Supplementary Information

Self-assembly of PEG/dodecyl-graft amphiphilic copolymers in water: consequences of the monomer sequence and chain flexibility on uniform micelles

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Experimental Section

Materials

Tetralin (1,2,3,4-tetrahydronaphthalene: TCI; purity >97%; an internal standard for ^{1}H NMR analysis) was dried overnight over calcium chloride and distilled from calcium hydride under reduced pressure before use. Triethylamine (TCI, purity >99.0%) was purified by distillation before use. Poly(ethylene glycol) methyl ether methacrylate [PEGMA: CH_2=$CMeCO_2(CH_2CH_2O)_nMe$, M_n = 475, n = 8.5 on average] (Aldrich), poly(ethylene glycol) methyl ether acrylate [PEGA: CH_2=$CHCO_2(CH_2CH_2O)_nMe$, M_n = 480, n = 9.0 on average] (Aldrich), dodecyl methacrylate (DMA) (Wako, purity >95%), and dodecyl acrylate (DA) (TCI, purity >98%) were purified by an inhibitor removal column (Aldrich) and degassed by triple vacuum-argon purge cycles before use. Ethyl 2-chloro-2-phenylacetate (ECPA: Aldrich, purity >97%) and ethyl 2-bromo-2-methylpropanoate (EMA-Br: Aldrich, purity <98%) were distilled under reduced pressure before use. $Ru(Ind)Cl(PPh_3)_2$ (Aldrich) and $RuCp^*Cl(PPh_3)_2$ (Cp*: pentamethylcyclopentadienyl, Aldrich, purity >97%) were used as received and handled in a glove box under moisture- and oxygen-free argon (H_2O < 1 ppm; O_2 < 1 ppm). Al(O*i*-Pr)$_3$ (Aldrich, purity >99.99%), *n*-Bu_3N (TCI, purity >98%), and methoxycyclopentane (ZEON, purity >99%) were degassed by triple vacuum-argon purge cycles before use. Toluene (solvent) was purified before use by passing it through a purification column (Glass Contour Solvent Systems: SG Water USA). 2-Bromoisobutyryl bromide (TCI, purity >98%), benzylalcohol (Wako, purity >99%), 1,4-benzenedimethanol (TCI, purity >99%), dry THF (Wako, dehydrated), and dry CH_2Cl_2 (Wako, dehydrated) were used as received.

Characterization

Molecular weight distribution (MWD) curves, number-average molecular weight (M_n), peak top molecular weight (M_p), and M_w/M_n ratio of the polymers were measured by SEC in DMF containing 10 mM LiBr at 40 ^oC (flow rate: 1 mL/min) on three linear-type polystyrene gel columns (Shodex KF-805L: exclusion limit = 4×10^6; particle size = 10 μm; pore size = 5000 Å; 0.8 cm i.d. × 30 cm) that were connected to a Jasco PU-2080 precision pump, a Jasco RI-2031 refractive index detector, and a Jasco UV-2075 UV/vis detector set at 270 nm. The columns were calibrated against 10 standard poly(MMA) samples (Polymer Laboratories: M_p = 2680–1250000; M_w/M_n = 1.02–1.09) or 14 standard poly(ethylene oxide) samples (Polymer Laboratories: M_p = 1470–863500; M_w/M_n = 1.02–1.16). MWD curves, M_n, M_p, and M_w/M_n of the polymers were also measured by SEC in H_2O at 30 ^oC (flow rate: 1 mL/min) on a silica gel column (TOSOH G4000SW_{XL}: exclusion limit = 7×10^6; particle size = 8 μm; 0.8 cm i.d. × 30 cm) that was connected to the same pump and detector

system as those used in DMF. The column was calibrated against 11 standard poly(ethylene oxide) samples (Polymer Laboratories: M_p = 1470–298000; M_w/M_n = 1.03–1.07). To remove the residue of catalysts and unreacted monomers, polymer samples for characterization were purified by preparative SEC in DMF at 25 °C (flow rate: 15 mL/min) on TOSOH TSKgel α-3000 (exclusion limit = 9×10^4; particle size = 13 μm; 5.5 cm i.d. × 30 cm). ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$, CD_3COCD_3, and D_2O on a JEOL JNM-ECA500 spectrometer operating at 500 (^{1}H) and 125 (^{13}C) MHz. Absolute weight-average molecular weight (M_w) of the polymers in DMF or H_2O was determined by multi-angle laser light scattering (MALLS) equipped with SEC on a Dawn HELEOS II instrument (Wyatt Technology, semiconductor laser, λ = 663 nm). The SEC was performed in DMF containing 10 mM LiBr at 40 °C (flow rate: 1 mL/min) on three linear-type polystyrene gel columns (Shodex KF-805L) or in H_2O at 30 °C (flow rate: 1 mL/min) on a silica gel column (TOSOH G4000SW_{XL}), that were connected to a Jasco PU-2080 precision pump, a Jasco RI-1530 refractive index detector, and a Jasco UV-1570 UV/vis detector set at 270 nm. Dynamic light scattering (DLS) was measured on Otsuka Photal ELSZ-0 equipped with a semi-conductor laser (λ = 658 nm) at 25 °C. The measuring angle was 165° and the data was analyzed by CONTIN method. Fourier transform infrared (FT-IR) spectra were recorded on Agilent Technologies Cary 630 FT-IR spectrometer at 25 °C. Cloud point of the aqueous solutions of polymers was measured on UV-1800 (Shimadzu, optical path length = 1.0 cm, λ = 670 nm, heating/cooling rate: 1 °C/min, temperature range: 40 – 95 °C). Differential scanning calorimetry (DSC) was performed for samples (ca. 5 mg weighed into an aluminum pan) under dry nitrogen flow on a DSC Q200 calorimeter (TA Instruments) equipped with a RCS 90 electric freezing machine. The polymer samples were heated to 150 ºC at the rate of 10 ºC/min and held at the temperature for 10 min to erase thermal history. Then, the samples were cooled to -80 ºC at the rate of -10 ºC/min and held at the temperature for 10 min, and again heated to 150 ºC at the rate of 10 ºC/min. The second heating runs were used for the thermal analysis of polymers.

^{1}H spin-spin relaxation time (T_2) measurement of polymers was conducted using degassed D_2O or acetone-d_6 solutions of polymers (except for PEGMA/DMA random copolymer, entry 6 in Table S2) at 30 °C. Degassed polymer solutions were added into NMR tubes by syringe; the tubes were then sealed under nitrogen before ^{1}H NMR analysis. ^{1}H T_2 values were determined by the Carr-Purcell-Meiboom-Gill (CPMG) pulse sequence using 16 values of τ (a minimum value of 25 ms, a maximum value of 5 s). The NMR samples were not spun during the measurement. The number of scans was set at 128 (data points = 16384, spectral width = 10 ppm. Other parameters were set as follows: 90° pulse width = 14 μs; relaxation delay = 7 s. For a PEGMA/DMA random copolymer (entry 6 in Table S2), 16 values of τ (a minimum value of 5 ms, a maximum value of 3 s) and relaxation delay (4.5 s) were employed.

Synthesis of Initiators

Benzyl 2-bromo-2-methylpropanoate (BzMA-Br): In 50 mL round-bottomed flask equipped with a three-way stopcock, benzyl alcohol (8 mmol, 0.52 mL), triethylamine (18 mmol, 2.51 mL), and CH_2Cl_2 (20 mL) were added at 25 ^oC under argon. Into the solution, 2-bromo-2-methylpropanoyl bromide (12 mmol, 1.48 mL) was added dropwise at 0 ^oC. The mixture was stirred at 25 ^oC for 2 days. Then, the reaction was terminated by adding water. The organic layer was washed with saturated aqueous Na_2CO_3 solutions (50 mL) two times, dilute aqueous HCl solutions (50 mL) two times, water (100 mL) three times, and brine (100 mL) once, and was dried on sodium sulfate for 1 h. After evaporating the organic solution, the resulting crude product was purified by column chromatography (hexane/ethyl acetate = 9/1) to give benzyl 2-bromo-2-methylpropanoate (BzMA-Br). Yield 0.99 g (48 %). ^1H NMR [500 MHz, $CDCl_3$, r.t., δ = 7.26 ppm ($CDCl_3$)]: δ 7.4-7.3 (m, 5H, aromatic), 5.2 (s, 2H, benzyl), 2.0 (s, 6H, methyl). ^{13}C NMR [125 MHz, $CDCl_3$, r.t., δ = 77.16 ppm ($CDCl_3$)]: δ 171.6 (-O-*C*O-), 135.6, 128.7, 128.5, 128.0 (C_6H_5-), 67.7 (-O-*C*H_2-C_6H_5-), 55.8 (-CO-*C*$(CH_3)_2$-Br), 30.9 ((*C*$H_3)_2$-CBr-CO-). FT-IR: ν/cm^{-1} = 1729 (carbonyl C=O stretch).

1,4-Bis(2-bromoisobutyryloxymethyl)benzene (BzDMA-2Br): In 50 mL round-bottomed flask equipped with a three-way stopcock, 1,4-benzenedimethanol (5 mmol, 0.69 mL), triethylamine (22.5 mmol, 3.32 mL), and THF (25 mL) were added at 25 ^oC under argon. Into the solution, 2-bromo-2-methylpropanoyl bromide (15 mmol, 1.84 mL) was added dropwise at 0 ^oC. The reaction mixture was stirred at 25 ^oC for 18 h and evaporated to remove THF. The resulting crude was dissolved in ethyl acetate. The organic mixture was washed with saturated aqueous Na_2CO_3 solutions (50 mL) two times, dilute aqueous HCl solutions (50 mL) two times, water (100 mL) three times, and brine (100 mL) once, and was dried on sodium sulfate for 1 h. After evaporating the organic solution, the resulting product was purified by column chromatography (hexane/ethyl acetate = 9/1) to give 1,4-bis(2-bromoisobutyryloxymethyl)benzene (BzDMA-2Br). Yield 1.66 g (76 %). ^1H NMR [500 MHz, $CDCl_3$, r.t., δ = 7.26 ppm ($CNCl_3$)]: δ 7.4 (s, 4H, aromatic), 5.2 (s, 4H, benzyl), 2.0 (s, 12H, methyl). ^{13}C NMR [125 MHz, $CDCl_3$, r.t., δ = 77.16 ppm ($CDCl_3$)]: δ 171.6 (-O-*C*O-), 135.7, 128.2 (-C_6H_4-), 67.3 (-O-*C*H_2-C_6H_4-), 55.7 (-CO-*C*$(CH_3)_2$-Br), 30.9 ((*C*$H_3)_2$-CBr-CO-). FT-IR: ν/cm^{-1} = 1733 (carbonyl C=O stretch).

Synthesis of Amphiphilic Copolymers

The synthesis of PEG/dodecyl-graft amphiphilic copolymers was carried out by syringe technique under argon in baked glass tubes equipped with a three-way stopcock. Typical procedures were given:

P4: PEGA/DA (19/12) random copolymer. RuCp*Cl(PPh_3)$_2$ (0.0045 mmol, 3.6 mg) was charged in a 30 mL glass tube. Then, methoxycyclopentane (2.2 mL), tetralin (0.24 mL), *n*-Bu_3N (0.18 mmol, 0.043mL), PEGA (2.7 mmol, 1.2 mL), DA (1.8 mmol, 0.50 mL), and a 40 mM methoxycyclopentane solution of benzyl 2-bromo-2-methylpropanoate (BzMA-Br, 1.8 mL, 0.072 mmol) were added sequentially into the tube at 25 °C under argon (the total volume: 6 mL). The glass tube was placed in an oil bath kept at 80 °C. At predetermined intervals, the mixture was sampled with a syringe under dry argon; the reaction was terminated by cooling the solution to –78 °C. The monomer conversion was determined by ^{1}H NMR in $CDCl_3$ with tetralin as an internal standard (Conv. PEGA/DA = 82%/77%, 77 h). The quenched reaction mixtures were evaporated to dryness. The crude product was purified by preparative SEC in DMF as an eluent to remove catalyst residue and unreacted monomers. The product was dried under vacuum at room temperature. SEC (DMF, PMMA std.): M_n = 11,000 g/mol; M_w/M_n = 1.26. *dn*/*dc* (DMF) = 0.043. SEC-MALLS (DMF, 0.01 M LiBr): M_w = 15,400 g/mol. ^{1}H NMR [500 MHz, acetone-d_6, 25 °C, δ = 2.05 (acetone)]: δ 7.5–7.3 (aromatic), 4.4–3.9 (-COOC$\underline{H}_2$CH$_2$O-, -COOC$\underline{H}_2$CH$_2$CH$_2$-), 3.8–3.7 (-COOCH$_2$C$\underline{H}_2$O-), 3.7–3.5 (-OCH$_2$CH$_2$O-), 3.5–3.4 (-C$\underline{H}_2$OCH$_3$), 3.4–3.3 (-OCH$_3$), 2.6–2.3 (-CH$_2$C$\underline{H}$CO-), 2.0–1.5 (-C$\underline{H}_2$CH-, -COOCHC$\underline{H}_2$(CH$_2$)$_9$CH$_3$), 1.5–1.2 (-COOCH$_2$CH$_2$(C$\underline{H}_2$)$_9$CH$_3$), 1.0–0.9 (-COO(CH$_2$)$_{11}$C$\underline{H}_3$). FT-IR: ν/cm^{-1} = 1729 (carbonyl C=O stretch).

P9: PEGA/DA random copolymer by FRP. AIBN (0.068 mmol, 11 mg) was charged in a 30 mL glass tube. Then, toluene (7.1 mL), tetralin (0.24 mL), PEGA (2.7 mmol, 1.2 mL), and DA (1.8 mmol, 0.50 mL) were added sequentially into the tube at 25 °C under argon (the total volume: 9 mL). The glass tube was placed in an oil bath kept at 80 °C. After 24 h, the reaction was terminated by cooling the solution to –78 °C. The monomer conversion was determined by ^{1}H NMR in $CDCl_3$ with tetralin as an internal standard (Conv. PEGA/DA = 91%/90%). The quenched reaction solution was evaporated to dryness. The crude product was purified by preparative SEC in DMF as an eluent to remove unreacted monomers. The product was dried under vacuum at room temperature. SEC (DMF, PMMA std.): M_n = 6,800 g/mol; M_w/M_n = 1.55. ^{1}H NMR [500 MHz, acetone-d_6, 25 °C, δ = 2.05 (acetone)]: 4.4–3.9 (-COOC$\underline{H}_2$CH$_2$O-, -COOC$\underline{H}_2$CH$_2$CH$_2$-), 3.8–3.7 (-COOCH$_2$C$\underline{H}_2$O-), 3.7–3.5 (-OCH$_2$CH$_2$O-), 3.5–3.4 (-C$\underline{H}_2$OCH$_3$), 3.4–3.3 (-OCH$_3$), 2.6–2.3 (-CH$_2$C$\underline{H}$CO-), 2.0–1.5 (-C$\underline{H}_2$CH-, -COOCH$_2$C$\underline{H}_2$(CH$_2$)$_9$CH$_3$), 1.5–1.2 (-COOCH$_2$CH$_2$(C$\underline{H}_2$)$_9$CH$_3$), 1.0–0.8 (-COO(CH$_2$)$_{11}$C$\underline{H}_3$). FT-IR: ν/cm^{-1} = 1729 (carbonyl C=O stretch).

P12: PEGMA/DA (46/30) gradient copolymer. RuCp*Cl(PPh_3)$_2$ (0.0045 mmol, 3.6 mg) was charged in a 30 mL glass tube. Then, toluene (2.7 mL), tetralin (0.24 mL), a 250 mM toluene solution of Al(O*i*-Pr)$_3$ (0.72 mL, Al(O*i*-Pr)$_3$ = 0.18 mmol), PEGMA (2.3 mmol, 0.99 mL), DA (2.3 mmol, 0.62 mL), and a 52 mM toluene solution of EMA-Br (0.70 mL, EMA-Br = 0.036 mmol) were added sequentially into the tube at 25 °C under argon (the total volume: 6 mL). The glass tube was placed in an oil bath kept at 80 °C. At predetermined intervals, the mixture was sampled with a syringe under dry argon. The reaction was terminated by cooling the solution to –78 °C. The monomer conversion was determined by ^{1}H NMR in $CDCl_3$ with tetralin as an internal standard (Conv. PEGMA/DA = 82%/62%, 47 h). The quenched reaction mixtures were evaporated to dryness. The crude product was purified by preparative SEC in DMF as an eluent to remove catalyst residue and unreacted monomers. The product was dried under vacuum at room temperature. SEC (DMF, PMMA std.): M_n = 23,900 g/mol; M_w/M_n = 1.26. *dn*/*dc* (DMF) = 0.044. SEC-MALLS (DMF, 0.01 M LiBr): M_w = 37,200 g/mol. ^{1}H NMR [500 MHz, acetone-d_6, 25 °C, δ = 2.05 (acetone)]: δ 4.3–3.9 (-COOC$\underline{H}_2$CH$_2$O-, -COOC$\underline{H}_2$CH$_2$CH$_2$-), 3.8–3.7 (-COOCH$_2$C$\underline{H}_2$O-), 3.7–3.5 (-OCH$_2$CH$_2$O-), 3.5–3.4 (-C$\underline{H}_2$OCH$_3$), 3.4–3.2 (-OCH$_3$), 2.6–2.2 (-CH$_2$C$\underline{H}$CO-), 2.2–1.8 (-C$\underline{H}_2$C(CH$_3$)-), 1.8–1.5 (-COOCH$_2$C$\underline{H}_2$(CH$_2$)$_9$CH$_3$), 1.5–1.2 (-COOCH$_2$CH$_2$(C$\underline{H}_2$)$_9$CH$_3$), 1.2–0.8 (-COO(CH$_2$)$_{11}$C$\underline{H}_3$, -CH$_2$C(C$\underline{H}_3$)-). FT-IR: ν/cm^{-1} = 1729 (carbonyl C=O stretch).

P14: PEGMA/DA bidirectional gradient copolymer. RuCp*Cl(PPh_3)$_2$ (0.0045 mmol, 3.6 mg) was charged in a 30 mL glass tube. Then, toluene (3.5 mL), tetralin (0.24 mL), a 400 mM toluene solution of *n*-Bu_3N (0.3 mL, *n*-Bu_3N = 0.12 mmol), PEGMA (2.3 mmol, 0.99 mL), DA (2.3 mmol, 0.62 mL), and a 51 mM toluene solution of BzDMA-2Br (0.35 mL, BzDMA-2Br = 0.018 mmol) were added sequentially into the tube at 25 °C under argon (the total volume: 6 mL). The glass tube was placed in an oil bath kept at 80 °C. At predetermined intervals, the mixture was sampled with a syringe under dry argon. The reaction was terminated by cooling the solution to –78 °C. The monomer conversion was determined by ^{1}H NMR in $CDCl_3$ with tetralin as an internal standard (Conv. PEGMA/DA = 84%/61%, 80 h). The quenched reaction mixtures were evaporated to dryness. The crude product was purified by preparative SEC in DMF as an eluent to remove catalyst residue and unreacted monomers. The product was dried under vacuum at room temperature. SEC (DMF, PMMA std.): M_n = 36,300 g/mol; M_w/M_n = 1.24. *dn*/*dc* (DMF) = 0.049. SEC-MALLS (DMF, 0.01 M LiBr): M_w = 57,800 g/mol. ^{1}H NMR [500 MHz, acetone-d_6, 25 °C, δ = 2.05 (acetone)]: δ 7.4 (aromatic), 4.3–3.9 (-COOC$\underline{H}_2$CH$_2$O-, -COOC$\underline{H}_2$CH$_2$CH$_2$-), 3.8–3.7 (-COOCH$_2$C$\underline{H}_2$O-), 3.7–3.5 (-OCH$_2$CH$_2$O-), 3.5–3.4 (-C$\underline{H}_2$OCH$_3$), 3.4–3.3 (-OCH$_3$), 2.6–2.2 (-CH$_2$C$\underline{H}$CO-), 2.2–1.7 (-C$\underline{H}_2$C(CH$_3$)-), 1.7–1.5 (-COOCH$_2$C$\underline{H}_2$(CH$_2$)$_9$CH$_3$), 1.5–1.2 (-COOCH$_2$CH$_2$(C$\underline{H}_2$)$_9$CH$_3$), 1.2–0.8 (-COO(CH$_2$)$_{11}$C$\underline{H}_3$, -CH$_2$C(C$\underline{H}_3$)-). FT-IR: ν/cm^{-1} = 1729 (carbonyl C=O stretch).

P15: PEGMA/DMA random block copolymer. $Ru(Ind)Cl(PPh_3)_2$ (0.012 mmol, 9.3 mg) was charged in a 30 mL glass tube. Then, toluene (4.0 mL), tetralin (0.16 mL), a 400 mM toluene solution of *n*-Bu_3N (0.3 mL, *n*-Bu_3N = 0.12 mmol), PEGMA (2.1 mmol, 0.92 mL), DMA (0.9 mmol, 0.26 mL), and a 42 mM toluene solution of ECPA (0.36 mL, ECPA = 0.015 mmol) were added sequentially into the tube at 25 ^oC under argon (the total volume: 6 mL). The glass tube was placed in an oil bath kept at 80 ^oC. After 12 h, monomer conversion was determined to be 52%/47% (PEGMA/DMA) by ^1H NMR in $CDCl_3$ with tetralin as an internal standard. Into the copolymerization mixture with 30 mol% DMA, a fresh DMA was directly fed by syringe under inert atmosphere to induce copolymerization with 50 mol% DMA. In 51 h, the reaction was terminated by cooling the solution to –78 °C. The monomer conversion was determined: PEGMA/DMA = 88%/128%. The quenched reaction mixture was evaporated to dryness. The crude product was purified by preparative SEC in DMF as an eluent. The product was dried under vacuum at room temperature. SEC (DMF, PMMA std.): M_n = 52,400 g/mol; M_w/M_n = 1.22. *dn*/*dc* (DMF) = 0.048. SEC-MALLS (DMF, 0.01 M LiBr): M_w = 91,200 g/mol. ^1H NMR [500 MHz, acetone-d_6, 25 ^oC, δ = 2.05 (acetone)]: δ 7.3–7.1 (aromatic), 4.2–4.1 (-COOC$\underline{H}_2$$CH_2O$-), 4.1–3.9 (-COOC$\underline{H}_2$$CH_2CH_2$-), 3.8–3.7 (-$COOCH_2C\underline{H}_2O$-), 3.7–3.6 (-$OCH_2CH_2O$-), 3.6–3.4 (-C$\underline{H}_2OCH_3$), 3.4–3.3 (-$OCH_3$), 2.2–1.8 (-C$\underline{H}_2C(CH_3)$-), 1.8–1.6 (-$COOCH_2C\underline{H}_2(CH_2)_9CH_3$), 1.6–1.3 (-$COOCH_2CH_2(C\underline{H}_2)_9CH_3$), 1.2–0.8 (-$COO(CH_2)_{11}C\underline{H}_3$, -$CH_2C(C\underline{H}_3)$-). FT-IR: ν/cm^{-1} = 1725 (carbonyl C=O stretch).

Supporting Data

1. Synthesis of PEG/Dodecyl-Graft Copolymers

1-1. PEGA/DA Random Copolymers

PEGA/DA random copolymers (**P1** – **P10**) with different hydrophobic DA content (23 – 50 mol%) and DP were synthesized by ruthenium-catalyzed controlled radical or free radical copolymerization of PEGA and DA (Table S1).

Table S1. Synthesis of PEGA/DA Random Copolymers[a]

Code	DA_{target}[b] (mol%)	Time (h)	Conv. (%)[c] PEGA/DA	M_n[d] (SEC)	M_w/M_n[d] (SEC)	DA[e] (mol%)	DP[f]	m/n[f]	m/n (calcd)[g]
P1	25	127	36/37	22,100	1.20	23	53	41/12	68/23
P2	30	36	35/38	12,300	1.18	26	33	21/7	31/14
P3	30	93	37/43	13,900	1.24	34	37	24/13	65/32
P4	40	77	82/77	11,000	1.26	38	31	19/12	31/19
P5	40	44	48/47	16,500	1.23	40	51	31/20	72/47
P6	45	118	74/73	16,600	1.35	46	59	32/27	41/33
P7	50	93	35/35	13,600	1.31	48	46	24/22	44/44
P8	50	44	46/44	9,200	1.31	50	30	15/15	29/28
P9	40	24	91/91	6,800	1.55	41	-	FRP	-
P10	40	43	78/77	33,300	1.94	40	-	FRP	-

[a] Conditions: $[PEGA]_0/[DA]_0/[BzMA\text{-}Br]_0/[RuCp^*Cl(PPh_3)_2]_0/[n\text{-}Bu_3N]_0$ = 563/188/3.0/0.75/30 (**P1**), 525/225/6.0/0.75/30 (**P2**), 525/225/3.0/0.75/30 (**P3**), 450/300/12/0.75/30 (**P4**), 450/300/3.0/0.75/30 (**P5**), 373/375/3.0/0.75/30 (**P7**), 375/375/6.0/0.75/30 (**P8**) mM in methoxycyclopentane and 550/450/10/1/20 (**P6**) mM in toluene at 80 °C. **P9**, **P10**: $[PEGA]_0/[DA]_0/[AIBN]_0$ = 300/200/7.5 mM in toluene at 80 (**P9**) or 40 (**P10**) °C.

[b] Target DA content (mol%): 100 x $[DA]_0/([PEGA]_0+[DA]_0)$.

[c] Monomer conversion determined by ^{1}H NMR with tetralin as an internal standard.

[d] Determined by SEC in DMF (10 mM LiBr) with PMMA standard calibration.

[e] DA content (mol%) of copolymers determined by ^{1}H NMR.

[f] Degree of polymerization (DP) (*m*/*n*: DP of PEGA and DA) determined with $M_{w,DMF}$ (MALLS), M_w/M_n (SEC), and DA content (^{1}H NMR).

[g] *m*/*n* calculated from the feed ratio of monomers to initiator and monomer conversion.

1-2. Synthesis of PEGMA/DA Gradient Copolymers

PEGMA/DA gradient copolymers (DA: 30 – 53 mol%, **P11** – **P13**) were synthesized by ruthenium-catalyzed living radical copolymerization of PEGMA and DA with a bromide initiator (Figures S1, S2).

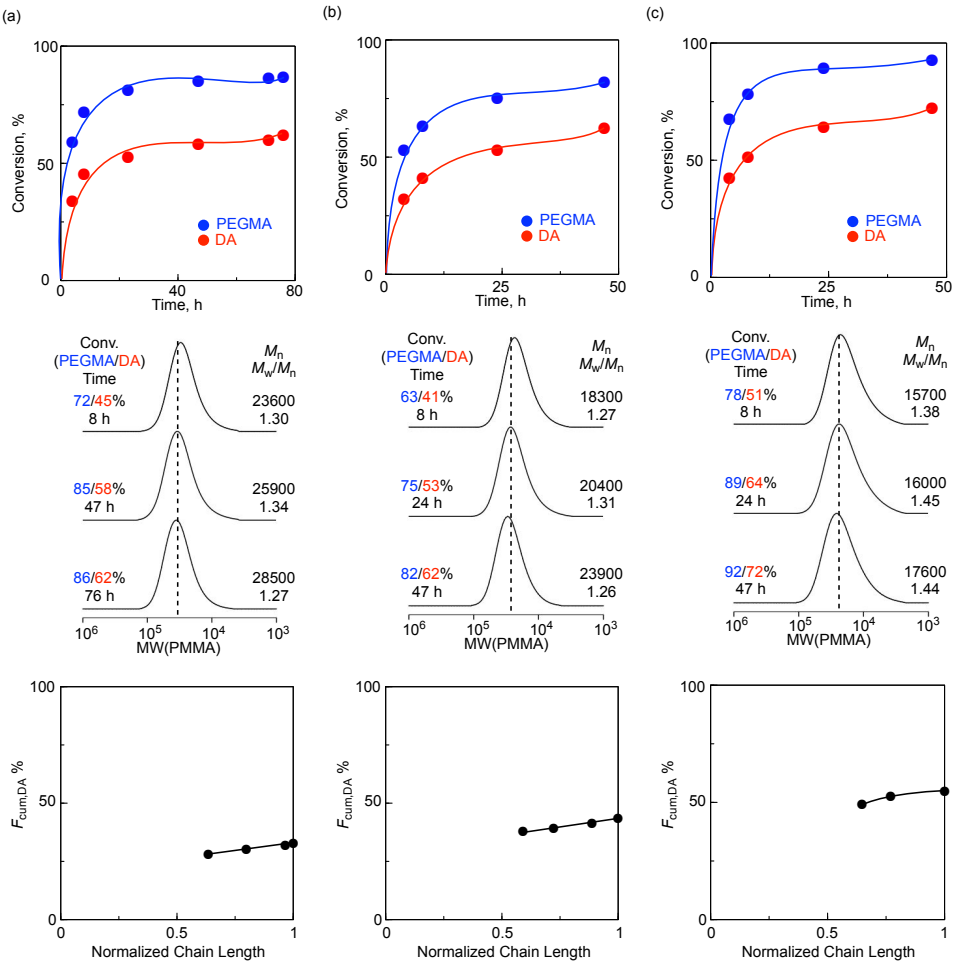

Figure S1. Ru-catalyzed living radical polymerization of PEGMA and DA with a bromide initiator for **P11** – **P13** (a: **P11**, b: **P12**, c: **P13**): $[PEGMA]_0/[DA]_0/[EMA\text{-}Br]_0/[Ru(Ind)Cl(PPh_3)_2]_0/[Al(O\textit{i}\text{-}Pr)_3]_0$ = 450/300/6.0/0.75/30 (**P11**), 375/375/6.0/0.75/30 (**P12**), and 300/450/6.0/0.75/30 (**P13**) mM in toluene at 80 °C. Upper: time conversion curves. Middle: SEC curves of products. Lower: cumulative DA content of copolymers ($F_{cum,DA}$) as a function of normalized chain length.

Cumulative DA content of copolymers ($F_{cum,DA}$) was determined with monomer feed ratio and conversion (determined by ^{1}H NMR).[S1] Instantaneous DA contents in copolymers ($F_{inst,DA}$) shown in Figure 1 (in main text) are calculated according to the following equation: $F_{inst,DA}$ = [$Conv_{total,i}$ x $F_{cum,DA,i}$ - $Conv_{total,i-1}$ x $F_{cum,DA,i-1}$]/[$Conv_{total,i}$ - $Conv_{total,i-1}$], where $F_{cum,DA}$ is cumulative DA contents in gradient copolymers.[S1-S3]

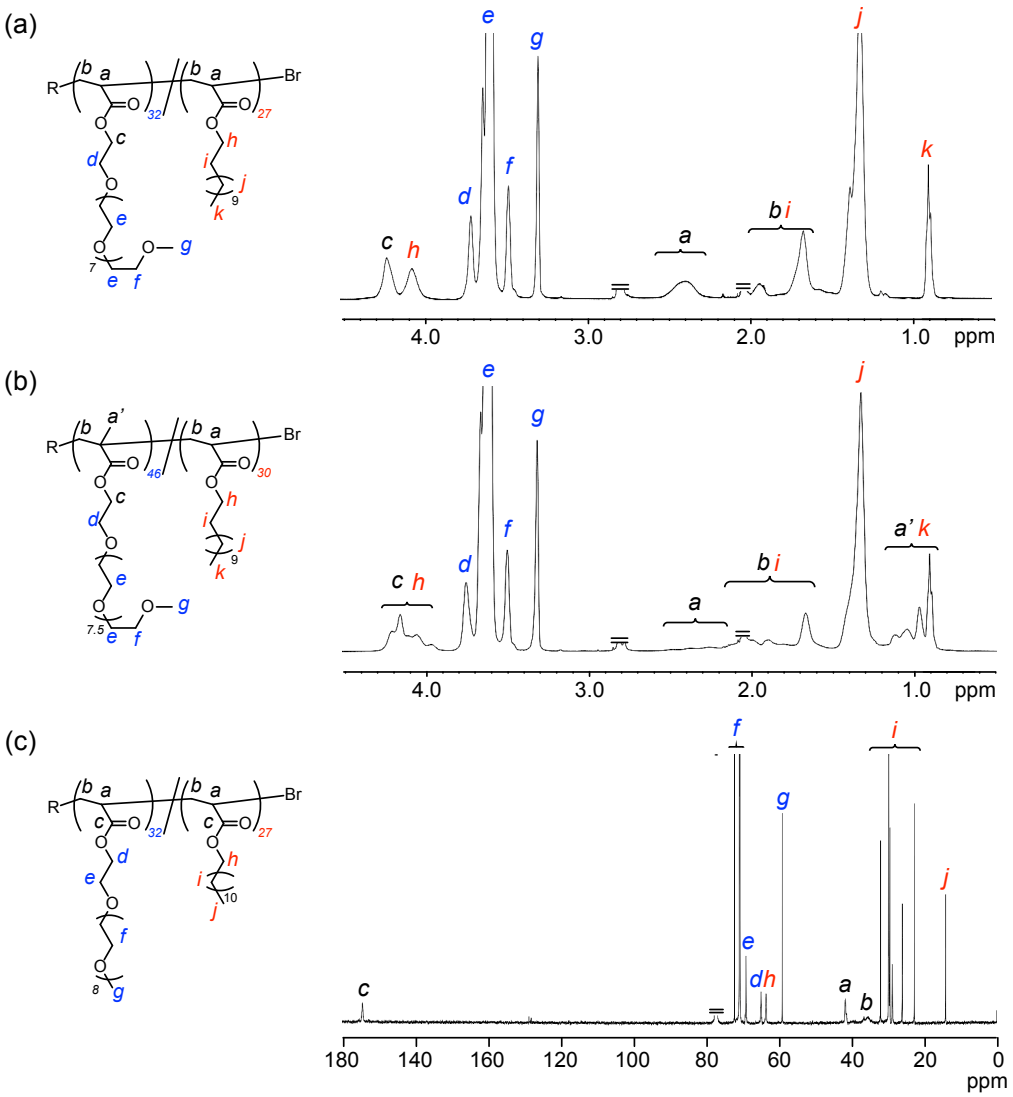

Figure S2. (a, b) ^{1}H NMR spectra of (a) a PEGA/DA random copolymer (**P6**) and (b) a PEGMA/DA gradient copolymer (**P12**) in acetone-d_6 at 25 ^{o}C. (c) ^{13}C NMR spectrum of **P6** in $CDCl_3$ at 55 ^{o}C.

1-3. Synthesis and Characterization of PEGMA/DMA Random Copolymers

PEGMA/DMA random copolymers (DMA: 20 – 50 mol%) were prepared according to the literature and characterized by SEC, SEC-MALLS, DLS, ^{1}H NMR, and UV-vis (Table S2).[S4]

Table S2. Characterization of PEGMA/DMA Random Copolymers[a]

entry	DMA[b] (mol%)	DP[b]	m/n[b]	M_n[c] (SEC)	M_w/M_n[c] (SEC)	$M_{w,DMF}$[d] (MALLS)	$M_{w,H2O}$[d] (MALLS)	N_{agg}[e]	$R_{h,H2O}$[f] (nm)	Cp[g] (^{o}C)
1	20	41	32/9	16,400	1.18	20,200	32,600	1.6	3.5	83
2	30	56	39/17	18,500	1.19	27,800	53,800	1.9	4.2	80
3	40	52	31/21	16,200	1.18	24,100	98,700	4.1	4.9	72
4	40	190	114/76	43,900	1.23	91,400	108,000	1.2	5.0	74
5	50	63	32/31	15,200	1.21	29,200	227,000	7.8	6.5	60
6	50	107	54/53	24,300	1.22	47,600	219,000	4.6	6.4	62

[a] Copolymers (entries 1 - 6) were synthesized by ruthenium-catalyzed radical copolymerization: $[PEGMA]_0/[DMA]_0/[ECPA]_0/[Ru(Ind)Cl(PPh_3)_2]_0/[n\text{-}Bu_3N]_0$ = 400/100/10/2.0/20 (entry 1), 350/150/8.0/2.0/20 (entry 2), 300/200/8.0/2.0/20 (entry 3), 300/200/2.0/1.0/20 (entry 4), 250/250/10/2.0/20 (entry 5), and 250/250/5.0/2.0/20 (entry 6) mM in toluene at 80 ^{o}C.[S4]

[b] DMA content (mol%), degree of polymerization (DP), and copolymer composition (m/n: DP of PEGMA and DMA) determined by ^{1}H NMR.

[c] Determined by SEC in DMF (10 mM LiBr) with PMMA standard calibration.

[d] Absolute weight-average molecular weight (M_w) determined by SEC-MALLS in DMF (10 mM LiBr) or H_2O.

[e] Aggregation number in H_2O: $N_{agg} = M_{w,\,H2O}$ (MALLS)/$M_{w,\,DMF}$ (MALLS).

[f] Hydrodynamic radius determined by DLS in H_2O at 25 ^{o}C: [polymer] = 10 mg/mL.

[f] Cloud points of the aqueous solution of polymers (90% transmittance): [polymer] = 4 mg/mL; λ = 670 nm; heating: 1^{o}C/min.

2. Thermal Properties of PEG/Dodecyl-Graft Copolymers

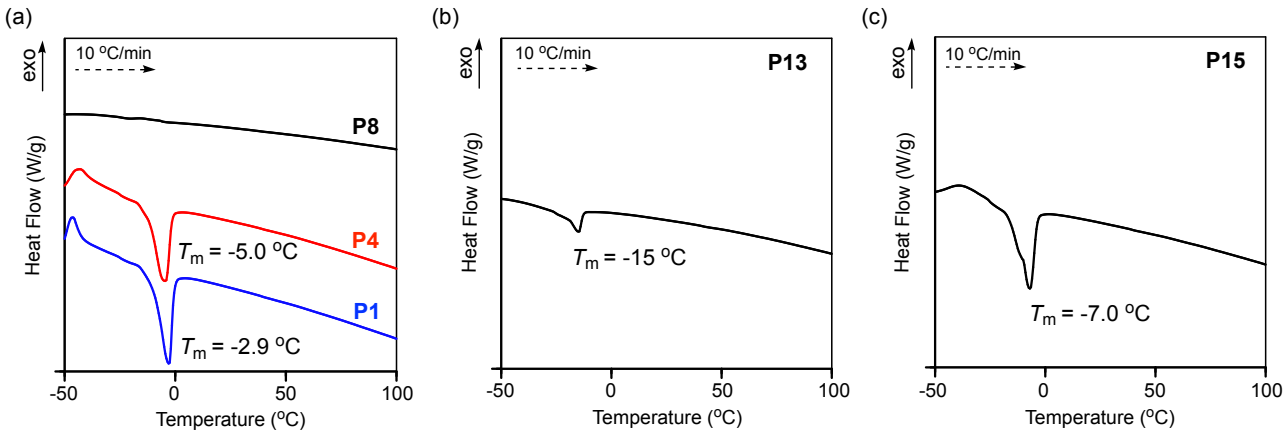

Figure S3. DSC curves of (a) PEGA/DA random copolymers (**P1**, **P4**, **P8**), (b) a PEGMA/DA gradient copolymer (**P13**), and (c) a PEGMA/DMA random block copolymer (**P15**): heating rate = 10 °C/min.

3. DLS Measurement of Amphiphilic Copolymers in Water

To investigate the effects of polymer concentration (10 – 100 mg/mL) and temperature on self-assembly in water, PEGA/DA random copolymers and PEGMA/DA gradient copolymers were analyzed by DLS in H_2O at various concentration and temperature (25 ^{o} – 70 ^{o}C) (Figures S4, S5).

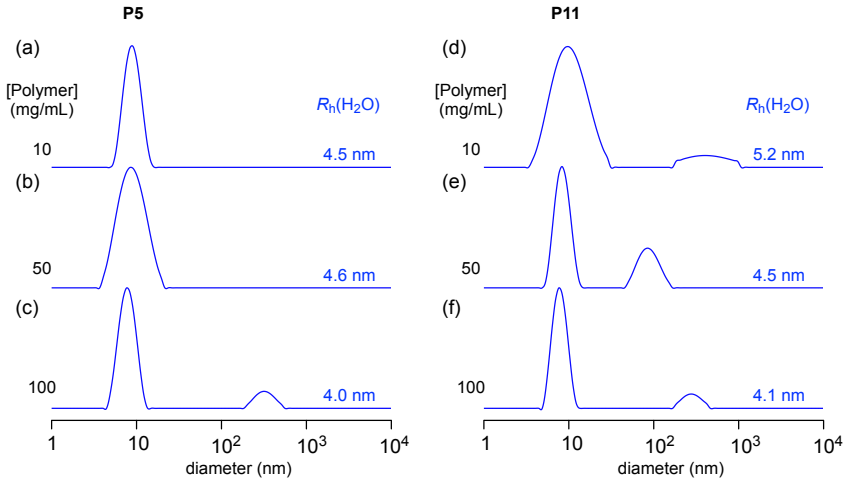

Figure S4. DLS intensity size distribution of a PEGA/DA random copolymer (a-c: **P5**) and a PEGMA/DA gradient copolymer (d-f: **P11**) in H_2O at 25 ^{o}C: [polymer] = (a, d) 10, (b, e) 50, and (c, f) 100 mg/mL. (c-f) Volume fraction of small size range (~10 nm) in bimodal distribution: >99%.

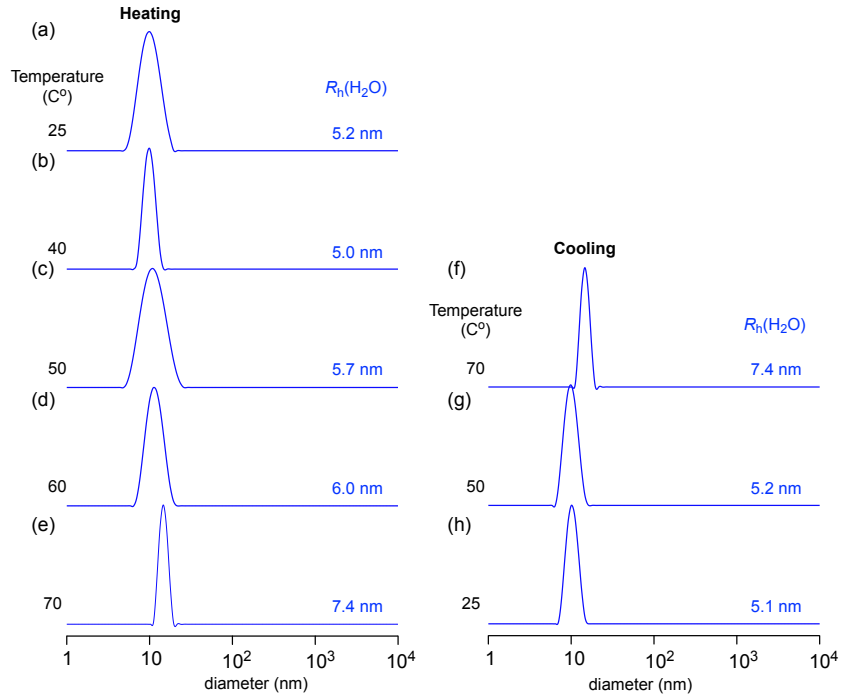

Figure S5. DLS intensity size distribution of a PEGA/DA random copolymer (**P6**) in H_2O upon heating from 25 ºC to 70 ºC (a-e) and by cooling from 70 ºC to 25 ºC (f-h): [polymer] = 10 mg/mL.

4. Thermoresponsive Solubility of Amphiphilic Copolymers in Water

Cloud points (Cp) measurement of PEGA/DA random and PEGMA/DA gradient copolymers in water was conducted by changing temperature. The transmittance of the solutions was monitored at λ = 670 nm. C_p was defined as the temperature at which the transmittance of the aqueous solutions reached 90% upon heating (Figure S6).

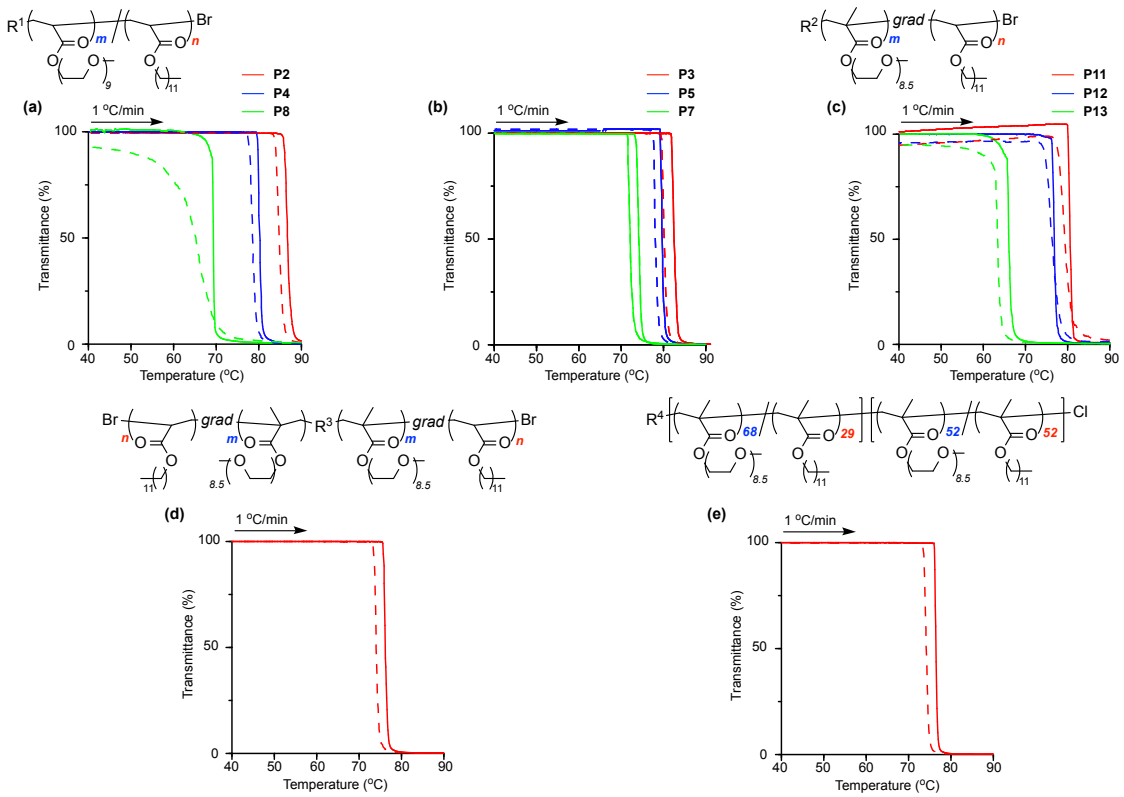

Figure S6. Temperature-dependent transmittance of the aqueous solutions of (a, b) PEGA/DA random copolymers (a: **P2**, **P4**, **P8**, b: **P3**, **P5**, **P7**), (c) PEGMA/DA gradient copolymers (**P11**, **P12**, **P13**), (d) a PEGMA/DA bidirectional gradient copolymer (**P14**), and (e) a PEGMA/DMA random block copolymers (**P15**) monitored at λ = 670 nm between 40 and 95 °C: [polymer] = 4 mg/mL; heating (solid line)/cooling (dash line) = 1 °C/min.

References

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S2) Ogura, Y.; Terashima, T.; Sawamoto, M. *ACS Macro Lett.* **2013**, *2*, 985-989.

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