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High Molecular Weight Poly(α,α′,β-trisubstituted β-lactones) As Generated by Metal-Free Phosphazene Catalysts.

Julien De Winter,[†,‡] Olivier Coulembier,*[,‡] Pascal Gerbaux,[†] and Philippe Dubois[‡]

[†]*Mass Spectrometry Research Group, Interdisciplinary Center of Mass Spectrometry (CISMa), and* [‡]*Center of Innovation and Research in Materials and Polymers (CIRMAP), Laboratory of Polymeric and Composite Materials, University of Mons (UMONS), Place du Parc 20, Mons, 7000, Belgium*

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ABSTRACT: The use of different phosphazene bases has been investigated as catalysts in polymerization of [*R,S*]-4-benzyloxycarbonyl-3,3-dimethyl-2-oxetanone (dMMLABz) in presence of carboxylic acids used as initiators. Whatever the catalyst considered (P_1-*t*-Bu, P_2-*t*-Bu, or P_4-*t*-Bu) a very good control over the polymerization has been obtained in terms of polyester molecular weights and end-groups fidelity as attested by spectroscopic techniques such as ^{1}H NMR, gel permeation chromatography (GPC) and matrix assisted laser desorption ionization-mass spectrometry (MALDI−MS) experiments. Characterized by a complete absence of transfer reactions, the system allows for the generation of very high molecular weight PdMMLABz trough a mechanism selectively involving the "O-alkyl" scission of the β-lactone monomer. A clear dependence of the basicity of the phosphazene catalyst on the overall polymerization kinetics has been observed where the most basic catalytic species, i.e., 1-*tert*-butyl-4,4,4-tris(dimethylamino)-2,2-bis[tris(dimethylamino)phosphoranyl-idenamino]-2Λ^5,4Λ^5-catenadi-(phosphazene) (P_4-*t*-Bu), shows the highest active ion-pair. Accordingly, P_4-*t*-Bu allowed for the synthesis of PdMMLABz chains characterized by a number-average molecular weight higher than 1.5×10^6 g mol^{-1}.

Introduction

To date, a widespread of research in polymeric materials has been devoted into the field of nanomedecine and, for most, on biodegradable drug delivery systems.[1] Over the last 2 decades, a large development of degradable drug delivery systems was carried out to adapt and tune the drug delivery in the human body. Those systems can be classified in two distinct categories that are implantable and injectable systems.[2] As compared to implantable one, injectable systems does not need surgery, becoming then the most widely studied since they can be easily introduced into a living body.[2] Nevertheless, those microparticles may induce in some cases diseases or be directly eliminated by macrophages.[3]

From the state of the art, a large range of polymers is available for drug delivery systems including polyethers, polycarbonates, polyamides and so forth.[1] Since both biodegradability and biocompatibility are a prerequisite for their applications, aliphatic polyesters such as polylactide, polyglycolide and poly(ε-caprolactone) have been defined as relevant candidates and widely investigated/used.[2] Poly(hydroxyalkanoate)s are then an important class of natural biomacromolecules used as metabolic storage materials and in metal ion transportation.[4,5] Initially prepared by fermentation, their high cost of production has paved the way to an alternative route, i.e., the ring-opening polymerization (ROP) of (substituted) β-butyrolactone (BL). Despite its attractiveness, the polymerization of BL is still considerably challenging. Poly(β-butyrolactone) (PBL) of rather limited molecular mass are usually recovered as a result of chain transfer side-reactions in competition with the chain-growth propagation and leading to the formation of crotonate end-groups.[6] Suffering from the same backbiting reactions, few examples of β-malolactonic acid esters, ultimately leading after selective deprotection to highly hydrophilic and biocompatible poly(β-malic acid), have also been used and polymerized by a ring-opening process. Whatever the β-lactone involved, when weak bases or ammonium carboxylates are used as initiators, a mechanism involving the carboxylate anions is responsible for the propagation. In comparison to conventional unsubstituted β-lactones, it has been confirmed that in the case of α,α′-dialkyl-β-propiolactone, no chain transfer could occur as α-proton abstraction could no longer take place.[7] Similar results have been highlighted by Guerin et al., who demonstrated that, compared to polymalolactonates obtained from α,α′,β-trisubstituated-β-lactones, polymers prepared from unsubstituted β-lactones were characterized by major discrepancies between the experimental and theoretical molecular weights due to substitution in α-position of the monomer.[8] Being not commercially available, such lactones need to be synthesized by a five-step reaction from the commercial [*R,S*]-diethyl oxalpropionate.[9] Poly([*R,S*]-3,3-dimethylmalic acid) (PdMMLA) ultimately obtained appears to be an attractive water-soluble aliphatic polyester with carboxylic acid groups dandling all along the chain (Scheme 1).[10] This polymer, easily obtained by catalytic hydrogenation of its benzylated precursor (PdMMLABz), itself generated by anionic ROP of the [*R,S*]-4-benzyloxycarbonyl-3,3-dimethyl-2-oxetanone (dMMLABz) (Scheme 1), proved to be biocompatible and biodegradable with the *in vivo* formation of nontoxic the [*R,S*] −3,3-dimethyl-malolactonic acid.[11]

While extraordinary advances have been made in organometallic catalysis for ring-opening polymerization reactions,[12] organocatalysts have recently proven to complement metal-based catalytic species regarding their different mechanisms of activation as well as their benefits in biomedical and microelectronic applications.[13] Among the several organic catalyst platforms already developed, researches have been mainly focused on using 4-dimethylaminopyridine (DMAP), alkylphosphine, N-heterocyclic carbenes (NHCs), thioureas, guanidines and amidines superbases, fluorinated alcohols (HFAs), iodide trichloride, and phosphazenes.[14] Quite interestingly, among the exhaustive list of organocatalysts, β-lactones such as BL have been mainly polymerized (with a limited success) by using NHC.

Herein we aim at reporting on the control polymerization of dMMLABz from poly(ethylene oxide) α-methoxy, ω-carboxylic

*Corresponding author. E-mail: olivier.coulembier@umons.ac.be.

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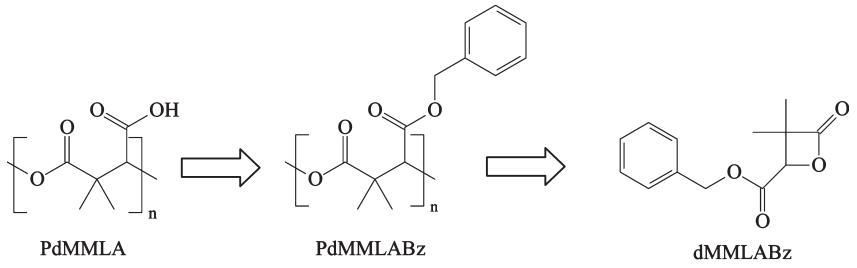
Scheme 1



Scheme 1

Table 1. Molecular Characterizations of PdMMLABz As Obtained by ROP of dMMLABz in THF at Room Temperature by Using a PEO−COOH Macroinitiator and Different Phosphazene Catalysts

				catalyst							
entry	sample	$[dMMLABz]_0$ (M)	$[initiator]_0$ (M)	nature	$[catalyst]_0$- mol L^{-1}	polymerization time (h)	conversion (%)	$M_{n.th}$ (g mol^{-1})	$M_{n.GPC}$[d] (g mol^{-1})	PDI	$M_{n.MALDI}$[e] (g mol^{-1})
1	**PdMMLABz 1**[a]	0.17	0.085	P_2-*t*-Bu	0.085	7.5	>99	4.8×10^3	2.4×10^3	1.18	4.6×10^3
2	**PdMMLABz 2**	0.24	1.7×10^{-4}	P_2-*t*-Bu	1.7×10^{-4}	768	>99	332.5×10^3	66×10^3	1.19	
3	**PdMMLABz 3**	0.17	1.7×10^{-3}	P_1-*t*-Bu	4.4×10^{-3}	144	81	21×10^3	16×10^3	1.13	21×10^3
4	**PdMMLABz 4**	0.17	1.7×10^{-3}	P_4-*t*-Bu	1.7×10^{-3}	6	>99	26×10^3	21×10^3	1.13	26×10^3
5	**PdMMLABz 5**	1.42	1.49×10^{-4}	P_4-*t*-Bu	1.42×10^{-4}	72	b	2.2×10^6	450×10^3	1.55	*b*

[a] Initiator: cinnamic acid. [b] Not determined. [c] Theoretical mass as determined by

$$M_{n.th} = \frac{234.25 \times [M]_0}{[initiator]_0} \times convn$$

[d] Experimental molar mass (following polystyrene calibration) as determined by gel permeation chromatography in THF/NEt_3 (0.2 wt % at 35 °C). [e] Experimental molar mass as determined by MALDI−MS using the formula

$$M_{n.MALDI} = \frac{\sum_i n_i M_i}{\sum_i n_i}$$

where n_i is the intensity in the mass spectrum and M_i the mass of the ion minus the mass of the cation.

acid (PEO−COOH) used as macroinitiator in the presence of various phosphazene catalysts. Whatever the phosphazene used, perfectly controlled and defined poly([*R,S*]-4-benzylcarbonyl-3,3-dimethyl-2-oxetanone) (PdMMLABz) were obtained. While P_1-*t*-Bu was revealed of low activity, the combination of P_4-*t*-Bu and a carboxylic acid initiator allowed the very fast generation of high molecular weight PdMMLABz.

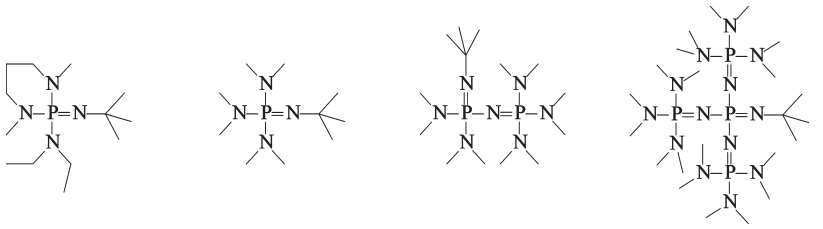
Experimental Section

Materials. [*R,S*]-4-Benzylcarbonyl-3,3-dimethyl-2-oxetanone (dMMLABz) was synthesized from diethyl oxalpropionate as already described.[9] After purification, the dMMLABz was stored at −18 °C. Poly(ethylene oxide) α-methoxy, ω-carboxylic acid (PEO−COOH) was synthesized according to literature,[15] starting from poly(ethylene oxide) α-methoxy-ω-hydroxyl (Fluka, M_n = 2080) and dried by three successive azeotropic distillations by addition of toluene before an extensive drying at 60 °C *in vacuo* overnight. Cinnamic acid (Aldrich, 99%) was dried by three successive azeotropic distillations H_2O/toluene by addition of dried toluene. Tetrahydrofuran (THF) and toluene (Labscan, 99%) were dried using an MBraun solvent purification system under N_2. Tert-butylimino-tris(dimethylamino)phosphorane (P_1-*t*-Bu, Sigma) was dried on a 4 Å molecular sieve. 1-*tert*-Butyl-2,2,4,4,4-pentakis(dimethylamino)-2Λ^5,4Λ^5-catenadi(phosphazene) (P_2-*t*-Bu, Sigma, ~2 M in THF) was dried on calcium hydride for 48 h before filtration and evaporation of the THF *in vacuo* at room temperature. An extensive drying process was performed by three successive azeotropic distillations by addition of dried toluene. 1-*tert*-butyl-4,4,4-tris(dimethylamino)-2,2-bis[tris(dimethylamino) phosphoranyl-idenamino]-2Λ^5,4Λ^5-catenadi(phosphazene) (P_4-*t*-Bu, Sigma, 1 M in hexane under argon) was dried by hexane solvent evaporation. All chemicals were stored and used in a glovebox (< 3 ppm of O_2, < 1 ppm of H_2O).

Preparation of Poly(dimethyl benzyl-β-malolactonate), PdMMLABz, As Initiated from Poly(ethylene oxide) α-Methoxy, ω-Carboxylic Acid, and 1-*tert*-Butyl-4,4,4-tris(dimethylamino)-2,2-bis[tris(dimethylamino)phosphoranylidenamino]-2Λ^5,4Λ^5-catenadi(phosphazene) Catalyst (Entry 4, Table 1). In glovebox, an equimolar mixture of poly(ethylene oxide) α-methoxy, ω-carboxylic acid (20 mg, 0.1×10^{-4} mol) and 1-*tert*-butyl-4,4,4-tris(dimethylamino)-2,2-bis[tris(dimethylamino)phosphoranylidenamino]-2Λ^5,4Λ^5-catenadi(phosphazene) catalyst (6.3 mg, 0.1×10^{-4} mol) was introduced in a vial and dissolved in 0.7 g of THF. Subsequently, in another vial, the monomer (0.234 mg, 0.1×10^{-2} mol) was dissolved in 4.4 g of THF. After complete solubilization, the as-prepared carboxylate solution was quickly added to the monomer solution. Along the polymerization, aliquots were withdrawn and analyzed by FT-IR in order to follow the evolution of the synthetic process. After 6 h, the medium was precipitated out from cold heptane (~50 g). The recovered polymer was then filtered out and dried under *vacuum* until constant weight (0.253 mg, yield >99%). $Conversion_{FTIR}$ > 99%, ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm), 1.15 (s, 6mH), 3.6 (s, 4nH), 5.05 (s, 2mH), 5.3 (s, mH). $M_{n.MALDI}$ = 26 000 g/mol, $M_{n.GPC}$ = 21 000 g/mol, PDI = 1.13.

Characterization. ^{1}H NMR spectra were recorded in $CDCl_3$ at a concentration of 30 mg/0.6 mL (^{1}H NMR) on a Bruker AMX500 (500 MHz), with shift reported in part-per-million downfield from tetramethylsilane used as internal reference. Size exclusion chromatography (SEC) was performed in THF

Scheme 2



(added with 2% triethylamine) at 35 °C using a Polymer Laboratories liquid chromatograph equipped with a PL-DG802 degasser, an isocratic HPLC pump LC 1120 (flow rate = 1 mL/min), a Marathon autosampler (loop volume = 200 μL, solution concentration = 1 mg/mL), a PL-DRI refractive index detector, and three columns: a PL gel 10 μm guard column and two PL gel Mixed-B 10 μm columns (linear columns for separation of MW_{PS} ranging from 500 to 10^6 daltons). Poly(styrene) standards were used for calibration. Fourier transform infrared (FT-IR) spectra were recorded using a BIO-RAD Excalibur spectrometer equipped with an ATR Harrick Split PeaTM. MALDI−MS mass spectra were recorded using a Waters QToF Premier mass spectrometer equipped with a nitrogen laser, operating at 337 nm with a maximum output of 500 $J.m^{-2}$ delivered to the sample in 4 ns pulses at 20 Hz repeating rate. Time-of-flight mass analyses were performed in the reflectron mode at a resolution of about 10,000. All the samples were analyzed using trans-2-[3-(4-*tert*-butylphenyl)-2-methylprop-2-enylidene]malononitrile (DCTB), that matrix was prepared as 20 mg/mL solution in CH_2Cl_2. The matrix solution (1 μL) was applied to a stainless steel target and air-dried. Polymer samples were dissolved in CH_2Cl_2 to obtain 1 mg/mL solutions. Aliquots (1 μL) of those solutions were applied onto the target area already bearing the matrix crystals, and air-dried. For the recording of the single-stage MS spectra, the quadrupole (rf-only mode) was set to pass all the ions of the distribution, and they were transmitted into the pusher region of the time-of-flight analyzer where they were mass analyzed with 1 s integration time. Data were acquired in continuum mode until acceptable averaged data were obtained.

Results and Discussion

Phosphazene bases developed by Schwesinger and proazaphosphatranes developed by Verkade are known as strong nonmetallic superbases.[16] Joining their exceptional basicity, phosphazenes derivatives such as 2-*tert*-butylimino-2-diethylamino-1,3-dimethylperhydro-1,3,2-diazaphosphine, BEMP, (Scheme 2) also proved to be chemically very stable, kinetically active and highly versatile. Such versatility, widely developed in organic reactions[17−19] was recently reinforced by the possibility to use phosphazene bases for the cyclopolymerization of phthalaldehyde[20] and the catalytic ring-opening polymerization (ROP) of various cyclic esters (e.g., lactide, ε-caprolactone and δ-valerolactone) both initiated from an alcohol.[21]

As reported, the aforementioned (di)lactone ROP and the cyclopolymerization of phthalaldehyde succeeded by using 1-*tert*-butyl-2,2,4,4,4-pentakis(dimethylamino)-2Λ^5,4Λ^5-catenadi(phosphazene) (P_2-*t*-Bu) as catalyst and proved to be very active even at low temperature. To the best of our knowledge, never any β-lactone (substituted or not) has been the object of a polymerization study by using phosphazene bases. For that reason, our first attempt was to assess the ability of P_2-*t*-Bu to catalyze the ring-opening process of the (*R,S*)-benzylcarbonyl-3,3-dimethyl-2-oxetanone (dMMLABz) from a carboxylic acid initiator in THF and at room temperature.

Since phosphazene catalysts have never been reported for the ROP of β-lactones and because, for the first time, a carboxylic acid initiator is tentatively used, the polymerization of dMMLABz ($[M]_0 = 0.17$ mol·L^{-1}) was first studied with P_2-*t*-Bu in THF at

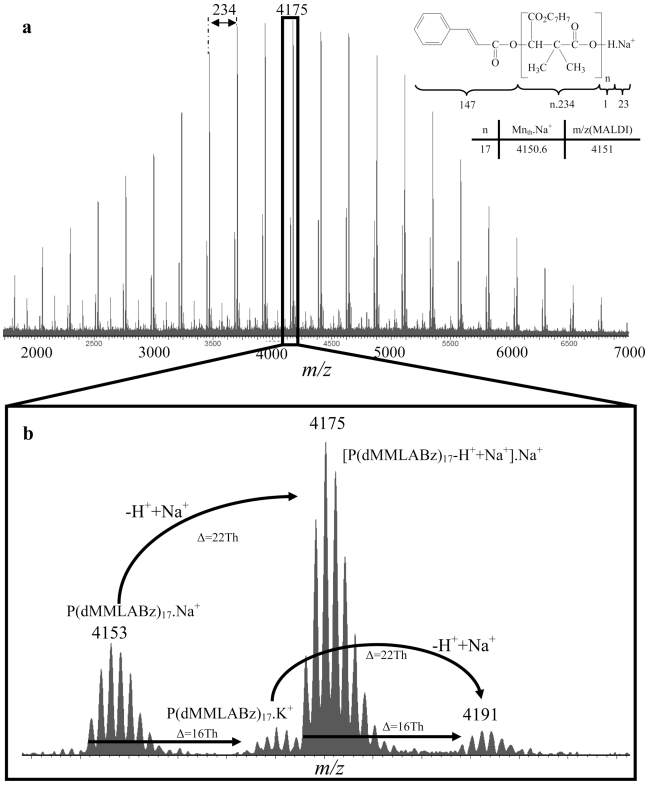


Figure 1. Poly(dimethyl benzyl-β-malolactonate) MALDI mass spectrum recorded after 5 h of polymerization ($[M]_0 = 0.17$ mol·L^{-1}; $[dMMLABz]_0/[RCOOH]_0/[P_2\text{-}t\text{-}Bu]_0 = 20/1/1$; THF; room temperature) (a) Full mass spectrum and (b) magnification between 4145 and 4205.

room temperarture using cinnamic acid as the initiator for a monomer-to-initiator-to-catalyst molar ratio of 20/1/1 (entry 1, Table 1).

After 5 h of reaction, few drops of the crude reaction medium were withdrawn and analyzed by mass spectrometry. Figure 1a shows the mass spectrum of the as-obtained poly(dimethyl benzyl-β-malolactonate) (PdMMLABz). From this first analysis, three main information may be extracted: (*i*) the ROP of dMMLABz using an equimolar mixture of RCOOH and P_2-*t*-Bu can successfully occur, (*ii*) since the difference between two consecutive signals corresponds to the monomer molar mass (234 Th), no degradation or modification of the monomeric repeating structure is to be bewailed, and (*iii*) the "*O*-alkyl" scission of the monomer is clearly highlighted (cf. hereafter). The ring-opening process taking place at both initiation and propagation steps is deduced from the nature of the polyester chain end-groups as observed all along the mass distribution, i.e., exclusively ω-carboxylic acid ω-end-groups. Actually the mass spectrum reveals two populations overlapping each other (from beginning to the end of the distribution), the less intense population corresponding to the sodium cationized oligomers initiated from the cinnamic acid group ($PdMMLABz.Na^+$) while the second distribution, higher in mass

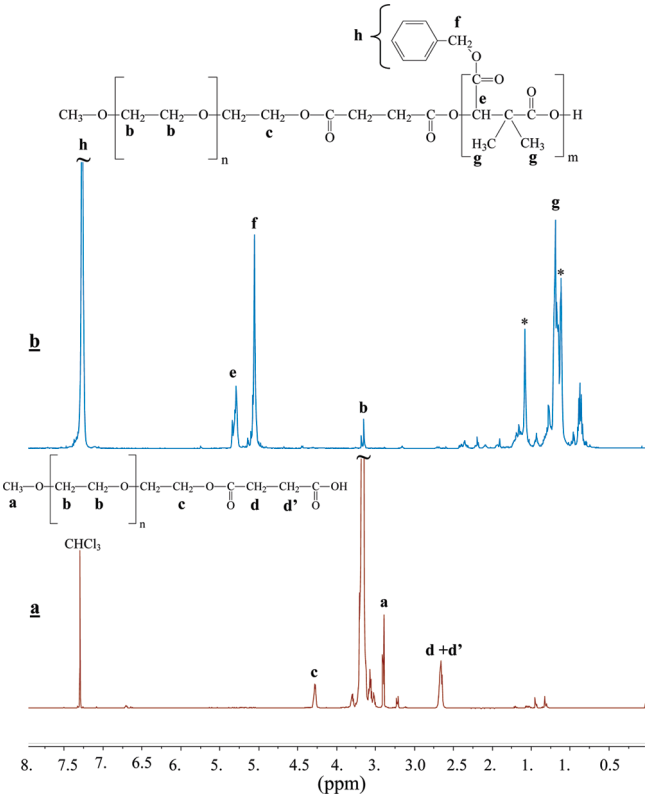


Figure 2. ^{1}H NMR spectra of α-methoxy, ω-carboxylic acid poly(ethylene oxide) (PEO−COOH) macroinitiator (a) and a corresponding poly(ethylene oxide)-*b*-poly(dMMLABz) (PEO-*b*-PdMMLABz) block copolymer (b) (entry 2, Table 1; solvent = $CDCl_3$) (∗: impurities).

of 22 Th, corresponds to the first one where a H^+ is exchanged with a Na^+ ([P(dMMLABz)$_{17}$-H^+ + Na^+]·Na^+). The observation of this second distribution can be considered as the "finger print" of the presence of the carboxylic acid end-group (Figure 1b),[22] confirming the privileged "*O*-alkyl" scission of the lactone monomer.

Finally, if the ROP reaction is pushed to completion (7.5 h), the as-obtained **PdMMLABz 1** (entry 1, Table 1) is characterized by a very good control over the molecular parameters as attested by the good accordance between both the theoretical molar mass ($M_{n.th}$) and the experimental one determined by MALDI−MS analysis ($M_{n,MALDI}$) as well as by the narrow polydispersity index (PDI) of 1.18.

In 2005, Ouhib et al. described the possibility to obtain PdMMLABz characterized by a $M_{n.exp}$ of 320 × 10^3 g mol^{-1} using tetrabutylammonium benzoate as initiator in bulk at 37 °C.[10] In order to get some light about the possibility to obtain PdMMLABz in the same range of high molar masses but using P_2-*t*-Bu as catalyst, the ROP of dMMLABz has been carried out from a α-methoxy, ω-carboxylic acid poly(ethylene oxide) (PEO−COOH, M_n ∼ 2000 g·mol^{-1}) used as a tag for the ^{1}H NMR and GPC characterizations. To that end, the preparation of PEO−COOH has been carried out according to Zalipsky et al. by reacting a α-methoxy, ω-hydroxyl poly(ethylene oxide) initiator (PEO−OH) with an excess of succinic anhydride for 24 h at room temperature in presence of *N*,*N*′-dimethylaminopyridine and triethylamine.[18] ^{1}H NMR spectroscopy attests for the completion of the reaction with the intensity ratio between α-methoxy protons (H_a) at 3.40 ppm and ω-carboxymethylene ones at 2.65 ppm ($H_{d,d'}$) being equal to the expected 3/4 ratio (Figure 2a). Note also that the complete modification of the hydroxyl end-groups has been assessed by MALDI−MS analysis prior and after esterification reaction (Figure 3).

The ROP of dMMLABz has then been conducted from the as-obtained PEO−COOH ($M_{n.MALDI}$ = 2025 g·mol^{-1}; PDI = 1.05)

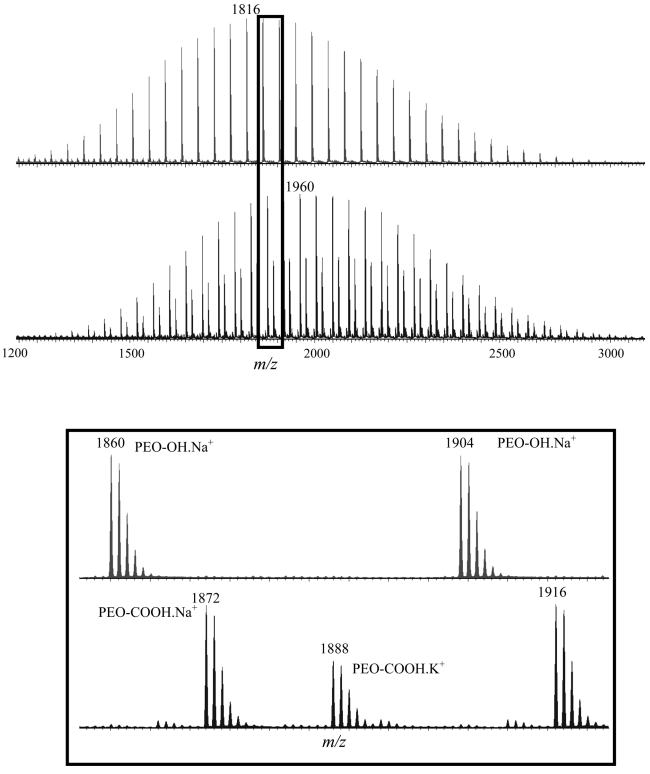


Figure 3. MALDI−MS mass spectra of both PEO−OH (top) and the corresponding PEO−COOH (bottom) attesting for the quantitative modification of hydroxyl end-groups.

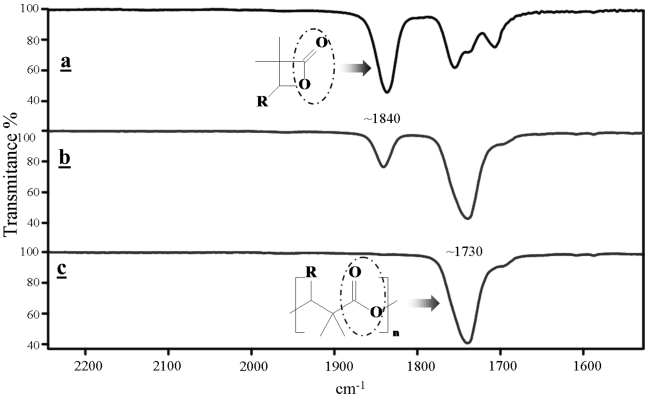


Figure 4. FT-IR evolution (zoom from 2200 to 1600 cm^{-1}) along the polymerization reaction leading to **PdMMLABz 2** as recorded after 0 (a), 123 (b), and 768 h (c). Disappearance of the vibrational absorbance at 1840 cm^{-1} to the benefit of 1730 cm^{-1}.

at room temperature in THF for an initial monomer concentration of 0.24 mol·L^{-1} and an initial monomer-to-macroinitiator ratio of 1400 ([PEO−COOH]$_0$/[P_2-*t*-Bu]$_0$). The evolution of the process was followed by FT-IR spectroscopy by the disappearance of the vibrational band at ∼1840 cm^{-1} (corresponding to the carbonyl function of the β-lactone monomer) to the benefit of a new absorption around 1730 cm^{-1} typical to the ester carbonyl group in linear aliphatic polyesters (Figure 4). After completion of reaction (32 days), the medium has been precipitated out and characterized by both ^{1}H NMR and GPC analyses (entry 2, Table 1). Experimental number-average molecular weight in PdMMLABz was determined by ^{1}H NMR measurement (not reported in Table 1) since, from Figure 2b, the repetitive proton signals of both PEO and PdMMLABz blocks can be readily observed. Assuming that all the PEO−COOH chains effectively promoted the ROP of dMMLABz, a

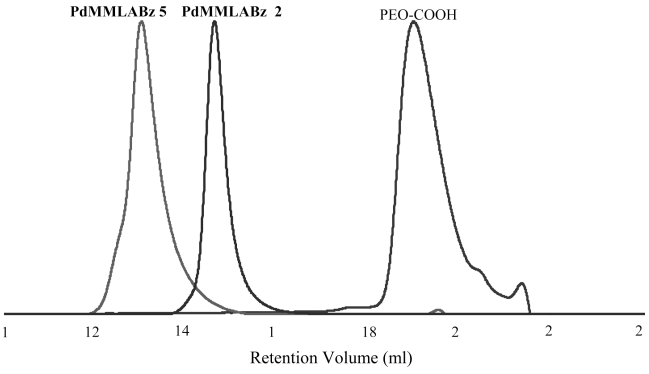


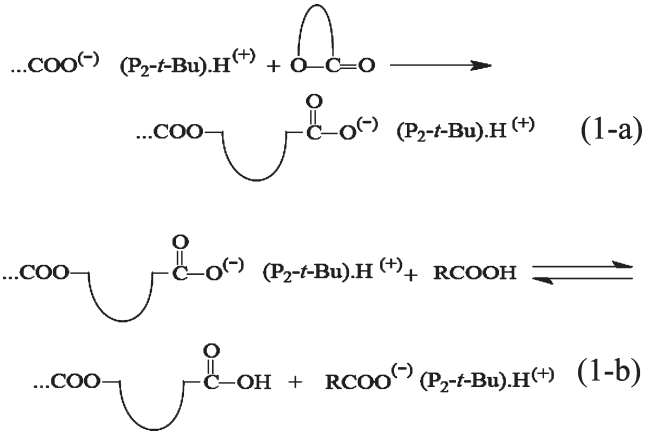
Figure 5. GPC traces of PEO−COOH macroinitiator (right) and its corresponding diblock copolymers, i.e., **PdMMLABz 2** (middle; entry 2, Table 1) and **PdMMLABz 5** (left; entry 5, Table 1).

Table 2. Solution Basicity Data for P_1-*t*-Bu, P_2-*t*-Bu, and P_4-*t*-Bu Phosphazene Catalysts[23]

	pK_a	
phosphazene	MeCN	DMSO
P_1-*t*-Bu·H^+	27	16
P_2-*t*-Bu·H^+	33.5	22
P_4-*t*-Bu·H^+	43	30

$M_{n,PdMMLABz,\ NMR}$ of 283×10^3 g mol^{-1} was determined based on the relative intensity of the repetitive methylene proton H_f of PdMMLABz at 5.1 ppm ($-CO_2CH_2C_6H_5$) and the repetitive methylene protons H_b of the PEO sequence at 3.7 ppm. Assuming an inherent experimental error close to 10%, a good agreement thus exists between the theoretical and the experimental molecular weights. As expected, the GPC trace of **PdMMLABz 2** is completely shifted to lower retention volume compared to PEO−COOH used as macroinitiator (Figure 5) and shows a very narrow PDI (1.19) attesting for the remarkable control over the polymerization process.

Even if the P_2-*t*-Bu catalyst presents a clear potential for the ROP of dMMLABz from a RCOOH initiator, its kinetic activity proved very poor with respect to other metal-free tetraethylammonium benzoate initiator systems.[10] Since P_2-*t*-Bu is only believed to activate an initiating carboxylic acid more likely generating carboxylate active species, it might be considered as a transfer agent (counterion) carrying the initiating functional group (eq 1, parts a and b, if P_2-*t*-Bu is used in default regarding the initiating carboxylic acid initiator).



Because there is an increase in basicity with increasing number of phosphorus atoms in the phosphazene structure (Table 2), it has been decided to enhance the kinetics of the ROP of dMMLABz by using P_4-*t*-Bu (1-*tert*-butyl-4,4,4-tris(dimethylamino)-2,2-bis[tris-(dimethylamino)-phosphoranyl- idenamino]-2Λ^5,4Λ^5-catenadi (phosphazene)) as catalyst. Note also that one reaction has also been attempted with P_1-*t*-Bu (*tert*-butylimino-tris(dimethylamino)phosphorane) as a comparatively less active system.

Basically, it is known that the anionic ROP of BL is kinetically improved when the size of the counterion of the initiating (and therefore propagating) carboxylate salt increases.[24] Since P_4-*t*-Bu is a stronger base than P_2-*t*-Bu by around 10 pK_a units and because its hydrodynamic radius is significantly larger, the kinetics of the polymerization reaction should be considerably modified.

While P_1-*t*-Bu is definitely gendering the less active (but controlled) system (entry 3, Table 1), the polymerization of dMMLABz in THF at room temperature for an initial monomer-to-initiator molar ratio of 100 by using P_4-*t*-Bu as catalyst is extremely fast (entries 4 and 5, Table 1). Interestingly enough, P_4-*t*-Bu catalyst appears even much more active than the previously discussed tetrabutylammonium benzoate-based system, thus active at high monomer concentration, actually in bulk conditions (absence of solvent) at 37 °C.[10] For instance, P_4-*t*-Bu allows for generating a highly active carboxylate ended PEO macroinitiator making possible the generation of a PdMMLABz of 26×10^3 g mol^{-1} in 6 h at room temperature with an excellent control (PDI ∼1.13) (entry 4, Table 1). The control in terms of molecular weights has also been complemented by the ROP of dMMLABz from a PEO−COOH/P_4-*t*-Bu initiating system by targeting an initial monomer-to-initiator molar ratio as high as 9500 (entry 5, Table 1). By comparison to other reactions, the initial monomer concentration has been increased to 1.42 mol·L^{-1} all other conditions unchanged. After 72 h, the reaction medium turned extremely viscous with a complete monomer conversion as attested by FT-IR spectroscopy. GPC analysis reveals a unimodal molecular weight distribution characterized a slightly higher PDI of 1.55 probably due to the very high viscosity of the reaction medium already observed after few hours of reaction. Neither ^{1}H NMR nor MALDI analyzes have been used for the determination of the absolute molecular weight of such high PdMMLABz chains. While GPC might lead to a reasonable estimate of molecular weight, true (absolute) molecular weights can be obtained only if the mathematical relationship describing the hydrodynamic volumes of the calibration standard (PS) and the polymer under investigation (PdMMLABz) is known, requiring the knowledge of the so-called Mark−Houwink parameters.[25] The intrinsic viscosity of a polymer chain is given by the Mark−Houwink expression:

$$[\eta] = KM^a \tag{2}$$

and the molecular weight of any polymer can be determined by GPC using:

$$\log M_2 = \left(\frac{1}{1+a_2}\right)\log\left(\frac{K_1}{K_2}\right) + \frac{1+a_1}{1+a_2}\log M_1 \tag{3}$$

where M_1 is the molecular weight of a polymer standard (polystyrene in this case) for which K_1 and a_1 are also known, and M_2, K_2, and a_2 represent the molecular weight and Mark−Houwink parameters of the unknown sample (PdMMLABz in this case).

Only interested by the M_n of the **PdMMLABz 5**, the eq 3 might be simplified as:

$$\log(M_{nPdMMLABz}) = \varphi + \theta \log(M_{nPS}) \tag{4}$$

where φ and θ are constant for a given system.

Taking into consideration the first four GPC analyses of PdMMLABz samples (in Table 1), a linear relationship between $\log(M_{nPdMMLABz})$ and $\log(M_{nPS})$ can be drawn (Figure 6) and

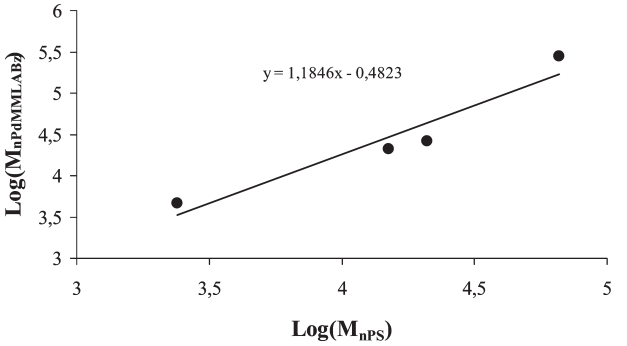


Figure 6. Calibration plot for the determination of absolute mass of **PdMMLABz 5**.

used as calibration plot for the determination of the **PdMMLABz 5** molecular weight.

Injecting the M_nGPC determined for the **PdMMLABz 5** (entry 5, Table 1), an absolute M_n of 1650000 g·mol^{-1} is calculated. This results is in rather acceptable agreement with the $M_{n.th}$ (~2 100 000 g·mol^{-1}) and attests for the remarkable control that can be achieved on the polymerization process.

Conclusion

Phosphazene bases have been investigated as catalysts for the polymerization of [*R,S*]-4-benzylcarbonyl-3,3-dimethyl-2-oxetanone (dMMLABz) in presence of a carboxylic acid initiator. As attested by GPC and MALDI−MS analyses, whatever the phosphazene used (P_1-*t*-Bu, P_2-*t*-Bu, or P_4-*t*-Bu), polymerization reactions proceed by an "*O*-alkyl" scission of the β-lactone monomer and are characterized by an excellent control in terms of polyester molecular weight and end-group fidelity. More than simply efficient, the use of P_4-*t*-Bu allowed for synthesizing a PdMMLABz characterized by a number-average molar mass higher than 1.5×10^6 g mol^{-1}.

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