

3-Miktoarm Star Terpolymers via Janus Polymerization: One-Step Synthesis and Self-Assembly

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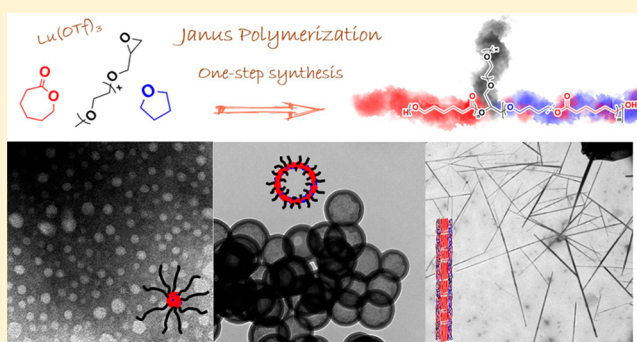
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S Supporting Information

ABSTRACT: Janus polymerization combines cationic and anionic polymerizations into the two ends of a single growing chain and presents a novel pathway to produce topologically defined polymers. In this contribution, we report a one-step synthesis of 3-miktoarm star terpolymers of poly(ethylene glycol)-*star*-poly(ϵ -caprolactone)-*star*-poly(ϵ -caprolactone-*co*-tetrahydrofuran) (PEG-*star*-PCL-*star*-P(CL-*co*-THF)) via Janus polymerization using lutetium triflates (Lu(OTf)₃) and methoxypoly(ethylene glycol) epoxy (mPEG-EO) as catalyst and macroinitiator, respectively. Self-assembly of PEG-*star*-PCL-*star*-P(CL-*co*-THF) into vesicles in aqueous solution depends on the ratio of hydrophilic and hydrophobic block of the terpolymers. Coassembly of the terpolymer with a PCL homopolymer (MW = 3000), on the other hand, increases shell thickness and vesicle diameter. Furthermore, nanorods and needle-shaped aggregates featuring high aspect ratios are obtained upon self-assembly at an interface. This unique behavior can be attributed to crystallization of the PCL segments. Based on the biocompatible and biodegradable nature of the constituting segments, the herein described 3-miktoarm star terpolymers might be promising materials for drug/gene delivery or as bionanoreactors, especially as wall thickness and stiffness of the structures observed can be tuned. With that control over (nano)local permeability might be feasible.



INTRODUCTION

Miktoarm star-shaped terpolymers, whose arms emanate from a central junction point with different chemical structures, have attracted much attention due to their unique properties.^{1–4} A great number of morphological studies have been reported, and it is concluded that the morphologies being accessible via self-assembly of ternary systems are much more complex and interesting than usually observed in the case of binary systems.^{5–7} Although 3-miktoarm star terpolymers are also ABC ternary systems, a single junction connects three different blocks, and hence, their microdomain morphology in the bulk⁸ and also their self-assembly behavior in solution^{9,10} are significantly different from the corresponding linear triblock terpolymers.¹¹

Compared to regular star-shaped polymers, the synthesis of asymmetric miktoarm terpolymers is more challenging, sometimes requiring several synthetic steps with strict purification of each intermediate. The first ABC miktoarm star terpolymer has been reported by Hadjichristidis and Iatrou featuring polyisoprene, polystyrene, and poly(1,4-butadiene) arms.¹² In general, three synthetic methods have been employed. The first method uses multifunctional chlorosilane

to react with different linear living polymer chain ends to form star polymers.^{6,13} The second is based on the diblock copolymer formed by the reaction between linear polymer with an end group of 1,1-diphenylethylene (DPE) or 1,4-bis(1-phenylethenyl)benzene (DDPE) and another living macroanion. The generated active site at the block junction is then capable of polymerizing the third arm.^{2,14} The third utilizes a polymer chain containing two different groups at the same chain end which are able to initiate two separate polymerizations.¹⁵ Also, trifunctional initiators can be employed for the miktoarm synthesis.¹⁶ As one disadvantage, these methods suffer from harsh polymerization conditions or difficulties in the preparation of multifunctional initiators.

Janus polymerization as introduced by our group combines cationic and anionic polymerizations into a single growing chain.¹⁷ A cationic random copolymerization of tetrahydrofuran (THF) with ϵ -caprolactone (CL) and a simultaneous anionic homopolymerization of CL can be performed at two

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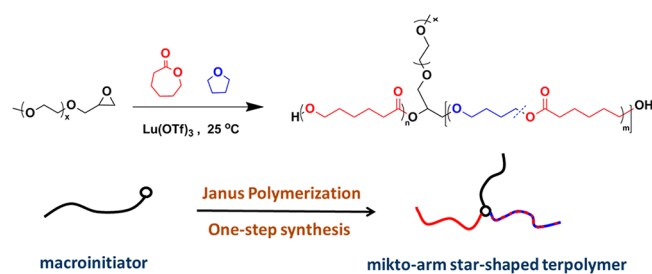
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ends of a growing polymer chain, respectively, catalyzed by lutetium triflates $[\text{Lu}(\text{OTf})_3]$ with propylene oxide as initiator under very mild conditions. Well-defined diblock poly(THF-*co*-CL)-*b*-PCL and multiblock $[(\text{THF-}i>co-CL)-*b*-PCL] $_m$ have been synthesized and exhibited excellent mechanical properties.¹⁸ Branched polymers are also synthesized by our group via Janus polymerization as an example for the topological design of polymers.¹⁹$

In this contribution, we synthesized 3-miktoarm star terpolymers containing hydrophilic PEG, semicrystalline PCL, and hydrophobic poly(THF-*co*-CL) chains (PEG-*star*-PCL-*star*-P(CL-*co*-THF)) directly by a one-step Janus polymerization with methoxypoly(ethylene glycol) epoxy (mPEG-EO) as macroinitiator (Scheme 1). The facile

Scheme 1. Synthesis of 3-Miktoarm Star Terpolymer (PEG-*star*-PCL-*star*-P(CL-*co*-THF)) Catalyzed by $\text{Lu}(\text{OTf})_3$ and mPEG-EO



synthetic approach simplifies both polymerization and purification. Subsequent self-assembly of the 3-miktoarm star terpolymer in aqueous media encompasses vesicles and worm-like micelles depending on the preparation conditions. Since PEG, PCL, and PTHF are recognized as biocompatible materials, PEG-*star*-PCL-*star*-P(CL-*co*-THF) polymers are promising with regard to future biomedical applications.^{20,21}

EXPERIMENTAL SECTION

Materials. Tetrahydrofuran (THF, AR, Sinopharm Chemical Reagent Company) was refluxed over potassium ketyl prior to use. ϵ -Caprolactone (CL, 99%, Acros) was distilled under reduced pressure over CaH_2 and stored under an argon atmosphere at room temperature. $\text{Lu}(\text{OTf})_3$ was synthesized from corresponding Lu_2O_3 (>99.99%, Beijing Founde Star Science and Technology Company) and triflic acid (99%, Energy Chemical) according to the reported method²² and dried in a vacuum (<0.5 mmHg) at 200 °C for 40 h. Methoxypoly(ethylene glycol) epoxy (mPEG-EO, $M_n = 2000$) was purchased from Suzhou Nord Derivatives Pharmaceutical Technology

Company and vacuum-dried for 24 h at room temperature before use. Other chemicals were used as received.

Measurements. Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Avance III 400 MHz (^1H : 400 MHz and ^{13}C : 100 MHz) spectrometer in CDCl_3 . Molecular weights (MWs) and polydispersity indices (D) were determined by size exclusion chromatography (SEC) using a Waters 150C apparatus equipped with Waters Styragel HR3 and HR4 columns and a Waters 2414 refractive index detector. THF was used as eluent with a flow rate of 1.0 mL/min at 40 °C, and narrow D polystyrene samples were used as calibration standard. Differential scanning calorimetry (DSC) analyses were performed on a TA Q20 instrument. Samples were heated from -90 to 90 °C at a rate of 5 °C/min under a nitrogen purge, held for 3 min to erase thermal history, cooled to -90 °C at a rate of 10 °C/min, and finally subjected to a second scan. X-ray diffraction (XRD) spectra were conducted with Shimadzu Lab XRD-60000 X-ray diffractometer (40 kV, 40 mA) using nickel-filtered $\text{Cu K}\alpha$ radiation. Samples were scanned from 2θ of 5° to 90°. The hydrodynamic diameters of nanoparticles were measured by dynamic light scattering (DLS) using a particle size analyzer (Zetasizer Nano Series, Malvern Instruments). The measurements were made at a fixed angle at 90° and a wavelength of 531 nm. Each reported measurement was conducted for three runs. Transmission electron microscopy (TEM) images were obtained using a HITACHI HT7700 instrument. A drop of nanoparticle solution in water with a concentration of 1 mg/mL was added onto the carbon film and followed by a drop of 2% phosphotungstic acid solution. The carbon film was dried under infrared lamp for 1 h before TEM analysis. Scanning electron microscopy (SEM) images were obtained using a SU-8010 instrument. Cryogenic transmission electron microscopy (cryo-TEM) measurements were performed on a FEI Tecnai G² 20 cryo-transmission electron microscope (FEI, Eindhoven, Netherlands). Acceleration voltages were set to 200 kV. Samples were prepared on Quantifoil grids (3.5/1) after cleaning by argon plasma treatment for 120 s. 8.5 μL of the solutions was blotted by using a Vitrobot Mark IV (FEI, Eindhoven, Netherlands). Samples were plunge-frozen in liquid ethane and stored under nitrogen before being transferred to the microscope utilizing a Gatan transfer stage. The images were acquired with a 4k \times 4k Eagle HS CCD and a 1k \times 1k Olympus MegaView camera. Further observation was carried out after heating to 55 °C and ultrasonication for 5 min. The sample was then cooled to room temperature and prepared as described before. Atomic force microscopy (AFM) images were recorded on a CSPM5500 microscope operated in tapping mode. The samples were prepared by spin-coating onto clean silicon wafers.

Janus Polymerization of THF and CL Initiated by $\text{Lu}(\text{OTf})_3$ /mPEG-EO. All polymerizations were performed using the Schlenk technique. All polymerization tubes were flame-dried and purged with argon. In a typical polymerization, a 20 mL tube was charged with lutetium triflate (31.4 mg, 0.05 mmol), THF (1.44 g, 20.0 mmol), and CL (0.57 g, 5.0 mmol) at room temperature. After lutetium triflate was dissolved, the mixture was added into another tube containing

Table 1. Ring-Opening Copolymerization of Tetrahydrofuran (THF) and ϵ -Caprolactone (CL) Catalyzed by $\text{Lu}(\text{OTf})_3$ /mPEG-EO in the Bulk

sample	[CL]:[THF] ^a (molar ratio)	T (°C)	time (days)	yield (%)	conv (%) ^b		$M_{n,\text{NMR}}^c$ (kDa)	$M_{n,\text{SEC}}^d$ (kDa)	D_{SEC}^d	PCL/PTC/PEG ^e in polymer	hydrophilic ratio (wt %)
					THF	CL					
P1	1:8	25	3	5.4	4.7	8.4	3.9	5.8	1.4	3/21/45	51.6
P2	1:4	25	4	7.7	6.4	11.0	5.0	11.7	1.25	8/28/45	40.7
P3	1:4	25	5	15.0	2.4	46.7	8.4	15.7	1.14	49/11/45	23.8
P4	1:4	40	2	25.5	4.2	79.2	13.0	26.5	1.14	84/19/45	15.4
P5	1:4	25	22	31.2	3.6	≥99	15.0	34.7	1.26	— ^f	13.3

^a $\text{Lu}(\text{OTf})_3$:mPEG-EO:THF = 1:1:400. ^bAs determined by ^1H NMR analysis. ^cAs calculated by ^1H NMR analysis. ^dAs determined by SEC. ^eTerpolymer composition was determined by reactivity ratios and ^1H NMR analysis. PTC is the abbreviation for P(CL-*co*-THF). ^fHere, coupling reactions between anionic and cationic chain ends occurred, rendering it difficult to calculate the composition in the P(CL-*co*-THF) arm by reactivity ratios.

mPEG-EO (100.0 mg, 0.05 mmol), and the reaction was carried out at 25 °C. After predetermined reaction time, the polymerization was terminated by water. The resulting viscous solution was added slowly to cold hexane with vigorous stir. The precipitation was filtrated and dried under vacuum.

Self-Assembly in Aqueous Solution. Polymer vesicles were prepared by a solvent switching method at an initial concentration of 3.0 mg/mL. A terpolymer sample was dissolved in 1 mL of THF, and 1 mL of deionized Milli-Q water was added slowly in 30 min at 25 °C under continuous shaking. The turbid mixtures were then dialyzed against water for 2 days to remove THF using a Spectra/Por regenerated cellulose membrane with a MW cutoff of 3500.

Annealing at an Interface. A 3-miktoarm star terpolymer was dissolved in THF at a concentration of 6 mg/mL and dropped onto a carbon film or a silicon wafer. After 10 min, the sample was annealed in 80 °C for 30 min and then cooled to 25 °C at a rate of 20 °C/h.

RESULTS AND DISCUSSION

Synthesis and Characterization of 3-Miktoarm Star Terpolymer. The 3-miktoarm star terpolymers, i.e., PEG-*star*-PCL-*star*-P(CL-*co*-THF), were synthesized via one-step Janus polymerization (Scheme 1) catalyzed by Lu(OTf)₃ and using mPEG-EO (MW = 2000) as initiator. A more detailed explanation of Janus polymerization as well as Figures S1 and S2 are included in the Supporting Information, and the results are listed in Table 1. The opening of the three-membered ring of mPEG-EO initiates both the anionic polymerization of PCL and the cationic copolymerization of THF with CL at the two ends in the presence of Lu(OTf)₃. This method represents a facile and straightforward alternative to classical approaches that would require several polymerization and purification steps. Furthermore, well-controlled Janus polymerization suppresses homopolymerization so that the final star polymer is free of any contaminations.

Through variation of the monomer feeding ratio and controlled reaction conditions, we can obtain star-shaped polymers with predetermined hydrophilic/hydrophobic ratios. It is confirmed that Janus polymerizations can be terminated before coupling reactions between cationic and anionic chain ends occur, i.e., the step-growth polymerization within 22 days (sample P5 in Table 1), which contributes to the slow chain movement of polymer stars involved with mPEG macro-initiator. The polymerization rate increases when the temperature rises from 25 to 40 °C as observed for samples P3 and P4.

The structure of the 3-miktoarm star terpolymer (sample P3 in Table 1) is characterized by ¹H NMR analysis (Figure 1). The backbone protons of PEG (H^b: 3.66 ppm), PTHF (H^c: 3.40 ppm and H^d: 1.64 ppm), and PCL (H^e: 2.30 ppm, H^f and H^g: 1.64 ppm, H^h: 1.37 ppm, and Hⁱ: 4.05 ppm) can be clearly identified. The signal at 5.12 ppm (H^a) is assigned to a methine proton in the macroinitiator and confirms the fact that the epoxide residue is located at the junction of the three arms. It needs to be mentioned that one arm of P(CL-*co*-THF) is a random copolymer segment of THF and CL units, and the ratio of THF/CL depends on their reactivity during cationic copolymerization. In order to obtain the exact ratio of two monomers in the P(CL-*co*-THF) arm, we terminate the polymerization during the first stage before chain coupling occurs. Here, the anionic ROP of CL proceeds much slower if compared to the cationic part.¹⁷ In that case, the conversion of CL is mainly attributed to the cationic copolymerization, and the THF/CL ratio between both comonomers in the resulting copolymer is only slightly lower than the ratio in P(CL-*co*-

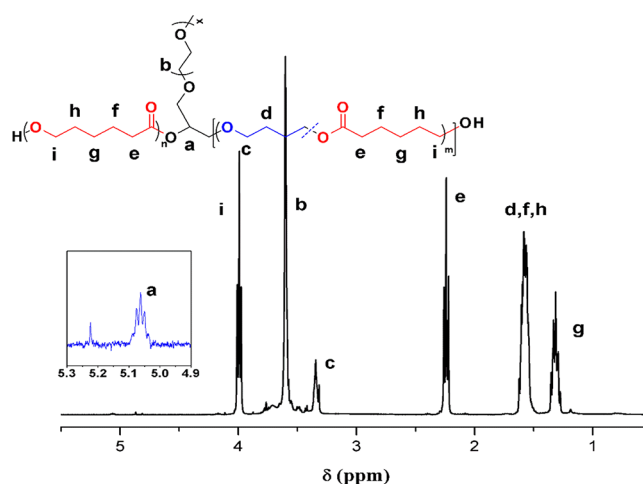


Figure 1. ¹H NMR spectrum of a 3-miktoarm star terpolymer (PEG₄₅-*star*-PCL₄₉-*star*-P(CL₁-*co*-THF₁₀)) terminated by H₂O (sample P3 in Table 1) with a magnified view in the inset.

THF) arm. According to our experiments (Table S1 and Figure S7), the reactivity ratios of CL and THF are 1.23 and 2.03, respectively, which indicates the molar ratio of CL to THF in the P(CL-*co*-THF) block.

The SEC traces of the terpolymers are shown in Figures 2A and 2B. Small distributions observed in the lower molecular weight region are ascribed to some remaining macroinitiator, whereas the higher molecular weight region of sample P3 is attributed to the polymerization of PEG-EO into the polymer chain as comonomer, which is also confirmed by our previous work.²³

The composition of the three constituting monomer units in the resulting star terpolymers is calculated from ¹H NMR spectra. By terminating the polymerization at different times, we can obtain different terpolymers with various hydrophilic/hydrophobic ratios, which significantly influences their solubility in water. As to P1 (PEG₄₅-*star*-PCL₃-*star*-P(CL₁-*co*-THF₂₀)) and P2 (PEG₄₅-*star*-PCL₈-*star*-P(CL₃-*co*-THF₂₅)) shown in Table 1, they can be directly dissolved in water due to a rather high content in hydrophilic material, whereas this is not possible for the other samples.

The thermal behavior of the terpolymer (sample P3 in Table 1) was investigated by DSC and XRD as shown in Figures 2C and 2D. The typical DSC melting peak at 49.2 °C with an enthalpy ΔH of 49.67 J/g and intense XRD diffraction peak at 21.3° and 23.7° confirms the existence of crystalline PCL domains and already indicates a strong influence of the PCL block on the thermal properties of the resulting terpolymer.

Self-Assembly of 3-Miktoarm Star Terpolymer in Aqueous Solution. Self-assembly of the 3-miktoarm star terpolymers (PEG-*star*-PCL-*star*-P(CL-*co*-THF)) was carried out via the nanoprecipitation process. PEG homopolymer is completely soluble in aqueous solution and will in our opinion not influence on the self-assembly of the 3-miktoarm star terpolymers. The self-assembly of star terpolymer depends very much on their hydrophilic/hydrophobic ratios and in this particular case also on the thermal history. It is necessary to perform a thermal treatment at a temperature higher than T_m of PCL in order to enhance the mobility of terpolymer chains and to assist in vesicle formation.²⁴ Therefore, before any further DLS and TEM analysis, the nanoparticle dispersions

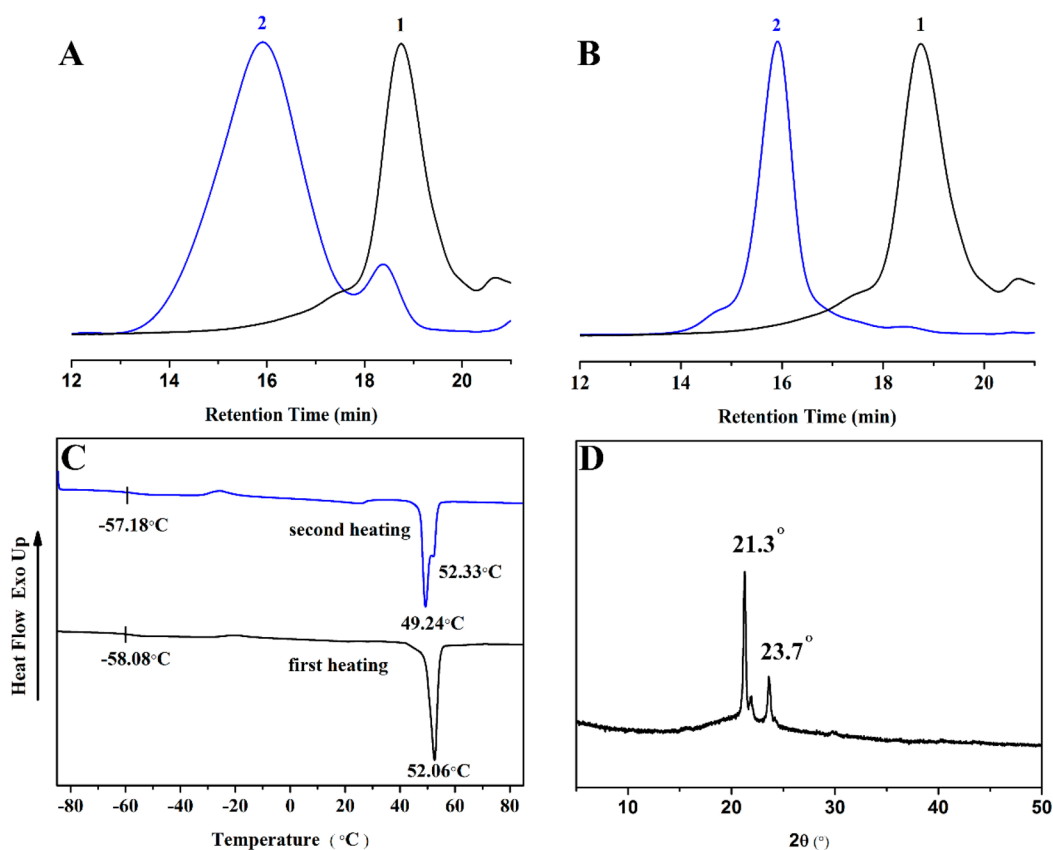


Figure 2. (A) (1) SEC trace of macroinitiator mPEG-EO; (2) SEC trace of 3-miktoarm star terpolymer PEG₄₅-star-PCL₈-star-P(CL₃-co-THF₂₅) (sample P2 in Table 1). (B) (1) SEC trace of macroinitiator mPEG-EO; (2) SEC trace of 3-miktoarm star terpolymer PEG₄₅-star-PCL₄₉-star-P(CL₁-co-THF₁₀) (sample P3 in Table 1). (C) DSC curves of 3-miktoarm star terpolymer PEG₄₅-star-PCL₄₉-star-P(CL₁-co-THF₁₀) (sample P3 in Table 1). (D) X-ray diffraction pattern of 3-miktoarm star terpolymer PEG₄₅-star-PCL₄₉-star-P(CL₁-co-THF₁₀) (sample P3 in Table 1).

are heated at 70 °C for 30 min, followed by a slow cooling to room temperature at about 1 °C/min.

The terpolymer PEG₄₅-star-PCL₈-star-P(CL₃-co-THF₂₅) (sample P2 in Table 1) with a high hydrophilic weight fraction of 40.7% is directly soluble in water and forms micelles. As shown in Figure 3, the hydrodynamic diameter of the micelles measured by DLS is 80 nm (Figure 3A) with a PDI of 0.261, whereas TEM analysis after staining by 2% phosphotungstic acid solution shows white spheres with a uniform size of about 30 nm (Figure 3C). It is reasonable that the diameters of micelles measured by DLS are somewhat larger if compared to TEM analysis since the PEG shell cannot be visualized in TEM. In addition, TEM shows nanoparticles in the dehydrated solid state while DLS assesses the hydrodynamic diameters of micelles swollen in an aqueous environment.²⁵

Sample P3 (PEG₄₅-star-PCL₄₉-star-P(CL₁-co-THF₁₀)) with a hydrophilic weight fraction of 23.8% forms vesicles in aqueous solution. After the thermal treatment, the vesicles are characterized by DLS and TEM as shown in Figure 3. The hydrodynamic diameter of the vesicles measured by DLS is about 185 nm (Figure 3B) with a moderately broad dispersity of 0.237. The TEM micrograph (Figure 3D) presents a cluster of spheres with an average diameter of 168 nm, which indicates the presence of a bilayer membrane with an average membrane thickness of ca. 21 nm. The vesicle diameter is in good agreement with the DLS data and features a rather low dispersity of 0.05. Interestingly, the structural integrity is maintained even after drying for TEM investigation. This is

further confirmed by SEM (Figure S11) where a number of spheres with diameters ranging from 150 to 200 nm are observed. The spherical morphology is preserved even without the aqueous environment confirming that these prepared vesicles are rather robust, which we attribute to semicrystalline PCL being part of the vesicle wall. Similar observations have been made earlier for vesicles formed from star-shaped PEO-*b*-poly(ferrocenyldimethylsilane) diblock copolymers featuring four arms.^{26,27} We also employed cryo-TEM to further confirm the presence of vesicular assemblies. Figure S12 shows a spherical bilayer structure with a diameter around 70 nm. After heating the samples to 55 °C and treating them with ultrasound for 5 min, we observe that the diameter of the vesicles approaches 200 nm or larger (Figure 3E). After this treatment, fused vesicles are also observed, indicating merging processes occurring during heating. Except the spherical vesicles, Figure 3F also reveals the presence of cylindrical micelles, which has also been reported earlier, the hypothesis was that at certain hydrophilic volume fractions lead to the formation of “mixed” assemblies due to interfacial tension mismatch.²⁸

The coassembly of 3-miktoarm star terpolymer (PEG₄₅-star-PCL₄₉-star-P(CL₁-co-THF₁₀)) (sample P3 in Table 1) and homopolymer PCL (MW = 3000) is carried out to investigate the morphology change of vesicles with varying hydrophilic/hydrophobic ratios. By adding PCL to the system, the hydrophilic weight fraction decreases from 23.8% to 17.5%, and the coassembly process is carried out as described previously. Afterward, TEM analysis shown in Figure 4B

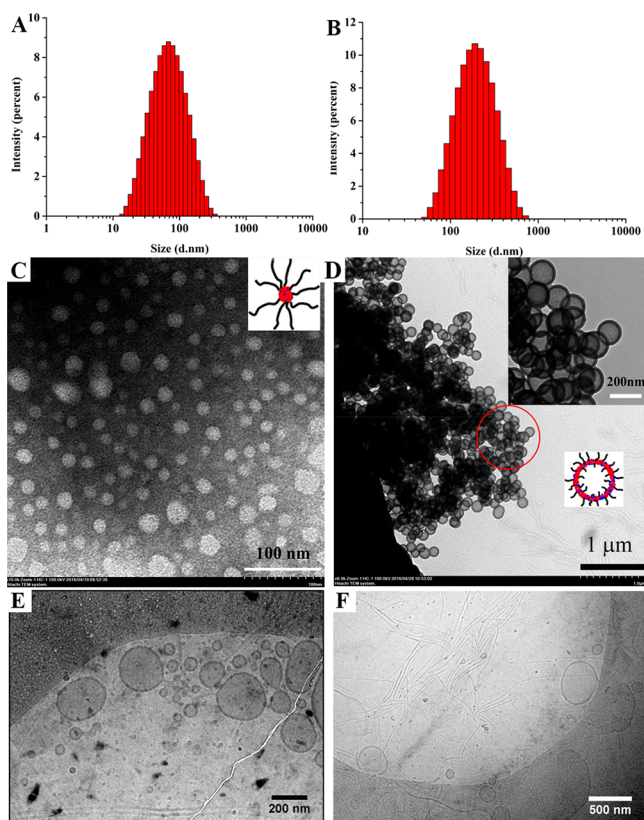


Figure 3. (A) Size distribution histogram of micelles self-assembled by 3-miktoarm star terpolymers ($\text{PEG}_{45}\text{-star-PCL}_8\text{-star-P}(\text{CL}_3\text{-co-THF}_{25})$) (sample P2 in Table 1) in water (1 mg/mL) at 25 °C. (B) Size distribution histogram of vesicles self-assembled by 3-miktoarm star terpolymers ($\text{PEG}_{45}\text{-star-PCL}_{49}\text{-star-P}(\text{CL}_1\text{-co-THF}_{10})$) (sample P3 in Table 1) in water (1 mg/mL) at 25 °C. (C) TEM image (stained by phosphotungstic acid solution) of micelles self-assembled by 3-miktoarm star terpolymers ($\text{PEG}_{45}\text{-star-PCL}_8\text{-star-P}(\text{CL}_3\text{-co-THF}_{25})$) (sample P2 in Table 1) in water. (D) TEM image of vesicles self-assembled by 3-miktoarm star terpolymers ($\text{PEG}_{45}\text{-star-PCL}_{49}\text{-star-P}(\text{CL}_1\text{-co-THF}_{10})$) (sample P3 in Table 1) in water. Scale bar = 1 μm . (E) cryo-TEM micrograph of vesicles self-assembled by 3-miktoarm star terpolymers ($\text{PEG}_{45}\text{-star-PCL}_{49}\text{-star-P}(\text{CL}_1\text{-co-THF}_{10})$) (sample P3 in Table 1) in water after thermal treatment. Scale bar = 200 nm. (F) Cryo-TEM micrograph of vesicles as well as cylindrical micelles self-assembled by 3-miktoarm star terpolymer ($\text{PEG}_{45}\text{-star-PCL}_{49}\text{-star-P}(\text{CL}_1\text{-co-THF}_{10})$) (sample P3 in Table 1) in water after thermal treatment. Scale bar = 500 nm.

depicts vesicular structures with an average diameter of 168–482 nm, and the ratio between membrane thickness and vesicle diameter increases from 25% (wall thickness is 21 nm) to 30.7% (wall thickness is 74 nm). The addition of PCL increases the bending rigidity energy necessary to bend the bilayer membrane during coassembly, which typically increases the vesicle diameter.^{29,30}

Self-Assembly of 3-Miktoarm Star Terpolymer at an Interface. This synthesized 3-miktoarm star terpolymer is able to self-assemble into acicular aggregates at an interface after cooling down from 80 to 25 °C with a rate of 20 °C/h. As shown in Figure 5A through TEM analysis, microscale acicular structures with large length to diameter ratio are formed after the heating treatment. The driving force of acicular aggregation is attributed to the PCL crystallization which is promoted through the evaporation of THF when heating to 80 °C, which allows the movement of individual chains and results in a

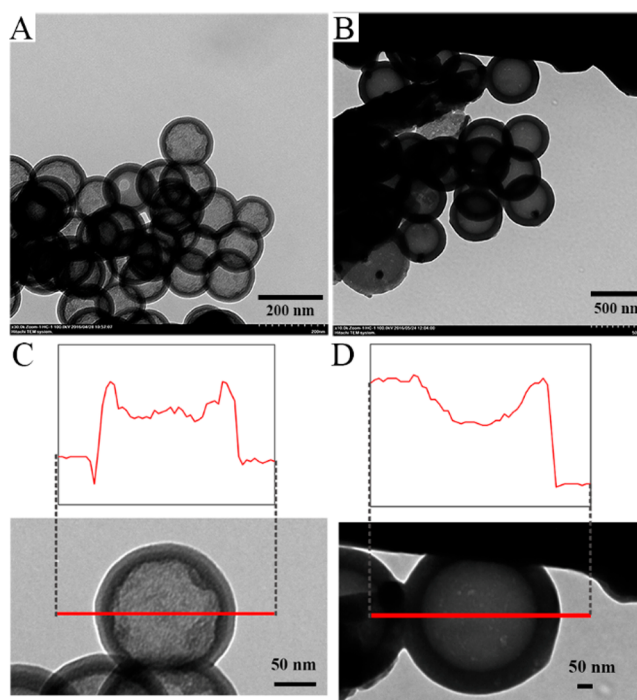


Figure 4. (A) TEM image of vesicles formed during self-assembly of 3-miktoarm star terpolymer ($\text{PEG}_{45}\text{-star-PCL}_{49}\text{-star-P}(\text{CL}_1\text{-co-THF}_{10})$) (sample P3 in Table 1) in water after thermal treatment. Scale bar = 200 nm. (B) TEM image of vesicles coassembled by 3-miktoarm star terpolymers ($\text{PEG}_{45}\text{-star-PCL}_{49}\text{-star-P}(\text{CL}_1\text{-co-THF}_{10})$) (sample P3 in Table 1) and PCL (MW = 3000) in water. Scale bar = 500 nm. (C) Change of gray degree along the red line on TEM image (vesicles shown in part A). (D) Change of gray degree along the red line on TEM image (vesicles shown in part B).

different morphology after annealing to 25 °C. Some nanorods are also found in TEM which is presented in Figure 5B; we suppose that the acicular aggregation is further promoted by these rod-like structures. We also observed a lamellar phase separation for this system after such an annealing process, presumably due to the high local terpolymer concentration (Figure S13).

By investigating such self-assembly behavior through AFM measurements, we can obtain more insight into the structure of these assemblies. Figures 5C to 5F show the height and phase images as well as section analyses for the acicular aggregates. The section in the height image shows that the height is around 25 nm; meanwhile, the section in the corresponding phase image demonstrates that different materials form the edges and the center of the structure. The middle part of the aggregates consists of PCL which crystallizes and acts as a hard compartment, whereas the rest is the soft part and most probably consists of PEG and P(THF-co-CL). Such self-assembled microstructures with 5–10 μm in length, a large length to diameter ratio, and an intriguing morphology have been rarely reported so far, not to mention the self-assembly behavior based on 3-miktoarm star terpolymers, and this might be interesting to further understand the phase behavior of such polymer topologies.

CONCLUSION

A one-step synthesis of 3-miktoarm star terpolymers ($\text{PEG}\text{-star-PCL}\text{-star-P}(\text{CL}\text{-co-THF})$) was achieved through Janus polymerization by using mPEG-EO as macroinitiator. Utilizing

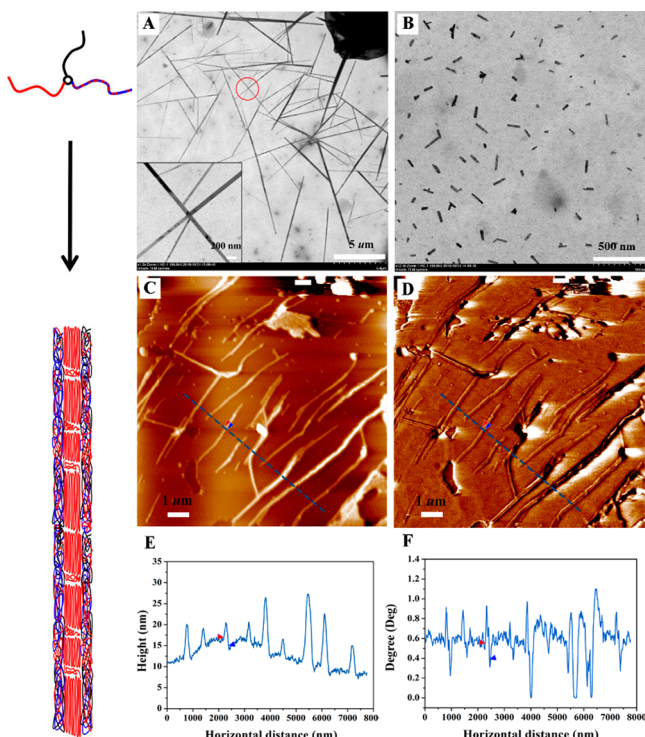


Figure 5. (A) TEM image of acicular aggregations self-assembled by 3-miktoarm star terpolymers (PEG₄₅-star-PCL₄₉-star-P(CL₁-co-THF₁₀)) (sample P3 in Table 1). Scale bar = 5 μm. (B) TEM image of rod-like aggregations self-assembled by 3-miktoarm star terpolymers (PEG₄₅-star-PCL₄₉-star-P(CL₁-co-THF₁₀)) (sample P3 in Table 1). Scale bar = 500 nm. (C) AFM height image of acicular aggregations self-assembled by 3-miktoarm star terpolymers (PEG₄₅-star-PCL₄₉-star-P(CL₁-co-THF₁₀)) (sample P3 in Table 1). Scale bar = 1 μm. (D) AFM phase image of acicular aggregations self-assembled by 3-miktoarm star terpolymers (PEG₄₅-star-PCL₄₉-star-P(CL₁-co-THF₁₀)) (sample P3 in Table 1). Scale bar = 1 μm. (E) Section analyses of acicular aggregations displayed in (C). (F) Section analyses of acicular aggregations displayed in (D).

the mechanistic differences of the individual stages during Janus polymerization, we were able to obtain polymers with different hydrophilic/hydrophobic ratios by terminating the polymerization at different time points. The self-assembly of 3-miktoarm star terpolymers (PEG-star-PCL-star-P(CL-co-THF)) in aqueous solution was investigated in detail. Samples with a high hydrophilic weight fraction could be directly dissolved in water and formed spherical micelles which were detected by both DLS and TEM. On the other hand, terpolymers with decreasing hydrophilic weight fractions tended to self-assemble into vesicles. These robust vesicles were clearly observed by cryo-TEM, TEM, and SEM and maintained their spherical morphology even after drying. Furthermore, the coassembly of 3-miktoarm star terpolymers (PEG₄₅-star-PCL₄₉-star-P(CL₁-co-THF₁₀)) and PCL (MW = 3000) was investigated, and a clear increase in membrane thickness and vesicle diameter was observed. Apart from aqueous solutions, this synthesized 3-miktoarm star terpolymer formed acicular superstructures after a further annealing process from a nonselective solvent (THF). Through TEM and AFM measurements, the morphology and the composition were investigated. As a biocompatible and biodegradable polymer, together with a broad range of morphologies being accessible using different self-assembly strategies, the 3-

miktoarm star terpolymers (PEG-star-PCL-star-P(CL-co-THF)) would be attractive for building a versatile drug delivery system.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.macromol.8b00949.

¹H NMR spectra, measurement of reactivity ratios, SEM and cryo-TEM images of vesicles, and TEM image of phase separation (PDF)

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Notes

The authors declare no competing financial interest.

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