

## Electronic Supplementary Information (ESI)

### Aqueous-only, pH-induced nanoassembly of dual pKa-driven contraphilic block copolymers

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**Materials.** The following materials were synthesized according to literature methods; 2,2,5-trimethyl-3-(1'-phenylethoxy)-4-phenyl-3-azahexane and 2,2,5-trimethyl-4-phenyl-3-azahexane-3-nitroxide.<sup>1</sup> *tert*-Butyl acrylate (*t*BA) and 4-acetoxystyrene (AcS) were filtered through a plug of aluminum oxide to remove the inhibitor. All other chemicals and reagents were obtained from Aldrich and used as received unless described otherwise. All reactions were performed under N<sub>2</sub> unless noted otherwise.

**Analysis.** <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were recorded at 500-MHz and 125 MHz, respectively, as solutions with the solvent proton or carbon signal as a standard. Gel permeation chromatography (GPC) was conducted on a Waters 1515 HPLC (Waters Chromatography, Inc.) equipped with a Waters 2414 differential refractometer, a PD2020 dual-angle (15° and 90°) light scattering detector (Precision Detectors, Inc.), and a three-column series PL gel 5μm Mixed C, 500 Å, and 10<sup>4</sup> Å, 300 x 7.5 mm columns (Polymer Laboratories, Inc.). The system was equilibrated at 35 °C in anhydrous THF, which

served as the polymer solvent and eluent with a flow rate of 1.0 mL/min. Polymer solutions were prepared at a known concentration (*ca.* 4-5 mg/mL) and an injection volume of 200  $\mu$ L was used. Data collection and analysis were performed, respectively, with Precision Acquire software and Discovery 32 software (Precision Detectors, Inc.). Interdetector delay volume and the light scattering detector calibration constant were determined by calibration using a nearly monodispersed polystyrene standard (Pressure Chemical Co.,  $M_p = 90$  kDa,  $M_w/M_n < 1.04$ ). The differential refractometer was calibrated with standard polystyrene reference material (SRM 706 NIST), of known specific refractive index increment  $dn/dc$  (0.184 mL/g). The  $dn/dc$  values of the analyzed polymers were then determined from the differential refractometer response. DLS analysis was performed using a Brookhaven Instruments Co (Holtsville, NY) system consisting of a model BI-200SM goniometer, a model EMI-9865 photomultiplier, and a model BI-9000AT digital correlator. Incident light was provided by a model 95-2 Ar<sup>+</sup> laser (Lexel Corp., Palo Alto, CA) operated at 514.5 nm. All measurements were made at  $25 \pm 1$  °C in water. Scattered light was collected at 90° angle. The digital correlator was operated with 522 channels, a dual sampling time of 100 ns, a 5s ratio channel spacing, and a duration time of 15 min. A photomultiplier aperture of 400  $\mu$ m was used, and the incident laser intensity was adjusted to obtain a photon counting rate between 200 to 300 kcps. Only measurements in which the measured and calculated baselines of the intensity autocorrelation function agreed to within 0.1% were used to calculate the particle size. The calculation of the particle size distribution and distribution averages was performed with the ISDA software package (Brookhaven Instruments Co., Holtsville, NY), which employed CONTIN particle size distribution analysis routines. A Corning pH meter 440

was used to measure pH of the solution. Samples for AFM imaging were prepared by drop-depositing *ca.* 2.0  $\mu\text{L}$  of the sample solution ( $\sim 0.1$  mg/mL) onto freshly cleaved mica plates. The AFM instrumentation consisted of a Nanoscope IIIa system, equipped with a J-type vertical engage piezoelectric scanner and operated in a tapping mode in air. Tapping-mode imaging was carried out with high resolution silicon probes. The average height values of micelles on mica were determined by section analysis, using the Nanoscope III software package.

**Synthesis of poly(*tert*-butyl acrylate)<sub>131</sub> (5):** To a flame-dried 25-mL Schlenk flask equipped with a magnetic stir bar and under N<sub>2</sub> atmosphere, at room temperature (rt), was added 2,2,5-trimethyl-3-(1'-phenylethoxy)-4-phenyl-3-azahexane (100 mg, 0.31 mmol), 2,2,5-trimethyl-4-phenyl-3-azahexane-3-nitroxide (3.4 mg, 0.015 mmol), and *tert*-butyl acrylate (6.56 g, 51.2 mmol). The reaction flask was sealed and stirred for 10 min at rt. The reaction mixture was degassed through three cycles of freeze-pump-thaw. After the last cycle, the reaction mixture was recovered back to rt and stirred for 10 min before being immersed into a pre-heated oil bath at 125 °C to start the polymerization. After 25 h, <sup>1</sup>H NMR analysis showed 80% monomer conversion had been reached. The polymerization was quenched by quick immersion of the reaction flask into liquid N<sub>2</sub>. The reaction mixture was dissolved in THF and precipitated into H<sub>2</sub>O/MeOH (v:v, 1:4) three times to afford **5** as a white powder, (4.4 g, 90% yield based upon monomer conversion);  $M_n^{\text{NMR}} = 16,400$  g/mol,  $M_n^{\text{GPC}} = 17,000$  g/mol,  $M_w/M_n = 1.19$ . <sup>1</sup>H NMR (CD<sub>2</sub>Cl<sub>2</sub>, ppm):  $\delta$  1.43 (br, 1370 H), 1.80 (br, 48 H), 2.21 (br, 120 H), 7.33-7.04 (m, 10 H). <sup>13</sup>C NMR (CD<sub>2</sub>Cl<sub>2</sub>, ppm):  $\delta$  27.8, 36.2, 41.8, 81.0, 174.5.

**Synthesis of poly(*tert*-butyl acrylate)<sub>131</sub>-*b*-poly(4-acetoxystyrene)<sub>76</sub> (4):** To a flame-dried 25-mL Schlenk flask equipped with a magnetic stir bar and under N<sub>2</sub> atmosphere at rt, **5**, (3.0 g, 0.18 mmol), 4-acetoxystyrene (3.73 g, 23 mmol), 2,2,5-trimethyl-4-phenyl-3-azahexane-3-nitroxide (1.9 mg, 8.8 μmol), and DMF (*ca.* 1 mL) were added. The reaction mixture was allowed to stir for 1 h at rt to obtain a homogeneous solution. The reaction mixture was degassed through three cycles of freeze-pump-thaw. After the last cycle, the reaction mixture was recovered back to rt and stirred for 10 min before being immersed into a pre-heated oil bath at 125 °C to start the polymerization. After 14 h, 58% monomer conversion was reached, as analyzed by <sup>1</sup>H NMR spectroscopy. After quenching by immersion of the reaction flask into a bath of liquid N<sub>2</sub>, THF was added to the reaction mixture and the polymer was purified by precipitating into H<sub>2</sub>O/MeOH (v:v, 1:4) three times to afford **4** as a white powder, (4.55 g, 88% yield);  $M_n^{\text{NMR}} = 28,700$  g/mol,  $M_n^{\text{GPC}} = 28,400$  g/mol,  $M_w/M_n = 1.26$ . <sup>1</sup>H NMR (300 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 1.43 (m, 1720), 1.80 (br, 130 H), 2.24 (br, 340 H), 6.55 (m, 280 H), 7.21 (m, 10 H). <sup>13</sup>C NMR (CD<sub>2</sub>Cl<sub>2</sub>, ppm): δ 21.5, 28.4, 35.9, 37.9, 40.6, 42.5, 80.9, 121.7, 128.9, 136.5, 143.0, 149.4, 174.5.

**Synthesis of poly(*tert*-butyl acrylate)<sub>131</sub>-*b*-poly(*p*-hydroxystyrene)<sub>76</sub> (3):** To a 25-mL round bottom (RB) flask, **4** (2.0 g, 71 μmol) and MeOH (10 mL) were added and stirred for 10 min at rt. The cloudy mixture was heated slowly to reflux. Immediately after the solution turned clear, a sodium methoxide solution in MeOH (25 wt%) (5.82 mg, 108 mmol) was added through syringe. The reaction mixture was further allowed to heat at reflux for 4 h. After cooling down to rt, the reaction mixture was precipitated in water with 4% acetic acid to afford **3** as white solid (1.7 g, 90 % yield).  $M_n^{\text{NMR}} = 26,200$  g/mol.

$^1\text{H}$  NMR ( $\text{CD}_3\text{OD}$ , ppm):  $\delta$  1.48 (br, 1200 H), 1.83 (br, 280 H), 2.27 (br, 300 H), 6.38 (m, 300 H), 7.26-7.16 (br, 10 H).  $^{13}\text{C}$  NMR ( $\text{CD}_3\text{OD}$ , ppm):  $\delta$  28.0, 37.1, 38.6, 40.8, 43.6, 82.2, 116.0, 129.9, 156.1, 175.8.

**Synthesis of poly(acrylic acid)<sub>131</sub>-*b*-poly(*p*-hydroxystyrene)<sub>76</sub> (1):** To a RB flask equipped with a magnetic stir bar, was added **2** (1.35 g, 71.0  $\mu\text{mol}$ ) and trifluoroacetic acid (20.2 g, 177 mmol). The reaction mixture was allowed to stir for 14 h at rt. Excess acid was removed under vacuum. The residue was dissolved into 10 mL of THF and purified by dialysis against nanopure water (18.0  $\text{M}\Omega\text{-cm}$ ) for three days and freeze-dried to afford **1** as a white powder (0.97 g, 95% yield).  $M_n^{\text{NMR}} = 19,000$  g/mol.  $^1\text{H}$  NMR ( $\text{DMSO-d}_6$ , ppm):  $\delta$  1.33 (m, 250 H), 2.18 (br, 50 H), 3.36 (br, 280 H), 6.45 (br, 300 H), 7.22 (m, 10 H), 8.94 (br, 80 H), 12.3 (br, 90 H).  $^{13}\text{C}$  NMR ( $\text{DMSO-d}_6$ , ppm):  $\delta$  26.1, 30.7, 67.9, 115.9, 128.0, 136.2, 156.1, 176.7.

**Preparation of micelle (2):** To a 25-mL RB flask equipped with a magnetic stir bar was added **1** (2 mg, 0.1  $\mu\text{mol}$ ) and nanopure water (15 mL). The pH value was adjusted to 12 by adding 1.0 M NaOH solution to afford a clear solution. The micellization was initiated after decreasing the pH value to 7 by adding dropwise 1.0 M HCl. The micelle solution was further allowed to stir for 12 h at rt.  $H_{\text{av}} = 5 \pm 2$  nm (AFM);  $D_{\text{av}} = 16 \pm 3$  nm (TEM);  $D_h$  as measured by DLS was pH dependent—see manuscript Fig. 4 for the data.

## References

- 1 D. Benoit, V. Chaplinski, R. Braslau, C. J. Hawker, *J. Am. Chem. Soc.* 1999, **121**, 3904-3920.