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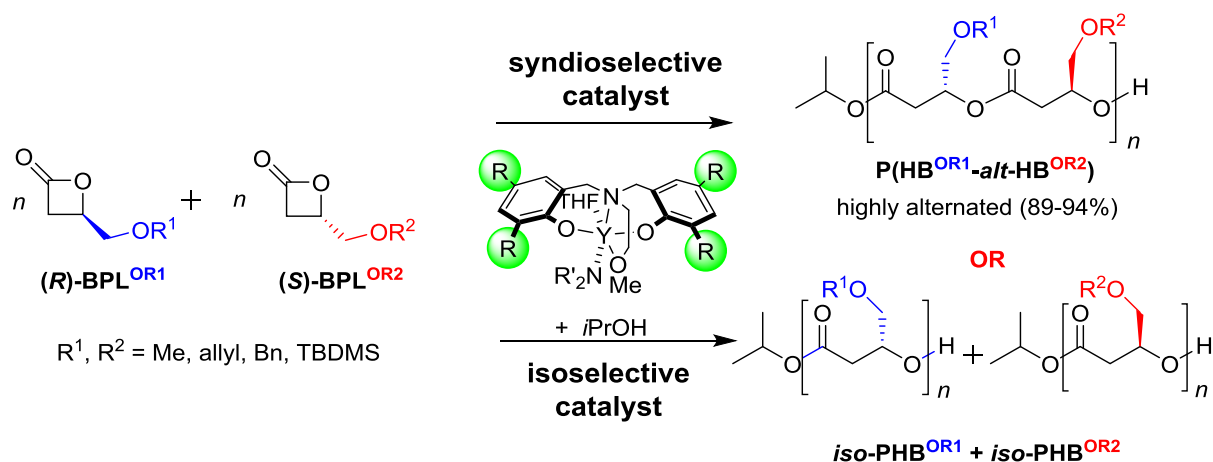
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Highly alternated copolymers or mixtures of isotactic enantiopure homopolymers can be synthesized on purpose from equimolar mixtures of two chemically different  $\beta$ -lactone monomers with opposite configuration, upon using a syndioselective or an isoselective yttrium-based catalyst, respectively.

**Yttrium-Mediated Ring-Opening Copolymerization of Oppositely-Configured 4-Alkoxymethylene- $\beta$ -Propiolactones. Effective Access to Highly Alternated Isotactic Functional PHAs.**

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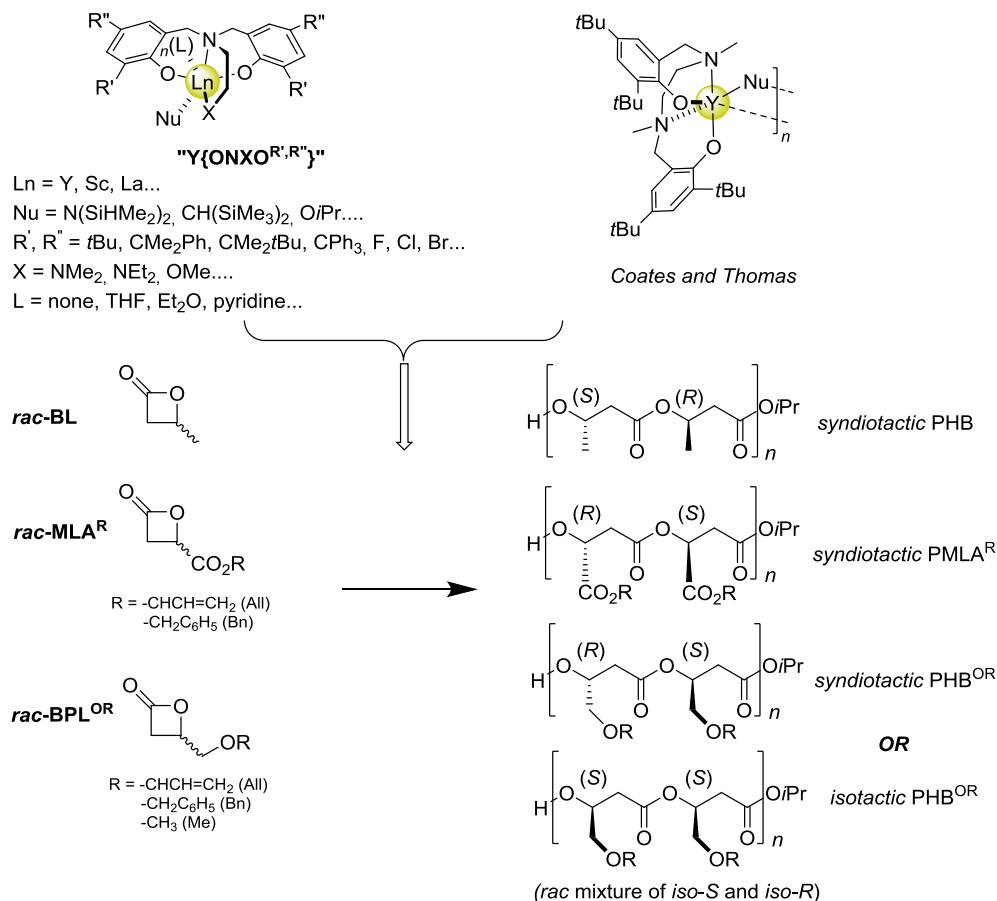
**Abstract:** The ring-opening copolymerization (ROCOP) of functional 4-alkoxymethylene- $\beta$ -propiolactones (BPL<sup>ORs</sup>) by yttrium-bisphenolate complexes has been investigated. The ROCOP of equimolar mixtures of BPL<sup>ORs</sup> of opposite configurations, namely (*R*)-BPL<sup>OR1</sup>/*(S)*-BPL<sup>OR2</sup> ( $R^1, R^2 = \text{OMe}, \text{OAllyl}, \text{OCH}_2\text{Ph} (= \text{OBn}), \text{OSiMe}_2t\text{Bu} (= \text{OTBDMS})$ ), by the syndioselective Y{ONOO<sup>cum</sup>}/*i*PrOH catalyst/initiator system affords P(HB<sup>OR1</sup>-*alt*-HB<sup>OR2</sup>) copolymers with high alternation degrees (altern. = 89–94%), as determined by comprehensive kinetic, <sup>13</sup>C{<sup>1</sup>H} NMR, MALDI-ToF-MS and ESI-MS-MS fragmentation studies. The ROCOP of the (*R*)-BPL<sup>OMe</sup>/*(S)*-BPL<sup>OTBDMS</sup> combination, featuring a large difference in the substituents' bulkiness, constitutes the only observed exception to this trend (altern. = 64%). On the other hand, the isoselectivity of the Y{ONNO<sup>Cl</sup>}/*i*PrOH catalyst/initiator system has been exploited to generate, in a one-pot/one-step procedure, original mixtures of isotactic PHAs. This system efficiently transforms equimolar mixtures of (*R*)-BPL<sup>OAll</sup>/*(S)*-BPL<sup>OMe</sup> into a 1:1 mixture of the corresponding isotactic *iso*-(*R*)-PHB<sup>OAll</sup> and *iso*-(*S*)-PHB<sup>OMe</sup> homopolymers; almost no copolymerization defects are observed. This new approach has been extended successfully to the ROCOP of equimolar mixtures of racemic monomers, *rac*-BPL<sup>OAll</sup>/*rac*-BPL<sup>OMe</sup>.

**Keywords:** alternated copolymer,  $\beta$ -lactone, polyhydroxyalkanoate (PHA), Ring-Opening Copolymerization (ROCOP), stereoselective polymerization, yttrium catalyst

## Introduction

Ring-opening polymerization (ROP) of  $\beta$ -lactones offers an efficient entry toward poly(hydroxyalkanoate)s (PHAs), an attractive class of (bio)degradable materials.<sup>[1]</sup> In particular, the stereoselective ROP of racemic chiral  $\beta$ -lactones has made significant progress over the past two decades.<sup>[2]</sup> In that very field and more generally in the ROP of cyclic esters, high stereoselectivities can be achieved only by metal-based catalyst/initiating systems.<sup>[3]</sup> This has enabled the preparation of either highly syndiotactic or highly isotactic synthetic PHAs, which complete the naturally occurring, exclusively isotactic PHAs produced by microorganisms. Although the ubiquitous zinc  $\beta$ -diketiminate system pioneered by Coates and coworkers proved much active towards the prototypic  $\beta$ -butyrolactone (*rac*-BL) and amenable to a good control of molar masses, it returned only atactic poly(3-hydroxybutyrate) (PHB).<sup>[4]</sup> Also, chromium complexes studied by Rieger and coworkers showed very modest abilities to stereocontrol the ROP of *rac*-BL, and lack any control of molar masses.<sup>[5]</sup> On the other hand, much success has been met with trivalent rare-earths, and most especially with yttrium complexes stabilized by tetradentate amino-alkoxy or diamino-bisphenolate ancillaries (Scheme 1).<sup>[6,7]</sup> By tailoring the nature of the *ortho*-substituents R' on this bisphenolate platform, taking profit of either steric or electronic interactions between these substituents and the growing polymer chain through chain-end stereocontrol mechanisms,<sup>[6a,8]</sup> syndiotactic PHB, syndiotactic poly(alkyl  $\beta$ -malolactonate)s (PMLA<sup>R</sup>s),<sup>[9]</sup> and syndiotactic or even quite uniquely isotactic<sup>[10]</sup> alkoxy-functionalized poly(3-hydroxyalkanoate)s (PHB<sup>ORs</sup>)<sup>[11]</sup> could be prepared by ROP of the corresponding *rac*-BL, the functional alkyl *rac*- $\beta$ -malolactonates (*rac*-MLA<sup>R</sup>s), and *rac*-4-alkoxymethylene- $\beta$ -propiolactones (*rac*-BPL<sup>ORs</sup>), respectively.<sup>[12]</sup> Very recently, Chen and coworkers demonstrated that upon tuning the capping X moiety of the tripodal ligand in such Y{ONXO<sup>R',R''</sup>} complexes, the stereoselectivity of the ROP of a *racemic* chiral  $\gamma$ -lactone can be switched from syndio- (X =

OMe) to isotactic ( $X = \text{NMe}_2$ ).<sup>[13]</sup> This further demonstrates the high versatility and immense potential of this class of unique catalysts/initiators.



**Scheme 1.** Some trivalent rare-earth complexes that incorporate dianionic diamino- or amino-alkoxy-bis(phenolate) ligands highly effective for the stereoselective ROP of chiral  $\beta$ -lactones.

Beyond “simple” homopolymerizations of a given racemic chiral monomer, these stereoselective catalyst systems are of high interest as well when applied toward mixtures of distinct  $\beta$ -lactones. Hence, Coates and Thomas demonstrated that a much related diamino-bis(phenolate) yttrium complex (Scheme 1) can generate highly alternated PHAs when applied to the ROP of equimolar mixtures of two different  $\beta$ -lactones of opposite absolute configuration.<sup>[14]</sup> The catalyst, which operates by a chain-end syndiocontrol mechanism,

selectively incorporates into the growing polymer chain a monomer of opposite configuration to the last inserted one, even though it is chemically different. Obviously, the essential challenge in this chemistry is to assess how chemically different the two monomers of opposite configuration can be, while still maintaining a high degree of catalyst “syndiocontrol”, that is a high degree of alternation in the eventually formed copolymer. In their pioneering work, Coates and Thomas applied this strategy to the copolymerization of mixtures of BL and 3-fluoroalkyl- $\beta$ -propiolactones, achieving alternation degrees in the range 90–94%.<sup>[14]</sup> However, the aliphatic/fluorinated nature of the monomers, did not allow further chemical modification of the resultant alternated polyesters. Our group later demonstrated that the strategy could be effectively extended to the preparation of highly alternated poly(alkyl  $\beta$ -malolactonate)s P(MLA<sup>R1</sup>-*alt*- MLA<sup>R2</sup>)s using equimolar mixtures of (*S*)-MLA<sup>R1</sup>/*(R)*-MLA<sup>R2</sup>. Thanks to the presence of pendant reactive benzyloxycarbonyl ( $R^1$ ) and allyloxycarbonyl ( $R^2$ ) groups, simple post-modification, notably hydrogenolysis/hydrogenation, respectively, offered original materials with a seldom-seen enchainment in a perfectly alternated fashion of highly hydrophilic (CO<sub>2</sub>H)/hydrophobic (CO<sub>2</sub>*n*Pr) functions. The preparation of such sequence-controlled polymers is currently of topical interest for a variety of potential applications.<sup>[15]</sup>

Herein we report on the preparation and characterization of new PHA copolymers from a class of functional  $\beta$ -lactones just recently released in ROP, 4-alkoxymethylene- $\beta$ -propiolactones (BPL<sup>OR<sub>s</sub></sup>).<sup>[11,12]</sup> The alkoxymethylene moiety in this class of  $\beta$ -lactones induces quite different interactions with the Y{ONXO<sup>R',R''</sup>} catalysts, in particular with halogenated complexes Y{ONXO<sup>hal,hal</sup>} (hal = F, Cl, Br) in which *hal*···HHCOR attractive contacts apparently enforce a unique isotactic stereocontrol.<sup>[11,12,16]</sup> The functionalities borne by the monomers (OR = OBn, OSiR<sub>3</sub>, OAllyl) used in this study have been selected for the potential post-functionalization of the resulting copolymers (debenzylation, desilylation,

hydrogenation ...), although chemical modification was not the objective of our present work. The actual aim of our initial investigations reported herein is two-fold: this first manuscript explores the potential of  $Y\{ONXO^{R',R''}\}$  catalyst/initiator systems at controlling the microstructure of  $P(HB^{OR1}-HB^{OR2})$  copolymers starting from *equimolar* mixtures of two different monomers  $(R)\text{-BPL}^{OR1}/(S)\text{-BPL}^{OR2}$ , and in particular the ability to achieve high degrees of alternation using syndioselective catalysts. Also, it reports on the preparation of original 1:1 mixtures of isotactic, chemically-different macromolecules of opposite configurations,  $(R)\text{-PHB}^{OR1}\text{-}(S)\text{-PHB}^{OR2}$ , starting from equimolar mixtures of two different monomers using an isoselective catalyst. To our knowledge, this is the first time that the straightforward one-pot, one-step preparation of such mixtures – otherwise reachable only by physical blending of separately prepared homochiral polyesters – is reported. A forthcoming manuscript will next report on the synthesis and characterization of more sophisticated  $[\text{isotactic-PHB}^{OR1}]\text{-}b\text{-}[\text{poly}(\text{HB}^{OR1}\text{-}alt\text{-HB}^{OR2})]$  microstructures resulting from the one-pot, one-step ROP of *non-equimolar* mixtures of two different 4-alkoxymethylene- $\beta$ -propiolactones.

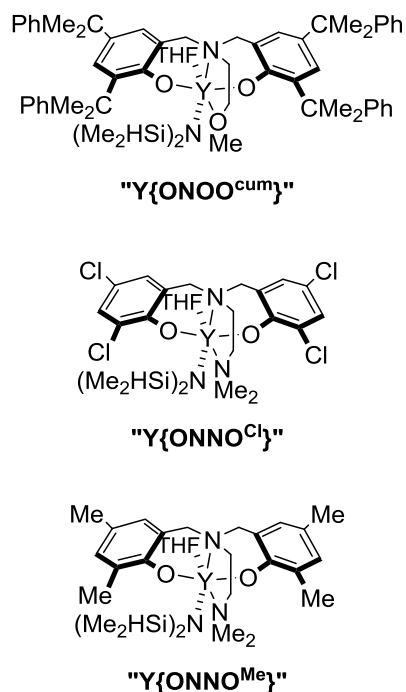
## Results and Discussions

### 1. Preparation and microstructural characterization of alternated PHA copolymers.

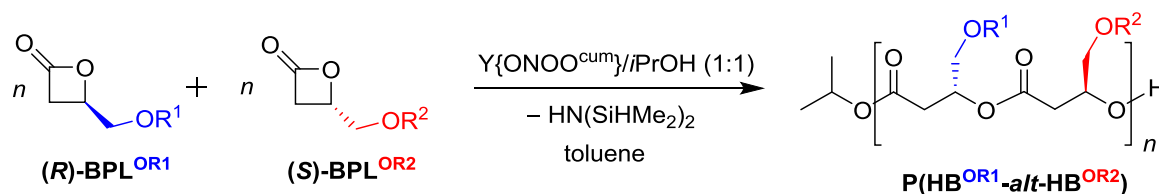
The  $Y\{ONOO^{cum}\}/iPrOH$  system (Chart 1) that combines high activities and syndiotacticities in the ROP of  $rac\text{-BPL}^{ORs[11]}$  was herein explored to promote the ROCOP of equimolar mixtures of two oppositely-configured 4-alkoxymethylene- $\beta$ -propiolactones bearing different substituents,  $(R)\text{-BPL}^{OR1}$  and  $(S)\text{-BPL}^{OR2}$  (Scheme 2). These experiments aimed at probing, beyond the anticipated control of classical parameters of the ROP (molar mass values and dispersity, terminal functionalities), the stereocontrol of the catalyst and the



targeted alternation of the enchainment of the two monomers. Representative results are summarized in Table 1.



**Chart 1.** Y{ONXO<sup>R',R''</sup>} pre-catalysts used in this study.



R<sup>1</sup>, R<sup>2</sup> = Me, allyl, -CH<sub>2</sub>Ph (= Bn), -SiMe<sub>2</sub>tBu (= TBDMS)

**Scheme 2.** Synthesis of alternated copolymers P(HB<sup>OR1</sup>-alt-HB<sup>OR2</sup>) by the ROCOP of equimolar mixtures of (R)-BPL<sup>OR1</sup>/(S)-BPL<sup>OR2</sup> with the Y{ONOO<sup>cumyl</sup>}/iPrOH (1:1) system.

**Table 1.** ROCOP of equimolar mixtures of (*R*)-BPL<sup>OR1</sup>/*(S)*-BPL<sup>OR2</sup> mediated by the Y{ONOO<sup>cum</sup>}/*i*PrOH (1:1) system.<sup>a</sup>

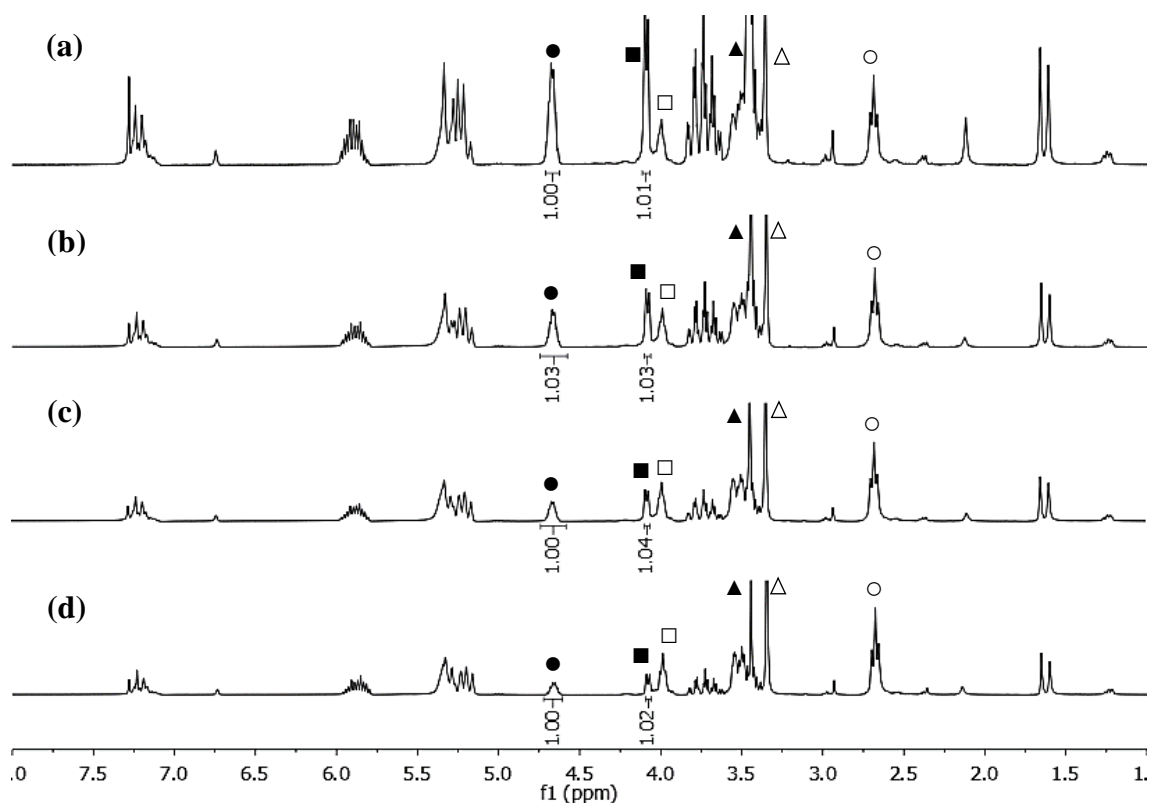
Entry	( <i>R</i> )-BPL <sup>OR1</sup> / ( <i>S</i> )-BPL <sup>OR2</sup>	[( <i>R</i> )-BPL <sup>OR1</sup> ] <sub>0</sub> : [( <i>S</i> )-BPL <sup>OR2</sup> ] <sub>0</sub> : [ <i>i</i> PrOH] <sub>0</sub>	BPL <sup>ORs</sup> Conv. <sup>c</sup> (%)	$M_{n,theo}$ <sup>d</sup> (g.mol <sup>-1</sup> )	$M_{n,NMR}$ <sup>e</sup> (g.mol <sup>-1</sup> )	$M_{n,SEC}$ <sup>f</sup> (g.mol <sup>-1</sup> )	$\bar{D}_M$ <sup>g</sup>	Altern. <sup>h</sup> (%)
1 <sup>b</sup>	( <i>R</i> )-BPL <sup>OAll</sup> / ( <i>S</i> )-BPL <sup>OMe</sup>	26:24:1	100	6 500	6 600	7 900	1.25	87
2	( <i>R</i> )-BPL <sup>OAll</sup> / ( <i>S</i> )-BPL <sup>OMe</sup>	25:26:1	100	6 600	6 600	11 800	1.38	90
3	( <i>R</i> )-BPL <sup>OBn</sup> / ( <i>S</i> )-BPL <sup>OMe</sup>	25:25:1	100	7 800	7 800	11 300	1.32	89
4	( <i>R</i> )-BPL <sup>OBn</sup> / ( <i>S</i> )-BPL <sup>OAll</sup>	25:25:1	100	8 400	8 900	11 300	1.17	91
5	( <i>R</i> )-BPL <sup>OAll</sup> / ( <i>S</i> )-BPL <sup>OTBDMS</sup>	25:25:1	90	9 000	8 300	11 500	1.05	93
6	( <i>R</i> )-BPL <sup>OBn</sup> / ( <i>S</i> )-BPL <sup>OTBDMS</sup>	26:25:1	100	10 500	10 300	14 500	1.05	94
7	( <i>R</i> )-BPL <sup>OMe</sup> / ( <i>S</i> )-BPL <sup>OTBDMS</sup>	25:25:1	100 62	6 300	6 400	<i>nd</i>	<i>nd</i>	67

<sup>a</sup> Reactions performed at [(*R*)-BPL<sup>OAll</sup> + (*S*)-BPL<sup>OMe</sup>]<sub>0</sub> = 1.0 M in toluene at -27 °C for 24 h (non optimized reaction time) unless otherwise stated. <sup>b</sup> Reaction conducted at 23 °C for 2 h. <sup>c</sup> Overall conversion of both monomers as determined by <sup>1</sup>H NMR of the crude reaction mixture (refer to the Experimental Section). <sup>d</sup> Theoretical molar mass determined from  $M_{n,theo} = \{([BPL^{OAll}]_0 \times conv_{BPL^{OAll}} \times M_{BPL^{OAll}}) + ([BPL^{OMe}]_0 \times conv_{BPL^{OMe}} \times M_{BPL^{OMe}})\} / [iPrOH]_0 + M_{iPrOH}$ , with  $M_{BPL^{OAll}} = 142 \text{ g.mol}^{-1}$ ,  $M_{BPL^{OMe}} = 116 \text{ g.mol}^{-1}$ ,  $M_{BPL^{OBn}} = 192 \text{ g.mol}^{-1}$ ,  $M_{BPL^{OTBDMS}} = 216 \text{ g.mol}^{-1}$ ,  $M_{iPrOH} = 60 \text{ g.mol}^{-1}$ . <sup>e</sup> Molar mass values determined by <sup>1</sup>H NMR analysis of the isolated polymer, from the signals of terminal *i*Pr vs. those of the repeating units. <sup>f</sup> Molar mass and dispersities determined by SEC in THF at 30 °C vs. polystyrene standards (uncorrected values). <sup>g</sup> Alternation degree, as determined by <sup>13</sup>C{<sup>1</sup>H} NMR analysis from the relation  $\%_{alt} = \frac{I_{alt}}{I_{alt} + I_{non-alt}} \times 100$ , with  $I_{alt}$  = sum of integral values of signals assigned to alternated sequences and  $I_{non-alt}$  = sum of integral values of signals assigned to non-alternated sequences.

#### a. ROCOP of (*R*)-BPL<sup>OAll</sup>/*(S)*-BPL<sup>OMe</sup> mixtures

The first ROCOP experiments were conducted on the (*R*)-BPL<sup>OAll</sup>/*(S)*-BPL<sup>OMe</sup> combination (entries 1 and 2). These comonomers were selected for in-depth studies because their NMR signals, in particular those of their side functional groups (allyl and methyl), are well differentiated both in the monomers and in the copolymer, thus allowing ready kinetic monitoring and microstructural analysis.

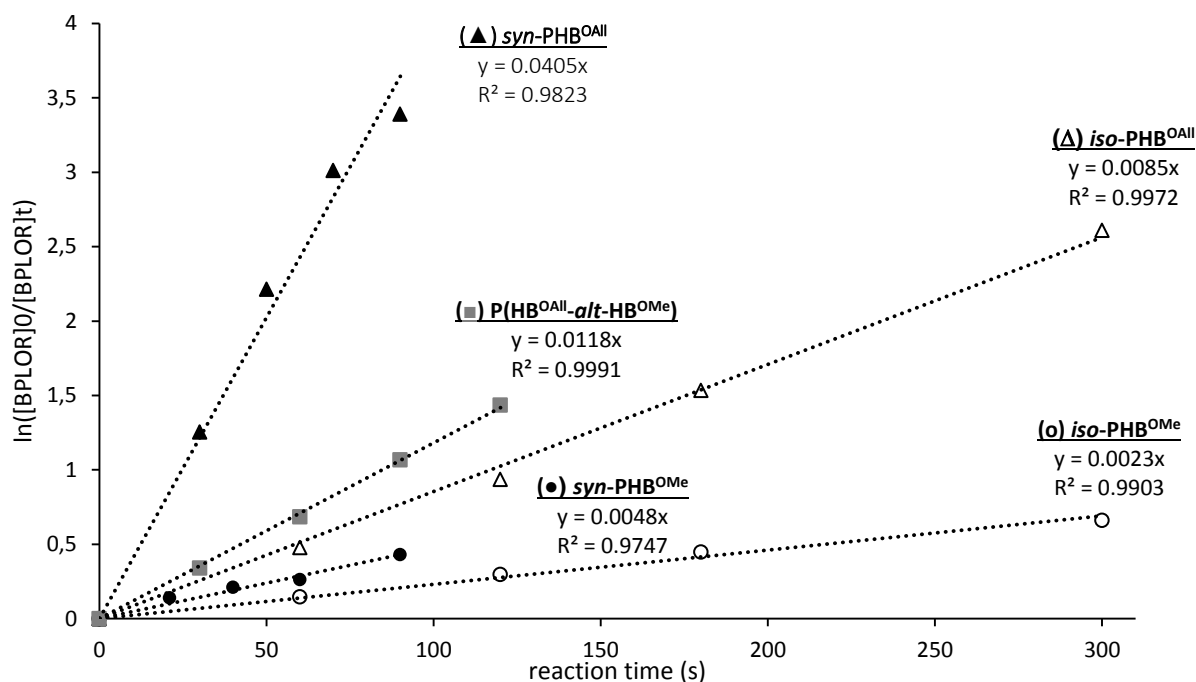
Monitoring of the characteristic <sup>1</sup>H NMR signals as a function of time evidenced the simultaneous consumption of both comonomers as the reaction proceeds (Figure 1); this is hinting at, or at least is consistent with the possible formation of an alternated microstructure.



**Figure 1.**  $^1\text{H}$  NMR kinetic monitoring (400 MHz,  $\text{CDCl}_3$ ,  $23\text{ }^\circ\text{C}$ ) of the ROCOP of an equimolar mixture of  $(R)\text{-BPL}^{\text{OAll}}/(S)\text{-BPL}^{\text{OMe}}$  mediated by the  $\text{Y}\{\text{ONOO}^{\text{cum}}\}/i\text{PrOH}$  system (50:50:1:1) at  $23\text{ }^\circ\text{C}$  after: (a) 30 s, (b) 60 s, (c) 90 s and (d) 120 s of reaction (■ :  $\delta_{\text{CH}_2\text{All-BPLOAll}} = 4.06\text{ ppm}$  vs. □ :  $\delta_{\text{CH}_2\text{All-PHBOAll}} = 3.96\text{ ppm}$  ; ▲ :  $\delta_{\text{CH}_3\text{-BPLOMe}} = 3.42\text{ ppm}$  vs. △ :  $\delta_{\text{CH}_3\text{-PHBOMe}} = 3.33\text{ ppm}$  ; ● :  $\delta_{\text{CH-BPLOAll/CH-BPLOMe}} = 4.64\text{ ppm}$  vs. ○ :  $\delta_{\text{CH}_2\text{OAll-PHBOAll/CH}_2\text{OMe-PHBOMe}} = 2.66\text{ ppm}$ ).

As depicted by the logarithmic plot in Figure 2, the reaction follows first-order kinetics in monomers. The ROCOP rate for the  $(R)\text{-BPL}^{\text{OAll}}/(S)\text{-BPL}^{\text{OMe}}$  combination ( $k_{\text{app}} = 11.8(1) \times 10^{-3}\text{ s}^{-1}$ ) falls in between those of the ROP of  $rac\text{-BPL}^{\text{OAll}}$  and  $rac\text{-BPL}^{\text{OMe}}$  determined under the same conditions, which lead to the corresponding syndiotactic homopolymers ( $k_{\text{app}} = 40.5(1) \times 10^{-3}\text{ s}^{-1}$  and  $4.8(2) \times 10^{-3}\text{ s}^{-1}$ , respectively). Also, the ROCOP rate is, under the same conditions, higher than that of the ROP of enantiopure monomers which give the corresponding isotactic homopolymers ( $k_{\text{app}} = 8.5(1) \times 10^{-3}\text{ s}^{-1}$  and  $2.3(1) \times 10^{-3}\text{ s}^{-1}$ , respectively). All together, this information is also consistent with the

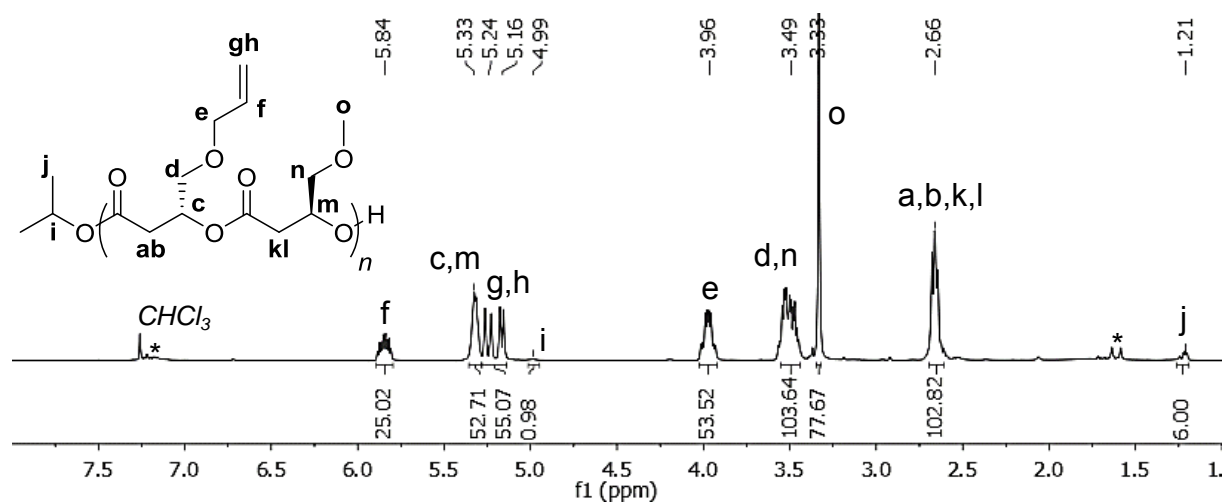
probable formation of an alternated copolymer and not of a mixture of isotactic homopolymers.



**Figure 2.** Logarithmic plot of the kinetics of the ROCOP of an equimolar mixture of (*R*)-BPL<sup>OAll</sup>/*(S)*-BPL<sup>OMe</sup> (■) and of the ROP of *rac*-BPL<sup>OAll</sup> (▲), *rac*-BPL<sup>OMe</sup> (●), (*R*)-BPL<sup>OAll</sup> (Δ), (*S*)-BPL<sup>OMe</sup> (○), mediated by the Y{ONOO<sup>cum</sup>}/*iPrOH* at 23 °C in toluene.

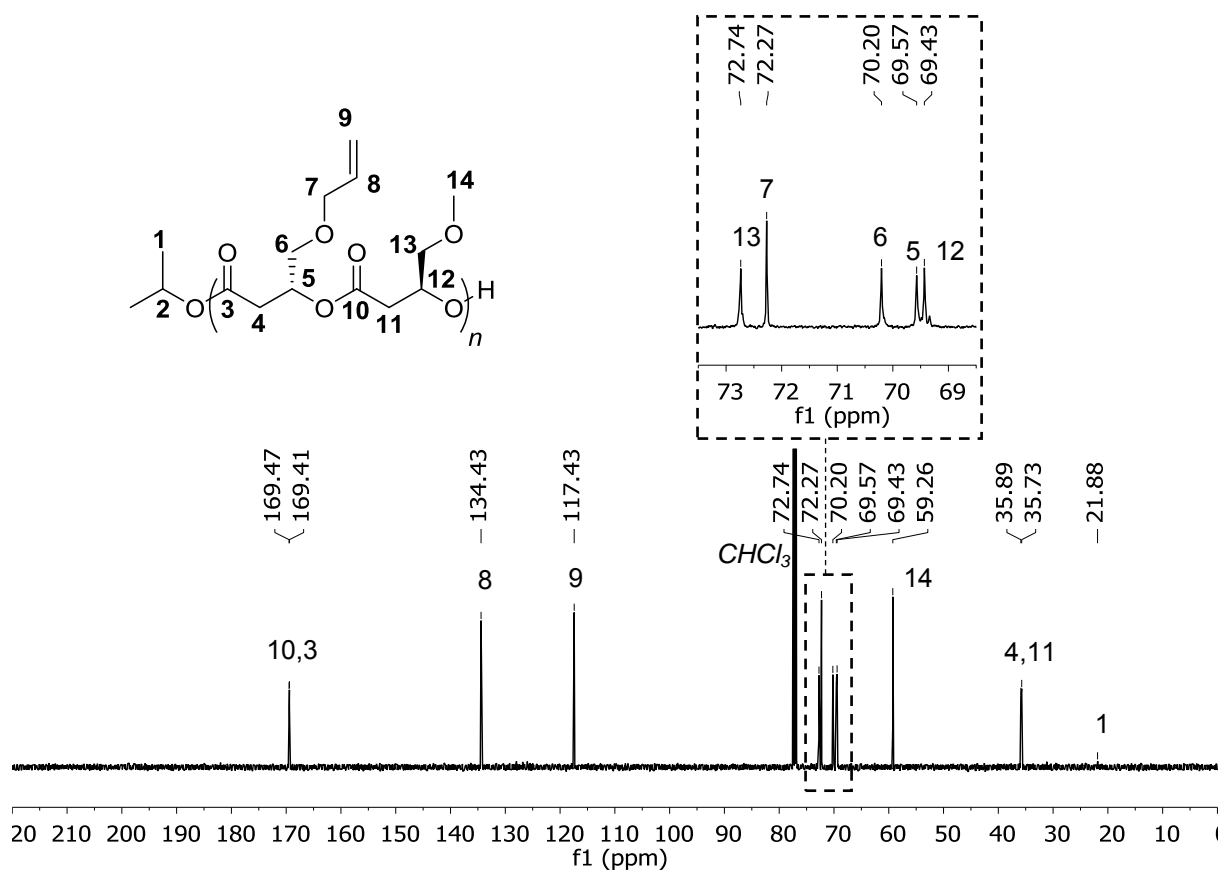
To further establish the microstructure, the two copolymers prepared at 23 °C and -27 °C (Table 1, entries 1, 2) were characterized by <sup>1</sup>H and <sup>13</sup>C{<sup>1</sup>H} NMR spectroscopy, MALDI-ToF and ESI mass spectrometry (MS), and SEC analysis.

<sup>1</sup>H NMR allows essentially determining the molar mass, by comparing the signal intensities from the repeating units of PHB<sup>OAll</sup> (H<sup>a</sup>-H<sup>h</sup>) and PHB<sup>OMe</sup> (H<sup>k</sup>-H<sup>o</sup>) and those of the terminal isopropoxy group (H<sup>i</sup>, H<sup>j</sup>) (Figure 3). The thus determined  $M_{n,NMR}$  values match perfectly the theoretical ones, following the same trends as those determined in homopolymerization studies.<sup>[11]</sup>

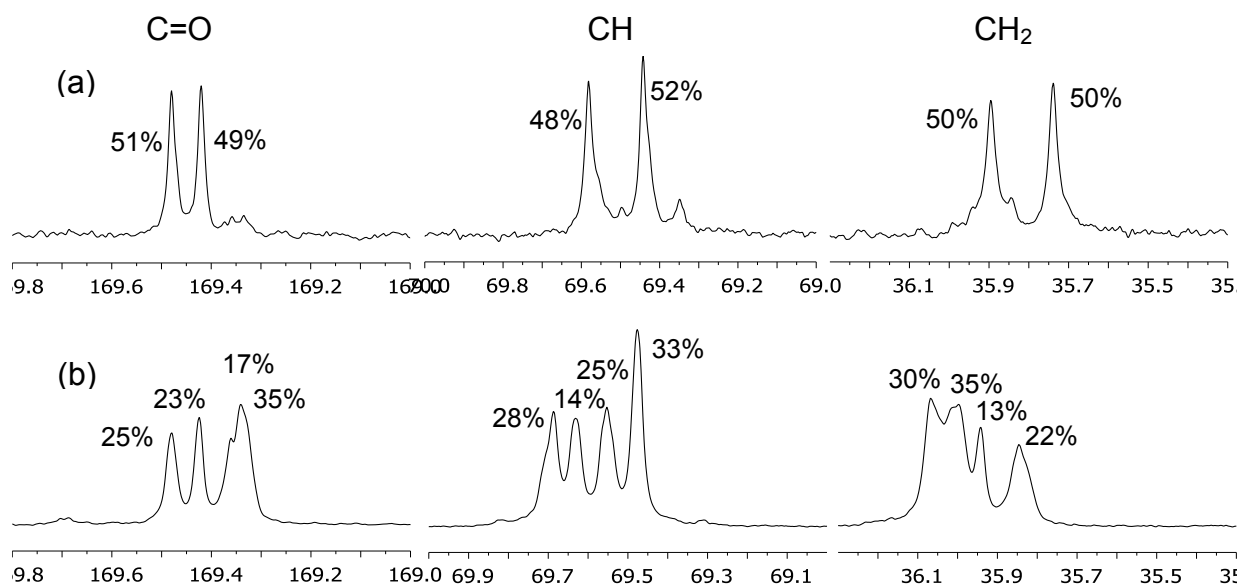


**Figure 3.**  $^1\text{H}$  NMR spectrum (500 MHz,  $\text{CDCl}_3$ , 25 °C) of a  $\text{P}(\text{HB}^{\text{OAll}}\text{-alt-HB}^{\text{OMe}})$  copolymer prepared from the ROCOP of an equimolar mixture of  $(R)\text{-BPL}^{\text{OAll}}/(S)\text{-BPL}^{\text{OMe}}$  with the  $\text{Y}\{\text{ONOO}^{\text{cum}}\}/i\text{PrOH}$  system (25:26:1:1; Table 1, entry 2). \* stands for signals from residual catalyst/ligand.

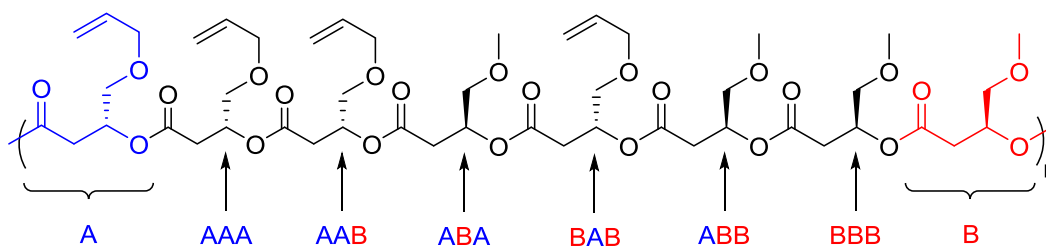
$^{13}\text{C}\{^1\text{H}\}$  NMR spectroscopy, beyond confirming the main chain repeating units  $\text{PHB}^{\text{OAll}}$  ( $\text{C}^3\text{-C}^9$ ) and  $\text{PHB}^{\text{OMe}}$  ( $\text{C}^{10}\text{-C}^{14}$ ) and the terminal group ( $\text{C}^1$ ) (Figure 4), provides a deeper appreciation of the microstructure. This latter can be assessed within the regions of the carbonyl ( $\text{C}^{3,10}$ ), methylene ( $\text{C}^{4,11}$ )<sup>[17]</sup> and methine ( $\text{C}^{5,12}$ ) groups, as established with the corresponding homopolymers.<sup>[11]</sup> Figure 5 illustrates these regions for two copolymers: one with a highly alternated microstructure thanks to the use of the “syndioselective”  $\text{Y}\{\text{ONOO}^{\text{cum}}\}$  catalyst, and another one with a random microstructure prepared with the non-stereoselective  $\text{Y}\{\text{ONNO}^{\text{Me}}\}$  catalyst (Chart 1) (due to the small methyl substituents installed on the ligand phenolate rings, as previously established).<sup>[11]</sup> In each region of the NMR spectra, the highly alternated copolymer features essentially two resonances of equal intensity assigned to the alternating  $\text{HB}^{\text{OAll}}$  and  $\text{HB}^{\text{OMe}}$  units (ABA and BAB triads, Chart 1), in contrast to the complex pattern displayed by the random copolymer.



**Figure 4.**  $^{13}\text{C}\{^1\text{H}\}$  NMR spectrum (125 MHz,  $\text{CDCl}_3$ , 25 °C) of a  $\text{P}(\text{HB}^{\text{OAll}}\text{-alt-HB}^{\text{OMe}})$  copolymer prepared from the ROCOP of an equimolar mixture of  $(R)\text{-BPL}^{\text{OAll}}/(S)\text{-BPL}^{\text{OMe}}$  with the  $\text{Y}\{\text{ONOO}^{\text{cum}}\}/i\text{PrOH}$  system at  $-27$  °C (25:26:1:1; Table 1, entry 2).



**Figure 5.** Details of the  $^{13}\text{C}\{^1\text{H}\}$  NMR spectra (125 MHz,  $\text{CDCl}_3$ , 23 °C) of (a) a  $\text{P}(\text{HB}^{\text{OAll}}\text{-alt-HB}^{\text{OMe}})$  highly alternated (altern. = 87%) copolymer, prepared from the ROCOP of an equimolar mixture of  $(R)\text{-BPL}^{\text{OAll}}/(S)\text{-BPL}^{\text{OMe}}$  with the  $\text{Y}\{\text{ONOO}^{\text{cum}}\}/i\text{PrOH}$  system at 23 °C (25:26:1:1; Table 1, entry 1); (b) an essentially random  $\text{P}(\text{HB}^{\text{OAll}}\text{-ran-HB}^{\text{OMe}})$  copolymer (altern. = 47%), prepared from the ROCOP of an equimolar mixture  $(R)\text{-BPL}^{\text{OAll}}/(S)\text{-BPL}^{\text{OMe}}$  with the  $\text{Y}\{\text{ONNO}^{\text{Me}}\}/i\text{PrOH}$  system (30:26:1:1).<sup>[11]</sup>



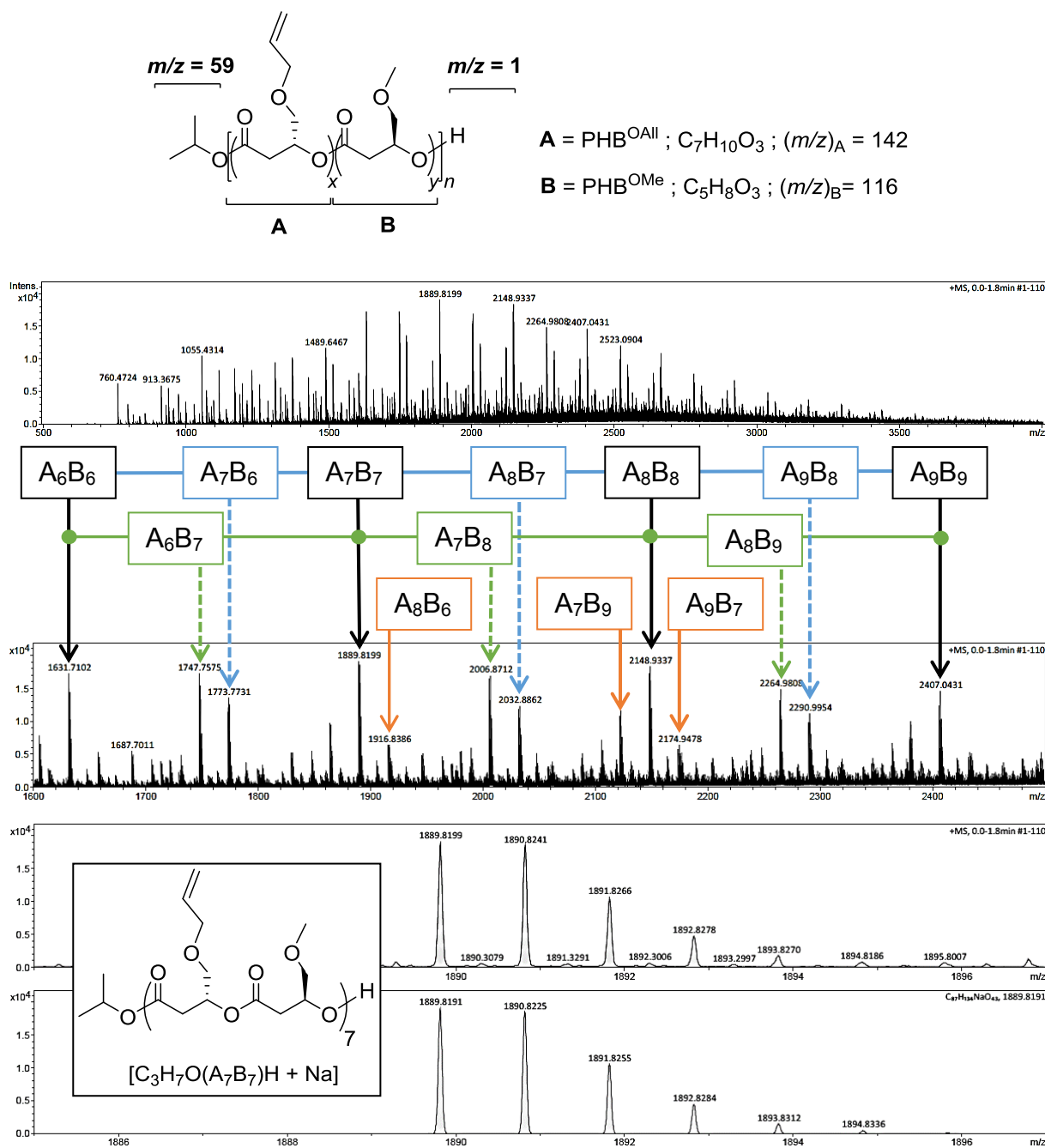
**Chart 1.** Representation of the possible triads in a  $\text{BPL}^{\text{OAll}}$  (A)/ $\text{BPL}^{\text{OMe}}$  (B) copolymer, upon varying the alternation degree.

A closer examination of the resonances in the carbonyl region, which is often the best resolved one in this family of copolymers (vide infra), further corroborates the formation of a highly alternated microstructure. Indeed, the two most (equally) intense resonances in the  $\text{P}(\text{HB}^{\text{OAll}}\text{-alt-HB}^{\text{OMe}})$  display the same chemical shifts ( $\delta_{\text{alt-ABA/BAB}} = 169.48$  and  $169.42$  ppm) as the alike resonances in the corresponding syndiotactic  $\text{PHB}^{\text{OAll}}$  and  $\text{PHB}^{\text{OMe}}$  homopolymers ( $\delta_{\text{syn-PHB}^{\text{OAll}}} = 169.47$  ppm;  $\delta_{\text{syn-PHB}^{\text{OMe}}} = 169.45$  ppm), respectively. On the other hand, the characteristic carbonyl resonances for the isotactic homopolymers are observed at higher field ( $\delta_{\text{iso-PHB}^{\text{OAll}}} = 169.36$  ppm;  $\delta_{\text{iso-PHB}^{\text{OMe}}} = 169.34$  ppm) (see Figure S6 in the Supporting Information). Comparatively, the latter signals are of very low intensity in the spectrum of the alternated copolymer. The virtual absence of isotactic sequences was further evidenced by analyzing, by  $^{13}\text{C}$  NMR spectroscopy, physical blends of the alternated copolymer with the corresponding isotactic  $\text{PHB}^{\text{OAll}}$  and  $\text{PHB}^{\text{OMe}}$  (see Figure S7 in the Supporting Information).

Hence, the alternation degree in the copolymers can be determined from the ratio of integral values corresponding to the resonances of alternated triads (ABA, BAB) to the total of triad resonances (ABA, BAB + AAB, BBA, AAA, and BBB, Chart 1).<sup>[9,14]</sup> For P(HB<sup>OAll</sup>-*alt*-HB<sup>OMe</sup>) prepared with the Y{ONOO<sup>cum</sup>}/*i*PrOH system, the alternation degree lies in the range 87–90%. As anticipated, a slightly higher value is reached when the ROCOP is performed at a lower temperature (entry 1 vs. 2); this was therefore systematically applied to all subsequent copolymerization experiments.

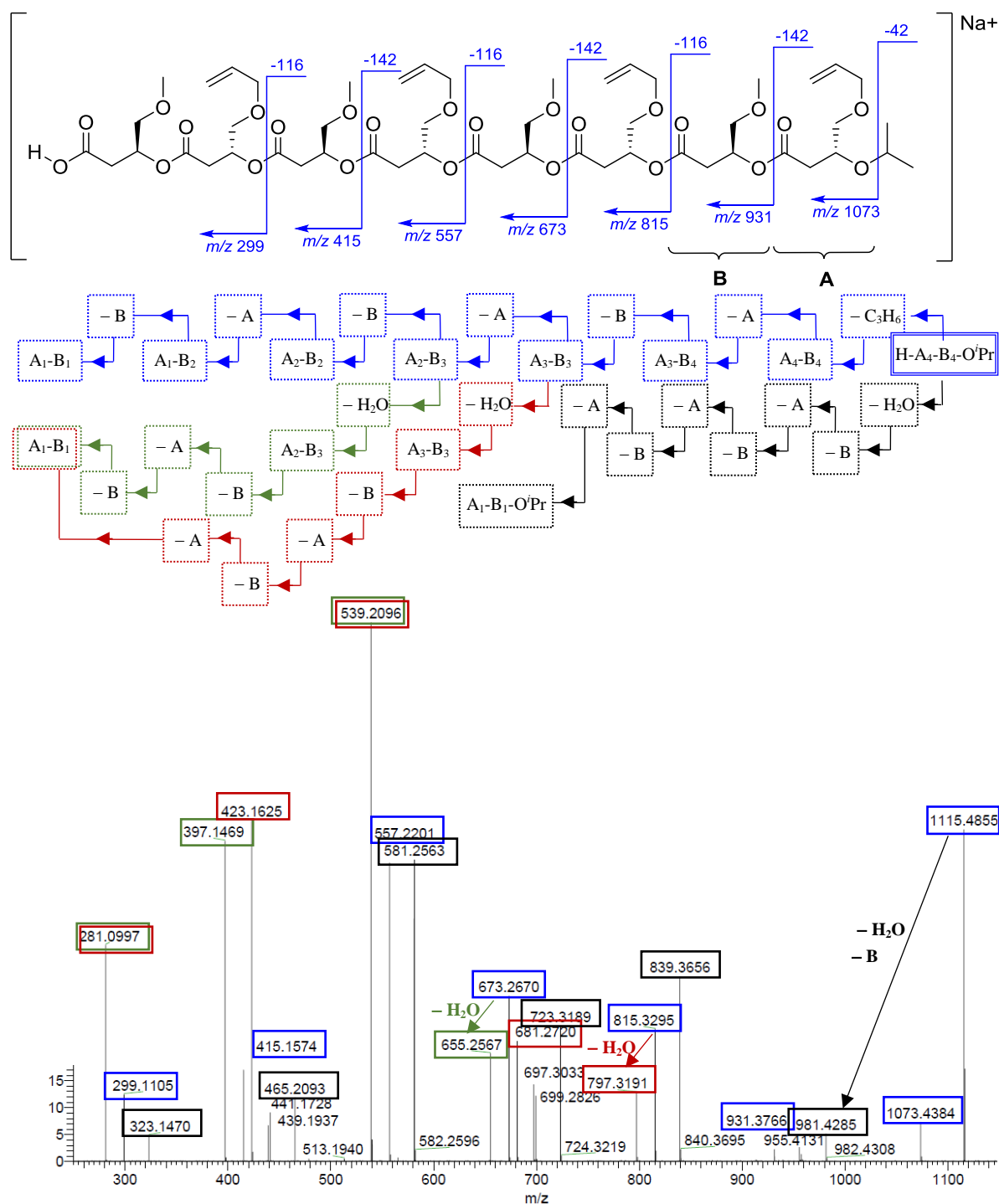
MALDI-ToF MS provides another strong support for a high degree of alternation in the P(HB<sup>OAll</sup>-*alt*-HB<sup>OMe</sup>) copolymers prepared with the Y{ONOO<sup>cum</sup>}/*i*PrOH system (Figure 6). The main population observed corresponds to macromolecules with a global repeating unit at  $m/z = 258 \text{ g.mol}^{-1}$ , that is the sum of the molar masses of both monomers ( $M_{\text{BPLOAll}} + M_{\text{BPLOMe}} = 142 + 116 \text{ g.mol}^{-1}$ ), end-capped by hydroxy and isopropoxy groups, and ionized by sodium, i.e. [*i*PrO-P(HB<sup>OAll</sup>-*alt*-HB<sup>OMe</sup>)<sub>*n*</sub>-H.Na<sup>+</sup>], with e.g.  $m/z_{\text{obsv}} = 1889.8$  (vs.  $m/z_{\text{theo}} = 1889.8$ ) for  $n = 7$  (in black). In addition to this main population, some peaks are observed for [*i*PrO(PHB<sup>OAll</sup>)<sub>*n+1*</sub>(PHB<sup>OMe</sup>)<sub>*n*</sub>-H.Na<sup>+</sup>] and [*i*PrO(PHB<sup>OAll</sup>)<sub>*n*</sub>(PHB<sup>OMe</sup>)<sub>*n+1*</sub>-H.Na<sup>+</sup>], with  $m/z_{\text{obsv}} = 2032.9$ <sup>[18]</sup> (vs.  $m/z_{\text{theo}} = 2032.9$ ) and  $m/z_{\text{obsv}} = 2006.9$ <sup>[18]</sup> (vs.  $m/z_{\text{theo}} = 2006.9$ ) for  $n = 7$  (populations shown in blue and green, respectively). These observations evidence the alternation of both monomers in the copolymer. Minor populations that correspond to alternation defects are identified with  $n(\text{HB}^{\text{OAll}}) = n(\text{HB}^{\text{OMe}}) + 2$  or  $n(\text{HB}^{\text{OAll}}) + 2 = n(\text{HB}^{\text{OMe}})$ , at  $m/z_{\text{obsv}} = 1916.8$ <sup>[18]</sup> (vs.  $m/z_{\text{theo}} = 1916.8$ ) for  $n(\text{HB}^{\text{OMe}}) = 6$  and  $m/z_{\text{obsv}} = 2174.9$ <sup>[18]</sup> ( $m/z_{\text{theo}} = 2174.9$ ) pour  $n(\text{HB}^{\text{OMe}}) = 7$ .





**Figure 6.** MALDI-ToF mass spectrum of a P(HB<sup>OAll</sup>-*alt*-HB<sup>OMe</sup>) copolymer prepared from the ROCOP of an equimolar mixture of (*R*)-BPL<sup>OAll</sup>/*(S)*-BPL<sup>OMe</sup> with the Y{ONOO<sup>cum</sup>} / *i*PrOH system (Table 1, entry 2). The main populations observed correspond to alternated copolymers starting with either a (*R*)-BPL<sup>OAll</sup> unit (A, blue) or a (*S*)-BPL<sup>OMe</sup> unit (B, green). Populations that correspond to copolymers featuring one alternation defect are shown in orange. All these major populations are ionized by Na<sup>+</sup>. At the bottom are shown the zoom regions of the experimental (top) and simulation (bottom) of the isotopic mass for an alternated macromolecule with  $n = 7$  ( $m/z_{obsv} = 1889.820$  vs.  $m/z_{theo} = 1889.819$ ).

These MALDI-ToF MS data were completed by ESI-MS/MS fragmentation studies. Figure 7 shows the fragmentation of a selected oligomer, namely  $[i\text{PrO-P}(\text{HB}^{\text{OAll-}alt}\text{-HB}^{\text{OMe}})_4\text{-H.Na}^+]$  ( $m/z_{\text{obsv}} = 1115.5$ ). The different fragmentation routes observed evidence the high degree of alternation within the copolymer chain. The fragmentation route featured in blue shows the initial loss of propene ( $m/z = 42$ ) from the terminal isopropoxy group to generate  $[\text{HO}(\text{A}_4\text{B}_4)\text{H.Na}^+]$  ( $m/z_{\text{obsv}} = 1073$ ) (note that in Figure 7, for the sake of clarity, all  $[\text{HO}(\text{A}_m\text{B}_n)\text{H.Na}^+]$  macromolecules are simplified as  $\text{A}_m\text{B}_n$ ). Subsequently observed signals corresponds to the perfectly regularly alternated loss of the two comonomers, i.e.  $[\text{HO}(\text{A}_3\text{B}_4)\text{H.Na}^+]$  ( $m/z_{\text{obsv}} = 931.3766$ ,  $\Delta m/z = 142.0618$  vs.  $M_{\text{BPLOAll}} = 142.06 \text{ g.mol}^{-1}$ ),  $[\text{HO}(\text{A}_3\text{B}_3)\text{H.Na}^+]$  ( $m/z_{\text{obsv}} = 815.3295$ ,  $\Delta m/z = 116.0471$  vs.  $M_{\text{BPLOMe}} = 116.05 \text{ g.mol}^{-1}$ ),  $[\text{HO}(\text{A}_2\text{B}_3)\text{H.Na}^+]$  ( $m/z_{\text{obsv}} = 673.2670$ ,  $\Delta m/z = 142.0625$ ),  $[\text{HO}(\text{A}_2\text{B}_2)\text{H.Na}^+]$  ( $m/z_{\text{obsv}} = 557.2201$ ,  $\Delta m/z = 116.0469$ ),  $[\text{HO}(\text{A}_1\text{B}_2)\text{H.Na}^+]$  ( $m/z_{\text{obsv}} = 415.1574$ ,  $\Delta m/z = 142.0627$ ) and  $[\text{HO}(\text{A}_1\text{B}_1)\text{H.Na}^+]$  ( $m/z_{\text{obsv}} = 299.1105$ ,  $\Delta m/z = 116.0469$ ) (pattern depicted in blue). Other fragmentation routes also evidence the perfectly alternated loss of the two comonomers, involving the loss of a hydroxy fragment (black) or of a water molecule (red and green) at different stages. Lower intensity signals were assigned to the fragmentation of pendant allyl and methoxy functionalities or to macromolecules containing one alternation defect. The latter error is for instance evidenced by the consecutive loss of two  $\text{HB}^{\text{OMe}}$  units from the peak at  $m/z_{\text{obsv}} = 931.3766$  to  $m/z_{\text{obsv}} = 815.3295$  ( $\Delta m/z = 116.0471$ ) and further to  $m/z_{\text{obsv}} = 699.2826$  ( $\Delta m/z = 116.0469$ ). However, signals showing more than one alternation defect were never observed, evidencing the high degree of alternation in those copolymers as already hinted by NMR analyses (vide supra), and hence, the high stereoselectivity of the  $\text{Y}\{\text{ONOO}^{\text{cum}}\}/i\text{PrOH}$  system.



**Figure 7.** ESI-MS/MS fragmentation spectrum of a selected oligomer, namely  $[iPrO-P(HB^{OAll}-alt-HB^{OMe})_4-H.Na^+]$  ( $m/z_{obsv} = 1115.5$ ) prepared from the ROCOP of an equimolar mixture of  $(R)$ -BPL<sup>OAll</sup>/ $(S)$ -BPL<sup>OMe</sup> with the  $Y\{ONOO^{cum}\}/iPrOH$  system (Table 1, entry 2). For clarity, the gross formula of the oligomer is simplified as  $[H-A_4-B_4-OiPr.Na^+]$  in the initial macromolecule, while terminal groups are not mentioned in the subsequent fragments.

*b. ROCOP of other (R)-BPL<sup>OR1</sup>/(S)-BPL<sup>OR2</sup> combinations*

The ROCOP of other equimolar mixtures of (R)-BPL<sup>OR1</sup>/(S)-BPL<sup>OR2</sup> comonomers with the Y{ONOO<sup>cum</sup>}/iPrOH system was studied. The main results are summarized in Table 1 (entries 3–7). Similarly to the (R)-BPL<sup>OAll</sup>/(S)-BPL<sup>OMe</sup> model combination, all copolymerizations were kinetically monitored by <sup>1</sup>H NMR spectroscopy. First-order kinetics and the corresponding apparent rate constants are displayed in Figures S2–S3 and Table 2, respectively. For comparison purposes, kinetics of homopolymerizations of the racemic and enantiomerically pure monomers *rac*-BPL<sup>OR</sup> and (R)- or (S)-BPL<sup>OR</sup> (which provide syndiotactic and isotactic PHB<sup>OR</sup>, respectively) are also reported.

**Table 2.** First-order apparent rate constants for the ROP of racemic and enantiomerically pure BPL<sup>OR</sup> monomers and for the ROCOP of equimolar mixtures of (R)-BPL<sup>OR1</sup>/(S)-BPL<sup>OR2</sup> mediated by the Y{ONOO<sup>cum</sup>}/iPrOH (1:1) system at 23 °C in 1.0 M toluene solutions with [Y]<sub>0</sub> = 13.1 mM.<sup>a</sup>

(Co)monomer(s)	(Co)monomer(s) vs. Y{ONOO <sup>cum</sup> } (equiv.)	<i>k</i> <sub>app</sub> (×10 <sup>-3</sup> s <sup>-1</sup> )
<i>rac</i> -BPL <sup>OAll</sup>	53	40.5(1)
<i>rac</i> -BPL <sup>OMe</sup>	53	4.8(2)
<i>rac</i> -BPL <sup>OBn</sup>	51	82(5)
<i>rac</i> -BPL <sup>OTBDMS</sup>	51	8.5(1)
(R)-BPL <sup>OAll</sup>	51	8.5(1)
(S)-BPL <sup>OMe</sup>	50	2.3(1)
(R)-BPL <sup>OBn</sup>	50	20.1(6)
(S)-BPL <sup>OTBDMS</sup>	51	8.4(2)
(R)-BPL <sup>OAll</sup> /(S)-BPL <sup>OMe</sup>	25:25	11.8(1)
(R)-BPL <sup>OBn</sup> /(S)-BPL <sup>OMe</sup>	25:25	15.8(1)
(R)-BPL <sup>OBn</sup> /(S)-BPL <sup>OAll</sup>	25:25	25.4(6)
(R)-BPL <sup>OAll</sup> /(S)-BPL <sup>OTBDMS</sup>	25:25	27.6(9)
(R)-BPL <sup>OBn</sup> /(S)-BPL <sup>OTBDMS</sup>	26:25	28.0(6)
(R)-BPL <sup>OMe</sup> /(S)-BPL <sup>OTBDMS</sup>	25:25	7.4(1)

In almost all cases, we observe the following trends: (i) in the ROCOP of equimolar mixtures of (*R*)-BPL<sup>OR1</sup>/*(S)*-BPL<sup>OR2</sup> by the Y{ONOO<sup>cum</sup>}/*i*PrOH system, both comonomers are consumed concomitantly, at the same rate; (ii) as mentioned above for the (*R*)-BPL<sup>OAll</sup>/*(S)*-BPL<sup>OMe</sup> combination, the observed ROCOP apparent rate constants fall in between those of the homopolymerizations of the racemic monomers; and (iii) the ROCOP is faster than the homopolymerization of either enantiopure monomer. These features are again compatible with an expected alternated microstructure of the copolymers.

We noted three exceptions to these kinetic trends: (a) the (*R*)-BPL<sup>OBn</sup>/*(S)*-BPL<sup>OMe</sup> combination for which the ROCOP rate ( $k_{\text{app}} = 15.8(1) \times 10^{-3} \text{ s}^{-1}$ ) is slightly lower than that for the formation of *iso*-PHB<sup>OBn</sup> from (*R*)-BPL<sup>OBn</sup> ( $k_{\text{app}} = 20.1(6) \times 10^{-3} \text{ s}^{-1}$ ); (b) the (*R*)-BPL<sup>OBn</sup>/*(S)*-BPL<sup>OAll</sup> combination for which the ROCOP rate ( $k_{\text{app}} = 25.4(6) \times 10^{-3} \text{ s}^{-1}$ ) is lower than those for the formation of *syndio*-PHB<sup>OBn</sup> ( $k_{\text{app}} = 82(5) \times 10^{-3} \text{ s}^{-1}$ ) and *syndio*-PHB<sup>OAll</sup> ( $k_{\text{app}} = 40.5(1) \times 10^{-3} \text{ s}^{-1}$ ) from the corresponding racemic monomers; and (c) the (*R*)-BPL<sup>OMe</sup>/*(S)*-BPL<sup>OTBDMS</sup> combination for which, most notably, the latter monomer is consumed at a slower pace than the former one in the ROCOP experiment (see Figure S23) and also the ROCOP apparent rate ( $k_{\text{app}} = 7.4(1) \times 10^{-3} \text{ s}^{-1}$ ) is slightly lower than that for the formation of *iso*-PHB<sup>OTBDMS</sup> ( $k_{\text{app}} = 8.4(2) \times 10^{-3} \text{ s}^{-1}$ ). Of these three exceptions, clearly the last one appears to be *a priori* incompatible with the formation of a copolymer with a highly alternated microstructure.

The microstructures of all copolymers were analyzed by <sup>13</sup>C{<sup>1</sup>H} NMR spectroscopy, by deconvolution of the carbonyl, methine and methylene regions, and also by mass spectrometry. As anticipated from the kinetic data, the <sup>13</sup>C NMR data (see the Supporting Information) revealed high alternation degrees (89–94%, Table 1) for all copolymers, except for the one issued from the (*R*)-BPL<sup>OMe</sup>/*(S)*-BPL<sup>OTBDMS</sup> combination, where intense signals

assigned to AAB, BBA, AAA/BBB, triads indicate important “misinsertions” along the alternated microstructure. The alternation degree for this copolymer was estimated at 67% by  $^{13}\text{C}$  NMR analysis.

MALDI-ToF-MS and ESI-MS/MS provided conclusive information about the degree of alternation, which is consistent with the NMR data (see the Supporting Information). As for the  $\text{P}(\text{HB}^{\text{OAll}}\text{-alt-HB}^{\text{OMe}})$  model copolymer, the MALDI-ToF mass spectra of the different  $\text{P}(\text{HB}^{\text{OR1}}\text{-alt-HB}^{\text{OR2}})$ s evidence major populations of  $\text{A}_n\text{B}_n$ ,  $\text{A}_{n+1}\text{B}_n$  and  $\text{A}_n\text{B}_{n+1}$  alternated macromolecules. Only macromolecules having a single alternation defect ( $\text{A}_{n+2}\text{B}_n$  or  $\text{A}_n\text{B}_{n+2}$ ) were observed as minor populations. ESI-MS/MS spectra featured fragmentation routes all derived from a major population of highly alternated macromolecules, with subsequent loss of A or B units, and secondary populations that correspond to the loss of propene and/or  $\text{H}_2\text{O}$  (see the Supporting Information).

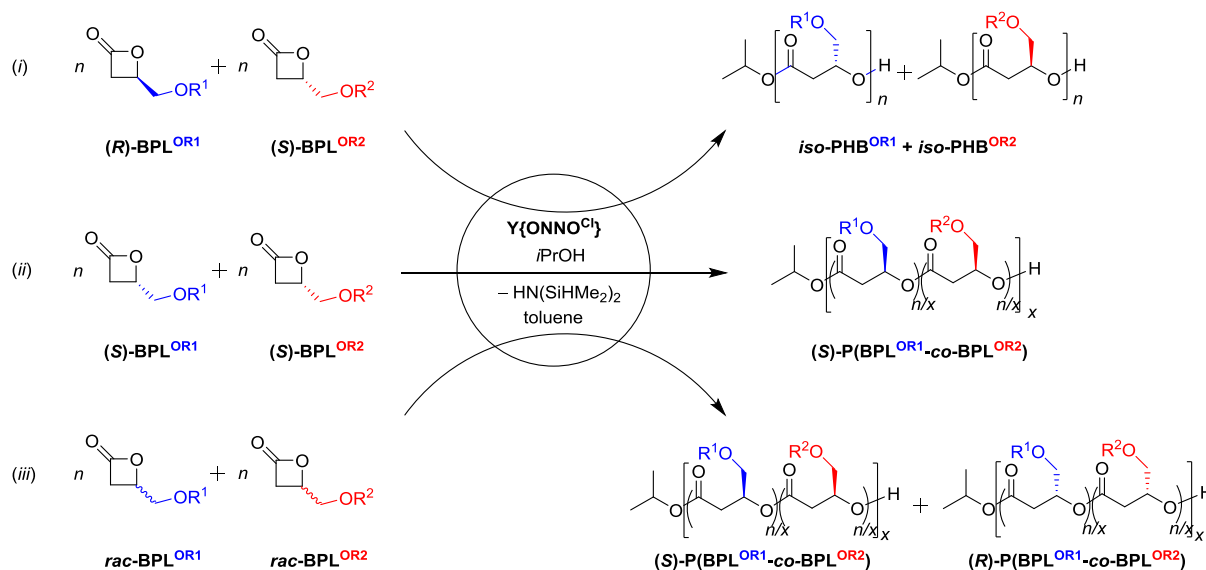
Thus, out of the six different  $(R)\text{-BPL}^{\text{OR1}}/(S)\text{-BPL}^{\text{OR2}}$  combinations investigated, the  $\text{Y}\{\text{ONOO}^{\text{cum}}\}/i\text{PrOH}$  system generates highly alternated microstructures for all of them but one; only the  $(R)\text{-BPL}^{\text{OMe}}/(S)\text{-BPL}^{\text{OTBDMS}}$  features significant alternation defects. We speculate that this may be due to the large steric difference between the relatively small OMe and the quite bulky OTBDMS groups; this may hinder the coordination and/or the ring-opening of the latter hindered monomer, offering the possibility to the  $\text{Y}\{\text{ONOO}^{\text{cum}}\}$  moiety to consecutively enchain two or more  $(R)\text{-BPL}^{\text{OMe}}$  units, despite the “syndioselective preference” of the active propagating species (made of the  $\text{Y}\{\text{ONOO}^{\text{cum}}\}$  moiety and the growing  $\text{PHB}^{\text{OR}}$  chain) to enchain successive monomer units with opposite configurations. This is essentially what kinetic studies teach, with a conversion rate of  $(S)\text{-BPL}^{\text{OTBDMS}}$  significantly lower than that of  $(R)\text{-BPL}^{\text{OMe}}$ .

2. *One-pot, one-step preparation and characterization of 1:1 mixtures of differently functionalized isotactic homoPHAs.*

As shown above, the synthesis of highly alternated PHAs is governed by the syndioselectivity exerted by the bulky  $Y\{ONOO^{cum}\}$  moiety, via a chain-end control mechanism as demonstrated earlier for “simple” homopolymerizations.<sup>[6b,8,12]</sup> The use of a sterically uncrowded, non discriminative catalyst system such as that based on  $Y\{ONNO^{Me}\}$  (Chart 1) onto equimolar mixtures of  $(R)$ -BPL<sup>OR1</sup>/ $(S)$ -BPL<sup>OR2</sup> leads to ill-defined materials, made essentially of random copolymers (vide supra, Figure 5).

To further probe the decisive influence of the  $Y\{ONXO^R\}$  moiety in these copolymerizations and to possibly access other original PHA topologies, we next explored the ROP/ROCOP of the BPL<sup>OAll</sup>/BPL<sup>OMe</sup> model combination by the  $Y\{ONNO^{Cl}\}/iPrOH$  system (Chart 1). This catalyst system (as other analogues bearing halogens at the phenolato R'/R" substituents) has been shown to be isoselective in the ROP of *rac*-BPL<sup>OR</sup> monomers, providing racemic mixtures of isotactic  $(R)$ - and  $(S)$ -PHB<sup>OR</sup>.<sup>[11]</sup> We therefore anticipated different scenarios by applying such a catalyst system, depending on the relative configuration of the BPL<sup>OAll</sup>/BPL<sup>OMe</sup> comonomers (Scheme 3): (i) the preparation of “clean” mixtures of isotactic, oppositely configured and differently functionalized PHB<sup>ORs</sup>; (ii) the preparation of an isotactic statistic copolymer; and (iii) the preparation of a racemic mixture of the former isotactic statistic copolymers.

The three different cases –  $(R)/(S)$ ,  $(S)/(S)$  or *rac/rac* BPL<sup>OAll</sup>/BPL<sup>OMe</sup>, respectively – were investigated and the results of the copolymerizations are summarized in Table 3.



**Scheme 3.** Envisioned possible scenarios for the ROP/ROCOP of equimolar mixtures of  $\text{BPL}^{\text{OR1}}/\text{BPL}^{\text{OR2}}$  by the isoselective  $\text{Y}\{\text{ONNOCl}\}/i\text{PrOH}$  system depending on the configuration of the starting comonomers.

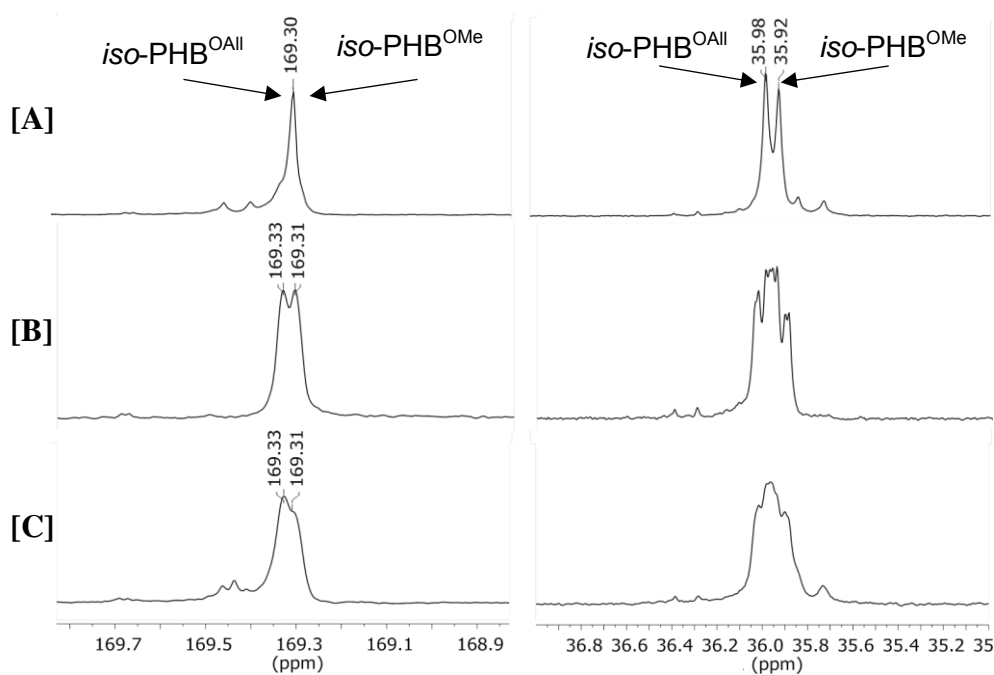
**Table 3.** ROP/ROCOP of equimolar mixtures of  $(R)/(S)$ ,  $(S)/(S)$  and  $\text{rac}/\text{rac}$   $\text{BPL}^{\text{OAll}}/\text{BPL}^{\text{OMe}}$  by the isoselective  $\text{Y}\{\text{ONNOCl}\}/i\text{PrOH}$  system.<sup>a</sup>

Entry	Comonomers	Comonomer loading vs. Y (equiv.)	$M_{n,\text{theo}}^b$ (g.mol <sup>-1</sup> )	$M_{n,\text{NMR}}^c$ (g.mol <sup>-1</sup> )	$M_{n,\text{SEC}}^d$ (g.mol <sup>-1</sup> )	$\mathcal{D}_M^d$
1	$(R)\text{-BPL}^{\text{OAll}}$	31	7 900	8 000	9 600	1.11
	$(S)\text{-BPL}^{\text{OMe}}$	30				
2	$(S)\text{-BPL}^{\text{OAll}}$	27	7 000	7 000	10 400	1.09
	$(S)\text{-BPL}^{\text{OMe}}$	27				
3	$\text{rac-BPL}^{\text{OAll}}$	25	6 000	5 700	8 500	1.10
	$\text{rac-BPL}^{\text{OMe}}$	21				

<sup>a</sup> Reactions performed in toluene at 20 °C for 4 h (unoptimized reaction time); full conversion of both monomers was observed in all cases. <sup>b</sup> Theoretical molar mass determined from  $M_{n,\text{theo}} = \{([\text{BPL}^{\text{OAll}}]_0 \times \text{conv.}_{\text{BPL}^{\text{OAll}}} \times M_{\text{BPL}^{\text{OAll}}}) + ([\text{BPL}^{\text{OMe}}]_0 \times \text{conv.}_{\text{BPL}^{\text{OMe}}} \times M_{\text{BPL}^{\text{OMe}}})\} / [i\text{PrOH}]_0 + M_{i\text{PrOH}}$ , with  $M_{\text{BPL}^{\text{OAll}}} = 142 \text{ g.mol}^{-1}$ ,  $M_{\text{BPL}^{\text{OMe}}} = 116 \text{ g.mol}^{-1}$ ,  $M_{i\text{PrOH}} = 60 \text{ g.mol}^{-1}$ . <sup>c</sup> Molar mass determined by <sup>1</sup>H NMR analysis of the isolated polymer, from the signals of terminal *i*Pr vs. those of the repeating units. <sup>d</sup> Molar mass values and dispersities determined by SEC in THF at 30 °C vs. polystyrene standards (uncorrected values).



$^1\text{H}$  NMR kinetic monitoring revealed nearly constant reaction rates for  $\text{BPL}^{\text{OAll}}$  ( $k_{\text{app}} = 10.8(3) \times 10^{-3} - 11.7(1) \times 10^{-3} \text{ s}^{-1}$ ) and  $\text{BPL}^{\text{OMe}}$  ( $k_{\text{app}} = 19.7(6) \times 10^{-3} - 22.9(3) \times 10^{-3} \text{ s}^{-1}$ ), regardless of their absolute/relative configurations in the starting mixture (see Figure S35 in the Supporting Information). The microstructure of the resulting materials was investigated by  $^{13}\text{C}\{^1\text{H}\}$  NMR spectroscopy using the carbonyl and main-chain methylene resonances (Figure 8). All materials featured in the carbonyl region major resonances consistent with isotactic microstructures ( $\delta \leq 169.33 \text{ ppm}$ ).<sup>[11]</sup> However, their complexity, as well as that for the methylene group, were much different.



**Figure 8.** Details of the carbonyl (left) and main-chain methylene (right) regions of the  $^{13}\text{C}\{^1\text{H}\}$  NMR spectra (125 MHz,  $\text{CDCl}_3$ , 23 °C) of polymers recovered from the ROP of equimolar mixtures of: **[A]** (*R*)- $\text{BPL}^{\text{OAll}}$ /*S*- $\text{BPL}^{\text{OMe}}$  (Table 3, entry 1), **[B]** (*S*)- $\text{BPL}^{\text{OAll}}$ /*S*- $\text{BPL}^{\text{OMe}}$  (entry 2), and **[C]** *rac*- $\text{BPL}^{\text{OAll}}$ /*rac*- $\text{BPL}^{\text{OMe}}$ , by the  $\text{Y}\{\text{ONNO}^{\text{Cl}}\}/i\text{PrOH}$  system (Table 3, entry 3).

As anticipated, the simplest situation turned out to arise from the (*R*)-BPL<sup>OAll</sup>/*(S)*-BPL<sup>OMe</sup> couple (Scheme 3, *i*). In that case, a single major resonance is observed in the carbonyl region, which incidently results from the overlapping of the isochronous resonances for *iso*-PHB<sup>OAll</sup> and *iso*-PHB<sup>OMe</sup> ( $\delta = 169.30$  ppm).<sup>[11]</sup> Besides, the methylene region features two equally intense, relatively sharp and well-resolved resonances ( $\delta = 35.98$  and  $35.92$  ppm), characteristic of those two latter isotactic sequences. These data are consistent with the selective formation of a 1:1 mixture of *iso*-(*R*)-PHB<sup>OAll</sup> and *iso*-(*S*)-PHB<sup>OMe</sup> homopolymers. The few low-intensity resonances observed account for minor stereo- and copolymerization defects.

The <sup>13</sup>C{<sup>1</sup>H} NMR spectra for the materials resulting from the (*S*)-BPL<sup>OAll</sup>/*(S)*-BPL<sup>OMe</sup> and *rac*-BPL<sup>OAll</sup>/*rac*-BPL<sup>OMe</sup> combinations are more complex but quite similar to one another. They indicate that, in these cases, copolymers resulting from the enchainment of both BPL<sup>OAll</sup> and BPL<sup>OMe</sup> in individual macromolecules, respectively, and not (isotactic) homopolymers, are produced. It is noteworthy that the material issued from *rac*-BPL<sup>OAll</sup>/*rac*-BPL<sup>OMe</sup> does not feature the low field carbonyl resonances characteristic of the P(HB<sup>OAll</sup>-*alt*-HB<sup>OMe</sup>) alternated structure (compare Figure 8 vs. Figure 5); this is logically accounted for by the isoselective (and not syndioselective) ability of the Y{ONNO<sup>Cl</sup>}/*i*PrOH system. Hence, we assume that the material produced from *rac*-BPL<sup>OAll</sup>/*rac*-BPL<sup>OMe</sup>, despite its higher complexity, is essentially the racemic equivalent of the enantiomerically pure copolymers produced from (*S*)-BPL<sup>OAll</sup>/*(S)*-BPL<sup>OMe</sup> (and (*R*)-BPL<sup>OAll</sup>/*(R)*-BPL<sup>OMe</sup>) (Scheme 3).

## Conclusion

The high stereoselectivity impaired by some Y{ONXO<sup>R',R''</sup>}/*i*PrOH catalyst/initiating systems in the ROP of racemic 4-alkoxymethylene- $\beta$ -propiolactones can be valuably implemented in the copolymerization of mixtures of such monomers bearing different functional substituents.

Using the syndioselective  $Y\{ONOOC^{cum}\}/iPrOH$  system, highly alternated copolymers were obtained by the ROCOP of equimolar mixtures of  $(R)$ -BPL<sup>OR1</sup>/ $(S)$ -BPL<sup>OR2</sup>. The alternation degree of the resulting  $P(HB^{OR1}\text{-}alt\text{-}HB^{OR2})$  copolymers can be quantitatively probed by <sup>13</sup>C NMR spectroscopy. MALDI-ToF-MS and ESI-MS-MS fragmentation techniques provide also very useful analytical tools for assessing the alternation in these copolymers; while the interpretation and processing of these MS data cannot be achieved readily in a manner as quantitative as <sup>13</sup>C NMR spectroscopy allows, the two MS techniques are quite complementary to the latter NMR one, and evidence in the present study, that only isolated alternation defects occur in the prepared  $P(HB^{OR1}\text{-}alt\text{-}HB^{OR2})$  copolymers. High alternation degrees can be reached upon using (i) obviously, a highly syndioselective catalyst, and (ii) “adequate” chemical combinations of  $(R)$ -BPL<sup>OR1</sup>/ $(S)$ -BPL<sup>OR2</sup> monomers. The “adequacy” here mentioned refers to the acceptable extent of chemical differentiation between the two monomers. Even in a given family of  $\beta$ -lactones such as the BPL<sup>OR</sup>s, our results evidence that when a too large difference in the pendant functionalities does exist, namely OMe vs. OTBDMS, the “syndio/alternating” control of the catalyst can be altered. We assume in the present case that this lack of control results from a too large difference in bulkiness between the monomers’ functional groups, as other combinations of  $(S)$ -BPL<sup>OTBDMS</sup> with other  $(R)$ -BPL<sup>OR1</sup> monomers bearing larger substituents (i.e. featuring a similar bulkiness to OTBDMS;  $R^1 = OBn, OAlI$ ) proved suitable to reach high alternation degrees. More studies are however required and currently under way in our laboratory to confirm this hypothesis. These results and limitations nonetheless confirm that the preparation of alternated copolymers from the ROCOP of combinations of even more chemically differentiated monomers (BPL<sup>OR</sup> / MLA<sup>R</sup> / 4-alkyl- $\beta$ -propiolactones / lactide, etc...) remains a highly challenging field.

For the first time, to our knowledge, the isoselectivity of a catalyst system, namely  $\text{Y}\{\text{ONNO}^{\text{Cl}}\}/i\text{PrOH}$ , has been exploited to generate, in a one-pot/one-step strategy, original mixtures of isotactic PHAs. This system efficiently transforms equimolar mixtures of  $(R)\text{-BPL}^{\text{OAll}}/(S)\text{-BPL}^{\text{OMe}}$  into a 1:1 mixture of the corresponding isotactic *iso*- $(R)\text{-PHB}^{\text{OAll}}$  and *iso*- $(S)\text{-PHB}^{\text{OMe}}$  homopolymers, with almost no copolymerization defect being observed. The approach has been extended to the ROCOP of equimolar mixtures of racemic comonomers,  $\text{rac-BPL}^{\text{OAll}}/\text{rac-BPL}^{\text{OMe}}$ , which provides the racemic equivalent of the enantiomerically pure copolymer produced from the corresponding enantiomerically pure monomers  $(S)\text{-BPL}^{\text{OAll}}/(S)\text{-BPL}^{\text{OMe}}$  (and  $(R)\text{-BPL}^{\text{OAll}}/(R)\text{-BPL}^{\text{OMe}}$ ). Theoretically, we assume that such an approach may allow in the future the preparation of blends that can generate the formation of stereocomplexes, different from those issued from two enantiomeric macromolecules of a given polyester.

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**Supporting information available.** General experimental and instrumental considerations, typical polymerization procedure, ROCOP kinetic data,  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of (co)polymers, MALDI-ToF-MS and ESI-MS-MS data of copolymers, representative SEC and DSC traces of copolymers.

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- [16] DFT computations did not suggest coordination of the *O* atom of the methylenealkoxy moiety onto the active yttrium center to be a favored process, although it cannot be completely ruled out at this stage (see ref [11] and [112]). The interference on stereocontrol of heteroatom(s) in functional side-arms of  $\beta$ -lactones is currently under investigation in our laboratory.
- [17] Note that in our initial communication (ref [11]), we inadvertently inverted the assignments of main-chain (backbone) and lateral (functional) methylene resonances; Main-chain methylene carbons (e.g. C<sup>4,11</sup> in Figure 4) are found at  $\delta$  ca. 36 ppm while carbons of the lateral methylene (e.g. C<sup>6,13</sup> and also C<sup>7</sup> in Figure 4) are found at  $\delta$  ca. 70–72 ppm.

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<sup>[18]</sup> Note that the  $m/z$  value here reported (and shown in Figure 6) corresponds to the  $^{13}\text{C}_1$  isotope, due to the high intensity of this peak.