Supporting information

Tuning the LCST of poly(2-oxazoline)s by varying composition and molecular weight: Alternatives to poly(N isopropylacrylamide)?

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Contents

1. Experimental details

Materials

Solvents were purchased from Biosolve. Acetonitrile (size 3 Å) was dried over molecular sieves. 2-Ethyl-2-oxazoline (EtOx; Aldrich) was distilled over barium oxide (BaO) and stored under argon. Methyl tosylate (Aldrich) was distilled without drying agent and stored under argon. Butyronitrile, ethanolamine and zinc acetate were obtained from Aldrich and used without further purification.

Instrumentation

Polymerizations were carried out in an Emrys Liberator microwave synthesizer (Biotage) utilizing capped reaction vials. These vials were heated to 105 ºC, allowed to cool to room temperature and filled with argon prior to use. All microwave polymerizations were performed with temperature control.

Size exclusion chromatography (SEC) was performed on a Shimadzu system with a SCL-10A system controller, a LC-10AD pump, a RID-10A refractive index detector and PSS gram 30 (pore size 30 Å; bead size 10 µm; 100 – 10,000 Da) and PSS gram 1000 (pore size 1000 Å; bead size 10 µm; 1,000 – 1,000,000 Da) columns in series at 60 °C. A solution of *N,N*-dimethylacetamide (DMAc) containing 2.1 g LiCl/L was used as an eluent at a flow rate of 1 mL/min. The average molecular weights were calculated against poly(styrene) (PS) calibration standards.

The compositions of the polymers were determined using ^{1}H NMR spectroscopy. Spectra were recorded on a Varian Mercury 400 MHz spectrometer in $CDCl_3$. The residual protonated solvent signals were used as reference.

Thermal transitions were determined by differential scanning calorimetry (DSC) using a DSC 204 F1 Phoenix by Netzsch (calibrated using Netzsch standards). Each measurement consisted of two heating cycles to 200 °C under a nitrogen flow. In the first cycle, heating to 200 °C and subsequent cooling to –100 °C occurred at a rate of 40 °C. The second cycle was used to determine the transition temperatures and was performed at a heating rate of 20 °C/min. The glass transitions were determined from the mid-temperature of the transition.

The cloud points were determined by turbidity measurements in a Crystal 16^{TM} by Avantium Technologies. Four blocks of four parallel temperature controlled sample holders are connected to a Julabo FP40 cryostat allowing 16 simultaneous measurements. Turbidity of the solutions was measured by the transmission of a red light through the sample vial as a function of the temperature. Solutions of the polymers were prepared in deionized water (Laborpure, Behr Labor Technik) and were stirred at room temperature until all polymer was dissolved or dispersed. Two heating cycles were applied from 0 °C to 100 °C at 1 °C/min with hold steps of 5 min at the extreme temperatures. The cloud points are given as the 50% transmittance point during the second heating ramp.

Synthesis of 2-n-propyl-2-oxazoline monomer synthesis

The monomer 2-*n*-propyl-2-oxazoline (*n*PropOx) was synthesized as reported previously (R. Hoogenboom, M. W. M. Fijten, H. M. L. Thijs, B. M. van Lankvelt, U. S. Schubert, *Design. Mon. Polym.* **2005**, *8*, 659-671): Butyronitrile (1 equivalent) and ethanolamine (1.1 equivalents) were mixed together with $Zn(OAc)_2$ as catalyst (0.02 equivalents). The resulting yellow suspension was stirred at 130 ºC for 16 hours. After cooling to ambient temperature, CH_2Cl_2 was added and the resulting mixture was washed with water (2 times) and brine (1 time). The resulting organic layer was dried with magnesium sulfate, filtered and the solvent was evaporated under reduced pressure. The final products were obtained as colorless liquid after vacuum distillation.

*n*PropOx: ^{1}H-NMR ($CDCl_3$): δ 4.15 (d, 9.5 Hz, 2H, OCH_2), 3.75 (d, 9.5 Hz, 2H, NCH_2), 2.18 (t, 8.1 Hz, 2H, CCH_2), 1.59 (sextet, 7.4 Hz, 2H, $CCH_2C\underline{H_2}$), 0.90 (t, 7.4 Hz, 2H, CH_3).

General polymerization procedure

For each polymerization, the polymerization mixture was automatically prepared using an automated synthesis robot (R. Hoogenboom, F. Wiesbrock, M. A. M. Leenen, M. A. R. Meier, U. S. Schubert, *J. Comb. Chem* **2005**, *7*, 10). The polymerization mixtures contain the monomers EtOx and *n*PropOx in the desired ratio with a total [M] of 4 M, acetonitrile and methyl tosylate (different amounts to vary the [M]/[I] ratio) as initiator. The polymerization mixtures were heated for 8.33, 16.66 or 25 minutes in the microwave synthesizer at 140 ºC for the [M]/[I] ratios of 50, 100 and 150, respectively. After microwave heating, the polymerization mixture was cooled to 38 ºC and quenched by the addition of water. The polymers were purified by drying overnight under reduced pressure to remove the solvent and minor amounts of residual monomer. The polymers were characterized by ^{1}H NMR spectroscopy, SEC and turbidimetry. Selected polymers were also analyzed by DSC.

2. Analytical data for the PEtOx and P*n*PropOx homopolymers

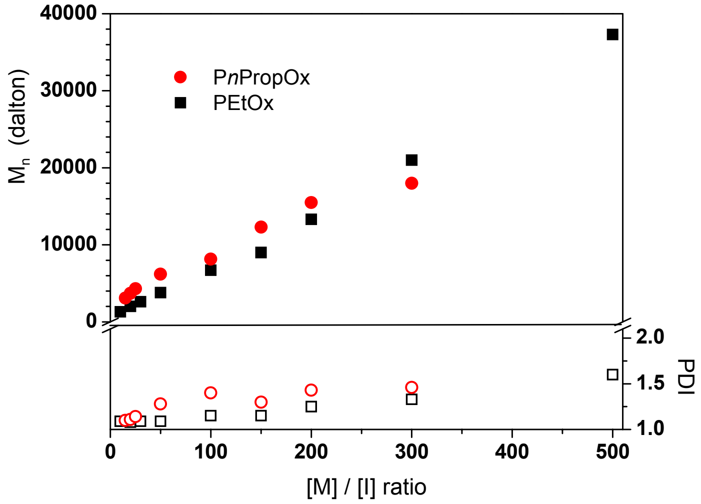

Figure S1. Molecular weight and polydispersity index of the PEtOx and P*n*PropOx homopolymers as function of the theoretical monomer to initiator ([M]/[I]) ratio.

Table S1. Properties of the PEtOx and P*n*PropOx homopolymers.

Polymer	$M_{n,SEC}$[a]	PDI_{SEC}[a]	Cloud point[b]
$PEtOx_{10}$	1,300	1.09	–
$PEtOx_{20}$	2,000	1.08	–
$PEtOx_{30}$	2,600	1.09	–
$PEtOx_{50}$	3,800	1.09	–
$PEtOx_{100}$	6,700	1.15	90.6
$PEtOx_{150}$	9,000	1.15	85.3
$PEtOx_{200}$	13,300	1.25	78.3
$PEtOx_{300}$	21,000	1.33	73.5
$PEtOx_{500}$	37,300	1.6	69.3
$PnPropOx_{15}$	3,100	1.1	42.9
$PnPropOx_{20}$	3,700	1.11	39.0
$PnPropOx_{25}$	4,300	1.14	37.5
$PnPropOx_{50}$	6,200	1.28	30.3
$PnPropOx_{100}$	8,140	1.4	29.6
$PnPropOx_{150}$	12,300	1.3	25.5
$PnPropOx_{200}$	15,500	1.43	24.1
$PnPropOx_{300}$	18,000	1.46	22.5

[a] SEC with *N*,*N*-dimethylacetamide containing 2.1 g LiCl/L as eluent. PS standards.

[b] Cloud points were extracted from the 50% transmittance point in the second heating run at 5 mg/mL.

3. Determination of reactivity ratios for the statistical EtOx-*n*PropOx copolymerizations

To determine the reactivity ratio of the statistical EtOx-*n*PropOx copolymerizations, kinetic studies were performed for copolymerizations at different monomer ratios, namely EtOx:*n*PropOx = 80:20, 60:40, 40: 60 and 20:80 (Figure S2). From these kinetic plots, the polymerization rates were determined for both monomers, which were used to calculate the polymer composition at 30% monomer conversion (Figure S3). The reactivity ratios were determined from these polymer compositions by non-linear fitting of the data in Figure S3.

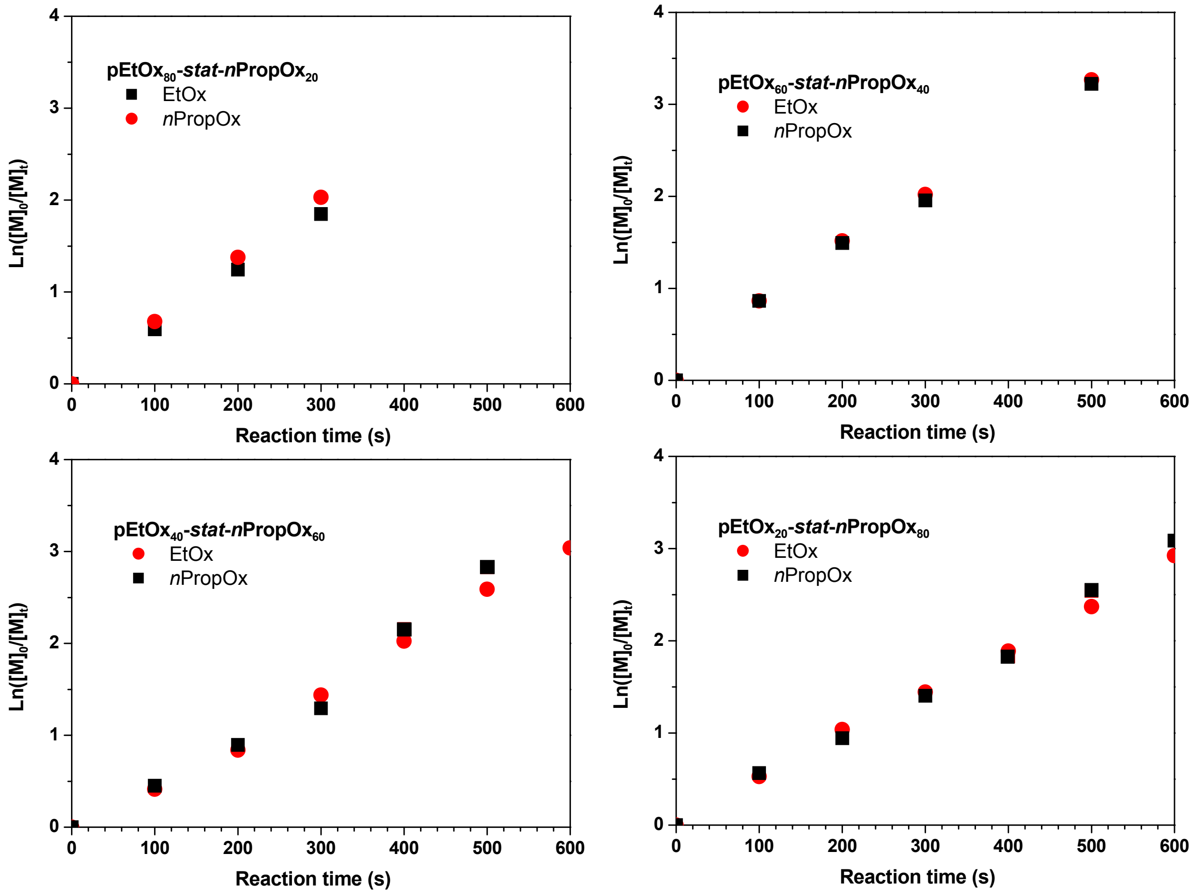

Figure S2. Kinetic plots for the statistical copolymerizations of EtOx and *n*PropOx.

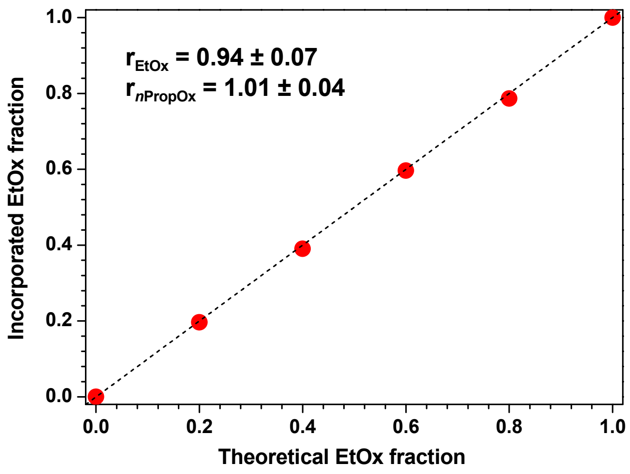

Figure S3. Incorporated *versus* theoretical EtOx fraction and corresponding reactivity ratios for the statistical EtOx-*n*Propox copolymerizations.

4. Analytical data for the copolymers with [M]/[I] = 50

Table S2. Properties of the EtOx-P*n*PropOx statistical copolymers with [M]/[I] = 50.

Polymer	$M_{n,SEC}$[a]	PDI_{SEC}[a]	Cloud point[b]
$PEtOx_{50}$	3,300	1.14	–
$PEtOx_{45}$-*stat*-$PropOx_{5}$	3,500	1.15	–
$PEtOx_{40}$-*stat*-$PropOx_{10}$	3,500	1.36	97.3
$PEtOx_{35}$-*stat*-$PropOx_{15}$	3,700	1.36	82.0
$PEtOx_{30}$-*stat*-$PropOx_{20}$	3,700	1.34	72.2
$PEtOx_{25}$-*stat*-$PropOx_{25}$	4,000	1.36	59.8
$PEtOx_{20}$-*stat*-$PropOx_{30}$	5,400	1.35	51.3
$PEtOx_{15}$-*stat*-$PropOx_{35}$	3,900	1.35	45.8
$PEtOx_{10}$-*stat*-$PropOx_{40}$	3,800	1.34	40.0
$PEtOx_{5}$-*stat*-$PropOx_{45}$	4,000	1.34	34.2
$PropOx_{50}$	4,200	1.32	29.6

[a] SEC with *N,N*-dimethylacetamide containing 2.1 g LiCl/L as eluent. PS standards.

[b] Cloud points were extracted from the 50% transmittance point in the second heating run at 5 mg/mL.

5. Analytical data for the copolymers with [M]/[I] = 100

Table S3. Properties of the EtOx-P*n*PropOx statistical copolymers with [M]/[I] = 100.

Polymer	$M_{n,SEC}$[a]	PDI_{SEC}[a]	Cloud point[b]
$PEtOx_{100}$	15,300	1.21	94.1
$PEtOx_{90}$-*stat*-$PropOx_{10}$	15,200	1.22	81.6
$PEtOx_{80}$-*stat*-$PropOx_{20}$	13,600	1.21	75.5
$PEtOx_{70}$-*stat*-$PropOx_{30}$	12,600	1.26	64.8
$PEtOx_{60}$-*stat*-$PropOx_{40}$	13,000	1.25	55.9
$PEtOx_{50}$-*stat*-$PropOx_{50}$	10,700	1.28	51.1
$PEtOx_{40}$-*stat*-$PropOx_{60}$	10,200	1.37	44.2
$PEtOx_{30}$-*stat*-$PropOx_{70}$	9,700	1.36	40.0
$PEtOx_{20}$-*stat*-$PropOx_{80}$	9,600	1.37	34.8
$PEtOx_{10}$-*stat*-$PropOx_{90}$	7,800	1.48	31.2
$PropOx_{100}$	8,140	1.4	28.0

[a] SEC with *N,N*-dimethylacetamide containing 2.1 g LiCl/L as eluent. PS standards.

[b] Cloud points were extracted from the 50% transmittance point in the second heating run at 5 mg/mL.

6. Analytical data for the copolymers with [M]/[I] = 100

Table S4. Properties of the EtOx-P*n*PropOx statistical copolymers with [M]/[I] = 150.

Polymer	$M_{n,SEC}$[a]	PDI_{SEC}[a]	Cloud point[b]
$PEtOx_{150}$	17,700	1.47	83.9
$PEtOx_{135}$-*stat*-$PropOx_{15}$	17,000	1.44	71.5
$PEtOx_{120}$-*stat*-$PropOx_{30}$	17,700	1.4	63.1
$PEtOx_{105}$-*stat*-$PropOx_{45}$	17,200	1.49	53.7
$PEtOx_{90}$-*stat*-$PropOx_{60}$	17,900	1.38	49.2
$PEtOx_{75}$-*stat*-$PropOx_{75}$	17,600	1.37	42.6
$PEtOx_{60}$-*stat*-$PropOx_{90}$	18,600	1.35	37.3
$PEtOx_{45}$-*stat*-$PropOx_{105}$	17,900	1.33	34.1
$PEtOx_{30}$-*stat*-$PropOx_{120}$	18,500	1.34	29.1
$PEtOx_{15}$-*stat*-$PropOx_{135}$	18,600	1.35	24.5
$PropOx_{150}$	17,200	1.45	24.1

[a] SEC with *N,N*-dimethylacetamide containing 2.1 g LiCl/L as eluent. PS standards.

[b] Cloud points were extracted from the 50% transmittance point in the second heating run at 5 mg/mL.

7. Graphical representation of the composition and molecular weight data for the copolymers with [M]/[I] of 50, 100 and 150

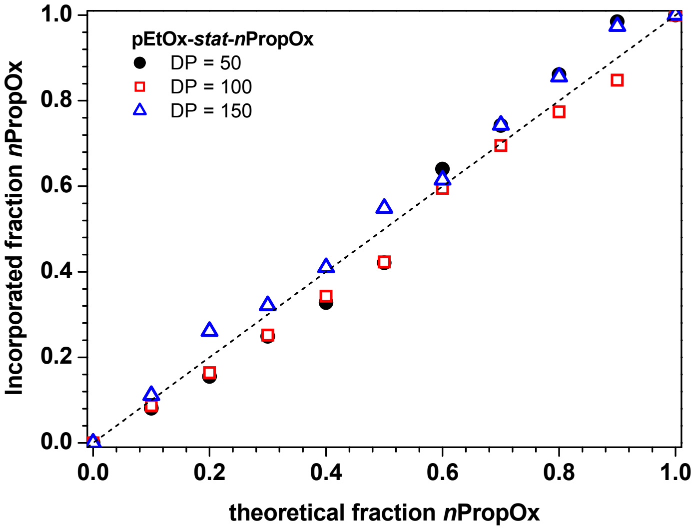

Figure S4. Incorporated mol-fraction of *n*PropOx (determined by ^{1}H NMR spectroscopy) *versus* the theoretical mol-fraction of *n*PropOx for the statistical copolymers of EtOx and *n*Propox with [M]/[I] of 50, 100 and 150 demonstrating that the copolymers have the desired compositions.

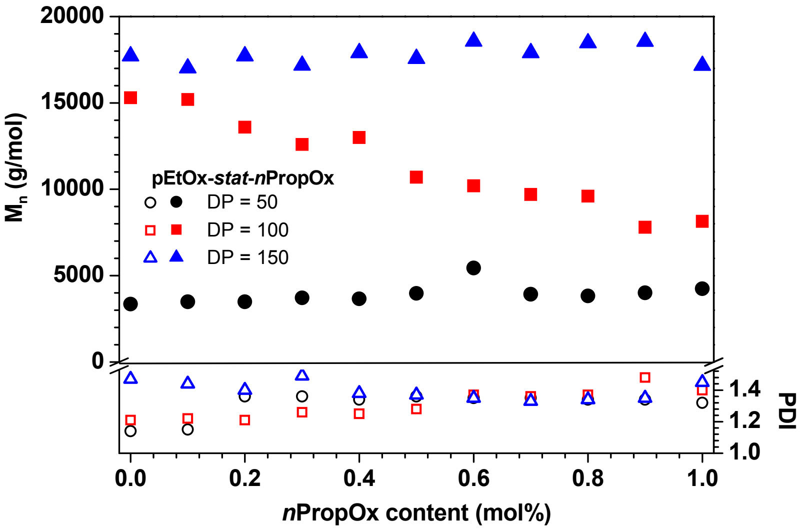

Figure S5. M$_n$ and PDI as function of mol-fraction *n*PropOx for the statistical copolymers of EtOx and *n*Propox with [M]/[I] of 50, 100 and 150. The decreasing M$_n$ for the [M]/[I] = 100 series is due to the steadily increasing PDI with incorporation of *n*PropOx.

8. Residuals for the empirical cloud point model

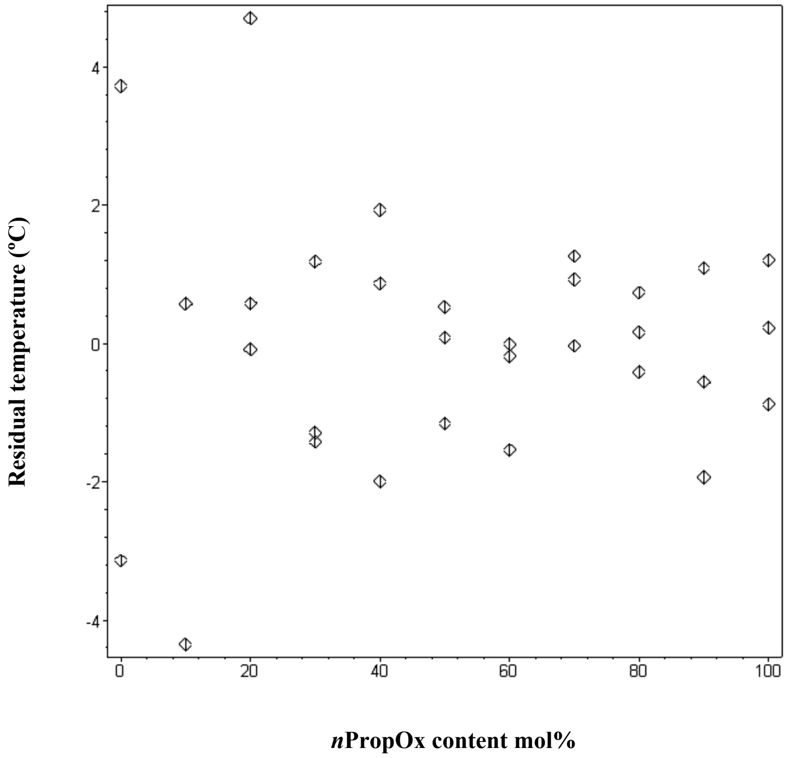

Figure S6. Residuals for the empirical model that was used to fit the cloud points (5 mg/mL) of the EtOx-*n*PropOx statistical copolymers with different [M]/[I] ratios demonstrating that most of the predicted values are within 2 ºC of the measured data.