Thio-Click Modification of Poly[2-(3-butenyl)-2-oxazoline]

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ABSTRACT: The radical addition of mercaptans (RSH) onto poly[2-(3-butenyl)-2-oxazoline], which is available through a living/controlled cationic isomerization polymerization, can proceed smoothly in the absence of side reactions, exhibiting the characteristics of a click reaction. The "thio-click" reaction can be performed under feasible ([RSH]/[C═C] ~ 1.2−1.5, no transition metal additives) and mild conditions (generation of radicals with UV light at room temperature) and goes to completion within a day. Hydrophobic fluoropolymers can be prepared in the same way as water-soluble (co-)polymers or glycopolymers, starting from readily available materials.

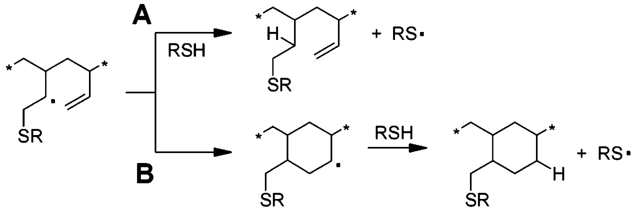
Introduction

Tailor-made polymers are key materials in many fields like for instance materials science[1,2] and biomedicine.[3,4] Especially interesting are "smart" polymers with stimuli-responsive and adjustable properties.[5] Nowadays, there exist a number of synthetic tools for producing sophisticated polymers with well-defined composition, microstructure, functionality, and architecture. A most successful and versatile strategy involves growth of a polymer backbone through a controlled ionic, radical, or metathesis polymerization reaction and subsequent chemical modification, for instance through hydrolysis, esterification, alkylation,[1] or "click chemistry"[6−9] (refs 8 and 9 provide comprehensive reviews on this topic).

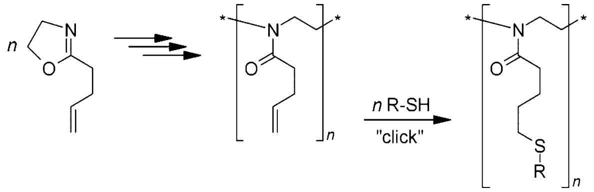
Click chemistry is a general concept introduced by Sharpless et al.,[6] which, however, is often reduced to the copper-catalyzed Huisgen 1,3-dipolar cycloaddition of azides and alkynes.[8] According to its original definition, a click reaction must be *modular, be wide in scope, give very high yields, generate only inoffensive byproducts, and be stereospecific (but not necessarily enantioselective*). Processes must therefore have a *high thermodynamic driving force*, like for instance carbon−heteroatom bond forming reactions. The most common examples comprise (I) cycloadditions of unsaturated species (Huisgen, but also Diels−Alder transformations[10]), (II) nucleophilic ring-opening of strained heterocyclic electrophiles, (III) carbonyl chemistry of the "non-aldol" type, and (IV) additions to carbon−carbon multiple bonds.[6] The above-mentioned hydrolysis, esterification, and alkylation reactions are thus no click reactions.

The radical addition of mercaptans (RSH) onto vinyl double bonds, on the other hand, could well be considered as a click reaction (type IV) as it can proceed smoothly in quantitative yields and be regioselective (anti-Markovnikov).[11,12] However, the modification of 1,2-polybutadienes with mercaptans suffers from a seemingly unavoidable side reaction of the intermediate radical species (see Scheme 1). The desired route is that the radical formed by the addition of RS• onto the double bond abstracts a hydrogen atom from another RSH molecule (pathway A). However, prior to hydrogen transfer, the radical may add to another double bond in its vicinity, leading to the formation of a six-member cyclic unit (pathway B). The degree of modification is therefore less than quantitative (<85%) at full conversion of double bonds.[13]

Scheme 1. Possible Reactions of the Intermediate Radical Species Formed by the Anti-Markovnikov Addition of RS• onto 1,2-Polybutadiene



Scheme 2. Synthesis and Click Modification of Poly[2-(3-butenyl)-2-oxazoline]



Our approach to eliminate the undesired pathway B is to increase the distance between intermediate radical and neighboring double bond, thus to replace 1,2-polybutadiene by for instance an unsaturated polyacrylate or poly[2-(3-butenyl)-2-oxazoline]. In this work, we report on the first synthesis and cationic isomerization polymerization of 2-(3-butenyl)-2-oxazoline and successful "thio-click" modification of poly[2-(3-butenyl)-2-oxazoline] with mercaptans (Scheme 2). For a proof of principle, poly[2-(3-butenyl)-2-oxazoline] homo- and copolymers of different molecular weights ($M_n = 3.0-10.9$ kg/mol) were reacted with five commercially available mercaptans exhibiting different functionality/polarity and sterics: methyl-3-mercaptopropionate, 1*H*,1*H*,2*H*,2*H*-perfluorooctanethiol, 3-mercapto-1,2-propanediol, thioacetic acid, and 2,3,4,6-tetra-*O*-acetyl-1-thio-*β*-D-glucopyranose. Polymer samples were characterized by means of NMR spectroscopy, Fourier-transform infrared spectroscopy (FT-IR), analytical ultracentrifugation (AUC), and size exclusion chromatography (SEC).[14]

Experimental Part

Chemicals. Chemicals and solvent were purchased from various suppliers and used, unless otherwise noted, as received. Acros: thioacetic acid (98%). Aldrich: 2-chloroethylamine hydrochloride (99%), *N*-hydroxysuccinimide (98%), methyl-3-mercaptopropionate (98%), methyl triflate (99%), 2-methyl-2-oxazoline (99%). Alfa

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Aesar: 4-pentonic acid (98%), 3-mercapto-1,2-propanediol (90+%). Iris Biotech: 1-(3-dimethylpropyl)-3-ethylcarbodiimide hydrochloride (EDAC, 99.4%). Fluka-Riedel-deHaën: dichloromethane (>99.9%), diethyl ether (>99.5%), methanol (>99.9%, over molecular sieve), tetrahydrofuran (THF, p.a.). Fluorochem Ltd.: 1*H*,1*H*,2*H*,2*H*-perfluorooctanethiol (99%). Glycon Biochemicals: 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranose (>99%). Merck: acetonitrile (>99.9%).

Monomer Synthesis. The synthesis of 2-(3-butenyl)-2-oxazoline involved three steps starting from 4-pentenoic acid (→ *N*-succinimidyl-4-pentenate → *N*-(2-chlorethyl)-4-pentenamide → 2-(3-butenyl)-2-oxazoline), based on a similar procedure described elsewhere.[15] (1) *N*-Succinimidyl-4-pentenate: To a solution of 16.0 g (0.160 mol) of 4-pentenoic acid in 800 mL of dry dichloromethane (distilled from CaH_2) were added 29.39 g (0.255 mol) of *N*-hydroxysuccinimide and 36.68 g (0.192 mol) of EDAC, and the mixture was stirred for 12 h at room temperature. After evaporation of the solvent, the residue was dissolved in a mixture of diethyl ether and water (3:1 v/v) and thereof extracted five times. After combined organic layers were dried with sodium sulfate, the solvent was removed to yield *N*-succinimidyl-4-pentenate as a colorless solid (yield: 27.72 g, 88%). (2) *N*-(2-Chloroethyl)-4-pentenamide: A solution of 27.72 g (0.141 mol) of *N*-succinimidyl-4-pentenate in 700 mL of dry dichloromethane was added drop by drop under vigorous stirring to a solution of 32.61 g (0.281 mol) of 2-chloroethylamine hydrochloride and 11.25 g (0.281 mol) of NaOH in 300 mL of deionized water. After being stirred overnight, the organic layer was separated and washed twice with 200 mL of deionized water. The combined fractions were dried over sodium sulfate and the solvent evaporated to give *N*-(2-chloroethyl)-4-pentenamide as a yellowish oil (yield: 19.94 g, 88%). ^1H NMR (400.1 MHz, $CDCl_3$): δ/ppm = 2.27−2.38 (m, 4H), 3.58 (m, 4H), 4.98−5.08 (m, 2H), 5.77−5.84 (m, 1H) 6.16 (bs, 1H). ^{13}C NMR (100.4 MHz, $CDCl_3$): δ/ppm = 27.50, 30.03, 54.50, 67.35, 115.51, 137.04, 168.05. (3) 2-(3-Butenyl)-2-oxazoline: In a flame-dried flask, 15.0 g (0.093 mol) of *N*-(2-chloroethyl)-4-pentenamide were dissolved in 50 mL of dry methanol. To this solution, a freshly ground solution of 5.21 g (0.093 mol) of KOH in 50 mL of dry methanol was added drop by drop. The reaction mixture was stirred for 12 h at 70 °C under an argon atmosphere (precipitation of KCl occurred after about 1 h). The salt was filtered off and the remaining solution was concentrated in vacuo. Additionally precipitated salt was removed by passing the solution through a 0.45 μm filter. For purification, the yellow solution was fractionally distilled at reduced pressure to give 2-(3-butenyl)-2-oxazoline as a colorless liquid ($bp^{20\ mbar}$: 67 °C; yield: 6.2 g, 53%). ^1H NMR (400.1 MHz, DMSO-d_6): δ/ppm = 2.28 (s, 4H), 3.68 (t, 2H, ^3J = 9.4 Hz), 4.15 (t, 2H, ^3J = 9.4 Hz), 4.96−5.08 (m, 2H), 5.80−5.86 (m, 1H). ^{13}C NMR (100.4 MHz, DMSO-d_6): δ/ppm = 26.6, 29.4, 53.9, 66.6, 115.0, 137.2, 166.1. MS: m/z = 125 ($M^{+\bullet}$, relative intensity: 16%), 124 (100%), 97 (23%), 69 (47%), 54 (30%).

Homopolymerization of 2-(3-Butenyl)-2-oxazoline. To a solution of 2.60 g (0.021 mol) of 2-(3-butenyl)-2-oxazoline in 7.4 mL of dry acetonitrile (freshly distilled from CaH_2) was added 0.076 mL (0.69 mmol) of methyl triflate under a dry argon atmosphere. The mixture was stirred for 24 h at 70 °C, followed by the addition of 0.1 mL (1.04 mmol) of piperidine at room temperature. After being stirred for another 5 h at 70 °C, the reaction mixture was submitted to dialysis against methanol (MWCO: 1 kDa) for 2 days. After evaporation of the solvent, the polymer (**2**) was collected in benzene and freeze-dried (gravimetric yield: 1.81 g, 70%). ^1H NMR (400.1 MHz, $CDCl_3$): δ/ppm = 1.09−1.42 (m, 0.1H), 2.06 (m, 0.1H), 2.34−2.43 (m, 4H), 2.95−3.01 (m, 0.1H), 3.44 (bs, 4H), 4.98−5.06 (m, 2H), 5.80−5.81 (m, 1H). ^{13}C NMR (100.4 MHz, $CDCl_3$): δ/ppm = 24.2, 26.0, 29.3, 32.1, 32.3, 43.7−47.4, 55.3, 115.6, 137.3, 172.5, 173.0. FT-IR: $\tilde{\nu}/cm^{-1}$ = 3076 (=CH_2 str), 2919 (C−H str), 1631 (C=O str, amide I), 1414 (CH_2−CO).

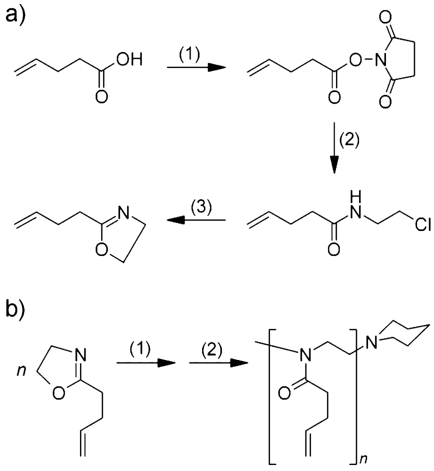
Copolymerization of 2-(3-Butenyl)-2-oxazoline and 2-Ethyl-2-oxazoline. To a mixture of 1.28 g (0.010 mol) of 2-(3-butenyl)-oxazoline and 2.66 g (0.031 mol) of 2-ethyl-2-oxazoline in 10 mL of dry acetonitrile (freshly distilled from CaH_2) were added 0.098 mL (0.89 mmol) of methyl triflate under a dry argon atmosphere. The mixture was stirred for 24 h at 70 °C, followed by the addition of 0.26 mL (2.68 mmol) of piperidine at room temperature. After being stirred for another 5 h at 70 °C, the reaction mixture was submitted to dialysis against deionized water (MWCO: 1 kDa) for 2 days. After evaporation of the solvent, the copolymer (**5**) was collected in water and freeze-dried (gravimetric yield: 2.0 g, 77%). ^1H NMR (400.1 MHz, $CDCl_3$): δ/ppm = 1.09 (bm, 2.1H), 2.36 (m, 2.9H), 2.94−3.00 (m, 0.1H), 3.43 (bs, 4H), 4.97−5.05 (m, 0.5H), 5.79−5.81 (m, 2.5H). FT-IR: $\tilde{\nu}/cm^{-1}$ = 3078 (=CH_2 str), 2938 (C−H str), 1629 (C=O str, amide I), 1419 (CH_2−CO).

Photoaddition of Mercaptan. To a ~4 wt % solution of 90 mg of poly[2-(3-butenyl)-oxazoline] (**1**) in 2.5 mL of dry THF (freshly distilled from Na/K alloy) in a glass vessel were added 93 μL (0.85 mmol) of methyl-3-mercaptopropionate (**a**, 1.2 equiv with respect to double bonds). The mixture was degassed twice, put under an argon atmosphere, and exposed to UV light (source: Heraeus TQ 150, 150 W, emphasis of intensity at λ = 303 nm) for 24 h. The polymer solution was then directly submitted to exhaustive dialysis against methanol (MWCO: 1 kDa). After evaporation of the solvent, the polymer (**1a**) was dissolved in benzene and freeze-dried (gravimetric yield: 79 mg, 88%).

Photoadditions of 1*H*,1*H*,2*H*,2*H*-perfluorooctanethiol (**b**), thioacetic acid (**d**), and 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranose (**e**) onto poly[2-(3-butenyl)-oxazoline]s (**2**−**4**) were carried out likewise, that of 3-mercapto-1,2-propanediol (**c**) was done in a THF/methanol 1/1 (v/v) mixed solvent. The modification of poly[(2-(3-butenyl)-2-oxazoline)-*co*-(2-ethyl-2-oxazoline)] (**5**) with 3-mercapto-1,2-propanediol (**c**) occurred in a THF/methanol 3/2 (v/v) mixed solvent; polymer concentration was ~8 wt % and the mercaptan was used in 50% excess with respect to double bonds. The polymer solution was dialyzed against deionized water (MWCO: 1 kDa) and the copolymer (**5c**) isolated by freeze-drying (gravimetric yield: 269 mg, 92%).

Analytical Instrumentation and Methods. ^1H NMR measurements were carried out at room temperature using a Bruker DPX-400 spectrometer operating at 400.1 MHz (^{13}C NMR: 100.4 MHz). $CDCl_3$, DMSO-d_6, and D_2O were used as solvents (Deutero GmbH, Germany); signals were referenced to the signal of solvent at δ = 7.26 (77.0), 2.50 (39.5), and 4.79 ppm, respectively. FT-IR spectra were recorded on a BioRad 6000 FT-IR; samples were measured in the solid state using a Single Reflection Diamond ATR. Gas chromatography−mass spectrometry (GC-MS) analysis was carried out on Agilent Technologies GC 6890N Series with a MS detector 5975. Differential scanning calorimetry (DSC) was performed on a Netzsch DSC 204 Phoenix. Measurements were done under nitrogen atmosphere at a heating/cooling rate of 10 K/min; glass transition temperature was determined from the second heating curve. Size-exclusion chromatography (SEC) with simultaneous UV and RI detection was performed (i) in THF at 25 °C using a column set of three 300 × 8 mm MZ-SD*plus* (spherical polystyrene particles with an average diameter of 5 μm) columns with porosities of 10^3, 10^5, 10^6 Å or (ii) in *N*-methyl-2-pyrrolidone (NMP + 0.5 wt % LiBr) at +70 °C using a column set of two 300 × 8 mm PSS-GRAM (spherical polyester particles with an average diameter of 7 μm) columns with porosities of 10^2 and 10^3 Å, respectively. Solutions containing ~0.15 wt % polymer were stirred overnight and filtered through 0.45 μm filters; injected volume was 100 μL. Calibration was done with polystyrene standards. Analytical ultracentrifugation (AUC) was done with an Optima XL-I ultracentrifuge (Beckmann-Coulter, Palo Alto, CA) equipped with Rayleigh interference optics. The sedimentation−velocity experiments were performed with 0.19 wt % solutions of polymer in methanol at a rotational speed of 60K rpm at 25 °C. Data were evaluated with the SEDFIT software package (Peter Schuck, Bethesda, MD)[16] to give sedimentation coefficient distributions ($g^*(s)$ and $c(s)$) and molar mass distributions ($c(M)$). Equilibrium experiments for every polymer sample (solution in methanol) were performed

Scheme 3. (a) Synthesis of 2-(3-Butenyl)-2-oxazoline from 4-Pentenoic Acid[a] and (b) Polymerization of 2-(3-Butenyl)-2-oxazoline[b]



[a] Key: (1) *N*-Hydroxysuccinimide, EDAC, dichloromethane, room temperature, 12 h; (2) 2-chloroethylamine hydrochloride, 0.94 N aqueous NaOH, dichloromethane, room temperature, 12 h; (3) KOH, methanol, 70 °C, 12 h. [b]Key: (1) Methyl triflate, acetonitrile, 70 °C, 24−72 h; (2) piperidine, 70 °C, 5 h.

at three different speeds (20K−60K rpm) and five to seven concentrations (0.13−0.51 wt %). Data were evaluated with the program MSTAR (Kristian Schilling, Nanolytics, Germany).[17] Density measurements were carried out on a density meter DMA5000 (Anton Paar, Graz, Austria).

Results and Discussion

Monomer Synthesis. 2-(3-Butenyl)-2-oxazoline was chosen as the monomer because its two reactive sites exhibit orthogonal reactivity. As will be demonstrated later, this monomer can undergo controlled cationic isomerization polymerization via the oxazoline group under preservation of the vinyl double bond − unlike for instance the commercial 2-isopropenyl-2-oxazoline, a derivative of methacrylic acid, which under otherwise identical polymerization conditions produced a gel (see also ref 18).

The new monomer 2-(3-butenyl)-2-oxazoline was synthesized in three steps starting from commercially available 4-pentenoic acid (Scheme 3a), as described in the Experimental Part (modified procedure reported by Binder et al.[15]). The first step includes an activation of the 4-pentenoic acid with the activation system 1-(3-dimethylpropyl)-3-ethylcarbodiimide hydrochloride (EDAC) and *N*-hydroxysuccinimide. The activated acid is then reacted with 2-chloroethylamine hydrochloride in the presence of NaOH, which is a heterogeneous reaction, to form the corresponding amide in a very good yield. Ring closure to 2-(3-butenyl)-2-oxazoline was achieved with KOH in methanol at 70 °C (Binder et al. used NaOH at room temperature). The chemical structure of the final product was confirmed by ^{1}H and ^{13}C NMR spectroscopy and GC−MS; purity is 99+% (GC).

Polymerization. Homopolymerization of 2-(3-butenyl)-2-oxazoline and copolymerization with 2-ethyl-2-oxazoline were performed in acetonitrile solution at 70 °C using methyl triflate as the initiator; the reaction was quenched with piperidine (cf. Jordan et al.;[19] Scheme 3b). For homopolymerization, initial concentrations of monomer and initiator were $[M]_0 = 2.3-4.7$ mol/L and $[I]_0 = 0.025-0.094$ mol/L, respectively, depending on the targeted molecular weight of the polymer. Monomer consumption came to completion within 24−72 h. Polymerization obeys pseudo-first-order kinetics and has a half-life period of a few hours (Figure 1a). The apparent number-average molecular weight (M_n^{app}) of the polymer, as determined by SEC applying a calibration with polystyrene, increases linearly with the conversion of monomer (x_p) (NMR). These results indicate that the polymerization of 2-(3-butenyl)-2-oxazoline can occur in the absence of termination and chain transfer reactions, thus exhibits living character.[20]

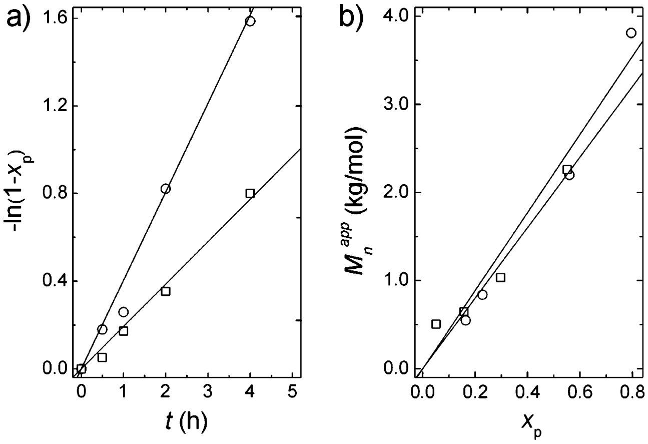


Figure 1. (a) First-order time−conversion plots for the polymerizations of 2-(3-butenyl)-2-oxazoline (M) in acetonitrile at 70 °C, initiator (I): methyl triflate; (○) $[M]_0 = 4.655$ mol/L, $[I]_0 = 0.155$ mol/L; (□) $[M]_0 = 2.793$ mol/L, $[I]_0 = 0.093$ mol/L. (b) Evolution of the apparent number-average molecular weight (M_n^{app}, SEC) with monomer conversion (x_p)

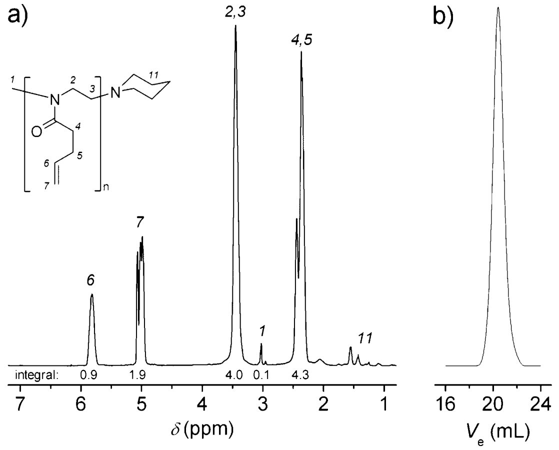


Figure 2. (a) ^{1}H NMR spectrum (400.1 MHz, $CDCl_3$) and (b) SEC trace (eluent, THF; detector, RI) of the poly[2-(3-butenyl)-2-oxazoline] sample **1**.

Four samples of poly[2-(3-butenyl)-2-oxazoline] (**1**−**4**) with different molecular weights were synthesized. The chemical structures of polymers were as expected, as confirmed by ^{1}H NMR spectroscopy (see the exemplary spectrum of **1** in Figure 2a). Importantly, quantitative evaluation of peak integrals showed that none of the vinyl double bonds had been affected during polymerization reaction, thus polymers exhibit a uniform microstructure (unlike polybutadienes). End group analysis, considering the signal of the methyl protons of the α-chain end (*1*) and of the methylene of the polymer backbone (*2*+*3*), allowed for the determination of absolute values of $M_n^{(NMR)}$ (or number-average degree of polymerization, *n*) of **1**−**3** (the end group signal of **4** was too weak for an accurate integration)− data are listed in Table 1. Values obtained for M_n are usually close to calculated ones. Absolute weight-average molecular weights (M_w) were determined from AUC sedimentation-velocity and equilibrium runs ($M_w^{(AUC)}$ in Table 1); deviation between the values obtained from these two independent AUC methods was 3% or less. The polydispersity index, PDI =

Table 1. Average Molecular Weights (M_n and M_w) and Glass Transition Temperatures (T_g) of Poly[2-(3-butenyl)-2-oxazoline]s (1−4) and Poly[(2-(3-butenyl)-2-oxazoline)-*co*-(2-ethyl-2-oxazoline)] (5)

	$M_n^{(NMR)}$ (kg/mol)[a]	$M_w^{(AUC)}$ (kg/mol)[c]	M_w/M_n	$M_n^{(SEC)}$ (kg/mol)[d]	$M_w^{(SEC)}$ (kg/mol)[d]	$(M_w/M_n)^{(SEC)d}$	T_g (°C)[e]
1	3.4	3.8	1.12	2.7	3.2	1.19	9
2	7.0	8.0	1.14	6.9	8.4	1.22	15
3	8.0	9.0	1.13	8.8	10.5	1.19	15
4	10.9[b]	12.6	(1.16)	11.5	13.3	1.16	17
5	3.0	3.2	1.06	3.3	3.7	1.12	38

[a] ^{1}H NMR end group analysis; solvent: $CDCl_3$. [b] N/A; calculated according to $M_w^{(AUC)}/(M_w/M_n)^{(SEC)}$. [c] AUC sedimentation-velocity. [d] SEC (eluent: THF): **1**−**4**, SEC (eluent: NMP): **5**. [e] DSC.

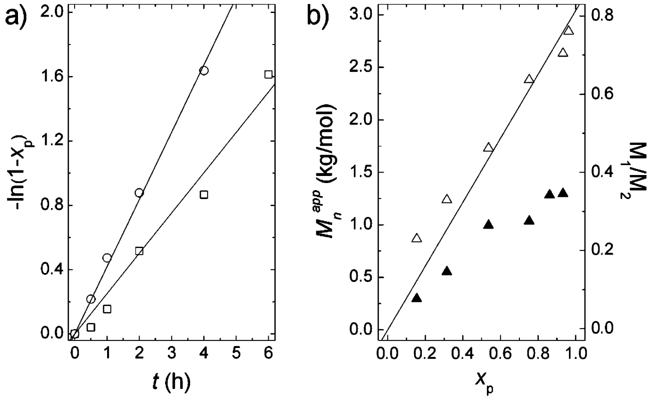


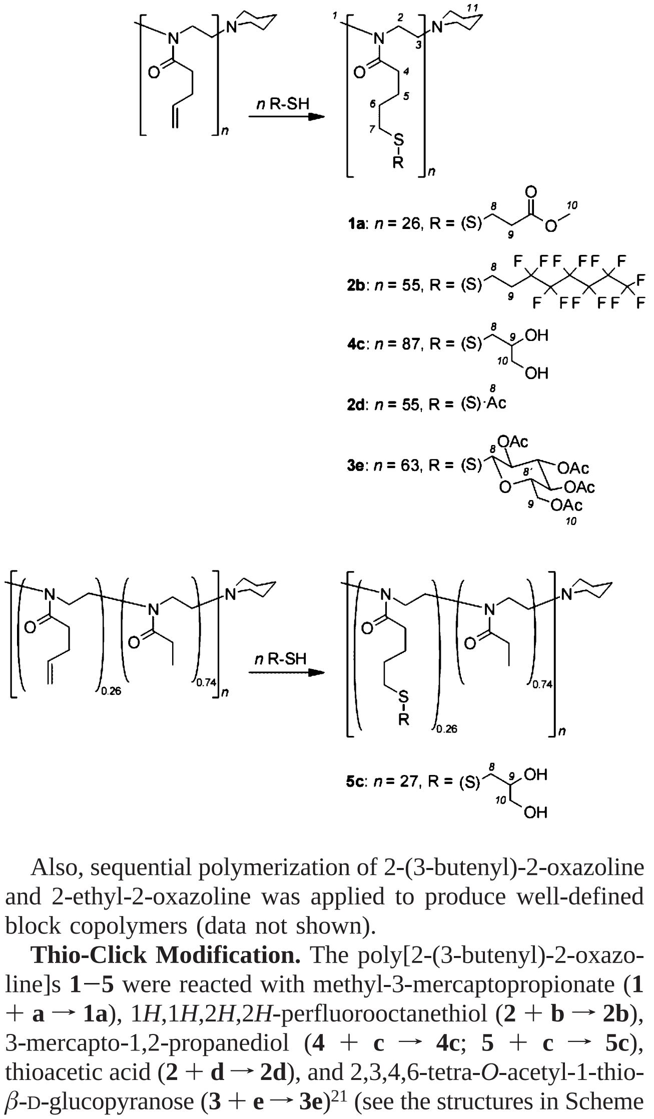
Figure 3. (a) First-order time−conversion plots for the copolymerization of 2-(3-butenyl)-2-oxazoline [(□) [M_1] = 1.026 mol/L] and 2-ethyl-2-oxazoline [(○) [M_2] = 2.678 mol/L] in acetonitrile at 70 °C, initiator: methyl triflate ($[I]_0$ = 0.089 mol/L). b) Evolution of the apparent number-average molecular weight [(△) M_n^{app}, SEC] and of the comonomer ratio [(▲) M_1/M_2, NMR] with over-all monomer conversion (x_p).

$M_w^{(AUC)}/M_n^{(SEC)}$, is about 1.2, indicating that the polymers exhibit a narrow molecular weight distribution. Monomodal and narrow distributions of **1**−**4** were also detected by SEC (see the exemplary chromatogram of **1** in Figure 2b). Evaluation of SEC data on the basis of a calibration with polystyrenes yields apparent molecular weight averages ($M_n^{(SEC)}$ and $M_w^{(SEC)}$ in Table 1) that deviate less than 20% from absolute values.

The polymers **1**−**4** are, unlike 1,2-polybutadiene, readily soluble in polar solvents (methanol, ethanol, acetonitrile, and *N*-methylpyrrolidone) as well as in nonpolar solvents (THF, chloroform, benzene, and cyclohexane); they are not soluble in water, diethyl ether, and *n*-hexane. The specific density of poly-[2-(3-butenyl)-2-oxazoline] is $\rho = 1.139 \pm 0.010$ g/mL (density oscillation tube). The glass transition occurs at below room temperature, $T_g \leq 17$ °C (DSC), depending slightly on the molecular weight of the sample (Table 1).

In the statistical copolymerization of 2-(3-butenyl)-2-oxazoline and 2-ethyl-2-oxazoline (initial monomer feed: $[M_1]_0$:$[M_2]_0$ = 0.32), the consumption of both monomers follows a pseudo-first-order kinetics (Figure 3a); monomer conversions were calculated by ^{1}H NMR analysis of the reaction solutions taken at different times. The polymerization of 2-ethyl-2-oxazoline proceeded faster than that of 2-(3-butenyl)-2-oxazoline and the composition of the copolymer changed gradually with increasing conversion (Figure 3b), suggesting that the final polymer (**5**) is a gradient rather that a random copolymer. As expected for living/controlled copolymerization process, the molecular weight ($M_n^{(SEC)}$) of the copolymer increases linearly with monomer conversion (Figure 3b). Further molecular characteristics of **5** are collected in Table 1.

Scheme 4. Samples Prepared by Modification of Poly[2-(3-butenyl)-2-oxazoline] with Mercaptans (RSH) (Ac = Acetyl)



Also, sequential polymerization of 2-(3-butenyl)-2-oxazoline and 2-ethyl-2-oxazoline was applied to produce well-defined block copolymers (data not shown).

Thio-Click Modification. The poly[2-(3-butenyl)-2-oxazoline]s **1**−**5** were reacted with methyl-3-mercaptopropionate (**1** + **a** → **1a**), 1*H*,1*H*,2*H*,2*H*-perfluorooctanethiol (**2** + **b** → **2b**), 3-mercapto-1,2-propanediol (**4** + **c** → **4c**; **5** + **c** → **5c**), thioacetic acid (**2** + **d** → **2d**), and 2,3,4,6-tetra-*O*-acetyl-1-thio-*β*-D-glucopyranose (**3** + **e** → **3e**)[21] (see the structures in Scheme 4). Solutions of the reactants in THF or THF/methanol mixed solvent were placed in a glass vessel and exposed to an UV light source for 24 h; modified polymers were purified by dialysis (see the Experimental Part for further details).

The ^{1}H NMR and FT-IR data of all products (see Table 2 and the exemplary ^{1}H NMR spectrum of **1a** in Figure 4a) agreed with the expected chemical structures. The degrees of modification, *f*, as calculated from the integrals of signals *8* (−SCH-(H)−) and *2* + *3* (polymer backbone) (Scheme 4), were found to be quantitative; traces of residual double bonds were only detected for **2b** (4%) and **3d** (<1%). Cyclic units in the backbone seem to be absent as well as Markovnikov addition products, which in ^{1}H NMR should have produced a doublet at $\delta \sim 1.22$ ppm ($-SCH(CH_3)-$). SEC analyses revealed narrow molecular weight distributions of samples **1a** (Figure 4b), **2b**, and **3e** (M_w/M_n < 1.15, Table 2), like the ones of the starting materials. Samples **2d**, **4c**, and **5c** could, however, not be analyzed by SEC irrespective of the eluent used. AUC sedimentation−velocity experiments revealed a monomodal sedimentation coefficient distribution of **2d** and **4c** (Figure 5).

The radical addition of mercaptans onto poly[2-(3-butenyl)-2-oxazoline] seems to have all the characteristics of a click reaction, namely it is modular and wide in scope and produces well-defined polymers without side reactions. It is especially

Table 2. Molecular Characteristics of Modified Poly[2-(3-butenyl)-2-oxazoline]s

	^{1}H NMR δ (ppm)[a]	FT−IR $\tilde{\nu}$ (cm^{-1})	f[b]	$(M_w/M_n)^{(SEC)c}$	T_g (°C)[d]
1a	1.63−1.71 (b, *5+6*), 2.29, 2.39 (b, *4*), 2.55−2.62 (b, *9*), 2.60 (t, *7*), 2.76 (t, *8*), 3.42, 3.47 (b, *2+3*), 3.69 (s, *10*)	2927 (C−H str), 1729 (OC═O str), 1634 (NC═O str, amide I), 1431(CH$_2$−CO)	1.00	1.18	−38
2b	1.65−1.71 (b, *5+6*), 2.33−2.37 (b, *4+9*), 2.58 (b, *7*), 2.71 (b, *8*), 3.43 (b, *2+3*), 5.01−5.06, 5.82 (−CH═CH$_2$)	2931 (C−H str), 1638 (C═O str, amide I), 1430 (CH$_2$−CO), 1182 (C−F str)	0.96 (0.04)	1.13	N/A
4c	1.65 (b, 5 + 6), 2.40−2.44 (b, *4+9*), 2.60−2.82 (b, *7+8*), 3.48−3.69 (b, *2 + 3+10*), 3.85 (b, *9*)	3333 (O−H), 2915, 2861 (C−H str), 1613 (NC═O str, amide I), 1417 (CH$_2$−CO)	1.00	N/A	6
2d	1.62−1.72 (b, *5+6*), 2.31−2.37 (b, *8+4*), 2.87 (b, *7*), 3.42 (b, *2+3*)	2928 (C−H str), 1778 (SC═O str), 1632 (C═O str, amide I), 1417 (CH$_2$−CO)	1.00	N/A	0
3e	1.66−1.75 (b, *5+6*), 2.00−2.08 (b, *10*), 2.22−2.36 (b, *4*), 2.69−2.71 (b, *7*), 3.41 (b, *2+3*), 3.76 (b, *8′*), 4.12−4.27 (b, *9*), 4.54 (b, *8*), 4.98−5.25 (b, *8′*)	2937 (C−H str), 1740 (OC═O str), 1639 (NC═O str, amide I), 1427 (CH$_2$−CO), 1211 (C−O str)	0.99 (0.01)	1.14	68
5c	1.06−1.07 (b, *5′*), 1.63 (b, *5+6*), 2.37−2.42 (b, *4+4′*), 2.61−2.82 (b, *7+8*), 3.53−3.68 (b, *2+2′+3+3′+10*), 3.84 (b, *9*)	3384 (O−H), 2938 (C−H str), 1613 (NC═O str, amide I), 1421 (CH$_2$−CO)	1.00	N/A	37

[a] Assignment of peaks according to the chemical structures in Scheme 4. [b] Degree of modification = integral(*8*) × 2/integral(*2* + *3*) (^{1}H NMR); the value in parentheses corresponds to the fraction of unreacted double bonds. [c] SEC (eluent: THF). [d] DSC.

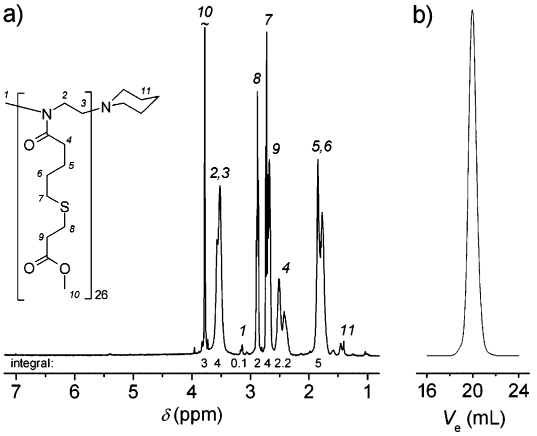


Figure 4. (a) ^{1}H NMR spectrum (400.1 MHz, CDCl$_3$) and (b) SEC trace (eluent, THF; detector, RI) of the modified poly[2-(3-butenyl)-2-oxazoline] sample **1a**.

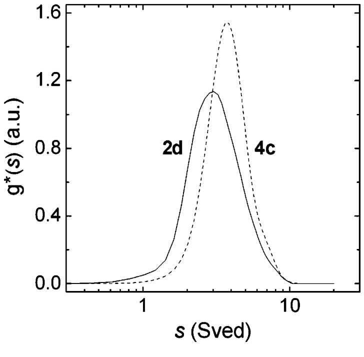


Figure 5. Sedimentation coefficient distributions ($g^*(s)$) of the modified poly[2-(3-butenyl)-2-oxazoline] samples **2d** (THF) and **4c** (methanol) at 60 K rpm, 25 °C.

noteworthy that these characteristics were achieved under feasible and mild conditions. Reactions were performed using just 1.2−1.5 equiv of mercaptan with respect to double bonds and thiyl radicals were directly generated through irradiation with UV light at room temperature, thus no extra radical initiator was necessary.[11] Formation of disulfide through a recombination of thiyl radicals is not evident for the given experimental conditions.[22] Earlier modifications of 1,2-polybutadiene were done at 10-fold excess of mercaptan (nonetheless considerable amounts of cyclic units were produced) with azoisobutyronitrile as the radical source.[13,23,24] Also, the synthetic procedure goes completely without toxic transition metals (not so the Huisgen reaction[19]), which simplifies the workup procedure.

Expectedly, the modified polymer samples exhibit different thermal properties (T_g, see Table 2) and solubility features as compared to the starting materials, which can be interesting for further potential applications as biomaterials. The change in physical properties after successful modification with different mercaptans can be also be recognized by the glass transition temperature. It may be shifted by several tens of degrees, for instance from +9 (**1**) to −38 °C (**1a**) or from +15 (**3**) to +68 °C (**3e**). The hydroxylated polymer **4c** turned out to be soluble in water and showed typical LCST behavior (LCST = lower critical solution temperature). The cloud point of a 1 wt % solution of **4c** in water is at about room temperature. Investigation of thermoresponsive properties and testing of the materials for bioinspired structure formation and biological applications is in progress.

Conclusion

We demonstrated the first synthesis and living/controlled cationic polymerization of 2-(3-butenyl)-2-oxazoline to give poly[2-(3-butenyl)-2-oxazoline] with a narrow molecular weight distribution. The copolymerization with 2-ethyl-2-oxazoline also proceeds in a living manner to yield gradient copolymers. The subsequent radical addition of mercaptans onto the poly[2-(3-butenyl)-2-oxazoline] homo- and copolymers was found to have the characteristics of a “click” reaction. The reaction can be performed under feasible ([RSH]/[C═C] ∼ 1.2−1.5, no transition metal additives) and mild conditions (in-situ generation of radicals with UV light at room temperature) and goes to completion within 1 day. Hydrophobic fluoropolymers can be prepared in the same way as water-soluble (co-)polymers or glycopolymers, starting from readily available materials.

Current work is devoted to the extension of the modular toolbox of poly(2-oxazolines) and to investigate the colloidal properties and application potential of these new materials.

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Supporting Information Available: Figures showing SEC traces and AUC sedimentation-velocity and equilibrium data of polymers **1**−**4**, ^{1}H NMR spectra of modified polymers **1a**, **2b**, **2d**, **3e**, **4c**, and **5c**, and SEC traces of **1a**, **2b**, and **3e**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(21) The thio-glucose derivative was used in the protected form because it is readily available as such and not because protection of hydroxyl groups would be needed for the free-radical addition onto poly[2-(3-butenyl)-2-oxazoline]. A subsequent hydrolysis of the acetyl protecting groups occurs readily by stirring the modified polymer in a mixture of chloroform and 0.5 M sodium methoxide in methanol 9:1 (v/v) for 45 min at room temperature.
(22) Noticeable amounts of disulfide were not produced during the irradiation of a 4 wt % solution of methyl-3-mercaptopropionate in THF with UV light for 24 h, as shown by GC analysis, even in the absence of poly[2-(3-butenyl)-2-oxazoline].
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