Supporting Information

Orthogonal Folding of Amphiphilic/Fluorous Random Block Copolymers for Double and Multicompartment Micelles in Water

Mayuko Matsumoto,1 Mitsuo Sawamoto,1,2 Takaya Terashima1*
1Department of Polymer Chemistry, Graduate School of Engineering, Kyoto University
Katsura, Nishikyo-ku, Kyoto 615-8510, Japan
2Institute of Science and Technology Research, Chubu University, 1200 Matsumoto-cho, Kasugai,
Aichi 487-8501, Japan
E-mail: terashima@living.polym.kyoto-u.ac.jp
*: corresponding authors

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Experimental Section

Materials.

Poly(ethylene glycol) methyl ether methacrylate [PEGMA: CH₂=CMcO₂(CH₂CH₂O)nMe, \( M_n = 475, n = 8.5 \) on average] (Aldrich), dodecyl methacrylate (DMA, Wako, purity >95%), and 1H,1H,2H,2H-perfluoroocetyl methacrylate (13FOMA, Aldrich, purity >97%) were purified by inhibitor removal column (Aldrich) and were degassed by triple vacuum-argon purge cycles before use. Ethyl 2-chloro-2-phenylacetate (ECPA, Aldrich, purity >97%) was distilled under reduced pressure before use. (Cp*: pentamethycyclopentadiene, Aldrich) and Ru(Ind)Cl(PPh₃)₂ (Aldrich) were used as received and handled in a glove box under moisture- and oxygen-free argon (H₂O < 1 ppm; O₂ < 1 ppm). Tetralin (1,2,3,4-tetrahydronaphthalene, TCI, purity >97% , an internal standard for ¹H NMR analysis) was dried overnight over calcium chloride and distilled from calcium hydride under reduced pressure before use. 4-Dimethylamino-1-butanol (4-DMAB, TCI, purity >98%), n-Bu₃N (TCI, purity >98%), 2,2-dichloroacetoephone (DCAP, TCI, purity >97%), and ethanol (Wako, dehydrated) were degassed before use. Toluene was purified before use by passing it through a purification column (Glass Contour Solvent Systems, Nikko Hansen & Co., Ltd).

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 °C (flow rate: 1 mL/min) on three linear-type polystyrene gel columns (Shodex KF-805L, exclusion limit = 4 × 10⁶, 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 H₂O at 30 °C (flow rate: 1 mL/min) on a silica gel column (TOSOH G4000SWXL, exclusion limit = 7 × 10⁶, particle size = 8 μm, 0.78 cm i.d. × 30 cm) that was connected to the same pump and detectors 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 residual monomers and catalysts, polymer samples were purified by preparative SEC (column: TOSOH TSKgel α-3000, exclusion limit = 9 × 10⁴, particle size = 13 μm, 5.5 cm i.d. × 30 cm) in DMF with a Jasco PU-2086...
precision pump, a Jasco RI-2031 refractive index detector, and a Jasco UV-2075 UV/vis detector set at 270 nm. The purified polymers were employed for characterization.

$^1$H and $^{19}$F nuclear magnetic resonance (NMR) spectra were recorded in acetone-$d_6$, CDCl$_3$, (CF$_3$)$_2$CDOD, and D$_2$O at 25 or 30 °C on a JEOL JNM-ECA500 spectrometer, operating at 500.16 ($^1$H) and 470.62 ($^{19}$F) MHz. $^1$H nuclear Overhauser effect (NOE) difference spectroscopy of polymers were obtained by irradiating the methylene protons of dodecyl methacrylate units [-($\text{CH}_2$)$_9$-, 1.5 -1.3 ppm] in D$_2$O at 30 °C. The number of scans was set at 1024 (spectral width = 15 ppm). Other parameters for pulse were as follows: 90° pulse width = 14 μs; irradiation position (on-resonance) = 1.36 ppm; off-resonance = -10 ppm; irradiation time (NOE-building up) = 5 s; attenuator = 60 dB; data points = 16384. Relaxation delay was determined with the equation ($T_{1,\text{max}} \times 1.3$): 2.33 s (P2) or 2.60 s (P4) in D$_2$O.

Aqueous solutions of polymers utilized for SEC, light scattering, transmission electron microscopy (TEM), and atomic force microscopy (AFM) measurement were prepared as follows: bulk polymers were mixed with water, and the aqueous solutions were sonicated for several minutes and filtrated with PTFE membrane filter (0.45 μm pore, Merck Millipore) before analysis. Absolute weight-average molecular weight ($M_w$) of polymers in DMF or H$_2$O was determined by multi-angle laser light scattering (MALLS) equipped with SEC on a Dawn HELEOS II instrument (Wyatt Technology, semiconductor laser, $\lambda = 663$ 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$_2$O at 30 °C (flow rate: 1 mL/min) on a silica gel column (TOSOH G4000SWXL). These columns 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) measurement was conducted on Otsuka Photom ELSZ-0 equipped with a semiconductor laser ($\lambda = 658$ nm, measuring angle: 165°) or Zetasizer Nano ZSP (Malvern) equipped with a He-Ne laser ($\lambda = 633$ nm, measuring angle: 173°) at 25 °C. Cloud point of the aqueous solutions of copolymers was measured on UV-1800 (Shimadzu, optical path length = 1.0 cm, $\lambda = 670$ nm, heating/cooling rate: 1 °C/min, temperature range: 40 – 95 °C).

Transmission electron microscopy (TEM) measurement of polymers was performed on HT7700 (Hitachi) at an accelerating voltage of 100 kV. The samples were prepared by the drop cast of the aqueous solutions of polymers (10 mg/mL) on carbon-coated grids (Okenshoji, ELS-C10 STEM Cu100P). The solutions (5 μL) were put on the grid for 5 min and blotted up with papers. The samples were then stained with the vapor of 1% OcO$_4$ aqueous solutions (TAAB, laboratories Equipment Ltd) for 5 min and dried overnight at 25 °C before TEM measurement.

Liquid-phase atomic force microscopy (AFM) measurement of polymer micelles was performed on Cypher ES (Asylum Research, Oxford Instruments) equipped with BlueDrive photothermal
excitation at 28 °C. In situ imaging of polymer micelles was performed in amplitude modulation mode with the aqueous solution droplet. Gold-coated cantilevers (ArrowUHF AuD, NanoWorld) were used with resonance frequencies of 400–420 kHz in the solution. Each cantilever was calibrated by the thermal fluctuation method. Igor Pro software (WaveMetrics) was used for data acquisitions, plane corrections and topographic analyses. All AFM images were collected in the solution in attractive tapping mode with a free amplitude of 50 mV at the set point of 90 mV with a scan rate of 4.88 Hz.

**Polymer Synthesis.**

The synthesis of amphiphilic/fluorous copolymers (P1-P7) was carried out by syringe technique under argon in baked glass flasks or tubes equipped with a three-way stopcock.

**PEGMA/DMA-PEGMA/13FOMA random block copolymer (P2):** In 50 mL round-bottom flask, RuCp*Cl(PPh₃)₂ (0.010 mmol, 8.3 mg) was weighed out. Then, EtOH (14.5 mL), tetralin (0.42 mL), a 500 mM EtOH solution of 4-DMAB (0.42 mL, 4-DMAB = 0.21 mmol), PEGMA (7.3 mmol, 3.2 mL), DMA (3.1 mmol, 0.92 mL), and a 30.4 mM EtOH solution of ECPA (1.38 mL, ECPA = 0.042 mmol) were added into the flask at 25 °C under argon (the total volume: 21 mL). The flask was placed in an oil bath kept at 40 °C. At predetermined intervals, the mixture was sampled with a syringe under dry argon, and the reaction was terminated by cooling the solution to -78°C. The monomer conversion was determined by ¹H NMR in CDCl₃ with tetralin as an internal standard: Conv. PEGMA/DMA = 49%/54% at 10 h. The crude product was dried under vacuum at room temperature and purified by preparative SEC in DMF to give a PEGMA/DMA random copolymer (P1) [Mₙ = 36800 g/mol, Mₘ/Mₙ = 1.13 by SEC with PMMA calibration, PEGMA/DMA (l/m) = 86/41 by ¹H NMR, dn/dc (for SEC-MALLS) = 0.0466 in DMF (10 mM LiBr), 0.130 in H₂O].

In 30 mL glass tube, P1 (macroinitiator, Cl = 9.1 µmol, 467 mg) was placed. Then, EtOH (2.2 mL), tetralin (0.056 mL), a 500 mM EtOH solution of 4-DMAB (0.056 mL, 4-DMAB = 0.028 mmol), and a EtOH solution of RuCp*Cl(PPh₃)₂, PEGMA, and 13FOMA (0.92 mL, RuCp*Cl(PPh₃)₂ = 1.15 mg, 1.44 µmol, PEGMA = 0.44 mL, 1.00 µmol, 13FOMA = 0.13 mL, 0.43 µmol, EtOH = 0.35 mL) were added into the tube at 25°C under argon (the total volume: 3.2 mL). The tube was placed in an oil bath kept at 40°C. At predetermined intervals, the mixture was sampled with a syringe under dry argon, and the reaction was terminated by cooling the solution to -78°C. The monomer conversion was determined by ¹H NMR in CDCl₃ with tetralin as an internal standard: Conv. PEGMA/13FOMA = 75%/84% at 19 h. The quenched reaction mixture was evaporated to dryness and the crude product was purified by preparative SEC in DMF to give a PEGMA/DMA-block-PEGMA/13FOMA copolymer (P2). SEC (DMF, PMMA std.): Mₙ = 72100,
was sampled with a syringe under dry argon, and the reaction was determined by reaction wa
the flask at 25 °C. 0.35 mmol, PEGMA/13FOMA random copolymer (P3): In 30 mL glass tube, RuCp*Cl(PPh₃)₂ (4.0 μmol, 3.2 mg) was weighed out. Then, EtOH (5.2 mL), tetralin (0.16 mL), a 500 mM EtOH solution of 4-DMAB (0.16 mL, 4-DMAB = 0.08 mmol), PEGMA (2.80 mmol, 1.23 mL), 13FOMA (1.2 mmol, 0.35 mL), and a 30.4 mM EtOH solution of ECPA (0.88 mL, ECPA = 0.027 mmol) were added into the flask at 25 °C under argon (the total volume: 8 mL). The tube was placed in an oil bath kept at 40 °C. At predetermined intervals, the mixture was sampled with a syringe under dry argon, and the reaction was terminated by cooling the solution to -78 °C. The monomer conversion was determined by ¹H NMR in CDCl₃ with tetralin as an internal standard: Conv. PEGMA/13FOMA = 77%/85% at 26 h. The quenched reaction mixture was evaporated to dryness and the crude product was purified by preparative SEC in DMF to give P3. SEC (DMF, PMMA std.): Mₙ = 39400, Mₘ/Mₙ = 1.13. PEGMA/13FOMA (l/n) = 86/43 by ¹H NMR, Mₙ = (NMR, α) = 59600. ¹H NMR [500 MHz, acetone-d₆, 25 °C, δ = 2.1 (acetone)]: δ 7.4–7.2 (aromatic), 4.4–4.3 (-COOCH₂CH₂CF₂⁻), 4.2–4.1 (-COOCH₂CH₂O⁻), 3.8–3.7 (-COOCH₂CH₂O⁻), 3.7–3.6 (-OCH₂CH₂O⁻), 3.6–3.4 (-CH₂OCH₃), 3.4–3.3 (-OCH₃), 2.8–2.6 (-COOCH₂CH₂CF₂⁻), 2.2–1.6 (-CH₂C(CH₃)⁻), 1.3–0.8 (-CH₂C(CH₃)⁻). ¹⁹F NMR [500 MHz, acetone-d₆, 25 °C, δ = -76.5 ppm (CF₃COOH in CDCl₃)]: δ -81 to -82 (-CF₃), -113 to -115 (-CH₂CF₂⁻), -122 to -125 (-CH₂CF₂CF₂CF₂CF₂⁻), -126 to -128 (-CF₃CF₃). dn/dc (for SEC-MALLS) = 0.0323 in DMF (10 mM LiBr), 0.109 in H₂O.

PEGMA/DMA/13FOMA random copolymer (P4): In 30 mL glass tube, RuCp*Cl(PPh₃)₂ (5.0 μmol, 4.0 mg) was weighed out. Then, EtOH (7.5 mL), tetralin (0.20 mL), a 500 mM EtOH solution of 4-DMAB (0.20 mL, 4-DMAB = 0.10 mmol), PEGMA (3.50 mmol, 1.54 mL), DMA (0.75 mmol, 0.22 mL), 13FOMA (0.75 mmol, 0.22 mL), and a 42.5 mM EtOH solution of ECPA (0.33 mL, ECPA = 0.014 mmol) were added into the flask at 25 °C under argon (the total volume: 10 mL). The tube was placed in an oil bath kept at 40 °C. At predetermined intervals, the mixture was sampled with a syringe under dry argon, and the reaction was terminated by cooling the solution to -78 °C. The monomer conversion was determined by ¹H NMR in CDCl₃ with tetralin as an internal standard: Conv. PEGMA/DMA/13FOMA = 75%/79%/80% at 22 h. The quenched
reaction mixture was evaporated to dryness and the crude product was purified by preparative SEC in DMF to give P4. SEC (DMF, PMMA std.): $M_n = 92200$, $M_w/M_n = 1.21$. PEGMA/DMA/13FOMA $(l/m/n) = 196/49/49$ by $^1$H NMR, $M_n = (NMR, \alpha) = 127000$. $^1$H NMR [500 MHz, acetone-$d_6$, 25 °C, $\delta = 2.1$ (acetone)]: $\delta$ 7.4–7.2 (aromatic), 4.4–4.3 (–COOCH$_2$CH$_2$CF$_2$–), 4.2–4.1 (–COOCH$_2$CH$_2$O–), 4.1–3.9 (–COOCH$_2$CH$_2$CH$_2$–), 3.8–3.7 (–COOCH$_2$CH$_3$O–), 3.7–3.6 (–OCH$_2$CH$_2$O–), 3.6–3.4 (–CH$_2$OCH$_3$), 3.4–3.3 (–OCH$_3$), 2.8–2.6 (–COOCH$_2$CH$_2$CF$_2$–), 2.2–1.8 (–CH$_2$C(CH$_3$)–), 1.7 (–COOCH$_2$CH$_2$(CH$_2$)$_3$CH$_3$), 1.6–1.3 (–COOCH$_2$CH$_2$(CH$_2$)$_9$CH$_3$), 1.3–0.8 (–COO(CH$_2$)$_1$CH$_3$, –CH$_2$C(CH$_3$)–). $^{19}$F NMR [500 MHz, acetone-$d_6$, 25 °C, $\delta = -76.5$ ppm (CF$_3$COOH in CDCl$_3$)]: $\delta$ –81 to –82 (–CF$_3$), –113 to –115 (–CH$_2$CF$_2$–), –122 to –125 (–CH$_2$CF$_2$(CF$_2$)$_3$–), –126 to –128 (–CF$_2$CF$_3$). dn/dc (for SEC-MALLS) = 0.0344 in DMF (10 mM LiBr), 0.115 in H$_2$O.

PEGMA/13FOMA-PEGMA/DMA-PEGMA-13FOMA random triblock copolymer (P5): In 100 mL round-bottom flask, Ru(Ind)Cl(PPh$_3$)$_2$ (0.036 mmol, 28 mg) was weighed out. Then, toluene (27 mL), tetralin (0.60 mL), a 400 mM toluene solution of n-Bu$_3$N (0.91 mL, n-Bu$_3$N = 0.36 mmol), PEGMA (12.8 mmol, 5.6 mL), DMA (5.48 mmol, 1.6 mL), and a 56 mM toluene solution of DCAP (0.93 mL, DCAP = 0.052 mmol) were added into the tube at 25 °C under argon (the total volume: 36.6 mL). The flask was placed in an oil bath kept at 80 °C. At predetermined intervals, the mixture was sampled with a syringe under dry argon, and 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/DMA = 37%/35% at 19 h. The crude product was purified by preparative SEC in DMF to give a PEGMA/DMA random copolymer as a bifunctional macroinitiator [$M_n = 43400$, $M_w/M_n = 1.19$ by SEC, PEGMA/DMA ($l/m$) = (45/19) x 2 by $^1$H NMR, dn/dc (for SEC-MALLS) = 0.0495 in DMF (10 mM LiBr, 0.125 in H$_2$O).

In 30 mL glass tube, the bifunctional PEGMA/DMA copolymer macroinitiator (polymer = 5.9 µmol, 312 mg) was placed. Then, toluene (2.6 mL), tetralin (0.10 mL), PEGMA (0.63 mL, 1.4 mmol), 13FOMA (0.18 mL, 0.61 mmol), a 400 mM toluene solution of n-Bu$_3$N (0.10 mL, n-Bu$_3$N = 0.04 mmol), and a toluene solution of Ru(Ind)Cl(PPh$_3$)$_2$ (0.50 mL, Ru(Ind)Cl(PPh$_3$)$_2$ = 2.0 µmol) were added sequentially in that order into the tube at 25°C under argon (the total volume: 4.1 mL). The tube was placed in an oil bath kept at 80°C. At predetermined intervals, the mixture was sampled with a syringe under dry argon, and 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/13FOMA = 79%/83% at 26 h. The quenched reaction mixture was evaporated to dryness and the crude product was purified by preparative SEC in DMF to give P5 SEC (DMF, PMMA std.): $M_n = 123000$, $M_w/M_n = 1.17$, (PEGMA/DMA- PEGMA/13FOMA)$_2$ ($l/m-o/n$)$_2$ = (45/19-69/36)$_2$ by $^1$H NMR, $M_n = (NMR, \alpha) = 150000$. $^1$H NMR [500 MHz, acetone-$d_6$,
25 °C, δ = 2.1 (acetone): δ 8.0–7.5 (aromatic), 4.4–4.3 (−COOCH₂CH₂CF₂−), 4.2–4.1
(−COOCH₂CH₂O−), 4.1–3.9 (−COOCH₂CH₂H₂−), 3.8–3.7 (−COOCH₂CH₂O−), 3.7–3.6
(−OCH₂CH₂O−), 3.6–3.4 (−CH₂OCH₃), 3.4–3.3 (−OCH₃), 2.8–2.6 (−COOCH₂CH₂CF₂−), 2.2–1.8
(−CH₂C(CH₃)₂), 1.7 (−COOCH₂CH₂H₂(CH₂)₀CH₃), 1.6–1.3 (−COOCH₂CH₂(CH₂)₀CH₃), 1.3–0.8
(−COO(CH₂)₁₁CH₃, -CH₂C(CH₃)₃). ¹⁹F NMR [500 MHz, acetone-d₆, 25 °C, δ = -76.5 ppm
(CF₃COOH in CDCl₃): δ -81 to -82 (−CF₃), -113 to -115 (−CH₂CF₂−), -122 to -125
(−CH₂CF₂CF₂CF₂CF₂−), -126 to -128 (−CF₂CF₃). dn/dc (for SEC-MALLS) = 0.0300 in DMF (10
mM LiBr), 0.106 in H₂O.

Asymmetric PEGMA/DMA-PEGMA/13FOMA random block copolymer (P₆): In 100 mL
round-bottom flask, Ru(Ind)Cl(PPh₃)₂ (25 µmol, 19 mg) was weighed out. Then, toluene (39 mL),
tetralin (1.0 mL), a 400 mM toluene solution of n-Bu₃N (1.25 mL, n-Bu₃N = 0.50 mmol), PEGMA
(12.7 mmol, 5.6 mL), DMA (12.6 mmol, 3.7 mL), and a 331 mM toluene solution of ECPA (0.62
mL, ECPA = 0.20 mmol) were added into the tube at 25 °C under argon (the total volume: 51 mL).
The flask was placed in an oil bath kept at 80 °C. At predetermined intervals, the mixture was
sampled with a syringe under dry argon, and the reaction was terminated by cooling the solution to
-78°C. The monomer conversion was determined by ¹H NMR in CDCl₃ with tetralin as an internal
standard: Conv. PEGMA/DMA = 43%/42% at 27 h. The crude product was dried under vacuum at
room temperature and purified by preparative SEC in DMF to give a PEGMA/13FOMA random
copolymer as a macroinitiator [Mₙ = 16300, Mₙ/Mₚ = 1.29 by SEC, PEGMA/DMA (l/m) = 37/39 by
¹H NMR, dn/dc (for SEC-MALLS) = 0.0464 in DMF (10 mM LiBr), 0.130 in H₂O].

In 30 mL glass tube, the PEGMA/DMA random copolymer macroinitiator (Cl = 9.7 µmol, 268
mg) was placed. Then, toluene (2.7 mL), tetralin (0.080 mL), PEGMA (0.60 mL, 1.4 mmol),
13FOMA (0.17 mL, 0.58 mmol), a 400 mM toluene solution of n-Bu₃N (0.20 mL, n-Bu₃N = 0.080
mmol), and a toluene solution of Ru(Ind)Cl(PPh₃)₂ (0.20 mL, Ru(Ind)Cl(PPh₃)₂ = 3.0 mg, 3.9
µmol) were added into the tube at 25°C under argon (the total volume: 3.9 mL). The tube was
placed in an oil bath kept at 80°C. At predetermined intervals, the mixture was sampled with a
syringe under dry argon, and the reaction was terminated by cooling the solution to -78°C. The
monomer conversion was determined by ¹H NMR in CDCl₃ with tetralin as an internal standard:
Conv. PEGMA/13FOMA = 79%/81% at 15.5 h. The quenched reaction mixture was evaporated to
dryness and the crude product was purified by preparative SEC in DMF to give P₆. SEC (DMF,
PMMA std.): Mₙ = 61100, Mₙ/Mₚ = 1.27, PEGMA/DMA-PEGMA/13FOMA (l/m-o/n) = 37/39-
105/50 by ¹H NMR, Mₙ = (NMR, α) = 99200. ¹H NMR [500 MHz, acetone-d₆, 25 °C, δ = 2.1
(acetone): δ7.4–7.2 (aromatic), 4.4–4.3 (−COOCH₂CH₂CF₂−), 4.2–4.1 (−COOCH₂CH₂O−), 4.1–3.9
(−COOCH₂CH₂H₂−), 3.8–3.7 (−COOCH₂CH₂O−), 3.7–3.6 (−OCH₂CH₂O−), 3.6–3.4 (−CH₂OCH₃),
3.4–3.3 (−OCH₃), 2.8–2.6 (−COOCH₂CH₂CF₂−), 2.2–1.8 (−CH₂C(CH₃)₃), 1.7
(-COOCH₂CH₃(CH₂)₆CH₃), 1.6–1.3 (-COOCH₂CH₂(CH₂)₆CH₃), 1.3–0.8 (-COO(CH₂)₁₁CH₃, -CH₂C(CH₃)₃). ¹⁹F NMR [500 MHz, acetone-d₆, 25 °C, δ = -76.5 ppm (CF₃COOH in CDCl₃)]: δ -81 to -82 (-CF₃), -113 to -115 (-CH₂CF₂⁻), -122 to -125 (-CH₂CF₂CF₂CF₂CF₂⁻), -126 to -128 (-CF₂CF₃). dn/dc (for SEC-MALLS) = 0.0249 in DMF (10 mM LiBr), 0.101 in H₂O.

Asymmetric PEGMA/13FOMA-PEGMA/DMA random block copolymer (P7): In 100 mL round-bottom flask, Ru(Ind)Cl(PPh₃)₂ (25 μmol, 19 mg) was weighed out. Then, toluene (38 mL), tetralin (1.0 mL), a 400 mM toluene solution of n-Bu₃N (1.25 mL, n-Bu₃N = 0.50 mmol), PEGMA (12.7 mmol, 5.6 mL), 13FOMA (12.7 mmol, 3.7 mL), and a 331 mM toluene solution of ECPA (0.62 mL, ECPA = 0.20 mmol) were added into the tube at 25 °C under argon (the total volume: 50 mL). The flask was placed in an oil bath kept at 80 °C. At predetermined intervals, the mixture was sampled with a syringe under dry argon, and the reaction was terminated by cooling the solution to -78°C. The monomer conversion was determined by ¹H NMR in CDCl₃ with tetralin as an internal standard: Conv. PEGMA/13FOMA = 32%/47% at 24 h. The crude product was dried under vacuum at room temperature and purified by preparative SEC in DMF to give a PEGMA/13FOMA random copolymer as a macroinitiator [Mₙ = 18100, Mₘ/Mₙ = 1.15 by SEC in THF, PEGMA/13FOMA (l/n) = 27/38 by ¹H NMR].

In 30 mL glass tube, the PEGMA/13FOMA random copolymer macroinitiator (Cl = 9.8 μmol, 286 mg) was placed. Then, toluene (2.7 mL), tetralin (0.08 mL), a 400 mM toluene solution of n-Bu₃N (0.20 mL, n-Bu₃N = 0.080 mmol), and a toluene solution of Ru(Ind)Cl(PPh₃)₂ (0.2 mL, Ru(Ind)Cl(PPh₃)₂ = 3.0 mg, 3.9 μmol) were added into the tube at 25°C under argon (the total volume: 3.9 mL). The tube was placed in an oil bath kept at 80°C. At predetermined intervals, the mixture was sampled with a syringe under dry argon, and the reaction was terminated by cooling the solution to -78°C. The monomer conversion was determined by ¹H NMR in CDCl₃ with tetralin as an internal standard: Conv. PEGMA/13FOMA = 84%/82% at 20 h. The quenched reaction mixture was evaporated to dryness and the crude product was purified by preparative SEC in DMF to give P7. SEC (DMF, PMMA std.): Mₙ = 72100, Mₘ/Mₙ = 1.26, PEGMA/DMA-PEGMA/13FOMA (l/m-o/n) = 27/38-135/55 by ¹H NMR, Mₙ = (NMR, α) = 94800. ¹H NMR [500 MHz, acetone-d₆, 25 °C, δ = 2.1 (acetone)]: δ7.4–7.2 (aromatic), 4.4–4.3 (-COOCH₂CH₂CF₂⁻), 4.2–4.1 (-COOCH₂CH₂O⁻), 4.1–3.9 (-COOCH₂CH₂H⁻), 3.8–3.7 (-COOCH₂CH₃O⁻), 3.7–3.6 (-OCH₂CH₂O⁻), 3.6–3.4 (-CH₂OCH₃), 3.4–3.3 (-OCH₃), 2.8–2.6 (-COOCH₂CH₂CF₂⁻), 2.2–1.8 (-CH₂C(CH₃)₃⁻), 1.7 (-COOCH₂CH₂(CH₂)₆CH₃), 1.6–1.3 (-COOCH₂CH₂(CH₂)₆CH₃), 1.3–0.8 (-COO(CH₂)₁₁CH₃, -CH₂C(CH₃)₃⁻). ¹⁹F NMR [500 MHz, acetone-d₆, 25 °C, δ = -76.5 ppm (CF₃COOH in CDCl₃)]: δ -81 to -82 (-CF₃), -113 to -115 (-CH₂CF₂⁻), -122 to -125 (-CH₂CF₂CF₂CF₂CF₂⁻), -126 to -128 (-CF₂CF₃). dn/dc (for SEC-MALLS) = 0.0348 in DMF (10 mM LiBr).
## Supporting Data

**Table S1.** Synthesis of PEGMA/DMA/13FOMA Amphiphilic Copolymers

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<th>Conv. (%)</th>
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* PEGMA/DMA/13FOMA copolymers were synthesized by ruthenium-catalyzed living radical polymerization with the following conditions:
  - entry 1: \([\text{PEGMA}]_x[\text{DMA}]_y[\text{ECPA}]_z[\text{RuCl(CP})\text{(PPh\text{3})}_2]_w[\text{I-DMAB}]_b = 350/150/2.0/0.5/10 \text{mM in ethanol at 40 }\text{°C}\).  
  - entry 2: \([\text{PEGMA}]_x[\text{13FOMA}]_y[\text{P1 (entry 1)}]_z[\text{RuCl(CP})\text{(PPh\text{3})}_2]_w[\text{I-DMAB}]_b = 313/134/2.84/0.45/8.8 \text{mM in ethanol at 40 }\text{°C}\).  
  - entry 3: \([\text{PEGMA}]_x[\text{13FOMA}]_y[\text{ECPA}]_z[\text{RuCl(CP})\text{(PPh\text{3})}_2]_w[\text{I-DMAB}]_b = 350/150/3.33/0.5/10 \text{mM in ethanol at 40 }\text{°C}\).  
  - entry 4: \([\text{PEGMA}]_x[\text{13FOMA}]_y[\text{ECPA}]_z[\text{RuCl(CP})\text{(PPh\text{3})}_2]_w[\text{I-DMAB}]_b = 350/75/75/1.41/0.5/10 \text{mM in ethanol at 40 }\text{°C}\).  
  - entry 5: \([\text{PEGMA}]_x[\text{DMA}]_y[\text{DCAP}]_z[\text{RuCl(CP})\text{(PPh\text{3})}_2]_w[\text{n-BuN}]_b = 350/150/1.43/1.0/10 \text{mM in toluene at 80 }\text{°C}\).  
  - entry 6: \([\text{PEGMA}]_x[\text{13FOMA}]_y[\text{entry 5}]_z[\text{RuCl(CP})\text{(PPh\text{3})}_2]_w[\text{n-BuN}]_b = 350/150/1.43/0.5/10 \text{mM in toluene at 80 }\text{°C}\).  
  - entry 7: \([\text{PEGMA}]_x[\text{DMA}]_y[\text{ECPA}]_z[\text{RuCl(CP})\text{(PPh\text{3})}_2]_w[\text{n-BuN}]_b = 250/250/4.0/0.5/10 \text{mM in toluene at 80 }\text{°C}\).  
  - entry 8: \([\text{PEGMA}]_x[\text{13FOMA}]_y[\text{entry 7}]_z[\text{RuCl(CP})\text{(PPh\text{3})}_2]_w[\text{n-BuN}]_b = 350/150/2.5/1.0/20 \text{mM in toluene at 80 }\text{°C}\).  
  - entry 9: \([\text{PEGMA}]_x[\text{13FOMA}]_y[\text{ECPA}]_z[\text{RuCl(CP})\text{(PPh\text{3})}_2]_w[\text{n-BuN}]_b = 250/250/4.0/0.5/10 \text{mM in toluene at 80 }\text{°C}\).  
  - entry 10: \([\text{PEGMA}]_x[\text{DMA}]_y[\text{entry 9}]_z[\text{RuCl(CP})\text{(PPh\text{3})}_2]_w[\text{n-BuN}]_b = 350/150/2.5/1.0/20 \text{mM in toluene at 80 }\text{°C}\).  

\(^a\) Conversion of PEGMA, DMA and 13FOMA determined by \(^1\text{H NMR.}\)  
\(^b\) Determined by SEC in DMF (10 mM LiBr) with PMMA standard calibration.  
\(^c\) Determined by SEC in THF with PMMA standard calibration.
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$^a$ Determined by SEC in DMF (10 mM LiBr) with PMMA standard calibration.
$^b$ Determined by SEC in THF with PMMA standard calibration.
$^c$ DP of PEGMA ($l(o)$), DMA ($m$) and 13FOMA ($n$) and $M_n$ of the copolymers determined by $^1$H NMR.
$^d$ Calculated weight-average molecular weight ($M_w$): $M_w$ (Calcd.) = $M_n$ (NMR) x $M_w/M_n$ (SEC).
$^e$ Absolute weight-average molecular weight ($M_w$) of the copolymers determined by SEC-MALLS in DMF (10 mM LiBr) or water.
$^f$ Aggregation number of the copolymers in water: $N_{agg} = M_{w,H_2O}/M_{w,DMF}$.
$^g$ Cloud point temperature of the aqueous solutions of the copolymers monitored at 670 nm upon heating (1 °C/min): [polymer] = 4 mg/mL in water.
Figure S1. Synthesis of (a, b) P1, (c, d) P2, (e, f) P3, and (g, h) P4 via ruthenium-catalyzed living radical copolymerization: (a, c, e, g) Time-conversion curves and (b, d, f, h) SEC curves of the intermediates and final products in DMF (10 mM LiBr). The final products (P1 – P4) were purified by preparative SEC to remove a catalyst residue and unreacted monomers. Polymerization conditions: see Table S1.
Figure S2. $^1$H NMR spectra of (a) P1, (b) P3, (c) P2, and (d) P4 in acetone-$d_6$ at 25 °C.
**Figure S3.** Synthesis of (a, b) P₅, (c, d) P₆, and (e, f) P₇ via ruthenium-catalyzed living radical copolymerization: (a, c, e) Time-conversion curves and (b, d, f) SEC curves of the crude products in (b, d) DMF (10 mM LiBr) or (f) THF. The final products were purified and/or fractionated by preparative SEC in DMF to give P₅, P₆, and P₇. Polymerization conditions: see Table S1.
Figure S4. (a, c) $^1$H and (b, d) $^{19}$F NMR spectra of P5 in (a, b) acetone-$d_6$ or (c, d) D$_2$O at 25 °C.
Figure S5. (a, b, d-f) DLS intensity size distribution of (a) P1, (b) P3, (d) P2, (e) P4, and (f) P5 in DMF (black lines) or water (blue lines) at 25 °C: [polymer] = 10 mg/mL. (c) SEC curves of P3 in DMF (10 mL LiBr, black) at 40 °C or water (blue) at 30 °C.
Figure S6. (a) $^1$H NMR and (b) $^1$H NOE difference spectra of P4 (30 mg/mL) in D$_2$O at 30 °C. (c) $^1$H NOE signal intensity for one proton (NOE/N$_{H}$) of poly(ethylene glycol) methyl ether [$d$: -CH$_2$(OCH$_2$CH$_2$)$_{7.5}$, 3.9 – 3.5 ppm, $e$: -OCH$_3$, 3.4 ppm] and fluorous units [$k$: -CH$_2$(CF$_2$)$_2$CF$_3$, 2.7 ppm] in P2 and P4 in D$_2$O at 30 °C. The peak assignment: see Figure S2. The NOE/N$_{H}$ values of $k$, $d$, and $e$ were estimated by irradiating the methylene protons of the dodecyl groups [$h$: -(CH$_2$)$_9$-, 1.5 – 1.3 ppm]. Here, the one methylene proton of the irradiated dodecyl units was set to 100 as integral normal.
Figure S7. (a, c) $^1$H and (b, d) $^{19}$F NMR spectra of P6 in (a, b) acetone-$d_6$ or (c, d) D$_2$O at 25 °C.

Figure S8. (a, c) $^1$H and (b, d) $^{19}$F NMR spectra of P7 in (a, b) acetone-$d_6$ or (c, d) D$_2$O at 25 °C.
**Figure S9.** Self-assembly behavior of asymmetric A/C-B/C random block copolymers (P6 and P7) in water. SEC curves (by the RI detector with PEO calibration) of (a) the macroinitiator of P6 and (b) P6 in DMF (10 mM LiBr, black lines) or H2O (blue lines). (b) M_w and N_agg of the P6 micelle were determined by SEC-MALLS in water. DLS intensity size distribution of (c) P6 and (d) P7 in DMF (black lines) or H2O (blue lines) at 25 °C: [polymer] = 10 mg/mL.

**Figure 10.** A TEM image of P7 micelles cast on carbon coat grids from the aqueous solution ([polymer] = 10 mg/mL). The sample was stained with the vapor of the aqueous solutions of OsO₄.