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Poly(glycidyl amine) and Copolymers with Glycidol and Glycidyl Amine Repeating Units: Synthesis and Characterization

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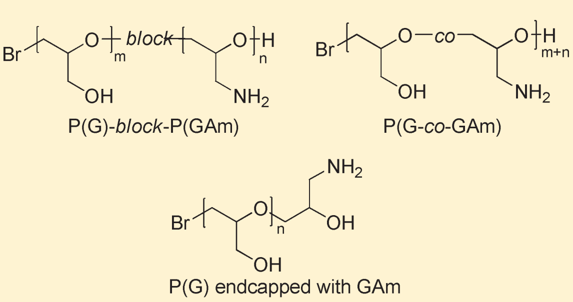
Ⓢ *Supporting Information*



ABSTRACT: The synthesis and characterization of poly(glycidol-*co*-glycidyl amine), poly(glycidol)-*block*-poly(glycidyl amine), and poly(glycidol) end-capped with a glycidyl amine unit is reported. Copolymerization of ethoxyethyl glycidyl ether with epichlorohydrin using tetraoctylammonium bromide/triisobutylaluminium as catalyst leads to statistical or block copolymers. Sequential addition of the monomers to the initiator leads to block copolymers while simultaneous copolymerization of the monomers results in statistical copolymers. The resulting polyethers with protected hydroxymethyl and chloromethyl side groups were converted in three steps to poly(epoxide)s with hydroxymethyl and aminomethyl side chains. These polymers have a high potential for the preparation of multifunctional polymers since amine and alcohol groups can be addressed selectively by electrophiles. An intermediate in the synthesis of these functional poly(epoxide)s are polyethers with hydroxymethyl and azidomethyl side chains. The azide group of these copolymers was further functionalized via a click reaction with propargyl alcohol proving the reactivity of the polymer bound azide group. Furthermore, preparation of poly(glycidol)s bearing a glycidyl amine end group is reported.

■ INTRODUCTION

Poly(glycidol) and its derivatives have recently received increasing attention. Although cationic polymerization of glycidol with Lewis acids is known in literature,[1,2] most publications focus on anionic ring-opening polymerization of glycidol or protected glycidols.[3−7] Their biocompatibility and high functionality make poly(glycidol)s interesting intermediates for biomedical and applications in many other fields.[8,9]

Early work on the synthesis of epoxides in the presence of trialkylaluminium compounds has been done by Vandenberg et al..[10] The copolymerization of epichlorohydrin and glycidol with boron trifluoro diethyl etherate was investigated by Royappa et al., leading to branching and the formation of small ring species.[11] Recently, Deffieux et al. have published a system using tetraalkylammonium salts as initiators in the presence of triisobutylaluminium ($i\mathrm{Bu_3Al}$) as activator for the polymerization of propylene oxide,[12] copolymerization of propylene oxide and ethylene oxide,[13] and polymerization of epichlorohydrin[14] as well as polymerization of ethoxyethyl glycidyl ether and *tert*-butylglycidyl ether.[15] The system allows the synthesis of polyethers under mild reaction conditions in a controlled manner.[15] The polymerization of epichlorohydrin occurs without nucleophilic attack of the propagating active species on the chloromethyl side groups;[14] transfer to the monomer as observed for ethoxyethyl glycidyl ether[16] and for other substituted oxiranes[15] using potassium alkoxide initiated polymerization was not observed up to now.

Amino alcohols are organic compounds that contain both an amine and an alcohol functional group. The combination of amine and alcohol groups in the same molecule plays an important role in biological membranes, e.g., ethanolamine is the second-most-abundant headgroup for phospholipids. In industry, ethanolamine, which is a weak base, is used in aqueous solutions for scrubbing of acid gases. In general, low molecular weight amino alcohols are used as feedstock in the production of detergents, emulsifiers, pharmaceuticals, corrosion inhibitors, and chemical intermediates. The combination of multiple amine and alcohol groups as side chains within a polymer is expected to result in multireactive polymers which can be addressed selectively by electrophiles generating multifunctional polymers. Polyethers with alcohol and amine groups are expected to substitute low molecular weight amino alcohols in many technical applications.

Amino-functionalized polyethers have gained growing interest. Among these, amino-functional PEGs are the most important; PEGylation is used for drug delivery, and for the protection of peptide/protein biopharmaceuticals.[17] Surfaces coated with star-shaped PEO were shown to be extremely resistant to unspecific adsorption of proteins.[18,19] A drawback is the fact, that PEG possesses functional groups only at the chain ends.

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Therefore, attempts to functionalize PEG focused on the modification of these groups,[20] including the use of dibenzyl protected amino ethanol as initiator for ethylene oxide to yield amino-functionalized PEGs.[21−23] Another way to increase the functionality is to synthesize copolymers of PEG and a monomer, that can be functionalized further,[24,25] as for example dibenzyl amino glycidol, as protected amino glycidol.[26]

In this study, we describe the synthesis of statistical and block copolymers of glycidol and glycidyl amine (statistical and block poly(epoxide)s with hydroxymethyl and amino methyl side groups). To reach this goal commercially available epichlorohydrin is copolymerized with ethoxyethyl glycidyl ether. The resulting copolymers are subject to polymer analogues reactions, yielding copolymers of glycidol and glycidyl azide, which may serve as substrates for "click reactions" with terminal alkynes. Furthermore, the azide is transformed into copolymers of glycidol and glycidyl amine, which may serve in a variety of applications, since both amine groups and hydroxyl groups can be addressed selectively by electrophilic reagents.

Furthermore, a poly(glycidol) bearing a glycidyl amine end group, analogue to Jeffamine was synthesized.[27,28] The poly(glycidol) with a glycidyl amine end group was used as macronitiator for the polymerization of L-alanine-*N*-carboxy anhydride to show its accessibility for bioconjugation. Bioconjugates may serve for the immobilization of enzymes or due to the known biocompatibility of poly(glycidol)s as peptide drug carriers. Polyethers (mainly poly(ethylene glycol)) are known to increase bioavailability and plasma half-lives, by reducing proteolysis and enhancing solubility and stability of biomedical relevant peptides.[2] Compared to PEG the polyethers described have the advantage of being multifunctional.

■ EXPERIMENTAL SECTION

Nomenclature. In this work, glycidyl derivatives are named using the prefix "glycidyl" followed by the group representing the rest, e.g., "glycidyl amine" (GAm) or "glycidyl azide" (GAz), and epichlorohydrin (ECH) (synonym with glycidyl chloride GCl).

Materials. Tetraoctylammonium bromide (+99%, Fluka), triisobutylaluminium (1M, in toluene, Acros Organics) triphenylphosphine (+99%, Merck), sodium azide ((+99%, Merck), potassium phthalimide (+98%, Merck), copper(I)bromide (+98%, Fluka), hydrazine monohydrate (+98%, Fluka), propargyl alcohol (+99%, Acros), hydrochloric acid (+36.5−38% solution, Merck) and dimethylformamide (99.8%, Merck) were used as received without further purification. The *N*-carboxy anhydride of L-alanine was received from SNPE GmbH in Frankfurt and dried under reduced pressure before use. Epichlorohydrin (+99%, Merck) was purified by stirring over CaH_2, distillation in vacuum and storage over molecular sieves. Toluene (+99%, Merck) was purified on sodium and distilled under vacuum. Ethoxyethyl glycidyl ether was synthesized from 2,3-epoxypropan-1-ol (glycidol) and ethyl vinyl ether according to Fitton et al.[29] purified by stirring over CaH_2 and distillation in vacuum and storage over molecular sieves. All reactions were carried out under nitrogen atmosphere. Nitrogen (Linde, 5.0) was passed over molecular sieves (4 Å).

Measurements. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker DPX-400 NMR spectrometer at 400 and 100 MHz, respectively. Deuterated chloroform ($CDCl_3$), deuterated dimethyl sulfoxide (DMSO-d_6) and deuterated trifluoroacetic acid were used as solvent, and tetramethylsilane (TMS) served as internal standard.

Size exclusion chromatography (SEC) analyses were carried out at 35 °C using a high-pressure liquid chromatography pump (ERC HPLC 64200) and a refractive index detector (ERC-7215a). The eluting solvent was tetrahydrofuran (HPLC grade) with 250 mg L^{-1} 2,6-di-*tert*-butyl-4-methylphenol and a flow rate of 1 mL min^{-1}. Five columns with MZ gel were applied. The length of the first column was 50 mm and 300 mm for the other four columns. The diameter of each column was 8 mm, the diameter of the gel particles was 5 μm and the nominal pore widths were 50, 50, 100, 1000, and 10000 Å. Calibration was achieved using poly(methyl methacrylate) standards.

For dimethylformamide (DMF) as eluting solvent for SEC measurements a high-pressure liquid chromatography pump (Bischoff 2250) and a refractive index detector (Jasco 2040+) were used at 30 °C. The DMF contained 1 g L^{-1} LiBr and a flow rate of 1 mL min^{-1} was applied. Four different columns with PSS GRAM gel were used: length of each column 30 cm, diameter of each column 8 mm, diameter of gel particles 10 μm, and nominal pore widths were 30, 1000, 1000, and 3000 Å. Calibration was achieved using poly(methyl methacrylate) standards.

For water as eluting solvent size exclusion chromatography (SEC) analysis was carried out at 30 °C using an isocratic pump (Agilent 1100 series) and a refractive index detector (Wyatt Optilab DSP). Water (HPLC gradient grade, Roth) with 0.1 M sodium nitrate ($NaNO_3$, p.a., AppliChem) and methanol (p.a., Gheyer) as internal standard was used at a flow rate of 1 mL·min^{-1}. Four PSS suprema columns filled with modified acrylate-copolymer-network particles were applied. The length of the precolumn was 50 mm and the other three separation columns had a length of 300 mm. The diameter of each column was 8 mm, the diameter of the copolymer particles 10 μm, and the nominal pore widths were 30, 1000, and 3000 Å, respectively. Calibration was achieved using narrow distributed poly(ethylene glycol)/poly(ethylene oxide) or pullulan standards.

DSC measurements were carried out on a Netzsch DSC 204 differential scanning calorimeter under nitrogen atmosphere. Samples were measured in perforated closed aluminum pans using approximately 3−6 mg of sample. The samples were measured between −80 and +150 °C. The heat flow was determined as a function of temperature. First-order transitions were reported as the maxima or minima of the endothermic or exothermic peaks during the third heating and the second cooling scans. To determine the glass transition temperature, the inflection point was taken.

FT-IR measurements were recorded on a NEXUS 470 FT-IR of Thermo-Nicolet with a spectral resolution of 8 cm^{-1} in KBr.

Synthesis of Poly(epichlorohydrin). Tetraoctylammonium bromide (20.6 mg, 0.072 mmol) and epichlorohydrin (1.667 g, 18.012 mmol) were dissolved in toluene (0.500 mL) under nitrogen atmosphere. The polymerization was started by adding a solution of triisobutylaluminium (700 μL, 0.77 mmol) at a constant temperature of 0 °C. The reaction mixture was kept overnight at this temperature. Monomer conversion was determined by ^1H NMR spectroscopy. After polymerization (complete monomer conversion) toluene was removed under reduced pressure. The colorless polymer was dissolved in tetrahydrofuran and precipitated in aqueous solution of sodium hydroxide (5 wt %). To remove traces of the tetraoctylammonium salts a polymer solution in THF was precipitated in methanol. The product was isolated as colorless oil with a yield of 98%.

^1H NMR(400 MHz, DMSO-d_6, TMS_{int}). Repeating unit δ = 3.58−3.83 (CH_2Cl; CH_2CHO, 5H) ppm.

^{13}C NMR(100 MHz, DMSO-d_6, TMS_{int}) Repeating units δ = 44.20 (CH_2Cl), 68.65 (CH_2O), 78.17 (CHO) ppm.

$M_{n,SEC,DMF} = 27500$, $M_w/M_n = 1.26$.

Synthesis of Poly(glycidyl azide). Poly(epichlorohydrin) (9.253 g, 100 mmol) was dissolved in dimethylformamide (200 mL) and sodium azide (7.801 g, 120 mmol) was added to the solution. The reaction mixture was stirred at 100 °C for 12 h. After completion of the reaction the polymer was precipitated in water. The polymer was filtered, washed with water and dried under reduced pressure. The product was isolated as yellowish oil with a yield of 97%.

^{1}H NMR(400 MHz, DMSO-d_6, TMS$_{int}$). Repeating units δ = 3.27−3.39 (CH_2N_3, 1H), 3.40−3.51 (CH_2N_3, 1H), 3.55−3.72 (CH_2CHO, 3H) ppm.

^{13}C NMR(100 MHz, DMSO-d_6, TMS$_{int}$). Repeating units δ = 51.04 (CH_2N_3), 68.58 (CH_2O), 78.05 (CHO) ppm.

$M_{n,SEC,DMF}$ = 21400, M_w/M_n = 1.26.

Synthesis of Poly(glycidyl amine). Poly(glycidyl azide) (9.904 g, 100 mmol), was dissolved in dimethylformamide (220 mL) and triphenylphosphine (28.850 g, 110 mmol) was added. The reaction mixture was stirred for 2 h and subsequently water (5 mL) was added. The solvents were removed under reduced pressure. The polymer was dissolved in water, triphenylphosphine oxide was filtered off and finally the polymer was washed with toluene. The product was isolated as yellowish oil with a yield of 96%.

^{1}H NMR(400 MHz, DMSO-d_6, TMS$_{int}$). Repeating units δ = 2.41−2.69 (CH_2NH_2, 2H) 3.09−3.70 (CH_2CHO, 3H) ppm.

^{13}C NMR(100 MHz, DMSO-d_6, TMS$_{int}$). Repeating units δ = 42.64 (CH_2NH_2), 69.83 (CH_2), 80.07 (CHO) ppm.

Synthesis of Poly(glycidyl acetamide). To a solution of poly(glycidyl amine) (73 mg, 1 mmol glycidyl amine groups) in dry DMF, *N*,*N*-diisopropyethylamine (1.292 g, 10 mmol) and acetic anhydride (1.021 g, 10 mmol) were added. The solution was stirred for 3 h and solvent and excess of amine and anhydride were removed under reduced pressure.

^{1}H NMR(400 MHz, DMF-d_7, TMS$_{int}$). Repeating units δ = 1.88−1.97 (H_3CON, 3H), 3.32−3.42 (CH_2N, 1H), 3.43−3.74 ($CH_2CH(CH_2N)O$, 4 H) ppm.

$M_{n,SEC,DMF}$ = 21500, M_w/M_n = 1.21.

Synthesis of Poly(ethoxyethyl glycidyl ether-co-epichlorohydrin). Tetraoctylammonium bromide (0.374 g, 0.684 mmol) was dissolved in dry toluene (2 mL) under nitrogen atmosphere. Epichlorohydrin (4.430 g, 47.9 mmol) and ethoxyethyl glycidyl ether (3.000 g, 20.5 mmol) were added. The polymerization was started by adding the triisobutylaluminium while cooling with an ice bath. The reaction mixture was allowed to warm up to room temperature and stirred overnight. The monomer conversion was monitored via ^{1}H NMR spectroscopy. After polymerization, toluene was removed under reduced pressure. The colorless polymer was dissolved in tetrahydrofuran and precipitated in an aqueous solution of sodium hydroxide (5 wt %). The product was isolated as colorless oil with a yield of 96%.

^{1}H NMR(400 MHz, DMSO-d_6, TMS$_{int}$). Repeating units δ = 1.05−1.13 (CH_2CH_3, 3H), 1.15−1.23 ($CHCH_3$, 3H), 3.42−3.87 ($CH_2CH(CH_2O)O$, CH_2CH_3, $CH_2CH(CH_2Cl)O$, 12H), 4.57−4.74 (OCHO, 1H) ppm.

^{13}C NMR(100 MHz, DMSO-d_6, TMS$_{int}$) Repeating units δ = 15.10 (CH_2CH_3), 19.62 ($CHCH_3$), 44.09 (CH_2Cl), 60.13 (CH_2CH_3), 64.39, 64.59 ($CH_2CH(CH_2OH)O$), 68.71 ($CH_2CH(CH_2OH)O$), 69.53 ($CH_2CH(CH_2Cl)O$), 78.57−79.15 (CH_2CHO), 99.07 ($CHCH_3$) ppm.

$M_{n,SEC,DMF}$ = 10200, M_w/M_n = 1.35.

Synthesis of Poly(glycidol-co-epichlorohydrin). Poly(ethoxyethyl glycidyl ether-*co*-epichlorohydrin) (10.941 g, 30 mmol EEGE) was dissolved in THF (25 mL) and an appropriate amount of hydrochloric acid (5 wt %) was added. The solution was stirred for 30 min. After stirring the solution for 30 min it was neutralized with sodium bicarbonate. The solvents were removed under reduced pressure, the polymer dissolved in dimethylformamide and the salts filtered off. The remaining dimethylformamide was removed under reduced pressure. The product was isolated as colorless oil with a yield of 96%.

^{1}H NMR(400 MHz, DMSO-d_6, TMS$_{int}$). Repeating units δ = 3.36−3.93 (polymer backbone, 10H), 4.46−4.64 (OH) ppm.

^{13}C NMR(100 MHz, DMSO-d_6, TMS$_{int}$). Repeating units δ = 44.23 (CH_2Cl), 60.77 (CH_2OH), 68.51, 69.46 ($CH_2CH(CH_2OH)O$, $CH_2CH(CH_2Cl)O$), 78.21 ($CH_2CH(CH_2OH)O$), 80.21 ($CH_2CH(CH_2Cl)O$) ppm.

$M_{n,SEC,DMF}$ = 8700, M_w/M_n = 1.39.

Synthesis of Poly(glycidol-co-glycidyl azide). Poly(glycidol-*co*-epichlorohydrin) (8.698 g, 70 mmol methylene chloride groups) was dissolved in dimethylformamide (100 mL) and sodium azide (5.006 g, 77 mmol) was added to the solution. The reaction mixture was stirred at 100 °C for 12 h. After completion of the reaction the amount of solvent was reduced and the salts filtered off. The remaining dimethylformamide was removed under reduced pressure. The product was isolated as yellowish oil with a yield of 96%.

^{1}H NMR(400 MHz, DMSO-d_6, TMS$_{int}$). Repeating units δ = 3.23−3.87 (polymer backbone, 10H), 4.43−4.78 (OH) ppm.

^{13}C NMR(100 MHz, DMSO-d_6, TMS$_{int}$). Repeating units δ = 50.95 (CH_2N_3), 60.57 (CH_2OH), 68.56, 69.29 ($CH_2CH(CH_2OH)O$, $CH_2CH(CH_2Cl)O$), 77.95 ($CH_2CH(CH_2OH)O$), 80.30 ($CH_2CH(CH_2\ N_3)O$) ppm.

$M_{n,SEC,DMF}$ = 10000, M_w/M_n = 1.32.

Reaction of Poly(glycidol-co-glycidyl azide) with Propargyl Alcohol. Poly(glycidol-*co*-glycidyl azide) (866 mg, 5.0 mmol azide groups) and propargyl alcohol (280 mg, 5.0 mmol) were dissolved in DMF (10 mL) and copper(I)bromide (72 mg, 0.5 mmol) was added to the reaction mixture. After overnight stirring, the copper bromide was filtered off and the solvent was removed under reduced pressure. The product was isolated as yellowish oil with a yield of 99%.

^{1}H NMR(400 MHz, DMF-d_7, TMS$_{int}$). Repeating units δ = 3.32−3.71 (CH_2CHO, 3H), 4.09−4.20 (CH_2N, 2H), 5.23 (triazole−CH_2−OH, 2H), 8.00 (triazole, 1H) ppm.

Synthesis of Poly(glycidol-co-glycidyl amine). Poly(glycidol-*co*-glycidyl azide) (9.156 g, 70 mmol) was dissolved in DMF (75 mL) and triphenylphosphine (20.196 g, 77 mmol) was added to the solution which was stirred at room temperature until gas formation stopped. Subsequently, water was added and the solvents were removed under reduced pressure. The polymer was washed with toluene and dried under reduced pressure (10^{-2} mbar). The product was isolated as yellowish oil with a yield of 95%.

^{1}H NMR(400 MHz, DMSO-d_6, TMS$_{int}$). Repeating units δ = 3.27−3.68 (polymer backbone) ppm.

^{13}C NMR(100 MHz, DMSO-d_6, TMS$_{int}$). Repeating units δ = 42.39 (CH_2NH_2), 60.39 (CH_2OH), 69.24 (CH_2CHO), 79.98 ($CH_2CH(CH_2OH)O$), 80.33 ($CH_2CH(CH_2\ NH_2)O$) ppm.

Synthesis of Poly(glycidol acetyl-co-glycidyl acetamide). To a solution of poly(glycidol-*co*-glycidyl amine) (74 mg, 0.7 mmol glycidyl amine groups, 0.3 mmol glycidol groups) in dry DMF and *N*,*N*-diisopropyethylamine (1.292 g, 10 mmol) acetic anhydride (1.021 g, 10 mmol) was added. The solution was stirred for 3 h and solvent and excess of amine and anhydride were removed under reduced pressure.

^{1}H NMR(400 MHz, DMF-d_7, TMS$_{int}$). Repeating units δ = 1.86−1.90 (H_3CON, 3H), 1.98−2.02 (H_3COO, 3H), 3.13−3.33 (CH_2N, 1H), 3.50−3.77 ($CH_2CH(CH_2N)O$, $CH_2CH(CH_2O)O$, 9 H), (CH_2OCO, 1H) ppm.

$M_{n,SEC,DMF}$ = 8400, M_w/M_n = 1.38.

Synthesis of Poly(epichlorohydrin)-block-poly(ethoxyethyl glycidyl ether). Tetraoctylammonium bromide (196 mg, 0.360 mmol) and epichlorohydrin (1.667 g, 18.000 mmol) were dissolved in toluene (1.000 mL) under nitrogen atmosphere. The polymerization was started by adding a solution of triisobutylaluminium (700 μL, 0.77 mmol) at a constant temperature of 0 °C. The reaction mixture was kept overnight at this temperature. Complete monomer conversion was confirmed by ^{1}H NMR spectroscopy. Ethoxyethyl glycidyl ether (2.631 g, 18 mmol) was added to the solution at a constant temperature of 0 °C, the reaction mixture was allowed to warm up to room temperature and kept overnight. Monomer conversion was again monitored via ^{1}H NMR spectroscopy. The colorless polymer obtained after removal of the solvent was dissolved in tetrahydrofuran and precipitated in an aqueous solution of sodium hydroxide (5 wt %). The product was isolated as colorless oil with a yield of 97%.

^{1}H NMR(400 MHz, $CDCl_3$, TMS$_{int}$). Repeating units δ = 0.99−1.13 (CH_2CH_3, 3H), 1.12−1.23 ($CHCH_3$, 3H), 3.17−3.96 ($CH_2CH(CH_2O)O$, CH_2CH_3, $CH_2CH(CH_2Cl)O$, 12H), 4.43−4.79 (OCHO, 1H) ppm.

^{13}C NMR(100 MHz, $CDCl_3$, TMS$_{int}$) Repeating units δ = 15.09 (CH_2CH_3), 19.59 ($CHCH_3$), 44.19 (CH_2Cl), 60.08 (CH_2CH_3), 63.97, 64.53 ($CH_2CH(CH_2OH)O$), 68.71 ($CH_2CH(CH_2OH)O$), 69.42 ($CH_2CH(CH_2Cl)O$), 78.24 (CH_2CHO), 99.14 ($CHCH_3$) ppm.

$M_{n,SEC,DMF}$ = 16200, M_w/M_n = 1.58.

Synthesis of Poly(epichlorohydrin)-block-poly(glycidol). Poly(ethoxyethyl glycidyl ether-*co*-epichlorohydrin) (11.934 g, 50 mmol EEGE) was dissolved in THF (25 mL) and an appropriate amount of hydrochloric acid (5 wt %) was added. After the solution was stirred for 30 min, sodium bicarbonate was added. The solvents were removed under reduced pressure, the polymer dissolved in dimethylformamide and the salts filtered off. The dimethylformamide was removed under reduced pressure. The product was isolated as colorless oil with a yield of 98%.

^{1}H NMR(400 MHz, DMSO-d_6, TMS$_{int}$). Repeating units δ = 3.42−3.93 (polymer backbone, 10H), 4.35−4.71 (O*H*) ppm.

^{13}C NMR(100 MHz, DMSO-d_6, TMS$_{int}$). Repeating units δ = 44.20 (CH_2Cl), 60.84 (CH_2OH), 68.62, 69.37 ($CH_2CH(CH_2OH)O$, $CH_2CH(CH_2Cl)O$), 78.20 ($CH_2CH(CH_2OH)O$), 79.97 ($CH_2CH(CH_2Cl)O$) ppm.

Synthesis of Poly(glycidyl azide)-block-poly(glycidol). Poly(glycidol)-*block*-poly(epichlorohydrin) (8.329 g, 50 mmol methylene chloride groups) was dissolved in dimethylformamide (100 mL) and sodium azide (3.576 g, 55 mmol) was added to the solution. The reaction mixture was stirred at 100 °C for 12 h. After completion of the reaction the amount of solvent was reduced and the salts filtered off. The remaining dimethylformamide was removed under reduced pressure. The product was isolated as yellowish oil with a yield of 96%.

^{1}H NMR(400 MHz, DMSO-d_6, TMS$_{int}$). Repeating units δ = 3.22−3.88 (polymer backbone, 10H), 4.45−4.70 (O*H*) ppm.

^{13}C NMR(100 MHz, DMSO-d_6, TMS$_{int}$). Repeating units δ = 51.04 (CH_2N_3), 60.85 (CH_2OH), 68.65, 69.36 ($CH_2CH(CH_2OH)O$, $CH_2CH(CH_2Cl)O$), 78.05 ($CH_2CH(CH_2OH)O$), 80.07 ($CH_2CH(CH_2\ N_3)O$) ppm.

Synthesis of poly(glycidyl amine)-block-poly(glycidol). Poly(glycidol-*co*-glycidyl azide) (8.654 g, 50 mmol) was dissolved in DMF (75 mL) and triphenylphosphine (14,425 g, 55 mmol) was added to the solution which was stirred at room temperature until gas formation stopped. Subsequently, water was added and the solvents were removed under reduced pressure. The polymer was washed with toluene and dried under reduced pressure (10^{-2} mbar). The product was isolated as yellowish oil with a yield of 95%.

^{1}H NMR(400 MHz, DMSO-d_6, TMS$_{int}$). Repeating units δ = 3.35−3.79 (polymer backbone) ppm.

^{13}C NMR(100 MHz, DMSO-d_6, TMS$_{int}$). Repeating units δ = 42.06 (CH_2NH_2), 60.62 (CH_2OH), 69.26 (CH_2CHO), 79.48−80.10 ($CH_2CH(CH_2OH)O$), ($CH_2CH(CH_2\ NH_2)O$) ppm.

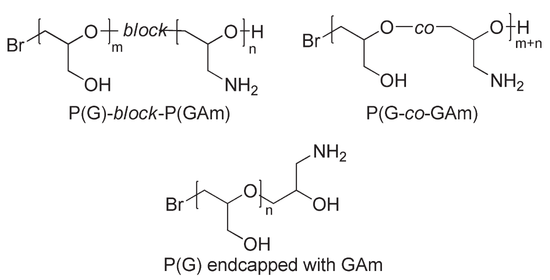
Synthesis of Glycidyl Phthalimide. Potassium phthalimide (100.00 g, 0.492 mol) was dispersed in epichlorohydrin (300.00 mL, 3.826 mol) and stirred under reflux for 8 h. The excess of epichlorohydrin was removed by distillation and the resulting mixture of glycidyl phthalimide and potassium chloride was extracted with chloroform. The product was purified by sublimation under reduced pressure (10^{-2} mbar) to receive a white powder with a yield of 95%.

^{1}H NMR(400 MHz, DMSO-d_6, TMS$_{int}$). δ = 2.70, 2.81 (2H, tr, J = 4.28, q, J = 2.51, $H_2C(O)CHCH_2$), 3.24 (1H, m, $H_2C(O)CHCH_2$), 3.78, 3.83 (1H, d, J = 4.97 $H_2C(O)CHCH_2$), 3.94, 3.99 (1H, d, J = 4.97 $H_2C(O)CHCH_2$), 7.74 (2H, m, ring), 7.88 (2H, m, ring).

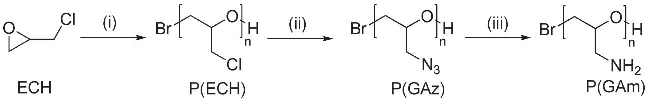
Synthesis of Amine-Terminated Poly(glycidol). Tetraoctylammonium bromide (0. 547 g, 1.00 mmol) was dissolved in dry toluene (3 mL) under nitrogen atmosphere. Ethoxyethyl glycidyl ether (1.462 g, 10.00 mmol) was added. The polymerization was started by addition of triisobutylaluminium 3 mL (3.3 mmol) while cooling with an ice bath. The reaction mixture was allowed to warm up to room temperature and stirred overnight. The reaction was followed via ^{1}H NMR spectroscopy. Subsequently glycidyl phthalimide (0.406 g, 2.00 mmol) was added. After stirring for 1 h toluene was removed under reduced pressure. The polymer was dissolved in tetrahydrofuran and an appropriate amount of diluted hydrochloric acid (5 wt %) was added. The solution was stirred for 30 min and neutralized with sodium bicarbonate. The solvents were removed under reduced pressure, the polymer dissolved in dimethylformamide and the salts filtered off. Hydrazine hydrate (105 mg, 2.10 mmol) were added to the solution. The solvent was removed under reduced pressure, the polymer dissolved and washed with chloroform. The product was isolated as yellowish oil with a yield of 95%.

^{1}H NMR(400 MHz, $CDCl_3$, TMS$_{int}$). Repeating units δ = 3.27−3.64 (backbone, 5H), 4.67−4.77 (CH_2OH) ppm.

Scheme 1. Copolymers with Glycidyl Amine and Glycidol Repeating Units Presented in This Study

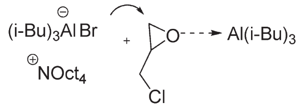


Scheme 2. Reaction Sequence for the Synthesis of Poly(glycidyl amine) Starting from Epichlorohydrin[a]



[a] Key: (i) $NOct_4Br$, $i$$Bu_3Al$, 0°C, room temperature, toluene; (ii) NaN_3, DMF, 110 °C; (iii) 1. PPh_3, DMF, room temperature. 2. H_2O, DMF, room temperature.

Scheme 3. Activation of the Monomer and the Initiator with Al(i-Bu)$_3$



Synthesis of Poly(glycidol)-block-poly(L-alanine). Glycidyl amine terminated poly(glycidol) (943 mg, 1 mmol) with a degree of polymerization of 10, was dissolved in dry dimethylformamide (5 mL) and added to a solution of L-alanine-*N*-carboxy anhydride (345 mg, 3 mmol) in dry dimethylformamide (5 mL) and stirred until the evolving of gas stopped. The solvent was removed under reduced pressure to isolate the product as a white powder with a yield of 98%.

^{1}H NMR(400 MHz, F_3CCO_2D, TMS$_{int}$). Repeating units δ = 1.75−1.83 (CH_3CH, 3H), 3.93−4.30 (CH_2CHO, 3H), 4.82−4.99 (CH_3CH, $CH_2OC(O)CF_3$, 3H) ppm.

RESULTS AND DISCUSSION

Functional polymers can be obtained via conversion of reactive repeating units within a copolymer. The introduction of functionalities can be facilitated by combining repeating units bearing side groups with different reactivity into one macromolecule.

Table 1. SEC Data for Poly(epichlorohydrin) (PECH), Poly(glycidyl azide), and Poly(glycidyl acetylamide)

no.	polymer	M_n(th) (g/mol)[a]	M_n (SEC) (g/mol)[b]	M_n/M_w(SEC)[b]	% conversion[c]
1	poly(epichlorohydrin)	23 133	27 500	1.26	100
2	poly(glycidyl azide)	24 773	21 400	1.26	100
3	poly(glycidyl acetamide)	28 783	21 500	1.21	

[a] Determined from the monomer to initiator ratio at full conversion. [b] Number-average molecular weight (M_n), weight-average molecular weight (M_w), and dispersity index (PI) of the were determined by SEC in DMF using PMMA standard. [c] Determined by ^{13}C NMR spectroscopy.

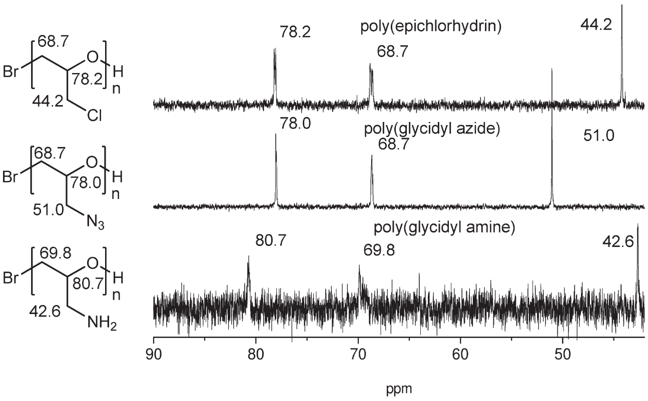


Figure 1. ^{13}C NMR spectra of poly(epichlorohydrin), poly(glycidyl azide), and poly(glycidyl amine) in DMSO-d_6.

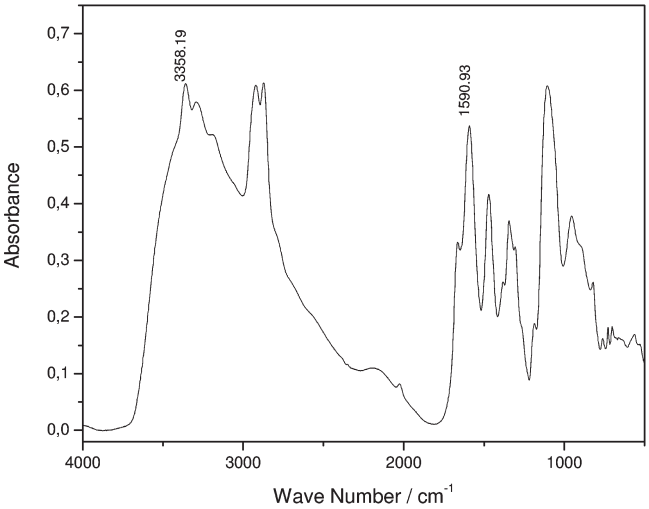


Figure 2. FT-IR spectrum of poly(glycidyl amine) (KBr) showing the two significant peaks of a primary amine.

For this concept, it is essential whether the reactive groups are distributed statistically, block-like or whether the second functionality is only present at the chain ends of the multifunctional polymer (Scheme 1).

In this work, we present a method to convert chloromethyl repeating units within linear polyethers to azido methyl and amino methyl repeating units via polymer analogous reaction. First, their conversions are presented for poly(epichlorohydrin), and then, these reactions were applied to statistical and block copolymers of epichlorohydrin and ethoxyethyl glycidyl ether. Finally, a route to poly(glycidol)s end-capped with a glycidyl amine unit is presented.

Synthesis of Poly(glycidyl amine) Homopolymer. To prepare a polyether with aminomethyl side groups of high molecular weight, epichlorohydrin was homopolymerized and further functionalized as illustrated in Scheme 2.

Epichlorohydrin was polymerized with a system introduced by Deffieux et al.[14] Tetraoctylammonium bromide was used as an initiator and triisobutylaluminium as a catalyst.

Using triisobutylaluminium (Scheme 3) in combination with tetraoctylammonium bromide for the polymerization of epichlorohydrin allows the preparation of well-defined poly(epichlorohydrin). The triisobutylaluminium (used as catalyst) first forms a weakly nucleophilic aluminate complex with N-tetraoctylammonium bromide, and the excess of AlR_3 acts as activator of the oxirane monomer via oxygen—aluminum coordination.[14] In contrast to the conventional anionic polymerization, the weakly nucleophilic aluminate species ensures the propagation without attack to the chloride function of epichlorohydrin, yielding well-defined poly(epichlorohydrin).

A poly(epichlorohydrin) sample with a degree of polymerization of $P_n = 250$ was prepared (Table 1).

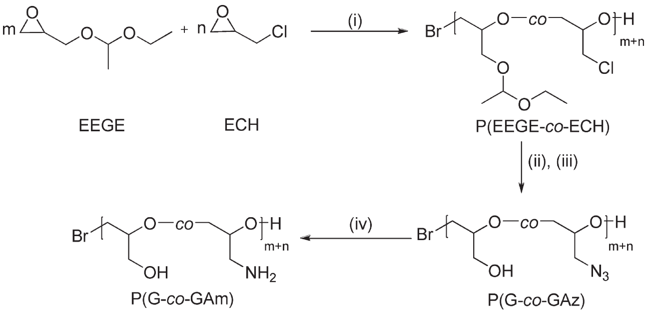
Assuming that exactly one molecule of tetraoctylammonium bromide is initiating one chain, the molar masses are in good agreement with the experimental values. As described in the literature, the polymerization shows no transfer reaction or side reactions with participation of the chloromethyl group. The degree of polymerization can be adjusted by the monomer to initiator ratio. Higher degrees of polymerization require a higher amount of catalyst, since beside the monomer—catalyst complex, the catalyst coordinates also to the polyether backbone.

To transfer the poly(epichlorohydrin) into poly(glycidyl amine), the polymer was first converted into poly(glycidyl azide). This could be achieved by reaction of the polymer with sodium azide in DMF at 110 °C, sodium chloride being the only side product of the reaction. The ^{13}C NMR spectrum of the product shows a quantitative conversion of the chloromethyl groups into azidomethyl groups, as indicated by the shift of the signal of the carbon atom attached to the functional group: $\delta = 44.2$ ppm for CH_2Cl and $\delta = 51.0$ ppm for CH_2N_3 (Figure 1). It is expected, that the bromide group in α-position of the chain is also substituted during azidation and further modification reaction, however, no experimental prove could be provided. To investigate the thermal stability of the resulting poly(glycidyl azide) a thermogravimetric analysis was conducted, which showed a significant mass change only at temperatures above 200 °C.

To yield poly(glycidyl amine) the poly(glycidyl azide) had to be reduced with a suitable agent. The reaction was performed by dissolving the polymer in DMF, adding triphenylphosphine and stirring for 2 h. The, so-called Staudinger reduction forms the corresponding phosphine—imine, which is easily hydrolyzed by the addition of water to release the amine, leaving gaseous nitrogen and triphenylphosphine oxide as only byproducts of the reaction. The reduction can also be performed by palladium-catalyzed hydrogenation, but under laboratory conditions, the Staudinger reduction appeared to be the best choice, as the hydrophobic byproduct triphenylphosphine can easily be separated from the water-soluble polymer. Successful functionalization of the polymers was confirmed by ^{13}C NMR spectroscopy, as indicated by the shift of the signal of the carbon atom attached to the functional group: δ = 51.0 ppm for CH_2N_3 and δ = 42.6 ppm for CH_2NH_2, Figure 1 showing the chemical shifts of the methylene carbon atoms bearing the functionality.

A positive ninhydrin test proved the presence of free amine groups as well. Furthermore, an IR spectrum was recorded, which shows the typical bands: at 3358 cm^{-1} the symmetrical and antisymmetrical stretching of the N−H bond, and at 1590 cm^{-1} a signal corresponding to the bending of the N−H bond of amine groups, where the high intensity indicates the presence of primary amine groups (Figure 2).

Scheme 4. Poly(glycidol-*co*-glycidyl amine): Synthetic concept[a]



[a] Key: (i) $NOct_4Br$, iBu_3Al, 0°C to room temperature, toluene; (ii) THF/HCl/H_2O, room temperature; (iii) NaN_3, DMF, 110 °C; (iv) 1. PPh_3, DMF, room temperature. 2. H_2O, DMF, room temperature.

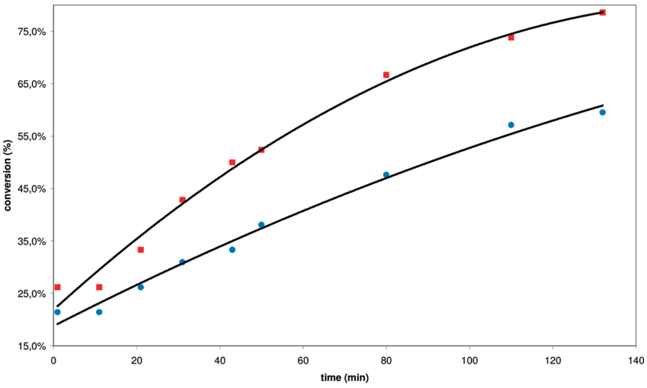


Figure 3. Monomer conversion versus time for the copolymerization of epichlorohydrin and ethoxyethyl glycidyl ether (toluene, 20 °C, [EEGE] = 1.8M, [ECH] = 1.8M, [$NOct_4Br$] = 3.8 × 10^{-2} M, [i-Bu_3Al]/[$NOct_4Br$] = 2.2 (■ = epichlorohydrin; ● = ethoxyethyl glycidyl ether).

SEC-Data obtained from the synthesized PECH and the following intermediates show narrow distributions and confirm, that no side reactions leading to intermolecular coupling occur during the polymer analogues reactions.

Since from copolymers with two reactive side groups multifunctional polymers are more easily accessible, copolymers with glycidol and glycidyl chloride, glycidyl azide or glycidyl amine repeating units were prepared. Poly(glycidol) is known for its biocompatibility[8] and has recently shown to be useful in a wide range of applications, and it is a polyether bearing nucleophilic side chains as well.

Statistical Copolymers of Glycidol and Glycidyl Amine. Epichlorohydrin and glycidol are two commercially available monomers, the polymerization of which was reported in the literature.[4] The copolymerization, however, was not reported to the best of our knowledge. To obtain linear copolymers ECH and protected glycidols have to be used as monomers. Our strategy for the preparation of polyethers with amino methyl and hydroxy methyl side chains comprises four steps (Scheme 4): (i) Copolymerization of ECH with ethoxyethyl glycidyl ether (EEGE) formation of P(EEGE-*co*-ECH). (ii) Removal of the acetal protection group with formation of P(G-*co*-ECH). (iii) Nucleophilic substitution of chlorine with azide with formation of P(G-*co*-GAz). (iv) Reduction of the azide groups to amine groups and formation of P(G-*co*-GAm).

(i). Copolymerization of ECH with Ethoxyethyl Glycidyl Ether (EEGE). The copolymerization of epichlorohydrin and ethoxyethyl glycidyl ether was readily performed by a system previously introduced by Deffieux et al..[14] Tetraoctylammonium bromide as an initiator was dissolved in toluene under nitrogen atmosphere and the desired amounts of monomers were added. The polymerization was started by adding triisobutylaluminium as a catalyst while cooling with an ice bath. Completion of the reaction was confirmed by ^{1}H NMR spectroscopy. To remove traces of the aluminum catalyst the polymer was precipitated in 5% aqueous solution of sodium hydroxide. The degree of polymerization was adjusted by the molar monomer to initiator ratio.

To follow the kinetics a copolymerization with a ratio of ethoxyethyl glycidyl ether to epichlorohydrin of one was analyzed by taking samples from the reaction mixture and quenching the reaction in a mixture of DMSO-d_6 and D_2O (Figure 3). The conversion of each monomer was calculated by comparing the signal intensity of the CH_2 group of epichlorohydrin at δ = 2.85 ppm and the signal intensity of the CH group of

Table 2. SEC Data for Statistical Copolymer of Ethoxyethyl Glycidyl Ether and Epichlorohydrin and Subsequent Modification Steps

no.	copolymers[a]	M_n(th) (g/mol)[b]	M_n(SEC) (g/mol)[c]	M_n/M_w (SEC)[c]	% conversion[d]
1	poly(ethoxyethyl glycidylether$_{30}$-epichlorhydrin$_{70}$)	10 943	10 200	1.35	100
2	poly(glycidol$_{30}$-epichlorohydrin$_{70}$)	8779	8700	1.39	100
3	poly(glycidol$_{30}$-glycidyl azide$_{70}$)	9238	10 000	1.32	100
4	poly(glycidol acetate$_{30}$-glycidyl acetamide$_{70}$)	11 619	8400	1.38	n.d.

[a] Monomer ratio in the feed. [b] Determined from the monomer to initiator ratio at full conversion. [c] Number-average molecular weight (M_n), weight-average molecular weight (M_w), and dispersity index (PI) of the statistical copolymers were determined by SEC in DMF using PMMA standards. [d] Determined by ^{13}C NMR spectroscopy.

ethoxyethyl glycidyl ether at δ = 3.05 ppm with the signal of the methyl group of toluene at δ = 2.30 ppm, used as solvent and standard.

The kinetics show an initially slightly faster consumption of epichlorohydrin compared to ethoxyethyl glycidyl ether. Starting from an equimolar amount of epichlorohydrin and ethoxyethyl glycidyl ether after 30% total monomer conversion the ratio of repeating units in the copolymer ECH:EEGE is equal to 55:45 (Figure 3). After 4 h, the conversion of epichlorohydrin was quantitative and the conversion of ethoxyethyl glycidyl ether reached a value of 98%.

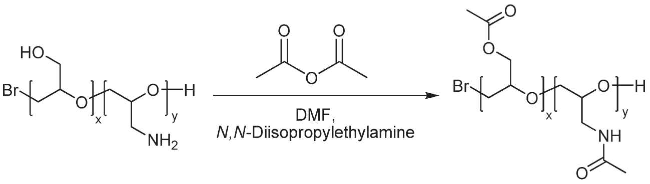
Removal of the acetal protection group of poly(ethoxyethyl glycidyl ether-*co*-epichlorohydrin) to form poly(glycidol-*co*-epichlorohydrin) is readily achieved by dissolving the polymer in THF and adding an appropriate amount of diluted hydrochloric acid to hydrolyze the acetal. The polymer was purified by neutralizing the solution with sodium hydrogen carbonate, removing the solvent and drying the polymer under reduced pressure. ^{1}H NMR spectroscopy proved a quantitative removal of the protection group; the chloromethyl group remained unchanged during this process. By this procedure polymers of different composition were prepared (Table 2).

To convert the chloromethyl groups of the epichlorohydrin repeating units to the azid methyl groups the poly(glycidol-*co*-epichlorohydrin) with a ratio of G/ECH = 1 was dissolved in dimethylformamide and sodium azide was added. The reaction mixture was stirred at 100 °C for 12 h. Under these conditions sodium azide is soluble in dimethylformamide, while the resulting sodium chloride is not. ^{13}C NMR spectroscopy proves a quantitative substitution of the chloride by azide.

The copolymer of poly(glycidol-*co*-glycidyl azide) was used for the reaction with propargyl alcohol and for the preparation of poly(glycidol-*co*-glycidyl amine).

Reduction of poly(glycidol-*co*-glycidyl azide) was performed by dissolving the polymer in DMF to react it with triphenylphosphine to form phosphine imines. The imines are easily hydrolyzed by addition of water to the reaction mixture. Finally, the solvents were removed and the polymer was washed with toluene and dried under reduced pressure. Also here ^{13}C NMR spectroscopy proves a quantitative substitution of the chloride by azide, without affecting the hydroxyl groups. Because of the cationic nature of the amine groups in the presence of water and hence possible interactions with the column material, the copolymer of poly(glycidyl amine) and poly(glycidol) was not analyzed by SEC. Instead the copolymer was reacted with acetic anhydride (Scheme 5) to yield an acetylated copolymer bearing acetate and acetamide side groups, with a procedure, that was previously used by Frey et al.[26]

Scheme 5. Derivatization of Poly(glycidol-*co*-glycidyl amine) with Acetic Anhydride



The conversion of a copolymer of ethoxyethyl glycidyl ether and epichlorohydrin to a copolymer of glycidol and glycidyl amine was followed by SEC. The SEC data of the different intermediates confirm, that no side reactions leading to cross-linking or intermolecular coupling occur during the polymer analogous reactions (Table 2).

Block Copolymers of Glycidol and Glycidyl Amine. Assuming a living controlled character of the polymerization block copolymers of glycidol and glycidyl amine were synthesized by sequential monomer addition followed by polymer analogous reaction. The desired block of epichlorohydrin was prepared first, and after full consumption of the monomer (confirmed by ^{1}H NMR), the calculated amount of ethoxyethyl glycidyl ether was added to prepare the second block. It appeared to be more advantageous to synthesize the poly(epichlorohydrin) block first, as this polymerization proved to be more reliable and the consumption is usually quantitative, while the conversion of ethoxyethyl glycidyl ether is usually below 96%. Table 3 shows the SEC values for two block copolymers prepared.

To determine the initiation efficiency of poly(epichlorohydrin)* (denotes the active polymer*) SEC of the first block, as well as of the block copolymer were recorded (Figure 4). The SEC trace corresponding to the first block poly(epichlorohydrin) is shifted completely to higher molar masses in agreement with quantitative formation of a diblock copolymer.

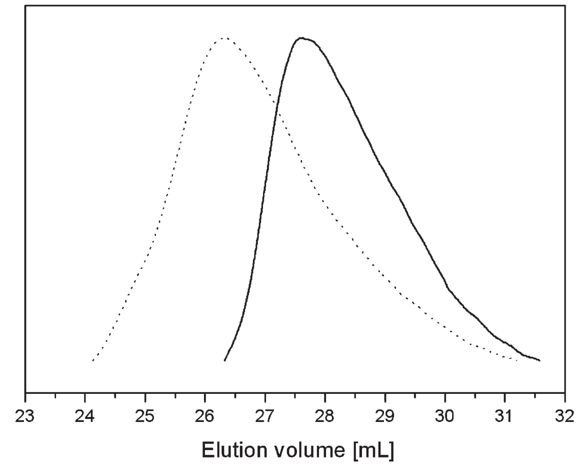


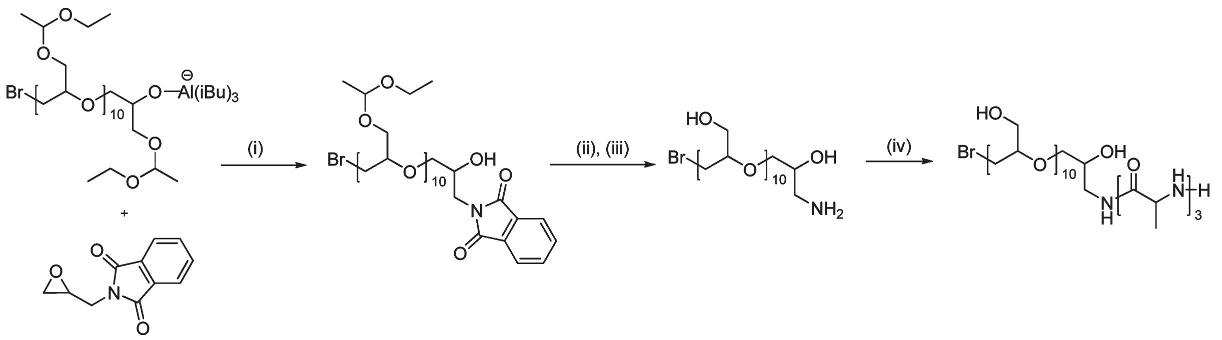
Figure 4. SEC traces corresponding to the different stages of the synthesis of a poly(epichlorohydrin)-*block*-poly(ethoxyethyl glycidyl ether): PECH block (solid line); block copolymer (dashed line).

Table 3. SEC-Data for block copolymers of epichlorohydrin and ethoxyethyl glycidyl ether

no.	ECH/EEGE (feed)[a]	M_n-P(ECH)-block (th) [g/mol][b]	M_n-P(EEGE)-block (th) [g/mol][b]	ECH/EEGE[c]	M_n(SEC)[d] [g/mol]	M_n/M_w[d]
1	50/50	4706	7309	47/53	16 200	1.58
2	20/160	1930	23 000	20/158	17 000	1.59

[a] Monomer ratio in the feed. [b] Determined from the monomer to initiator ratio at full conversion. [c] Ratio of repeating units in the copolymer, determined by ^{1}H NMR spectroscopy. [d] Number-average molecular weight (M_n), weight-average molecular weight (M_w), and dispersity index (PI) of the block copolymer were determined by SEC in DMF using PMMA standards.

Scheme 6. Synthesis of Amino End-Capped Poly(glycidol)[a]



[a] Key: (i) *i*Bu$_3$Al, Oct$_4$NBr, toluene, room temperature; (ii) tetrahydrofuran, HCl/H$_2$O, room temperature; (iii) dimethylformamide, hydrazine monohydrate, room temperature, (iv) dry dimethylformamide, room temperature, L-Ala-NCA.

In the following the block copolymers of epichlorohydrin and ethoxyethyl glycidyl ether were treated in the same way as the statistical copolymers. The acetal group was removed by hydrolysis in tetrahydrofuran with diluted hydrochloric acid and the polymer was subsequently reacted with sodium azide to yield poly(glycidyl azide)-*block*-poly(glycidol). Then the azide was reduced to the amine following the Staudinger reaction. Successful functionalization was proven by ^{13}C NMR spectroscopy as well, by the shift of the signal of the carbon atom attached to the functional group. No difference in reactivity compared to the statistical copolymers was observed.

Synthesis of Amino End-Capped Poly(glycidol) and Its Use as Initiator for L-Alanine-*N*-carboxy Anhydride (L-Ala-NCA). Since amino telechelic PEGs show a growing importance in the synthesis of drug carriers, it was our aim to achieve an amino terminated poly(glycidol) and to show its potential as initiator for the polymerization of *N*-carboxy anhydrides of amino acids. To ensure that end-capping occurs only with one building block a monomer with high steric hindrance, glycidyl phthalimide, was chosen. In a model experiment glycidyl phthalimide (M) and potassium *tert*-butoxide (I) were reacted in dioxane and DMSO under the conditions suitable for anionic polymerization in molar ratio of one [M]/[I] = 10. Only nonconverted glycidyl phthalimide and the 1:1 addition product of potassium *tert*-butoxide and glycidyl phthalimide were observed. The same result was obtained for the earlier described system of *i*Bu$_3$Al and Oct$_4$NBr in toluene. This observation applies not only for homopolymerization of glycidyl phthalimide; it applies for copolymerization with ethoxyethyl glycidyl ether as well, proving the high steric hindrance of the phthalimide groups, inhibiting the chain growth reactions. Therefore, it is a convenient method for end-capping of poly(ethoxyethyl glycidyl ether). The synthetic concept is illustrated in Scheme 6. First, ethoxyethyl glycidyl ether is polymerized using tetraoctylammonium bromide as initiator and triisobutylaluminium as catalyst. After full conversion of ethoxyethyl glycidyl ether glycidyl phthalimide is added (i). Then the ethoxyethyl glycidyl ether is readily hydrolyzed to poly(glycidol) by using hydrochloric acid in tetrahydrofuran (ii), the phthalimide is converted with hydrazine in DMF to amine and phtalhydrazide(iii), and to show its ability for the functionalization with peptides, the polymer was reacted with L-alanine-*N*-carboxy anhydride. Glycidyl phthalimide monomer was synthesized in a convenient method by refluxing epichlorohydrin in the presence of potassium phthalimide and potassium carbonate and was purified by sublimation (the ^{1}H NMR spectrum is in good accordance with the literature[30,31]). To clearly detect the end group a poly(ethoxyethyl glycidyl ether) with a degree of polymerization of five was synthesized in toluene with tetraoctylammonium bromide as initiator and triisobutylaluminium as catalyst and end-capped by addition of glycidyl phthalimide. SEC analysis with tetrahydrofuran as the eluting solvent revealed an increase of the molecular weight from 2000 g/mol to 2200 g/mol a decrease of the dispersity index from 1.17 to 1.10. Subsequent removal of the acetal protection group in the way described before yields poly(glycidol) end-capped with a phthalimide group. The successful end-capping reaction—addition of the phthalimide to the growing poly(ethoxyethyl glycidyl ether) chain—was confirmed by SEC analysis of poly(glycidol) with a phthalimide terminus in water using an UV detector and a refractive index detector. The overlap of the distribution curves obtained proves the successful end-capping (Figure 5) and shows a narrow dispersity index of 1.09.

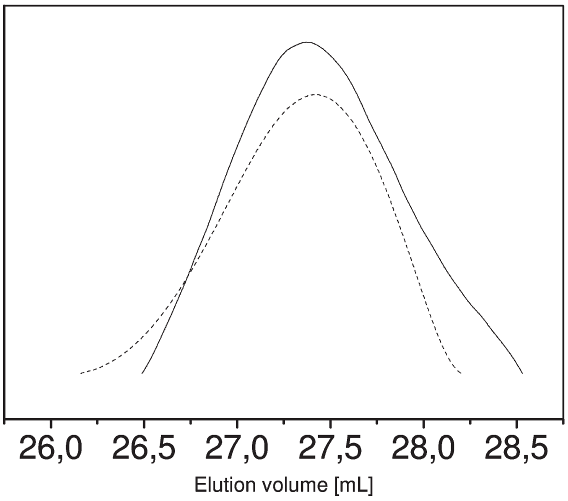


Figure 5. SEC traces (H$_2$O) for phthalimide terminated poly(glycidol), obtained with refractive index detector and UV light detector, respectively: UV (solid line); RI (dashed line).

The poly(glycidol) end-capped with glycidyl phthalimide was readily transformed into an amino terminated poly(glycidol) by reaction of the phthalimide with hydrazine to yield the free amine and phthalhydrazide (Scheme 6).

To show its ability for the functionalization with peptides, the polymer was reacted with L-alanine-*N*-carboxy anhydride in a

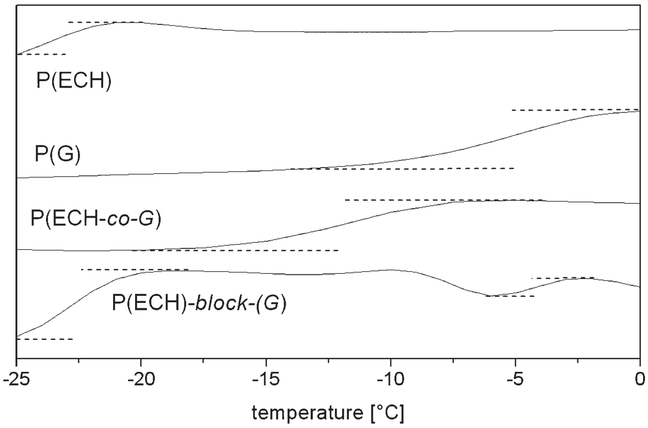


Figure 6. DSC measurements of poly(epichlorohydrin), poly(glycidol), and a statistical copolymer of a ratio of 60 to 40.

ratio of three units of α-amino acid for each polymer chain. The reaction was performed by mixing the polymer and L-alanine-*N*-carboxy anhydride in dry dimethylformamide, to yield a white powder. After removing the solvent, the block copolymer of poly(glycidol) and L-alanine was soluble in trifluoroacetic acid and showed the expected chemical shifts in the ^{1}H NMR spectrum.[32]

Thermal Properties. In order to determine the thermal properties of the copolymers, DSC measurements of poly(epichlorohydrin), poly(glycidol), and a statistical copolymer with a molar ratio of repeating units of one were performed. The glass transition temperatures of poly(epichlorohydrin) and poly(glycidol) were determined to be at −23.8 and −4.8 °C respectively, in accordance with literature values.[33,34] Taking into account the T_g values of the homopolymers the T_g value of a copolymer with a mass fraction epichlorohydrin (w_1) to glycidol (w_2) repeating units of $w_1/w_2 = 55.6/44.4$ was calculated using Fox's equation[35]

$$\frac{1}{T_g} = \frac{w_1}{T_{g1}} + \frac{w_2}{T_{g2}}$$

giving a value of $T_g = -15.7$ °C. The experimental glass transition temperature was determined to be −11.6 °C, close to the calculated value, this result further proves the statistical distribution of the repeating within the copolymer (Figure 6). A diblock copolymer with equimolar amounts of epichlorohydrin and ethoxyethyl glycidyl ether was also analyzed by DSC and shows two glass transition temperatures ($T_{g1} = -22.9$ and $T_{g2} = -4.5$ °C), close to the ones of the homopolymers, indicating microphase separation.

CONCLUSIONS

For the first time poly(glycidyl amine) homopolymer and statistical copolymers with glycidol and glycidyl amine repeating units as well as block copolymers were synthesized and characterized. The polyethers were prepared by (co)polymerization of epichlorohydrin and ethoxyethyl glycidyl ether and subsequent polymer analogous reactions. NMR analysis proves for all reactions a quantitative degree of functionalization. Poly(glycidyl azide-*co*-glycidol), as an intermediate of these reactions proved to be a useful reagent for the functionalization of polyethers by the Huisgen−1,3-dipolar cycloaddition (click reaction).

Furthermore, we found a convenient method for synthesizing poly(glycidol) with a terminal amino glycidyl group, which was used for functionalization with L-alanine-NCA. Thus, poly(glycidol)s with an amino end group are good alternatives for Jeffamines.

ASSOCIATED CONTENT

Ⓢ **Supporting Information.** ^{1}H and ^{13}C NMR spectra, as well as SEC elugrams. This material is available free of charge via the Internet at http://pubs.acs.org.

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