Electronic Supplementary Material (ESI) for Chemical Science

Metastable Single-Chain Polymer Nanoparticles Prepared by Dynamic Cross-Linking with *nor-seco*-Cucurbit[10]uril

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S.1 Instrumentation and Materials

^{1}H NMR (500 MHz) spectra was recorded using a Bruker Avance BB 500. Chemical shifts are recorded in ppm (δ) in D_2O with the internal reference set to δ 4.79 ppm. ATR FT-IR spectroscopy was performed using a Perkin-Elmer Spectrum 100 series FT-IR spectrometer equipped with a universal ATR sampling accessory. UV-VIS studies were performed on a Varian Cary 4000 UV-Vis spectrophotometer. Gel permeation chromatography (GPC) was carried out in water (H_2O) on a Shodex glucose column with a Shimadzu SPD-M20A prominence diode array detector, Optilab refractive index detector and dynamic light scattering detector (both Wyatt). Samples were filtered over 0.2 μm PVDF filters before injection using a 0.6 mL / min flow rate.

AFM measurements were obtained in tapping mode using a PICOPLUS 5 μm scanning probe microscope (both Molecular Imaging) with Bruker RTESPA cantilevers (tip radius = 8 nm, f_0 = 305-356 kHz, k = 20-80 N/m). Samples were prepared by dropcasting 100 nM solutions of the nanoparticles on mica with drying in a vacuum oven for 30 min at 60 °C. AFM data were processed using Gwyddion 2.25 imaging software. The data were collected using Pro Data SX software and was analyzed using Origin 7.0 software.

MV-NCO[1] and *ns*CB[10][2] were prepared according to a literature procedures. All other materials were purchased from Aldrich and used as received.

S.2 General Synthetic Protocols

General synthesis of Poly(*N*-hydroxyethylacrylamide). *N*-Hydroxyethylacrylamide (0.5 g, 4.3 mmol) and methyl 2-chloropropanoate (MCP) (1.1 mg, 0.98 μL, 8.7 μmol, Target DP = [M]/[I] = 500) were dissolved in a 1:1 (v/v) mixture of deionized water and ethanol (0.75 mL) and the solution was degassed by bubbling nitrogen for 5 min. CuCl (0.9 mg, 8.7 μmol) and Me_6TREN (2.0 mg, 2.4 μL, 8.7 μmol) were dissolved in a 1:1 (v/v) mixture of deionized water and ethanol (0.25 mL) and the solution was degassed by bubbling nitrogen for 5 min. The monomer and initiator solution was then added via syringe into the copper and ligand solution and the mixture was allowed to stir at 20 °C for 30 min. Aliquots were removed periodically to analyze conversion. The reaction mixture was then diluted with ethanol (5 mL) and precipitated into acetone. The solid was filtered and dried under vacuum yielding the title compound as a white solid (0.48 g, 96 %). ^{1}H-NMR Spectroscopy (D_2O, 500 MHz) δ (ppm) = 3.50-3.32 (2H, HO-CH_2-CH_2), 3.25-2.87 (2H, HEAm, HO-CH_2-CH_2), 2.2-0.8 (polymer backbone). GPC (H_2O): M_n (PDI) = 59.2 kDa (1.10).

Table S1: Polymerization of *N*-hydroxyethylacrylamide using the CuCl/Me_6-TREN catalyst system.

Entry	$[M]_o/[I]_o$	Solvent (EtOH:H_2O)	Conversion (%)^a	M_n (kDa)^b	PDI^b
1	1000	50:50	86	133	1.15
2	2500	50:50	82	256	1.24
3	5000	50:50	78	440	1.23

^{a} determined by ^{1}H NMR. ^{b} determined by GPC using H_2O as eluent.

General synthesis of functional PHEAm polymers. PHEAm (0.5 g, 4.34 mmol relative to hydroxyl functionality) was dissolved in *N*-methyl-1-pyyrolidone (NMP) (5 ml). MV-NCO (121.8 mg, 0.217 mmol) was added as solids to the polymer solution. Dibutyltindilaurate (3 drops) was added to the solution to catalyse the isocyanate coupling. The reaction was stirred at room temperature for 5 hours. The resulting orange solution was precipitated from acetone to yield the yellow-orange polymer **1** (0.58 g, 95%). ^{1}H-NMR Spectroscopy (H_2O, 500 MHz) δ (ppm)= 9.28 (4H, d, MV-*H*), 8.76 (4H, d, MV-*H*), 5.01-4.92 (2H, MV-CH_2-CH_2-OCN-), 4.45 (3H, CH_3-MV), 4.11-4.01 (2H, MV-CH_2-CH_2-OCN-), 3.78-3.50 (R-OCN-CH_2-, R-NCO-CH_2-CH_2-polymer), 3.50-2.89 (R-NCO-CH_2-CH_2-polymer), 2.20-1.10 (polymer backbone). GPC (H_2O): M_n (PDI) = 168 kDa (1.15).

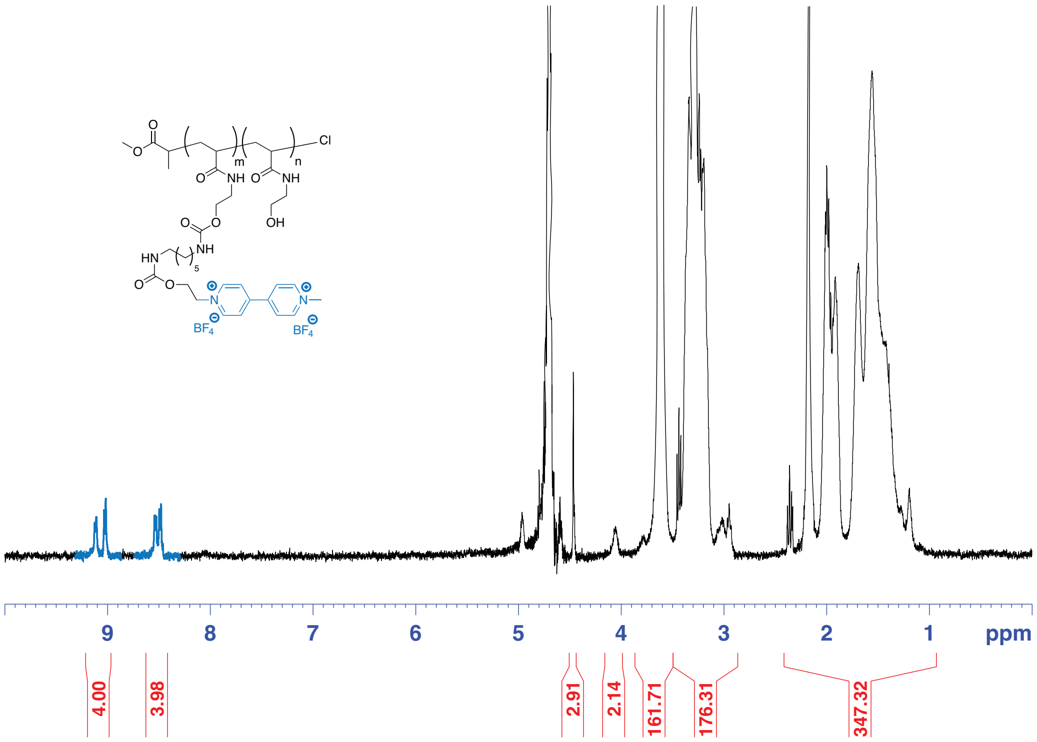

Figure S1: ^{1}H-NMR characterization of functional polymer **P1**.

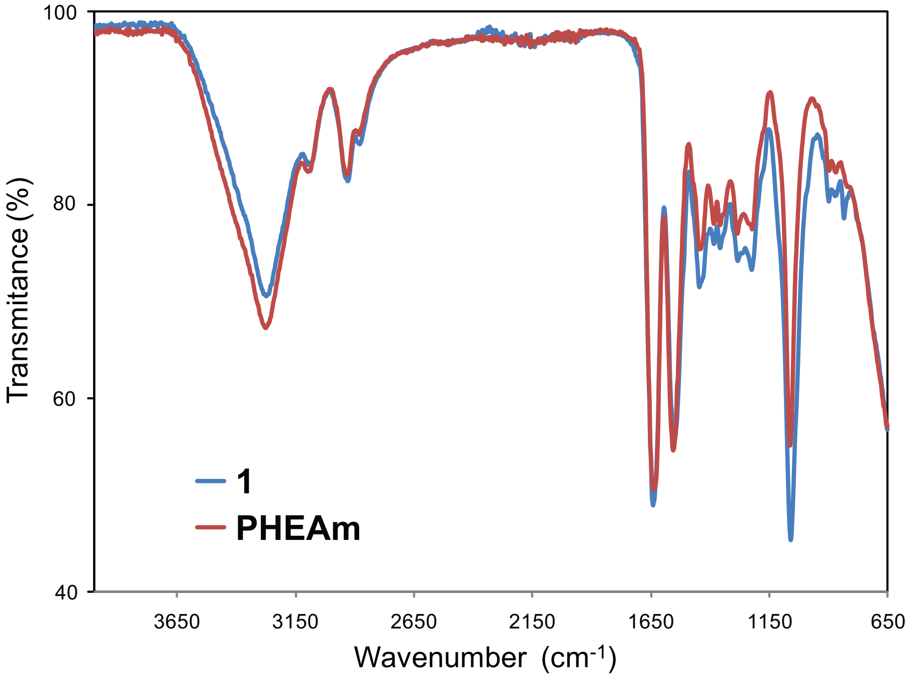

Figure S2: FT-IR characterization of functional polymer **P1**.

General preparation of supramolecular single-chain polymeric nanoparticles. A solution of **P1** (10 ml, 1 mg/mL, 0.38 mM relative to MV) in H_2O was stirred vigorously with slow addition of *nor-seco*-cucurbit[10]uril (5.06 mg, 3.8 μmol) as a solid over a period of 10 minutes. The solution of the particles was stirred for a further 2 hours.

Table S2: Dynamic light scattering analysis of single-chain polymer nanoparticles.

Polymer	MV[a] (%)	*ns*CB[10] (%)	NP[b]	R_h^c (nm)	PDI
1	5	0	-	42 ± 2	0.38
1	5	5	**NP1**	38 ± 1	0.25
2	5	0	-	48 ± 2	0.33
2	5	5	**NP2**	43 ± 1	0.26
3	15	0	-	92 ± 3	0.36
3	15	5	**NP3a**	79 ± 2	0.33
3	15	10	**NP3b**	57 ± 2	0.37
3	15	15	**NP3c**	43 ± 1	0.39
4	5	0	-	57 ± 2	0.39
4	5	5	**NP4**	52 ± 1	0.36
4	5	0[d]	-[d]	63 ± 3	0.39

[a] Molar loading of both MV moieties on the functional polymer. [b] Single-chain polymer nanoparticle formed.

[c] Hydrodynamic diameter taken from DLS measurements. [d] Control experiment where CB[7] (5%) was added instead of *ns*CB[10] to demonstrate the absence of single-chain folding/collapse without ternary complex formation.

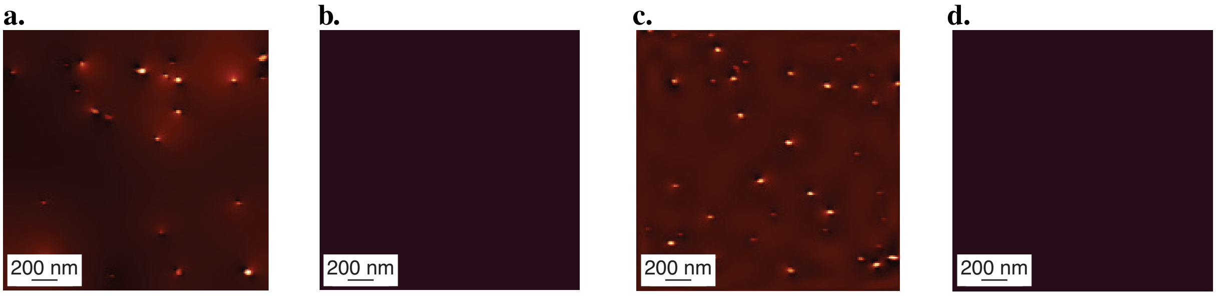

Figure S3: AFM imaging of single-chain polymeric nanoparticles drop-cast from dilute solutions onto mica substrates: a) **NP2**. b) Image of the control experiment where polymer **P2**, without the addition of *ns*CB[10], was imaged to demonstrate that no nanoparticles form and that only a flat polymer film is observed. c) **NP4**. d) Image of the control experiment of the addition of CB[7] to polymer **P4** demonstrating that no nanoparticles form.

References

[1] Biedermann, F.; Appel, E. A.; del Barrio, J.; Gruendling, T.; Barner-Kowollik, C.; Scherman, O. A. *Macromolecules* **2011**, *44*, 4828–4835.

[2] Huang, W.-H.; Liu, S.; Zavalij, P. Y.; Isaacs, L. *J. Am. Chem. Soc.* **2006**, *128*, 14744–14745.