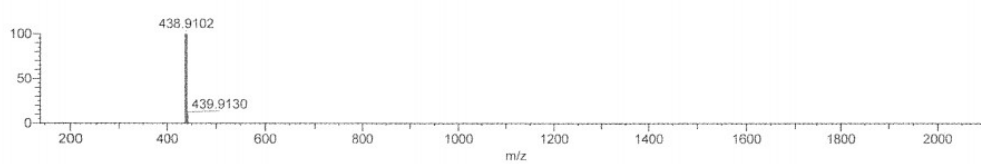
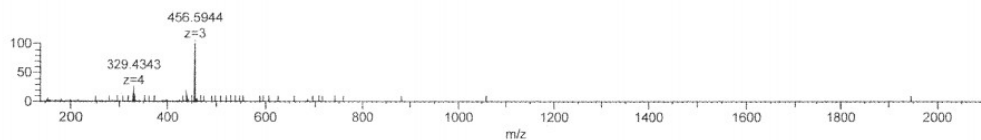
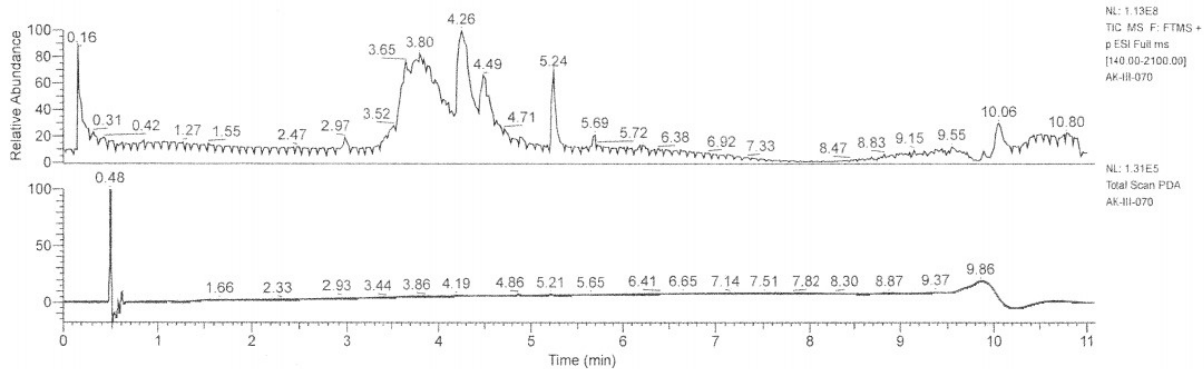


Figure S68 HPLC chromatogram of purified III-6(b,d)(2,4,6)



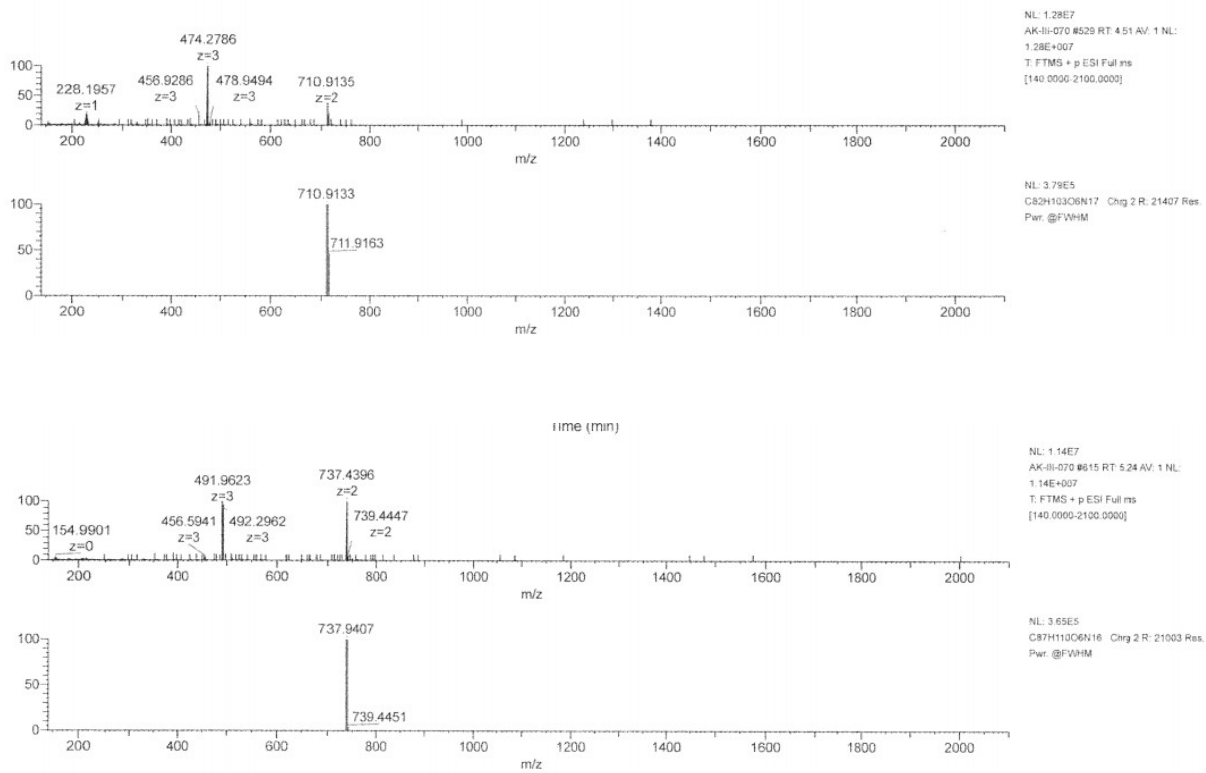
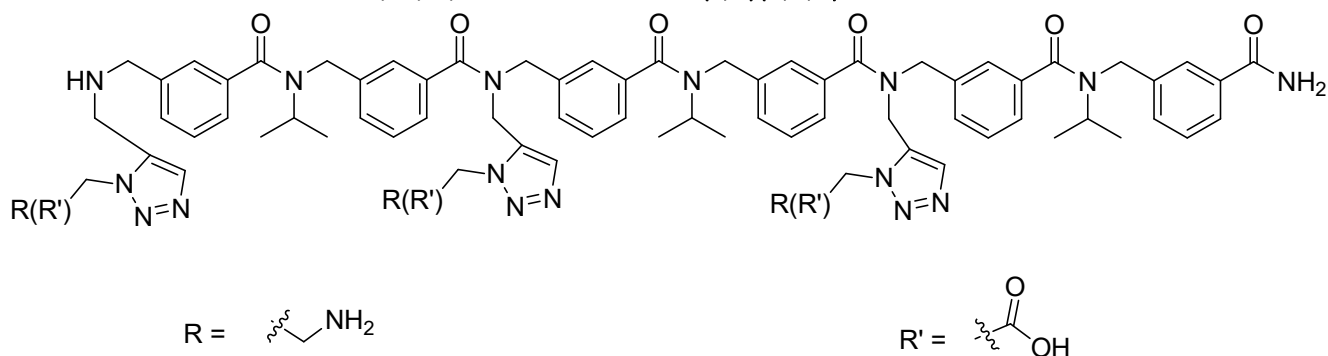


Figure S69 LCMS spectra of III-6(b,d)(2,4,6).

5.3.4- meta-arylopeptoid hexamer, III-6(c,d)(2,4,6).



Hexamer III-6(c,d)(2,4,6) was synthesised according general procedure A then general procedure B using 50 mg of RA resin (0.031 mmol)

$m_{\text{crude}} = 46 \text{ mg}$ (purity 86%), crude yield 110%

$m_{\text{pure}} = 33.8 \text{ mg}$ (purity 97.8%), isolated yield 81%

LCMS pic at 3.29 min: HRMS (TOF MS ES⁺): m/z calcd for C₇₂H₈₇N₁₈O₈ [M+3H]³⁺: 443.89793 found: 443.8988 (1.97 ppm).

LCMS pic at 3.19 min: HRMS (TOF MS ES⁺): m/z calcd for C₇₂H₈₇N₁₈O₈ [M+3H]³⁺: 443.89793; found: 443.8989 (-2.11 ppm).

LCMS pic at 3.56 min: HRMS (TOF MS ES⁺): m/z calcd C₇₂H₈₃N₁₇O₁₀ [M+2H]²⁺: 672.82489; found: 672.8253 (0.63 ppm).

LCMS pic at 4.13 min: HRMS (TOF MS ES⁺): m/z C₇₂H₈₀N₁₆O₁₂ [M+2H]²⁺: 680.30653; found: 680.3075 (1.42 ppm).

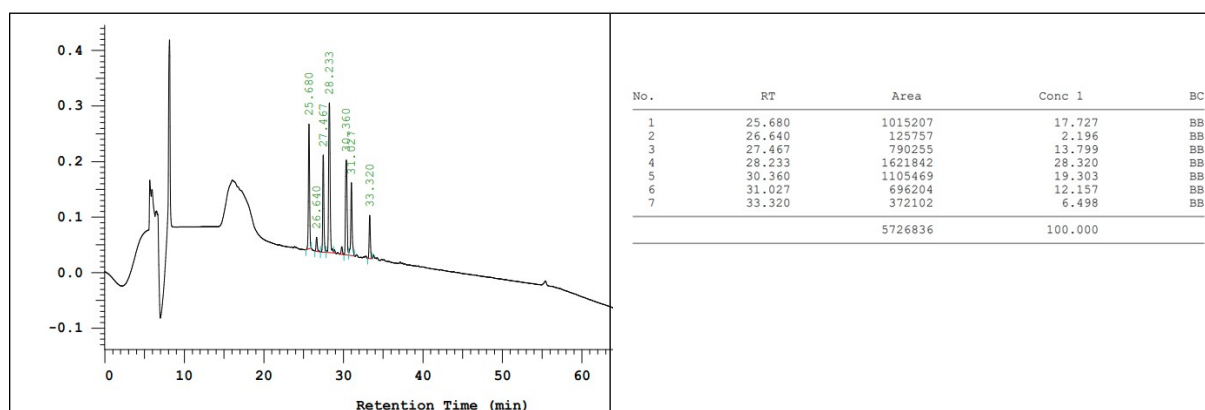


Figure S70 HPLC chromatogram of purified III-6(c,d)(2,4,6).

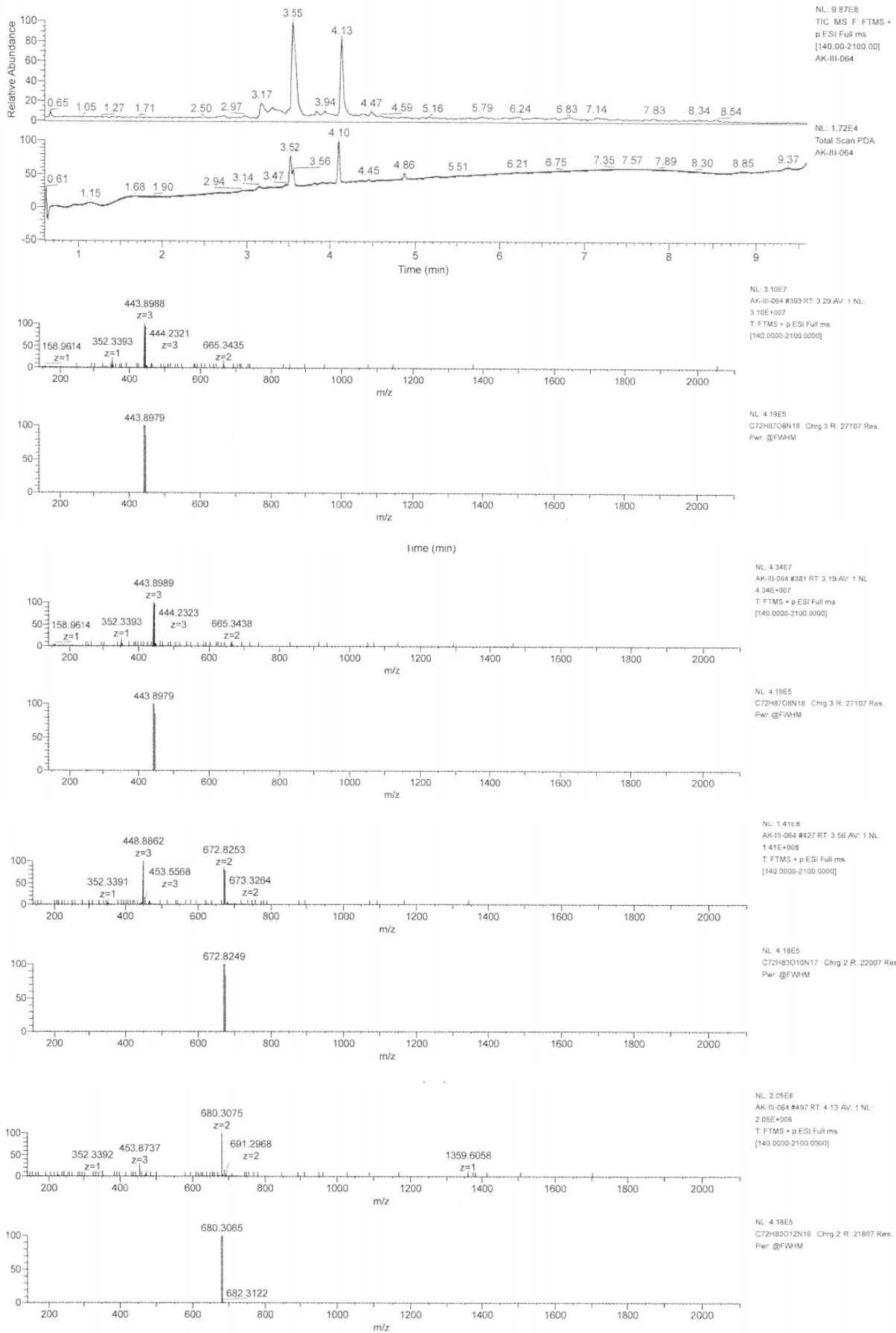
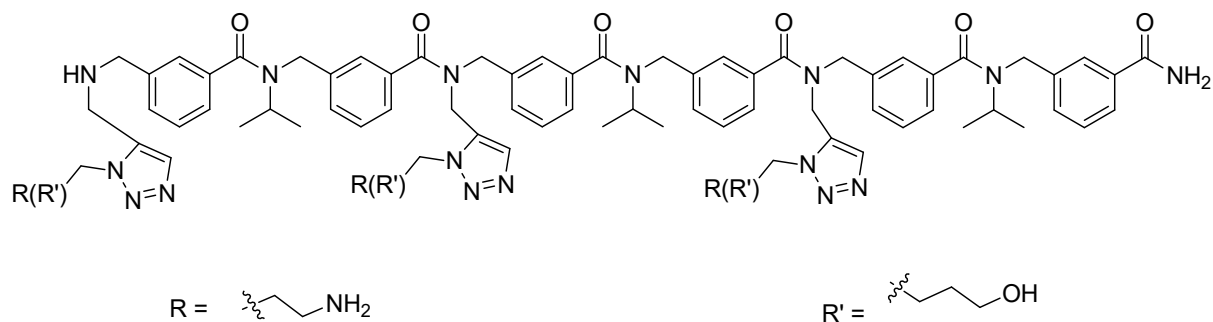


Figure S71 LCMS spectra of III-6(c,d)(2,4,6).

5.3.5- Meta-arylopeptoid hexamer, III-6(d,e)(2,4,6).



Hexamer III-6(d,e)(2,4,6) was synthesised according general procedure A then general procedure B using 50 mg of RA resin (0.031 mmol)

$m_{\text{crude}} = 46$ mg (purity 89%), crude yield 111%

$m_{\text{pure}} = 33.8$ mg (purity 98%), isolated yield 81%

LCMS pic at 2.77 min: HRMS (TOF MS ES+): m/z calcd for $C_{72}H_{89}N_{16}O_6$ $[M+2H]^{2+}$: 657.86161 found: 657.8613 (-0.52 ppm)

LCMS pic at 2.89 min: HRMS (TOF MS ES+): m/z calcd for $C_{73}H_{90}N_{18}O_7$ $[M+2H]^{2+}$: 665.36145 found: 665.3611 (-0.54 ppm)

LCMS pic at 3.18 min: HRMS (TOF MS ES+): m/z calcd for $C_{74}H_{91}N_{17}O_8$ $[M+2H]^{2+}$: 672.86128 found: 672.8617 (0.62 ppm)

LCMS pic at 3.58 min: HRMS (TOF MS ES+): m/z calcd for $C_{75}H_{92}N_{16}O_9$ $[M+2H]^{2+}$: 680.36111 found: 680.3611 (0.05 ppm)



Figure S72 HPLC chromatogram of purified III-6(d,e)(2,4,6).

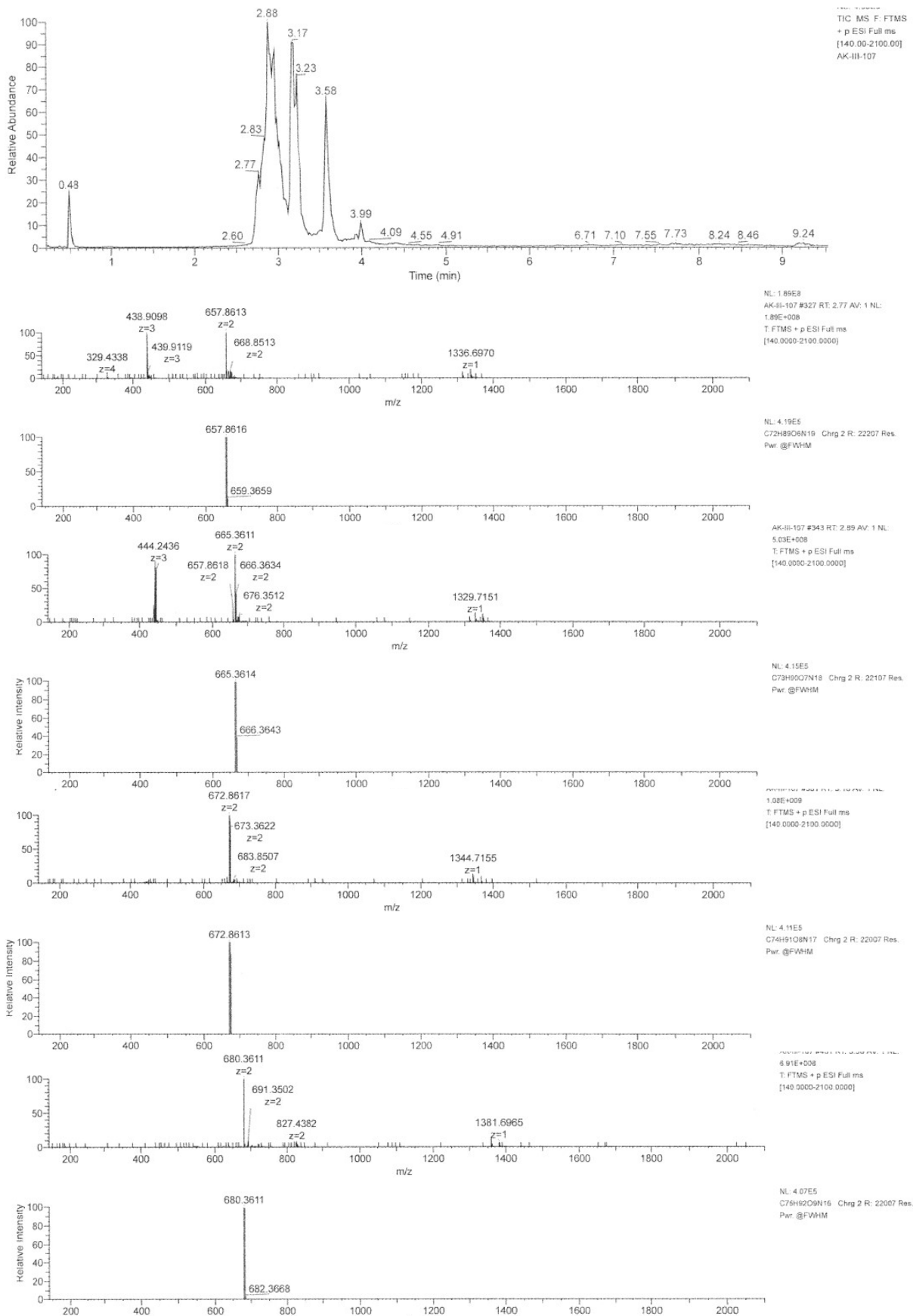
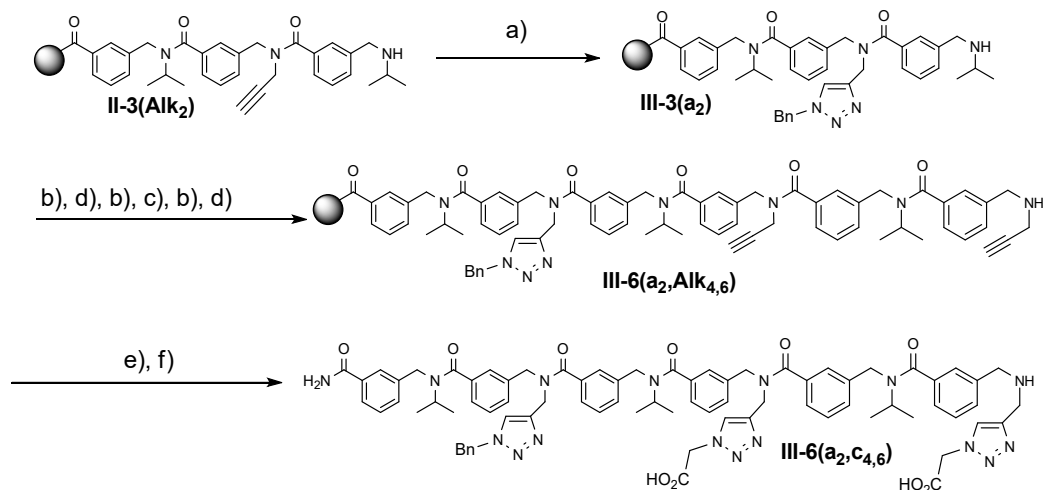


Figure S74 LCMS spectra of III-6(d,e)(2,4,6).

6-Sequential click to access regioisomers

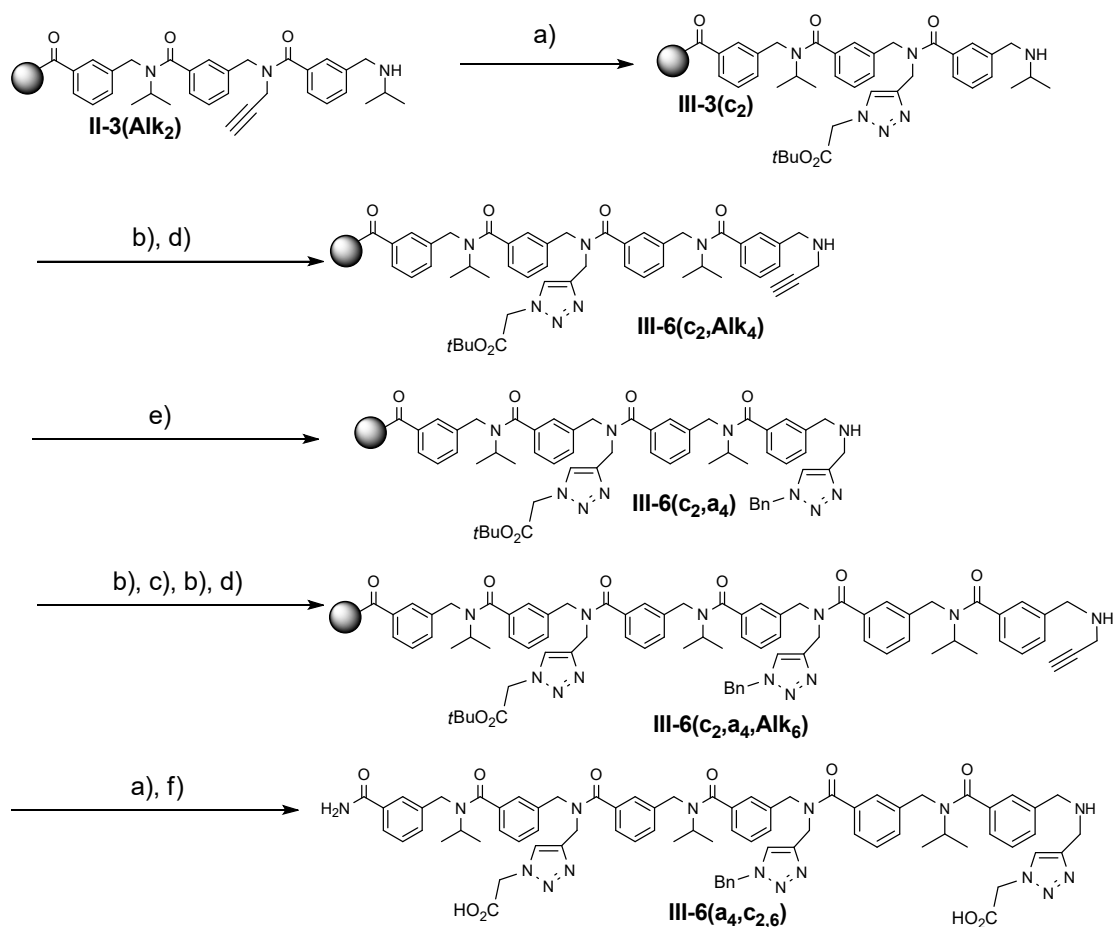
6.1- Synthetic paths

6.1.1. Synthetic path for III-6(a₂,c_{4,6})



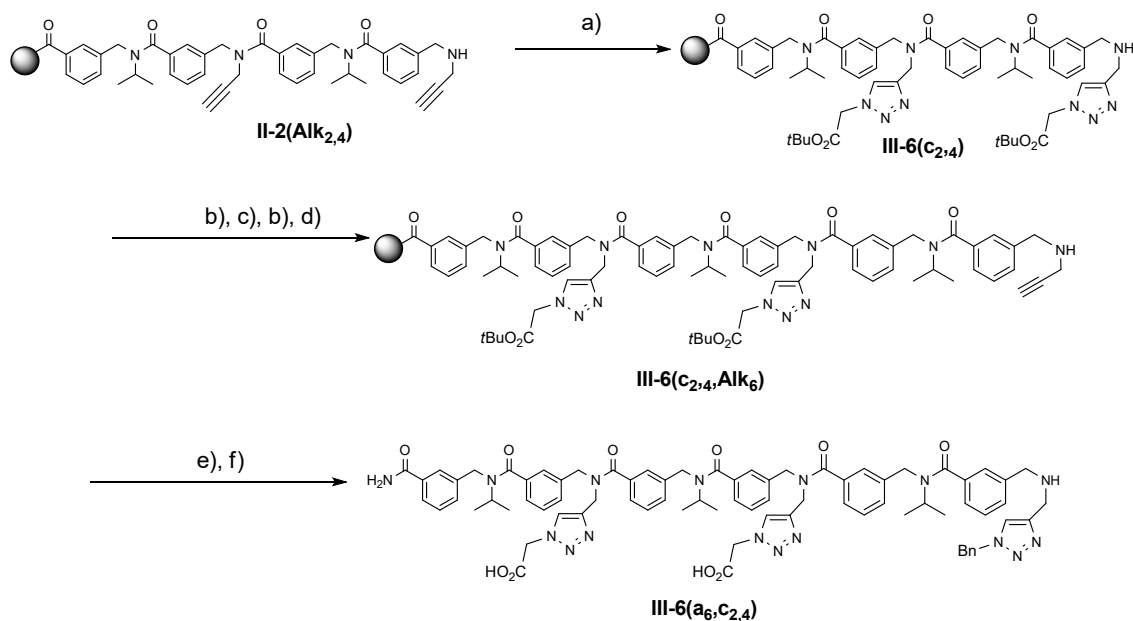
- a) DCM/MeOH ($v/v=8/2$), Cata (5mol-%), **1a**, 50°C. b) 3-(chloromethyl)-benzoyl chloride, DIPEA, DCM, RT. c) *isopropyl* amine, dmsO, 50°C. d) Propargyl amine, dmsO, 50°C. e) DCM/MeOH ($v/v=8/2$), Cata (5mol-%), **1c**, 50°C. f) TFA/H₂O/*tri isopropyl* silane (95/2.5/2.5).

6.1.2. Synthetic path for III-6(a₄,c₂,6)



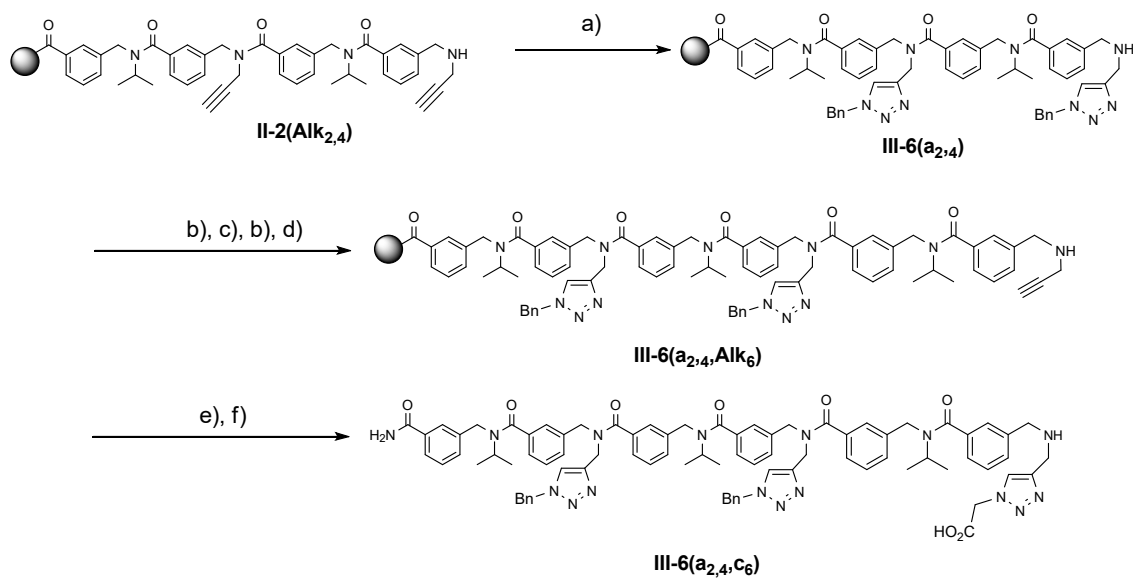
- a) DCM/MeOH (v/v=8/2), Cata (5mol-%), **1c**, 50°C. b) 3-(chloromethyl)-benzoyl chloride, DIPEA, DCM, RT. c) *i*sopropyl amine, dmso, 50°C. d) Propargyl amine, dmso, 50°C. e) DCM/MeOH (v/v=8/2), Cata (5mol-%), **1a**, 50°C. f) TFA/H₂O/tri *i*sopropyl silane (95/2.5/2.5).

6.1.3. Synthetic path for III-6-(a₆,c_{2,4})



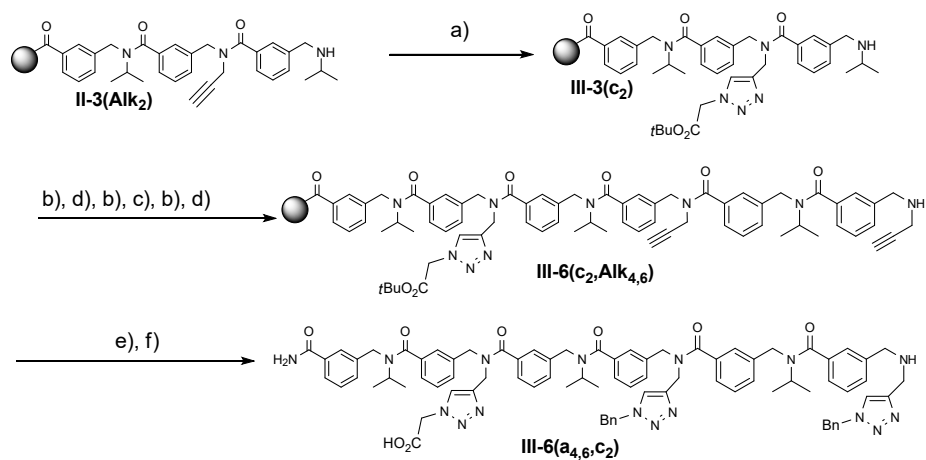
- a) DCM/MeOH ($v/v=8/2$), Cata (5mol-%), **1c**, 50°C. b) 3-(chloromethyl)-benzoyl chloride, DIPEA, DCM, RT. c) *i*sopropyl amine, dmsO, 50°C. d) Propargyl amine, dmsO, 50°C. e) DCM/MeOH ($v/v=8/2$), Cata (5mol-%), **1a**, 50°C. f) TFA/H₂O/*tri isopropyl silane* (95/2.5/2.5).

6.1.4. Synthetic path for III-6-(a_{2,4},c₆)



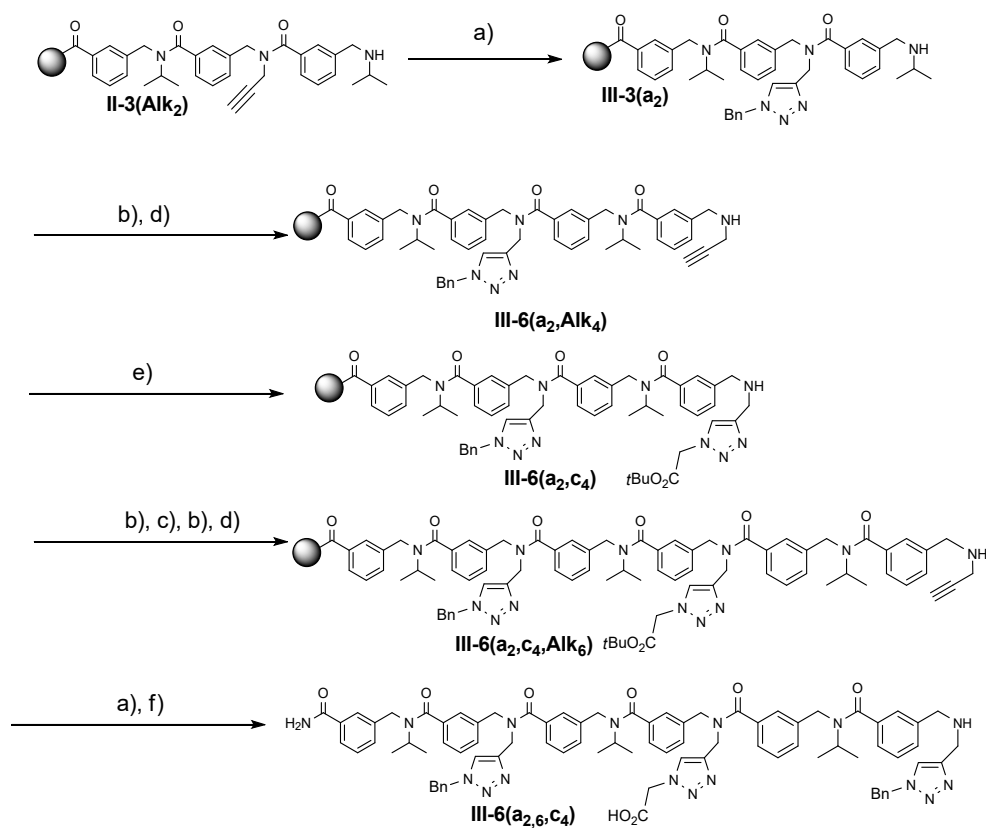
a) DCM/MeOH ($v/v=8/2$), Cata (5mol-%), **1a**, 50°C. b) 3-(chloromethyl)-benzoyl chloride, DIPEA, DCM, RT. c) *isopropyl* amine, dmsO, 50°C. d) Propargyl amine, dmsO, 50°C. e) DCM/MeOH ($v/v=8/2$), Cata (5mol-%), **1c**, 50°C. f) TFA/H₂O/*tri isopropyl* silane (95/2.5/2.5).

6.1.5- Synthetic path for III-6(a_{4,6},c₂)



a) DCM/MeOH ($v/v=8/2$), Cata (5mol-%), **1c**, 50°C. b) 3-(chloromethyl)-benzoyl chloride, DIPEA, DCM, RT. c) *isopropyl* amine, dmsO, 50°C. d) Propargyl amine, dmsO, 50°C. e) DCM/MeOH ($v/v=8/2$), Cata (5mol-%), **1a**, 50°C. f) TFA/H₂O/*tri isopropyl silane* (95/2.5/2.5).

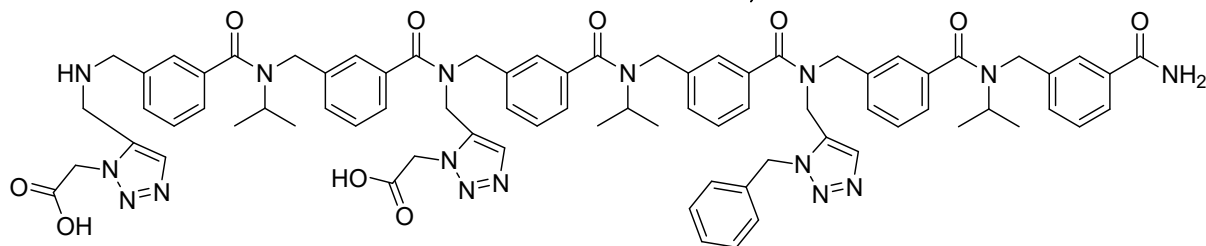
6.1.6. Synthetic path for III-6-(a₂,c₄)



a) DCM/MeOH (v/v=8/2), Cata (5mol-%), **1a**, 50°C. b) 3-(chloromethyl)-benzoyl chloride, DIPEA, DCM, RT. c) *isopropyl* amine, dmsO, 50°C. d) Propargyl amine, dmsO, 50°C. e) DCM/MeOH (v/v=8/2), Cata (5mol-%), **1c**, 50°C. f) TFA/H₂O/tri *isopropyl* silane (95/2.5/2.5).

6.2- Characterisation data

6.2.1- Synthesis of meta-arylopeptoid hexamer, III-6-(a₂,c_{4,6}):



$m_{\text{crude}} = 118 \text{ mg}$ (purity 81%), crude yield 157%

$m_{\text{pure}} = 63 \text{ mg}$, (purity 85%), isolated yield 84%

HRMS (TOF MS ES⁺): m/z calcd for C₇₇H₈₃N₁₆O₁₀ [M+H]⁺: 1391.64726 found: 1391.6487 (1.02 ppm)

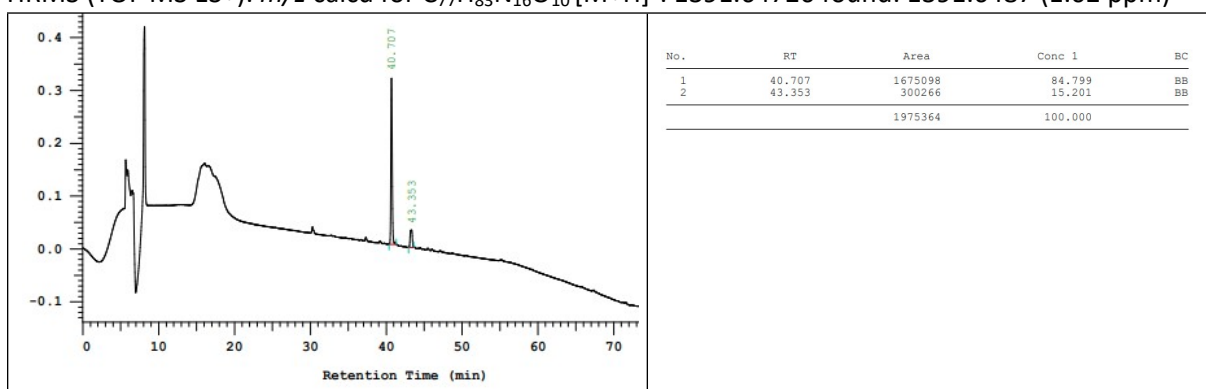


Figure S75 HPLC chromatogram of purified III-6-(a₂,c_{4,6}).

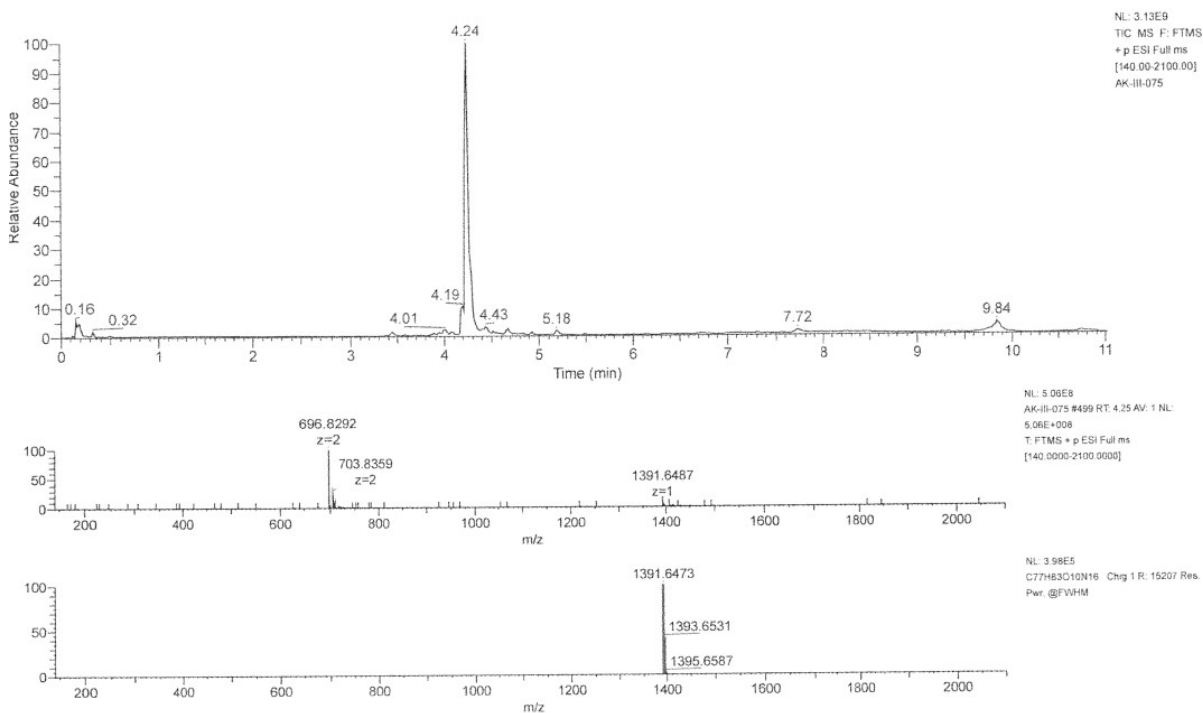
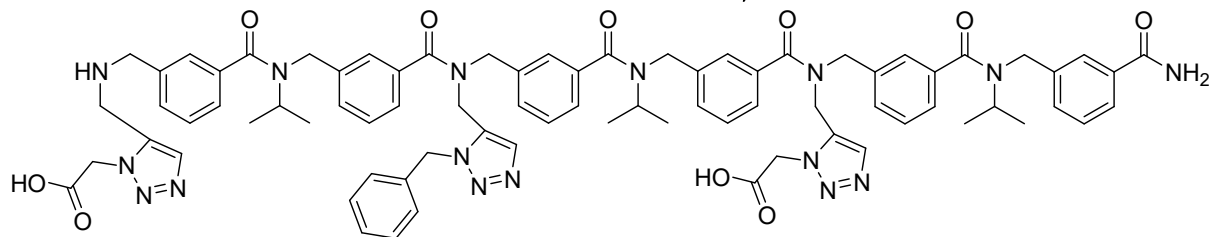


Figure S76 LCMS spectra of III-6-(a₂,c_{4,6}).

6.2.2-Synthesis of meta-arylopeptoid hexamer, III-6-(a₄c₂,6):



$m_{\text{crude}} = 109 \text{ mg}$, (Purity 85%), crude yield 145%

$m_{\text{pure}} = 70 \text{ mg}$, (Purity 97%), isolated yield 93%

HRMS (TOF MS ES+): m/z calcd for $C_{77}H_{83}N_{16}O_{10}$ [M+H]⁺: 1391.64726 found: 1391.6487 (1.02 ppm)

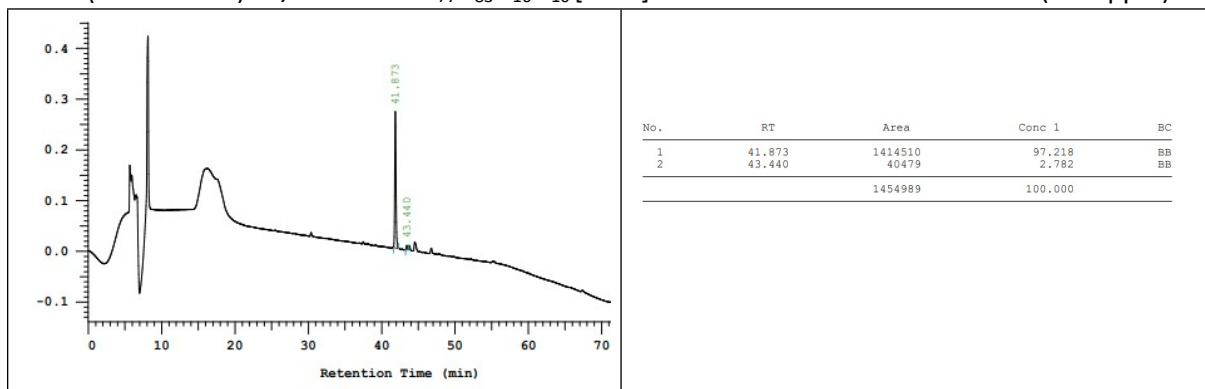


Figure S77 HPLC chromatogram of purified III-6-(a₄c₂,6).

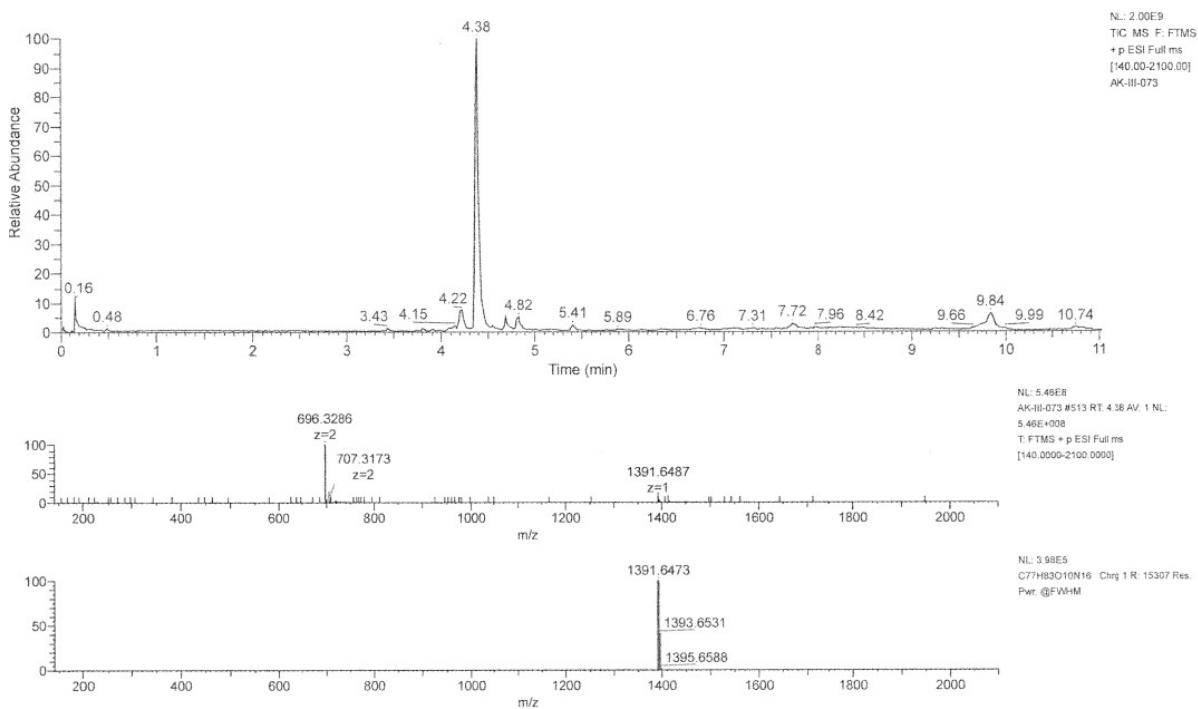
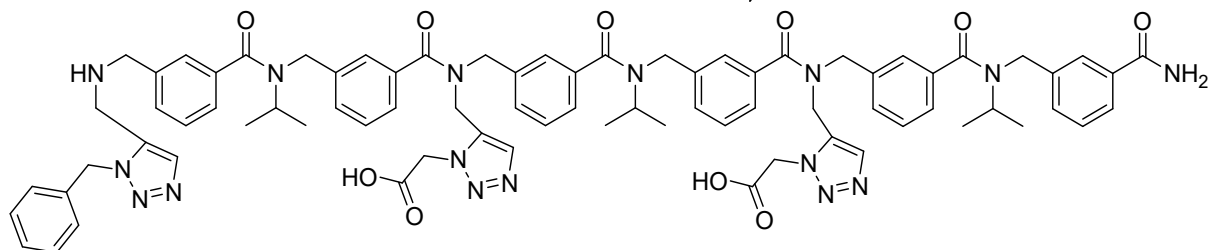


Figure S78 LCMS spectra of purified III-6-(a₄c₂,6).

6.2.3- Synthesis of meta-arylopeptoid hexamer, III-6-(a₆,c_{2,4}):



$m_{\text{crude}} = 112 \text{ mg}$, (Purity 69%), crude yield 149%

$m_{\text{pure}} = 50 \text{ mg}$, (Purity 87%), isolated yield 67%

HRMS (TOF MS ES⁺): m/z calcd for C₇₇H₈₃N₁₆O₁₀ [M+H]⁺: 1391.64726 found: 1391.6487 (1.02 ppm)

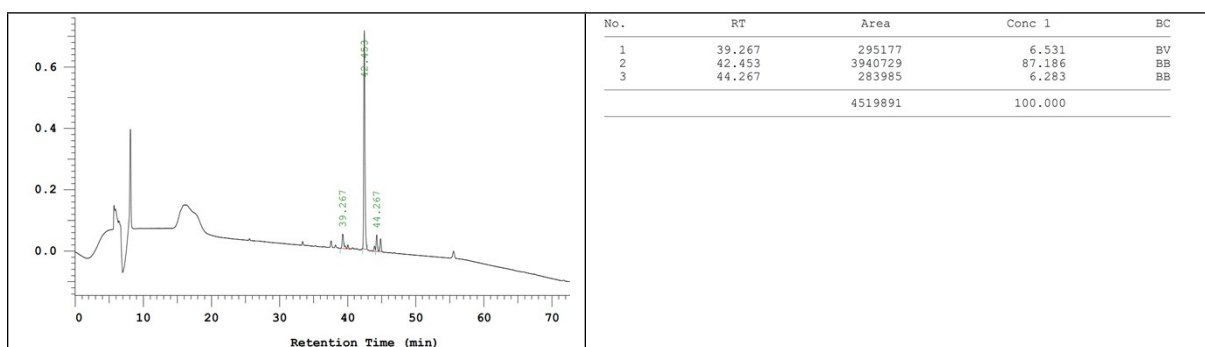


Figure S79 HPLC chromatogram of purified III-6-(a₆,c_{2,4}).

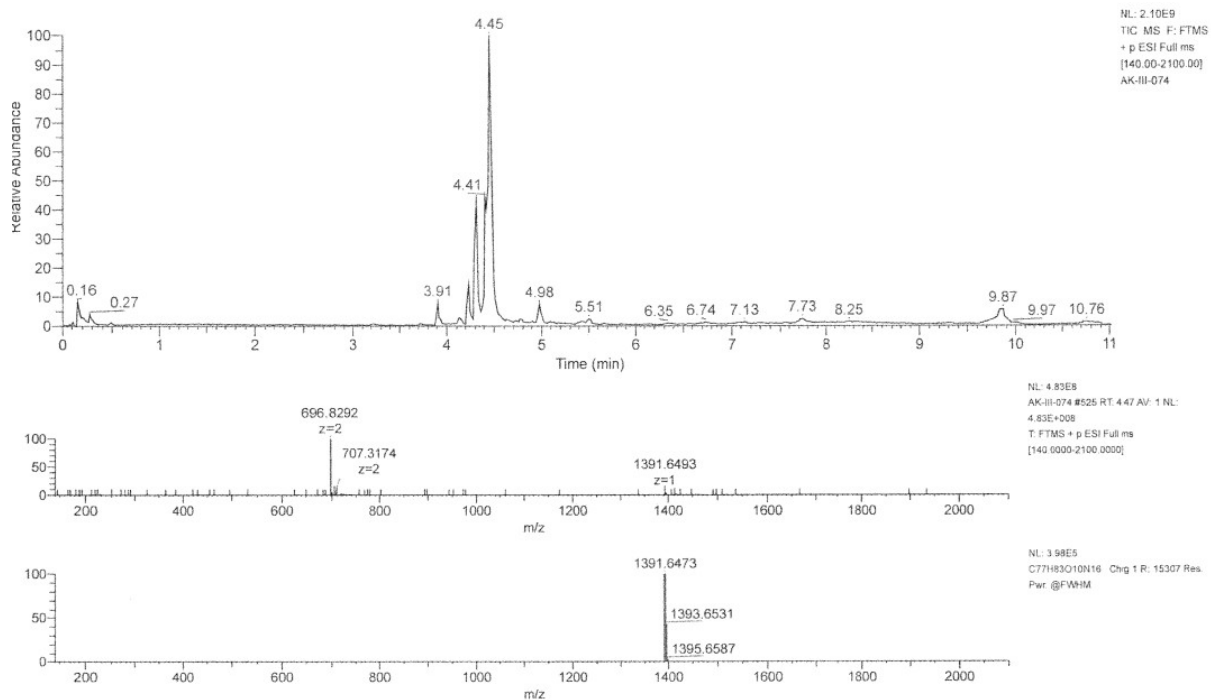
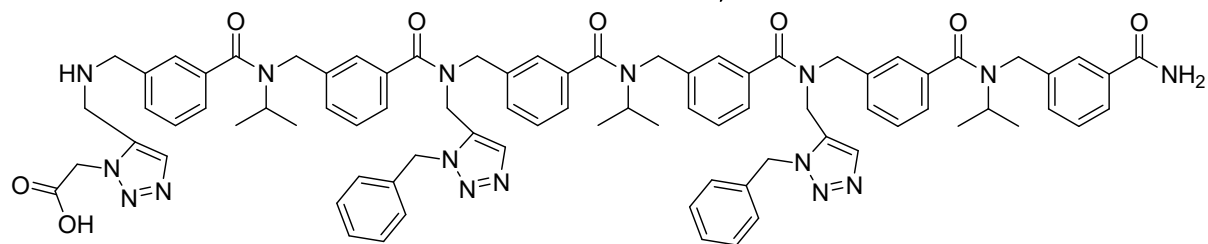


Figure S80 LCMS spectra of III-6-(a₆,c_{2,4}).

6.2.4- Synthesis of meta-arylopeptoid hexamer, III-6-(a_{2,4},c₆):



$m_{\text{crude}} = 23.65 \text{ mg}$, (Purity 78%), crude yield 105%

$m_{\text{pure}} = 20.1 \text{ mg}$, (purity 83%), isolated yield 90%.

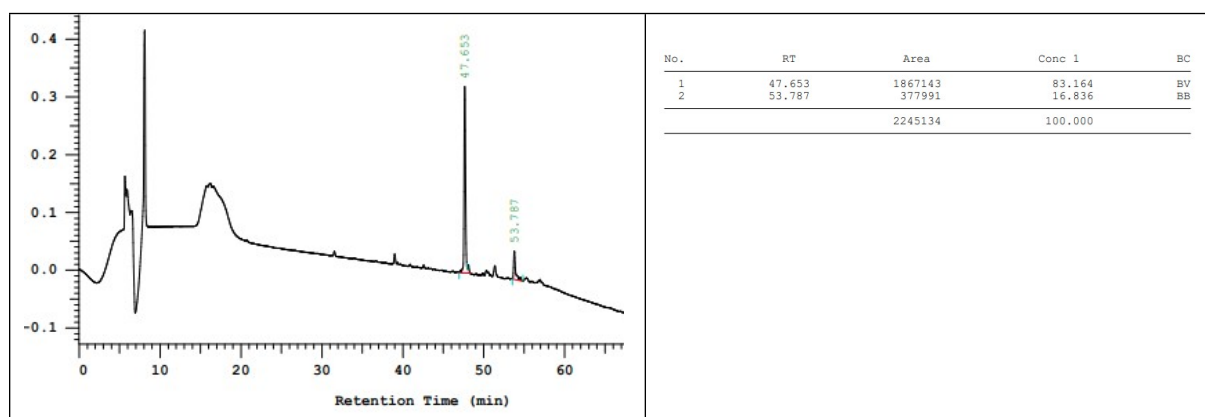
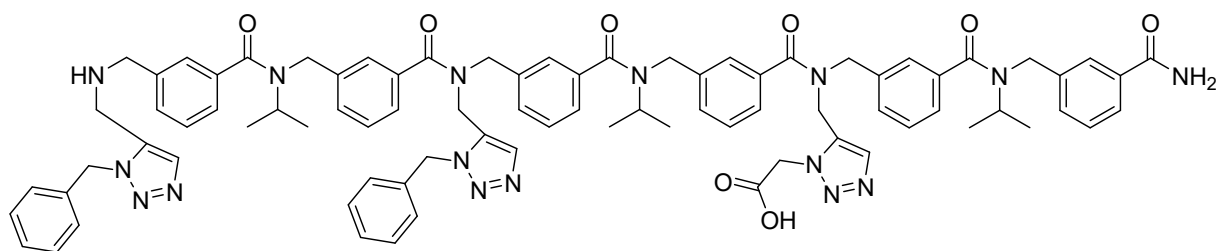


Figure S81 HPLC chromatogram of purified III-6-(a_{2,4},c₆).

6.2.5- Synthesis of meta-arylopeptoid hexamer, III-6-(a_{4,6},c₂):



$m_{\text{crude}} = 24.6 \text{ mg}$, (purity 82%), crude yield 109 %

$m_{\text{pure}} = 18.6 \text{ mg}$ (purity 92%), isolated yield 83%

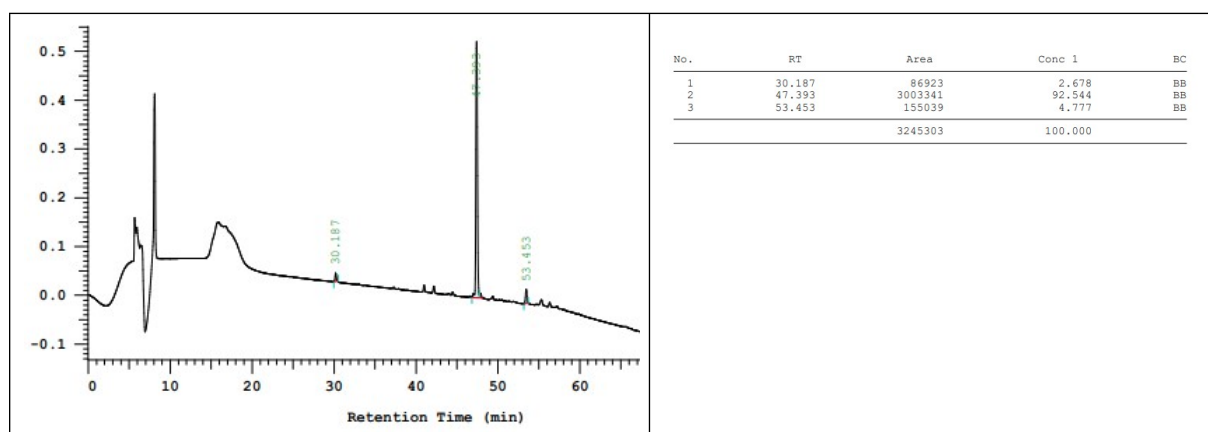
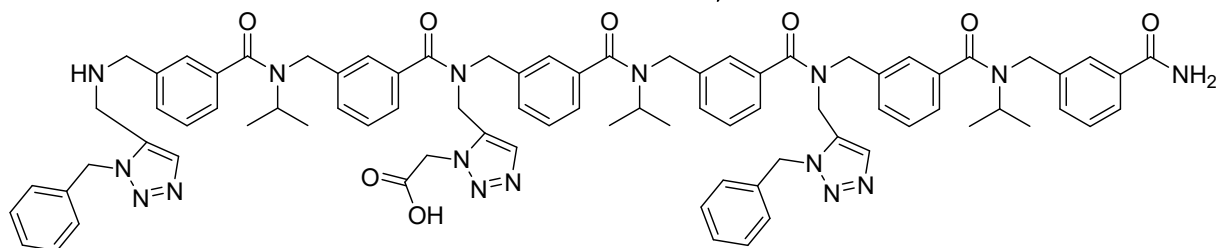


Figure S82 HPLC chromatogram of purified III-6-(a_{4,6},c₂).

6.2.6- Synthesis of meta-arylopeptoid hexamer, III-6-(a_{2,6},c₄):



m_{crude} = 25 mg (purity 87%), crude yield 111%

m_{pure} = 19 mg (purity 93%), isolated yield 84%

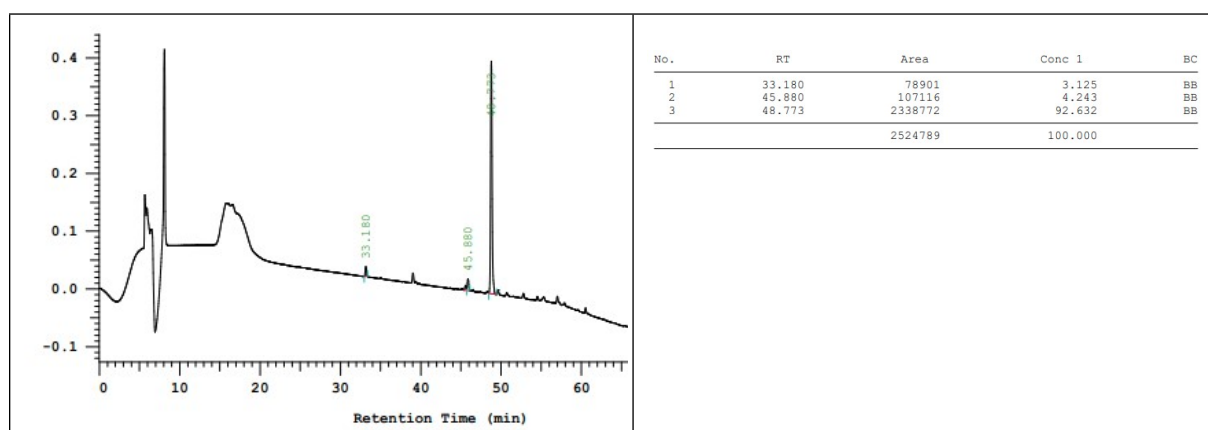
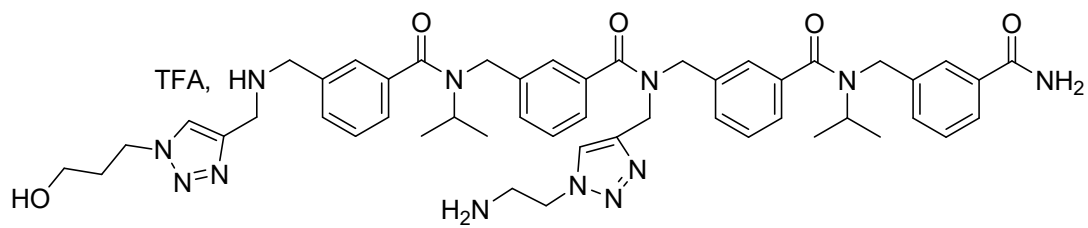


Figure S83 HPLC chromatogram of purified III-6-(a_{2,6},c₄)

6.2.7- Synthesis of meta-arylopeptoid hexamer, III-4(d₂,e₄):



$m_{\text{crude}} = 16.7 \text{ mg}$ (purity 87%), crude yield 117%

$m_{\text{pure}} = 11.6 \text{ mg}$ (purity 92%), isolated yield 82%

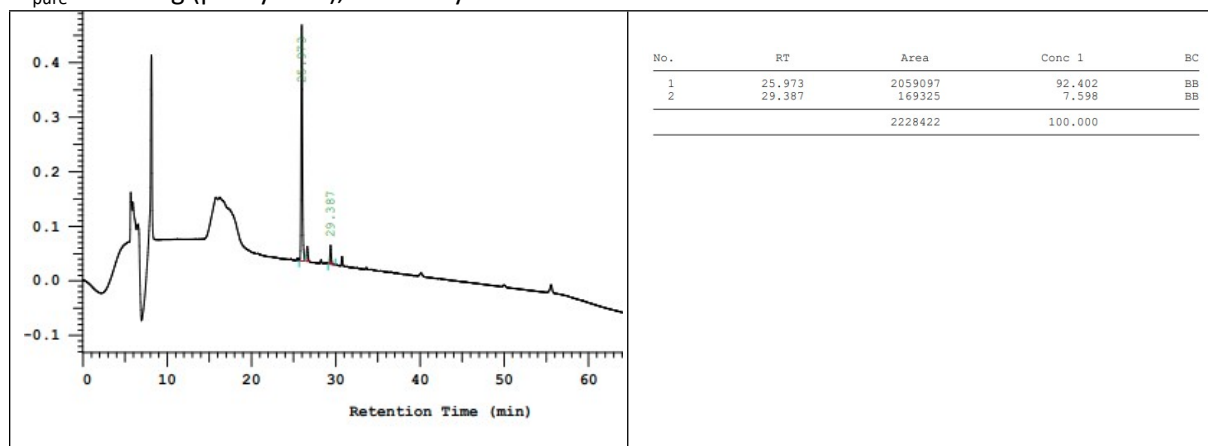
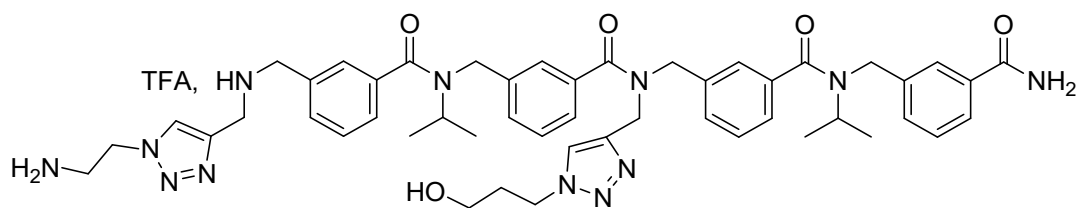


Figure S84 HPLC chromatogram of purified III-4(d₂,e₄).

6.2.8- Synthesis of meta-arylopeptoid Hexamer, III-4(e₂,d₄):



$m_{\text{crude}} = 17.2 \text{ mg}$, (purity 83%) crude yield 121%

$m_{\text{pure}} = 11.2 \text{ mg}$, (purity 87%), isolated yield 79%

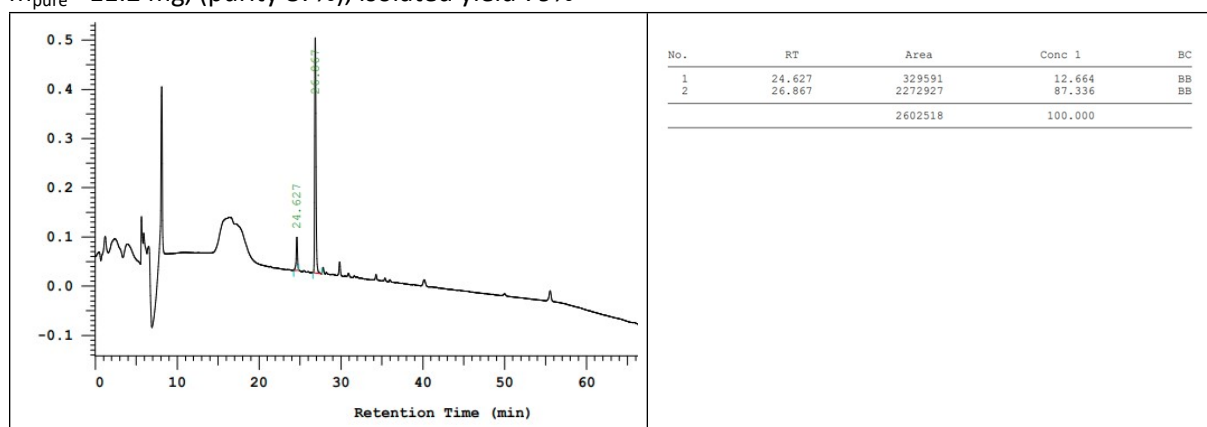


Figure S85 HPLC chromatogram of purified III-4(e₂,d₄).

7-Table of retention times.

Arylopeptoid	Retention time	Identification
III-4-(e,d)(2,4)	26.0	III-4(d₂,e₄)
	26.9	III-4(d₄,e₂)
III-6(a,c)(2,4,6)	40.8	III-6-(a₂)(c_{4,6})
	41.8	III-6-(a₄)(c_{2,6})
	42.5	III-6-(a₆)(c_{2,4})
	47.7	III-6-(c₂)(a_{4,6})
	48	III-6-(c₆)(a_{2,4})
	49.1	III-6-(c₄)(a_{2,6})

Table S1: HPLC retention time for each tetrameric and hexameric regioisomers

8-References

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