Supporting information

Crystallization in sequence-defined peptoid diblock copolymers induced by microphase separation

Jing Sun[1,4], Alexander A. Teran[2,5], Xunxun Liao[3,6], Nitash P, Balsara[2,4,5] and Ronald N. Zuckermann[1,4]**

[1]Molecular Foundry, Lawrence Berkeley National Laboratory
[2]Department of Chemical and Biomolecular Engineering, University of California, Berkeley 94720
[3]Department of Materials Science and Engineering, University of California, Berkeley 94720
[4]Materials Sciences Division, Lawrence Berkeley National Laboratory
[5]Environmental Energy Technologies Division, Lawrence Berkeley National Laboratory
[6]National Center for Electron Microscopy, Lawrence Berkeley National Laboratory

Experimental section

Synthesis of peptoid polymers

Polypeptoids were synthesized on an automated robotic synthesizer or a commercial Aapptec Apex 396 robotic synthesizer on 100 mg of Rink amide polystyrene resin (0.61 mmol/g, Novabiochem, San Diego, CA). One of the primary amine submonomers, 2-(2-(2-methoxyethoxy)ethoxy)ethyl amine was synthesized as previously described.[30] All the other monomers, solvents, and reagents described here were purchased from commercial sources and used without further purification. The synthesis procedure was a modified version of methods previously described.[33] The Fmoc group on the resin was deprotected with 20% (v/v) 4-

methylpiperidine/DMF before starting the submonomer cycle. An acylation step was then performed on the amino resin by the addition of 1.0 mL of 1.2 M bromoacetic acid in DMF and 0.18 mL of *N*,*N*'-diisopropylcarbodiimide (DIC, 1.15mmol, neat) and mixing for 20 min. Displacement of the bromide with various submonomers occurred by adding a 1.0-2.0 M solution of the primary amine in N-methyl-2-pyrrolidone, followed by agitation for 120 min. All the polymers were acetylated on the resin after synthesis using a mixture (2.0 mL per 100 mg of resin) of 0.4 M acetic anhydride and 0.4 M pyridine in DMF for 30 min. The crude peptoid products were cleaved from the resin by the addition of 50% (v/v) trifluoracetic acid (TFA) in DCM for 20 min, followed by evaporation under a stream of N_2. The crude products were then dissolved in 1:1 mixture (v/v) of (50:50 isopropanol: acetonitrile)/water and lyophilized. The peptoids were then purified by reverse-phase HPLC on a C4 column (Vydac, 10-15 μm, 22mm x 250 mm) using a linear gradient of 50-100% (50:50 isopropanol:acetonitrile) in water with 0.1% TFA over 60 min at a flow rate of 10 mL/min. The polypeptoid pNia-*b*-pNtw was purified by reverse-phase HPLC on a C18 column (Vydac, 10 μm, 22mm x 250 mm). The polypeptoid $pNdc_{24}$-*b*-$pNte_{12}$ and homopeptoid $pNdc_{20}$ were directly precipitated from water.

Each final product was characterized by analytical reverse-phase HPLC using a C4 column (Vydac 214TP, 5 μm, 4.6 mm x 150 mm) with 50-100% gradient at 1 mL/min over 30min at 60 ^{o}C. The polypeptoid pNia-*b*-pNte was characterized using a C18 column (5 μm, 2 mm x 50 mm). Peptoid purity was determined using the analytical reverse-phase HPLC conditions detailed above, and the molecular weight was determined by matrix-assisted laser desorption/ionization mass spectrometry (Applied Biosystems MALDI TOF/TOF Analyzer 4800 with a 1:1 (v/v) mixture of peptoid [2 mg/mL in 1:1 (50:50 isopropanol: acetonitrile):water] and 1,8,9-

dianthracenetriol dissolved in tetrahydrofuran at 10 mg/mL. The final polypeptoids were then lyophilized prior to subsequent measurements.

Small/Wide angle X-ray scattering (SAXS/WAXS)

The polypeptoids were loaded into the center of Garolite G-10 spacers with 0.125 μm thickness and a central hole with a diameter of 3.86 mm. The samples were then sealed off in a custom-designed sample holder with Kapton windows and well annealed (at various temperatures depending on the block copolymer) over night. Measurements were performed at beamline 7.3.3 at the Advanced Light Source (ALS) at Lawrence Berkeley National Laboratory and beamline 1-4 at the Stanford Synchrotron Radiation Laboratory (SSRL). Samples were loaded on a custom-built temperature stage and annealed at each temperature for 15-20 min before taking measurements. A silver behenate sample was used as a standard. Full two-dimensional scattering patterns were collected on an ADSC CCD detector. The scattering patterns from the ALS were reduced using the Nika program for Igor Pro available from Jan Ilavsky at Argonne National Laboratory,[1] and data from SSRL were reduced using a program written by John Pople at SSRL.

Differential scanning calorimetry (DSC)

Differential scanning calorimetry (DSC) experiments were performed to determine the thermal behavior of the synthesized peptoids using a TA Q200 Differential Scanning Calorimeter. In all measurements, a scan rate of 10 K/min was used in the temperature range of -60 to 200^{o}C for three heating and cooling cycles.

Atom force microscopy (AFM)

AFM images were performed on an Asylum MFP-3D atomic force microscope in the tapping mode at room temperature in air. A polypeptoid in $CHCl_3$ solution (10 mg/mL) was spin coated onto mica at room temperature. Samples were then annealed at 120 ^oC for several hours and cooled slowly to room temperature.

Density measurement

The density of poly(*N*-(2-(2-(2-methoxyethoxy)ethoxy)ethyl)glycine) (pNte) and poly(*N*-decylglycine) (pNdc) was measured to be 1.23 ± 0.01 g/cm^3 and 0.95 ± 0.004 g/cm^3 respectively using a density gradient column at room temperature.[35] An aqueous sucrose gradient and alcohol/ water gradient were used in the density gradient column method. The measured density was used to calculate the volume fraction of the polypeptoids.

Polarized optical microscopy

Approximately 1-2 mg of samples were placed between two glass slides secured to an Instec HCS302 heating stage controlled by an Instec STC 200 temperature controller. The heating stage was further equipped with recirculating cooling water. The sample apparatus was placed in a Leica DM 4500P microscope, and data were collected using a 5×lens. Polarizers were placed over the lens to view the birefringence of the sample.

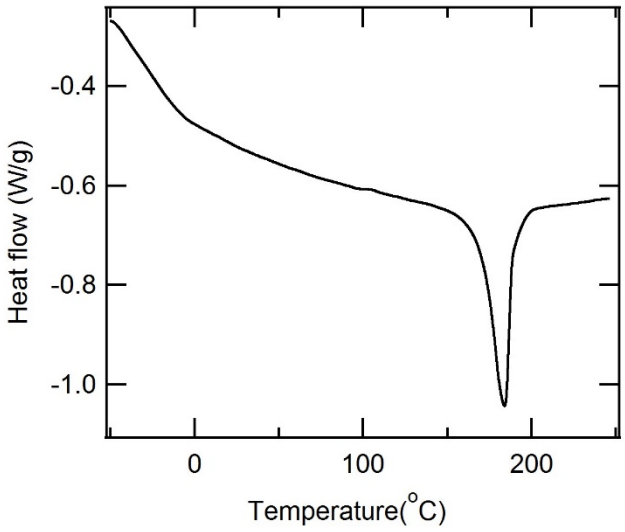

Figure S1. DSC endotherm of block copolypeptoid $pNia_{18}$-*b*-$pNte_{18}$.

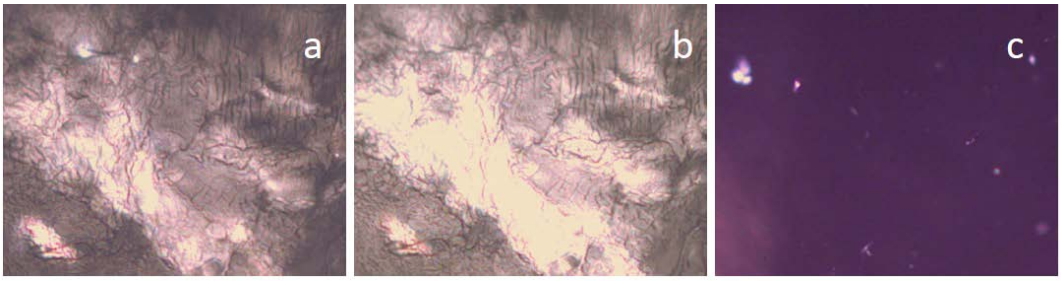

Figure S2. Polarized optical microscopy for $pNdc_{12}$-*b*-$pNte_{21}$ exhibits birefringent patterns at room temperature (a) and 90 °C (b), the temperature when pNte is amorphous but pNdc is crystalline). Upon heating to higher temperature (145 °C), birefringence is lost and leave an isotropic melt.

Symbol definitions:

ϕ_{Nte} is volume fraction of the pNte block.

ϕ_{Ndc} is volume fraction of the pNdc block.

$T_{L''-L}$ is transition temperature from L''phase to L phase.

T_{L-M} is transition temperature from L phase to M phase.

T_{M-D} is transition temperature from M phase to D phase.

$T_{m,Ndc}$ is melting temperature of the pNdc block.

$T_{m,Nte}$ is melting temperature of the pNte block.

$\Delta H_{m,Ndc}$ is entropy change of the pNdc block.

$\Delta H_{m,Nte}$ is entropy change of the pNte block.

$T_{wm,Ndc}$ is transition temperature of the pNdc from crystal to melt, obtained by WAXS.

$T_{wm,Nte}$ is transition temperature of the pNte from crystal to melt, obtained by WAXS.

D implies the disordered phase.

M implies the metastable phase.

L implies the lamellar phase with crystalline pNdc block.

L" implies the lamellar phase with two crystalline blocks.

References

1. Ilavsky, J. *J. Appl. Crystallogr.* **2012**, *45*, 324-328.