Supplementary Material (ESI) for Journal of Materials Chemistry
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Electronic supplementary information

for

Rod-Coil Copolymers from Oligo(p-benzamide) Foldamers

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Experimental

Materials
Technical solvents were purchased from Acros Organics, solvents of p. a. quality from Fisher Scientific. All chemical reagents including compounds 1 and 2 were obtained from Acros Organics and were used as received. N-Methylpyrrolidinone was dried over calcium hydride followed by distillation and storage over molecular sieve (4 Å). Deuterated solvents (DMSO-d₆ and CDCl₃) were purchased from Deutero GmbH and used as received.

Techniques
Standard ¹H and ¹³C nuclear magnetic resonance spectra were recorded at a frequency of 300 MHz (75 MHz for ¹³C) on a Bruker AC 300. For two dimensional COSY and NOESY experiments a Bruker AMX 400 was used working at 400 MHz. Infrared spectra were recorded on a Nicolet 5 DXC FT-IR spectrometer. X-ray crystal structures were obtained on a Turbo CAD 4. The RP HPLC analysis was performed on a HP 1090 Liquid Chromatograph of Hewlett Packard by using a PerfectSil column (MZ Analysentechnik, Mainz, Germany, 250 x 4.0 mm; 120 ODS-2 5 μm). The samples were eluted with an acetonitrile/water gradient that started from 10% acetonitrile rising to 90% over a period of 35 min. Both solvents were buffered with 0.1% TFA. UV-detection was performed at 254 nm. Melting points were recorded on a FP 62 Mettler Toledo in a capillary tube and are uncorrected. Field desorption mass spectra were measured on a Finnigan MAT 95 and ESI mass spectra on a
Micromass Q-TOF Ultima 3. Gel permeation chromatography with chloroform was performed on an instrument consisting of a Waters 717 plus auto sampler, a TSP Spectra Series P 100 pump and a set of three PSS SDV columns (10^6/10^5/10^4 g/mol for high molecular masses, 10^4/10^3/10^2 g/mol for low molecular masses). Signal detection occurred by use of a TSP Spectra System UV 2000 (UV 254 nm) and a Wyatt Optilab DSP (refractive index). For measurements in DMF containing 1 g/L of lithium bromide, an Agilent 1100 Series was used as an integrated instrument including a PSS Gral column (10^6/10^5/10^4 g/mol), a UV (254 nm) and RI detector. Calibration was done using poly(styrene) standards provided by Polymer Standards Service. MALDI-TOF mass spectra were recorded on a Kratos Axima CFR in linear, positive mode using dithranol or CHCA as matrix.

A Philips EM 420 transmission electron microscope using a LaB₆ cathode at an acceleration voltage of 120 kV was used to obtain TEM-images. TEM grids (carbon film on copper, 300 mesh) were obtained from Electron Microscopy Sciences, Hatfield, PA, USA. For cryo-TEM Quantifoil R1.2/1.3 copper grids were used. AFM measurements were performed as previously reported.

**Synthesis of 4-(2,4-Dimethoxybenzylamino)benzoic acid, 4**

4-Aminobenzoic acid (80 g; 0.583 mol) and 2,4-dimethoxybenzaldehyde (97 g; 0.584 mol) were suspended in toluene (1 L) and refluxed under Dean-Stark conditions until ca. 11 ml of water had been removed. The solvent was removed under reduced pressure and the yellow solid (3) dissolved in THF (ca. 4 L). Sodium borohydride (48 g; 1.27 mol) was added in small portions while stirring and cooling with an ice-bath. The colour of the reaction mixture changed from yellow to colourless over a period of 72h. Water was added until hydrogen formation could no longer be observed and all NaBH₄ was quenched. THF was removed under reduced pressure and the aqueous phase neutralized with HCl (1 M). The colourless precipitate was recovered by filtration and dried under vacuum at 40°C to yield 4-(2,4-dimethoxybenzylamino)benzoic acid (83.32 g; 50 %).

mp: 185-187 ºC.

\[^1^1^1\]H-NMR: δ (300 MHz, DMSO-d₆) 3.73 (s, 3 H); 3.81 (s, 3 H); 4.18 (d, J = 5.52 Hz, 2 H); 6.46 (dd, J₁ = 8.09 Hz, J₂ = 2.39 Hz, 1 H); 6.54 – 6.57 (m, 3 H); 6.76 (t, 1 H); 7.10 (d, J = 8.09 Hz, 1 H); 7.63 (d, J = 8.82 Hz, 2 H).

**Synthesis of N-(2,4-Dimethoxybenzyl)-4-(4-nitrobenzamido)benzoic acid, 5**

A solution of 4-nitrobenzoyl chloride (39 g; 0.21 mol) in dry NMP (500 ml) was added to a solution of 4 (48.6 g; 0.169 mol) in dry NMP (1 L) while stirring and cooling with an ice-bath. The reaction mixture was stirred for 1h and left at rt for 2 days. The yellow solid was recovered by vacuum filtration, washed neutral with water and re-crystallized from ethanol to give N-(2,4–dimethoxybenzyl)-4-(4-nitrobenzamido)benzoic acid (60.5 g; 82 %).

mp: 228 ºC.

\[ ^1H \text{-NMR (400 MHz, DMSO-d}_6\text{)}: \delta 3.63 (s, 3 H); 3.70 (s, 3 H); 5.03 (s, 2 H); 6.45 (dd, } J_1 = 2.20 \text{ Hz, } J_2 = 8.25 \text{ Hz, 1 H}); 6.47 (d, } J = 2.20 \text{ Hz, 2 H}); 7.18-7.22 (m, 3 H); 7.58 (d, } J = 8.44 \text{ Hz, 2 H}); 7.72 (d, } J = 8.44 \text{ Hz, 2 H}); 8.10 (d, } J = 8.80 \text{ Hz, 2 H}), 12.94 (br. s, 1 H). \]

\[ ^{13}C \text{-NMR and DEPT (300 MHz, DMSO-d}_6\text{)}: \delta 47.60 (-); 55.12 (+); 55.30 (+); 98.25 (+); 104.59 (+); 116.24; 123.24 (+); 127.85 (+); 128.88; 129.42 (+); 129.92 (+); 130.08 (+); 142.50; 145.93; 147.59; 158.01; 160.05; 166.55; 167.76. \]

IR \( \nu (\text{cm}^{-1}) \): 3424, 2931, 2632, 1708, 1594, 1508 (, 1272, 1031, 862.

RP-HPLC (min): 22.63.

M (FD): \( m/z \) (%) = 436.2 (100); 437.2 (23.4); 438.2 (4.1). calc.[C\(_{23}\)H\(_{22}\)N\(_2\)O\(_5\)] = 436.13.

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**General activation method for the in situ preparation of acid chlorides 6, 10 and 12**

A Schlenk-flask was equipped with the compound carrying a carboxylic acid dissolved in dry NMP. The solution was evacuated and re-filled with dry nitrogen gas. This procedure was repeated three times. One equivalent (with respect to the carboxylic acid) of thionyl chloride was added dropwise to the solution while stirring and cooling with an ice-bath. The reaction mixture was stirred for an additional 2h at rt. The activated carboxylic acid was used in the next reaction step without characterization.
Synthesis of \(N\)-(2,4-Dimethoxybenzyl)-4-(4-aminobenzamido)benzoic acid, 7

A solution of ammonium formate (21.7 g; 0.344 mol) in methanol (400 ml) was added dropwise to a solution of 5 (15 g; 34.4 mmol) in NMP (150 ml) while stirring and cooling with an ice-bath. Pd/C (10%, 0.8 g) was added in small portions to the cold solution while maintaining a slight flow of nitrogen gas over the reaction mixture. After stirring for 36 h at rt the suspension was filtered through Celite and the methanol removed under reduced pressure. Water was added to the residue to give a colourless precipitate which was isolated via vacuum filtration. The crude solid was washed with water and dried under vacuum at 60°C to give \(N\)-(2,4-dimethoxybenzyl)-4-(4-aminobenzamido)benzoic acid (12.5 g; 90%).

\[\text{mp: 207 ºC.}\]

\[^1\text{H-NMR (300 MHz, DMSO-d}_6\text{) \delta: 3.66 (s, 3 H); 3.71 (s, 3 H); 4.97 (s, 2 H); 6.35 (d, } J = 8.46 \text{ Hz, 2 H); 6.47 – 6.49 (m, 2 H); 7.04 (d, } J = 8.46 \text{ Hz, 2 H); 7.11 (d, } J = 8.83 \text{ Hz, 2 H); 7.20 (d, } J = 7.72 \text{ Hz, 1 H); 7.74 (d, } J = 8.46 \text{ Hz, 2 H).}\]

\[^{13}\text{C-NMR und DEPT (300 MHz, DMSO-d}_6\text{) \delta: 47.55 (-); 55.12 (+); 55.31 (+); 98.22 (+); 104.60 (+); 112.30 (+); 117.54; 121.71; 126.43 (+); 127.25; 128.96 (+); 129.84 (+); 130.86 (+); 148.80; 150.88; 157.70; 159.68; 166.79; 169.94.}\]

\[\text{IR } \nu (\text{cm}^{-1}): 3363 (\text{N-H}), 2937, 2823, 1662, 1600, 1403, 1299, 1027.\]

\[\text{RP-HPLC (Min): 15.26.}\]

\[\text{M (FD): } m/z (%) = 406.1 (100); 407.2 (24.8); 408.1 (2.7). \text{ calc.} [\text{C}_{23}\text{H}_{22}\text{N}_{2}\text{O}_{5}] = 406.15.\]

Synthesis of 4-(\(N\)-(2,4-Dimethoxybenzyl)-4-(\(N\)-(2,4-dimethoxybenzyl)-4-nitrobenzamido)benzamido)benzamido)benzoic acid, 8

Thionyl chloride (1.60 ml; 22.14 mmol) was added to a solution of 6 (9.66 g; 22.14 mmol) in dry NMP (150 ml) according to the general activation method (GAM). The reaction mixture was stirred for 90 minutes at rt. A solution of 7 (4.66 g; 11.46 mmol) in dry NMP (30 ml) was added dropwise to the mixture while cooling the reaction flask with an ice bath. After stirring for 12 h at rt under a N\(_2\)-atmosphere the reaction product was precipitated from solution by adding water to the reaction mixture (300 ml). The precipitate was isolated by vacuum filtration, washed with water and dried. The solid was suspended in ethanol (1 L) and stirred for 5 h. The white insoluble solid was isolated by filtration and dried under vacuum at 40°C to give 4-(\(N\)-(2,4-dimethoxybenzyl)-4-(4-(\(N\)-(2,4-dimethoxybenzyl)-4-nitrobenzamido)benzamido)benzamido)benzoic acid (12.35 g; 68%).

\[\text{mp. 223-225 ºC.}\]

Supporting Information 4/21
Supplementary Material (ESI) for Journal of Materials Chemistry
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$^1$H-NMR (400 MHz, DMSO-d$_6$) δ: 3.63 (s, 3 H); 3.65 (s, 3 H); 3.71 (s, 6 H); 5.01 (s, 2 H); 5.04 (s, 2 H); 6.44 – 6.48 (m, 4 H); 7.14 (d, $J = 8.41$ Hz, 2 H); 7.20 – 7.25 (m, 4 H); 7.28 (d, $J = 8.80$ Hz, 2 H); 7.57 – 7.62 (m, 4 H); 7.72 (d, $J = 8.80$ Hz, 2 H); 7.73 (d, $J = 8.41$ Hz, 2 H); 8.11 (d, $J = 8.22$ Hz, 2 H); 10.23 (s, 1 H).

$^{13}$C-NMR (400 MHz, DMSO-d$_6$) δ: 47.57; 55.12; 55.36; 98.24; 98.27; 104.60; 116.23; 116.92; 119.15; 123.27; 127.26; 127.73; 128.07; 128.44; 129.29; 129.46; 129.84; 130.06; 130.89; 132.64; 140.33; 142.64; 144.92; 147.47; 147.58; 157.83; 158.03; 159.83; 160.03; 164.71; 166.68; 167.87; 169.23.

IR ν (cm$^{-1}$): 3295, 2937, 1654, 1598, 1506, 1407, 1313, 1255, 1207, 1120, 1031, 848, 707.

RP-HPLC (Min): 27.51.

M (ESI-MS): m/z (%) = [M + Na]$^+$ 847.32 (100); 848.32 (41.5); 849.32 (1.7). calc. [C$_{46}$H$_{40}$N$_4$O$_{11}$Na]$^+$ = 847.26.

Crystallographic data: molecular weight = 842.84; crystal dimensions = 0.064 x 0.128 x 0.128 mm$^3$; space group = Pna2$_1$ (orthorhombic); Z = 4; lattice constants: a = 14.0604(5) Å, b = 10.721(2) Å, c = 27.612(3) Å; V = 4162.1(9) Å$^3$; density: $\rho_{\text{x-ray}}$ = 1.345 g cm$^{-3}$; R1 = 8.78 %.

**Synthesis of 4-(N-(2,4-Dimethoxybenzyl)-4-(4-(N-(2,4-dimethoxybenzyl)-4-aminobenzamido)benzamido)benzamido)benzoic acid, 9**

A solution of 8 (5 g; 6.06 mmol) in NMP (60 ml) was added to a solution of ammonium formate (3.82 g; 60.6 mmol) in methanol (160 ml). Pd/C (10%; 0.32 g) was added to the reaction mixture under a gentle flow of nitrogen gas while cooling the reaction vessel with an ice-bath. After stirring the reaction for 48h, 96h and 118h more Pd/C (0.5 g) was added to the reaction mixture in the manner described above. 12h after the last addition of Pd/C the reaction mixture was filtered through Celite and the methanol evaporated under reduced pressure. Water was added to the remaining solution. The white precipitate was recovered by filtration and dried under vacuum to give 9 (4.4 g; 90 %).

m.p. 197-198 °C

$^1$H-NMR (300 MHz, DMSO-d$_6$) δ: 3.64 (s, 3 H); 3.66 (s, 3 H); 3.71 (s, 3 H); 3.72 (s, 3H); 4.97 (s, 2 H); 5.01 (s, 2 H); 6.33 (d, $J = 8.46$ Hz, 2 H); 6.45-6.48 (m, 4 H); 7.03 (d, $J = 8.82$ Hz, 2 H); 7.12 – 7.23 (m, 6 H); 7.29 (d, $J = 8.82$ Hz, 2 H); 7.60 (d, $J = 8.82$ Hz, 2 H); 7.70-7.74 (m, 4 H); 10.24 (s, 1 H).

IR ν (cm$^{-1}$): 3355, 2935, 1596, 1506, 1401, 1284, 1207, 1176, 1031, 835.
Synthesis of Octamer-(DMB)$_4$, 11

Thionyl chloride (364 μl; 5.03 mmol) was added to a solution of 8 (4.14 g; 5.02 mmol) in dry NMP (35 ml) according to the general activation method (GAM). The reaction mixture was stirred for 2h before a solution of 9 (4 g; 5.02 mmol) in dry NMP (35 ml) was added. After further stirring for 94h at rt the reaction mixture was cooled with an ice-bath and water (600 ml) was added to the mixture. An off-white solid precipitated and was recovered by filtration. The solid was stirred in either isopropanol or methanol at rt for 3 h and then recovered by filtration to give 11 (4.19 - 4.92 g; 52-61 %).

$^1$H-NMR (300 MHz, DMSO-d$_6$) δ: 3.64 (s, 12 H); 3.70 – 3.71 (m, 12 H); 5.00 – 5.03 (m, 8 H); 6.43 – 6.47 (m, 8 H); 7.12 – 7.31 (m, 18 H); 7.56 – 7.61 (m, 8 H); 7.68 – 7.74 (m, 8 H); 8.10 (d, $J = 8.46$ Hz, 2 H); 10.21 – 10.23 (m, 3 H); 12.93 (s, 1 H).

$^{13}$C-NMR (300 MHz, DMSO-d$_6$) δ: 47.58; 55.10; 55.28; 55.31; 98.22; 104.59; 116.21; 116.90; 119.09; 119.15; 123.22; 127.13; 127.20; 127.71; 128.01; 128.31; 128.37; 129.26; 129.39; 129.44; 129.47; 129.81; 130.04; 130.77; 130.90; 130.98; 131.89; 132.58; 140.26; 140.37; 140.43; 142.63; 146.45; 147.45; 147.54; 157.82; 157.85; 158.01; 159;80; 159.83; 160.01; 164.68; 164.86; 166.64; 167.84; 169.20; 169.28.

IR ν (cm$^{-1}$): 3303, 2940, 1637, 1598, 1504, 1403, 1263, 1207, 1157, 1118, 1031, 835, 759.

RP-HPLC (min.): 32.04.

M (MALDI-TOF): $m/z = 1640$ [M + K]$^+$. calc.[C$_{92}$H$_{80}$N$_8$O$_{19}$K$^+$/] = 1640.

GPC (DMF + 1 g/L LiBr): Mn = 510, Mw = 540 g/mol; PDI = 1.04.

Synthesis of alkyne functionalized octamer-(DMB)$_4$, 13

Thionyl chloride (0.97 ml; 13.4 mmol) was added to a solution of 11 (3.07 g; 1.91 mmol) in dry NMP (50 ml). Propargylamine (0.58 ml; 10.7 mmol) was added to the reaction mixture after stirring for 10 min. at rt. After that the reaction mixture was stirred at rt for further 36 h. Addition of cold water (500 ml) resulted in the precipitation of a brown resin-like compound which was stirred under cooling for
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further 3h resulting in a brown solid which was dried under vacuum at 40 °C (3 g; 1.83 mmol; 95 %).

$^1$H-NMR (300 MHz, DMSO-d$_6$) $\delta$: 3.07 (t, 1 H); 3.64 (s, 12 H); 3.70 – 3.71 (m, 12 H), 3.97 – 3.99 (m, 2 H); 5.01 – 5.03 (m, 8 H); 6.43 – 6.48 (m, 8 H); 7.11 – 7.32 (m, 18 H); 7.59 – 7.76 (m, 16 H); 8.10 (d, $J = 8.46$ Hz, 2 H); 8.91 (t, 1 H); 10.30 – 10.32 (m, 3 H).

IR (13) ν (cm$^{-1}$): 3293, 2927, 1643, 1598, 1502, 1403, 1286, 1207, 1155, 1110, 1029, 829, 759.

RP-HPLC (Min.): 32.25

M (MALDI-TOF): $m/z = 1645$ [M + Li]$^+$. calc.[C$_{98}$H$_{83}$N$_{9}$O$_{18}$Li]$^+$] = 1645.

GPC (DMF + 1g/L LiBr): Mn = 1500, Mw = 1550 g/mol; PDI = 1.04.

**Synthesis of octamer-(DMB)$_4$ block copolymer, 14**

A solution of 13 (2.9 g; 1.8 mmol) in NMP (20 ml) was added to a solution of PEG-N$_3$ (Mn$_{\text{PEG}}$ = 2000 g/mol; 1.67 g; 0.82 mmol) in NMP (10 ml). This was followed by the addition of solid CuI (60 mg, 0.31 mmol) and DBU (4.5 ml, 30 mmol). After stirring the reaction mixture at rt for 2 days, diethyl ether (300 ml) was added upon which a brown oil separated from the ether phase. The crude product was dried under vacuum to yield 2.5 g of a mixture of 14 and 13. The crude product mixture (1.2 g) was dissolved in tetrahydrofuran and purified by column chromatography. Eluting with THF, the excess of 13 could be removed. Elution with DMF gave the block copolymer 14 (500 mg).

$^1$H-NMR (400 MHz, DMSO-d$_6$) $\delta$: 3.23 (s, 3 H); 3.35 (s, 162 H); 3.63 – 3.66 (m, 12 H); 3.69 – 3.71 (m, 12 H); 3.75 (t, 2 H); 3.41 – 3.44 (m, 4 H); 4.98 – 5.01 (m, 8 H); 6.43 - 6.47 (m, 8 H); 7.11 – 7.30 (m, 18 H); 7.55 – 7.59 (m, 16 H); 7.87 (s, 1 H); 8.09 (d, $J = 8.51$ Hz, 2 H); 8.91 (t, 1 H); 10.17 – 10.20 (m, 3 H).

RP-HPLC (min.): 28.14

M (MALDI-TOF): $m/z = 3508$ [M + Li]$^+$; repeat unit 44. calc.[C$_{98}$H$_{90}$N$_{12}$O$_{19}$(C$_2$H$_4$O)$_{40}$ Li]$^+$] = 3508.

GPC (TCM): Mn = 6000, Mw = 6600 g/mol; PDI = 1.08.
Synthesis of octamer-PEG block copolymer, 15

14 (500 mg; 0.13 mmol) was dissolved in a mixture of TFA (12 ml), chloroform (5 ml) and anisole (4 ml) and stirred at rt for 15 h. After that, the volatiles were removed under reduced pressure. The crude product was dried under vacuum, dissolved in tetrahydrofuran and purified by column chromatography. With THF the cleaved off protective groups could be removed. Elution with DMF gave the block copolymer 15. Several product containing fractions were collected, the purest one contained 40 mg of 15.

$^1$H-NMR (400 MHz, DMSO-d$_6$) δ: 3.5 (s, 180 H), 4.49 (t, 2 H), 6.5 – 8.5 (m, 5 H); 9 (s, NH), 10.45 – 11 (m, NH).

$^1$H-NMR (400 MHz, D$_2$SO$_4$) δ: 3.57 (s, 180 H), 4.35 (s, N-CH$_2$-CH$_2$-O-), 6.8-8.1 (m, 20 H), 16-18 (m, NH).
Figure SI-1. X-ray single crystal structure of 8. Top: CPK model, bottom: shown as a stereo image with displacement ellipsoids drawn at the 50 % probability level. The bottom phenyl ring of the tetramer points towards, the top phenyl ring away from the viewer.
HPLC elugrams, mass- and NMR-spectra

Figure SI-2 RP-HPLC-traces of compounds 5,7,8,9,11,13 and 14.

Figure SI-3 MALDI-ToF mass spectrum of 11.
Figure SI-4 MALDI-ToF mass spectrum of 13.
Figure SI-5 $^1$H-NMR (DMSO-d$_6$) of 4.

Figure SI-6 $^{13}$C-NMR (DMSO-d$_6$) of 4.
Figure SI-7 $^1$H-NMR (DMSO-d$_6$) of 5.

Figure SI-8 $^{13}$C-NMR (DMSO-d$_6$) of 5.
Figure SI-9 $^1$H-NMR (DMSO-d$_6$) of 7.

Figure SI-10 $^{13}$C-NMR (DMSO-d$_6$) of 7.
Figure SI-11 ¹H-COSY (DMSO-d₆) of 8 (full spectrum).
Figure SI-12 $^1$H-COSY (DMSO-$d_6$) of 8 (aromatic region). (Protons H2 and H3 do not show a cross-peak, see NOESY spectrum Fig. SI-13)

Figure SI-13 $^1$H-NOESY (DMSO-$d_6$) of 8 (full spectrum).
Figure SI-14 $^1$H-NOESY (DMSO-d$_6$) of 8 (aromatic region). The cross-peak between protons H$^2$ and H$^3$ is circled in red.

Figure SI-15 $^{13}$C-NMR (DMSO-d$_6$) of 8.
**Figure SI-16** $^1$H-NMR (DMSO-$d_6$) of 9.

**Figure SI-17** $^{13}$C-NMR (DMSO-$d_6$) of 9.
**Figure SI-18** $^1$H-NMR (DMSO-d$_6$) of 11.

**Figure SI-19** $^{13}$C-NMR (DMSO-d$_6$) of 11.
Figure SI-20 $^1$H-NMR (DMSO-d$_6$) of 13.

Figure SI-21 $^{13}$C-NMR (DMSO-d$_6$) of 13.
Figure SI-22 $^1$H-NMR (DMSO-d$_6$) of 14. The spectrum also shows residual peaks for DMF and BHT. This is due to the chromatographic purification in DMF and THF (which was stabilized with BHT).

Figure SI-23 $^1$H-NMR spectra of 15 in A) DMSO-d$_6$ and B) D$_2$SO$_4$. 

Supporting Information 21/21