Structure elucidation and control of cyclic peptide-derived nanotube assemblies in solution

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SUPPORTING INFORMATION

Polymer and conjugate synthesis data:

Table S1: Conditions and characterization data for polymer synthesis

Polymer	[M]:[CTA]	Time (min)	^{1}H-NMR				DMF SEC Conventional calibration[a]	
			X (%)	DP_{Theo}	DP_{Actual}	M_n (g.mol^{-1})	M_n (g.mol^{-1})	M_w/M_n
pBA16	18	157	79	14	16	2,320	2,250	1.15
pBA30	35	140	79	28	30	4,150	3,450	1.16
pBA70	120	55	56	67	70	9,280	6,590	1.15
pBA91	120	100	73	88	91	11,940	8,450	1.16
pBA108	120	135	84	101	108	14,150	11,400	1.15
pBA195	250	123	79	198	195	25,240	18,500	1.19

Notes: [a] Conventional calibration relative to pS standards. Uncorrected with Mark Houwink parameters.

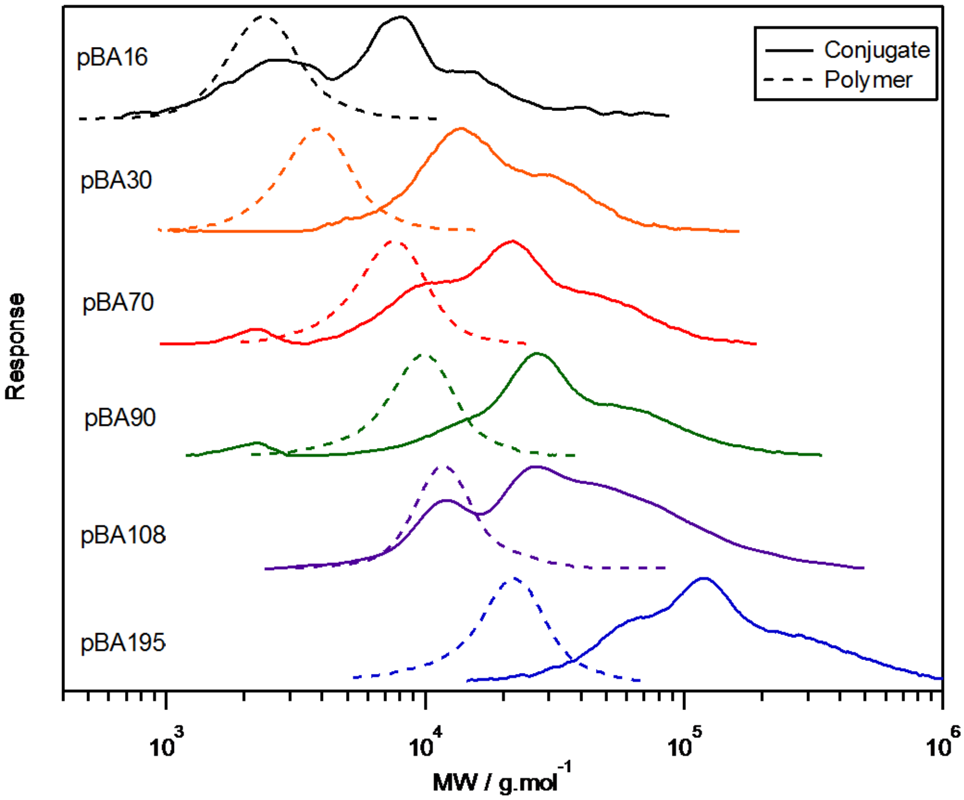


Figure S1: SEC traces of pBA-CP conjugates prepared in the microwave reactor at 100 °C for 15 min. 2.10 equivalents of polymer per peptide were used in each case.

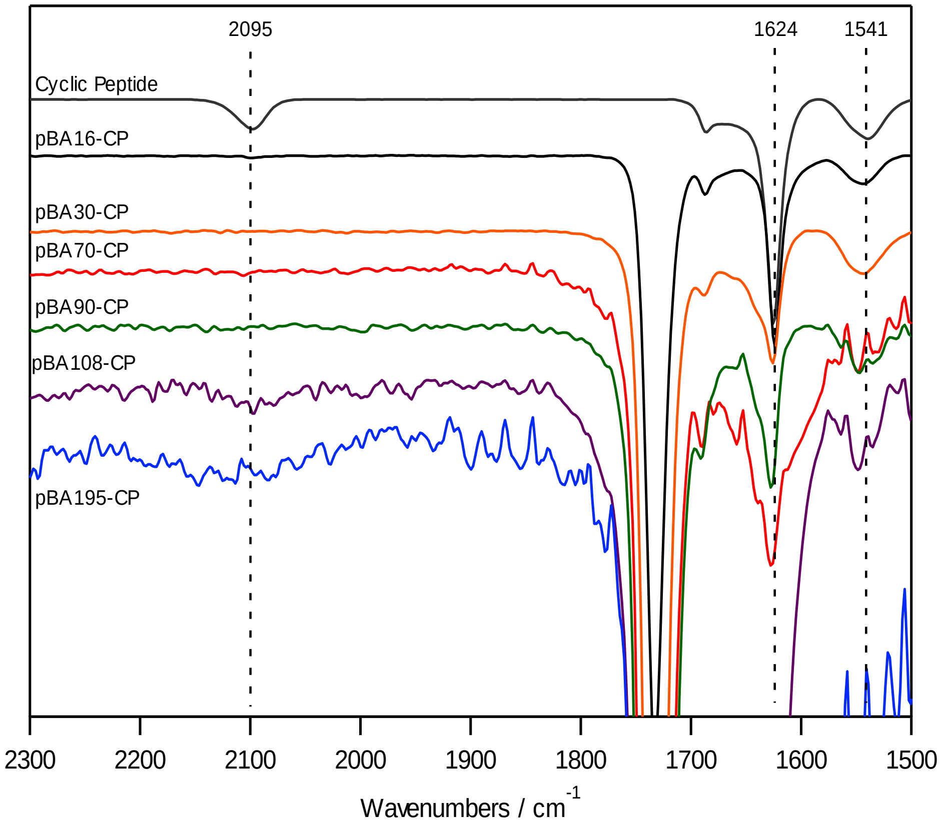


Figure S2: ATR-IR traces of the 2 arm cyclic peptide and pBA-CP conjugates prepared in the microwave reactor at 100 °C for 15 min. 2.10 equivalents of polymer per peptide were used in each case.

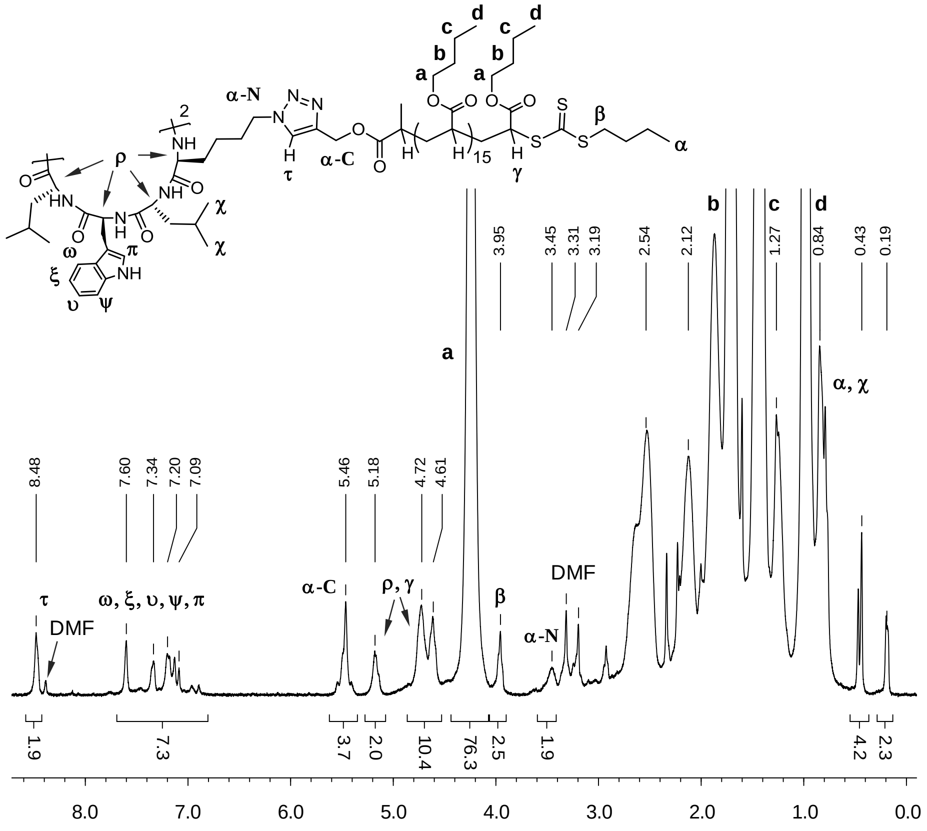


Figure S3: ^{1}H-NMR of $(pBA_{16})_2$-CP in *d*-TFA

Stability of the conjugates to TFA:

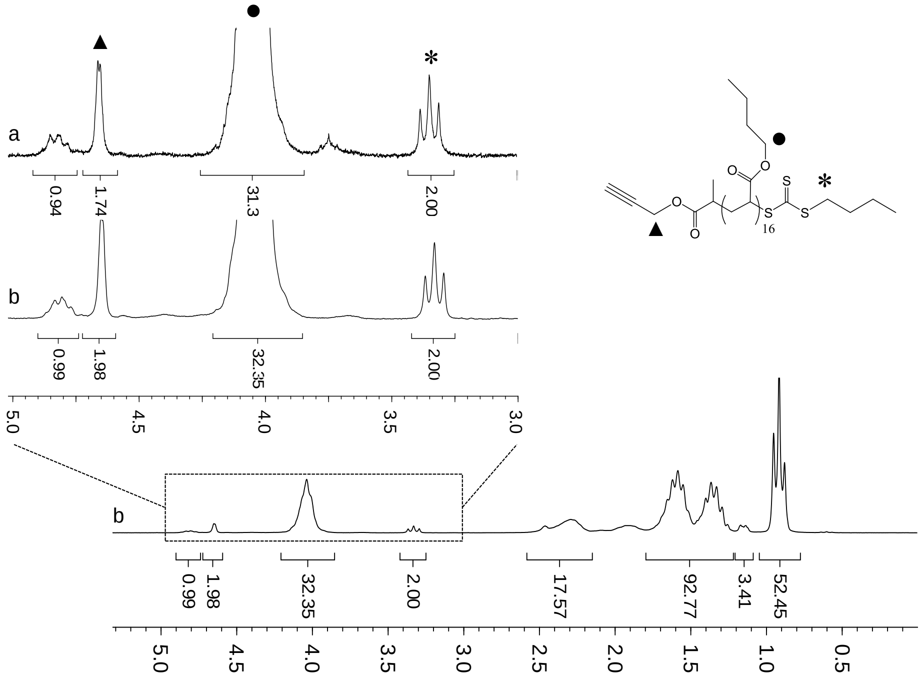


Figure S4: ^{1}H-NMR ($CDCl_3$) of pBA_{16} a) before and b) after heating in TFA at 60 °C

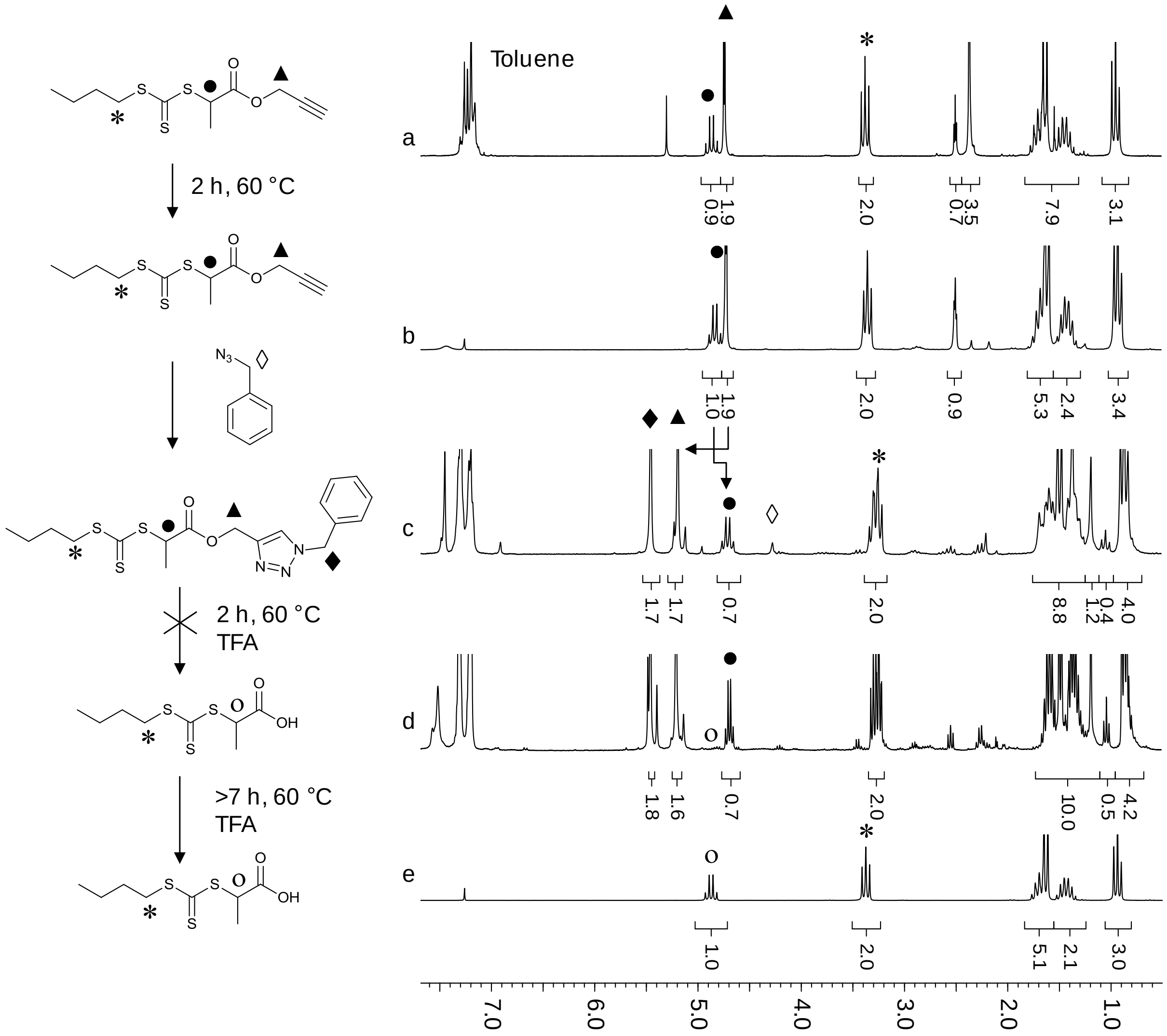


Figure S5: ^{1}H-NMR ($CDCl_3$) of PABTC a) before and b) after, and a model conjugate c) before, and d) after heating in TFA at 60 °C. e) ^{1}H-NMR ($CDCl_3$) spectrum of hydrolysed RAFT agent.

Self assembly DLS

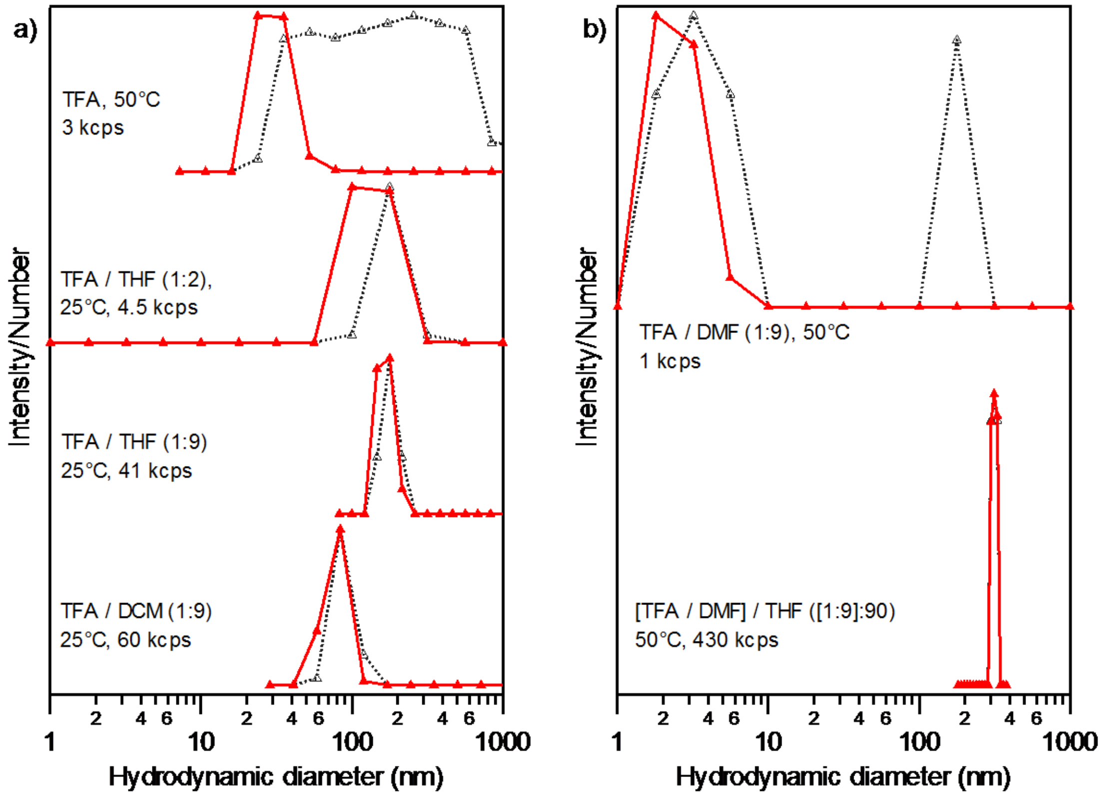


Figure S1: Dynamic light scattering intensity (Δ) and number (▲) distributions for $(pBA_{16})_2$-CP conjugates a) 10 mg in 0.25 ml TFA, diluted with THF or with DCM to a final concentration of 4 mg/ml; b) in TFA / DMF (1:9) diluted with THF to a final concentration of 10 mg/ml

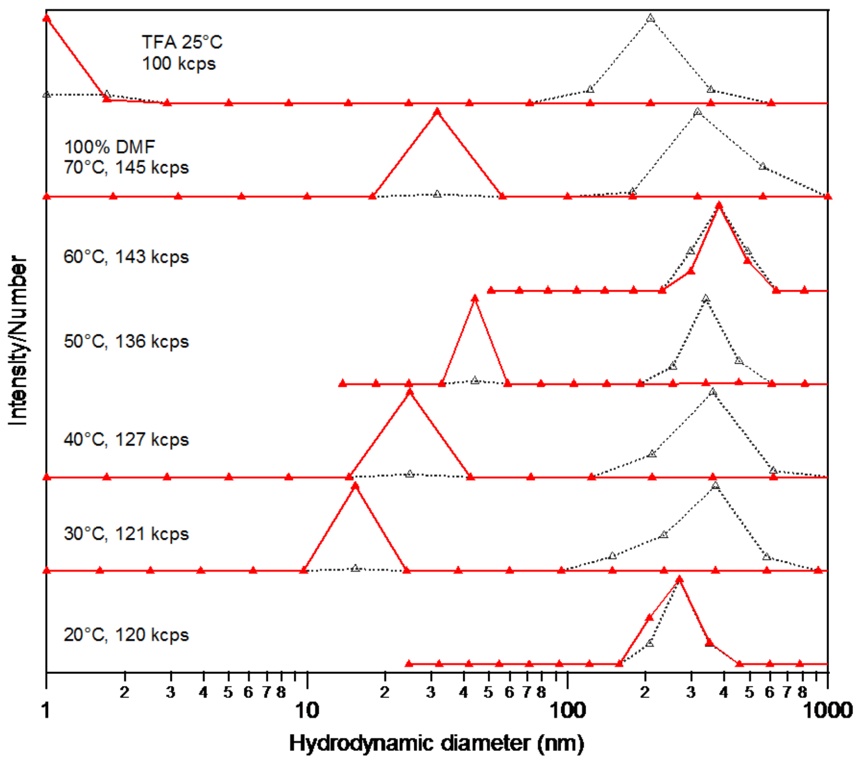
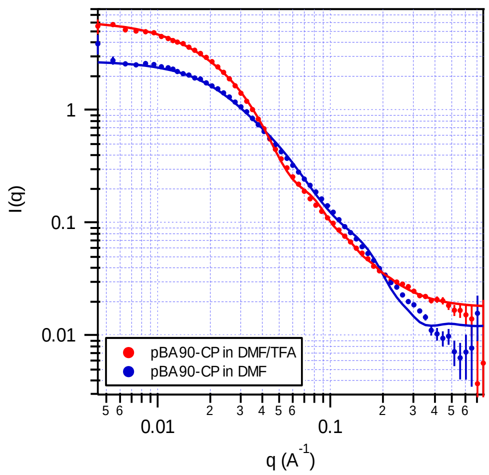


Figure S7: DLS intensity (Δ) and number (▲) distributions for 0.2 mM solutions of $(pBA_{90})_2$-CP in TFA, and DMF heated to 70 °C

SANS model output

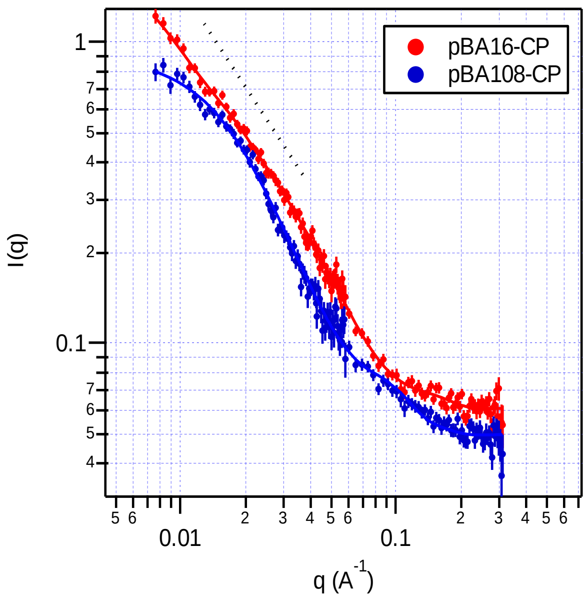
pBA90-CP in DMF / TFA (3:1)



Stacked disc model	pBA90-CP TFA/DMF (1:3)
Volume Fraction	0.10
Disc Radius (Å)	68.0
Core Thickness (Å)	5.5
Layer Thickness (Å)	7.7
Core SLD (Å^{-2} / 10^{6})	0.00
Layer SLD (Å^{-2} / 10^{6})	5.90
Solvent SLD (Å^{-2} / 10^{6})	6.09
# of Stacking	2.9
GSD of d-Spacing	6.0
Incoherent background (cm^{-1})	0.018

Figure S8: SANS data for dilution of $(pBA_{90})_2$-CP from TFA with DMF

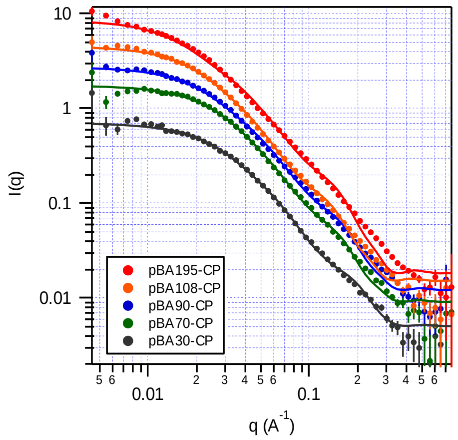
Various DP's in THF / DMF / TFA (90 : 9 : 1)



Core-Shell-Shell Cylinder Model	pBA 16-CP	pBA 108-CP
Volume Fraction	0.007	0.018
Core radius (Å)	13.10	15.2
Shell 1 thickness (Å)	11.03	13.6
Shell 2 thickness (Å)	22.80	50.2
Total Thickness (Å)	46.9	79.0
Core length (Å)	>1000	203.2
SLD core (Å^{-2} / 10^{6})	0.00	0.00
SLD shell 1 (Å^{-2} / 10^{6})	5.83	6.04
SLD shell 2 (Å^{-2} / 10^{6})	6.03	6.25
SLD solvent (Å^{-2} / 10^{6})	6.36	6.36
Incoherent background (cm^{-1})	0.060	0.049

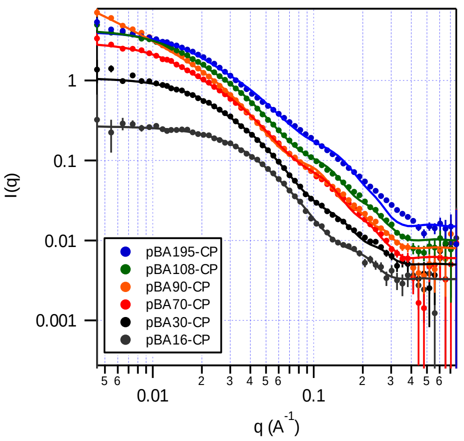
Figure S9: SANS of pBA-CP dissolved in TFA/DMF (1:9) and diluted with THF (1:9)

Various DP's in DMF, TFA / THF and TFA / $CDCl_3$



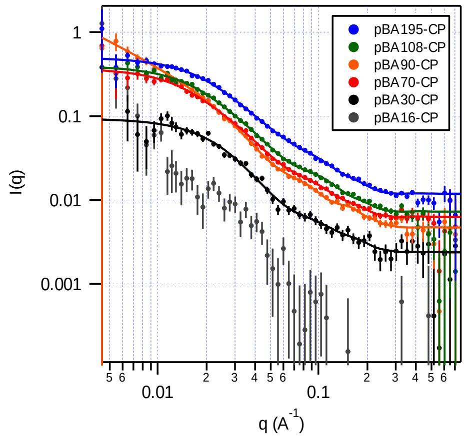
Core-Shell-Shell (CSS) Cylinder Model	pBA30-CP 25 °C	pBA70-CP 25 °C	pBA90-CP 25 °C	pBA108-CP 25 °C	pBA195-CP 25 °C
Volume Fraction	0.034	0.093	0.120	0.149	0.235
Core radius (Å)	9.8	10.3	10.1	11.3	10.7
Shell 1 thickness (Å)	25.2	14.4	15.3	19.3	17.0
Shell 2 thickness (Å)	8.3	26.1	24.1	27.5	26.1
Total Thickness (Å)	43.3	50.8	49.5	58.2	53.8
Core length (Å)	142.0	135.8	176.3	186.1	259.3
SLD core (Å-2 / 106)	0.00	0.00	0.00	0.00	0.00
SLD shell 1 (Å-2 / 106)	6.56	6.45	6.53	6.51	6.55
SLD shell 2 (Å-2 / 106)	6.68	6.67	6.67	6.67	6.67
SLD solvent (Å-2 / 106)	6.79	6.79	6.79	6.79	6.79
Incoherent background (cm-1)	0.005	0.009	0.012	0.015	0.018

Figure S10: SANS data for $(pBA_n)_2$-CP conjugates in *d7*-DMF



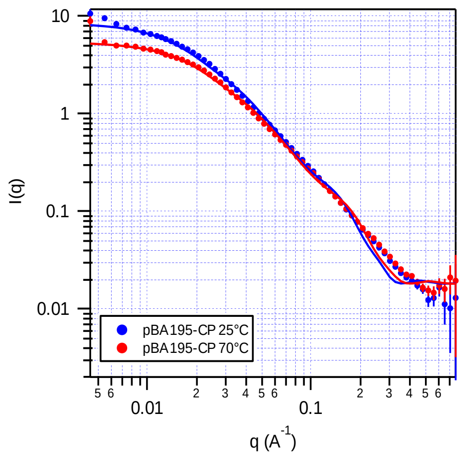
Core-Shell-Shell Cylinder Model	pBA16-CP	pBA30-CP	pBA70-CP	pBA90-CP	pBA108-CP	pBA195-CP
Volume Fraction	0.010	0.055	0.142	0.181	0.263	0.283
Core radius (Å)	10.2	9.0	9.4	8.7	8.8	9.7
Shell 1 thickness (Å)	20.0	20.0	20.0	20.0	20.0	20.0
Shell 2 thickness (Å)	7.3	25.2	36.3	47.4	35.4	27.7
Total Thickness (Å)	37.5	54.2	65.7	76.1	64.1	57.3
Core length (Å)	102.1	190.3	312.9	3,525.8	292.6	244.2
SLD core ($Å^{-2}$ / 10^6)	-0.40	-0.40	-0.40	-0.40	-0.40	-0.40
SLD shell 1 ($Å^{-2}$ / 10^6)	5.77	5.74	5.84	5.79	5.86	5.99
SLD shell 2 ($Å^{-2}$ / 10^6)	5.80	5.99	6.03	6.03	6.03	6.03
SLD solvent ($Å^{-2}$ / 10^6)	6.09	6.09	6.09	6.09	6.09	6.09
Incoherent background (cm^{-1})	0.0033	0.0050	0.0060	0.0080	0.0100	0.0150

Figure S11: SANS data for $(pBA_n)_2$-CP conjugates in TFA / THF (1:9) at 25 °C



Core-Shell-Shell Cylinder Model	pBA16-CP	pBA30-CP	pBA70-CP	pBA90-CP	pBA108-CP	pBA195-CP
Scale	-	0.044	0.065	0.089	0.082	0.150
Core radius (Å)	-	10.7	12.1	10.2	11.7	12.1
Shell 1 thickness (Å)	-	36.3	32.3	36.4	26.6	30.8
Shell 2 thickness (Å)	-	31.6	37.0	47.4	36.1	36.3
Total Thickness (Å)	-	78.6	81.3	94.0	74.4	79.2
Core length (Å)	-	123.8	250.0	4,413.3	213.2	187.7
SLD core (Å^{-2} / 10^{6})	-	0.00	0.00	0.00	0.00	0.00
SLD shell 1 (Å^{-2} / 10^{6})	-	3.15	3.14	3.14	3.15	3.16
SLD shell 2 (Å^{-2} / 10^{6})	-	3.20	3.20	3.20	3.19	3.20
SLD solvent (Å^{-2} / 10^{6})	-	3.22	3.22	3.22	3.22	3.22
Incoherent background (cm^{-1})	-	0.002	0.006	0.005	0.007	0.012

Figure S12: SANS data for $(pBA_n)_2$-CP conjugates in TFA / CDCl3 (1:9)

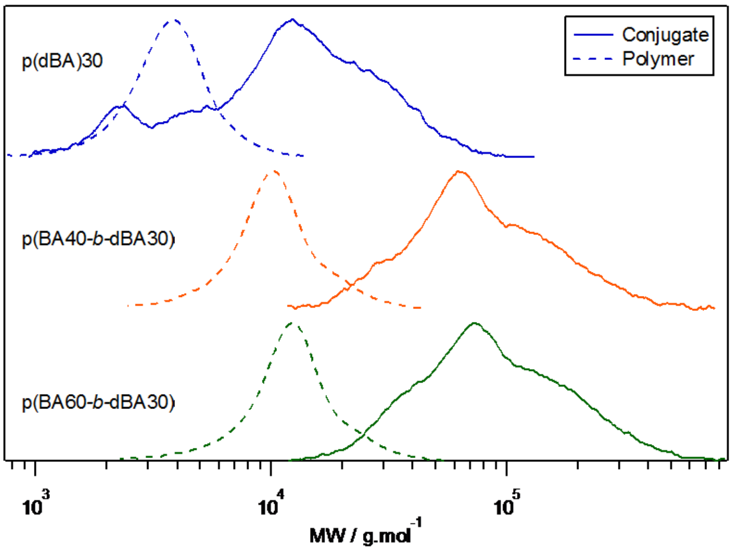


Core-Shell-Shell (CSS) Cylinder Model	pBA30-CP 70 °C	pBA70-CP 70 °C	pBA90-CP 70 °C	pBA108-CP 70 °C	pBA195-CP 70 °C
Scale	0.034	0.093	0.120	0.149	0.235
Core radius (Å)	9.7	8.9	9.0	9.7	9.6
Shell 1 thickness (Å)	0.3	6.5	7.3	10.9	10.8
Shell 2 thickness (Å)	32.4	26.9	25.5	27.8	26.1
Total Thickness (Å)	42.5	42.4	41.7	48.4	46.4
Core length (Å)	130.4	133.5	157.4	176.3	214.4
SLD core (Å^{-2} / 10^{6})	0.00	0.00	0.00	0.00	0.00
SLD shell 1 (Å^{-2} / 10^{6})	6.56	6.45	6.53	6.51	6.55
SLD shell 2 (Å^{-2} / 10^{6})	6.68	6.67	6.67	6.67	6.67
SLD solvent (Å^{-2} / 10^{6})	6.79	6.79	6.79	6.79	6.79
Incoherent background (cm^{-1})	0.0050	0.0090	0.0120	0.0150	0.0180

Figure S13: Effect of heating $(pBA_n)_2$-CP conjugates measured by SANS in DMF from 25 °C to 70 °C

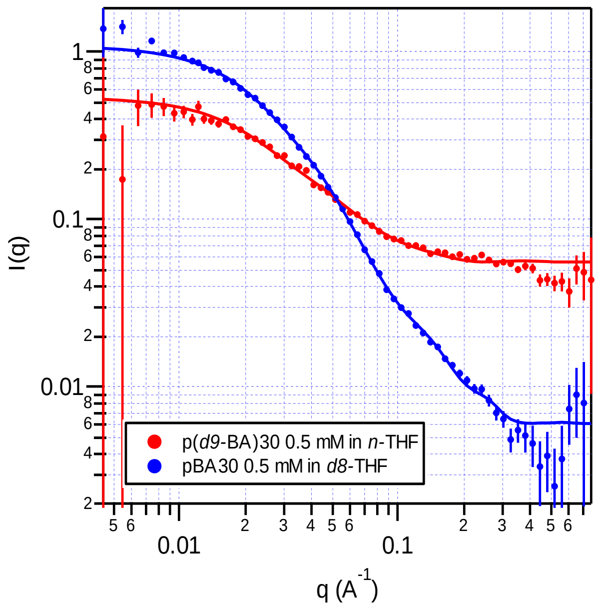
Tubes with deuterated cores:

Synthesis:



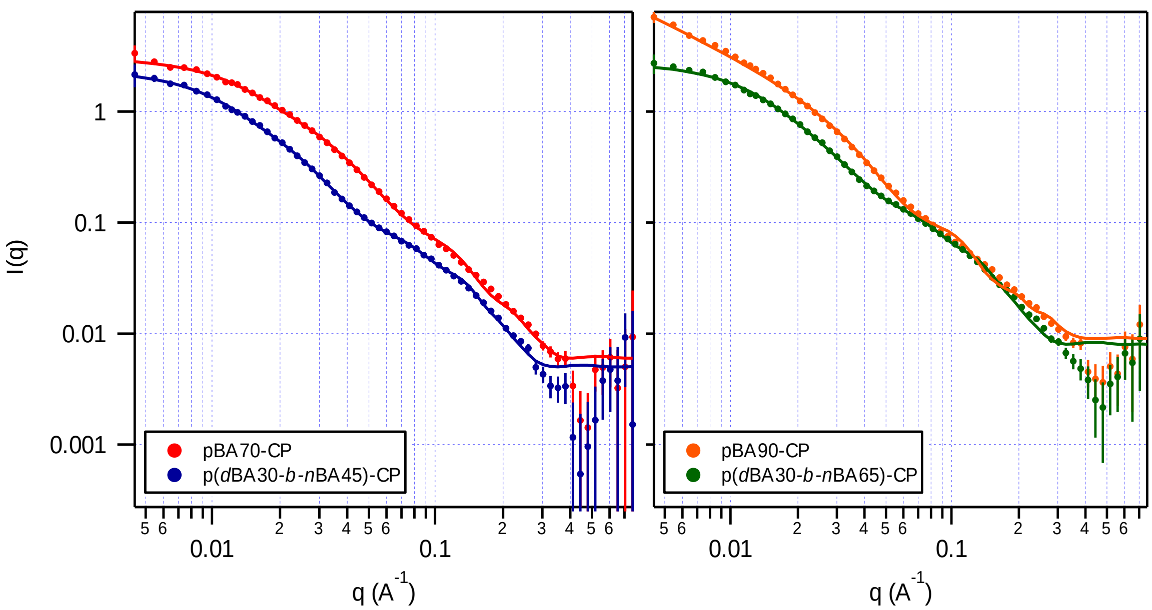
Polymer		p(d9-BA)29	p(*d9*-BA)29-*b*-BA45	p(*d9*-BA)29-*b*-BA65
[M] : [CTA]		35	45	68
Polymerisation time (min)		130	130	130
Conversion (X)		90%	90%	87%
Theoretical DP [a]		31.3	40.5	59.2
DP from 1H-NMR		29	45	65
Mn (g.mol-1) from 1H-NMR		4,200	9,904	12,467
SEC: DMF + LiBr. Conventional calibration	M_n (g.mol^{-1})	3,350	9,350	10,850
	M_w / M_n	1.19	1.22	1.23
SEC: THF Conventional calibration	M_n (g.mol^{-1})	4,100	11,100	13,400
	M_w / M_n	1.122	1.174	1.172
SEC: THF Light scattering	dn/dc [b]	0.0588	0.0576	0.0571
	M_n (g.mol^{-1})	5,200	13,000	15,800
	M_w / M_n	1.043	1.095	1.093

Figure S14: SEC traces of the three polymers and conjugates prepared from deuterated BA monomer. Notes: [a] Theoretical DP calculated based on conversion, measured by ^{1}H-NMR, [b] dn/dc calculated based on the assumption of 100% elution of the polymer by the SEC.



Core-Shell-Shell Cylinder Model	pBA30-CP in *d8*-THF	p(*d9*-BA)30-CP in *n*-THF
Scale	0.055	0.0582
Core radius (Å)	9.0	5.0
Shell 1 thickness (Å)	20.0	7.8
Shell 2 thickness (Å)	25.2	33.9
Total Thickness (Å)	54.2	46.8
Core length (Å)	190.3	190.3
SLD core (Å^{-2} / 10^{6})	-0.40	-0.40
SLD shell 1 (Å^{-2} / 10^{6})	5.74	4.10
SLD shell 2 (Å^{-2} / 10^{6})	5.99	0.86
SLD solvent (Å^{-2} / 10^{6})	6.09	0.80
Incoherent background (cm^{-1})	0.005	0.055

Figure S15: SANS pattern for [p(d_9-BA)$_{29}$]$_2$-CP in n-THF/ d-TFA (9:1) compared to (pBA$_{30}$)$_2$-CP in d8-THF / d-TFA (9:1)



Core-Shell-Shell (CSS) Cylinder Model	pBA70-CP	p(*d9*-BA)29-*b*-BA45-CP	pBA90-CP	p(*d9*-BA)29-*b*-BA65-CP
Scale	0.142	0.127	0.181	0.160
Core radius (Å)	9.4	11.2	8.7	12.0
Shell 1 thickness (Å)	20.0	45.1	20.0	47.3
Shell 2 thickness (Å)	36.3	43.3	47.4	41.6
Total Thickness (Å)	65.7	99.5	76.1	100.9
Core length (Å)	312.9	380.1	>1500	356.4
SLD core (Å^{-2} / 10^{6})	-0.40	-0.40	-0.40	-0.40
SLD shell 1 (Å^{-2} / 10^{6})	5.84	6.02	5.79	6.02
SLD shell 2 (Å^{-2} / 10^{6})	6.03	6.06	6.03	6.06
SLD solvent (Å^{-2} / 10^{6})	6.09	6.09	6.09	6.09
Incoherent background (cm^{-1})	0.006	0.005	0.008	0.008

Figure S16: SANS pattern and fits for tubes with deuterated cores in *d8*-THF / *d*-TFA (9:1)

SANS Error fitting:

The error in the length dimension from the model fitting, was obtained using the NIST IGOR Pro Macros. Once the best fit was obtained, all constants but the length were held constant, and the error in the length was determined. In all cases the error fit from the model was less than instrumental error, and so carries little real meaning. The error for conjugates assembled in 100% DMF at 25°C and 70°C are shown below.

Table S2: Model fitting errors for $p(BA_n)_2$-CP tubes in 100% DMF as measured by SANS

Polymer DP	DMF, 25°C		DMF, 25°C	
	Length (Å)	Model Fitting Error (Å)	Length (Å)	Model Fitting Error (Å)
30	229	0.784	215	0
70	237	0.454	218	0.843
90	275	0.6	241	0.513
108	303	0.527	273	0.564
195	367	0.744	307	0.568

Cross-linkable tubes

Synthesis:

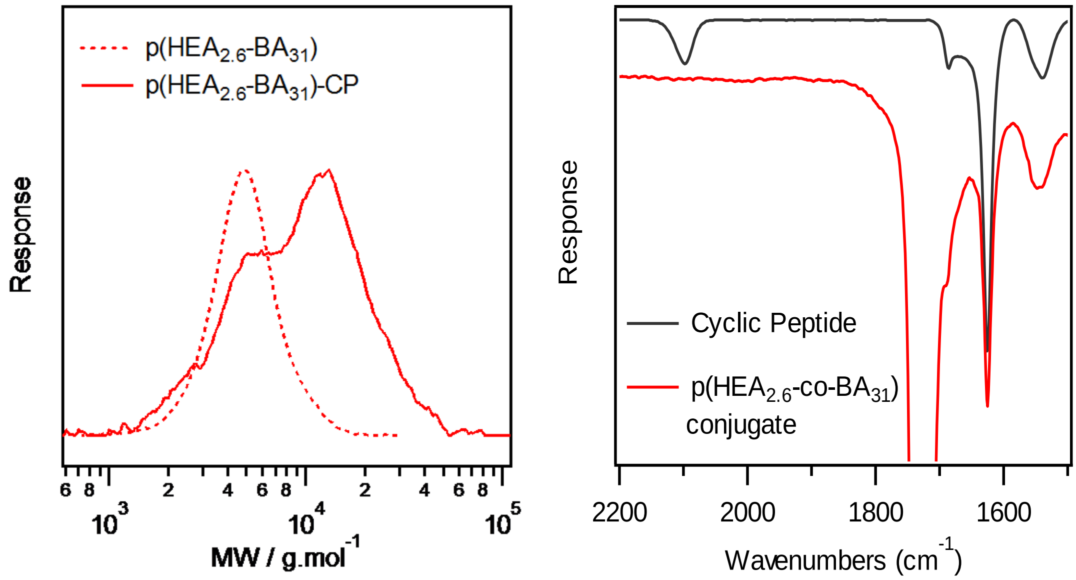


Figure S17: SEC and IR traces for p(HEA-*co*-BA) polymer and conjugate

DLS:

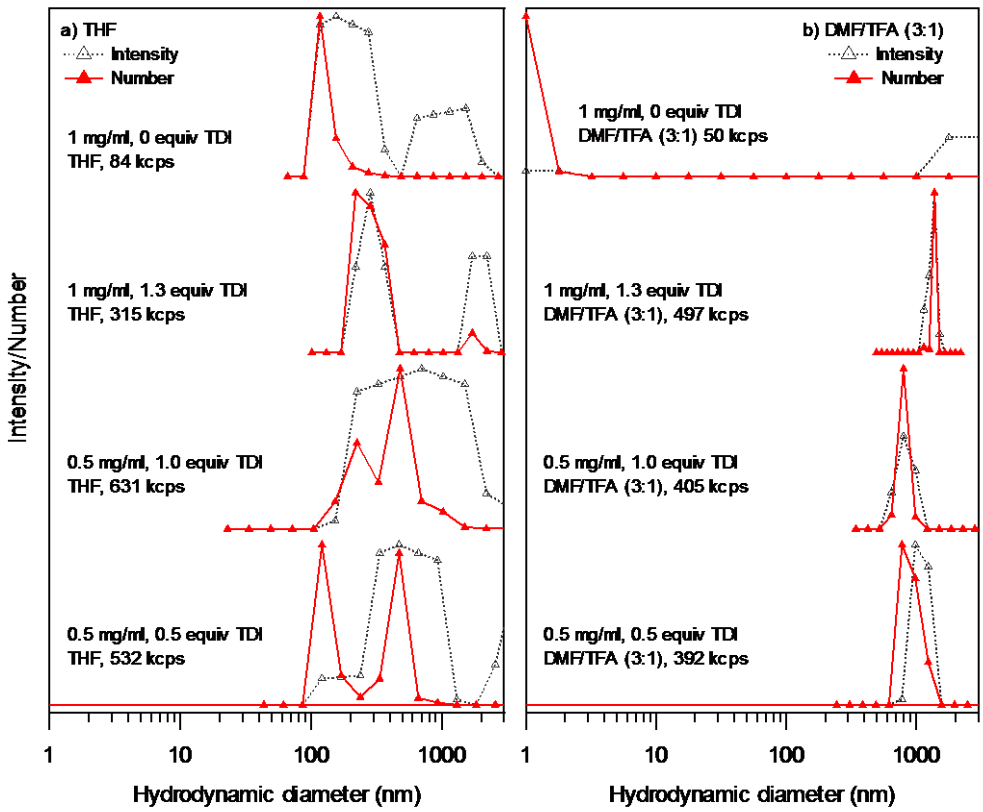


Figure S18: DLS intensity (Δ) and number (▲) distributions after cross-linking for 1 h of assembled (p(HEA-*co*-BA))$_2$-CP conjugates in a) THF, b) DMF/TFA (3:1) after 2h at 70 °C.