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Anionic ring opening polymerization of *N*-glycidylphthalimide: combination of phosphazene base and activated monomer mechanism

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ABSTRACT : Anionic ring-opening polymerization of glycidyl phthalimide, initiated with alcohol - phosphazene base systems and based on monomer activation with a Lewis acid (iBu$_3$Al), has been studied. No propagation occurred for initiator : iBu$_3$Al ratios less or equal to 1 : 3. For larger Lewis acid amounts, the first anionic ring-opening polymerizations of glycidyl phthalimide were observed. Polymers were carefully characterized by NMR, MALDI-TOF mass spectrometry and size exclusion chromatography and particular attention was given to the detection of eventual transfer or side-reactions. However, polymer precipitation and transfer reaction to aluminum derivative were detrimental to monomer conversion, polymerization control and limited polymer chain molar masses. The influence of reaction temperature and solvent on polymer precipitation and transfer reactions were studied and reaction conditions have been optimized leading to afford end-capped poly(glycidyl phthalimide) with narrow molar mass distributions. **Keywords :** Anionic polymerization; Ring Opening Polymerization; Phosphazene bases; epoxy; living polymerization.

INTRODUCTION

The field of anionic ring-opening polymerization (AROP) of epoxides experiences a recent revival.[1] Polyethers are a very important class of materials that are industrially produced in million tons scale per year. They are used in high diffusion applications (e.g. surfactants, cosmetics) or in more advanced applications (e.g. biomedical field).[2] The polymerization of functional epoxide monomers that possess reactive groups either directly accessible or protected are of particular interest. However, even if the demand for functional polyethers increases steadily, the number of functional epoxide monomers that can be polymerized by AROP is still limited.[1,3]

Amino functional polyethers are of particular interest due to the number of potential applications, such as heavy metal recovery,[4] gene delivery,[5,6] wastewater treatment,[7] surface engineering.[8] Polyfunctional primary amine-containing polyethers can be prepared by two different strategies. The first one is the postmodification of a precursor polymer using, for example, thiol-ene addition of poly(allyl glycidyl ether),[9] azidation-reduction of polyepichorhydrine[10] or reduction of poly(epicyanohydrin).[11] However, postmodification reactions often result in non-quantitative conversion or require multi-step syntheses. Therefore, the second strategy consisting in the direct polymerization of protected amine groups is an interesting but under-explored solution. There are a few epoxide monomers functionalized with protected amino groups reported to be polymerized by AROP: *N,N*-dibenzylglycidylamine (DBGA),[12,13] *N,N*-diallyglycidylamine (DAGA),[14] Boc-protected butanolamine glycidyl ether (BBAG).[15] Moreover, glycidyl phthalimide is an interesting protected-amine-containing monomer which has been used to functionalize hyperbranched polyglycerols with amine groups.[16,17] However,

the homopolymerization of the monomer by AROP has never been successfully achieved and only single additions of epoxides were observed. Möller and coworkers reacted glycidyl phthalimide with potassium *tert*-butoxide in dioxane and DMSO but no polymerization took place.[10] The use of Oct_4NBr in combination with triisobutylaluminum (*i*Bu₃Al) Lewis acid according to an activated monomer mechanism in toluene initiated the polymerization, but it did not enable further growth of polymer chains.[10]

Protic species - phosphazene base systems have emerged as efficient catalyst systems for the living polymerization of various functional monomers.[13,18-20] Protic groups are deprotonated by phosphazene bases and initiated the anionic polymerization. The protonated bulky cations formed by the deprotonation process generate highly reactive ion pairs which results in an increase of the propagation rate. Satoh and coworkers reported that the combination of *t*BuP₄ and alcohol is an excellent catalytic system for the living ring-opening polymerization of several *N,N*-disubstituted glycidyl amine derivatives, such as *N,N*-dibenzylglycidylamine, *N*-benzyl-*N*-methylglycidyl amine or *N*-glycidylmorpholine.[13]

Nevertheless, attempts to apply the previous initiating system to *N*-glycidylphtalimide failed to obtain corresponding polymers.[13] This lack of polymerizability has been attributed to the high steric hindrance of the phthalimide group.[3] To the best of our knowledge, poly(glycidylphthalimide) was only synthesized once according to a cationic ring-opening polymerization mechanism with Lewis acid and methylaluminium bis(2,6-di-tert-butyl-4-methylphenoxide) (MAD) as initiator by Kanoh et al.[21] The synthesis was performed in toluene at 100 °C and a polymer with a 1700 g.mol⁻¹ number average molar mass (*M*n) and a large dispersity (Đ = 1.63) was reported. Harsh polymerization conditions are required to obtain a polyether backbone with phthalimide pendant groups. Only one reaction was carried out and the polymer was not thoroughly characterized, e.g.

end-chains were not identified. In addition, the difference between theoretical and experimental molar masses has not been explained.

In this paper, polymerization of the very challenging glycidyl phthalimide monomer by AROP is reported for the first time. For this purpose, we used a Lewis acid which activates the monomer by increasing its electrophilicity and a phosphazene base resulting in highly nucleophilic propagating centers due to a high degree of ion-pair separation with phosphazenium counterion.[22] In addition, we have also studied the effect of solvent in polymerization, since the solubility of polyglycidylphthalimide is a limiting factor in chain growth. The resulting polymers were fully characterized by NMR, SEC and MALDI-TOF. A particular attention was given to the determination of molar masses, potential transfer reactions as well as end-groups.

EXPERIMENTAL

Materials.

Phosphazene base *t*BuP₄ solution (0.8 mol L⁻¹ in hexane, Aldrich), 2-methyltetrahydrofuran (98%, Aldrich), benzyl alcohol (99%, Aldrich) and triisobutylaluminium *i*Bu₃Al solution (1.1 mol L⁻¹ in toluene, Acros) were used without further purification and were stored in a glove box. *N*-(2,3-Epoxypropyl)phthalimide (95%, Acros, glycidyl phthalimide) was sublimated at 90°C under reduce pressure. Toluene, dichloromethane and tetrahydrofuran were dried with an MBRAUN MB SPS-800 solvent purification system under nitrogen. *N*-dimethylformamide (anhydrous, 99.8%, Aldrich) was distilled over CaH_2 two times prior to use.

Instruments

¹H and ¹³C NMR analyses were performed on a Bruker Avance 300 MHz and a Bruker Avance 400 MHz spectrometers. All spectra are internally referenced to residual proton signals of the deuterated solvent: $CDCl_3$ or CD_2Cl_2. Polymer

molar masses were determined by size exclusion chromatography (SEC) using DMF (containing 1.0 g L^{-1} lithium bromide as an additive) or THF as eluent. In DMF, the analyses were performed at 60°C, and at a flow rate of 0.8 mL.min^{-1}, at a polymer concentration of 5 mg.mL^{-1} after filtration through 0.22 μm. The steric exclusion was carried out on two PSS GRAM 1000 Å columns (8 × 300 mm; separation limits: 1 to 1000 kg.mol^{-1}) and one PSS GRAM 30 Å (8 × 300 mm; separation limits: 0.1 to 10 kg.mol^{-1}) coupled with three detectors (Viscotek, TDA 305) : a differential refractive index (RI) detector and an UV detector. In THF measurements were carried out on three PL Gel Mixte C 5μm columns (7,5 × 300 mm; separation limits: 0,2 to 2000 kg.mol^{-1}) maintained at 40°C coupled with 2 modular detectors: a differential refractive index (RI) detector Viscotek 3580 and a Diode Array UV Detector Shimadzu SPD20-AV. THF was used as the mobile phase at a flow rate of 1 mL.min^{-1}, toluene was used as a flow rate marker. All polymers were injected (50 μL) at a concentration of 5 mg.mL^{-1} after filtration through a 0.45 μm pore-size membrane. In both cases, the OmniSEC 4.6.2 software was used for data acquisition and data analysis. The number-average molar masses (M_n), the weight-average molar masses ($\bar{M}_w$), and the molar mass distributions ($Đ = M_w/M_n$) were determined by SEC with a calibration curve based on narrow poly(methyl methacrylate) (PMMA) standards (from Polymer Standard Services), using the RI detector.

Flight (MALDI-TOF) mass spectrometry (MS). Mass spectra were recorded by matrix-assisted laser desorption and ionization time-of-flight (MALDI-TOF) mass spectrometry (MS) using a Bruker autoflex III smartbeam mass spectrometer, equipped with the laser that produces pulses at 337 nm using dithranol as a matrix and NaI as cationizing agent. Spectra were recorded in reflector or in linear mode at an accelerating potential of 20 kV. Samples were prepared by dissolving the polymer in THF at a concentration of 5 mg.mL^{-1}. A 10 μL aliquot of this solution was mixed with 20 μL of matrix solution and 10 μL of NaI solution (both at 20 mg.mL^{-1} in THF). Standards (poly(ethylene oxide) of known structures, M_n = 1120, 3500 and 5500 g.mol^{-1} purchased from Polymer Standards Service) were used to calibrate the mass scale. In all cases, to determine m/z, the molar mass of the sodium cation was added.

Anionic ring opening polymerization of glycidylphthalimide

Polymerizations were carried out in polymerization tubes equipped with a magnetic stirrer according to the following procedure. All the mixtures were performed in a glovebox under a nitrogen atmosphere. In the polymerization tube, benzyl alcohol (1 equiv, 3 μL, 0.03 mmol) was deprotoned by the phosphazene base (1 equiv, 37 μL, 0.03 mmol) in dried toluene (2,5 mL) into polymerization tube for 10 min. In a separate vial, triisobutylaluminium (7 equiv, 190 μL, 0.21 mmol) was added on sublimated monomer (50 eq, 0.3 g, 1.50 mmol) in 2.5 mL of dried toluene. The monomer mixture was added dropwise in the polymerization tube. The polymerization was stirred at 25°C, left to react for 3h and quenched with acetic acid. The solvent was evaporated yielding a brown product. This product was solubilized in methylene chloride and precipitated into 150 mL diethyl ether to remove the phosphazene base (tBuP$_4$), monomer and triisobutylaluminium. A white solid was obtained. The polymer conversion was determined by ^{1}H NMR spectroscopy and molar masses were determined by SEC.

RESULTS AND DISCUSSION

Initially, polymerization reactions were carried out in toluene (Table 1, run 1-12).[21] For all the experiments, targeted degrees of polymerization (Xn), as calculated from $[M]_0/[ROH]_0$ ratio (i.e. assuming quantitative initiation), were deliberately set between 20 and 100 so that chain ends could be easily characterized by ^{1}H NMR and MALDI-TOF mass spectrometry. In our first trial, 1 equiv of the phosphazene base with respect to the primary alcohol initiator (benzyl alcohol) was used and

this condition did not lead to polymerization
(Table 1, run 1), which is

Table 1. Experimental conditions and molecular characteristics of Poly(glycidylphthalimide) samples initiated benzyl alcohol in the presence of tBuP$_4$ and iBuAl$_3$ in toluene.

Run	[M] (mol.L^{-1})	[M]$_0$/[ROH]$_0$/[tBuP$_4$]/[iBu$_3$Al]	T°C	Time (h)	Conv[a] (%)	$M_{n,th}$[b] (g.mol^{-1})	$M_{n,sec}$[c] (g.mol^{-1})	Đ	% $_{ISO}$
1	0.3	50/1/1/0	25	15	0	-	-	-	-
2	0.3	50/1/1/2.5	25	21	0	-	-	-	-
3	0.3	50/1/1/3	25	21	0	-	-	-	-
4	0.3	50/1/1/3.6	25	21	31	3250	1500	1.50	1
5	0.3	50/1/1/3.6	25	3	36	3800	1900	1.51	2
6	0.07	20/1/1/3.6	25	3	43	1900	1600	1.60	36
7	0.03	50/1/1/3.6	25	21	53	5400	1800	1.24	70
8	0.3	50/1/1/7.5	25	21	35	3700	2100	1.71	41
9	0.3	100/1/1/7.5	25	21	-	-	3800	1.60	-
10	0.3	50/1/1/7.5	25	48	32	3300	2100	1.57	69
11	0.3	50/1/1/7.5	0	48	52	5300	3100	2.37	43
12	0.3	100/1/1/7.5	0	18	40	8200	3300 + 18000	3.02	-

[a] Determined by ^{1}H NMR spectra in CDCl$_3$, [b]$M_{n,th}$(g.mol^{-1}): theoretical number average molecular weight Mn=(Xn*conv*Mo)+M(alcohol), [c]$M_{n,sec}$ (g.mol^{-1}): number average molecular weight determined by SEC in DMF (60°C, PMMA standards), % ISO = percentage of chains with isobutyl end group.

supporting the earlier results published by Isono et *al*.[13]

Further, we included iBu$_3$Al to our system in addition to tBuP$_4$ and benzyl alcohol. Therefore, for the rest of the polymerization experiments, 1 equiv of the phosphazene base with respect to benzyl alcohol and an increasing amount of iBu$_3$Al, were used.[23,24] Experiments performed with 2.5 equiv (Table 1, run 2) and 3.0 equivalents of iBu$_3$Al (Table 2, run 3) did not generate polymers. Several authors used glycidyl phthalimide monomer to end-cap polyglycidol

by ring-opening reaction,[10,16] and they interpreted this lack of homopolymerization to high steric hindrance or aggregation issue caused by the phthalimide group rather than the monomer reactivity.

The anionic ring-opening polymerization of glycidyl phthalimide has been observed for the first time when [iBu$_3$Al]/[ROH] ratio ≥ 3.6 (Table 1, runs 4-12). A minimum amount of Lewis acid is required for the propagation step to occur. This ratio is still unexplained but we assume this might result from the establishment of
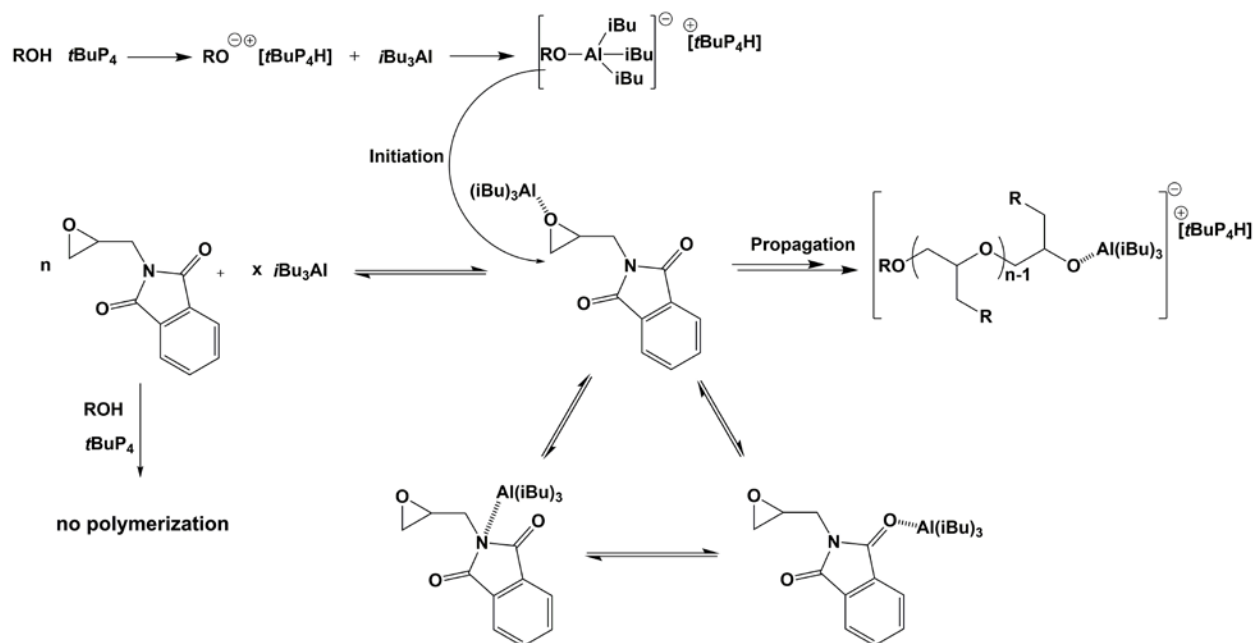
SCHEME 1 Postulated activated mechanism for the ROP of glycidylphthalimide using phosphazene base and *i*Bu₃Al as catalytic system.

coordination complexes between propagating center, Lewis acid and phosphazenium cation and by the necessity to activate monomers by coordination of an excess of Lewis acid with glycidylphthalimide molecules (Scheme 1). A complexation equilibrium is established between free monomer, monomer complexed with *i*Bu₃Al either on carbonyl groups, on nitrogen atom or on ether linkage. When *i*Bu₃Al interacts with ether linkage, electrons are transferred from the oxygen atom to the aluminum, generating a strong electron-withdrawing effect on the α-carbon.[23] The α-carbon electrophilicity is increased resulting in monomer activation followed by an attack of the nucleophilic alcoholate complex and the ring-opening of the monomer.

FIGURE 1 SEC trace of poly(glycidylphthalimide) initiated by benzyl alcohol in the presence of 1equiv of *t*BuP₄ and 3.6 equiv of *i*Bu₃Al (Table 1, run 5)

For experiments carried out with 3.6 equiv *i*Bu₃Al (Table 1, run 4-5) at $[M]_0$ = 0.3 mol.L⁻¹, monomer conversion and molar masses are limited by the precipitation of polymer chains during propagation step and the resulting polymers exhibit quite large molar mass distributions (Đ = 1.5-1.6) (Figure 1). Polyglycidylphthalimide (PGht) polymers were purified by precipitation in diethyl ether. The ¹H NMR spectrum displays all the characteristic signals of poly(glycidylphthalimide) (Figure S.1a). Protons of the polyether main-chain and
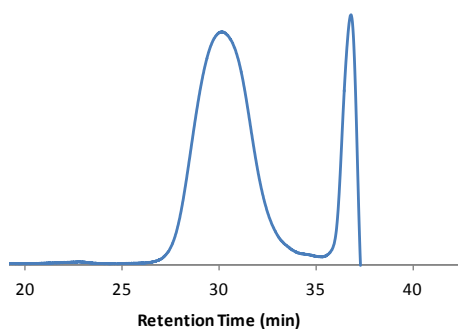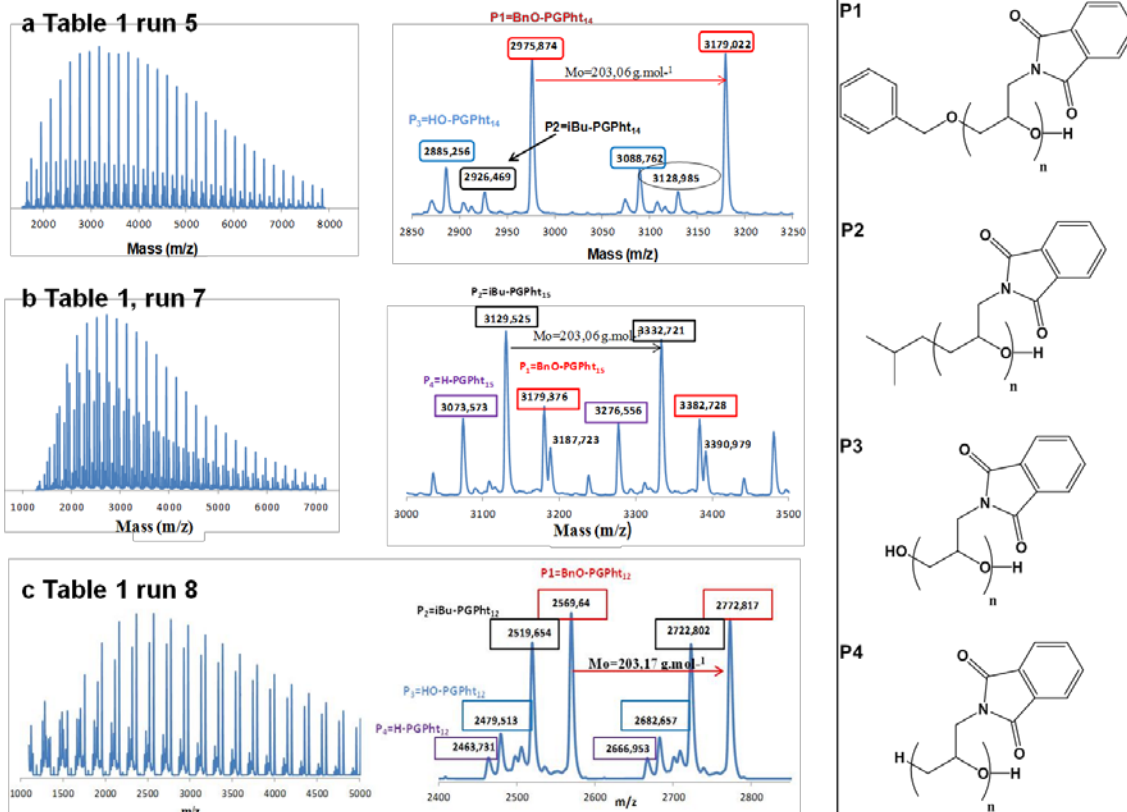
FIGURE 2 MALDI-TOF spectra (linear mode) of poly(glycidylphthalimide) initiated by benzyl alcohol/ tBuP$_4$/iBu$_3$Al (1/1/3.5) under different reaction conditions.

methylene bridge protons of the lateral substituents can be observed between 3.5 and 4.0 ppm. Aromatic protons of the phthalimide groups are visible between 7.5 and 8.0 ppm. After polymer purification by precipitation in diethyl ether, the signals associated with the -CH$_2$- and aromatic proton coming from benzyl end-group are still observed at 4.5 and 7.2 ppm, respectively.

Polymer (Table 1, run 5) was subjected to MALDI-TOF analysis to precisely determine the macromolecular chain structures. The spectrum shows one main population (P1), two minor populations (P2 and P3) (Figure 2) and three very minor populations. As expected, the molecular weight difference between two successive peaks of all the distributions is strictly equal to the molecular weight of one repeat unit (203.06 mass units). The main population (P1) corresponds to the [2]

expected polymer cationized with sodium ion and end-terminated by a benzyl alkoxy group on one end and by hydroxyl group on the other end: e.g. 2975,87 m/z = M_{Na^+} + M_{C7H7O^-} + n × $M_{C11H9NO3}$ + M_H with n=14. A second population (P2) can be attributed to an initiation by an isobutyl group due to transfer reaction to iBu$_3$Al (Figure S2): P$_2$= 2926.46 m/z = M_{Na^+} + M_{C4H9^-} + n × $M_{C11H9NO3}$ + M_H with n=14. A third population P3 can be attributed to an initiation by hydroxyl group coming from moisture traces: P$_3$= 2885,25 m/z = M_{Na^+} + M_{HO^-} + n × $M_{C11H9NO3}$ + M_H with n=14. The 3 minor distributions could not be identified but do not correspond to any of the structure that could be envisioned on the basis of probable mechanisms and reactivities.

Molar masses were determined by SEC using PMMA standards. PGht was obtained with molecular weights, Mn up to 1900 g mol^{-1} (Table

6

1, run 4-7, X_n= 9, figure 1) and molar mass distributions ranged from 1.5 to 1.6.

Molar masses given by the MALDI-TOF spectra are higher than M_n obtained by SEC (approx. 3000 vs 1900). We assume that molar masses determined by SEC are strongly underestimated due to interaction between phthalimide lateral substituents and the column stationary phase. Molecular weight is limited by transfer reactions with triisobutylaluminium (Figure S2). One iBu$_3$Al molecule forms four-center aluminate-type complex with alkoxide and phosphazenium cation according to a similar mechanism to the one proposed by Rejsek et al. in the case of ethylene oxide polymerization initiated by butyl lithium in the presence of iBu$_3$Al.[24] Inside the complex, a ligand exchange can be observed followed by a new complex formation (iBu$_2$AlOR) and isobutyl-phosphazenium moieties. Then, the isobutyl group attacks activated glycidylphthalimide and initiates a new macromolecular chain.

Experiments were performed at lower monomer concentrations in order to minimize the precipitation of the growing polymer chains and thus to increase monomer conversion (Table 1, runs 6-7). As expected, monomer conversion increases when decreasing initial monomer concentrations. But at the same time, undesirable transfer side reactions become more and more important, limit molar masses and negatively affect the control of polymer end-groups. For example, on the MALDI-TOF spectrum of run 7 Table 1, benzyl terminated chains (P1) are not the main distribution anymore which now consists of isobutyl-terminated chains (P2) (Figure 2.b). Another major peak series can be attributed to polyglycidylphthalimide chains with methyl and hydroxyl end groups (P4), which indicates the occurrence of a transfer reaction to the aluminum derivative resulting in hydride initiation.[25] Peaks corresponding to isobutyl end-groups are observed at 0.61, 0.77 and 1.15 ppm in ^{1}H NMR spectra. The molar fraction of macromolecular chains resulting from transfer reactions to aluminum derivative (%$_{ISO}$, Table 1)

was roughly calculated by ^{1}H NMR using the end-group aromatic protons and the CH$_3$ end-group protons resulting from transfer reactions. Chains initiated by moisture traces are neglected in the previous calculation. These values are in good agreement with the relative sizes of the different populations in the MALDI-TOF spectra. A kinetic study was carried out (Table 1, run 6). According to an activated monomer mechanism,[23] we assume an apparent zero monomer order with respect to the monomer. Plot of monomer conversion versus time is shown in Supporting Information (Figure S3). The monomer conversion rapidly increased during the first minutes up to 30 %. Then, the increase is greatly slowed down but the propagation is not fully stopped. This event was observed in parallel to the polymer precipitation.

In the next step, the amount of aluminum derivative was increased, in order to shift the chemical equilibrium toward the activated form of the monomer, promoting the propagation rate versus the precipitation rate. The following experiments were carried out with a ratio [iBu$_3$Al]/[ROH] = 7,5 (Table 1, run 8-10) at 25°C. However, a higher ratio of iBu$_3$Al did not help to prevent polymer precipitation and we did not observe a significant improvement on the monomer conversion rate or molar masses. In addition, these conditions favored transfer reaction as illustrated by the comparison between the MALDI-TOF spectra (Figures 2a and 2c) and the ^{1}H NMR spectra (Figures S1a and S1c) of reactions performed with 3.6 and 7.5 equivalents of iBu$_3$Al, respectively.

On the other hand, decreasing the reaction temperature to 0°C led to an increase of the monomer conversion and of the M_n (3100 g.mol^{-1}, Table 1, runs 11). However, we obtained the polymer with a high polydispersity (Đ = 2.4) and having a low molecular weight fraction (red line-Figure 3). MALDI TOF analysis confirmed the occurrence of transfer reactions to the aluminum derivative and that polymer end-groups are not controlled. For a targeted degree of polymerization of 100 (Table 1, run 12), the dispersity was higher and the molar mass distribution was clearly bimodal: one high molar

mass population with a number-average molar mass equal to 18 000 g.mol⁻¹ and a low molar mass distribution with M_n equal to 2200 g.mol⁻¹.
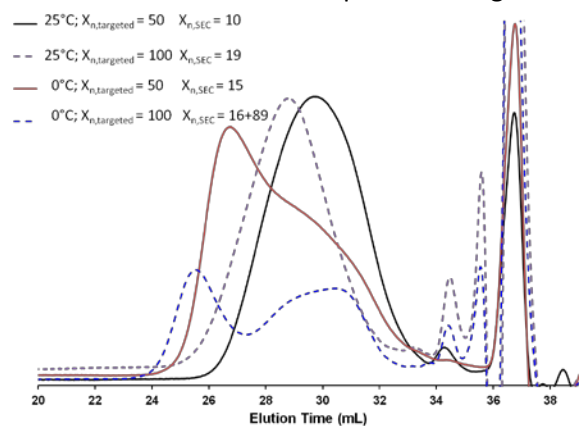

FIGURE 3 SEC profiles in DMF of poly(glycidylphthalimide) synthesized at $[M]_0$=0.3 mol.L⁻¹ with 7.5 equiv iBu$_3$Al.

A polymerization reaction was carried out a second time under the same conditions (Table 1, run 12).) and after 1 h reaction time, precipitate and supernatant were analyzed separately. Both size exclusion chromatograms are superimposed in Figure 4. The precipitate essentially consisted of large macromolecules (Mn = 6700 g.mol⁻¹, Đ = 1.66) while the supernatant mostly contained macromolecules with lower molar masses. One possible explanation is that macromolecules grew until their precipitation when the solubility limit of the polymer is exceeded. This solubility limit is temperature dependant: increase of the solubility limit with lower temperatures. Smaller macromolecules in the supernatant are generated by transfer reactions mostly to the aluminum derivative. In conclusion, the limitation of the achievable molar masses is related to a physical issue rather than a chemical reactivity issue.

Table 2. Experimental conditions and molecular characteristics of Poly(glycidylphthalimide) samples initiated benzyl alcohol in the presence of phosphazene base and iBu$_3$Al in polar solvent at 25°C.

Run	Solvent	ε	$[M]_0$ (mol.L⁻¹)	$[M]_0/[ROH]_0/$ $[tBuP_4]/[iBu_3Al]$	Times (h)	Conv[a]	$M_{n,th}$[b] (g.mol⁻¹)	$M_{n,sec}$ (g.mol⁻¹)	Đ	M_n (NMR)
1	DMF	38.3	0.3	50/1/1/7.5	94	0	-	-	-	-
2	CH$_2$Cl$_2$	8.93	0.3	50/1/1/7.5	48	20	2500	1100	1.22	-
3	THF	7.58	0.3	50/1/1/7.5	93	20	2100	1100	1.45	-
4	MeTHF	6.29	0.15	50/1/1/7.5	18	48	5000	2000	1.40	4100
5	MeTHF	6.29	0.15	25/1/1/7.5	16	54	3000	1700	1.15	3900
6	MeTHF	6.29	0.3	15/1/1/3.6	12	55	1800	1100	1.24	4100[d]

[a] Determined by ¹H NMR spectra in CD$_2$Cl$_2$, [b]$M_{n,th}$(g.mol⁻¹): theoretical number average molecular weight Mn=(Xn*conv*M$_0$)+M(alcohol), [c]$M_{n,sec}$ (g.mol⁻¹): number average molecular weight estimated by SEC in DMF (60°C, PMMA standard),[d] This value is overestimated due to the presence of macromolecular chains initiated by moisture traces.
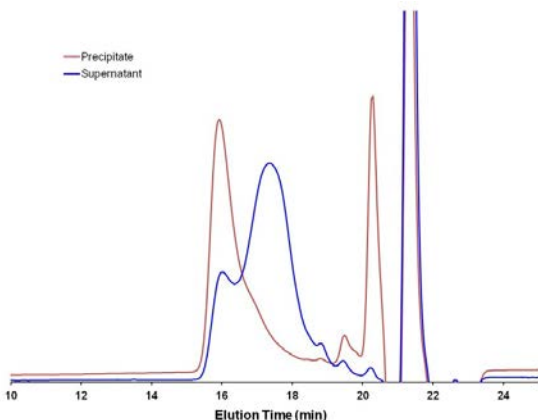
FIGURE 4 SEC in THF profiles of the precipitate (red line) and the supernatant (blue line) of Table 1 run 12 after 1 h reaction time.

Polymerization reactions were investigated in solvents of moderate polarity (i.e. dichloromethane, THF and MeTHF) and high polarity (i.e. DMF) in order to concomitantly increase the solvatation of the propagating anions and the polymer chain solubility. The stabilization of the propagating center by solvatation should also slightly decrease the interaction between the propagating center and the aluminum derivative resulting in a decrease of the transfer reaction to the aluminum derivative

DMF has already been used as solvent for the anionic polymerization of oxirane monomers.[26] However, no glycidylphtalimide polymerization was observed after 94 h for a reaction performed at 25°C in this polar solvent (Table 2, run 1). The strong interaction between the highly polarized carbonyl and triisobutylaluminum is one plausible explanation for this result.

Poly(glycidylphthaliminde) is soluble in dichloromethane, which has been used for NMR analyses. In addition, Carlotti and coworkers have shown that a living polymerization of ethylene or propylene oxide can be achieved in dichloromethane.[24] A reaction was carried out in this solvent (Table 2, run 2). The polymerization system stayed homogenous and no precipitation was observed. But the MALDI-TOF spectrum (Figure S4) shows a major distribution corresponds to polymer chains initiated by

chloride anions resulted from transfer reactions to the solvent. Therefore, use of dichloromethane was ruled out.

Run 3 Table 2 was performed in THF. The reaction mixture stayed homogenous during all the polymerization time. The MALDI-TOF spectrum (Figure S5) shows that the main distribution corresponds to polymer chains with the expected end-chains and the number-average molar mass value is in agreement with the theoretical one. Nevertheless, even after 4 days, monomer conversion was low compared to reaction performed in toluene (Table 1). THF behaves like a Lewis base and interact with trialkylaluminum decreasing the monomer activation efficiency. This result is in agreement with Carlotti and coworkers who showed that THF is not a suitable solvent for epoxide polymerization in the presence of triisobutylaluminum due to competitive complexation.[27]

Later, we used MeTHF as a solvent. Compared to THF, the methyl group of MeTHF decreases its polarity and thus the aforementioned interaction should be reduced.[28] Moreover, MeTHF is a biomass-derived chemical, which is currently considered as a promising environmentally friendly alternative to petro-based solvents. For a $[ROH]/[tBuP_4]/[iBu_3Al]$ ratio = 1/1/7.5 (Table 2, run 4) the polymerization system was homogenous for 1 hour and then a heteregeous system was observed. A MALDI-TOF spectrum of the final polymer (Figure 5) displays a major peak distribution corresponding to the expected polymer cationized by a sodium ion and end-terminated by a benzyloxy group on one end and by an hydroxyl group on the other end. As expected the molecular weight difference between two successive peaks is strictly equal to the molecular weight of one repeat unit (203.06 mass units). Figure 5 shows this mass difference between two monoisotopic ions, m/z 1959.60 and 2162.68, corresponding to the Na^+-cationized oligomers containing 9 and 10 repeat units. Four very minor distributions with the
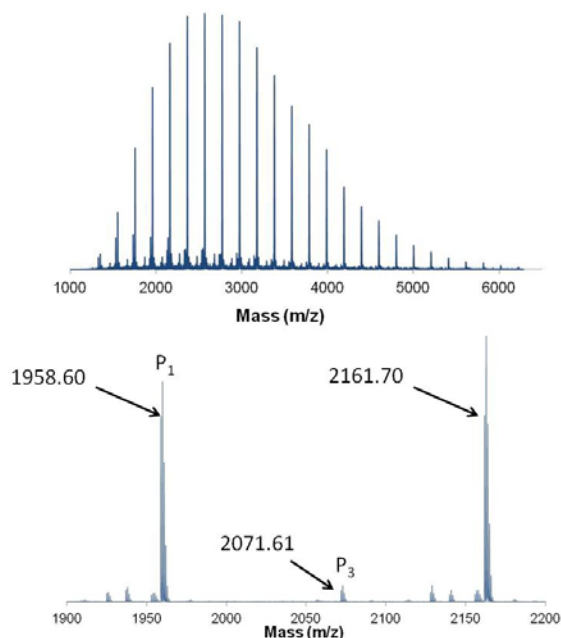
FIGURE 5 **.** MALDI-TOF spectrum of a poly(glycidylphthalimide) synthesized in MeTHF with benzyl alcohol as initiator and in the presence of 1 equiv tBuP$_4$ and 7.5 equiv of iBu$_3$Al (Table 2, run 5).

same isotopic distribution and unit distribution as the main one could also be observed on the spectrum. Transfer reactions were suppressed in MeTHF for these molar masses.

A reaction was carried out with 3.6 equiv of iBu$_3$Al in MeTHF. The polymerization kinetics was followed by ^{1}H NMR, SEC and MALDI-TOF (Figures S6 and S7). As previously, monomer conversion increased over time and reached a plateau corresponding to polymer precipitation. M_n increasing of the only peak series is clearly evidenced on the MALDI-TOF spectra. $M_{n, MALDI}$ is equal to 2275 g.mol^{-1} and is in a very good agreement with the theoretical value. None of the side reactions described previously has been evidenced by NMR or by MALDI-TOF. A kinetic study in MeTHF (Table 2, run 6; Figure S6) shows that before polymer precipitation, the propagation rate is much higher than in THF but slightly lower than in toluene, which confirms that the interactions between MeTHF and iBu$_3$Al

are strongly reduced compared to THF, leading to more efficient monomer activation. At the beginning of the precipitation, the achieved monomer conversion in MeTHF was higher than in toluene (40% and 29%, respectively). In conclusion, the synthesis of heterotelechelic polymers with controlled end-groups and low dispersities is possible in MeTHF.

Table 3. Ring Opening Polymerization of glycidylphthalimide using benzyl alcohol (ROH) as initiator, in the presence of tBuP$_4$ and iBu$_3$Al in toluene/MeTHF (1/4 v/v).

Run	[M]$_0$ (mol.L^{-1})	[M]$_0$/[ROH]$_0$/[tBuP$_4$]/[iBu$_3$Al]	Time s (h)	Conv[a]	$M_{n,th}$ (g.mol^{-1})[b]	$M_{n,NMR}$ (g.mol^{-1})	$M_{n,SEC}$ (g.mol^{-1})[c]	Đ
1	0.30	50/1/1/7.5	24	29	3000	3200	1900	1.32
2	0.30	50/1/1/3.6	94	43	4500	3900	2000	1.18
3	0.30	20/1/1/3.6	0.75	46	2000	3000	1700	1.12

[a] Determined by ^{1}H NMR spectra in CDCl$_3$, [b]$M_{n,th}$(g.mol^{-1}): theoretical number average molecular weight Mn=(Xn*conv*M$_0$)+M(alcohol), [c]$M_{n,sec}$ (g.mol^{-1}) were determined by SEC in DMF (60°C, PMMA standards)

To complete the polyglycidylphtalimide solubilization study, toluene-MeTHF (1/4 v/v) mixture was also used as reaction solvent (Table 3). The MALDI-TOF spectra of reactions with 7.5 or 3.6 equiv of iBu$_3$Al (Table 3, run 1 and 2) are shown in Figure S8. In both cases, the major population corresponds to the expected structure and only very minor populations coming from side-reaction were visible. Side-reactions (initiation with water, transfer reaction to iBu$_3$Al) were slightly more present for the reaction with 7.5 equiv of iBu$_3$Al which is consistent with a slightly lower molar mass as measured by SEC, ^{1}H-NMR and MALDI-TOF. The overlay of the size exclusion chromatography elution profiles reveals a slightly higher dispersity as well (Figure S9). A ^{13}C NMR of run 2 Table 3 is shown in Supporting Information (Figure S11): signals associated with benzyl end-groups are observed around 128 ppm. A kinetic study was performed with 3.6 equiv of iBu$_3$Al (Table 3, run 3) and experimental data were fitted according to a zero-order equation. Polymer precipitation was observed after 45 minutes of reaction and 45 % monomer conversion. Before precipitation, the degree of polymerization increases linearly with conversion and narrow molar mass distribution are observed for the various aliquots (Figure 6) with a fairly good control of the polymerization. On the whole, results obtained in toluene/MeTHF and in MeTHF are very similar.
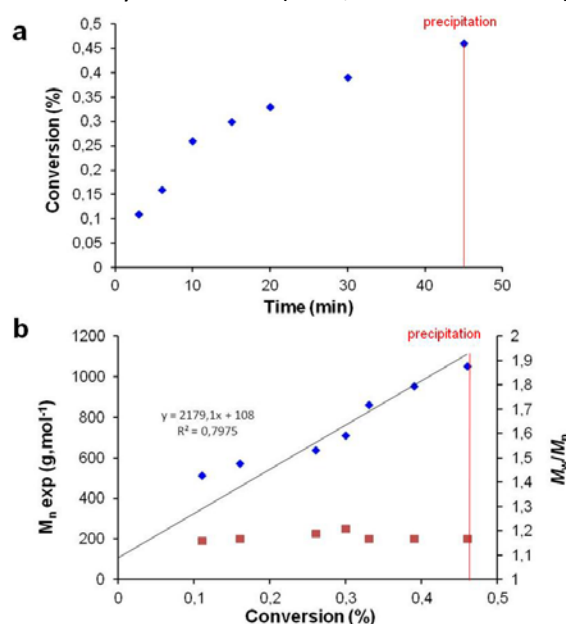
FIGURE 6 AROP of glycidylphalimide synthesized with *benzyl alcohol* / iBu$_3$Al / tBuP$_4$ as initiating system at 25 °C in toluene-MeTHF (Table 3, run 3: [I]$_0$ = 0.02 mol.L^{-1}, [M]$_0$ = 0.3 mol.L^{-1}, M/benzyl alcohol/iBu$_3$Al/tBuP$_4$ = 20/1/3.6/1): (a) zero-order kinetic plot ; (b) relationship observed between Mn (diamond; linear trend is indicated by the dashed line) or Mw/Mn (squares) and monomer conversion.

CONCLUSIONS

In summary, this article has demonstrated the first anionic ring-opening polymerization of glycidyl phthalimide monomer using benzyl alcohol / phosphazene base as initiating system and iBu$_3$Al as monomer activator. Optimal conditions for the polymerization have been

studied. A minimal amount of iBu$_3$Al is necessary for the polymerization to occur but the addition of a too large amount favors transfer reactions. MeTHF is particularly suitable solvent which allows a fairly good control of the polymerization. Heterotelechelic polymers with narrow molar mass distributions were prepared. However, the achievable molar masses are limited by polymer precipitation above a specific degree of polymerization. A decrease of the reaction temperature allowed an increase of the prepared molar masses but led cocomitently to an increase of transfer reaction frequency and is therefore detrimental to polymer dispersities. These results combined with the well-known deprotection reaction of the amine groups open a new synthetic pathway for the preparation by anionic ring-opening polymerization of homopolymer or copolymers of polyethers possessing pendant amine groups with potential applications in the field of drug delivery or nonviral vectors for gene transfection.

ACKNOWLEDGEMENTS

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GRAPHICAL ABSTRACT
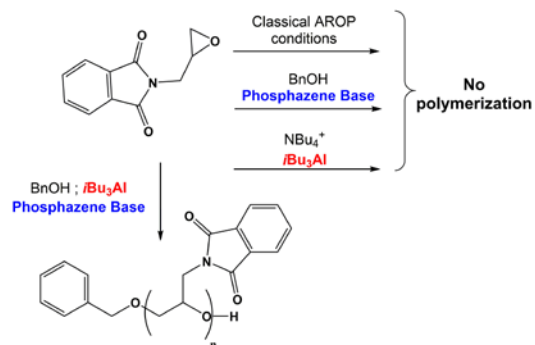
AUTHOR NAMES

Somasoudrame Rassou, Nicolas Illy, Ozgul Tezgel and Philippe Guégan*

TITLE

Anionic ring opening polymerization of *N*-glycidylphthalamide: combination of phosphazene base and activated monomer mechanism

TEXT

First demonstration of the *N*-glycidylphthalamide anionic ring opening polymerization is provided thanks to the combination of superbases such as phosphazene bases, and monomer activation. Demonstration of the expected polymer structure is ensured by SEC, NMR and MALDI-TOF mass spectrometry, and best conditions to afford narrow molar mass distribution are determined.

Les paramètres requis sont manquants ou erronés.

Figure S1. ^{1}H NMR spectra in CD_2Cl_2 at room temperature of poly(glycidylphthalimide) synthesized in toluene with benzyl alcohol-tBuP$_4$ as initiating system in the presence of 3.6 eq. of iBu$_3$Al with $[M]_0 = 0.3$ mol.L^{-1} (a, Table 1 run 5), with $[M]_0 = 0.07$ mol.L^{-1} (b, Table 1 run 6), or in the presence of 7.5 eq. of iBu$_3$Al with $[M]_0 = 0.3$ mol.L^{-1} (c, Table 1 run 9).
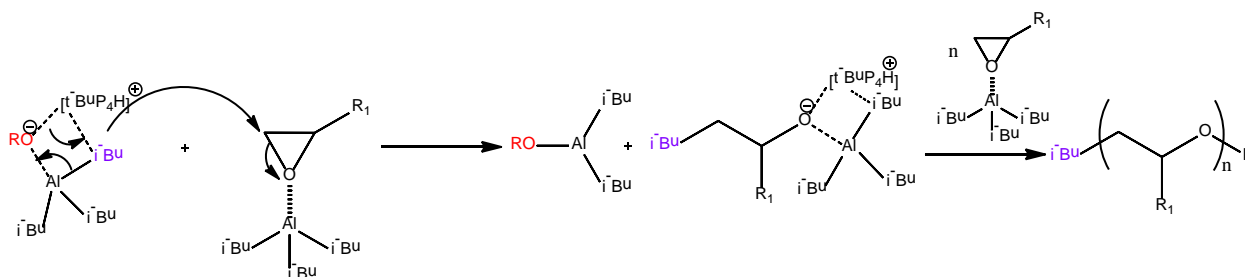

Figure S2. Proposed mechanisms for the transfer reactions during the anionic ring-opening polymerization of glycidylphthalimide in the presence of triisobutylaluminum.

Les paramètres requis sont manquants ou erronés.

Figure S3. Anionic ring-opening polymerization of glycidylphalimide synthesized with *benzyl alcohol* / iBu$_3$Al / tBuP$_4$ as initiating system at 25 °C in toluene (Table 1, run 6: $[I]_0 = 0.00375$ mol.L^{-1}, $[M]_0 = 0.07$ mol.L^{-1}, M/benzyl alcohol/iBu$_3$Al/tBuP$_4$ = 20/1/3.6/1): (a) zero-order kinetic plot ; (b) relationship observed between number-average molar mass (diamond; linear trend is indicated by the dashed line) or dispersity (squares) and monomer conversion.
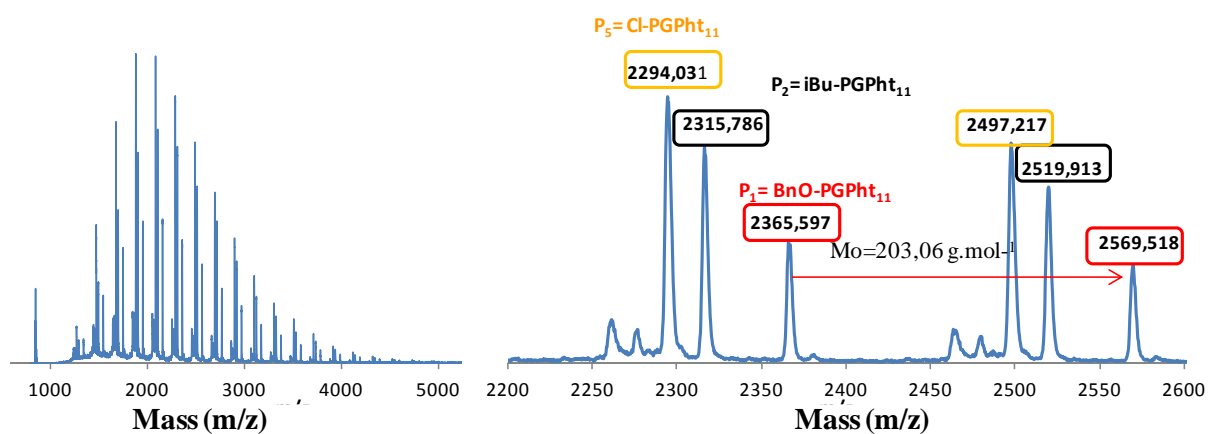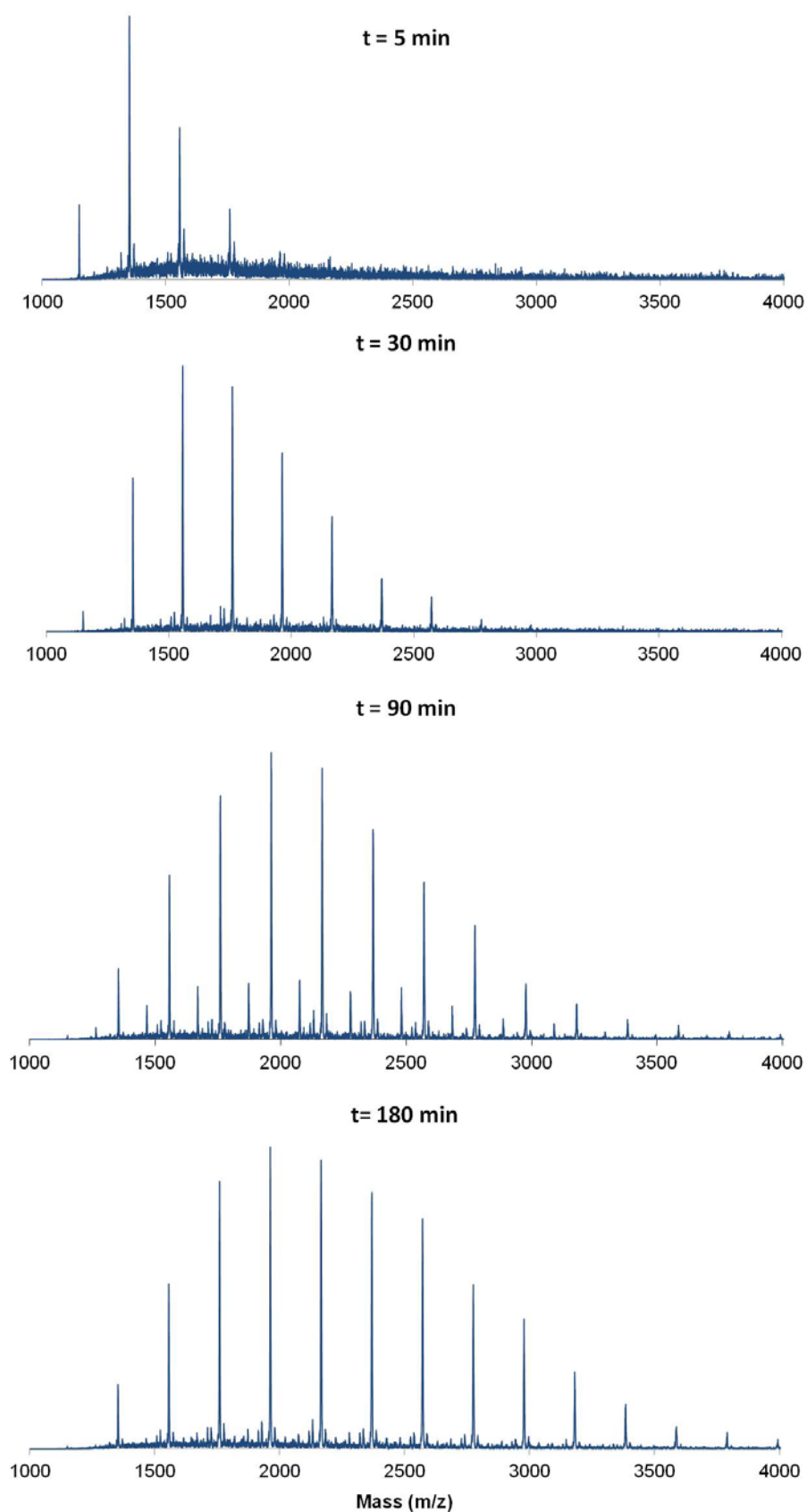
Figure S4. MALDI-ToF spectrum of a poly(glycidylphthalimide) synthesized in CH_2Cl_2 with benzyl alcohol as initiator and in the presence of 1 eq. $tBuP_4$ and 7.5 eq. of iBu_3Al (Table 2, run 2).
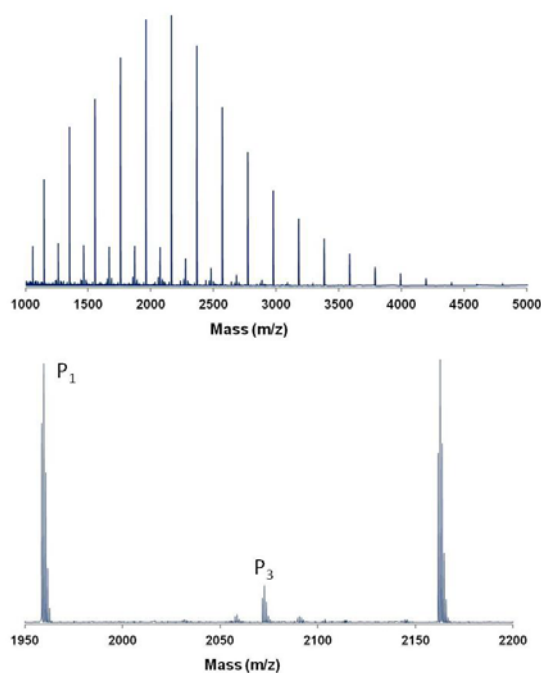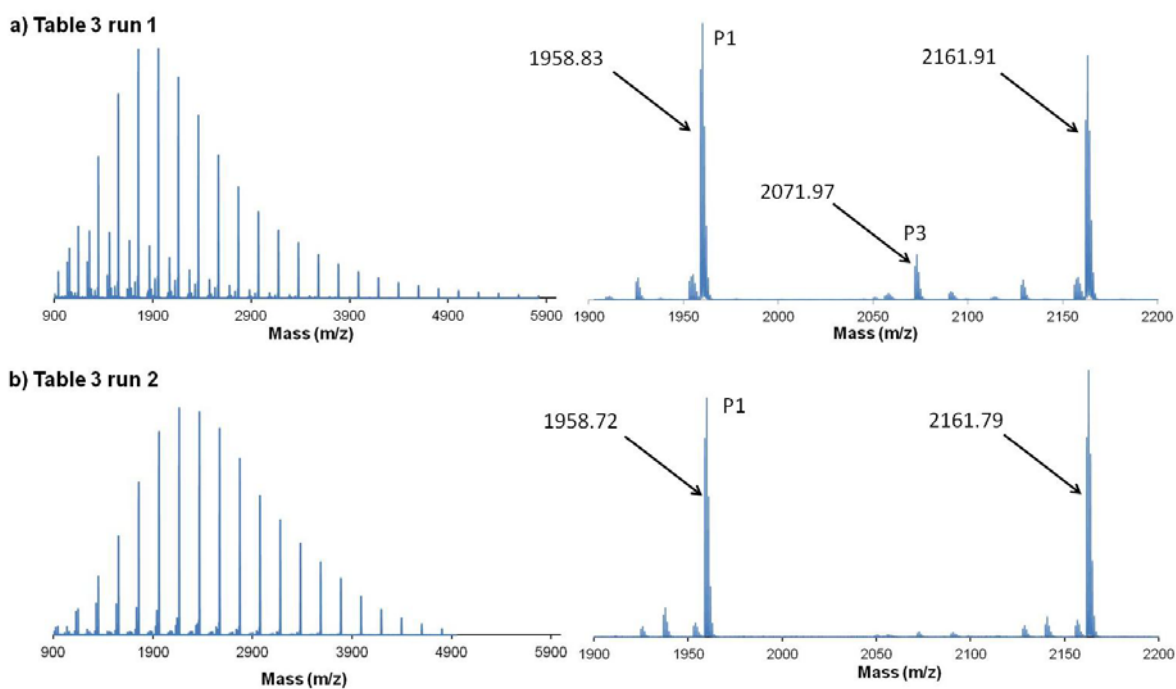

Figure S5. MALDI-ToF spectrum of a poly(glycidylphthalimide) synthesized in THF with benzyl alcohol as initiator and in the presence of 1 eq. $tBuP_4$ and 7.5 eq. of iBu_3Al (Table 2, run 3).

Figure S6. MALDI-ToF spectra of poly(glycidylphthalimide)s synthesized in MeTHF with benzyl alcohol as initiator and in the presence of 1 eq. *t*BuP$_4$ and 3.6 eq. of *i*Bu$_3$Al at various reaction times (Table 2, run 6).

Figure S7. Anionic ring-opening polymerization of glycidylphalimide synthesized with *benzyl alcohol* / *i*Bu$_3$Al / *t*BuP$_4$ as initiating system at 25°C in MeTHF (Table 2, run 6: [I]$_0$ = 0.02 mol.L^{-1}, [M]$_0$ =0.3 mol.L^{-1}, M/benzyl alcohol/*i*Bu$_3$Al/*t*BuP$_4$ = 15/1/3.6/1): (a) zero-order kinetic plot ; (b) relationship observed between number-average molar mass (diamond; linear trend is indicated by the dashed line) or dispersity (squares) and monomer conversion.

Figure S8. MALDI-TOF spectra of a poly(glycidylphthalimide) synthesized in toluene-MeTHF (1/4 v/v) with benzyl alcohol as initiator and in the presence of 1 equiv tBuP$_4$ and 7.5 equiv (a, Table 3 run 1) or 3.6 (b, Table 3 run 2) equiv of iBu$_3$Al.
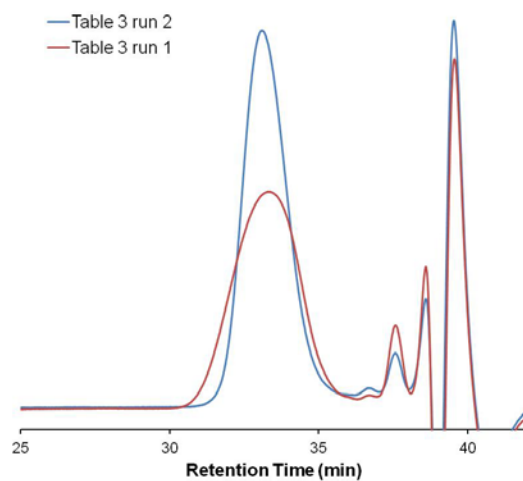
Figure S9. SEC profiles of poly(glycidylphthalimide) synthesized in toluene-MeTHF (1-4) under different reaction conditions.
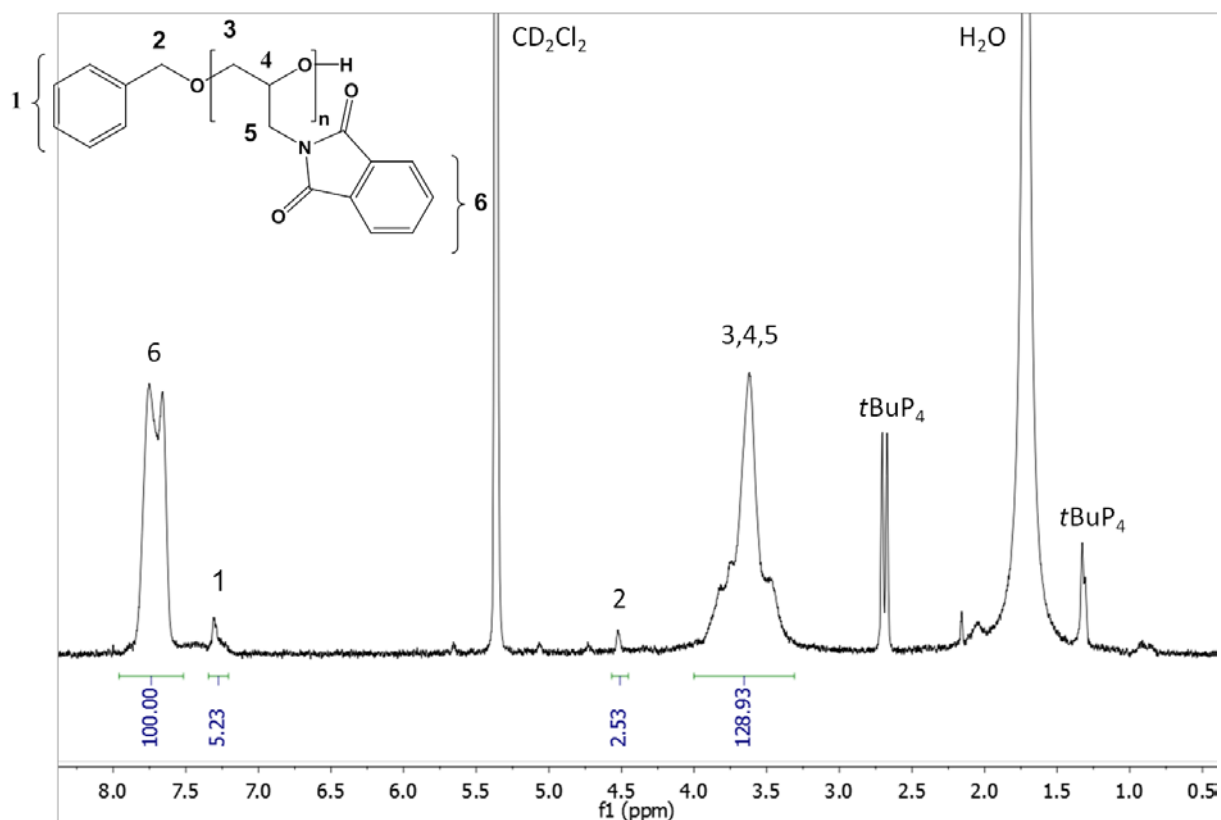
Figure S10. ^{1}H NMR spectra in CD_2Cl_2 at room temperature of poly(glycidylphthalimide) synthesized in Toluene-MeTHF (4-1) with benzyl alcohol-tBuP$_4$ as initiating system in the presence of 7.5 eq. of iBu$_3$Al with $[M]_0 = 0.3$ mol.L^{-1} (Table 2, run 4).
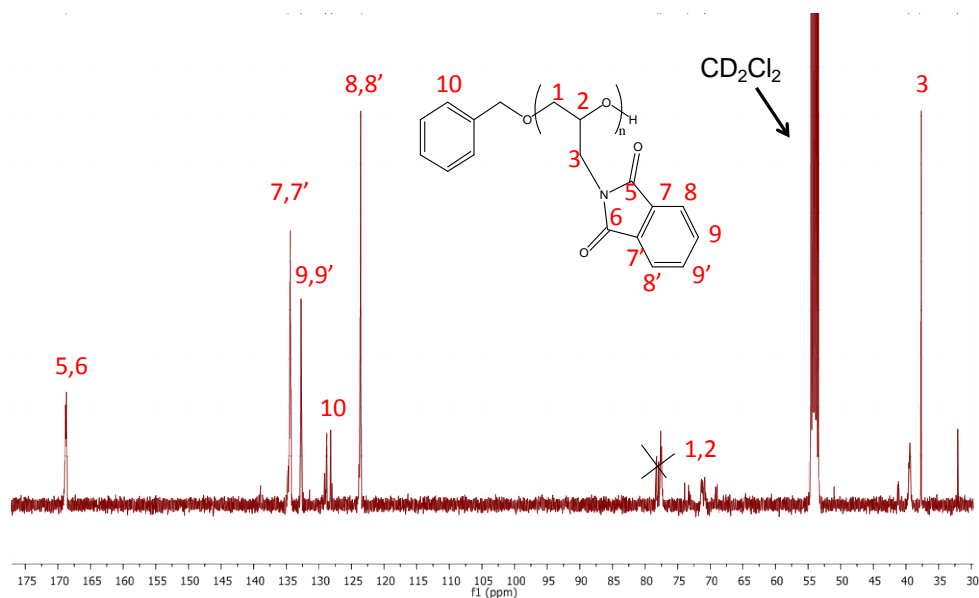
Figure S11. ^{13}C NMR spectra in CD_2Cl_2 at room temperature of poly(glycidylphthalimide) synthesized in Toluene-MeTHF (4-1) with benzyl alcohol-tBuP$_4$ as initiating system in the presence of 7.5 eq. of iBu$_3$Al with $[M]_0 = 0.3$ mol.L^{-1} (Table 3, run 2).