

Supplementary Information

Synthesis of defined high molar mass poly(2-methyl-2-oxazoline)

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Materials

2-Ethyl-2-oxazoline (EtOx) was kindly donated by Polymer Chemistry Innovation and was distilled over BaO before use. Methyl-2-oxazoline (MeOx) was purchased from Acros Organics and was distilled from barium oxide before use. Methyl *p*-toluenesulfonate (MeOTs) was obtained from Sigma-Aldrich and was distilled from CaH₂ prior to use. Acetonitrile (Sigma-Aldrich) was purified over aluminum oxide using a solvent purification system from J.C. Meyer. Sulfolane (Sigma-Aldrich) was purified by two consecutive distillations, first over barium oxide and then over 2-phenyl-2-oxazolinium tetrafluoroborate. All other chemicals, including triethyl amine, acetic anhydride and sodium azide were purchased from Sigma-Aldrich and were used as received. 2-Phenyl-2-oxazolinium tetrafluoroborate (HPhOxBF₄) was synthesized according to reference literature procedure.¹ Low molar mass PEtOx (DP 50 and 100) were synthesized by cationic ring-opening polymerization (CROP) of EtOx at 140°C in a microwave reactor using acetonitrile as a solvent and MeOTs as initiator according to reference published procedure.² The high molar mass PEtOx (DP > 250) were synthesized according to the recently reported low temperature polymerization of EtOx in chlorobenzene using HPhOxBF₄ as an initiator according (Table S2, Figure 3).¹ The obtained PEtOx polymers were hydrolyzed to well-defined linear polyethyleneimine (PEI) according to reference published procedure.³

Synthesis of poly(2-methyl-2-oxazoline) (PMeOx) by CROP of MeOx

The MeOx monomer was first purified under deep vacuum by low-temperature static distillation in presence of an oxazolinium initiator (sacrificial initiator method). The purified MeOx was collected into the reaction flask containing a calculated amount of initiator.¹ In the cleaning Schlenk flask, MeOx (4.6 g, 101 mmol) and the 2-phenyl-2-oxazolinium tetrafluoroborate (50 mg) were degassed by three freeze-pump-thaw cycles and stirred at room temperature for 1 h, allowing all nucleophilic impurities to be scavenged by the initiator. Afterwards, the solution was frozen with liquid nitrogen and evacuated using an oil pump coupled with an oil diffusion pump. After a deep vacuum was reached, the system was isolated from the pump, the cooling of the cleaning flask was removed and the monomer was distilled under static vacuum into the liquid nitrogen-cooled reaction flask containing the calculated amount of initiator. After the distillation was complete, the monomer was melted, and the reaction flask was isolated from the system and transferred to a glove-box, where freshly distilled sulfolane (13.4 mL) was added to reach a monomer concentration of 3 M. The reaction

mixture was stirred at 50°C in a glovebox, while samples for GC and SEC analysis were periodically taken.

Synthesis of PMeOx by acetylation of PEI

PEI (1 eq. of amines) was dissolved in *N,N*-dimethylacetamide (DMA, 20 mL) upon heating. The mixture was cooled down in an ice-water bath (fine suspension of PEI appeared) and acetanhydride (2 mL) was added, resulting in immediate dissolution of PEI. Triethylamine (1.5 eq) was added and the reaction mixture was purged with argon and allowed to stir at 0 °C for 1 h and overnight at room temperature. All volatiles were then removed under reduced pressure and the residue was dissolved in distilled water and purified by dialysis (MWCO 1 kDa for DP 50 polymer, respectively 3.5 kDa for longer polymers). PMeOx was recovered by freeze-drying as white or pale yellow solid (yield 72-95%).

Characterization of polymers.

Gas chromatography (GC) was used to monitor the kinetics of the CROP employing an Agilent 7890A system equipped with a VWR Carrier-160 hydrogen generator and an Agilent HP-5 column of 30 m length and 0.32 mm diameter. An FID detector was used, and the inlet was set to 240 °C with a split injection ratio 25:1. Hydrogen was used as carrier gas at a flow rate of 2 mL min⁻¹. *Size exclusion chromatography (SEC)* was used to determine the molecular weights (M_w - weight-averaged molecular weight, M_n - number-averaged molecular weight) and dispersity ($D = M_w/M_n$) of the prepared polymers. This was performed using an Agilent 1260-series HPLC system equipped with a 1260 ISO-pump, a 1260 automatic liquid sampler, a thermostatted column compartment at 50 °C equipped with two PLgel 5 µm mixed-D columns and a precolumn in series, a 1260 diode array detector 1260 RI detector and multi-angle light scattering detector (Wyatt miniDawn Treos II). The used eluent was DMA containing 50 mM of LiCl at a flow rate of 0.5 ml min⁻¹. Molar mass values and D values are calculated using refractive index increments $dn/dc_{PEIOx} = 0.078$ and $dn/dc_{PMeOx} = 0.092$, respectively. For the kinetics measurement, aliquots of the reaction mixture (300 µL) were taken in glovebox and passed through the Sephadex PD-10 column using water as an eluent and freeze-dried, as the residual sulfolane influences the SEC results. *Nuclear magnetic resonance (NMR)* spectra were measured with a Bruker Advance MSL 400 MHz NMR spectrometer. All chemical shifts are given in ppm. *Matrix assisted laser desorption/ionization time of flight mass spectrometry (MALDI-TOF MS)* was performed on an Applied Biosystems Voyager De STR MALDI-TOF

mass spectrometer equipped with 2 m linear and 3 m reflector flight tubes. All mass spectra were obtained with an accelerating potential of 20 kV in positive ion mode and in reflectron mode (matrix: 2-[3-(4-*tert*-butylphenyl)-2-methyl-2-propenyldene] malononitrile (DCTB)). Samples were applied to the MALDI plate *via* the dried drop method. All measurements were calibrated using methoxy poly(ethylene glycol) (mPEG, $M_n = 2000$ Da) as calibration standard. *Dynamic light scattering (DLS) measurements* was used to measure hydrodynamic diameters (D_h) of prepared polymers using a Zetasizer NanoZS instrument, Model ZEN3600 (Malvern Instruments, UK). The polymer samples ($c_{\text{pol}} = 2$ mg mL⁻¹) in phosphate buffer-saline (PBS, pH = 7.4) were filtered through an 0.22 μm PTFE syringe filter. Due to the potential high-molar mass shoulders (that would overweight the intensity-weighted values), the apparent volume-weighted mean hydrodynamic diameter of polymers, D_h , was determined at a scattering angle of $\theta = 173^\circ$ and the DTS (Nano) program was used to evaluate the data. The volume distribution was derived from the intensity distribution using Mie theory.

Table S1. Experimental details and obtained propagation rate constants (k_p 's) for low-temperature CROP of MeOx in sulfolane.

Run	$[\text{M}]_0:[\text{I}]_0^{\text{a}}$	$[\text{M}]_0^{\text{b}}$ (M)	Initiator	T ($^\circ\text{C}$) ^c	$k_p * 10^{-4}$ (L mol ⁻¹ s ⁻¹) ^d
1	100	3	HPhOxBF ₄	50	5.00
2	250	3	HPhOxBF ₄	50	3.35
3	500	3	HPhOxBF ₄	50	2.03

^aInitial monomer-to-initiator ratio. ^bInitial monomer concentration. ^cPolymerization temperature. ^dPropagation rate constant calculated from the monomer conversion plot assuming pseudo-first order reaction kinetics, the total concentration of living chain-ends equal to $[\text{I}]_0$ and rate equation $v = k_p [\text{I}]_0 [\text{M}]$.

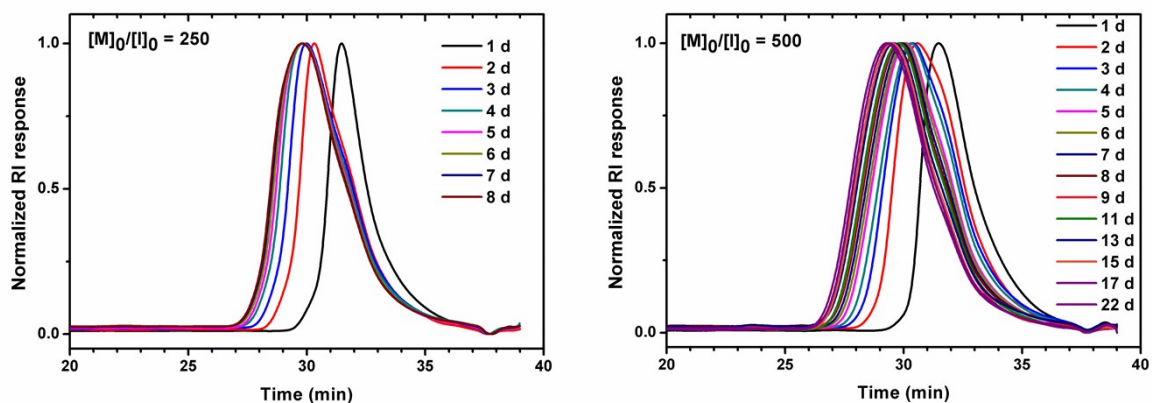


Figure S1. SEC traces of PMeOx prepared by low-temperature CROP after different reaction time eluted with DMA/LiCl. Initial monomer-to-initiator ratio 250 (left), respectively 500 (right).

Table S2. Polymerization details and characteristics of prepared PEtOx

Polymer	$[M]_0:[I]_0^a$	$[M]_0^b$ (M)	Initiator	T ($^{\circ}\text{C}$) ^c	end-group	M_w (kDa) ^d	M_n (kDa) ^d	D^d
PEtOx 1	50:1	4	MeOTs	140	-piperidyl	5.5	5.3	1.03
PEtOx 2	100:1	4	MeOTs	140	-N ₃	10.8	10.2	1.06
PEtOx 3	250:1	3.2	HPhOxBF ₄	50	-N ₃	22.9	22.2	1.03
PEtOx 4	500:1	3.2	HPhOxBF ₄	50	-N ₃	44.3	42.4	1.05
PEtOx 5	750:1	3.2	HPhOxBF ₄	50	-N ₃	58.0	54.6	1.06
PEtOx 6	1000:1	3.2	HPhOxBF ₄	50	-N ₃	87.4	80.7	1.08
PEtOx 7	2000:1	3.2	HPhOxBF ₄	42	-OH	97.0	87.3	1.11

^aInitial monomer-to-initiator ratio. ^bInitial monomer concentration. ^cPolymerization temperature. ^dDetermined by SEC-MALS using DMA/LiCl as an eluent.

Table S3. Characteristics of PMeOx prepared by acylation of linear polyethylenimine.

Polymer	Starting PEtOx	end-group	M_w (kDa) ^a	M_n (kDa) ^a	\bar{D}^a	Elution volume (mL) ^a
PMeOx 1	PEtOx 1	-piperidine	5.1	4.8	1.05	16.6
PMeOx 2	PEtOx 2	-N ₃	9.5	8.7	1.09	15.8
PMeOx 3	PEtOx 3	-N ₃	18.6	18.0	1.03	14.9
PMeOx 4	PEtOx 4	-N ₃	33.3	31.5	1.06	14.2
PMeOx 5	PEtOx 5	-N ₃	42.5	38.6	1.10	13.8
PMeOx 6	PEtOx 6	-N ₃	58.0	54.0	1.07	13.6
PMeOx 7	PEtOx 7	-OH	73.4	64.8	1.13	13.3

^aDetermined by SEC-MALS using DMA/LiCl as an eluent.

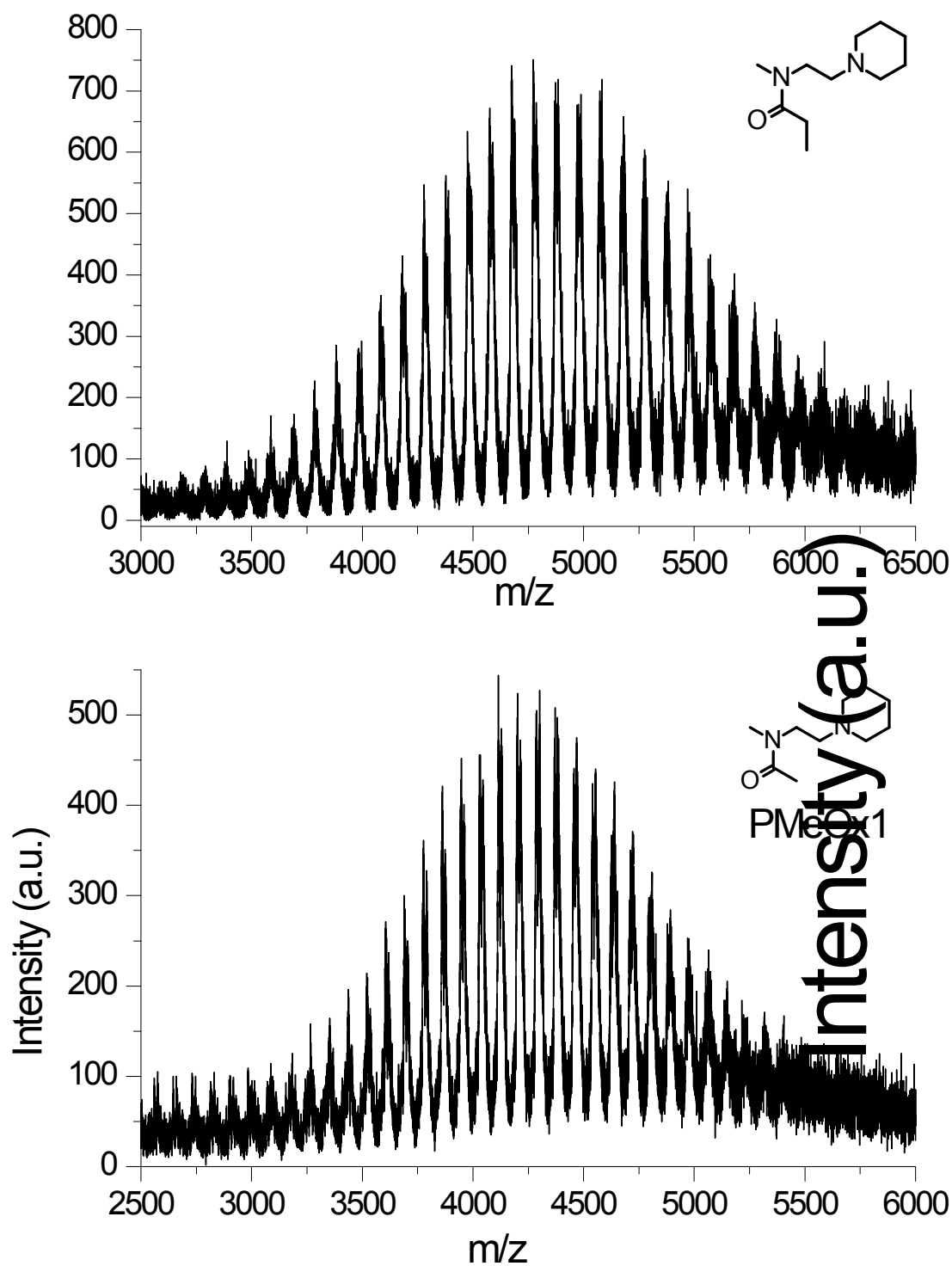


Figure S2. MALDI-TOF spectra of PEtOx 1 (top), respectively PMeOx 1 (bottom). The two homologous series represent $[M+Na]^+$, respectively $[M+K]^+$ values.

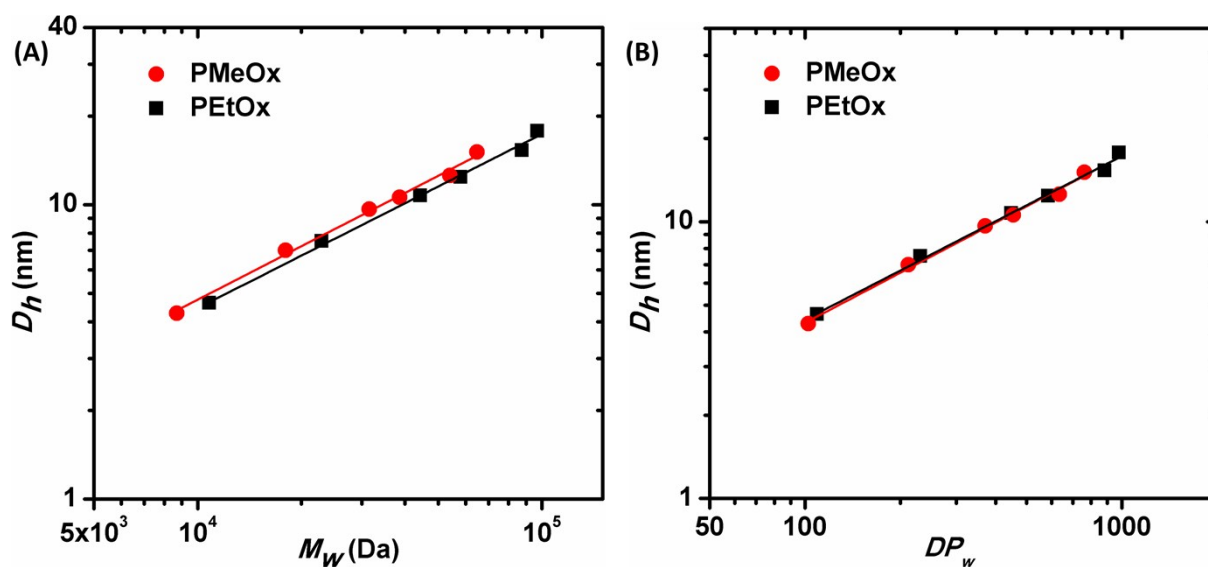


Figure S3. Double logarithmic plot of the hydrodynamic diameter (D_h) against values of the weight-averaged molar mass (A), respectively degree of polymerization (B), for synthesized PEtOx, respectively PMeOx ($c_{\text{pol}} = 2 \text{ mg mL}^{-1}$).

References

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