Supplementary Information

Synthesis of Amphiphilic, Janus Diblock Hyperbranched Copolyamides and Their Self-Assembly in Water

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Measurements

¹H and ¹³C spectra were obtained on JEOL ECA-600 and ECA-500 instruments operating in the pulsed Fourier-transform (FT) mode, using tetramethylsilane (TMS, 0.00 ppm) and the midpoint of CDCl₃ (77.0 ppm) as internal standards of ¹H, and ¹³C NMR spectra. IR spectra were recorded on a JASCO FT/IR-410. Purification was conducted with a JAI LC-908 preparative HPLC (eluent: CHCl₃) with two TOSOH TSKgel columns (2 × G2000H_{HR}), and with a JAI LC908-C60 recycling preparative HPLC (eluent, CHCl₃) with two JAIGEL columns (1H-40 and 2H-40). The M_n and M_w/M_n values of polymers were measured on a

Shodex GPC-101 (eluent, THF; calibration, polystyrene standards) equipped with Shodex UV-41, Shodex RI-71S, and Wyatt Technology DAWN EOS multiangle laser light scattering (MALLS, Ga-AS laser, $\lambda = 690$ nm) detectors and two Shodex KF-804-L columns. Transmission electron microscope (TEM) imaging was performed using a JEOL JEM-1230 microscope operating at 100 kV with a Gatan Dual Vision CCD camera. The method was basically drop-cast the solution on a TEM carbon coated copper grid while the TEM copper grid was placed on a hot plate to maintain with a specified temperature (25, 50, and 70 °C). Dynamic light scattering (DLS) measurements were performed with an OTSUKA ELECTRONICS particle sizer (FPAR-1000).

Materials

Lithium 1,1,1,3,3,3-hexamethyldisilazide (LiHMDS, Aldrich; 1.0 M solution in THF), dehydrated tetrahydrofuran (dry THF, Kanto), dehydrated *N*,*N*-dimethylformamide (dry DMF, Kanto), and dehydrated dichloromethane (dry CH_2Cl_2 , Kanto) were used as received. AB₂ monomers **4**, **8**, and initiator **9** were prepared according to the literature.^{1, 2}

Synthesis of initiator 5



Scheme S1. Synthesis of initiator 5.

Compound 11. Into a solution of 5-aminoisophthalic acid (10.08 g, 55.6 mmol) in triethylene glycol monomethyl ether (180 mL) was added thionyl chloride (15.0 mL, 206 mmol) at 0 °C. The mixture was stirred at 80 °C for 8 h, then the reaction was quenched with sat. NaHCO₃. The whole was extracted with ethyl acetate. The combined organic layers were washed with water and brine, dried over anhydrous MgSO₄, and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (ethyl acetate) to give 13.29 g of **11** as a yellow liquid (54%). ¹H NMR (500 MHz, CDCl₃): δ (ppm): 8.07 (t, *J* = 1.4 Hz, 1 H), 7.53 (d, *J* = 1.7 Hz, 2 H), 4.47 (t, *J* = 4.9 Hz, 4 H), 4.00 (br s, 2 H), 3.83 (t, *J* = 4.8 Hz, 4 H), 3.74-3.63 (m, 12 H), 3.56-3.50 (m, 4 H), 3.37 (s, 6 H). ¹³C NMR (150 MHz, CDCl₃): δ (ppm): 165.9, 146.8, 131.4, 120.7, 119.8, 71.9, 70.7, 70.58, 70.54, 69.1, 64.2, 58.9. IR (neat): *v* (cm⁻¹): 3450, 3363, 3243, 2875, 1959, 1720, 1631, 1605, 1455, 1341, 1234, 1108, 1037, 998, 948, 887, 851, 759.

Compound 12. To a solution of **11** (1.99 g, 4.20 mmol) in dry DMF (13.0 mL) was added 4-(*tert*-butyldimethylsilyloxymethyl)benzoic acid (0.984 g, 3.69 mmol), 4-(dimethylamino)pyridine (DMAP) (0.684 g, 5.60 mmol) and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDCI) (0.902

g, 4.71 mmol) at ambient temperature. The mixture was stirred for 23 h, and then the reaction was quenched with water. The whole was extracted with ether. The combined organic layers were washed with 1 M HCl, sat. NaHCO₃ and brine, dried over anhydrous MgSO₄, and concentrated in vacuo to give **12** as a viscous yellow liquid (2.44 g, 90%). ¹H NMR (600 MHz, CDCl₃): δ (ppm): 8.70 (s, 1 H), 8.53 (d, *J* = 1.7 Hz, 2 H), 8.41 (t, *J* = 1.7 Hz, 1 H), 7.93 (d, *J* = 8.0 Hz, 2 H), 7.44 (d, *J* = 8.0 Hz, 2 H), 4.81 (s, 2 H), 4.48 (t, *J* = 4.8 Hz, 4 H), 3.83 (t, *J* = 4.8 Hz, 4 H), 3.73-3.64 (m, 12 H), 3.53-3.50 (m, 4 H), 3.32 (s, 6 H), 0.96 (s, 9 H), 0.12 (s, 6 H). ¹³C NMR (125 MHz, CDCl₃): δ (ppm): 166.0, 165.3, 145.8, 138.8, 132.8, 130.9, 127.3, 126.2, 125.9, 125.5, 71.7, 70.6, 70.5, 70.4, 68.9, 64.4, 64.3, 58.8, 25.8, 18.3, -5.38. IR (neat): *v* (cm⁻¹): 3338, 2952, 2928, 2883, 2858, 1725, 1677, 1609, 1551, 1452, 1426, 1336, 1276, 1236, 1102, 1037, 940, 840, 778, 757.

Initiator 5. To a suspension of NaH (0.041 g, 1.71 mmol) in dry DMF (13.0 mL) was added a solution of **12** (0.890 g, 1.23 mmol) in dry DMF (6.5 mL) at 0 °C. The mixture was stirred at 0 °C for 40 min, and iodomethane (0.10 mL, 1.6 mmol) was added at 0 °C. The mixture was stirred at 0 °C for 3 h, and then the reaction was quenched with water. The whole was extracted with ether. The combined organic layers were washed with 1 M HCl and brine, dried over anhydrous MgSO₄, and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (ethyl acetate) to give **5** as a viscous colorless liquid (0.458 g, 50%). ¹H NMR (600 MHz, CDCl₃): *δ* (ppm): 8.46 (t, *J* = 1.4 Hz, 1 H), 7.93 (d, *J* = 1.7 Hz, 2 H), 7.28 (d, *J* = 8.0 Hz, 1 H), 7.15 (d, *J* = 8.5 Hz, 2 H), 4.65 (s, 2 H), 4.45 (t, *J* = 4.8 Hz, 4 H), 3.81 (t, *J* = 4.8 Hz, 4 H), 3.71-3.64 (m, 12 H), 3.55-3.53 (m, 4 H), 3.52 (s, 3 H), 3.36 (s, 6 H), 0.90 (s, 9 H), 0.03 (s, 6 H). ¹³C NMR (125 MHz, CDCl₃): *δ* (ppm): 170.6, 164.7, 145.4, 143.6, 133.5, 131.8, 131.5, 128.6, 128.4, 125.4, 71.8, 70.5, 70.4, 68.9, 64.5, 64.3, 58.9, 38.3, 25.8, 18.2, -5.43. IR (neat): *v* (cm⁻¹): 3445, 2927, 2882, 1725, 1653, 1599, 1455, 1355, 1335, 1240, 1108, 1039, 1018, 940, 840, 779, 758.

Synthesis of 1



Scheme S2. Synthesis of 1.

Compound 6. A flask, equipped with a three-way stopcock, was purged with argon and then charged with 1.0 M LiHMDS in THF (2.3 mL, 2.3 mmol). The flask was cooled to -40 °C under an argon atmosphere with stirring. Into the flask was added a solution of **5** (0.158 g, 0.215 mmol) in dry THF (4.0 mL) under dry nitrogen, followed by dropwise addition of a solution of **4** (1.019 g, 2.09 mmol) in dry THF (14.0 mL) over ca. 3 h at -40 °C with stirring under dry nitrogen. The mixture was stirred at -40 °C for 3 h, and then the reaction was quenched with sat. NH₄Cl. The whole was extracted with CH₂Cl₂. The combined organic layers were washed with water, dried over anhydrous MgSO₄, and concentrated under reduced pressure. The residue was purified by preparative HPLC (eluent: CHCl₃) to give **6** as a viscous yellow solid (0.485 g, 58%, M_n (MALLS) = 8710, $M_w/M_n = 1.22$).

Compound 1. To a solution of **6** (0.485 g, 0.0557 mmol) in dry THF (3.0 mL) was added 1 M HCl (0.5 mL) at ambient temperature. The reaction mixutre was stirred for 24 h, and then the reaction was quenched with sat. NaHCO₃. The whole was extracted with CH₂Cl₂. The combined organic layers were washed with water and brine, dried over anhydrous MgSO₄, and concentrated in vacuo. The residue

was purified by preparative HPLC (eluent: $CHCl_3$) to give **1a** as a viscous reddish brown solid (0.143 g, 30%, M_n (MALLS) = 7580, M_w/M_n = 1.08).

Synthesis of 2



Scheme S3. Synthesis of 2.

Compound 10. LiCl (1.445 g, 53.6 mmol) was placed in a flask equipped with a three-way stopcock, and dried at 250 °C under reduced pressure. The flask was cooled to room temperature under an argon atmosphere, and then charged with 1.0 M LiHMDS in THF (7.4 mL, 7.4 mmol). The flask was cooled to -35 °C under an argon atmosphere with stirring. A solution of **9** (0.212 g, 0.424 mmol) in dry THF (10.0 mL) was added to the flask under dry nitrogen, then a solution of **8** (2.158 g, 6.18 mmol) in dry THF (30 mL) was added dropwise over ca. 2 h at -35 °C with stirring under dry nitrogen. The mixture was stirred at -35 °C for 4 h, and then the reaction was quenched with saturated aqueous NH₄Cl. The whole was extracted with CH₂Cl₂. The organic layer was washed with water, dried over anhydrous MgSO₄, and concentrated under reduced pressure to give **10** as a yellow solid (1.976 g, 77%, M_n (GPC) = 5860, $M_w/M_n = 1.08$).

Compound 7. To a solution of **10** (1.220 g, 0.221 mmol) in dry THF (15.0 mL) was added 1 M HCl (1.6 mL) at ambient temperature. The reaction mixutre was stirred for 15 h, and then the reaction was quenched with sat. NaHCO₃. The whole was extracted with CH_2Cl_2 . The combined organic layers were washed with water, dried over anhydrous MgSO₄, and concentrated in vacuo to give **7** as a yellow solid (1.036 g, 80%, M_n (MALLS) = 4050, M_w/M_n = 1.09).

Compound 2. To a solution of **7** (0.408 g, 0.0699 mmol) and triethylamine (0.10 mL, 0.72 mmol) in dry CH₂Cl₂ (2.0 mL) was added DMAP (0.099 g, 0.81 mmol) and succinic anhydride (0.086 g, 0.86 mmol) at ambient temperature. The reaction mixutre was stirred for 14 h. Water was added and the whole was extracted with CH₂Cl₂. The combined organic layers were washed with 1 M HCl and brine, dried over anhydrous MgSO₄, and concentrated under reduced pressure. The residue was purified by preparative HPLC (eluent: CHCl₃) to give **2a** as a reddish brown solid (0.220 g, 53%, M_n (MALLS) = 6250, $M_w/M_n = 1.08$).

Synthesis of 3

Condensation of 1 with 2. To a solution of **1a** (0.0403 g, 0.00532 mmol) in dry DMF (0.5 mL) was added **2a** (0.0319 g, 0.00510 mmol), DMAP (0.0077 g, 0.0630 mmol), and EDCI (0.0140 g, 0.0730 mmol) at ambient temperature. The mixture was stirred for 43 h, and then the reaction was quenched with water. The whole was extracted with CH_2CI_2 . The combined organic layers were washed with 1 M HCl and brine, dried over anhydrous MgSO₄, and concentrated in vacuo. The residue was purified by preparative HPLC (eluent: CHCl₃) to give **3a** as a colorless solid (0.0460 g, 65%, M_n (MALLS) = 9280, $M_w/M_n = 1.08$).

The similar procedure afforded **3b** as a light yellow solid (16%, M_n (MALLS) = 22100, M_w/M_n = 1.07).



Figure S1. ¹H NMR spectrum of **2a** in CDCl₃ at 25 °C.



Figure S2. GPC profiles of (A) **2b**, (B) **1b**, (C) the products obtained by the reaction of **1b** with **2b** in the presence of EDCI and DMAP in DMF at room temperature for 44 h, and (D) the products purified by means of preparative HPLC (eluent: CHCl₃).



Figure S3. ¹H NMR spectrum of **3b** in CDCl₃ at 25 °C.

Reference

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