Supporting information

for

Well-defined linear and grafted poly(2-isopropenyl-2-oxazoline)s prepared *via* copper-mediated RDRP methods

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EXPERIMENTAL

Materials

2-Chloropropionitrile (CPN; Aldrich, 95%), methyl 2-chloropropionate (MCP; Aldrich, ≥99%), α-chlorophenylacetate (ECPA; Aldrich, 97%), ethyl 2-bromoisobutyrate (EBiB; Aldrich, 98%), CuCl (Aldrich, 99%), $CuCl_2$ (Aldrich, 99%), CuBr (Fluka, ≥ 98%), NaCl (p.a., Lach-Ner, Czech Republic), 1,1,4,7,10,10-hexamethyltriethylenetetramine (HMTETA; Aldrich, 97%), 2,2'-bipyridyl (bpy; Aldrich, ≥ 99%), Q-water (Millipore), dimethyl sulfoxide (DMSO; Aldrich, absolute, over molecular sieves), *N*-methylpyrrolidone (NMP; Acros Organics, 99.5 %, Extra dry), and *N,N*-dimethylacetamide (DMAc; Acros Organics, 99.5 %, Extra dry, over molecular sieves) were used as received. 2-Isopropenyl-2-oxazoline (IPOx; Aldrich, 98%) was distilled under reduced pressure and stored under argon at -20°C. Tris(2-pyridylmethyl)amine (TPMA) was synthesized as a yellow-brownish solid according to a literature protocol[1] and purified by repeated recrystallizations from diethyl ether and hexane to obtain a white crystalline product that was stored at 4°C. 1,1,4,7,7-Pentamethyldiethylenetriamine (PMDETA; Aldrich, 99%) was distilled under reduced pressure before use and kept under argon at 4°C. Tris[2-(dimethylamino)ethyl]amine (Me_6TREN) was synthesized and purified according to the literature[1] and kept under argon at 4°C. The solvents were bubbled with argon for at least 1 hour and stored under argon. The CuCl catalyst was stored under argon to avoid its oxidation and to ensure experimental reproducibility.

Cu(0)-RDRP of IPOx

In a typical experiment, CuCl (9.4 mg, 0.0954 mmol), $CuCl_2$ (6.4 mg, 0.0477 mmol), and TPMA (41.5 mg, 0.1431 mmol) were placed into a reaction flask equipped with a magnetic stirring bar and a three-way stopcock connected to an argon/vacuum inlet. After thorough de-oxygenation by several vacuum-argon

cycles, degassed water solution of NaCl (0.67 M, 1 mL) was added, and the green mixture containing dark brown precipitate was stirred for 30 min. Afterwards, IPOx (1 mL, 9.538 mmol) was added, which made the mixture turn light green, turbid, with the brown precipitate dissolving quickly. Then, the polymerization was started by adding the CPN stock solution in DMSO (10% (v/v), 84 µL, 0.0954 mmol). The clear, light blue mixture was stirred at r.t. for 26 h. Then, a sample was removed for the determination of conversion by NMR, and the solidified mixture was diluted with 4 mL of water and dialyzed (MWCO = 1 000) overnight with several water exchanges. After freeze drying, PIPOx was obtained as a white powder having no perceptible discoloration.

Synthesis of PIPOx-based macroinitiators

The synthesis of CPA-modified PIPOx is given as an example. In a reaction flask equipped with a magnetic stirring bar and a three-way stopcock connected to an argon/vacuum inlet, CPA (97 µL, 1.125 mmol) was added to a solution of PIPOx (0.25 g, 2.249 mmol of monomeric units) in 2 mL of dried NMP. The mixture was stirred at 60°C (oil bath) for 5 h. Then, the product was precipitated in diethyl ether, collected on a frit, washed thoroughly by diethyl ether, and dried in vacuum at room temperature (r.t.).

ATRP grafting of PIPOx-based macroinitiators

The grafting of styrene is given as an example. In a reaction flask, equipped with a magnetic stirring bar and a three-way stopcock connected to an argon/vacuum inlet, DMAc (5 mL) and styrene (5 mL, 43.49 mmol) were added to the macroinitiator (PIPOx modified with CPA, DS = 20 %, average MW = 132.84 per monomeric unit, 48.1 mg, 0.07249 mmol of initiation sites), CuCl (7.2 mg, 0.07249 mmol), and $CuCl_2$ (4.9 mg, 0.03625 mmol). The polymerization was started by the addition of PMDETA (23 µL, 0.1087 mmol), and the flask was immersed into an oil bath pre-heated to 100°C for 18 h. After cooling down to room temperature, the clear, greyish blue, slightly viscous mixture was diluted with 5 mL of THF and precipitated in methanol. The precipitate was filtered, washed with methanol, and dried at 30°C in vacuum. Monomer conversion (15 %) was determined gravimetrically. For SEC analysis, the grafts were released from the copolymer under alkaline conditions following a literature procedure.[2]

Characterization

The number-average molecular weights (M_n), weight-average molecular weights (M_w), and dispersity ($Đ$) of the polymers were determined using two systems: 1) Size-exclusion chromatography (SEC) system Shimadzu equipped with an RI detector and two PSS GRAM-type columns (8×300 mm; Polymer Standards Services GmbH, Mainz, Germany). The system was operated in DMAc + 0.1 % LiBr at the flow rate of 1 mL/min and r.t. PMMA (Polymer Standards Services GmbH) calibration was used. 2) SEC-MALS system combining the Shimadzu HPLC system equipped with a Superose 12 column and an online UV detector (Shimadzu), a differential refractive index detector Optilab T-rEX, and a multi-angle light scattering detector DAWN® HELEOS II (Wyatt Technology, USA). The flow rate of the mobile phase (0.3 M sodium acetate buffer (pH 6.5) with 1 g/L of sodium azide) was 0.5 mL/min. The ASTRA software was used for the calculation of molecular weights using the refractive index increment dn/dc = 0.1761 mL/g

determined with a Brookhaven Instruments BI-DNDC differential refractometer. ^{1}H NMR spectra were measured in DMSO-d6 (monomer conversion determination) or $CDCl_3$ (polymer characterization) using a Bruker DPX 300 spectrometer at 300.1 MHz.

Table S1. Cu(0)-RDRP of IPOx in water at M/I = 100:1 (30 min disproportionation, r.t., solvent/M = 1:1 v/v)

No.	Initiation and catalytic system	Stoichiometry	Time (h)	Conv. (%)[a]	M_n (theor.)[b]	M_n (SEC)[c]	$Đ$[c]
1	CPN/CuCl/ Me_6TREN	1/1/1	48	78	8 700	16 700	1.40
2	CPN/CuCl/PMDETA	1/1/1	72	61	6 800	18 100	2.02
3[d]	CPN/CuCl/TPMA	1/1/1	48	97	10 800	20 100	1.55
4[e]	CPN/CuCl/TPMA	1/1/1	24	71	7 900	4 800	10.77[f]
5	CPN/CuBr/TPMA	1/1/1	48	63	7 000	14 800	4.63[f]
6	EBiB/CuCl/TPMA	1/1/1	72	23	2 600	7 100	2.86[f]
7[g]	CPN/CuCl/TPMA	1/1/1	144	96	10 700	12 300	1.56
8[h]	CPN/CuCl/TPMA	1/1/1	144	13	1 400	3 500	1.22

[a] Determined by ^{1}H NMR.

[b] Theoretical M_n calculated from the M/I ratio and conversion.

[c] Determined by SEC in DMAc with PMMA calibration.

[d] The product had bimodal SEC trace. However, a sample collected at 24 h showed a unimodal MWD with much lower dispersity of 1.21 at 58% conversion. Therefore, the bimodality could result from recombination reactions occurring at higher conversions.

[e] Conducted at 60 °C.

[f] Bimodal SEC trace.

[g] H_2O/IPOx = 3:1 (v/v).

[h] Conducted in H_2O/DMSO = 1:1 (v/v).

Table S2. Cu(0)-RDRP of IPOx in water/NaCl mixtures at M/I = 100:1 (30 min disproportionation, r.t., solvent/M = 1:1 v/v)

No.	Initiation and catalytic system	Stoichiometry	Solvent	Time (h)	Conv. (%)[a]	M_n (theor.)[b]	M_n (SEC)[c]	$Đ$[c]	IE (%)[d]
1[e]	CPN/CuCl/$CuCl_2$/TPMA	1/1/0.5/1.5	0.67 M NaCl	21	85	9 400	22 600	1.19	42
2	CPN/CuCl/$CuCl_2$/TPMA	1/1/0.5/1.5	1 M NaCl	19	>99	11 100	24 100	1.25	46
3[f]	CPN/CuCl/$CuCl_2$/TPMA	1/1/0.5/1.5	1 M NaCl	30	94	10 500	24 200	1.53	nd
4[g]	CPN/CuCl/$CuCl_2$/TPMA	1/1/0.5/1.5	1 M NaCl	23	99	11 000	29 200	1.44	nd
5	CPN/CuCl/$CuCl_2$/bpy	1/1/0.5/1.5	1 M NaCl	72	63	7 000	11 600	1.51	nd
6	ECPA/CuCl/$CuCl_2$/TPMA	1/1/0.5/1.5	0.67 M NaCl	28	80	8 900	23 900	1.33	nd
7	MCP/CuCl/$CuCl_2$/TPMA	1/1/0.5/1.5	0.67 M NaCl	36	84	9 300	35 300	1.49	nd
8	CPN/CuCl/$CuCl_2$/TPMA	1/0.8/0.7/1.5	0.67 M NaCl	98	29	3 200	5 600	1.11	57
9	CPN/CuCl/$CuCl_2$/TPMA	1/0.9/0.6/1.5	0.67 M NaCl	23	94	10 400	19 300	1.34	nd
10	CPN/CuCl/$CuCl_2$/TPMA	1/2/1/3	0.67 M NaCl	36	11	1 200	27 200	1.81	nd

[a] Determined by ^{1}H NMR.

[b] Theoretical M_n calculated from the M/I ratio and conversion.

[c] Determined by SEC MALS in acetate buffer.

[d] Initiation efficiency calculated as the ratio of M_n(theor.) and M_n(SEC). Determined only for samples with low dispersity.

[e] Cooled to 0 °C during the first 15 min of polymerization.

[f] 1M NaCl/IPOx = 3:1 (v/v).

[g] No disproportionation period.

In a series of experiments collected in **Table S2**, we attempted at further optimizing the polymerization conditions. Firstly, we tried to introduce a cooling period during the initial stages of polymerization (entry 1) as decreased temperature has been previously shown to have a beneficial effect on polymerization control in aqueous Cu-RDRP.[3-5] Unfortunately, this approach did not bring a substantial improvement in the present system. Note though that the cooling period had to be rather short (15 min) because the polymerization mixture tended to solidify soon after it was placed into an ice bath. In another experiment, we tried to increase the concentration of the salt in the polymerization medium (1 M NaCl). This, however, had rather negligible influence on the course of polymerization and the shape of the SEC trace (entry 2). Interestingly, higher dilution of the polymerization mixture resulted into high dispersity (entry 3), corroborating the results obtained in neat water. Furthermore, we confirmed that the disproportionation period is necessary for the polymerization control. When the monomer and the

initiator were added immediately after the solvent, the control was lost as illustrated by the increased dispersity (entry 4). In the following experiments, we studied the influence of changes to the catalytic/initiation system. In the entry 5 experiment, we replaced TPMA with its linear analogue, 2,2'-bipyridine (bpy). However, this resulted into a considerably slower polymerization reaching only 63% conversion in 3 days, and dispersity was high (1.51). Further, we replaced CPN with a more active initiator, ethyl α-chlorophenylacetate (ECPA), that represents a chlorine-based analogue of methyl α-bromophenylacetate, introduced by Haddleton and coworkers as a "universal" initiator for styrene, acrylates, and methacrylates.[6] In our system, ECPA provided relatively high conversion of 80 %, but dispersity was slightly higher than with CPN (entry 6). On the other hand, the replacement of CPN with methyl 2-chloropropionate (MCP), a less active, widely utilized, chlorine-based initiator, led to a more significant dispersity increase to 1.49 (entry 7). In the following three experiments, we utilized alternative stoichiometries that have been shown to provide controlled polymerization in aqueous Cu(0)-RDRP.[3] The CPN/CuCl/$CuCl_2$/TPMA = 1/0.8/0.7/1.5 stoichiometry yielded a polymer of very low dispersity (1.11), but the polymerization stopped at the conversion of just 29 % (entry 8). Interestingly, a slight increase in the concentration of CuCl at the expense of the $CuCl_2$ deactivator resulted into a much faster polymerization reaching 94% conversion in 23 h, but the $Đ$ value increased to 1.34 (entry 9). Finally, the experiment involving doubled concentration of the catalytic system (CPN/CuCl/$CuCl_2$/TPMA = 1/2/1/3) afforded only very low conversion in an uncontrolled process (entry 10). It is noteworthy that, with the exception of entry 7, all the polymers from **Table S2** showed SEC MALS elugrams of similar shape as that presented in **Figure 1**.

Table S3. Cu(0)-RDRP of IPOx with MCP and HMTETA at M/I = 100:1 (30 min disproportionation, r.t., solvent/M = 1:1 v/v)

No.	Initiation and catalytic system	Stoichiometry	Solvent	Time (h)	Conv. (%)[a]	M_n (theor.)[b]	M_n (SEC)[c]	$Đ$[c]
1	MCP/CuCl/HMTETA	1/1/1	0.67 M NaCl	3.5	96	10 700	24 700	1.67
2	MCP/CuCl/$CuCl_2$/HMTETA	1/1/0.5/1.5	0.67 M NaCl	3.5	93	10 300	24 700	1.61
3	MCP/CuCl/$CuCl_2$/HMTETA	1/1/0.5/1.5	H_2O	3	97	10 800	26 300	1.67
4	MCP/CuCl/$CuCl_2$/HMTETA	1/0.8/0.7/1.5	0.67 M NaCl	5	84	9 300	32 300	1.63
5[d]	MCP/CuCl/$CuCl_2$/HMTETA	1/0.8/0.7/1.5	0.67 M NaCl	5	82	9 100	39 300	1.62
6	MCP/CuCl/$CuCl_2$/HMTETA	1/2/1/3	0.67 M NaCl	3.5	98	10 900	22 900	1.60

[a] Determined by ^{1}H NMR.

[b] Theoretical M_n calculated from the M/I ratio and conversion.

[c] Determined by SEC MALS in acetate buffer.

[d] 0.67 M NaCl/IPOx = 3:1 (v/v).

Table S4. Optimization of the synthesis of ATRP macroinitiators from PIPOx

No.	Acid (eq.)	PIPOx[a]		Solvent	Temp. (°C)	Time (h)	DS[b]	M_n[c]	$Đ$[c]
		M_n	$Đ$						
1	CPA (0.5)	22 900	1.60	NMP	60	24	36	55 500	3.84
2	CPA (0.5)	26 300	1.67	NMP	r.t.	24	2	26 000	1.76
3	CPA (4)	26 300	1.67	NMP	50	5	25	36 300	2.15
4	CPA (0.5)	26 300	1.67	NMP	60	5	15	31 100	1.78

[a] Characteristics of the starting PIPOx polymers as obtained by SEC MALS.

[b] Degree of substitution as determined by ^{1}H NMR analysis.

[c] Characteristics of the product as determined by SEC in DMAc (PMMA calibration; apparent values).

In the experiment shown in entry 1, we modified a higher-dispersity PIPOx (from entry 6, **Table S3**) with 0.5 eq. of CPA at the same conditions as in the analogous experiment with BIBA (entry 3, **Table 3**). This led to the DS of 36 % in 24 h, showing that the modification efficiency (ca 70 %) was not influenced by changing the carboxylic acid. Unfortunately, also with CPA a clearly bimodal SEC trace was obtained, and the product dispersity was high (3.84), probably due to the high dispersity of the starting PIPOx. Subsequently, we investigated the possibility of performing the modification at r.t. (entry 2). As could be expected, the reaction proceeded extremely slowly at this temperature, yielding a product with DS of just 2 %. In another experiment (entry 3), we tried to decrease the temperature to 50°C while increasing CPA concentration to 4 eq. at the same time, obtaining a product with the DS of 25 % and a SEC curve showing only a hint of bimodality. Notably, we finally managed to obtain a product with a unimodal SEC trace and the DS of 15 % when we applied the conditions employed previously in entry 1, only with shorter reaction time of 5 h (entry 4). This highlights that the presumed side reactions may be largely suppressed at shorter reaction times. It should be also mentioned that the product dispersity was only slightly higher than that of the starting PIPOx (1.78 vs. 1.67, respectively).

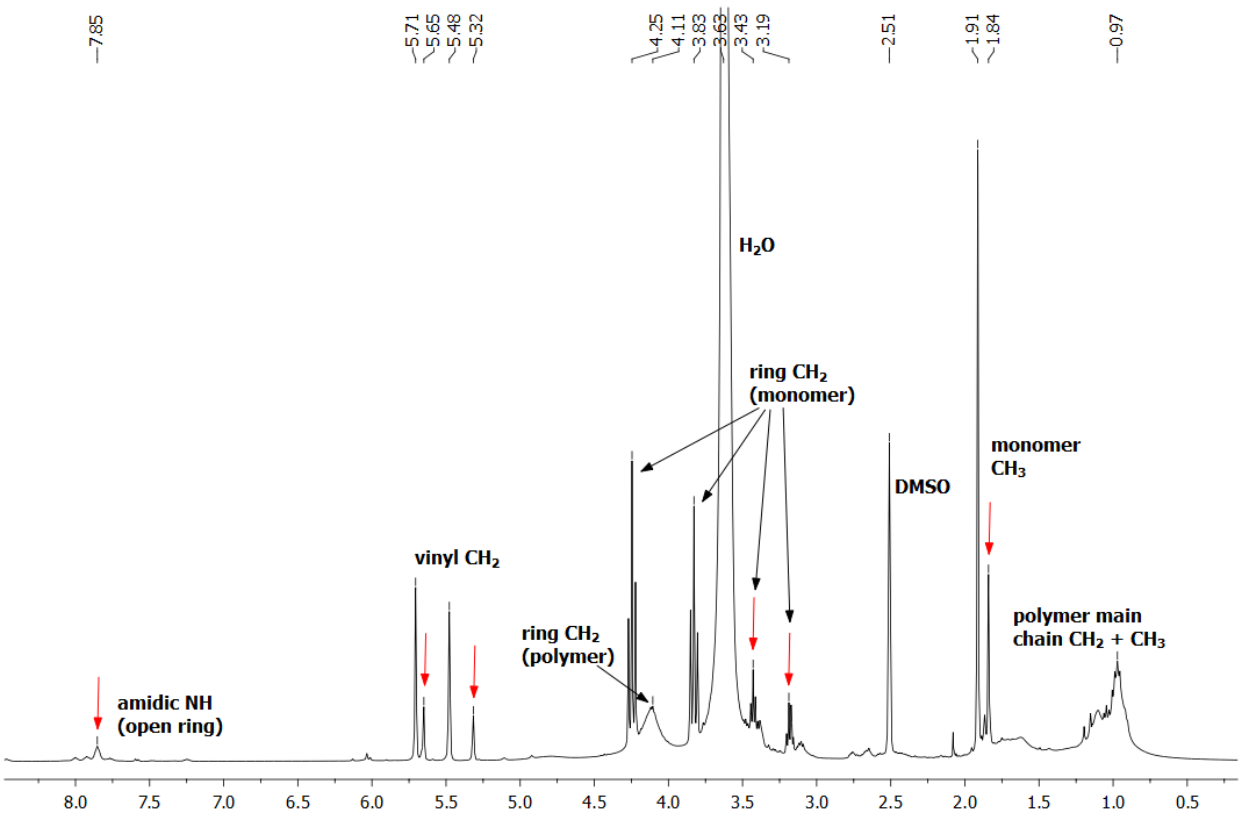

Figure S1. ^{1}H NMR of the polymerization mixture from entry 4, Table S1 (measured in DMSO-d6). The signals assigned to the hydrolyzed IPOx are marked by red arrows. Note that one signal of the ring CH_2 in polymer is completely overlapped by the signal of water.

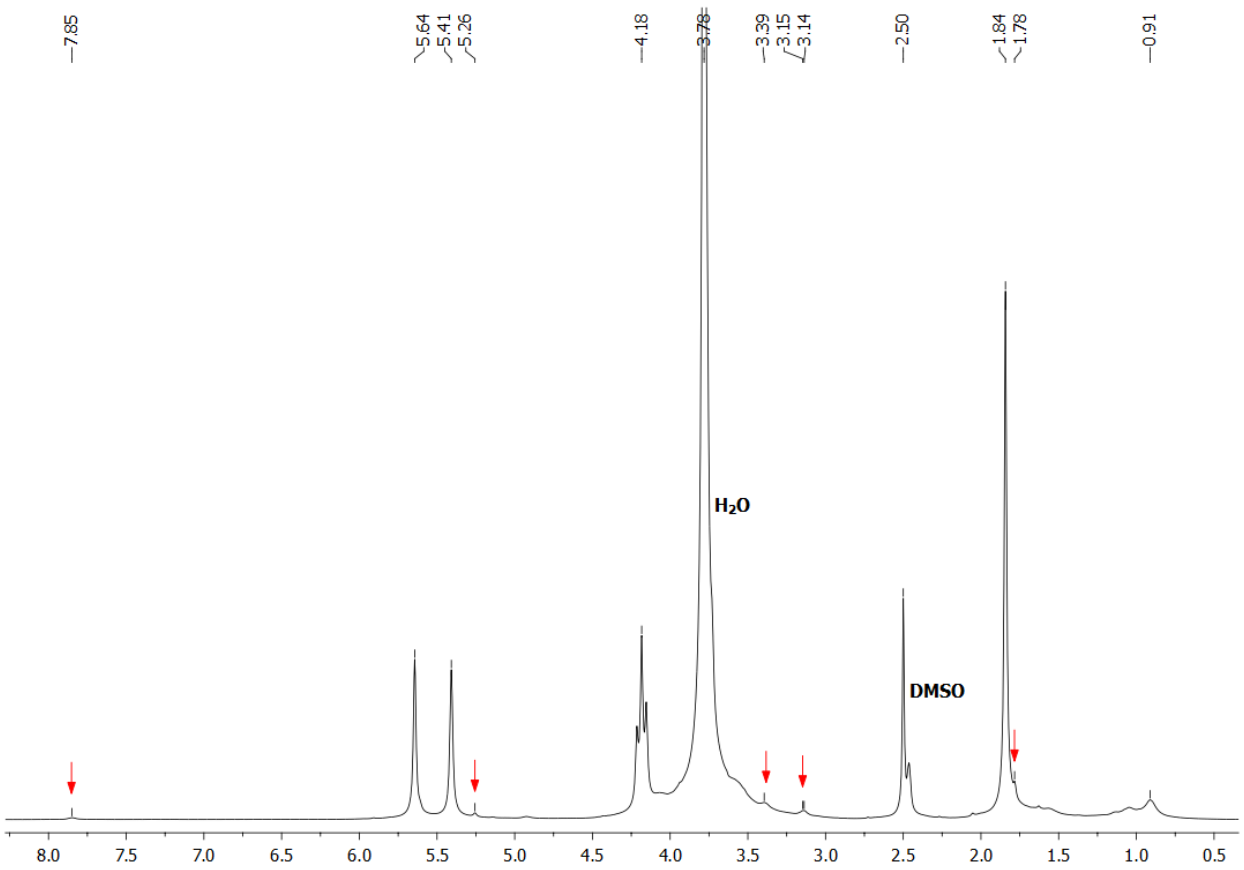

Figure S2. ^{1}H NMR of the polymerization mixture from entry 6, Table 1 (measured in DMSO-d6). The weak signals assigned to the hydrolyzed monomer are marked by red arrows.

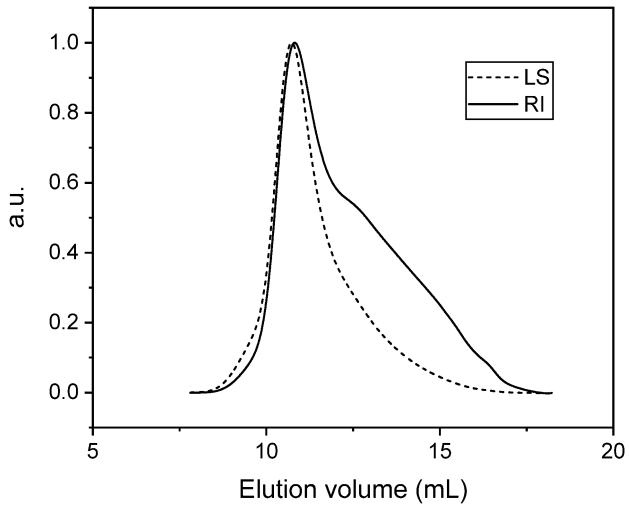

Figure S3. SEC MALS elugram of PIPOx shown in entry 5, Table 2.

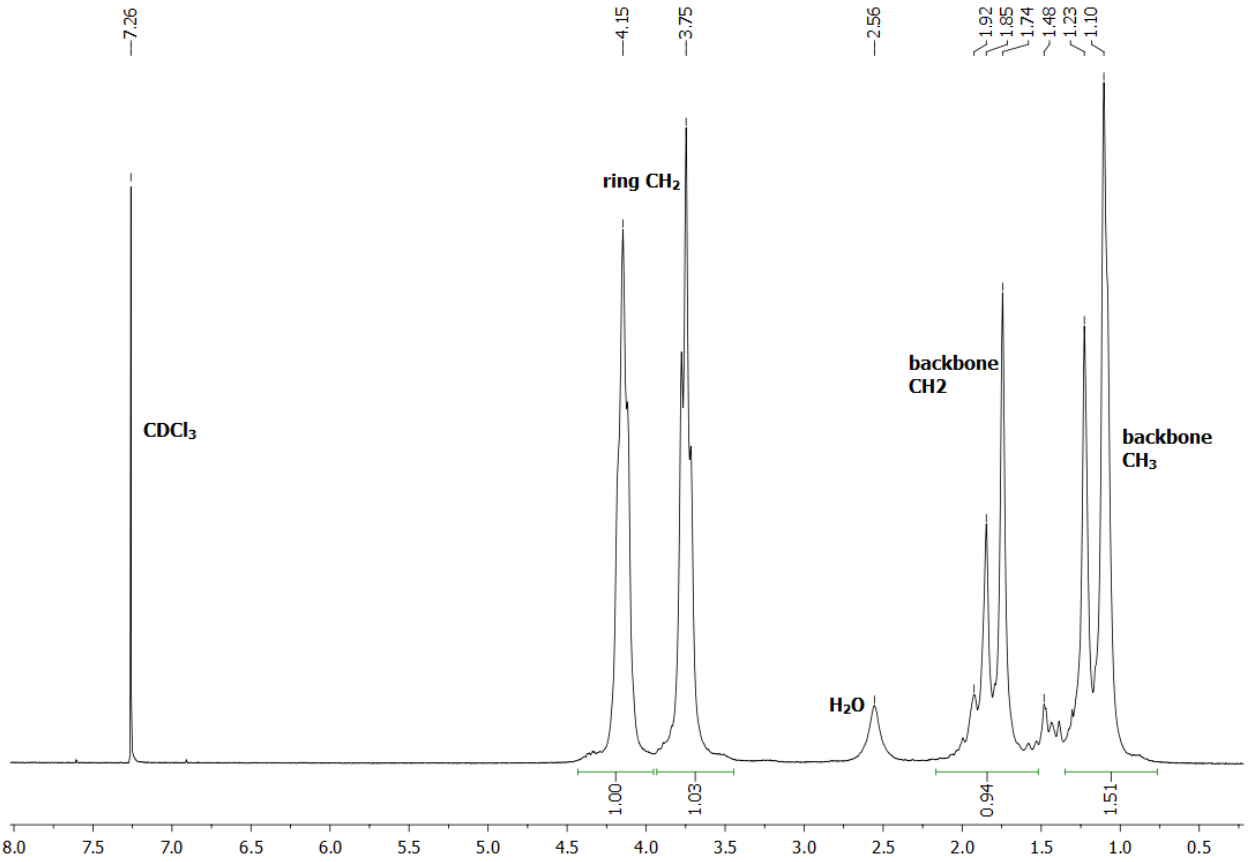

Figure S4. ^{1}H NMR of the isolated PIPOx polymer (measured in $CDCl_3$). Note that the signal at 2.56 ppm was identified as the signal of water. When ca 100 µl of water was added into the NMR cuvette, the intensity of the signal at 2.56 ppm increased considerably, and an additional signal at 4.78 ppm appeared. This highlights the strong interaction of PIPOx with water.

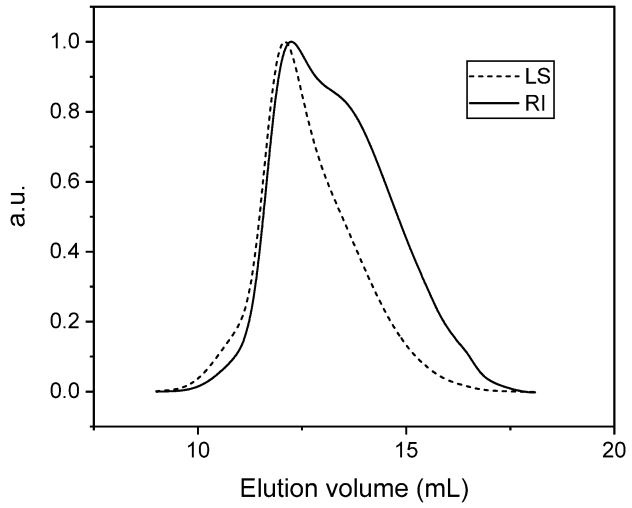

Figure S5. SEC MALS elugram of PIPOx from entry 7, Table 2.

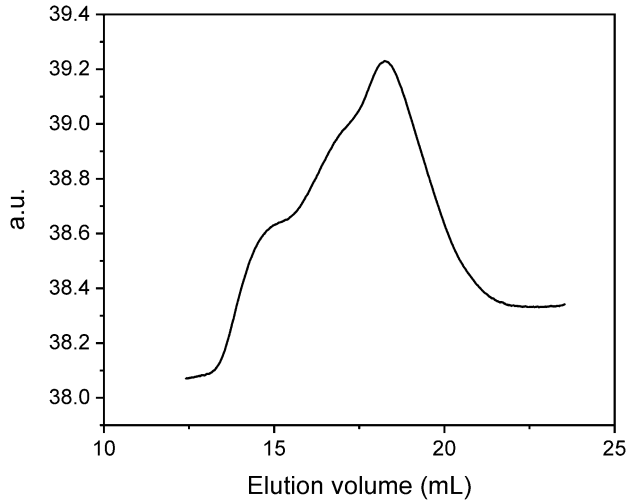

Figure S6. SEC elugram of the PIPOx-based macroinitiator shown in entry 2, Table 3.

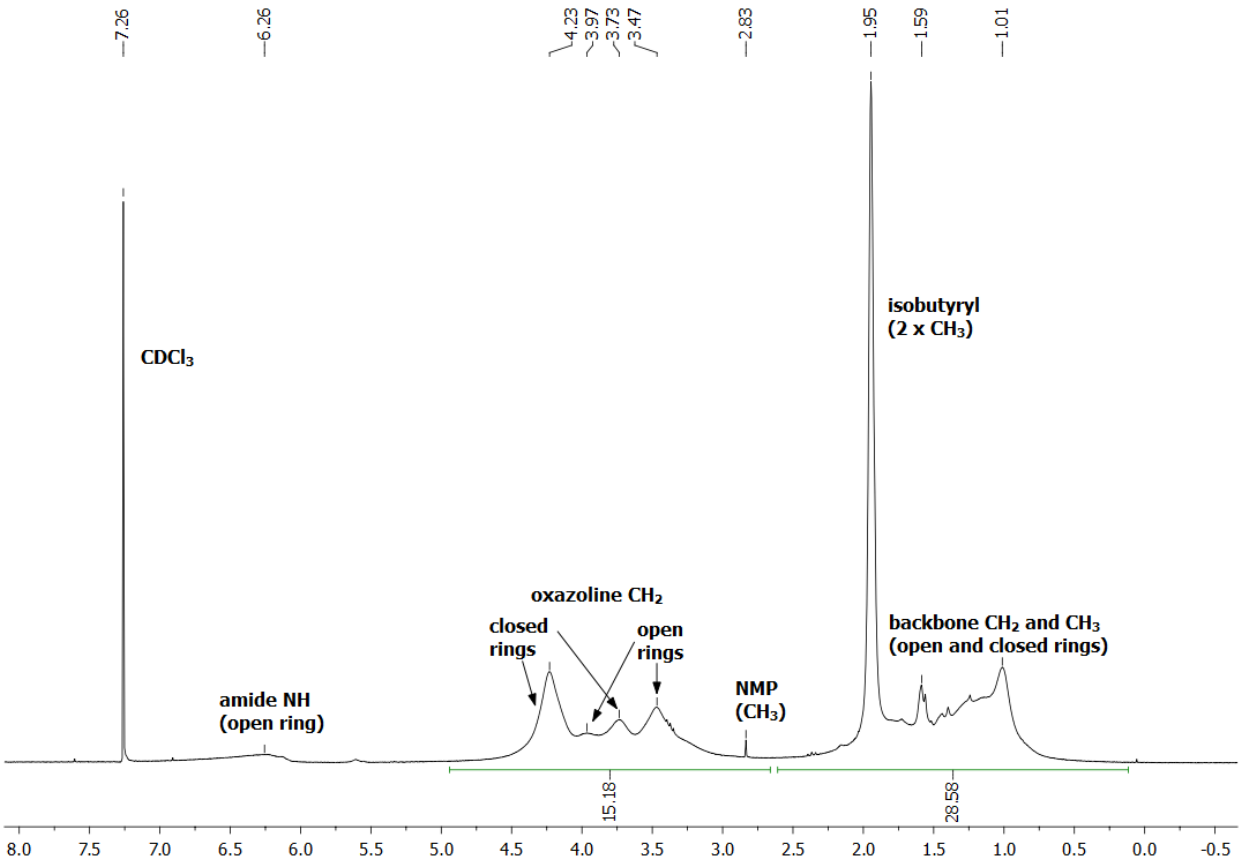

Figure S7. ^{1}H NMR spectrum of the isolated PIPOx-based macroinitiator (modification by BIBA) shown in entry 3, Table 3. The spectrum was measured in $CDCl_3$. For the calculation of the degree of substitution (DS), the total intensity of the backbone signals (5 H) was estimated from the total intensity of the oxazoline signals (4 H), based on which, the intensity of the overlapping isobutyryl signal (6 H) was determined. The contribution of the low-intensity signals of NMP (partially overlapping with the polymer signals) was found to be negligible and was thus neglected. The accuracy of this determination was confirmed by an independent calculation based on the data from the elemental analysis of the product.

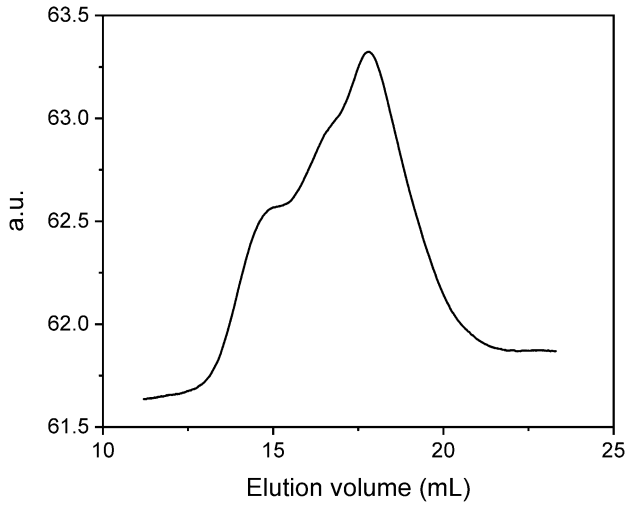

Figure S8. SEC elugram of the macroinitiator shown in entry 3, Table 3.

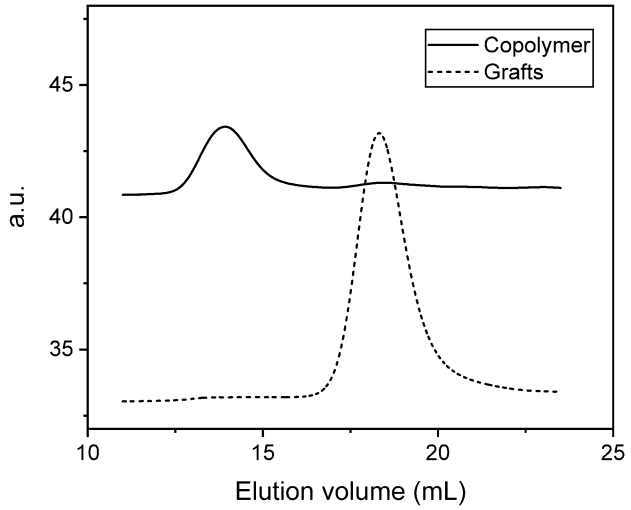

Figure S9. SEC elugrams of the PIPOx-*graft*-PS copolymer shown in entry 3, Table 4 and of the PS grafts released from the copolymer under alkaline conditions. The SEC analysis was performed in DMAc.

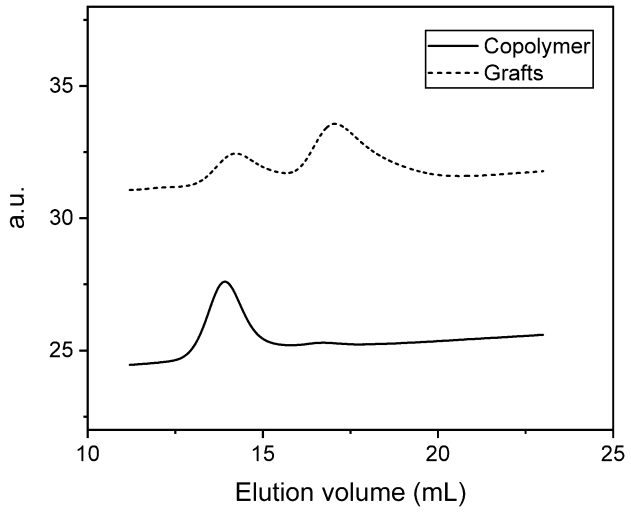

Figure S10. SEC elugrams of the PIPOx-*graft*-PMMA copolymer shown in entry 4, Table 4 and of the PMMA grafts released from the copolymer under alkaline conditions. The SEC analysis was performed in DMAc.

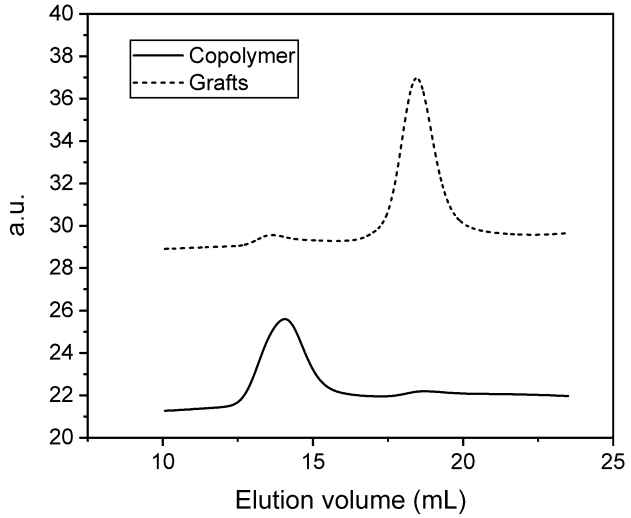

Figure S11. SEC elugrams of the PIPOx-*graft*-PS copolymer shown in entry 5, Table 4 and of the PS grafts released from the copolymer under alkaline conditions. The SEC analysis was performed in DMAc.

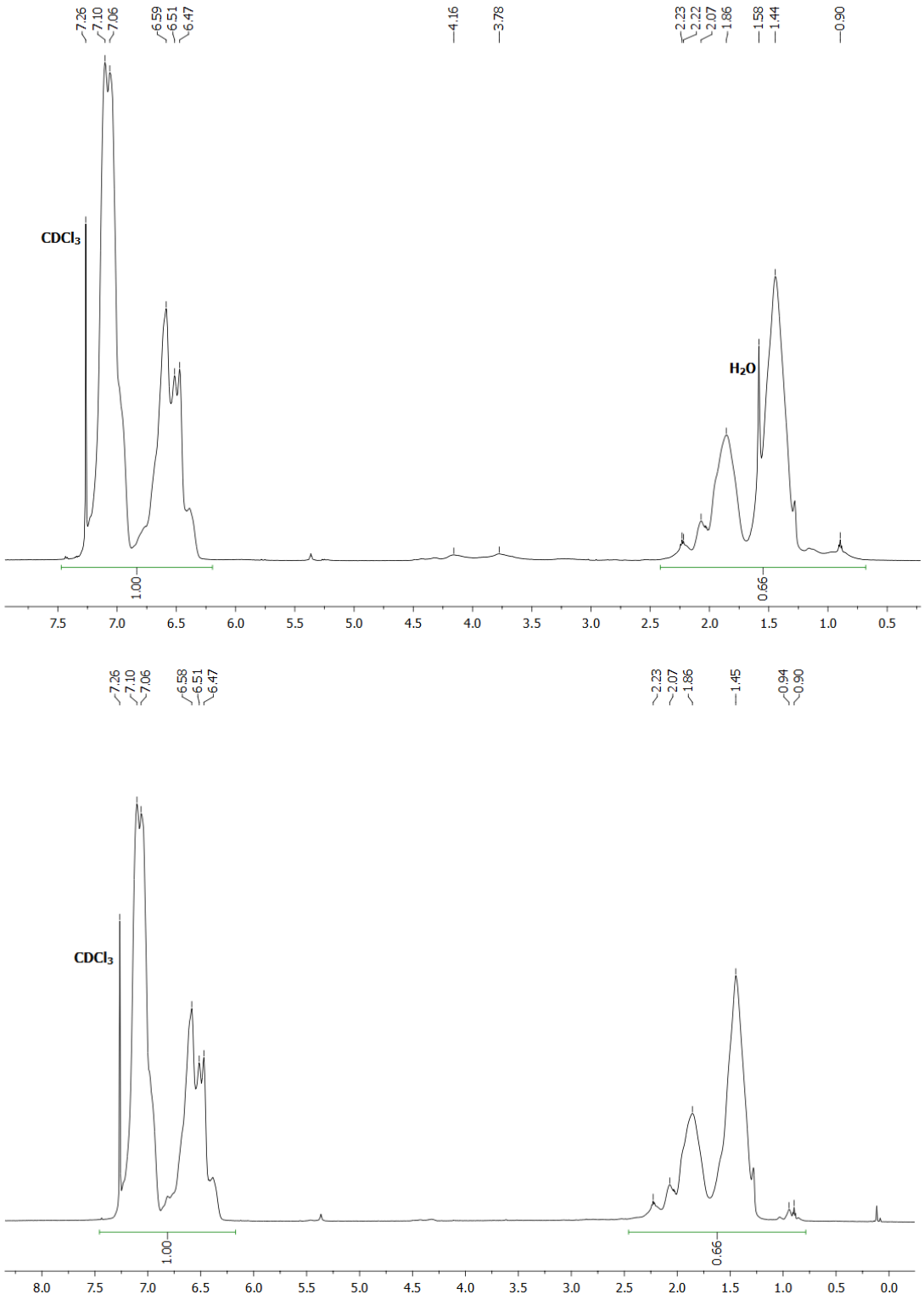

Figure S12. [1]H NMR spectra of the PIPOx-*graft*-PS copolymer shown in entry 6, Table 4 (top) and of the PS grafts released from the copolymer under alkaline conditions (bottom).[2] The spectra were acquired in $CDCl_3$.

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