

Supporting information for:

**Poly(2-isopropenyl-2-oxazoline) as versatile platform towards
thermoreponsive polymers**

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EXPERIMENTAL

1. Materials

2-Isopropenyl-2-oxazoline (Sigma-Aldrich, 98%, iPOx) was distilled over CaH₂ under reduce pressure before use. Tetrahydrofuran (Sigma-Aldrich, THF) was freshly distilled over Na/benzophenone under Ar flow before use. *n*-Butyllithium solution 2.5 M in hexanes (Sigma-Aldrich, *n*-BuLi) was used as received. Acetic acid (99.5%, AAc), propionic acid (99%, APr), butyric acid (99%, ABu), and isobutyric acid (99%, AiBu) purchased from TCI Europe were used as such. The deuterated N, N'-dimethylformamide (Isotope Europe, 99%, DMF-d₇) was used for the kinetics of polymer modifications. For all other

reactions N, N'-dimethylformamide (Acros Organics, DMF) 99.8%, extra dry over molecular sieve was used.

2. Synthesis

2.1. Living anionic polymerization of poly(2-isopropenyl-2-oxazoline) (PiPOx, small batch run4).

In a typical run, the anionic polymerization of iPOx and all manipulations were performed in clean/dry glassware and under Ar flow. A 1.6 M solution of 0.5 g (4.77 mmol) of iPOx in 2.5 mL of THF is cooled down to $-20\text{ }^{\circ}\text{C}$. Then 12.7 μL of n-BuLi (0.0318 mmol) in hexanes is injected into the reaction flask. The polymerization was kept for 10 min at this temperature and terminated with 1 mL of methanol. The reaction mixture is allowed to warm up to room temperature, then diluted with 1 mL of methanol, precipitated from diethyl ether twice, and dried in a vacuum oven at $55\text{ }^{\circ}\text{C}$. The PiPOx polymer is obtained with a 95% yield as a fine white powder. The absolute molar mass of the analyzed polymer was determined by SEC-LS (**Table S1** and **Fig. S1**). The specific refractive index increment value was determined ($dn/dc = 0.0902\text{ mL/g}$).

2.2. Living anionic polymerization of poly(2-isopropenyl-2-oxazoline) (PiPOx large batch run 6).

The anionic polymerization of iPOx and all manipulations were carried out as previous described for small batch runs. A 1.6 M solution of 6.36 g (57.2 mmol) of iPOx in 30 mL of THF is cooled down to $-40\text{ }^{\circ}\text{C}$. Then 0.15 mL of n-BuLi (0.37 mmol) in hexanes is injected into the reaction flask. The polymerization was kept for 10 min at this temperature and terminated with 6 mL of methanol. The reaction mixture is allowed to warm up to room temperature, then diluted with 15 mL of methanol, precipitated from diethyl ether twice, and dried in a vacuum oven at $55\text{ }^{\circ}\text{C}$. The PiPOx polymer is obtained with a 93% yield as a fine white powder. The absolute molar mass of the analyzed polymer was determined by SEC-LS and the chemical structure was confirmed by ^1H NMR spectroscopy (**Table S1** and **Fig. S2**).

2.3. The kinetics for the chemical modification of PiPOx with AAc, APr, ABu and AiBu acids.

In a typical run, a 0.5 M stock solution of 0.453 g (4.08 mmol of 2-oxazoline units) of PiPOx in 8.15 mL of DMF-d₇ and 8.16 mmol of acid is prepared under argon. During all chemical modifications the molar feed ratio of PiPOx:Acid = 1:2 is used. Then the resulting stock solution is divided between multiple vials containing ~0.6 mL each, which are sealed-off and then put to react on drysyn heating-block at 140 °C. The vials are removed one by one and cooled swiftly after 15, 22.5, 30, 45, 60, 90, 120, 150, 195, 260 and 360 min for acetic acid; 10, 20, 30, 40, 60, 75, 90, 105, 120, 150, 180, 240, 300 and 360 min for propionic acid; and after 5, 10, 15, 20, 25, 30, 35, 40, 60, 90, 120, 150, 210 and 300 min for butyric and isobutyric acids. Then the cooled solutions are carefully placed in the NMR tubes. The fully modified homopolymers are obtained after 6 hours. SEC samples are prepared by diluting 0.1 mL of the reaction mixtures with 0.9 mL of DMA (**Figs. S3-S5**).

2.4. The synthesis of the partially modified thermoresponsive polymers (PiPOx-Acids).

The thermoresponsive structures described in **Scheme 1** are prepared following the protocol described for the kinetics, except that this time regular hydrogenated DMF is used. In a typical run, a stock solution is prepared from 0.375 g (3.378 mmol) of PiPOx and 0.405 g (6.75 mmol) of acetic acid in 6.36 mL of DMF, then divided between multiple vials which are sealed-off and put to react. To obtain the thermoresponsive compositions of interest for each polymer series the vials are removed and cooled swiftly after 45, 90, and 360 min for the acetic acid; 5, 10, 15, 20, 25, 30, 40, 50, 65, 90, 120, 180, and 360 min for propionic acid, 5, 7.5, 10, 13, 15, 17.5, 20, 22.5, 25, 30, 35, 40, and 45 for butyric acid, while for isobutyric acid the vials were removed after: 5, 7.5, 10, 13, 15, 20, 22.5, 25, 30, 35, 40, and 45. The cooled solutions are diluted with chloroform, precipitated two times in cold diethylether, and dried at 55 °C. All samples, including the samples that are cloudy at room temperature, were left to slowly dissolve in distilled water in an ice-bath (0-3 °C) followed by freeze-drying. All polymers are obtained as fluffy white solids with yields between 90-95%. The compositions are estimated from ¹H-NMR spectroscopy using chloroform-d₁ as solvent (**Table S2** and **Fig. S6**). The cloud points are measured by turbidimetry, using 10 mg polymer/ mL of distilled water and 0.5 °C/min heating rate (**Table S2** and **Fig. S7**).

3. Characterization

The SEC-LS measurements are performed on a 3-angle static light scattering (MALS) detector, i.e. miniDAWN TREOS, from Wyatt Technology. The detector is coupled on-line to an Agilent 1260 infinity HPLC system (vide DMA-SEC) and used to determine absolute molar mass of the analyzed polymer samples. The measurements are performed at ambient temperature. The refractive index (RI) increment (dn/dc) values are determined via online size-exclusion chromatography (SEC) equipped with an RI detector, which measures the RI increase for a 1-10 mg/mL concentration series of the mentioned polymer. The LS results are further analyzed with the provided Astra 7 software, also designed by Wyatt Technology.

Size-exclusion chromatography (SEC) is performed on an Agilent 1260-series HPLC system equipped with a 1260 online degasser, a 1260 ISO-pump, a 1260 automatic liquid sampler (ALS), a thermostatted column compartment (TCC) at 50°C equipped with two PL gel 5 μ m mixed-D columns and a precolumn in series, a 1260 diode array detector (DAD) and a 1260 refractive index detector (RID). The used eluent is DMAc containing 50 mM of LiCl at a flow rate of 0.5 mL/min. The spectra are analyzed using the Agilent Chemstation software with the GPC add on. Molar mass values and \bar{M}_w values are calculated against PMMA standards from PSS.

The cloud point temperatures (T_{CP} 's) are measured on a Crystal 16™ parallel crystallizer turbidimeter developed by Avantium Technologies connected to a recirculation chiller and dry compressed air. Polymer solutions (10 mg/mL) in distilled water are heated from 2 up to 5 °C above the cloud point with a heating rate of 0.5 °C/min followed by cooling to 2 °C at a cooling rate of 0.5 °C/min. This cycle was repeated two times. The T_{CP} 's are reported as the 50% transmittance temperature in the 2nd heating run.

¹H NMR spectra were recorded at 25 °C on a Bruker instrument operating at 400 MHz. Chemical shifts (δ) are referenced to CDCl₃ (δ 7.26 ppm).

Differential scanning calorimetry (DSC) was performed on a Mettler-Toledo DSC1 Module in a nitrogen atmosphere with a heating/cooling rate of 5 °C/min. Indium was used as a standard for temperature and enthalpy calibrations. For the determination of the glass transition temperature (T_g), values were taken from the second heating run.

RESULTS AND DISCUSSION

Table S1. Living anionic polymerization runs of iPOx in THF in the presence of n-BuLi

Run	C _{iPOx} (mol/L)	^a M/I	T (°C)	^b Yield (%)	M _{n theo} (kDa)	^c M _{n exp} (kDa)	^c D	^d Tacticity i : h : s	^e T _g (°C)
1-small batch	3	150	-78	50	16.8	40.8	1.73	2:30:68	172.9
2-small batch	1.6	150	-78	67	16.8	25.1	1.43	2:28:70	169.8
3-small batch	1.6	150	-40	92	16.8	24.1	1.22	3:33:64	167.5
4-small batch	1.6	150	-20	95	16.8	17.5	1.12	4:31:65	168.2
5-large batch	1.6	150	-20	95	16.8	15.4	1.34	5:41:54	166.5
6-large batch	1.6	150	-40	93	16.8	17.1	1.22	4:30:66	167.9

^aMonomer to initiator ratio in the feed; ^bThe yield was calculated gravimetrically based on the precipitated polymer; ^cDetermined by SEC-LS in DMAc; ^dTacticity ratio isotactic (i):heterotactic (h):syndiotactic (s) determined from ¹H-NMR spectra based on α-methyl protons; ^eSecond heating run using a 5 °C/min heating rate.

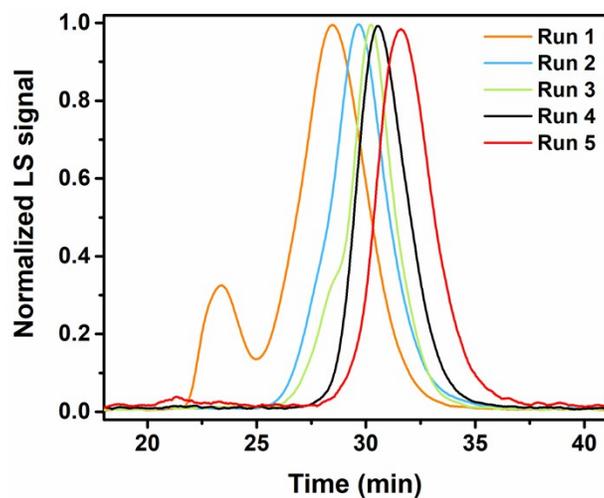


Fig S1. SEC-LS traces of PiPOx polymers obtained via anionic polymerization initiated with *n*-BuLi, runs 1-5.

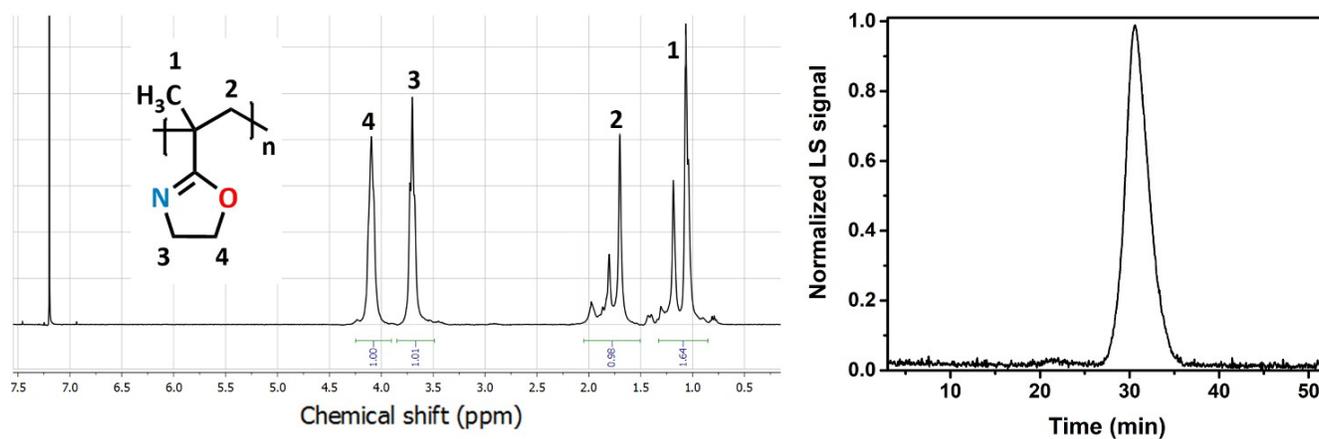


Figure S2. ^1H NMR spectrum in chloroform- d_1 (left) and SEC-LS trace of PiPOx polymer obtained via anionic polymerization (right) in run 6.

1. Kinetics for the chemical modification of PiPOx

If we assume that the polymer analogous reaction is a second order reaction (see Scheme 1.I.) with excess of one reactant, then the rate of PiPOx-Acid formation can be expressed by relation (S1).

$$\frac{1}{C_{Acid}^0 - C_{PiPOx}^0} \cdot \ln \frac{C_{PiPOx}^0 \cdot (C_{Acid}^0 - C_{PiPOx-Acid}^t)}{C_{Acid}^0 \cdot (C_{PiPOx}^0 - C_{PiPOx-Acid}^t)} = kt, \quad (S1)$$

Where C_{Acid}^0 is the initial concentration of acid (AAc, APr. ABu or AiBu), C_{PiPOx}^0 is the initial concentration of PiPOx, and $C_{PiPOx-Acid}^t$ is the concentration of PiPOx-Acid at time t.

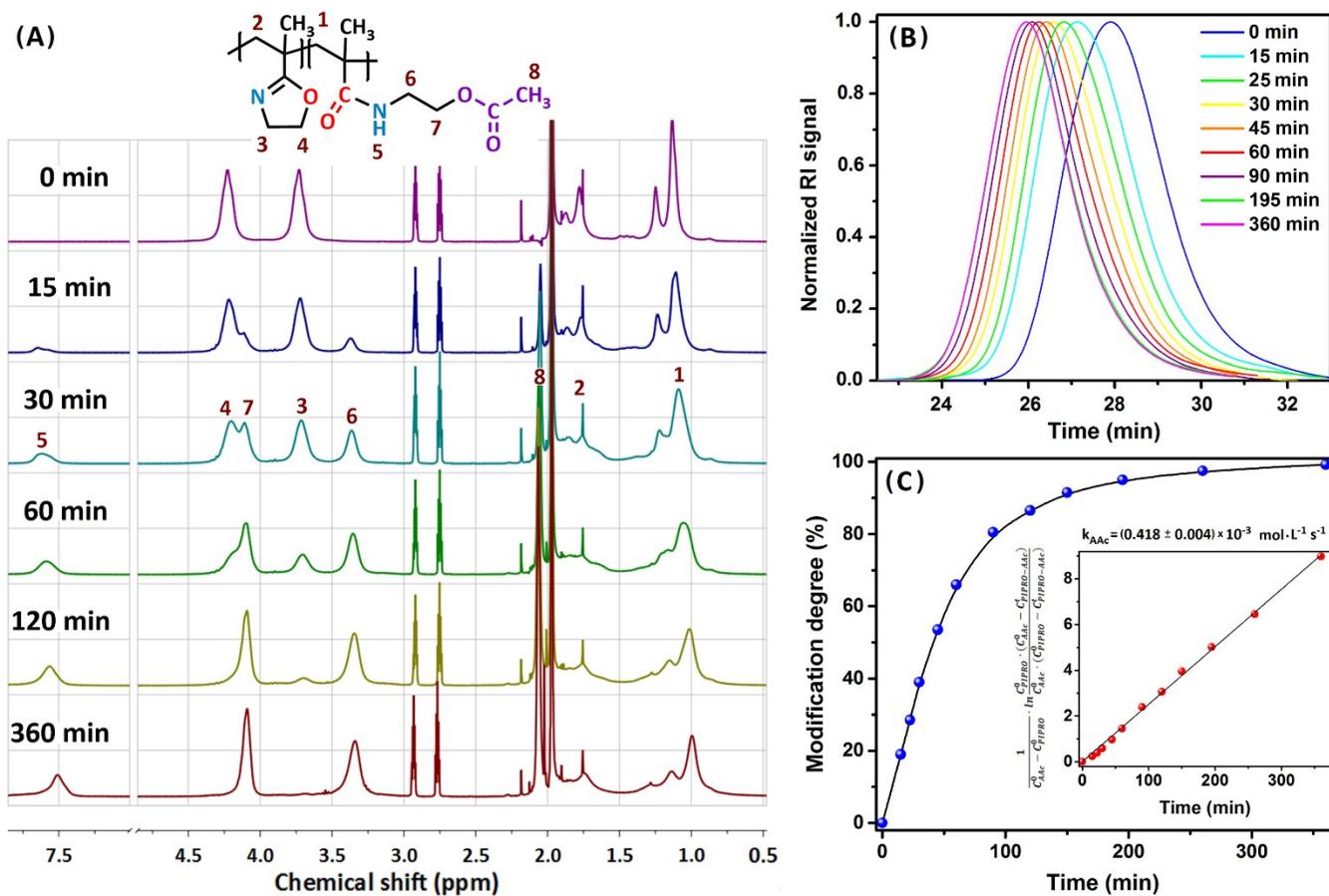


Figure S3. ^1H NMR spectra in DMF-d_7 for samples taken during the kinetic study of the PiPOx modification with acetic acid (A); Corresponding SEC traces for PiPOx-AAc series that shows the constant progress of the modification reaction (B); The time conversion plot for PiPOx-AAc series, with an inset showing the second order kinetic plot for the modification reaction (C).

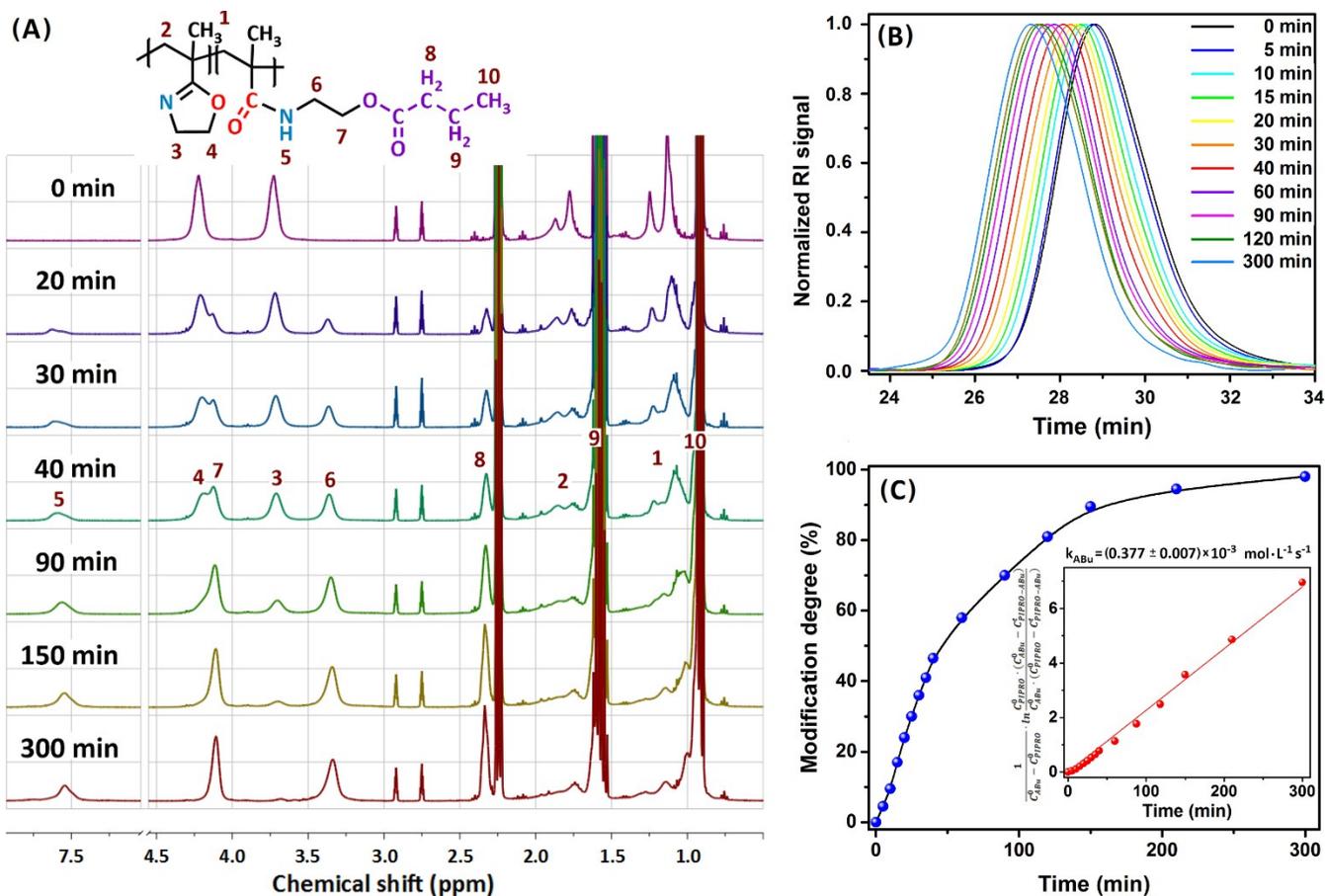
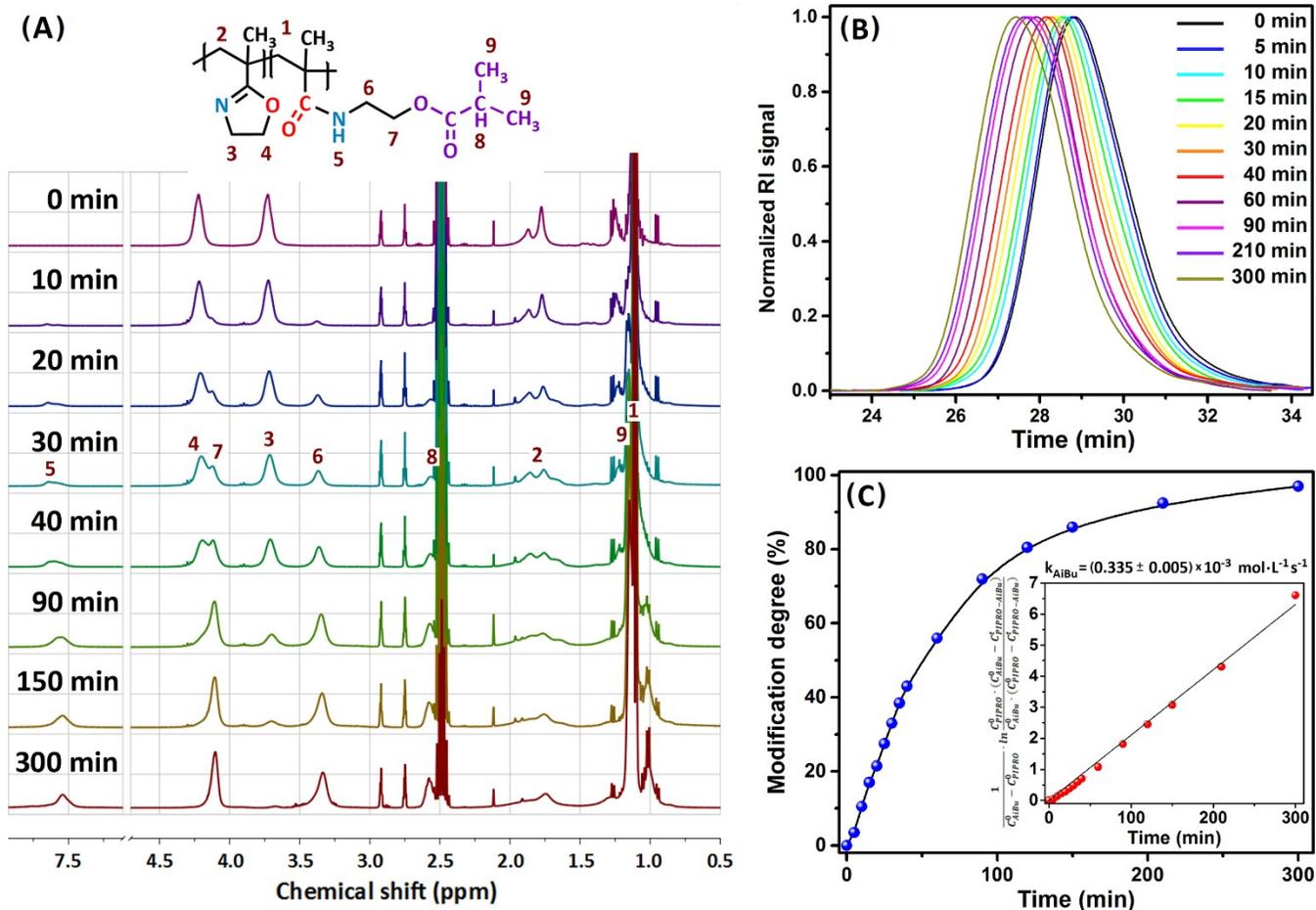


Figure S4. ^1H NMR spectra in DMF-d_7 for samples taken during the kinetic study of the PiPOx modification with butyric acid (A); Corresponding SEC traces for PiPOx-ABu series that shows a constant progress of the modification reaction (B); The time conversion plot for PiPOx-ABu series, with an inset showing the second order kinetic plot for the modification reaction (C).



2. Thermoresponsive behavior of PiPOx-Acids copolymers

Table S2. Characterization data for partially modified polymers

Polymer series	Time (min)	^a Deg. (%)	^b Mn (Da)	^b Đ	^c T _{CP} (°C)
PiPOx-AAc	45	54	22000	1.23	-
PiPOx-AAc	90	85	25000	1.22	-
PiPOx-AAc	360	100	27100	1.25	78.9
PiPOx-APr	5	3	15200	1.22	-
PiPOx-APr	10	15	18000	1.27	82.4
PiPOx-APr	15	21	20600	1.23	64.8
PiPOx-APr	20	27.5	21000	1.28	53.4
PiPOx-APr	25	32.5	21600	1.28	48.2
PiPOx-APr	30	39	23100	1.26	40.7
PiPOx-APr	40	48	24600	1.26	33.4
PiPOx-APr	50	55	25700	1.25	29.3
PiPOx-APr	65	68	27200	1.27	21.1
PiPOx-APr	90	77	27600	1.22	18.3
PiPOx-APr	120	85	30100	1.27	15.9
PiPOx-APr	180	96	30500	1.28	12.6
PiPOx-APr	360	100	31900	1.21	11.2
PiPOx-ABu	5	4	15400	1.21	-
PiPOx-ABu	7.5	7	16800	1.27	97.8
PiPOx-ABu	10	15	17800	1.28	58.5
PiPOx-ABu	13	18.5	18600	1.26	47.9
PiPOx-ABu	15	20	18900	1.28	44.4
PiPOx-ABu	17.5	27	19600	1.27	33.4
PiPOx-ABu	20	30	20000	1.28	26.9

Polymer series	Time (min)	^a Deg. (%)	^b Mn (Da)	^b Đ	^c T _{CP} (°C)
PiPOx-ABu	22.5	32.5	20900	1.27	22.1
PiPOx-ABu	25	36	21600	1.28	18.9
PiPOx-ABu	30	43	23000	1.25	11.7
PiPOx-ABu	35	49.5	24600	1.27	7.5
PiPOx-ABu	40	52.5	25300	1.27	5.6
PiPOx-ABu	45	57	25600	1.24	4.5
PiPOx-AiBu	5	3	15300	1.24	-
PiPOx-AiBu	7.5	5	15900	1.23	-
PiPOx-AiBu	10	12	17100	1.22	77.6
PiPOx-AiBu	13	22	19000	1.23	49.1
PiPOx-AiBu	15	24.5	19300	1.27	43.4
PiPOx-AiBu	20	27.5	24100	1.23	34.9
PiPOx-AiBu	22.5	35	21500	1.26	24.5
PiPOx-AiBu	25	38	21300	1.23	22.3
PiPOx-AiBu	30	43	21600	1.28	17.1
PiPOx-AiBu	35	45	22200	1.26	15.2
PiPOx-AiBu	40	49	23200	1.28	12.3
PiPOx-AiBu	45	51	23400	1.27	11.1

^aCopolymer compositions determined from ¹H NMR spectroscopy; ^bThe molar mass of fully modified copolymers determined by SEC in DMAc against PMMA standards; ^cThe cloud point temperatures in distilled water measured by turbidimetry at 10 mg/mL at 0.5 °C/min.

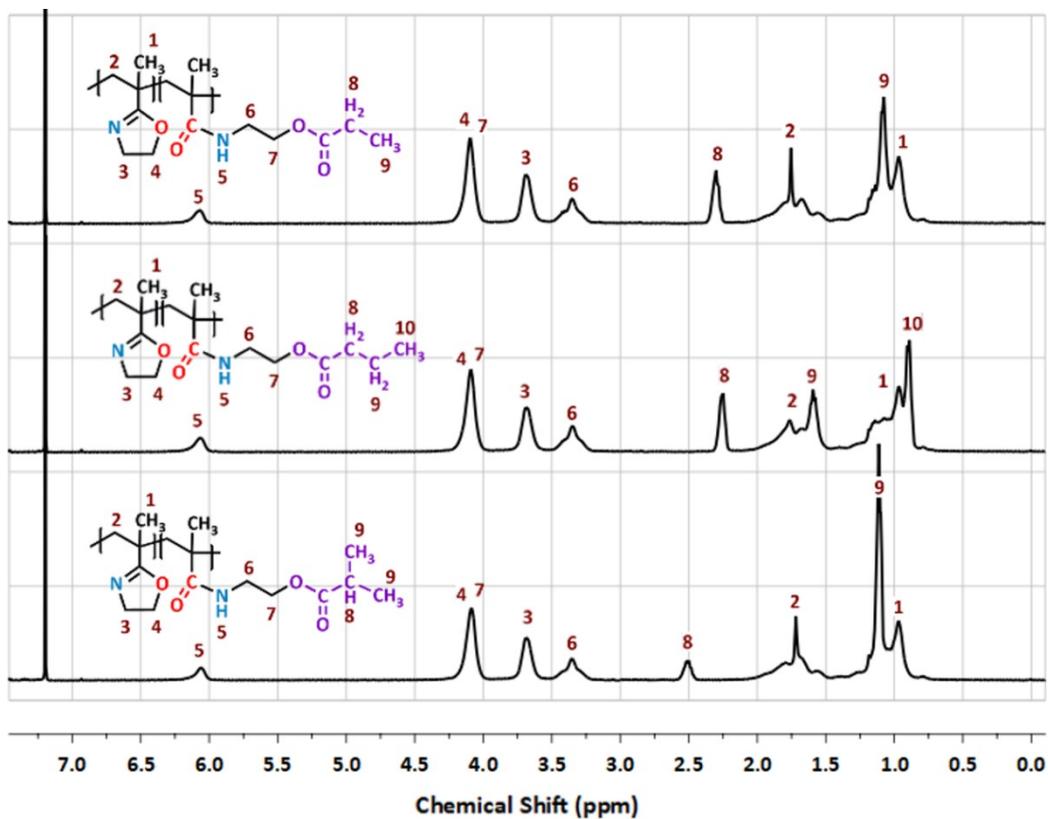


Figure S6. Selected ^1H NMR spectra in chloroform- d_1 for PiPOx-APr, PiPOx-ABu, and PiPOx-AiBu copolymers measured after 30 min of reaction.

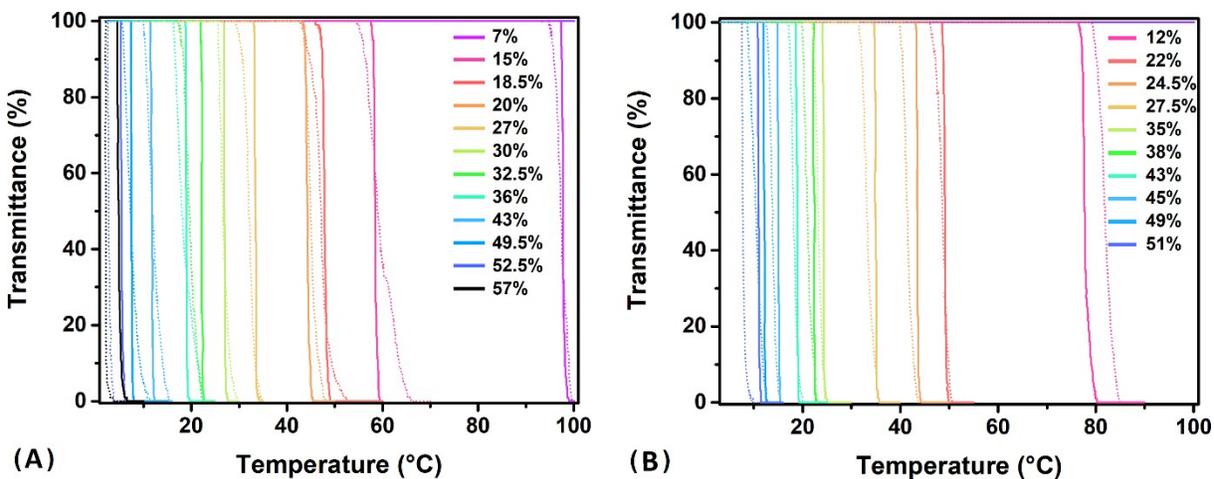


Figure S7. Transmittance versus temperature profiles for heating (solid lines) and cooling cycles (dashed lines) of PiPOx-ABu (A) and PiPOx-AiBu (B) series in distilled water (10 mg/mL, 0.5 $^{\circ}\text{C}/\text{min}$).