Supporting information for

Bioinspired Assembly of Functional Block-Copolymer Nanotemplates

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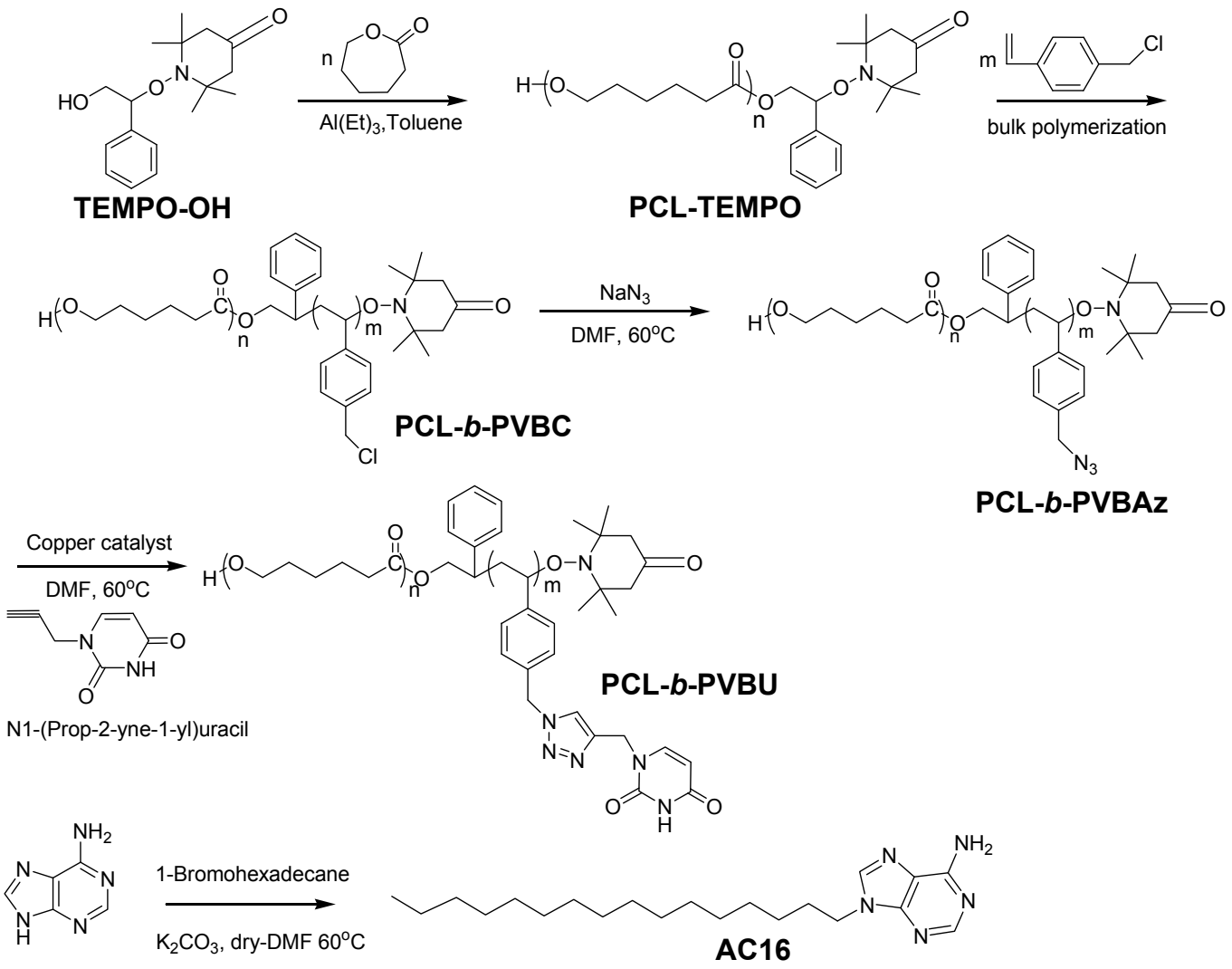
Experiment Section.

Materials. ε-Caprolactone (ε-CL, 99.5 %, ACROS), styrene (99 %, ACROS), dichloromethane (DCM, 99 % ACROS), dimethyl sulfoxide (DMSO, 99 %, ACROS), and dimethyl formamide (DMF, 99 %, Fisher Chemical) were dried over calcium hydride (CaH_2, 95 %, ACROS) for 24 h and then distilled under reduced pressure prior to use. Uracil (U, 99 %, ACROS), adenine (A, 99 %, Sigma), triethylaluminum ($AlEt_3$, 0.9 M in hexane, Fluka), glacial acetic acid (HPLC grade, TEDIA), tetrahydrofuran (THF, HPLC grade, TEDIA), acetonitrile (ACN, anhydrous, Aldrich), ethyl acetate (EtOAc, ACS reagent, Sigma-Aldrich), hexane (HPLC grade, Sigma-Aldrich), sodium azide (SHOWA, 98 %), propargyl bromide (Fluka, 80 % in Tolune), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, ACROS, 98 %), vinylbenzyl chloride (4-VBC, 96 %, ACROS), methanol (MeOH, HPLC grade, TEDIA), and *N*,*N*′,*N*″,*N*″-Pentamethyldiethylenetriamine (PMDETA, 99%, Aldrich) were all used as received. Benzoyl peroxide (BPO, 97 %, Fluka) was recrystallised from chloroform-methanol (1:1) mixture. 4-hydroxy-2,2,6,6-tetramethyl-1-piperidinyloxy (4-OH-TEMPO, 98 %, ACROS) and sodium hydroxide were laboratory grade (NaOH, 98 %, Aldrich) and used as received. Copper(I) bromide (CuBr) was stirred in glacial acetic acid overnight, filtered, and then rinsed with absolute ethanol under a blanket of argon and dried under vacuum at 60 °C overnight. 1-hydroxy-2-phenyl-2-(2’,2’,6’,6’-tetramethyl-1-piperidinyloxy) ethane (TEMPO-OH) was synthesized according to the literature.[S1]

Synthetic Routes. To obtain a nucleobase-containing block copolymers, a dual initiator, the hydroxyl-4-oxo-*N*-alkoxyamine, was chosen. This dual initiator contains a single primary alcohol as the initiating center for the living ROP of cyclic lactones, and a secondary benzylic group as an efficient initiator for the nitroxide-mediated "living" free radical polymerization of vinyl monomers. The nucleobase-containing block copolymers were synthesized via a four steps synthesis as shown in Scheme 1. The first step involved the synthesis of the well-defined PCL macroinitiator, which was prepared using ring-opening polymerization as reported previously.[S1] In the second step, the PCL-*b*-PVBC polymer was prepared via nitroxide-mediated radical polymerization. In the third step, the PCL-*b*-PVBC was modified by azidation using NaN_3 to obtain copolymers with azide groups. The presence of the azide group was confirmed by the occurrence of the characteristic peak of azide group at 2100 cm^{-1} in the FT-IR spectrum (**Figure S1**) and the methylene resonance at δ 4.2 ppm ($-CH_2N_3$) in the ^1H NMR spectrum (**Figure S2**). Finally, uracil was acetylmethylated by reacting with propargyl bromide under the catalysis of DBU unit, then grafted onto the azide group containing PCL-*b*-PVBAz copolymers, and the nucleobase grafted block copolymers (PCL-*b*-PVBU) were obatined.

Scheme S1. Synthetic Route to PCL-*b*-PVBU copolymer and AC16



Synthesis of N^1-(Prop-2-yne-1-yl)uracil. This compound was prepared according the literature procedure.[S2] (yield = 78 %). Mp: 169-170 °C. ^{1}H NMR (500 MHz, DMSO, δ): 11.35 (br s, 1H, –N*H*–), 7.68 (d, *J* = 6.0 Hz, 1H, –N–C*H*–), 5.61 (d, *J* = 6.0 Hz, 1H, –CO–C*H*–), 4.49 (d, *J* = 3.0 Hz, 2H, –CH_2–), 3.37 (t, *J* = 3.0 Hz, 1H, –C≡C*H*).

Synthesis of the Polycaprolactone Prepolymer (PCL-TEMPO). The TEMPO-OH (0.0728 g, 2.5×10^{-4} mol) dissolved in toluene (5 mL) was added into 0.2 mL of a toluene solution of triethyaluminum (0.1

mol/L) under an argon atmosphere. The reaction mixture was stirred at room temperature for 30 min, then evaporated to dryness and removed the 2-propanol byproduct. After repeating this procedure three times, 5 mL caprolactone (0.044 mol) dissolved in 25 mL dry toluene was added to the reaction mixture in ice bath. The polymerization was carried out at 25 °C for 4 h under an argon atmosphere and terminated by adding excess acetic acid (0.2 mL acetic acid/0.8 ml toluene). Finally, two-thirds of the initial solvent was evaporated, and the residue was precipitated into methanol. The product was dried until constant weight under vacuum and gave yield of 3.6 g (72%). ^{1}H NMR (500 MHz, $CDCl_3$, δ): 3.9–4.2 (polycaprolactone, 2H per repeating unit, –COOC*H*$_2$–), 2.1–2.4 (polycaprolactone, 2H per repeating unit, –CO=C*H*$_2$CH$_2$–), 1.5–1.8 (polycaprolactone, 2H per repeating unit, –COCH$_2$C*H*$_2$–, 2H per repeating unit, –COOCH$_2$C*H*$_2$–), 1.2–1.4 (polycaprolactone, 2H per repeating unit, –COCH$_2$CH$_2$C*H*$_2$–).

Synthesis of the PCL-*b*-PVBC Diblock Copolymer. The prepolymer, PCL-TEMPO, was added into a dry glass flask containing the vinylbenzyl chloride monomer. Twice freeze-pump-thaw cycles were preformed to remove residual solvent. The flask was sealed under vacuum and placed in an oil bath maintained at 120 °C. After 24 h, the polymerization was terminated by cooling the tube using ice water. After being dissolved in THF, the copolymer was precipitated in methanol and dried in an oven at 50 °C for 24 h to obtain a white powder (yield = 78%). ^{1}H NMR (500 MHz, $CDCl_3$, δ): 6.3–7.5 (aromatic protons: 5H × repeating units), 4.2–4.4 (–C*H*$_2$–N$_3$–), 3.9–4.2 (polycaprolactone, 2H per repeating unit, –COOC*H*$_2$–), 2.1–2.4 (polycaprolactone, 2H per repeating unit, –CO=C*H*$_2$CH$_2$–), 1.5–1.8 (polycaprolactone, 2H per repeating unit, –COCH$_2$C*H*$_2$–, 2H per repeating unit, –COOCH$_2$C*H*$_2$–, poly(styrene) backbone: 1H per repeating units), 1.2–1.4 (polycaprolactone, 2H per repeating unit, –COCH$_2$CH$_2$C*H*$_2$–), 1.0–1.8 ppm (poly(styrene) backbone: 2H × repeating units).

Synthesis of the PCL-*b*-PVBAz Diblock Copolymer. PCL-*b*-PVBC (2g, 0.067 mmol) was dissolved in 10 mL of DMF, and then NaN_3 (0.044g, 0.67 mmol) was added to the solution. The resulting solution was allowed to stir at 60 °C overnight and precipitated in excess methanol. After filtration, the polymer

was dried for 24 h in a vacuum oven at 25 °C (yield = 83.5 %). ^{1}H NMR (500 MHz, $CDCl_3$, δ): 6.3–7.5 (aromatic protons: 5H × repeating units), 4.0–4.2 (–C*H*$_2$–), 3.9–4.2 (polycaprolactone, 2H per repeating unit, –COOC*H*$_2$–), 2.1–2.4 (polycaprolactone, 2H per repeating unit, –CO=C*H*$_2$CH$_2$–), 1.5–1.8 (polycaprolactone, 2H per repeating unit, –COCH$_2$C*H*$_2$–, 2H per repeating unit, –COOCH$_2$C*H*$_2$–, poly(styrene) backbone: 1H per repeating units), 1.2–1.4 (polycaprolactone, 2H per repeating unit, –COCH$_2$CH$_2$C*H*$_2$–), 1.0–1.8 (poly(styrene) backbone: 3H × repeating units).

Modification of PCL-*b*-PVBC with Uracil via "Click" Reaction. PCL-*b*-PVBAz (0.5 g, 0.16 mmol azide group), N^1-(Prop-2-yne-1-yl)uracil (0.05g, 0.32 mmol), and 30 μL PMDETA were dissolved in 20 mL of DMF in a round-bottomed flask. The flask was subjected to twice-pump-thaw cycles under an argon atmosphere and then Cu(I)Br (30mg, 0.2 mmol) was quickly added. The solution was stirred at 60 °C until the IR absorption of azide at 2100 cm^{-1} disappeared completely. The mixture was diluted with DMF and passed through a short column of neutral aluminum oxide to remove copper salt. The solution was concentrated and precipitated into methanol to completely remove the excess N^1-(Prop-2-yne-1-yl)uracil. Finally, PCL-*b*-PVBU was further purified by washing several times with toluene (50 mL) in order to remove unpolymerized PCL-TEMPO (**Figure S6**). The product was dried until constant weight under vacuum (yield = 74%). ^{1}H NMR (500 MHz, d_6-DMSO, δ): 11.2–11.4 (1H, –CO–N*H*–CO–), 8.0–8.2 (1H, *H*C=C–), 7.56–7.8 (1H, –N–C*H*–), 5.2–5.6 (1H, –CO–C*H*–, 2H, –NC*H*$_2$–), 5.0–5.2 (1H, –C*H*$_2$–N–N–). M_n = 34332, M_w/M_n = 3.81 (GPC), M_n = 58553 (calculated from the ^{1}H NMR integration ratio of methylene protons at 5.0–5.2 ppm compared to –COOC*H*$_2$– at 3.9–4.2 ppm).

Complex preparation. Adenine was condensed with 1-bromohexadecane in hot DMF to afford the 9-hexadecyladenine [AC16] with 85 % yield after recrystallization from ethanol as previously reported.[S3] For preparing complexes from the copolymers and AC16, the copolymers and AC16 were dissolved separately in DMF to form clear solutions with the concentration of 5 wt %. The complexes were then prepared by mixing appropriate amounts of the two solutions; the solvent was then left to evaporate

slowly at 60 °C for 24 h. Finally, the samples were dried under vacuum at 120 °C for 48 h to remove the residual solvent. All the complexes with AC16 were further annealed at 160 °C for 48 h to enhance the long-range order of the copolymer domains.

Characterizations. FT-IR spectra were recorded using a Nicolet Avatar 320 FTIR Spectrometer; 32 scans were collected at a spectral resolution of 1 cm^{-1}. The conventional KBr disk method was employed: the sample was dissolved in DMF, then cast onto a KBr disk, and dried under vacuum at 120 °C. ^{1}H NMR spectra were recorded on a Varian Inova 500 MHz spectrometer equipped with a 9.395 T Bruker magnet and operated at 500 MHz. The weight-average molecular weight (M_w), number-average molecular weight (M_n), and PDI (M_w/M_n) were measured using a Waters 410 GPC system equipped with a refractive index detector and three Ultrastyragel columns (100, 500, and 1000 Å) connected in series. DMF was used as solvent and the system was operated at 25 °C and calibrated using polystyrene (PS) standards. Thermal analysis was carried out using a DSC instrument (TA Instruments Q-20) under an atmosphere of dry N_2. Samples were weighed (3-5 mg) and sealed in an aluminum pan, which was scanned from -90 to 250 °C at a scan rate of 20 °C/min. WAXD spectra of powders were obtained using a Rigaku D/max-2500 X-ray diffractometer. The radiation source was Ni-filtered Cu Kα radiation at a wavelength of 0.154 nm. The voltage and current were set at 30 kV and 20 Ma, respectively. Bragg's law ($\lambda = 2d \sin\theta$) was used to compute the *d*-spacing corresponding to the complementary behavior. Real-time small-angle X-ray scattering (SAXS) measurement was performed at BL01B SWLS beamline in the National Synchrotron Radiation Research Center (NSRRC), Taiwan. The incident X-ray beam was focused vertically by a mirror and monochromated to the energy of 10.5 keV by a germanium (111) double-crystal monochromator. The wavelength (λ) of the X-ray beam was 1.18095 Å. TEM images were taken for the samples with the phenyl segment stained with RuO_4, using a Hitachi H-7500 transmission electron microscope operated at an accelerating voltage of 100 kV. Ultrathin sections of the TEM samples (ca. 70 nm thickness) were prepared using a Leica Ultracut UCT microtome equipped with a diamond knife.

Table S1. Compositions, molecular weight distributions and thermal properties of PCL_n-*b*-$PVBU_m$ diblock copolymers

Entry	Compositions PCL-*b*-PVBU			Molecular weight distribution			Thermal properties			Morphology
	n[a]	m[a]	n/m[b]	M_w,[c] g/mol	M_n,[d] g/mol	M_w/M_n[d]	T_d,[e] °C 5 wt % loss	T_g,[f] °C PCL	T_g,[f] °C PVBU	
CU1	175	75	3.43	34332	58553	3.81	324	-60	168.4	Lamellar
CU2	175	105	1.62	49842	67700	4.3	316	-59.2	164.1	Lamellar
CU3	175	180	0.8	76914	84201	4.52	313	-60.92	170.4	HP cylinder
CU4	175	233	0.76	84810	96354	4.16	358	-59.6	178	sphere

[a] btained from kinetic studies of ^{1}H NMR spectra, where n and m are the number of repeat units for the PCL and PVBU blocks, respectively. **[b]** Obtained from integration of the signal at 4.14 and 4.4 ppm in the ^{1}H NMR spectra for the PCL and PVBC respectively. **[c]** Calculated from the ^{1}H NMR data using the expression $nM_{\varepsilon\text{-CL}}$ (114.1 g/mol) + mM_{VBU} (282.1 g/mol) + $M_{\text{initiator}}$ (291.4 g/mol). **[d]** Obtained from GPC trace (eluent: DMF; 0.6 mL/min; PS-standard calibration): M_n, number-average molecular mass with the highest RI intensity; PDI, molecular mass distribution. **[e]** Obtained from TGA thermograms recorded at a heating rate of 20 °C/min. **[f]** Obtained from second-run DSC thermograms recorded at a heating rate of 20 °C/min.

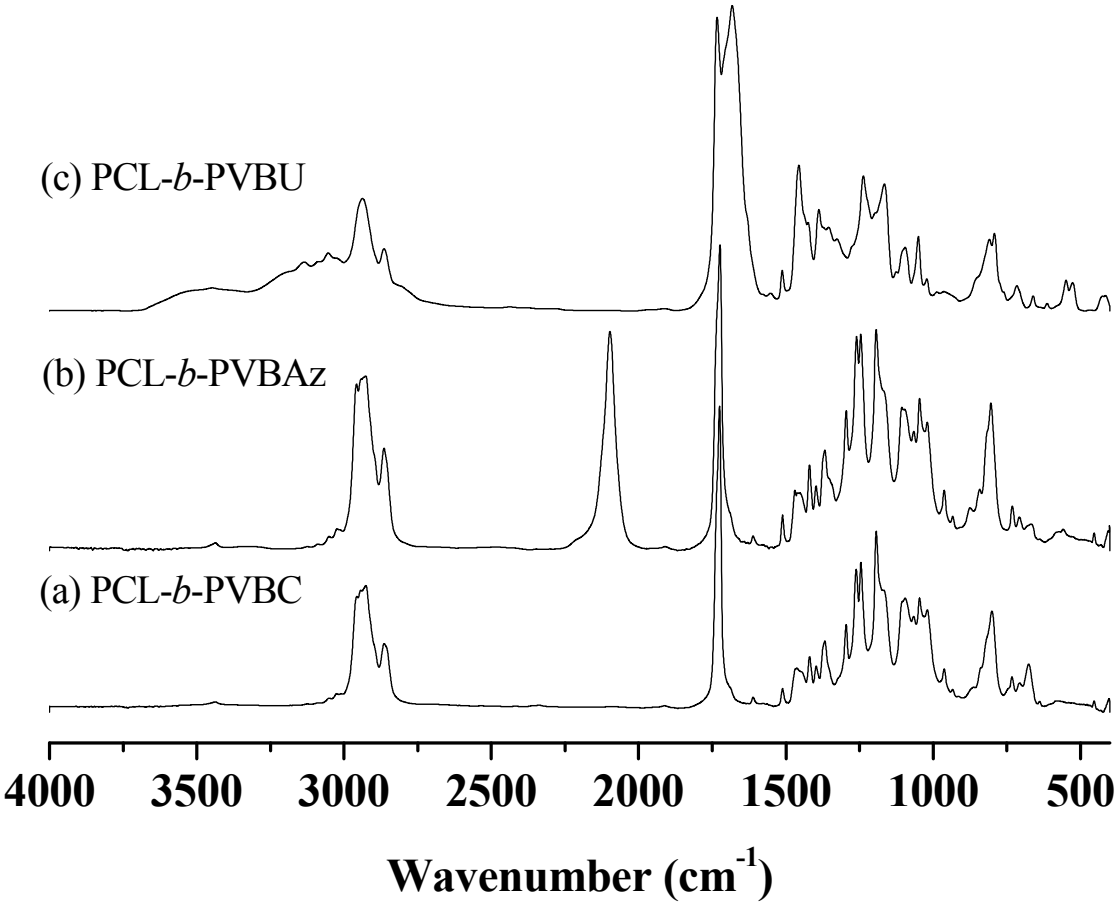


Figure S1. IR spectra of (a) PCL-*b*-PVBC, (b) PCL-*b*-PVBAz, and (c) PCL-*b*-PVBU.

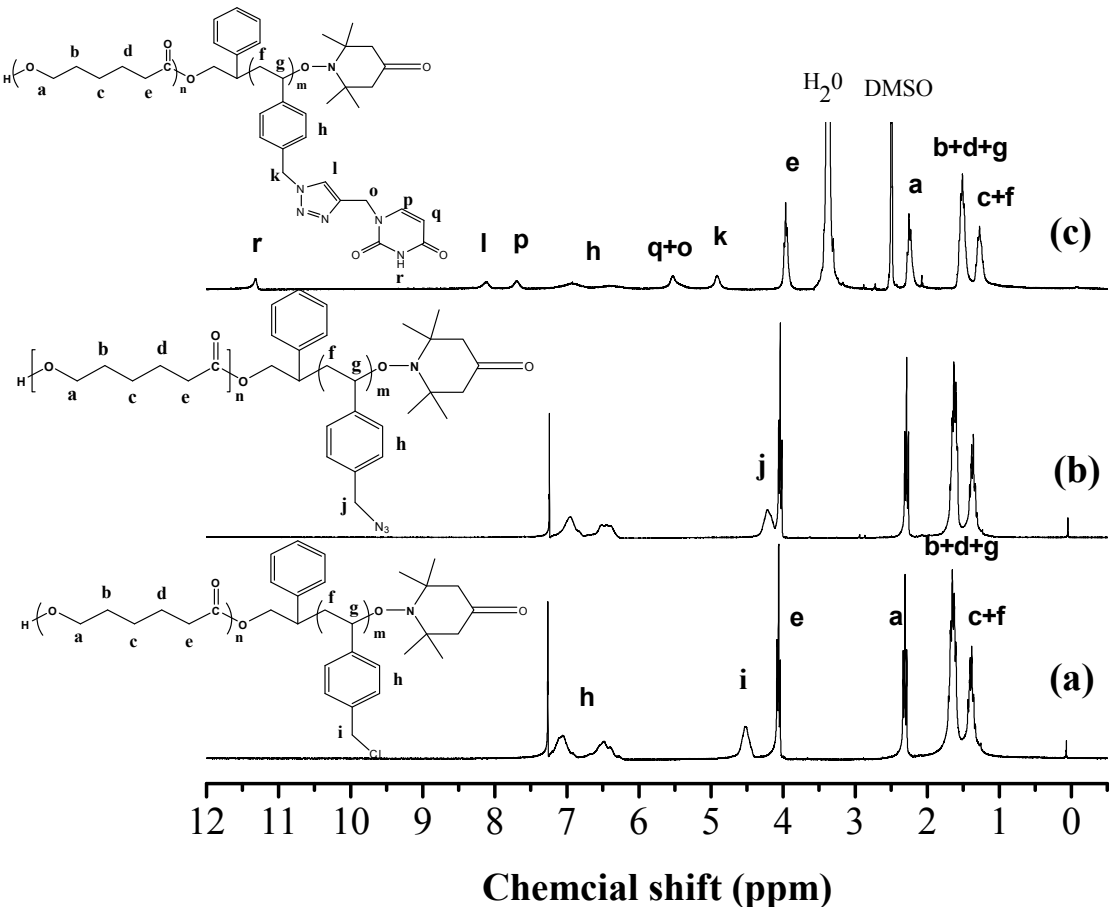


Figure S2. ^{1}H NMR spectra of (a) PCL-*b*-PVBC (b) PCL-*b*-PVBAz (c) after the "click"addition of N^{1}-(Prop-2-yne-1-yl)uracil.

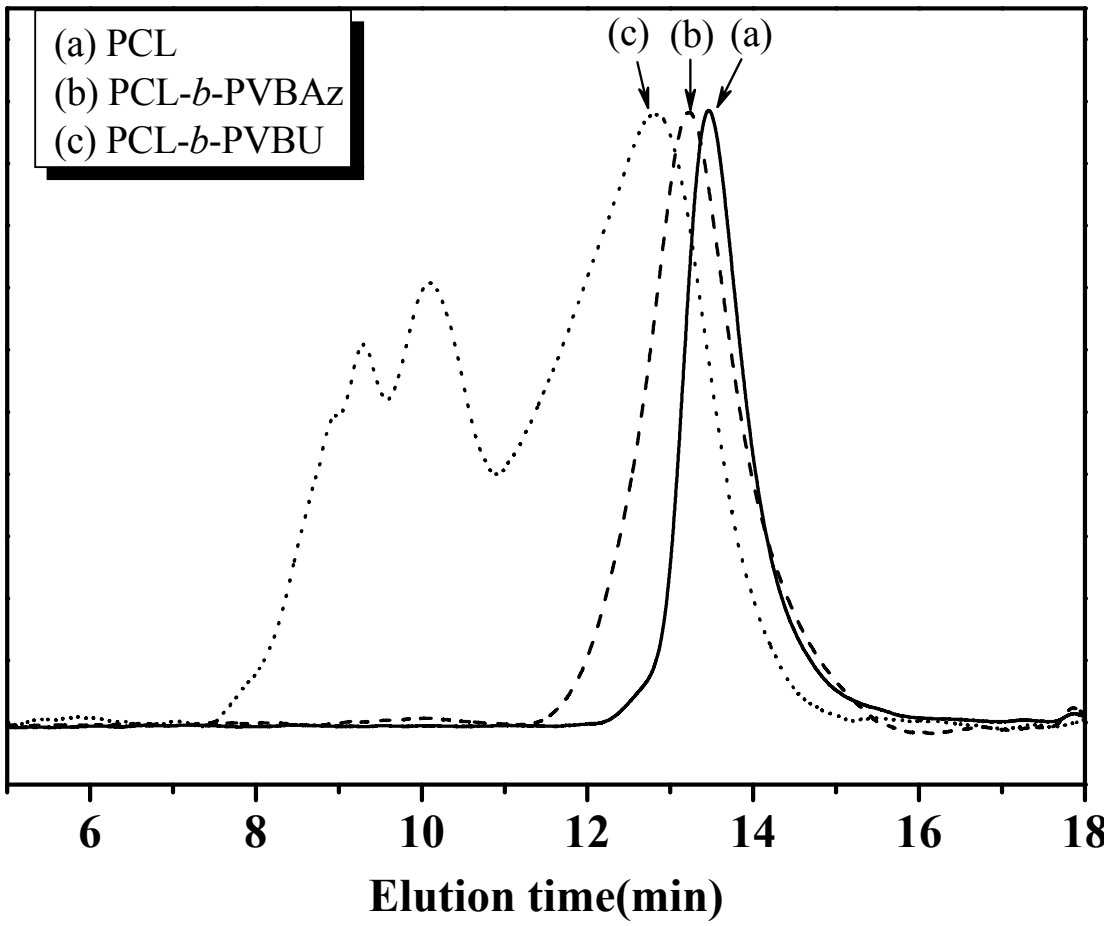


Figure S3. GPC traces of PCL, PCL-*b*-PVBAz, and PCL-*b*-PVBU in DMF. Ten microliters of the solution (~2.3g/dL) were injected.

GPC with RI detection was employed to examine the aggregation of PCL-b-PVBU and their precursors in DMF solution. Using GPC for supramolecular interaction can greatly facilitate the analysis of the relative size and stability of hydrogen-bonded supramolecular aggregates. **Figure S3** reveals that the molecular weight distribution for the uracil-grafted PCL-b-PVBU is increased relative to its individual components, indicating that aggregates of large size supramolecular polymers are formed through multiple hydrogen bonding interactions between base pair of the PVBU segments.

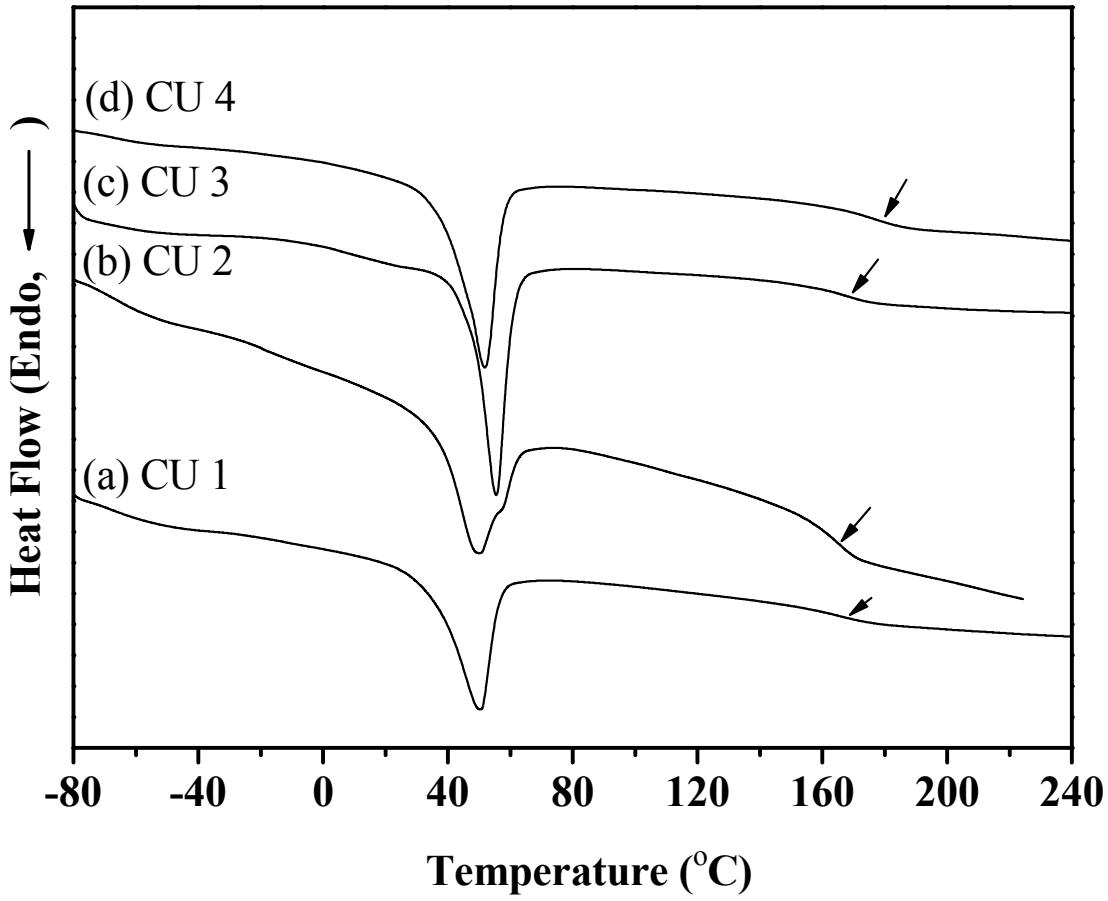


Figure S4. DSC traces of PCL-*b*-PVBU copolymers with various PVBU contents.

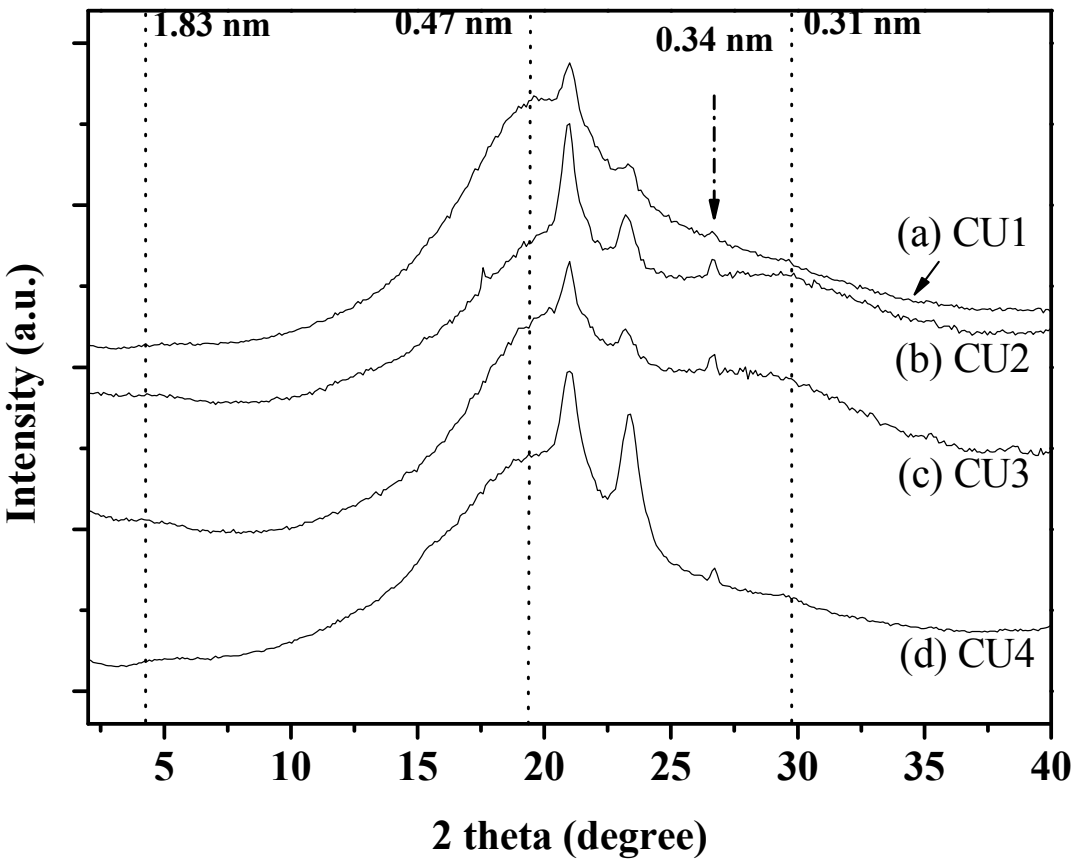


Figure S5. WXRD data for PCL-*b*-PVBU in various molecular weights: (a) CU1 (b) CU2 (c) CU3 (d) CU4.

Enzymatic degradation

The enzymatic degradation of PCL-*b*-PVBU films was carried out 37 °C in a 0.025 M, pH 7 phosphate buffer solution containing PS lipase. The PS lipase was purified before use. PCL-*b*-PVBU films with an initial weight ca. 10 mg were placed in a bottle containing the buffer solution. The composition of the solution in the bottle was 1 mg PS lipase per ml of phosphate buffer solution. After predetermined periods of time the samples was taken out by centrifugation from the buffer, then was washed with distilled water and dried in vacuum at room temperature.

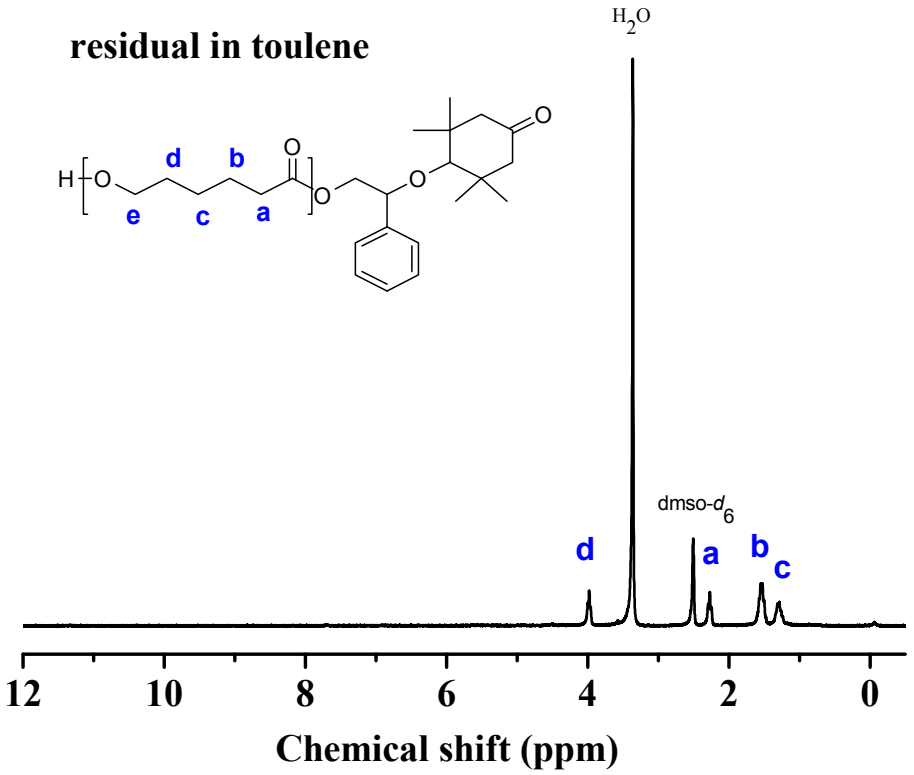


Figure S6. ^{1}H NMR spectra of residual unpolymerized PCL-TEMPO in d_6-DMSO at room temperature.

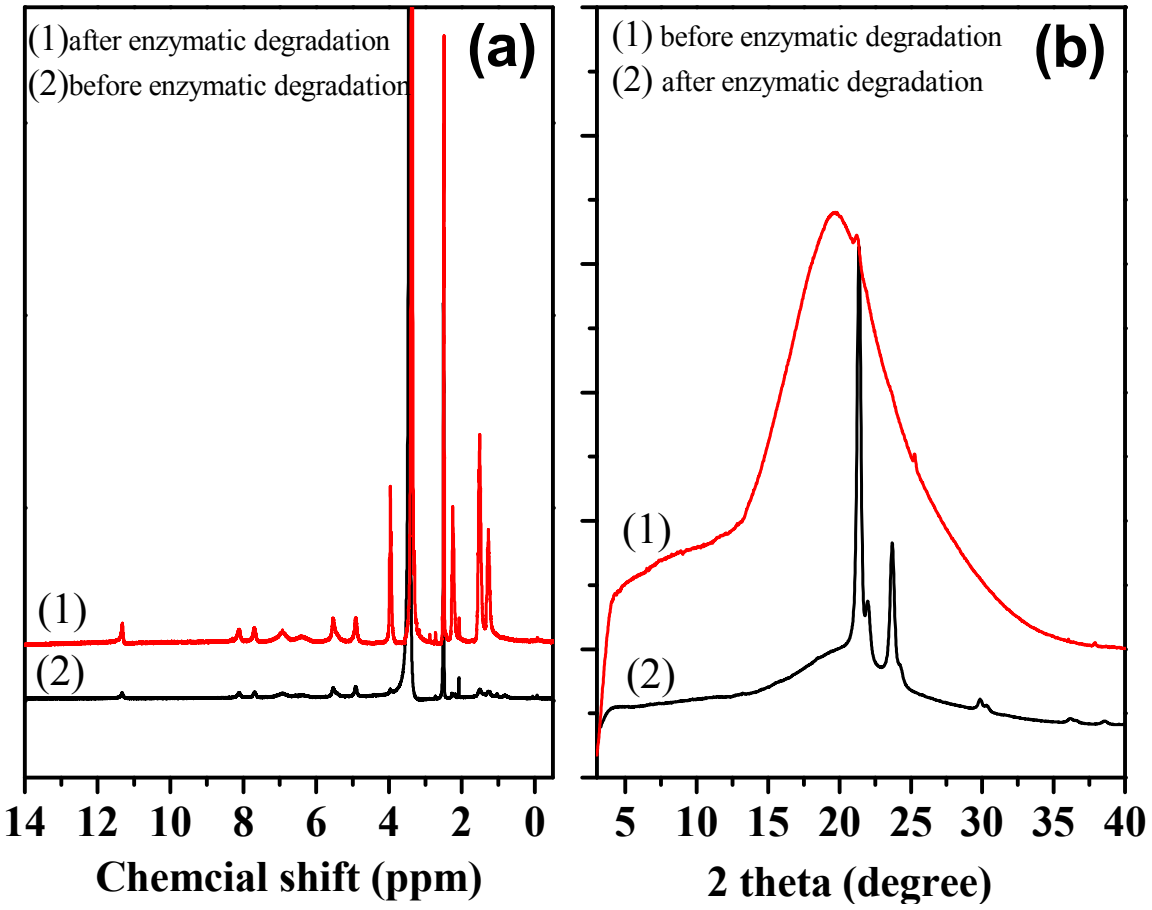


Figure S7. (a) ^{1}H NMR spectra of PCL-*b*-PVBU film before and after enzymatic degradation (3 day) at 37 °C. (b) WAXD patterns of PCL-*b*-PVBU film before and after enzymatic degradation (3day) at 37 °C.

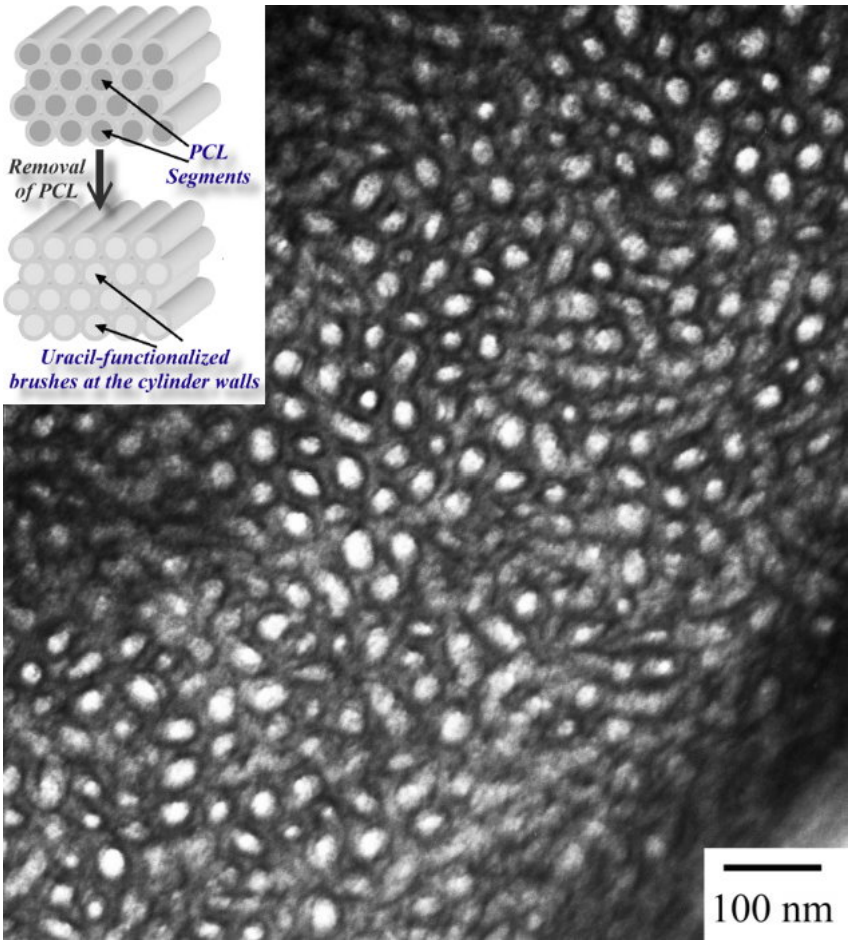


Figure S8. Cylinder structure for the enzymatic treatment and unstained sample, where the electron deficient air domain is white. It should be noted that if the PCL was not removed, the PVBU domain would always be dark in the images, with or without staining.

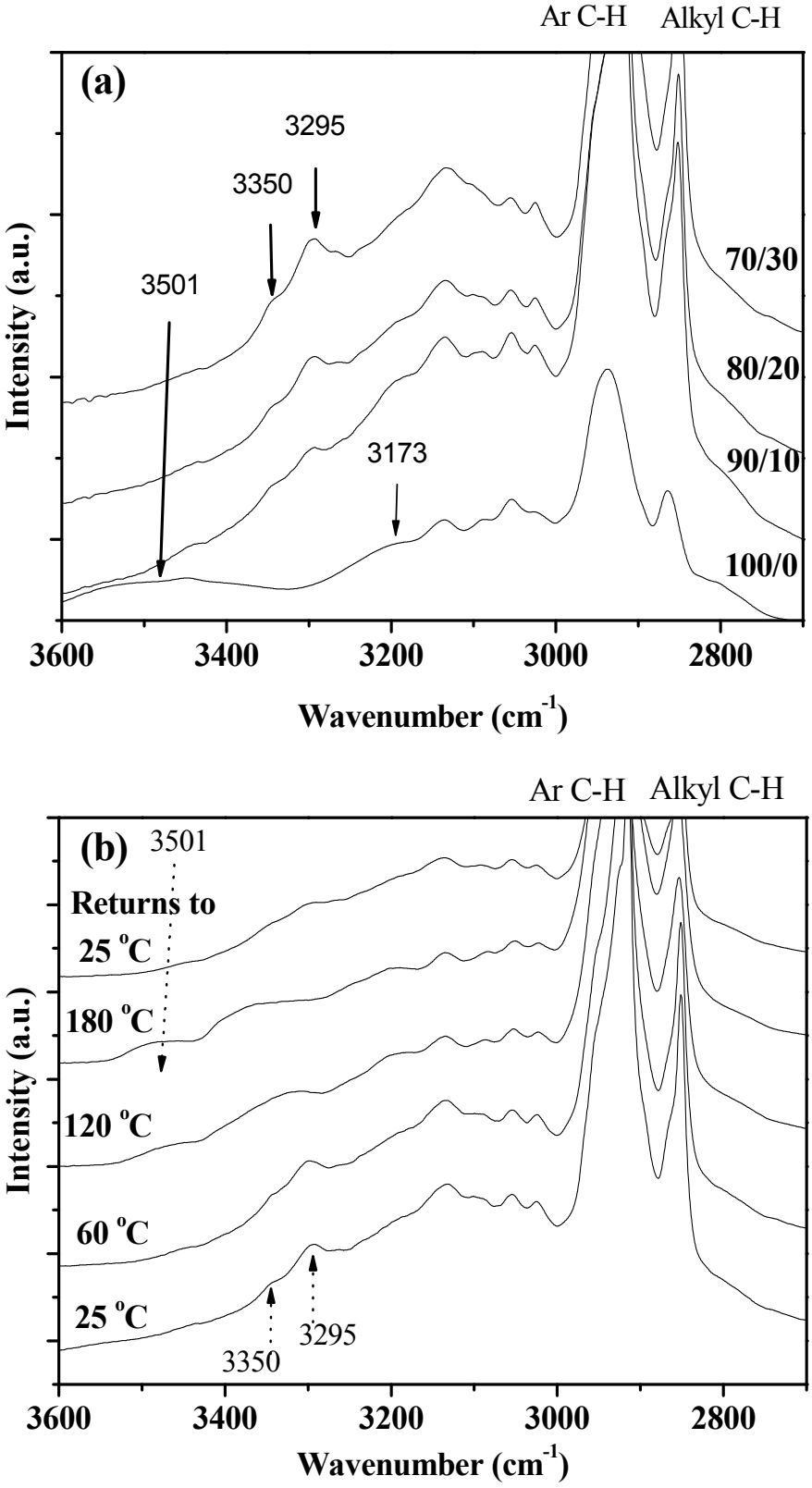


Figure S9. (a) FTIR spectra recorded at room temperature in the range of 2700-3600 cm^{-1} for PCL-*b*-PVBU in the bulk state in presence of various amounts of AC16. (b) Variable-temperture FTIR spectra of PCL-*b*-PVBU/AC16 (80/20) recorded in the range of 2700-3600cm^{-1}.

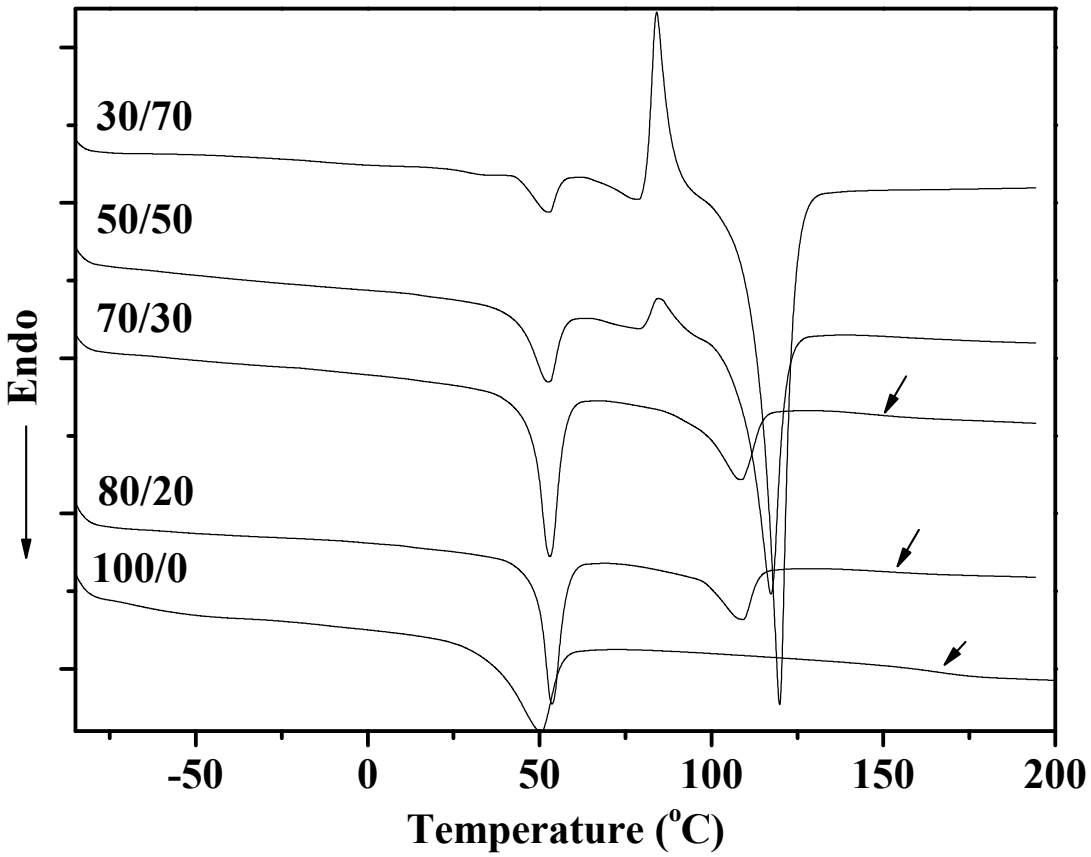


Figure S10. DSC thermograms of CU1/AC16 blends during heating.

References

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S3. Michas, J.; Paleos, C. M.; Skoulios, A.; Weber, P. *Mol Cryst Liq Cryst* **1995**, *239*, 245.