

Supporting Information for

Towards the Synthesis of Polythiazolines: A *Post-polymerization Approach*

Aikaterini Mathianaki,¹ Aysha Kinjo Demeler,¹ Adrian Dömling,² Federico Ferrari,³ Frieda Clara M. Scheelje,³ Hilke Bahmann,^{2,4} Guillaume Delaître^{1,4*}

1. Organic Functional Molecules, Organic Chemistry, University of Wuppertal, Gaußstraße 20, 42119 Wuppertal, Germany

2. Physical and Theoretical Chemistry, University of Wuppertal, Gaußstraße 20, 42119 Wuppertal, Germany

3. Laboratory of Applied Chemistry, Institute of Organic Chemistry (IOC), Karlsruhe Institute of Technology (KIT), Straße am Forum 7, 76131 Karlsruhe, Germany

4. Wuppertal Center for Smart Materials & Systems (CM@S), University of Wuppertal, Gaußstraße 20, 42119 Wuppertal, Germany

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Materials

2-Ethyl-2-oxazoline (EtOx) (99+%, Thermo Scientific Chemicals), methyl *p*-toluenesulfonate (MeOTs) (98%, Merck), methyl trifluoromethanesulfonate (MeOTf) (Merck), 2-methyl-2-thiazoline (MeThz) (97%, Alfa Aesar), and sulfolane (99%, Merck) were left stirring over CaH₂ overnight prior their purification by vacuum distillation. After the distillation, EtOx, MeOTs, MeOTf and MeThz were kept under argon and over molecular sieves at 3 °C. Sulfolane was kept under argon and molecular sieves at room temperature. Lawesson's reagent (LR) (99%, Thermo Scientific Chemicals), tetramethylammonium hydroxide (TMAH) (25 wt% in methanol, Thermo Scientific Chemicals), acetonitrile (MeCN) (99.9%, extra dry over molecular sieves, Thermo Scientific Chemicals), *N,N*-dimethylacetamide (DMAc) (99.5%, extra dry over molecular sieves, Acros Organics), diethyl ether (\geq 98%, Julius Hoesch), *n*-heptane (99+%, Thermo Scientific Chemicals), dichloromethane (DCM) (\geq 98%, Julius Hoesch), and chloroform (\geq 99.8%, Fisher Chemicals) were used as received. Double deionized water (18.2 M Ω) was collected from a Barnstead Genpure Pro system (Thermo Fisher Scientific).

General Characterization Methods

Nuclear magnetic resonance (NMR) spectroscopy measurements were conducted in a BRUKER AVANCE III 600 MHz or a BRUKER AVANCE 400 MHz spectrometer. CDCl₃ and TFA-d were used as deuterated solvents and the residual peaks $\delta(\text{CHCl}_3) = 7.26$ ppm and $\delta(\text{TFA-d}) = 11.5$ ppm were employed for shift correction.

Size-exclusion chromatography (SEC) with *N,N*-dimethylacetamide (DMAc) and 0.7 wt% LiBr as eluent was accomplished on a Polymer Standards Service PSS/Agilent SECurity²-GPC system. The system included an autoinjector, a PSS PFG precolumn (50 × 8 mm, 7 μm), three PSS PFG separating columns (7 μm , 8 × 300 mm, porosities: 100, 1000, 4000 Å), and a refractive-index detector (P/N 404-2106). A flow rate of 1 mL min⁻¹ was used at 50 °C with 2 g L⁻¹ as sample concentration. Linear poly(methyl methacrylate) standards were used to calibrate the system. Prior to injection, the samples were filtered through polytetrafluoroethylene (PTFE) membranes with 0.2 μm pore size.

Size-exclusion chromatography (SEC) in hexafluoroisopropanol (HFIP) was conducted on a Tosoh EcoSEC HLC-8320 SEC system. HFIP with 0.1 % (w/w) of KTFA 0.1 at 0.40 mL min⁻¹ flow rate at 35 °C was used as eluent. The system included a PSS PFG Analytical pre-column (50 × 8 mm, 5 μm) and a PSS PFG Analytical Linear S (300 × 8 mm, 5 μm). Linear poly(methyl

methacrylate) standards were used to calibrate the system (2000–981000 Da). Samples were prepared in a concentration of 1 mg mL⁻¹ and were filtered prior to injection.

Fourier transform infrared (FT-IR) spectroscopy was conducted on a Bruker Alpha II compact FT-IR spectrometer. The system included a diode laser and platinum attenuated total reflection. The reported signals were presented as the frequency of absorption in [cm⁻¹].

Dynamic light scattering (DLS) measurements were performed on an Amerigo particle size & Zeta potential analyzer from Cordouan Technologies equipped with a 50 mW diode at 635 nm coupled to automated optical attenuation system. Analysis of the data was carried out using the AmeriQ software. For the lower critical solution temperature monitoring, each sample was prepared with 5 mg mL⁻¹ concentration in double deionized water and measured using a temperature ramp starting from 10 to 70 °C (heating cycle) and 70 to 10 °C (cooling cycle) at an angle of 17° (forward scattering mode). A temperature equilibrium of 1 min was used between each degree.

Experimental part

2-Methyl-2-thiazoline (co)polymerization attempts

The monomer(s), the initiator, and the solvent were introduced into a well-dried and argon-filled Schlenk tube. The resulting mixture was stirred until homogeneous and then placed in a preheated oil bath and left to react. After the desired amount of time, the solution, which had turned from colorless to yellow, was quenched with an excess of TMAH. During quenching, the reaction turned from yellow to colorless. After stirring overnight at room temperature, it turned yellowish again and a sample was collected to monitor the conversion.

Table S1. Different conditions of the MeThz polymerization attempts.

Code	Initiator	Solvent	[I:M]	[MeThz:EtOx]	T (C°)	Reaction Time(h)	Concentration(M)
MeThz 1	MeOTs	MeCN	1:60	-	100	2	4.0
MeThz 2	MeOTs	MeCN	1:60	-	140	2	4.0
MeThz 3	MeOTs	DMAc	1:69	-	100	25	4.3
MeThz 4	MeOTs	DMAc	1:211	-	100	20	4.4
MeThz 5	MeOTs	DMAc	1:475	-	100	20	4.4
MeThz 6	MeOTs	Sulfolane	1:60	-	100	18	4.0
MeThz 7	MeOTf	MeCN	1:66	-	100	30	4.5
MeThz 8	MeOTf	MeCN	1:203	-	100	30	4.1
MeThz 9	MeOTs	MeCN	1:40	1:0.11	100	1	3.9
MeThz 10	MeOTs	MeCN	1:33	1:0.24	100	1	3.9
MeThz 11	MeOTs	MeCN	1:33	1:0.98	100	1	3.9
MeThz 12	MeOTs	MeCN	1:33	1:3.8	100	1	3.9

Synthesis of poly(2-ethyl-2-oxazoline)s

1.22 M and 1.26 M MeOTs stock solutions in dry acetonitrile were used for the synthesis of PEtOx A and PEtOx B, respectively.

PEtOx A

In a well-dried and argon-filled Schlenk flask, 2-ethyl-2-oxazoline (4.95 g, 49.93 mmol, 59 eq.), methyl *p*-toluenesulfonate (0.61 g of stock solution, 0.85 mmol, 1 eq.), and dry acetonitrile (5.36 g) were added to achieve a concentration of 4 M. The resulting mixture was stirred until homogeneous and then placed in a preheated oil bath at 100 °C for 1 hour and 20 min. Subsequently, the reaction mixture was cooled down in an ice bath. Termination was carried out under vigorous stirring with a 5 wt% Na₂CO₃ aqueous solution (2.98 mmol, 3.5 eq.). After stirring overnight at room temperature, 0.5 M HCl was added slowly until the pH became neutral and the water phase was extracted thrice with DCM. The organic phase was washed once with brine and the combined organic phases were dried over MgSO₄ before being concentrated under reduced pressure. The polymer solution was passed through a basic alumina column using DCM as eluent. followed by precipitation in an excess of cold diethyl ether. The polymer was dried extensively under vacuum.

PEtOx B

Similarly to the synthesis of PEtOx A, in a well-dried and argon-filled Schlenk flask, 2-ethyl-2-oxazoline (5.45 g, 54.98 mmol, 60 eq.) and methyl *p*-toluenesulfonate (0.63 g of stock

solution, 0.92 mmol, 1 eq.) were added. Subsequently, dry acetonitrile (5.73 g) was added to achieve a concentration of 4 M. The resulting mixture was stirred until homogeneous and then placed in a preheated oil bath at 100 °C for 1 hour. Then, the flask was cooled down in an ice bath and an equimolar amount of TMAH (0.36 ml, 0.86 mmol) was added for termination. The mixture was left to stir overnight. The solvent was removed under reduced pressure and the residue was redissolved in DCM before precipitation in an excess of cold diethyl ether. The polymer was additionally purified by passing through a basic aluminum oxide column using DCM as eluent, reprecipitated in an excess of cold diethyl ether, and dried extensively under vacuum.

General protocol for the synthesis of PEtThz-co-PEtOx copolymers with 5–33% thionation degrees by one-step thionation

A two-neck flask was charged with PEtOx A and was left drying at 45 °C under vacuum overnight. Next, the flask was filled with argon, equipped with a reflux condenser, and LR was added, followed by the addition of anhydrous MeCN. Please refer to Table S2 for exact quantities. The mixture was placed in a preheated oil bath at 90 °C and was left to stir for 2.5 hours. Initially, LR remained insoluble but after 15 minutes in the oil bath a homogeneous yellowish solution was formed. After the initial 2.5 hours, the flask was left stirring at room temperature overnight and the solvent was removed under reduced pressure. The polymer was redissolved in DCM and precipitated in an excess of cold Et₂O followed by drying under vacuum. Subsequently, the polymer was redissolved in CHCl₃ and passed through a basic alumina column using CHCl₃ as the eluent, before the copolymer-dependent steps described below.

Purification of PEtThz-co-PEtOx 5% copolymer

The precipitated material (0.1717 g) was dissolved in CHCl₃ (3.5 mL) and passed through the basic alumina column. The resulting solution was concentrated under reduced pressure. The copolymer was recovered by precipitation in an excess of cold Et₂O as a white solid and dried extensively under vacuum. Overall isolated yield: 10.5 %

Purification of PEtThz-co-PEtOx 11% copolymer

The precipitated material (0.1118 g) was dissolved in CHCl₃ (3 mL) and passed through the basic alumina column. The resulting solution was concentrated under reduced pressure. The residue was redissolved in DCM followed by precipitation in an excess of cold Et₂O. The heterogeneous mixture remained at –24 °C overnight, affording the copolymer as a white

sediment, which was collected after carefully decantation and extensively dried under vacuum. Overall isolated yield: 15.7 %

Purification of PEtThz-co-PEtOx 23–33% copolymers

After passing through a basic alumina column, the solvent was removed under reduced pressure. The residue was redissolved in CHCl_3 and precipitated in an excess of *n*-heptane. The mixture remained at $-24\text{ }^\circ\text{C}$ overnight, affording the copolymer as a white sediment which was collected after carefully decantation and extensively dried under vacuum.

Table S2. Detailed amounts before and after the purification of the 23–33% copolymers.

Sample Code	Residue from 1st precipitation (g)	CHCl_3 (mL)	Purified polymer (g)	Overall isolated yield (%)	Physical aspect
23%	0.1011	3	0.0433	11.9	White flaky powder
28%	0.1250	2	0.0612	16.7	
33%	0.1212	2	0.0434	35.8	

General protocol for the synthesis of the PEtThz-co-PEtOx 40–91% copolymers by one-step thionation

A two-neck flask was charged with PEtOx B and left to dry for 30 minutes at $40\text{ }^\circ\text{C}$ under vacuum. Next, LR and anhydrous MeCN were added. The flask was equipped with a reflux condenser, placed in a preheated oil bath at $90\text{ }^\circ\text{C}$, and left to stir for 2 hours. Initially, LR remained insoluble but after 15 minutes in the oil bath a homogeneous yellow solution was formed. After 2 hours, the reaction was allowed to stir at room temperature overnight. The purification steps for each thionation grade are described in the following.

Purification of PEtThz-co-PEtOx 40–55% copolymers

After cooling down to room temperature, MeCN was removed under reduced pressure. The residue was redissolved in DCM followed by precipitation in an excess of cold Et_2O . Subsequently, the polymer was redissolved in methanol followed by filtration. Methanol was removed. The polymer was redissolved in DCM and precipitated in an excess of cold Et_2O once (55%) or thrice (40%), to obtain a white flaky solid. Isolated yields: 74.9% (for sample 40%), 19.7% (for sample 55%).

Purification of PEtThz-co-PEtOx 91% copolymer

After cooling down the reaction mixture to room temperature, a white flaky precipitate was formed which was collected by filtration and dried under vacuum. Isolated yield: 87.6%

Synthesis of the PEtThz-co-PEtOx 95% copolymer by stepwise thionation

A two-neck flask was charged with PEtOx B (0.25 g, 2.53 mmol) and was left drying for 30 minutes at 40 °C under vacuum. Next, LR (0.256 g, 0.63 mmol, 0.25 eq.) was added, followed by the addition of anhydrous MeCN (7 mL). The flask was equipped with a reflux condenser and was placed in a preheated oil bath at 90 °C. After 30 minutes, remaining LR (0.256 g, 0.63 mmol) was split equally into 8 portions which were added with 1 mL of anhydrous MeCN in intervals of 15 minutes until a final ratio of [PEtOx B]:[LR] = 2 was attained (1.5 h). The mixture was left to react for an additional hour at 90 °C. Then, the flask was left to stir at room temperature overnight. The formation of a white precipitate was observed which was collected by filtration and dried under vacuum. 0.162 g of the copolymer were collected in the form of a white solid. Isolation yield: 56.3%

Table S3. Detailed amounts of each component for the synthesis of the PEtThz-co-PEtOx copolymers.

Sample Code	PEtOx A	PEtOx B	LR	MeCN	[LR:PEtOx]	Reaction Time (h)
5%	0.7666 g (7.73 mmol)	-	0.1565 g (0.39 mmol)	21.1 mL	1:20	2.0
11%	0.35 g (3.53 mmol)	-	0.0714 g (0.18 mmol)	9.6 mL	1:20	2.5
23%	0.35 g (3.53 mmol)	-	0.1428 g (0.35 mmol)	9.6 mL	1:10	2.5
28%	0.35 g (3.53 mmol)	-	0.1785 g (0.44 mmol)	9.6 mL	1:8	2.5
33%	0.1517 g (1.53 mmol)	-	0.0928 g (0.23 mmol)	4.2 mL	1:6.7	2.5
40%	-	0.25 g (2.52 mmol)	0.17 g (0.42 mmol)	7 mL	1:6	2.0
55%	-	0.25 g (2.52 mmol)	0.26 g (0.63 mmol)	7 mL	1:4	2.0
91%	-	0.25 g (2.52 mmol)	0.41 g (1.01 mmol)	7 mL	1:2.5	2.0
95%	-	0.25 g (2.52 mmol)	0.53 g (1.34 mmol)	15 mL	1:2	2.0

Additional characterization data

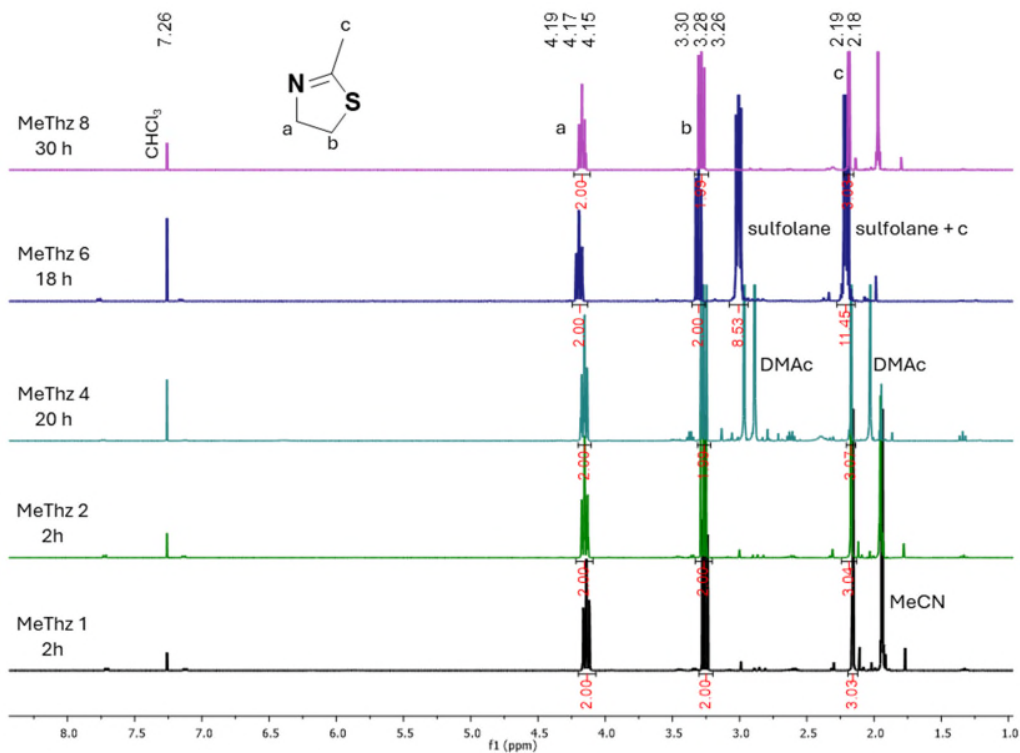


Figure S1. Representative ¹H NMR spectra of the polymerization attempts of 2-methyl-2-thiazoline in different conditions and reaction times (see Table S1).

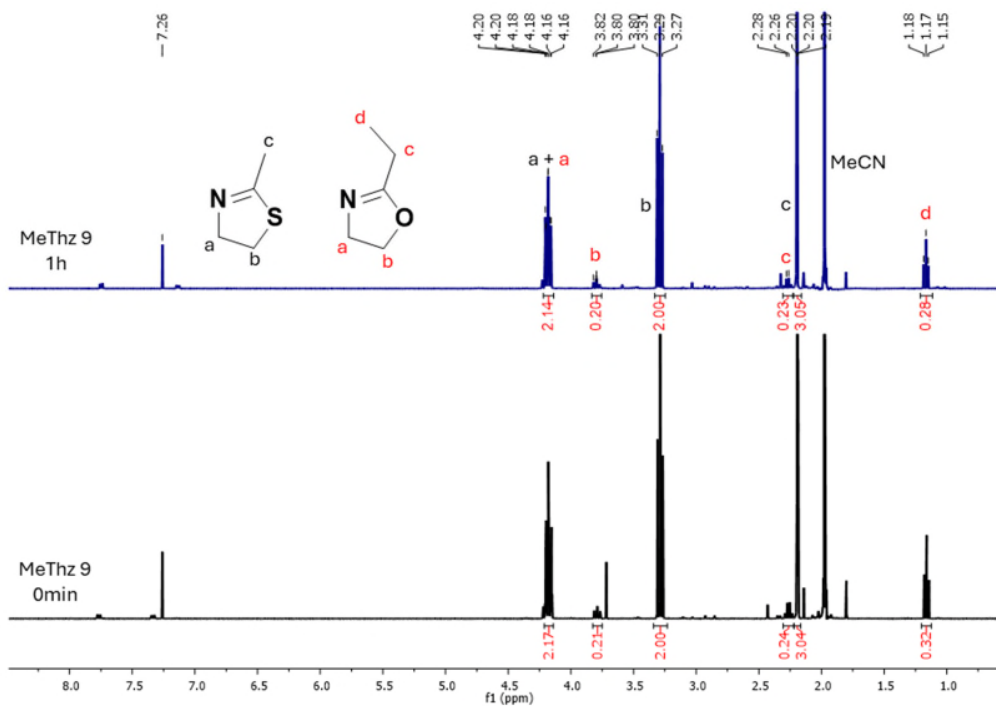


Figure S2. Representative ^1H NMR spectra of the copolymerization attempts of 2-methyl-2-thiazoline and 2-ethyl-2-oxazoline in 1:0.11 ratio: (bottom) initial mixture and (top) after 1 h reaction time.

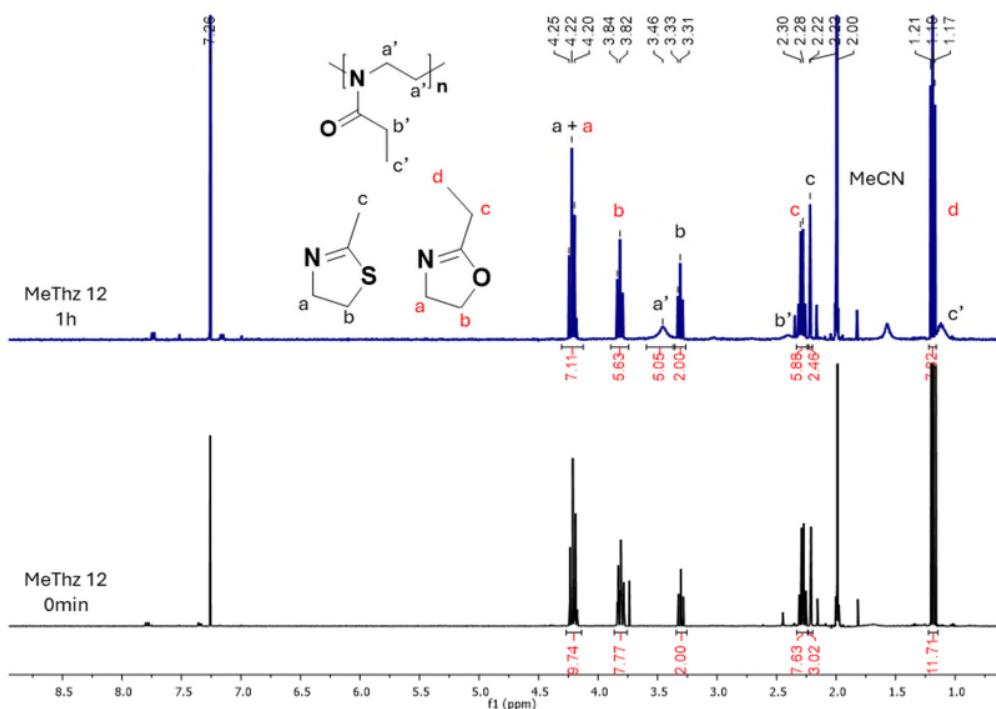


Figure S3. Representative ^1H NMR spectra of the copolymerization attempts of 2-methyl-2-thiazoline and 2-ethyl-2-oxazoline in 1:3.8 ratio: (bottom) initial mixture and (top) after 1 h reaction time.

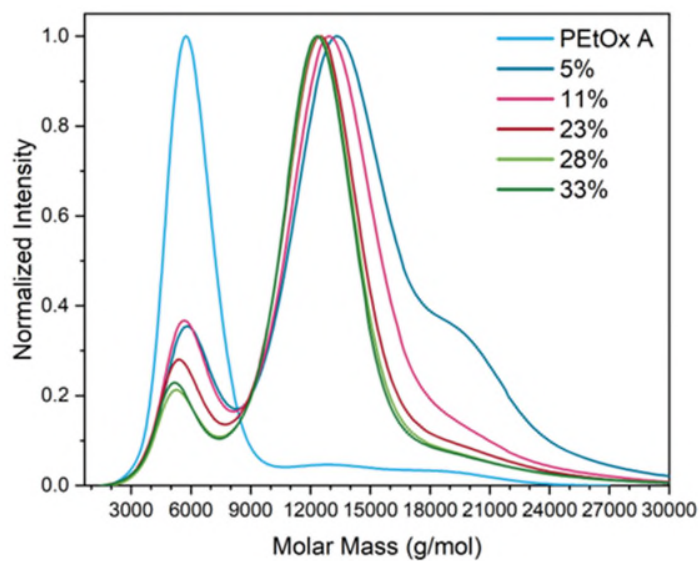


Figure S6. HFIP SEC chromatograms of pristine PETox A and PETox-co-PETox copolymers with different thionation degrees.

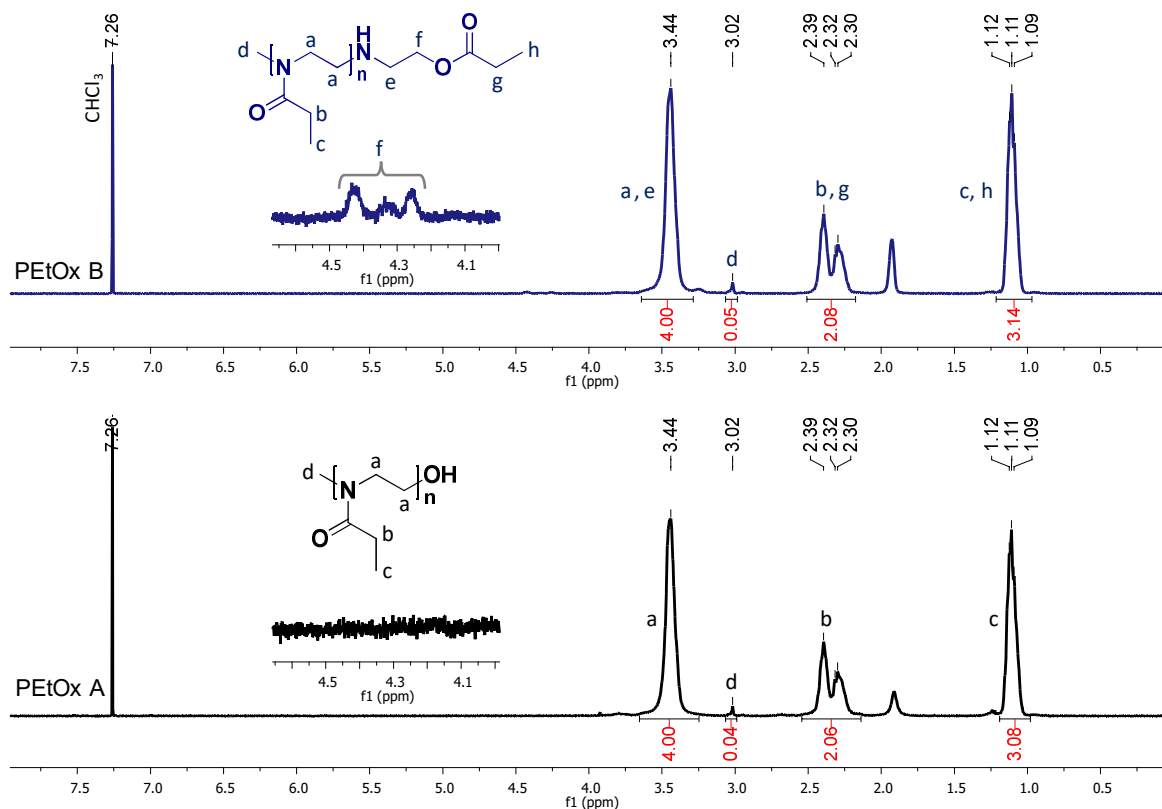


Figure S7. ¹H NMR spectra of PETox A and PETox B, highlighting the presence in PETox B and the absence in PETox A of ester ω-end groups.

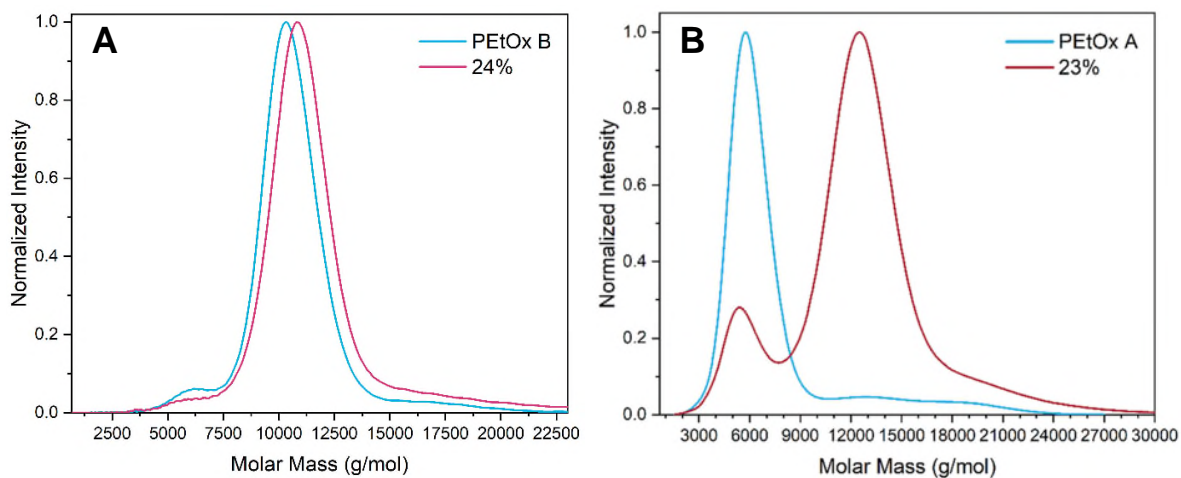


Figure S8. HFIP SEC chromatograms of (A) pristine PEtOx B and the corresponding copolymer obtained with 24 mol% thionation and (B) and pristine PEtOx A and sample 23%, as already reported in the main text.

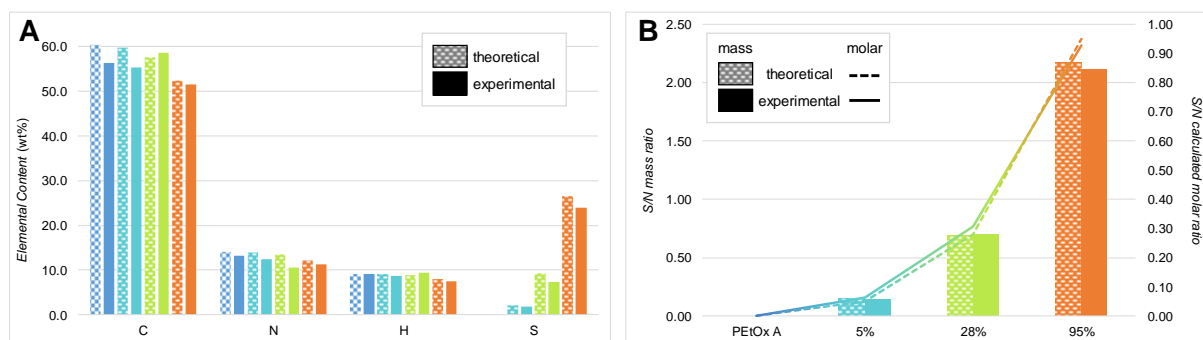


Figure S9. Elemental analysis results for PEtOx A and copolymers obtained with [LR]:[PEtOx] equals 0.025 (5%), 0.125 (28%), and 0.500 (95%). (A) CNHS elemental content and (B) S/N mass and calculated molar ratio.

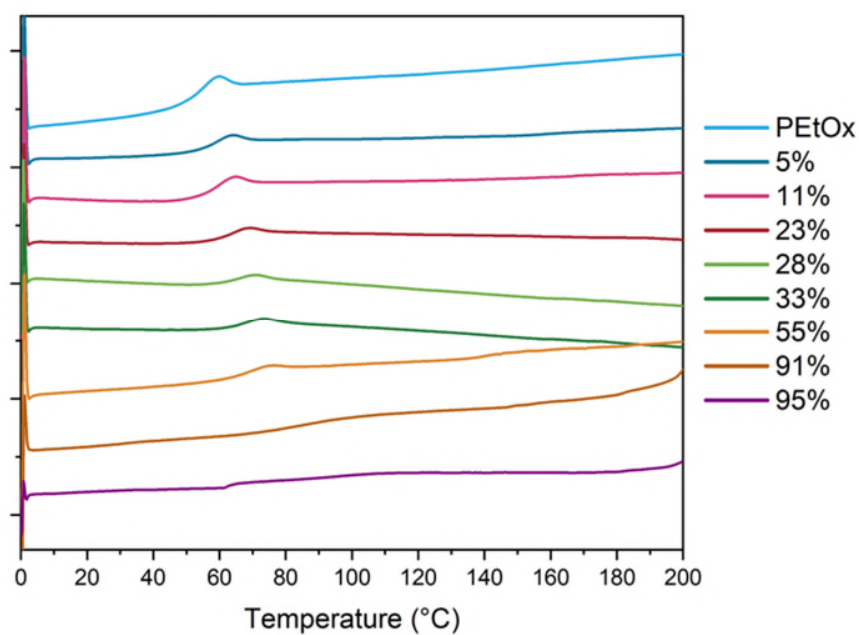


Figure S10. DSC thermograms of PEtOx A and of the synthesized copolymers with different thionation degrees. The 3rd heating cycle is shown.

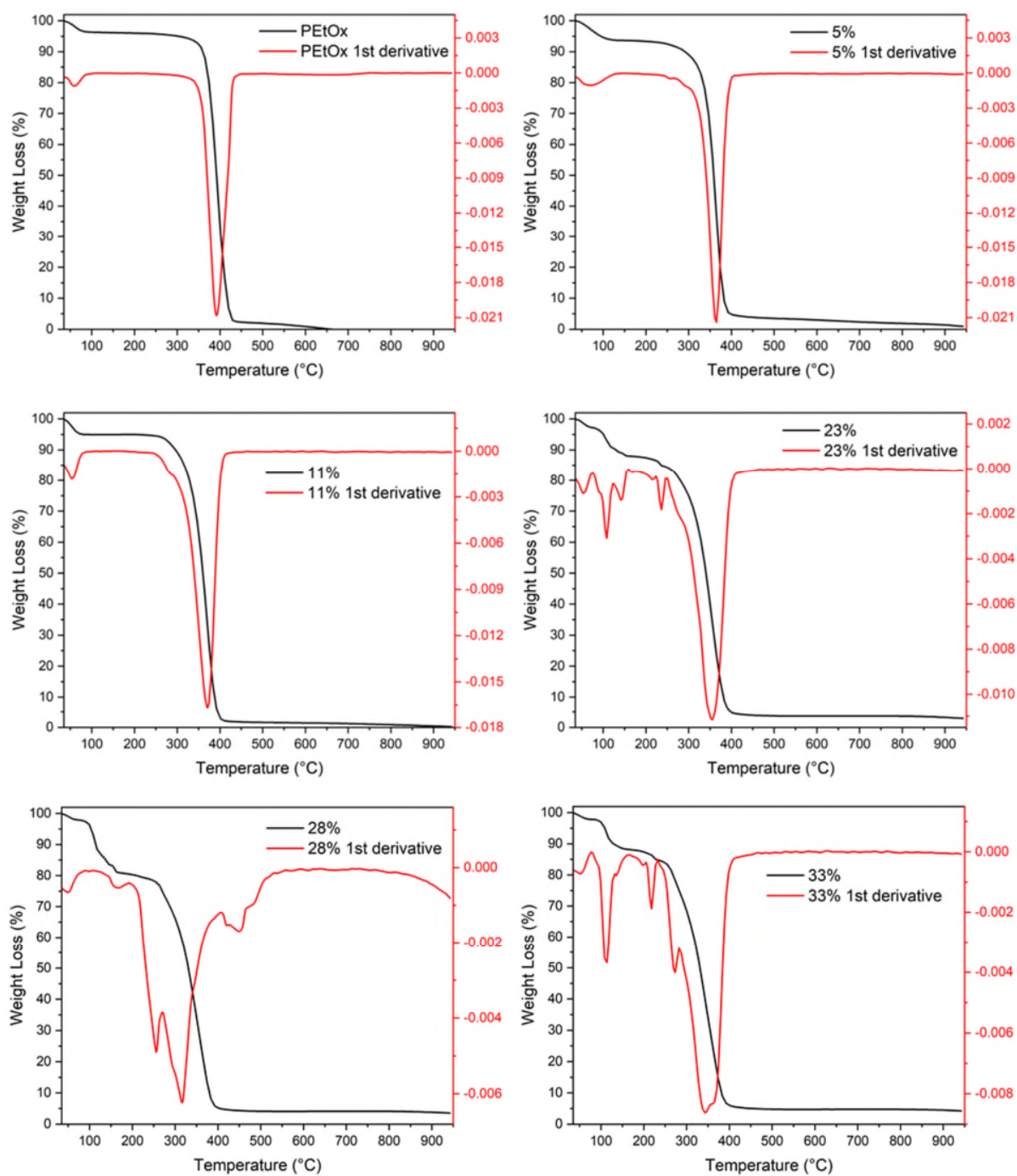


Figure S11. TGA thermograms of PETox A and of the synthesized copolymers with different thionation degrees. Black trace: weight loss versus the temperature, red trace: 1st derivative.

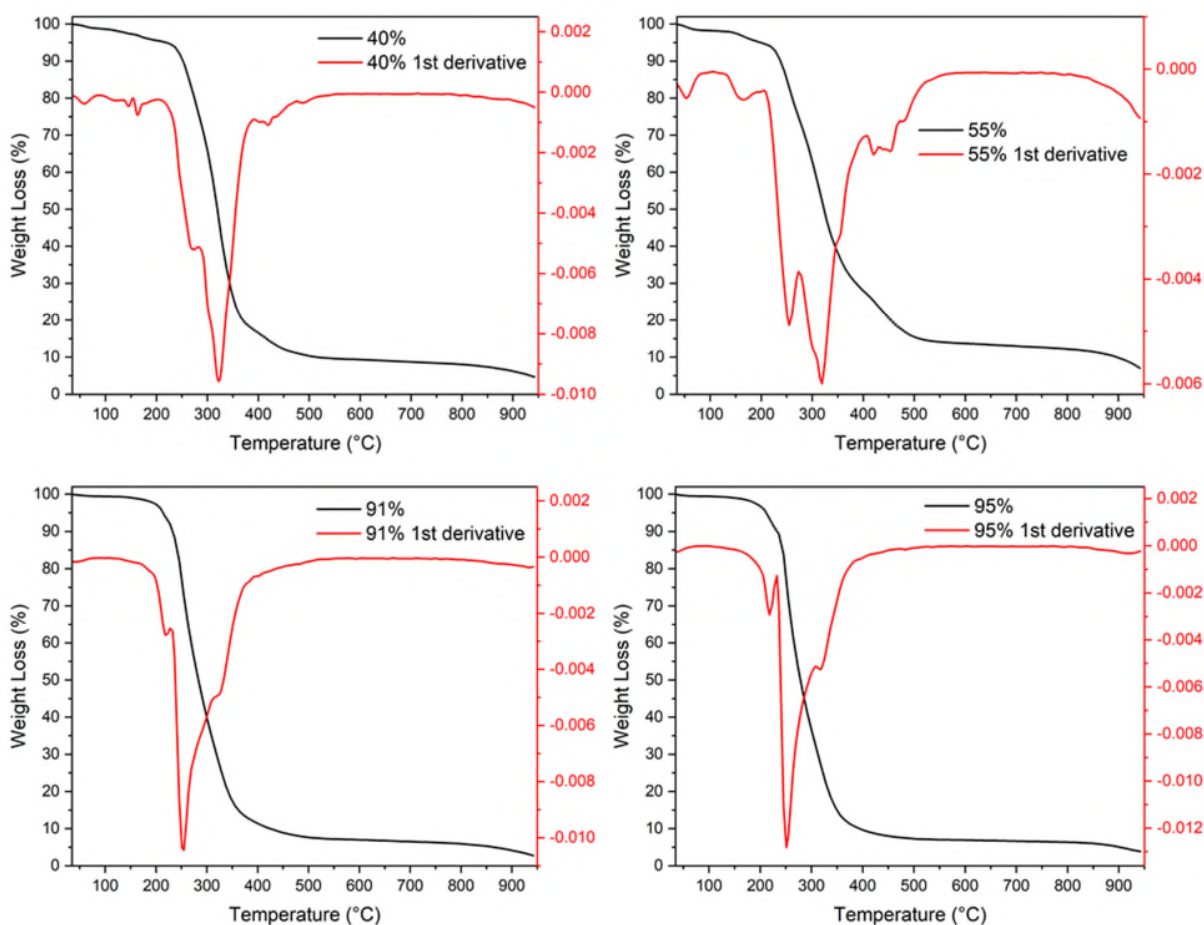


Figure S11. (continued)

Density Functional Theory Calculations

The density functional theory calculations were performed with the Turbomole program package.¹ The B3LYP exchange-correlation functional² was employed along with the def2-TZVP basis set.³ To account for intramolecular dispersion effects, the Grimme D3 correction⁴ with the Becke-Johnson damping⁵ was applied. Solvent effects were considered through COSMO (COnductor-Like Screening-MOdel).⁶ The harmonic frequencies were obtained with the numforce module in Turbomole to avoid spurious imaginary frequencies in combination with COSMO. For the calculation of enthalpies and free energies (Figure S10), the usual scaling factor of 0.9614 was applied to the harmonic B3LYP frequencies.

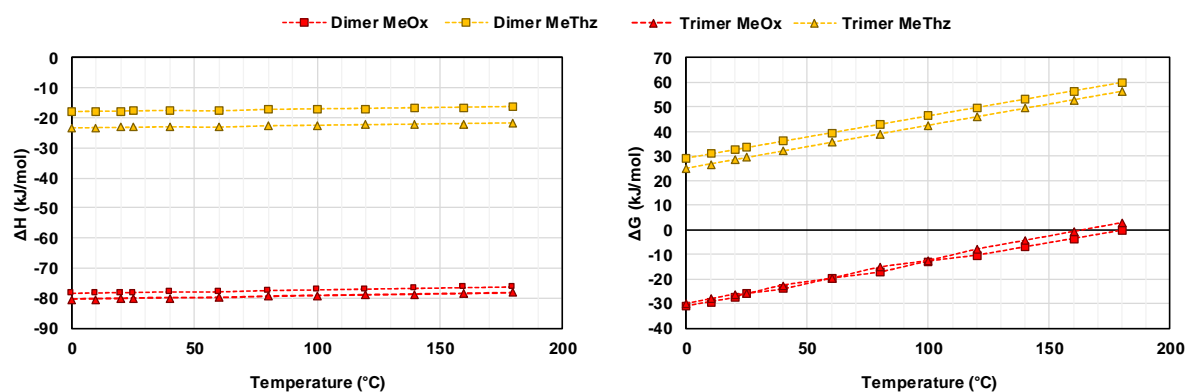


Figure S12. Variation of the enthalpy (left) and Gibbs free energies (right) of dimerization and trimerization for MeOx and MeThz in MeCN depending on the temperature.

In our calculations, we have considered the influence of the solvents through a continuum model that is determined by the dielectric constant alone. Within this approximation, the influence of the solvent on the reaction energies for both species lies within a few kJ/mol and does not explain the observation in the experimental setup (Figure S11).

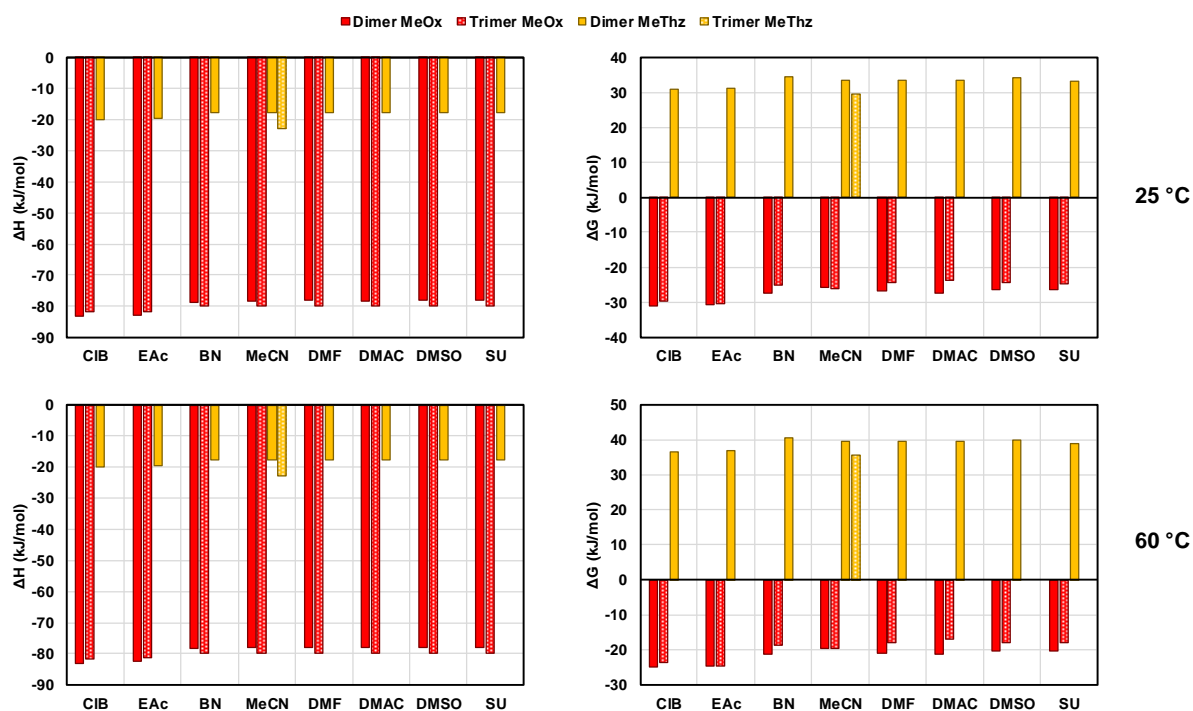


Figure S13. Variation of the enthalpy (left) and Gibbs free energy (right) of dimerization and trimerization for MeOx and MeThz at 25 °C (top) and 60 °C (bottom) for various solvents spanning low to high dielectric constants:⁷ CIB (chlorobenzene; 5.64), EAc (ethyl acetate, 6), benzene (25.59), MeCN (acetonitrile, 35.8), DMF (*N,N*-dimethylformamide, 37.65), DMAC (*N,N*-dimethylacetamide, 37.78), DMSO (dimethylsulfoxide, 40.82), SU (sulfolane, 43.3).

It is thus likely that the transition state involves a direct interaction with solvent molecules, thus lowering the activation energies for certain solvents. In the following, solvent effects are disregarded for simplicity. The transition state for the oxazoline dimerization is depicted in Figure S12. The Gibbs free energies along the full reaction coordinate in Figure S13 confirm an S_N2 mechanism with a reaction barrier of 85.6 kJ/mol and a reaction energy of -54.4 kJ/mol.

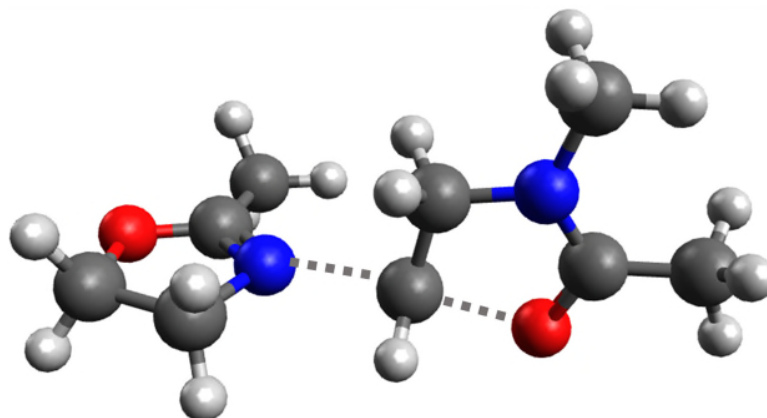


Figure S14. S_N2 transition state structure for the dimerization step of MeOx from DFT calculations at the B3LYP/def2-TZVP level with D3 dispersion and Becke-Johnson damping without solvent.

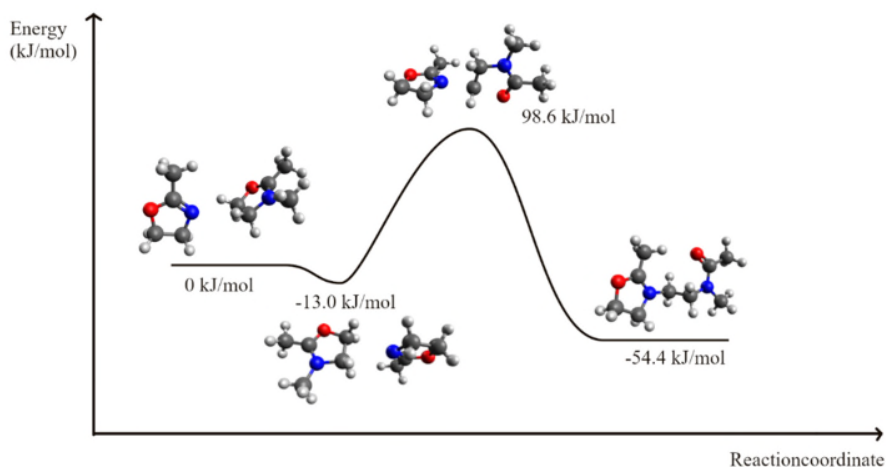


Figure S15. Gibbs free energy along the reaction path at 60 °C for the dimerization step of MeOx, obtained from DFT calculations at the B3LYP/def2-TZVP level with D3 dispersion and Becke-Johnson damping without solvent.

A direct comparison between the monomeric and dimeric structures of both compounds in Figure S14 reveals a significant difference: While the ring in the oxazoline is planar, it is slightly distorted in thiazoline. Consequently, the transition state structures could differ considerably which should be investigated in future studies.

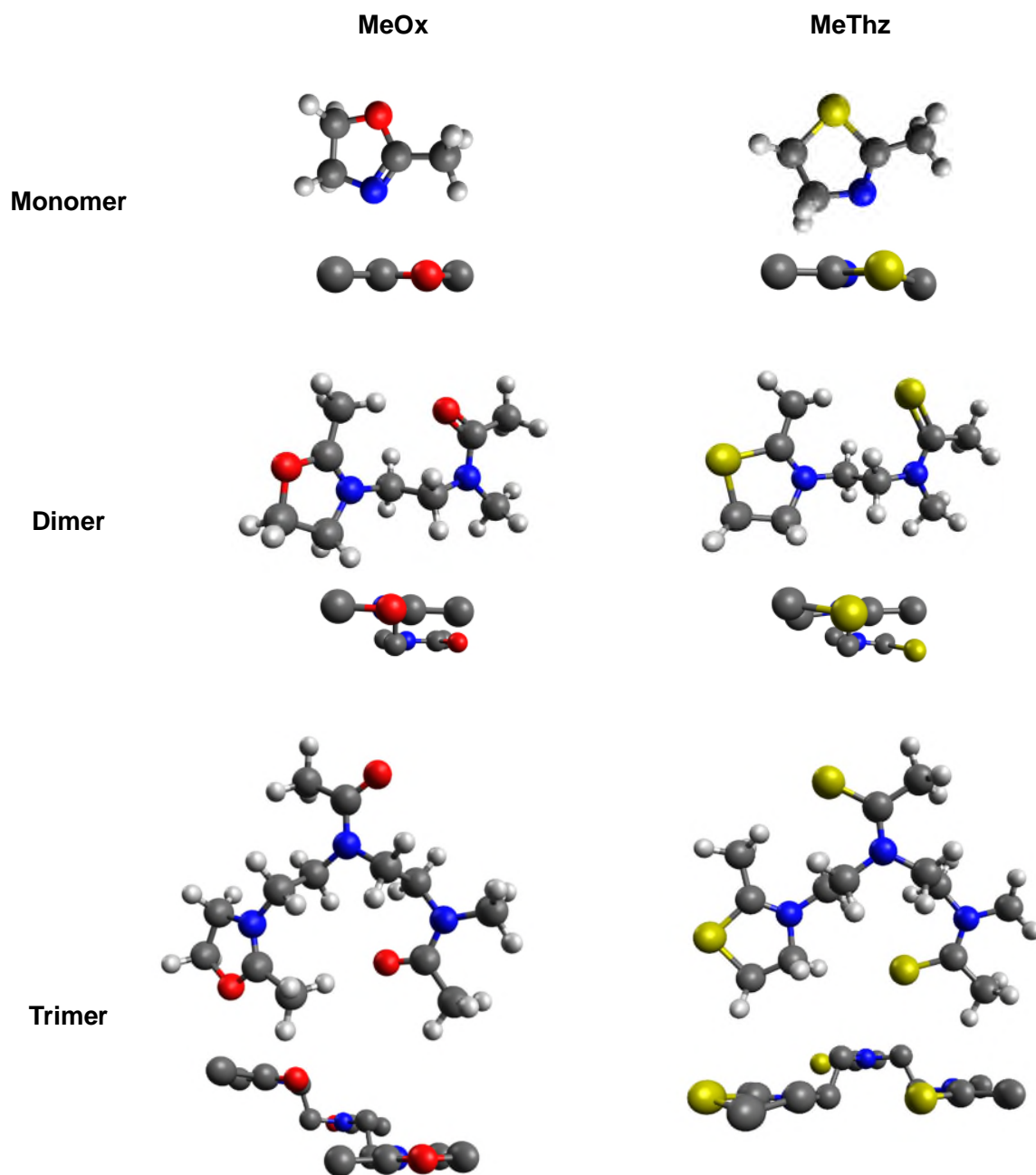


Figure S16. Structures of the MeOx and MeThz monomers, dimers, and trimers optimized at the B3LYP/def2-TZVP level with D3 dispersion and Becke-Johnson damping with DMAc as solvent. Full 3D structures are shown on top of side views of reduced (H-atoms removed for clarity) structures.

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