Linear High Molar Mass Polyglycidol and its Direct α-Azido Functionalization

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Summary: Linear polyglycidols with narrow chain dispersity and controlled high molar masses were prepared in a few hours by monomer-activated anionic polymerization of protected monomers, ethoxyethyl glycidyl ether and *tert*-butyl glycidyl ether, using a system composed of tetraoctylammonium bromide as initiator and triisobutylaluminum, used in 1.5 to 5-fold excess compared to the initiator, as co-initiator and monomer activator. This synthetic approach was shown to give various polyglycidol-based copolyethers in particular with propylene oxide or butene oxide. α-Azido,ω-hydroxy-poly(ethoxyethyl glycidyl ether) and other polyethers were directly prepared when tetrabutylammonium azide was used as initiator. Size exclusion chromatography and matrix-assisted laser desorption/ionization time-of-flight characterizations as well as ''click'' reactions were used to demonstrate the efficiency of the functionalization.

Keywords: anionic polymerization; click chemistry; copolymerization; glycidol; monomer activation

Introduction

Polyglycidol, a water-soluble polymer, and its copolymers are of great interest for biomedical applications, due to its biocompatibility and high hydroxyl functionality.[1–3] Many polymerization studies of protected glycidol have been conducted to get linear and high molar mass polymers using anionic and coordinated type mechanisms.[4–11] The efficiency and ease of the monomer protection step and its deprotection by acidic treatment makes ethoxyethyl glycidyl ether (EEGE) a good candidate as monomer for the synthesis of linear polyglycidols. *Tert*-butyl glycidyl ether (*t*BuGE) appears also interesting due to its commercial availability.[6] Coordinated polymerization using diethylzinc/water or calcium amide alkoxide allows to get high molar mass with a broad distribution whereas an anionic one permits the synthesis of limited molar masses due to chain transfer.[11] Despite this drawback and to take advantage of the hydrophilic behaviour and the high functionality of polyglycidol, a series of block and random copolymers with ethylene oxide or others were already proposed.[5,8,12–18] However, the polyglycidol part remained limited to low polymerization degrees. The synthesis of high molar mass polyglycidol and copolymers still remains a challenge in order to enlarge the scope of applications, especially in the biomedical field.

Chain ends functionalization appears also essential for the preparation of reactive polymers and for their selective conjugation to organic and inorganic substrates as well as to their end coupling to other polymer chains. The ''click chemistry'' based on the Huisgen's 1,3 dipolar cycloaddition between an azide and an alkyne function in presence of a copper catalyst[19,20] can be carried out in various media, including water, and can be very efficiently applied to the preparation of

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linear block copolymers, dendrimers, gels, surface functionalization, as well as to cells and virus modifications in biomolecular engineering.[21–23] The azide group is so far introduced by mesylation of the hydroxyl terminus of previously formed polymers followed by its subsequent substitution with sodium azide.[24,25] Indeed, most of the poly(ethylene glycol) (PEG) azidation routes reported in the literature involve so far the chemical modification of previously formed hydroxyl-terminated PEGs.[26–28]

The present study deals with the use of ammonium salts as initiators in the presence of triisobutylaluminum (*i*-Bu_3Al) as co-initiator and activator for the homopolymerization of protected glycidol and for their copolymerization with hydrophobic propylene oxide (POx) or butene oxide (BOx) in the aim to synthesize (co)polymers with linear and controlled high molar masses. The direct synthesis of α-azido, ω-hydroxy terminated polyglycidols and other polyethers, starting from tetrabutylammonium azide, will be also presented.

Experimental Part

Materials

Triisobutylaluminum (1 mol/L in toluene, Aldrich) was used without further purification. 2,3-Epoxypropan-1-ol (glycidol, 96%, Aldrich) and ethyl vinyl ether (99% Aldrich) were used as received. Propylene oxide (99%, Fluka), butene oxide (99%, Aldrich) and *tert*-butylglycidyl ether (99%, Aldrich) were purified over CaH_2, distilled under vacuum, and stored for 15 min in a glass flask equipped with PTFE stopcocks in the presence of i-Bu_3Al to remove traces of impurities. They were finally distilled under vacuum and stored under vacuum at RT in calibrated glass tubes until use. Toluene (98%, J.T. Baker) was purified with polystyryllithium seeds. It was distilled under vacuum and then stored in calibrated glass tubes under vacuum. Tetraoctylammonium bromide ($NOct_4Br$) (98%, Aldrich) and tetrabutylammonium azide (NBu_4N_3) (97%, Aldrich) were solubilized into dried toluene. A solution of each compound was then stored in graduated glass tubes fitted with PTFE stopcocks at 4 °C. Ethoxyethyl glycidyl ether was synthesized from glycidol and ethyl vinyl ether as already reported[29] with a yield of 90%, dried with CaH_2 and distilled prior to use. N,N-dimethylformamide (HPLC grade, Scharlau) and N,N,N′,N‘,N′-pentamethyldiethylenetriamine (99%, Aldrich) were used without further purification. Copper bromide (I) (Aldrich, 98%) was washed with a water/acetic acid (1:2) solution then filtered and washed again with methanol before use. 1,7-octadiyne (98%, Aldrich) was diluted with butanol and used without further purification. Toluene (98%, J.T. Baker) was purified with polystyryllithium seeds. It was distilled under vacuum and then stored in graduated glass tubes under vacuum.

Procedures

All (co)polymerizations were performed between −30 °C and 25 °C under argon in a glass reactor equipped with a magnetic stirrer and fitted with PTFE stopcocks. As example, 1 mL of ethoxy ethyl glycidyl ether ($n_{EEGE} = 6.85$ mmol) is added to 11.4 mL of toluene. 0.33 mL of a toluene solution of NBu_4N_3 ($n_{initiator} = 0.1$ mmol) and 0.5 mL of a triisobutylaluminum solution in toluene ($n_{i\text{-}Bu3Al} = 0.5$ mmol) were then added via a syringe under argon at −30 °C. The reaction is stirred and left to increase to 25 °C for 4 hours. Ethanol (1mL) was used to stop the reaction. The polymer conversions were determined gravimetrically after complete drying of the polymer under vacuum at 50 °C. Conversion: 100%. Theoretical $\overline{M}_n = 10\,000$ g/mol and SEC $\overline{M}_n = 9\,900$ g/mol. $I_p = 1.30$. ^{1}H NMR of PEEGE: $-O-CH_2(1)-CH(2)[CH_2(3)-O-CH(4)-CH_3(5)-O-CH_2(6)-CH_3(7)]$: 1,2,3,6, 3.35-3.75 ppm; 4, quadruplet at 4.75 ppm; 5, 1.27 ppm; 7, 1.17 ppm.

Deprotection of PEEGE was carried out in ethanol with 3% HCl and stirred for four hours. The polymer was then evaporated under reduced pressure and finally dried under vacuum. Deprotection of PtBuGE

was done in ethanol with 3% HCl under stirring for 24 hours at 60 °C. After neutralization by adding sodium carbonate, ethanol was evaporated under reduced pressure and polyglycidol finally dried under vacuum. ^{1}H NMR of Polyglycidol: O−CH_2(1)−CH(2)[CH_2(3)−OH]−O: 1, 2, 3, 3.60-3.85 ppm.

For the ''click'' reaction, 0.74 g of α-azido functionalized PEEGE (n_{PEEGE} = 0.067 mmol) was solubilized into 7 mL of dimethylformamide (DMF). 0.02 g of CuBr (n_{CuBr} = 0.134 mmol), 0.028 mL of pentamethyldiethylenetriamine (PMDETA) (n_{PMDETA} = 0.0134 mmol) and 0.22 mL of a solution of octadiyne in toluene ($n_{Octadiyne}$ = 0.033 mmol) were then added. The reaction was stirred at room temperature for 48 hours. The polymer was recovered by drying under vacuum, re-dissolved in pure toluene and precipitated in pentane several times at low temperature before analysis. $\overline{M}_n$ = 11 000 g/mol and I_p = 1.25 before reaction and $\overline{M}_n$ = 20 000 g/mol and I_p = 1.60 after reaction.

Analysis

Polymer molar masses were determined by Size Exclusion Chromatography (SEC) at 40 °C using tetrahydrofuran (THF) as eluent. Measurements in THF were performed on a PL GPC50 integrated system with RI and UV detectors and three TSK columns G4000HXL (particles of 5 μm, pore size of 200 Å and exclusion limit of 400 000 Da), G3000HXL (particles of 5 μm, pore size of 75 Å and exclusion limit of 60 000 Da), G2000HXL (particles of 5 μm, pore size of 20 Å and exclusion limit of 10 000 Da) at an elution rate of 1mL/min. Polystyrene were used as standards (except for PEO where PEO standards were used). Measurements in dimethylformamide (DMF) were performed for polyglycidols on a similar apparatus with the same kind of columns, elution rate and standards.

^{1}H (400 MHz) NMR measurements of the polymers and copolymers were performed on a Brüker Avance 400 spectrometer, in $CDCl_3$ or D_2O at room temperature.

^{1}H NMR of P*t*BuGE: −O−CH_2(1)−CH(2)-[CH_2(3)−O−[CH_3(4)]$_3$]: 1,2,3, 3.35-3.70 ppm; 4, 1.17 ppm.

^{1}H NMR of P(EEGE-co-POx): −O−CH_2(1)−CH(2)[−CH_2(3)−O−CH(4)-−CH_3(5)−O−CH_2(6)−CH_3(7)]−co−O-−CH_2(8)−CH(9)[CH_3(10)]: 1,2,3,6,8,9, 3.35-3.75 ppm; 4, quadruplet at 4.75 ppm; 5, 1.27 ppm; 7 and 10, 1.17 ppm.

^{1}H NMR of P(t-BuGE-co-BOx): −O−CH_2(1)−CH(2)[−CH_2(3)−O−C(CH_3)$_3$-(4)]-co-O−CH_2(5)−CH(6)[−CH_2(7)−CH_3-(8)]: 1,2,3,5,6, 3.35-3.75 ppm; 4, 1.17 ppm; 7, 1.35–1.65 ppm; 8, triplet at 0.90 ppm.

Osmometric measurements were performed on a Gonotec Osmomat 090 device in toluene with a Tac 5kD membrane. Osmotic pressures were measured for each sample at 5 concentrations: 0.2; 0.5; 1; 2 and 5 mg/mL.

Matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) spectra were performed on a Voyager mass spectrometer (Applied Biosystems). The instrument was equipped with a pulsed N_2 laser (337 nm) and a time-delayed extracted ion source. Spectra were recorded in the positive-ion mode using the reflectron and with an accelerating voltage of 20 kV. Samples were dissolved in CH_2Cl_2 at 10 mg/mL. The DCTB matrix (trans-2-(3-(4-t-butyl-phenyl)-2-methyl-2-propenylidene)malononitrile) solution was prepared by dissolving 10 mg in 1 mL of CH_2Cl_2. A MeOH solution of cationization agent (NaI, 10 mg/mL) was also prepared. The solutions were combined in a 10:1:1 volume ratio of matrix to sample to cationization agent. 1–2 μl of the obtained solution was deposited onto the sample target and vacuum-dried.

Results and Discussion

Polymerization of Ethoxyethyl Glycidyl ether and t-butyl Glycidyl Ether

A binary initiating system constituted of $NOct_4Br$ as initiator and *i*-Bu_3Al as catalyst/activator has been recently reported by us for the controlled anionic polymerization of epoxides[30–33] in hydrocarbon

media. This system was investigated for the polymerization of EEGE and t-BuGE, as a protected form of glycidol. As indicated in Table 1, polymerization of EEGE proceeds in toluene at low temperature, for [*i*-Bu_3Al]/[$NOct_4Br$] ratios equal to 4 or 5. In such conditions high molar mass PEEGE (85 000 g/mol) were prepared in a few hours. At lower ratios, polymerization occurs but non complete monomer conversions can be observed. Experimental molar masses, determined by SEC on the basis of a polystyrene calibration, are in the range of the calculated ones, assuming the formation of one PEEGE chain per $NOct_4Br$. A good correlation between SEC PS molar masses and PEEGE ones was shown by osmometry measurements performed on PEEGE samples with molar masses ranging from 10 000 g/mol to 30 000 g/mol (see Table 1). Transfer to monomer limiting the molar masses described by Keul and Moeller[11] with conventional initiator like potassium alkoxides was not observed with the initiating system we have used. Indeed, no characteristic peaks of allylic end groups at 4, 5 and 6.6 ppm appeared in the ^{1}H NMR spectra of all protected polyglycidol synthesized (Figure 1).

Table 1.
Polymerization of ethoxyethyl glycidyl ether (EEGE) and t-butyl glycidyl ether (t-BuGE) with $NOct_4Br$/*i*-Bu_3Al (toluene, 0 °C, conversion = 100%).

Monomer	[*i*-Bu_3Al]/[$NOct_4Br$]	[M] (mol/L)	Time (h)	$\overline{M}$n th[a] (g/mol)	$\overline{M}_n$exp (g/mol)		$\overline{M}_w/\overline{M}_n$[b]
					SEC [b]	Osmo[c]	
EEGE	4	0.5	9	10 000	10 300	11 000	1.06
EEGE	4	1	19	30 000	29 600	31 000	1.06
EEGE	5	2	15	100 000	85 000		1.27
t-BuGE	2	1	3	20 200	20 000		1.02
t-BuGE	3	1	3	30 000	26 000		1.15
t-BuGE	4	3	7[d]	65 000	52 000		1.37

[a] $\overline{M}_n th = [M]_0/[NOct_4Br] \times M_{Monomer}$. [b] determined by Size Exclusion Chromatography in tetrahydrofuran using a calibration with polystyrene standards. [c] determined by osmometry in toluene. [d] the temperature was left to increase up to 25 °C.

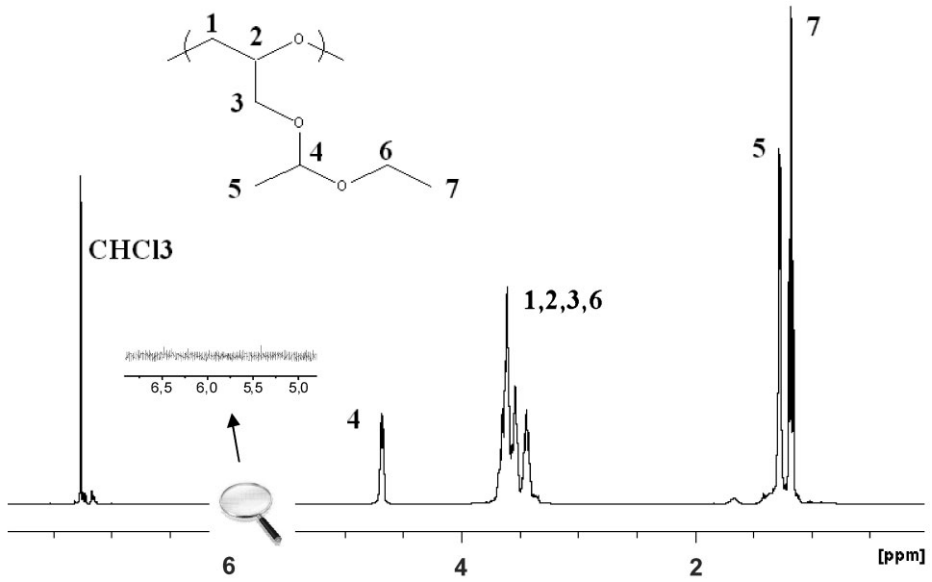


Figure 1.
Typical ^{1}H NMR spectrum of PEEGE synthesized using $NOct_4Br$/*i*-Bu_3Al as initiating system (see Table 1, run 2).

EEGE polymerization kinetics were carried out by dilatometry. Typical conversion *vs* time curves are plotted Figure 2 for [*i*-Bu_3Al]/[$NOct_4Br$] ratios 2 and 4 as well as $\ln([M]_0/[M])$ *vs* time for a ratio equal to 4. For 2 equivalents of [*i*-Bu_3Al], the monomer consumption levels off at about 60% conversion and does not reach completion, although the final molar masses remains in good agreement with theoretical values at the obtained conversion. Indeed, the PEEGE molar mass increases linearly with the monomer conversion up to the final yield, whereas molar mass distribution remains narrow, see Figure 3. This behaviour can be explained by a living-like reaction, without termination and transfer, in which the *i*-Bu_3Al fraction used to trigger the reaction is trapped by complexation with the oxygen of poly(EEGE) chain. In contrast, for 4 equivalents of *i*-Bu_3Al, a linear consumption, up to 90%, of EEGE is observed in a few minutes, at 0 °C, yielding PEEGE of 10 000 g/mol with a dispersity of 1.11. The $([M]_0 - [M]/[M]_0) = f(t)$ plot follows a linear rate law up to high EEGE conversion, whereas the $\ln([M]_0/[M])$ *vs* time plot is not linear. This suggests an apparent zero monomer order for the propagation reaction as already proposed for the monomer-activated mechanism of propylene oxide.[30]

Compared to EEGE, polymerization of *t*BuGE proceeds more readily and goes to completion in a few hours using only 2 equivalents of triisobutylaluminum with respect to the tetraoctylammonium bromide initiator. This can be explained by the presence of a single oxygen atom on the *t*BuGE and on P*t*BuGE units, without counting the oxygen atom of the reactive and reacted epoxide function, which is moreover greatly hindered by its *tert*-butyl substituent. This limits strongly the non-desired complexation of the aluminium compound by the chain. P*t*BuGE experimental molar masses are in the range of calculated ones and dispersities remain narrow for a molar mass up to 26 000 g/mol or slightly broad for a sample at 52 000 g/mol. This indicates that no significant side reaction occurs during propagation. But the preparation of much higher molar masses starting with this

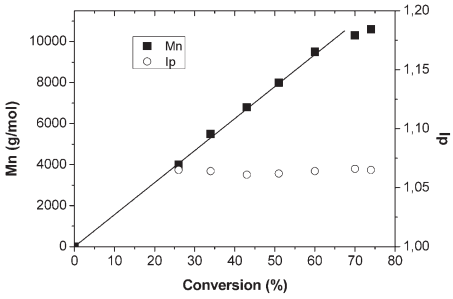


Figure 3.
Evolution of molar masses and molar mass distribution (Ip) versus conversion in the polymerization of (EEGE) (toluene, 0 °C, [EEGE] = 0.5 M, [$NOct_4Br$] = 7.10^{-3} M, [*i*-Bu_3Al]/[$NOct_4Br$] = 2).

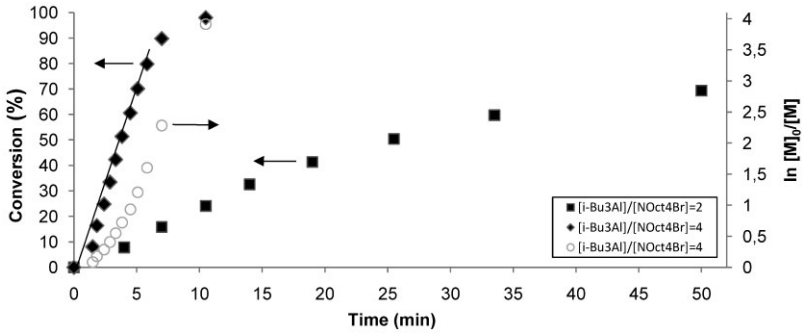


Figure 2.
Conversion (filled squares) and $\ln[M]_0/[M]$ (open circles) versus time plots for the polymerization of ethoxyethyl glycidyl ether (EEGE) (toluene, 0 °C, [EEGE] = 0.5 M, [$NOct_4Br$] = 7.10^{-3} M, [*i*-Bu_3Al]/[$NOct_4Br$] = 2 (■) or 4 (○)).

monomer appeared more problematic than EEGE. Polymer solubility difficulties appeared in many solvents and can be one reason. Despite this limitation the data reported and its commercial availability makes *t*BuGE a first ranked raw material for the synthesis of linear polyglycidol by the reported polymerization system, assuming that the deprotection step would proceed cleanly.

All the results agrees with the formation of a 1:1 initiating and propagating complex of low basicity, which strongly minimizes transfer reactions to monomer, and of high nucleophilicity, due to the activation role of the excess of Lewis acid, allowing fast reactions at low temperatures.

Deprotection of Poly(EEGE) and Poly(tBuGE) Units

Both acetal and *tert*-butyl protecting groups of glycidol units respectively in PEEGE and P*t*BuGE can be removed by acidic treatment although the deprotection conditions are quite different. Acetal groups of PEEGE can be quantitatively removed by treatment of the polymer in an acidic ethanol solution (3% vol of HCl) in 4 hours at room temperature. Removal of the *tert*-butyl groups of P*t*BuGE using the same acidic ethanol solution requires 24 h at 60 °C. SEC analysis carried out in DMF on protected and deprotected polyglycidol shows no peak broadening in agreement with a clean deprotection step, Figure 4. The apparent polyglycidol molar mass are higher than that of the initial PEEGE, although the repetitive unit decrease from 146 g/mol to 74 g/mol, leading to a loss of around half of the polymer molar mass. This may be explained by the difference of hydrodynamic volume of PEEGE and polyglycidol.

Copolymerization Studies

The copolymerization of EEGE and *t*BuGE with other epoxides mixed at the same time, respectively propylene oxide and butene oxide, were investigated to examine the possibility of synthesizing copolyethers of various hydrophilicity or amphiphilicity (Table 2, Figure 5 and 6).

Copolymerizations proceed to complete monomers consumption, yielding copolymers with similar average composition as the comonomer feed, experimental molar

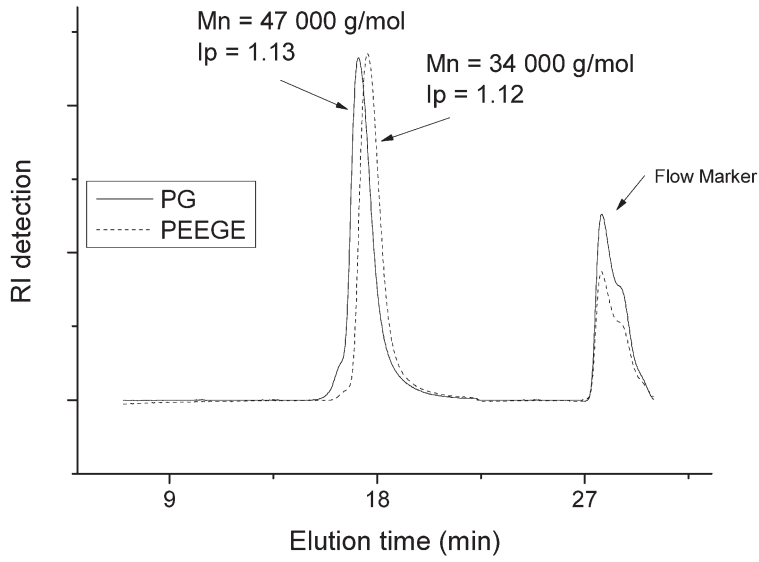


Figure 4.
SEC chromatograms and apparent molar mass (polystyrene calibration) of a PEEGE prepared using $NOct_4Br/i\text{-}Bu_3Al$ (1/5) as initiating system before and after deprotection using HCl/ethanol (3/97 in volume).

Table 2.
Copolymerization of EEGE with propylene oxide and *t*BuGE with butene oxide initiated with $NOct_4Br$ / i-Bu_3Al (toluene, [M] = 1–2 M, −30 °C, conversion = 100%).

Theoretical Composition (A–B)	[i-Bu_3Al]/[$NOct_4Br$]	Time (h)	$\overline{M}_w/\overline{M}_n$	DP_A/DP_B Theoretical	DP_A/DP_B Experimental[a)]
$EEGE_{68}$-POx_{172}	5	3	1.53	0.40	0.48
$EEGE_{68}$-POx_{172}	5	0.5	1.43	0.40	0.44
$EEGE_{25}$-POx_{262}	5	17	1.58	0.25	0.22
$EEGE_{137}$-POx_{172}	5	17	1.34	0.80	0.82
t-$BuGE_{42}$-BOx_{69}	2	3	1.14	0.61	0.52
t-$BuGE_{77}$-BOx_{139}	2	5	1.16	0.55	0.57

[a)]Determined by ^1H NMR

masses in the range of theoretical ones and low dispersities particularly for t-BuGE-based copolymers. Some broadening can be attributed to the high $NOct_4Br/i\text{-}Bu_3Al$ ratio used (1/5), necessary to quantitatively polymerize EEGE, which induces a very high reactivity for POx and results in a slight contribution of transfer reaction.[30] The reactivity ratios between EEGE and POx were determined in a series of copolymerization experiments stopped at low conversion, using the Kelen-Tudös method.[34] This yields $r_{POx} = k_{POxPOx}/k_{POxPEEGE} = 3.58$ and $r_{PEEGE} = k_{PEEGEPEEGE}/k_{PEEGEPOx} = 0.18$ indicating, in living-like conditions, the formation of copolymers with a gradient composition constituted by a predominant incorporation of POx units at the beginning of the chains and EEGE units at the end. This yield after release of the hydroxyl groups of the glycidol units copolymers with an amphiphilic character. Indeed, a preliminary study of their behaviour in water showed the formation of micelles.

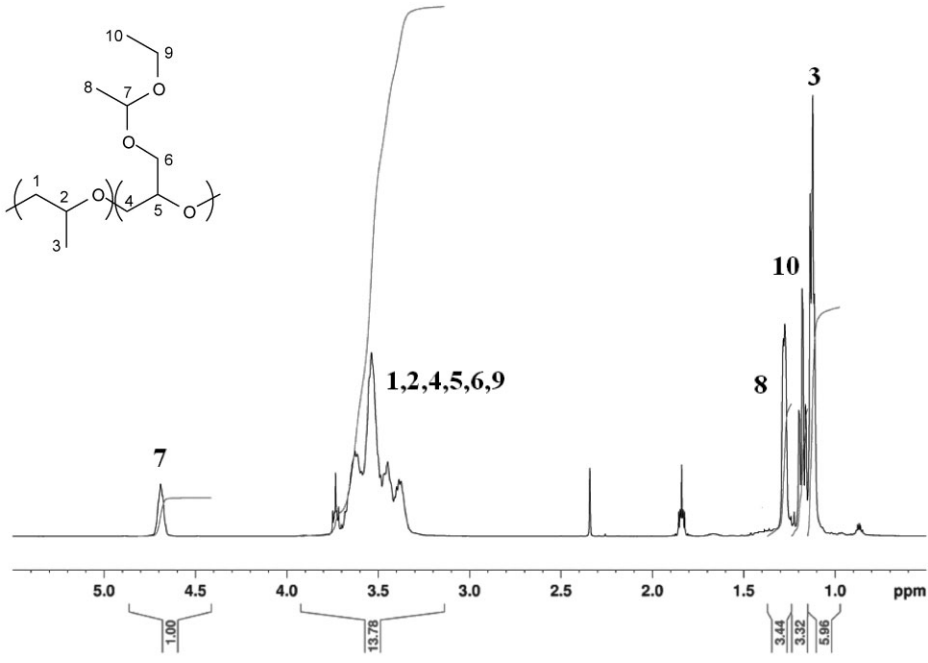


Figure 5.
^1H NMR spectrum of a P($EEGE_{68}$-stat-POx_{172}) (run 1, Table 2).

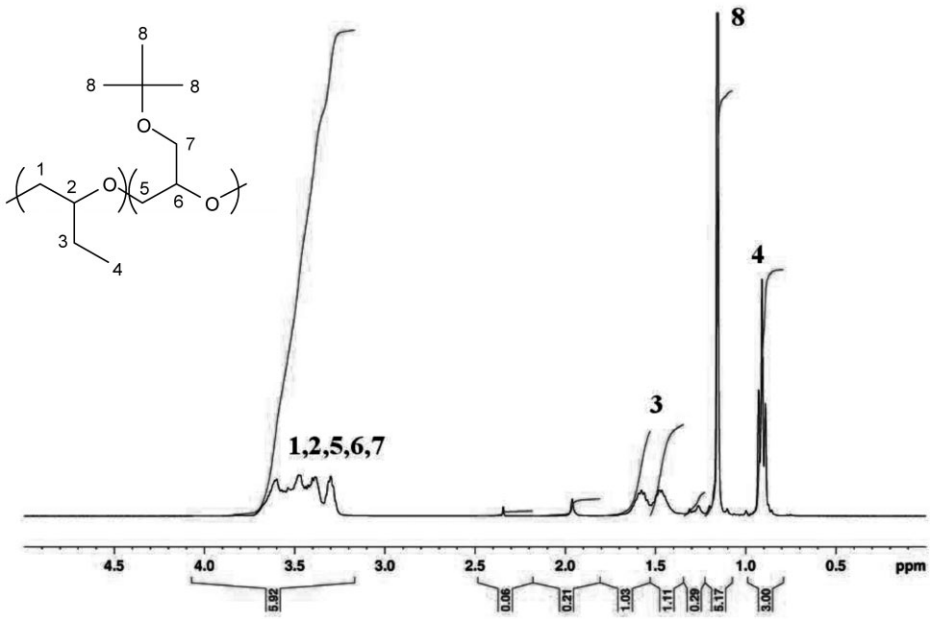


Figure 6.
^{1}H NMR spectrum of a P(t-BuGE$_{77}$-stat-POx$_{139}$) (run 6, Table 2).

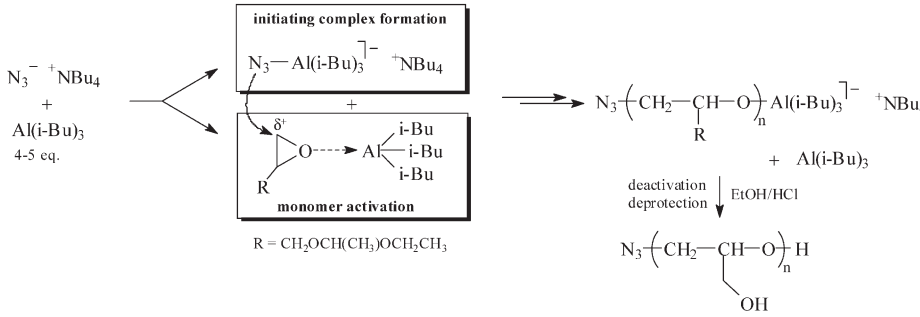
Direct α-azido Functionalization

To get in one step an azide function in α-position of polyglycidol, the ring opening polymerization of EEGE initiated by tetrabutylammonium azide (NBu_4N_3) in the presence of triisobutylaluminum as activator was studied (Table 3). The formation of narrowly dispersed PEEGE with experimental molar masses in good agreement with theoretical values, calculated assuming one chain formed per NBu_4N_3 initiator molecule, proceeds readily and quantitatively at room temperature. The reaction mechanism involves a complexation of the propagating active species with one equivalent of *i*-Bu_3Al and a strong nucleophilic activation of the oxirane ring via complexation with the remaining *i*-Bu_3Al molecules (Scheme 1). After insertion of the activated monomer in the growing chain, the Lewis acid is released, becoming able again to complex and activate another monomer molecule.

In order to get some information on the initiation selectivity by tetrabutylammonium azide, a MALDI-TOF analysis of a PEEGE was performed. The mass spectrum (enlarged region around 3000 g/mol), presented in Figure 7, shows five different peak series corresponding to distinct X-PEEGE-OH populations, all of them possessing an ω-hydroxyl end but carrying different head groups, i.e., $P_n = M^+_{Na} + nM_{EEGE} + M_H + M_x$. The two main

Table 3.
Anionic polymerization of ethoxyethyl glycidyl ether initiated by tetrabutylammonium azide in the presence of triisobutylaluminum (toluene, T = 20 °C, time = 3h, conversion = 100%)

[*i*-Bu_3Al]/[NBu_4N_3]	[Monomer] (mol/l)	$\overline{M}_n$ (th.) (g/mol)	$\overline{M}_n$ (exp.) (g/mol)	$\overline{M}_w/\overline{M}_n$
5.0	0.6	10 000	9900	1.30
4.0	0.5	10 000	11 000	1.25
4.0	0.5	30 000	28 000	1.09



Scheme 1.
Mechanism for the monomer activated anionic polymerization of ethoxyethyl glycidyl ether initiated by the NBu_4N_3/i-Bu_3Al system.

populations P_1 ($P_1n = M^+_{Na} + n\ M_{EEGE} + M_{N3} + M_H$) ($P_1 = 2988.16$ for $n = 20$) and P_2 ($P_2n = M^+_{Na} + n\ M_{EEGE} + M_H + M_N$) ($P_2 = 2962.51$ for $n = 20$) exhibit peak molar masses in agreement with the formation of N_3-PEEGE-OH chains, the presence of P_2 being explained by the fragmentation of N_3 with loss of N_2 during MALDI-TOF analysis. As for P_1 and P_2 populations P_1' and P_2' exhibit peak molar masses which

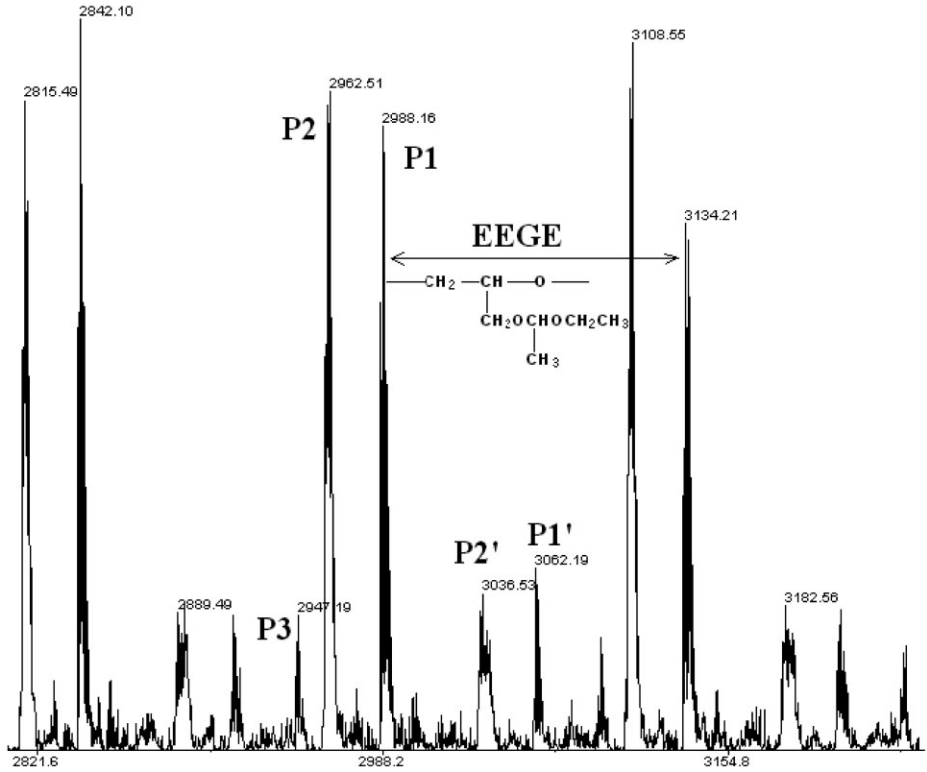


Figure 7.
Enlarged region of the matrix-assisted laser desorption/ionisation time-of-flight mass spectrum (trans-2-(3-(4-t-butyl-phenyl)-2-methyl-2-propenylidene)malononitrile as matrix and NaI as cationisation agent) of Poly(-ethoxyethyl glycidyl ether) (PEEGE) synthesized with NBu_4N_3/*i*-Bu_3Al ($\overline{M}_n = 9\,900$ g/mol, $I_p = 1.30$, Table 3).

Table 4.
Coupling reaction of α-N_3 polyethers with octadiyne by "Click" chemistry.

Polymer	$\overline{M}_n$ (exp.) precursor (g/mol)	$\overline{M}_n$ (exp.) final (g/mol)	$\overline{M}_w/\overline{M}_n$
N_3-PEO-OH	14 000	30 000	1.20
N_3-PPOx-OH	3000	5200	1.18
N_3-PEEGE-OH	11 000	20 000	1.60
N_3-PECH-OH	12 500	22 000	1.54

are also consistent with N_3-PEEGE-OH chains (respectively with N_3- and N- on the spectrum), which have lost a side hydroxyl protective group (-$C(CH_3)OCH_2CH_3$, M = 72 g/mol) of one of their EEGE units ($P'_1 = P_1$-72 and $P'_2 = P_2$-72). The last and small population observed P_3 ($P_3n = M^+_{Na} + n\,M_{EEGE} + 2M_H$) (P3 = 2947.19 for n = 20) corresponds to chains with a hydrogen in α-position which result as already indicated from a side hydride initiation.[30,32] Although it cannot be precisely quantified the amount of H-PEEGE-OH chains resulting from this side initiation process appears almost negligible as compared to the azido-functionalized ones.

Other α-azido polyethers like poly(ethylene oxide) (N_3-PEO-OH), poly(propylene oxide) (N_3-PPOx-OH) and polyepichlorohydrin (N_3-PECH-OH) were prepared in order to validate and extend this approach.[35] They were then reacted with octadiyne, at the 1:1 stoichiometry, in order to get chain-to-chain coupling. For each polymer an increase of the molar mass by a factor of about two tends to confirm the efficiency of the reaction and the high functionality of the polymer chains (Table 4). These results show the relatively broad scope of this chain end α-azido functionalization of polyethers through initiation of the anionic polymerization of the corresponding oxirane monomers by tetraalkylammonium azide in the presence of triisobutylaluminum.

Conclusion

The anionic polymerization of protected glycidols (ethoxyethyl glycidyl ether and *tert*-butylglycidyl ether) in the presence of a binary initiating system consisting of tetraoctylammonium bromide and an excess of triisobutylaluminum (*i*-Bu_3Al) appears as a good method to allow the controlled syntheses of PEEGE and P*t*BuGE of high molar masses in short reaction time. The use of tetrabutylammonium azide as initiator permits a direct and efficient α-azido functionalization of the chains. A 1:1 initiating or propagating complex of weak basicity is believed to be formed, suppressing transfer reactions to monomer. Fast polymerizations at low temperatures support a high nucleophilicity of the system due to the monomer-activation role of the excess of Lewis acid. After a quantitative acidic deprotection, polyglycidol and a large variety of glycidol-based copolymers as well as α-azido, ω-hydroxy polyethers with controlled molar masses can be obtained. This approach offers new possibilities of applications, in particular in the field of biomaterials using for instance "click" chemistry.

[1] R. K. Kainthan, M. Gnanamani, M. Ganguli, T. Ghosh, D. E. Brooks, S. Maiti, J. N. Kizhakkedathu, *Biomaterials* **2006**, *27*, 5377–5390.
[2] B. Klajnert, W. Walach, M. Bryszewska, A. Dworak, D. Shcharbin, *Cell Biology International* **2006**, *30*, 248–252.
[3] R. K. Kainthan, J. Janzen, E. Levin, D. V. Devine, D. E. Brooks, *Biomacromolecules* **2006**, *7*, 703–709.
[4] D. Taton, A. Le Borgne, M. Sepulchre, N. Spassky, *Macromol. Chem. Phys* **1994**, *195*, 139–148.
[5] A. A. Toy, S. Reinicke, A. E. Müller, H. Schmalz, *Macromolecules* **2007**, *40*, 5241–5244.
[6] M. Erberich, H. Keul, M. Möller, *Macromolecules* **2007**, *40*, 3070–3079.
[7] A. Dworak, G. Baran, B. Trzebicka, W. Walach, *Reactive and Functional Polymers* **1999**, *42*, 31–36.
[8] Z. Li, P. Li, J. Huang, *Journal of Polym. Science: Part A: Polym. Chemistry* **2006**, *44*, 4361–4371.
[9] S. Halacheva, S. Rangelov, C. Tsvetanov, *Macromolecules* **2006**, *39*, 6845–6852.
[10] a) P. Dimitrov, S. Rangelov, A. Dworak, N. Haraguchi, A. Hirao, C. Tsvetanov, *Macromol. Symp.* **2004**, *215*, 127–140. b) P. Dimitrov, E. Hasan, S. Rangelov, B. Trzebicka, A. Dworak, C. Tsvetanov, *Polymer* **2002**, *43*, 7171–7178.

[11] M. Hans, H. Keul, M. Moeller, *Polymer* **2009**, *50*, 1103–1108.
[12] K. Kaluzynski, J. Petrula, G. Lapienis, M. Basko, Z. Bartczak, A. Dworak, S. Penczek, *Journal of Polymer Science Part A: Polymer Chemistry* **2001**, *39*, 955–963.
[13] S. Penczek, J. Petrula, K. Kaluzynski, *Journal of Polymer Science Part A: Polymer Chemistry* **2004**, *42*, 432–443.
[14] P. Dimitrov, A. Utrata-Wesolek, S. Rangelov, W. Walach, B. Trzebicka, A. Dworak, *Polymer* **2006**, *47*, 4905–4915.
[15] P. Dimitrov, A. Porjazoska, C. P. Novakov, M. Cvetkovska, C. B. Tsvetanov, *Polymer* **2005**, *46*, 6820–6828.
[16] P. Dimitrov, S. Rangelov, A. Dworak, C. B. Tsvetanov, *Macromolecules* **2004**, *37*, 1000–1008.
[17] A. Dworak, I. Panchev, B. Trzebicka, W. Walach, *Macromolecular Symposia* **2000**, *153*, 233–242.
[18] S. Mendrek, A. Mendrek, H.-J. Adler, A. Dworak, D. Kuckling, *Journal of Polymer Science Part A: Polymer Chemistry* **2009**, *47*, 1782–1794.
[19] R. Huisgen, 1,3-Dipolar Cycloaddition Chemistry, Padwa A., Wiley, New-York 1984, 1–176
[20] H. C. Kolb, M. G. Finn, K. B. Sharpless, *Angew. Chem. Int. Ed.* **2001**, *40*, 2004–2021.
[21] L. Chen, C. J. Li, *Adv. Synth. and Cat.* **2006**, *348*, 1459–1484.
[22] J.-F. Lutz, *Angew. Chem. Int. Ed.* **2007**, *46*, 1018–1025.
[23] W. H. Binder, R. Sachsenhofer, *Macromol. Rapid Commun.* **2007**, *28*, 15–54.
[24] S. Hiki, K. Kataoka, *Bioconjugate Chem.* **2007**, *18*, 2191.
[25] S. Iyer, A. Anderson, S. Reed, B. Swanson, *Tetrahedron Lett.* **2004**, *45*, 4285.
[26] W. J. Wang, T. Li, T. Yu, F. M. Zhu, *Macromolecules* **2008**, *41*, 9750.
[27] C. Hua, S.-M. Peng, C. M. Dong, *Macromolecules* **2008**, *41*, 6686.
[28] M. J. Stefanko, Y. K. Gun'ko, D. K. Rai, P. Evans, *Tetrahedron* **2008**, *64*(44), 10132.
[29] A. O. Fitton, J. Hill, D. E. Jane, R. Millar, *Synthesis* **1987**, 1140–1142.
[30] A. Labbe, S. Carlotti, C. Billouard, P. Desbois, A. Deffieux, *Macromolecules* **2007**, *40*, 7842–7847.
[31] V. Rejsek, D. Sauvanier, C. Billouard, P. Desbois, A. Deffieux, S. Carlotti, *Macromolecules* **2007**, *40*, 6510–6514.
[32] C. Billouard, S. Carlotti, P. Desbois, A. Deffieux, *Macromolecules* **2004**, *37*, 4038–4043.
[33] S. Carlotti, A. Labbe, V. Rejsek, S. Doutaz, M. Gervais, A. Deffieux, *Macromolecules* **2008**, *41*, 7058–7062.
[34] F. Tüdos, T. Kelen, T. Földe-Berezsnich, B. Turcsanyi, *J. Macromol. Sci. Chem.* **1976**, *A10*, 1513–1540.
[35] M. Gervais, A. Labbe, S. Carlotti, A. Deffieux, *Macromolecules* **2009**, *42*, 2395–2400.

