Steric vs. electronic stereocontrol in syndio- or iso-selective ROP of functional chiral β-lactones mediated by achiral yttrium-bisphenolate complexes

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Steric vs. Electronic Stereocontrol in Syndio- or Iso-selective ROP of Functional Chiral β-Lactones Mediated by Achiral Yttrium-Bisphenolate Complexes

Romain Ligny,[a] Mikko M. Hänninen,[b] Sophie M. Guillaume,[a,*] and Jean-François Carpentier[a,*]

Origins of stereoselectivity in ROP of *racemic* chiral cyclic esters promoted by achiral yttrium complexes, resulting in the formation of highly heterotactic polylactide, and highly syndiotactic or, more uniquely, highly isotactic poly(3-hydroxybutyrate)s, are discussed. A close interplay between the nature of the cyclic ester, most particularly of the exocyclic functional chain installed on the chiral center of β-lactones, and the *ortho*-substituents installed on the phenolate rings of the ligand, results in various determining secondary interactions of steric and also electronic nature.

Introduction

Considerable work over the past three decades has revealed the unique propensity of rare earth complexes to act as highly effective initiators for the ring-opening polymerization (ROP) of cyclic esters.[1] The latter process is nowadays, undoubtedly, the method of choice for preparing polyesters with a bespoke architecture.[2] Fine-tuning of the organometallic catalyst, which initiates the chain-growth process and enchains all subsequent cyclic ester monomer units, allows for precise control of the molar mass, terminal groups and the microstructure of the polymers. Most attractive properties of rare earth complexes in this chemistry include in particular their high reactivity, which enables the ROP of stable, low-strained, and hence usually reluctant to ring-open cyclic esters,[3] and probably even more their stereocontrol ability when using *racemic* mixtures of chiral cyclic monomers. This peculiar stereocontrol ability has been first unveiled in the ROP of *racemic* lactide (*rac*-LA) for the synthesis of polylactide (PLA), arguably one of the most ubiquitous biosourced, degradable materials nowadays offering an alternative to common petrochemical-based plastics.[4]

Many rare earth complexes incorporating multidentate ancillary ligands have been reported to generate heterotactic PLA from *rac*-LA, *via* a so-called "chain-end stereocontrolled" (CEC) mechanism.[1,5] In such a CEC mechanism, ROP is usually assumed to proceed so as to minimize steric interactions between the last inserted monomer unit in the growing polymer chain and the new incoming monomer unit; this most often results in the alternation of monomer units with opposite configuration (*R*,*R*/*S*,*S* in the case of *rac*-LA) and, in turn, in a heterotactic PLA. This way of viewing stereocontrol provides a "common sense" rationale for the beneficial influence of bulky substituents installed on the multidentate ancillary ligand platform that coordinates the active rare earth metal center also flanked by its reactive nucleophilic moiety in the efficient systems reported for the heterotactic ROP of *rac*-LA. Hence, the more crowded the coordination sphere, the less conformational freedom for the growing polyester chain, the more discriminating the approach of the incoming chiral monomer –and most often the better chance to next incorporate one with an absolute configuration opposite to that of the last inserted one (Figure 1).

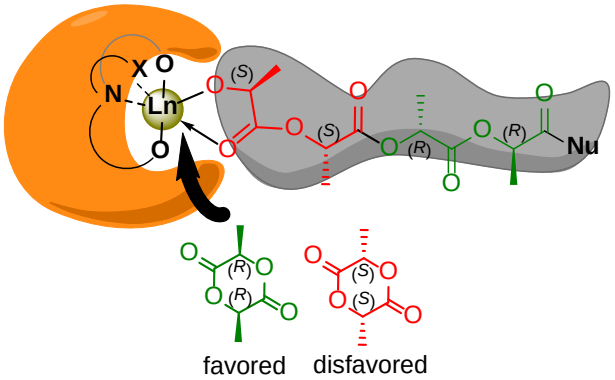

Figure 1. Simplistic illustration of the resting state of a *rac*-lactide ROP initiated by a Ln{ONXO^{R1,R2}}(Nu) complex and influence of ligand bulkiness on the discrimination between incoming chiral monomer units in a chain-end stereocontrolled (CEC) mechanism leading to heterotactic PLA.

[a] *Univ. Rennes, CNRS, Institut des Sciences Chimiques de Rennes, UMR 6226, F-35042 Rennes, France. E-mail: sophie.guillaume@univ-rennes1.fr, jean-francois.carpentier@univ-rennes1.fr*

[b] *University of Jyväskylä, Department of Chemistry, Jyväskylä, P.O. Box 35, FI-40014, Finland.*

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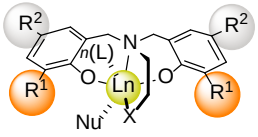
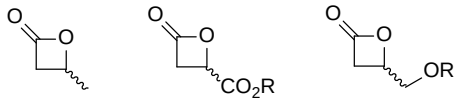
Yet, the actual processes at work in stereoselective ROP of cyclic esters can be much more complicated and can lead to unexpected microstructural control on the growing polymer chain. The aim of this Feature Article is to discuss the dramatic influence of ancillary ligands on the stereocontrol abilities of a family of rare earth complexes that we have been developing and investigating in details over the past 15 years (Figure 2).[6] Early up to very recent studies of their use in the stereoselective ROP of a series of *racemic* chiral cyclic esters, namely, *rac*-LA, the four-membered lactone *rac*-β-butyrolactone (*rac*-BL) and its functional alkyl *rac*-β-malolactonate (*rac*-MLA^{R}s) and *rac*-4-alkoxymethylene-β-propiolactone (*rac*-BPL^{OR}s) derivatives (Figure 2), have revealed unsuspected existence of various secondary interactions of steric and also electronic nature. Predominance of steric vs. electronic influences appears to be highly dependent on the nature of the cyclic ester/complex assemblage. This has led to a so far unique example of highly isoselective ROP of *racemic* functional β-lactones.

Background: ROP of *rac*-lactide and *rac*-β-butyrolactone

Our group has been developing since the early 2000s some rare earth complexes of the type Ln{ONXO^{R1,R2}}(Nu)(L)$_n$ (Nu = nucleophilic moiety initiating the ring opening = alkyl, amide, alkoxide; L = donor or solvent molecules such as THF; n = 0, 1), which incorporate tripodal dianionic diamino- or amino-alkoxy-bis(phenolate) ligands {ONXO^{R1,R2}}$^{2-}$ (X = NR$_2$, OR) (Figure 2).[6] These achiral complexes, most especially yttrium ones, constitute a kind of "privileged class" of initiators/catalysts for the ROP of cyclic esters, as they afford high activity, high degree of control, and special stereocontrol abilities.[6b]



Ln = Y, Sc, La...
Nu = N(SiHMe$_2$)$_2$, CH(SiMe$_3$)$_2$, O*i*Pr....
R^1, R^2 = Me, *t*Bu, adamantyl, CMe$_2$Ph, CMe$_2$*t*Bu, CPh$_3$, F, Cl, Br...
X = NMe$_2$, NEt$_2$, OMe....
L = none, THF, Et$_2$O, pyridine...



***rac*-BL** ***rac*-MLA^{R}** ***rac*-BPL^{OR}**

R = -CHCH=CH$_2$ (All), -CH$_2$C$_6$H$_5$ (Bn)

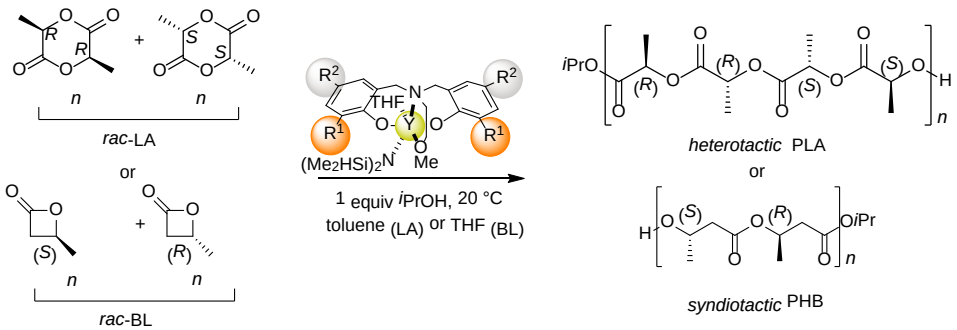
R = -CHCH=CH$_2$ (All), -CH$_2$C$_6$H$_5$ (Bn), -CH$_3$ (Me)

Figure 2. Typical rare earth complexes of the type Ln{ONXO^{R1,R2}}(Nu)(L)$_n$ that incorporate tripodal dianionic diamino- or amino-alkoxy-bis(phenolate) ligands (top)[6b] and some chiral β-lactones investigated in stereoselective ROP (bottom).

When applied to the ROP of *rac*-LA,[6a,7] the above-mentioned principle of achieving high heteroselectivity via incorporation of bulky substituents (R^1) on the *ortho*-positions of the phenolate rings, that is those substituents that affect the immediate metal coordination sphere (in contrast to R^2 substituents that point in the opposite direction),[‡] proved particularly efficient: PLAs ranging from atactic (P_r = P_m = 0.50* with small R^1 substituents = Me, Cl) to moderately heterotactic (P_r ≈ 0.80 with moderately large R^1 substituents = *t*Bu, adamantyl) to highly heterotactic (P_r = 0.91–0.96 with highly sterically crowding R^1 substituents = CMe$_2$Ph, CPh$_3$) were thus prepared (Scheme 1). Microstructural studies of the resulting PLAs by ^{13}C{^{1}H} NMR spectroscopy, cross-checked with statistical Bernoullian models of stereocenters distributions, revealed a pure CEC operative mechanism

Building up on these promising results with *rac*-LA, we have extended the use of Ln{ONXO^{R1,R2}}(Nu)(L)$_n$ complexes to the polymerization of the more challenging 4-membered β-lactones. The ROP of the simplest chiral member, *rac*-BL, seemed to follow – at first sight – basically the same trends as those for *rac*-LA: it affords highly syndiotactic poly(3-hydroxybutyrate) (PHB), formed by the successive enchainment of BL units of opposite absolute configuration (just as for heterotactic PLA), only with highly sterically crowding R^1 substituents.[8] In fact, yttrium complexes with {ONXO^{R1,R2}} ligands incorporating cumyl (CMe$_2$Ph) or trityl (CPh$_3$) R^1 substituents give syndio-PHB with P_r = 0.91 and 0.95, respectively. However, unexpectedly, not all bulky R^1 substituents do so: the purely aliphatic CMe$_2$*t*Bu, despite its bulkiness arguably comparable to the previous cumyl, gave only syndio-enriched PHB with P_r = 0.70! Also, we showed that a complex bearing the electron-depleted ligand with R^1 = CMe$_2$(*p*-CF$_3$-Ph) is significantly less syndioselective than the parent cumyl-substituted ligand (P_r = 0.83 vs. 0.91, respectively), despite again their much similar bulkiness. Hence, not only steric but also *electronic* considerations appear to be at work to stereocontrol the ROP of *rac*-BL. As for the ROP of *rac*-LA, a statistical Bernoullian analysis of the distribution of ^{13}C{^{1}H} NMR resonances at the diad and triad levels unambiguously evidenced that syndioselectivity in these ROPs of *rac*-BL originates from a CEC mechanism.

We have tentatively accounted for this apparent electronic influence on the stereocontrol by the intervention of C–H…π attractive interactions[9] involving, on one hand, the acidic methylene moiety of the alkoxy-butyrate group in the growing poly(3-hydroxybutyrate) chain and, on the other hand, the aryl rings present in R^1 substituents. H…π interactions were actually observed in solution, in the NOESY ^{1}H-^{1}H NMR spectrum of the initiating isopropoxide species Y{ON(OMe)O^{CMe2Ph,CMe2Ph}}(O*i*Pr)(THF) (OC*H*…π phenyl interactions) and also, in the solid state, by single-crystal X-ray diffraction of the parent amido complex Y{ONOO^{CMe2Ph,CMe2Ph}}(N(SiHMe$_2$)$_2$)(THF) (SiMe$_2$*H*…π phenyl ~ 3.0 Å).[8b]



R¹ R²	Me/Me	tBu/tBu	CMe$_2$Ph/Me	CMe$_2$tBu/Me	CPh$_3$/Me	CMe$_2$(4-CF$_3$Ph)/Me
***rac*-LA** P_r	0.55	0.81	0.91	0.95	0.95	-
***rac*-BL** P_r	0.56	0.80	0.91	0.70	0.96	0.83
TOF (h^{-1})	*nd*	*>>200*	*22,000*	*400*	*7,900*	*340*

Scheme 1. Influence of ligand substituents in the heteroselective ROP of *rac*-LA and in the syndioselective ROP of *rac*-BL promoted by in situ generated Y{ONXO^{R1,R2}}(O*i*Pr) complexes.[6a,7,8] Values on the bottom line correspond to average TurnOver Frequencies (TOF) determined for ROP of *rac*-BL at 20 °C at 1-2 M in toluene.

DFT computations performed on putative intermediates involved in the ROP of *rac*-BL, *i.e.* Y{ONOO^{CMe2Ph,Me}}(OCH(Me)CH$_2$CO$_2$CH$_2$CH(Me)CO$_2$*i*Pr), showed that such C*H*$_2$…π phenyl interactions may stabilize the active species by 5–10 kcal.mol^{-1} and contribute "freezing" the conformation of the growing macromolecular chain (Figure 3).[10] Interestingly, no such favorable C–H…π interactions were observed in the DFT-computed analogous intermediates for the ROP of LA, *i.e.* Y{ONOO^{CMe2Ph,Me}}(OCH(Me)CO$_2$CH(Me)-CO$_2$*i*Pr). This was not unexpected due to the lower acidity of the OC*H*(Me)CO$_2$ hydrogen in the *O*-lactyl-lactate moiety (as compared to that of OCH(Me)C*H*$_2$CO$_2$).

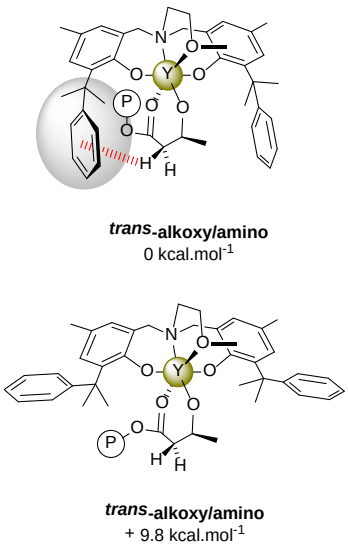
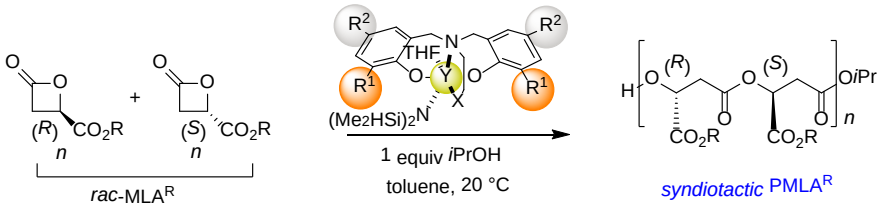


Figure 3. Schematic representation of two DFT-optimized model intermediates in the ROP of *rac*-BL mediated by Y{ONOO^{CMe2Ph,Me}}(O*i*Pr) species, showing stabilizing C–H…π interactions (relative computed energies; **P** stands for the polymeryl chain).[10]

ROP of alkyl *rac*-β-malolactonates: Smaller is better than larger

Driven by our interest to expand on this chemistry and to address the preparation of functional poly(hydroxyalkanoate)s, we have investigated on the ROP of alkyl *rac*-β-malolactonates (*rac*-MLARs) (Figure 2), to eventually take profit of the pendant carboxylate moieties, which are easily prone to chemical transformations. The literature discloses a variety of effective ROP catalysts/initiators for this class of functional β-lactones, but none of them has shown any stereoselective ability toward *racemic* monomers.[11] Thus, high syndiotacticity was achieved using Y{ONXO^{R1,R2}}(Nu)(L)$_n$ complexes; however, it followed a completely different trend than those observed for *rac*-LA and *rac*-BL (Scheme 2).[12] Independently of the nature of the alkoxycarbonyl side chain (R = allyl, benzyl, methyl), yttrium complexes that bear highly sterically bulky R^1 substituents on the ligand and that proved so effective in the syndioselective ROP of *rac*-LA and *rac*-BL, offered only syndio-biased/enriched alkyl poly(β-malolactonate)s (PMLA^{R}s); in fact, the system based on the larger trityl proved less stereoselective than that with cumyl (P_r = 0.68 vs. 0.81–0.82, respectively), and the purely aliphatic CMe$_2$*t*Bu was even better (P_r = 0.86–0.87) than the two former ones. Incidentally we found that the *o,p*-dichloro-substituted complex afforded highly syndiotactic PMLA^{R}s (P_r > 0.95).[12] It is noteworthy that the [Y{ON(OMe)O^{Cl,Cl}}(O*i*Pr)] catalyst is essentially non-stereoselective in the ROP of *rac*-LA (P_r = 0.56) and *rac*-BL (P_r = 0.42–0.45).[8b]

We initially envisioned a possible electronic contribution to be at the origin of this peculiarity, as hinted, at that time, by the positive π-aryl-influence in the syndioselective ROP of *rac*-BL (vide supra), and also because Gibson et al. pinpointed the unique stereocontrol of *o,p*-dichloro-substituted systems in the heteroselective ROP of *rac*-LA mediated by aluminum salan complexes, calling also for operative electronic contributions.[4e,f] Indeed, with these Al complexes, heteroselectivity of the sterically comparable *o,p*-dimethyl derivative is lower than



	R^1 / R^2 / X	CPh_3/Me	CMe_2Ph/Me	CMe_2tBu/Me	Br/Br	Cl/Cl	F/F	Me/Me
		OMe	NMe_2	OMe	OMe	OMe or NMe_2	NMe_2	OMe or NMe_2
***rac*-MLA^{Bn}**	P_r	0.68	0.81	0.86	0.91-0.92	> 0.95	> 0.95	> 0.95
***rac*-MLA^{All}**	P_r	0.68	0.82	0.87	0.95	> 0.98	nd	0.92
TOF (h^{-1})		*50*	*>3000*	*360-1100*	*50-300*	*500 / 1400*	*>25*	*>25*

Scheme 2. Influence of substituents in the syndioselective ROP of *rac*-MLA^R (R = Bn, All) promoted by in situ generated Y{ONXO^{R1,R2}}(O*i*Pr) complexes. Values on the bottom line correspond to average TurnOver Frequencies determined for ROP of *rac*-MLA^R (R = Bn, All) at 20 °C at 1 M in toluene. Data from ref 12 except with *o,p*-difluoro and -dimethyl systems (this work).

that of the *o,p*-dichloro analogue (P_r = 0.83 vs. 0.96, respectively), "*implying that the chloro substituents exert an influence beyond a straightforward steric effect*".[4e]

Yet, the experimental data we gathered in the ROP of *rac*-MLA^{Bn} were not much informative about electronic influences: first, the *o,p*-dibromo-substituted yttrium complex gave just slightly lower syndiotacticity than the analogous chloro- and fluoro- systems (P_r = 0.91–0.92 vs. > 0.95, respectively; Scheme 2).[12b] Furthermore, DFT computations performed on mononuclear and dinuclear model intermediates did not enable identifying any favorable interactions of C–X···O=C halogen-bonding type.[12b,13]

Maybe surprisingly enough, it is only very recently that we have investigated complexes bearing methyl-substituted ligands in the ROP of *rac*-MLA^R … and these proved just as syndioselective as the halogenated ones (P_r > 0.95; Scheme 2). Hence, in sharp contrast with *rac*-LA and *rac*-BL, the ROP of *rac*-MLA^{R}s is controlled by steric factors but requires small substituents to afford high syndiotacticity. Retrospectively, this diagnostic accounts for the lower selectivity of the larger *o,p*-dibromo-substituted system (as compared to the smaller Cl and F) that we prepared initially to probe the pertinence of halogen-bonding (known to be more pronounced for Br and I than Cl).[13] Our recent (and so far undisclosed) observations with the *o,p*-difluoro systems provide another clear evidence that halogen-bonding is not at work in these polymerizations.

We have investigated many models by DFT to rationalize this conclusion, somehow puzzling in view of the usual CEC model (Figure 1; vide supra). As expected, an additional donor atom (–CH*C(=O)*OR) enables numerous coordination modes (and hence many possible intermediates to compute) for the growing polymer chain but also for coordination of the monomer to the resting state of the catalyst.[14] The propagating polymer chain can be either κ^2- or κ^3-coordinated to the metal center (Figure 4, **A**/**A1**, respectively). In the resting state of the catalyst, the higher (κ^3-) coordination number geometries tend to be more stable (up to 7 kcal.mol^{-1}) but complexes with κ^2-coordinated ligand can end up to virtually identical activation energy in the following step. Addition of a monomer onto yttrium (Figure 4, **B**/**B1**) is exothermic in all studied coordination modes of the propagating chain. The monomer will most likely attach through the endocyclic carbonyl, as in regularly reported ROP mechanism of cyclic esters. Although other, potentially multi-dentate, coordination modes cannot be completely ruled out, the calculations indicate that these structures are energetically unfavorable or fail to produce the experimentally observed stereoselectivity. It should be also noted that if the propagating chain is already κ^3-coordinated, there seems to be an energetic penalty for the monomer coordination, indicating that the intermediates/products with coordination numbers higher than seven are generally unfavorable (Figure 4, bottom). After monomer coordination (**B**), the mechanism appears to track the route previously suggested for BL.[15] The formation of the four-membered metallacycle (**C**) is followed by ring opening and chain rearrangement leading to the resting state of the catalyst.

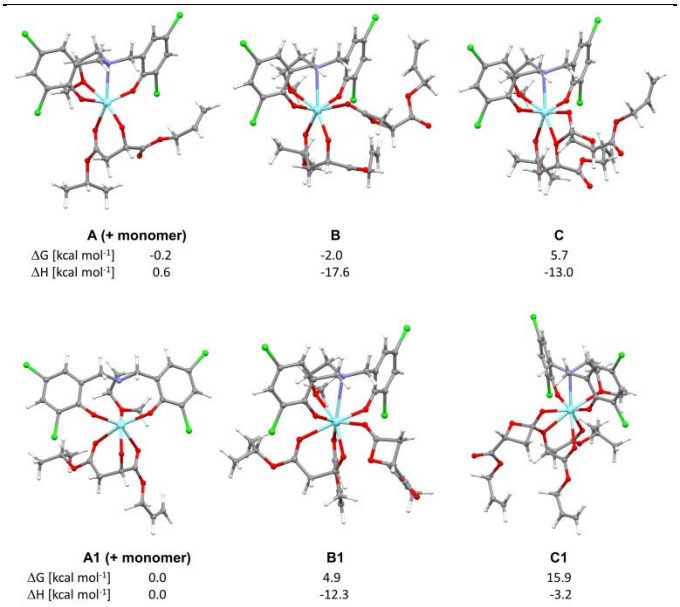


Figure 4. DFT-optimized possible intermediates (κ^2-, top; κ^3-, bottom) in the ROP of MLA^{All} initiated by the Y{ON(OMe)O^{Cl,Cl}}-(O*i*Pr) complex. The presented energy differences (ΔG and ΔH) are related to the corresponding **A1**(+monomer) values.

Although we have not yet been able to establish a complete mechanism for the ROP of MLA^{All}, the thus far studied intermediates and transition states suggest that the smaller ligand R^1 substituents, such as halides or methyl, enable a sufficiently high coordination number but also flexibility around the central metal, eventually leading to a good stereocontrol and to syndiotactic PMLA^{All}.

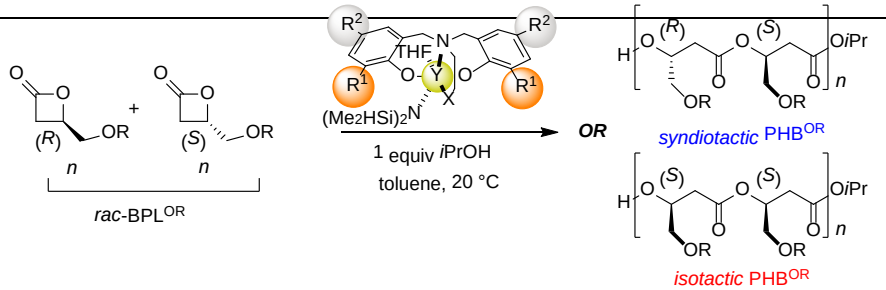
ROP of *rac*-4-alkoxymethylene-β-propiolactones: Syndio- vs. iso-selectivity, sterics vs. electronics

To further probe the influence of the pendant functional groups, in order to simultaneously expand on the scope and better understand factors that drive the stereoselectivity of these polymerizations, we have more recently investigated the ROP of *rac*-4-alkoxymethylene-β-propiolactones (*rac*-BPL^{OR}s). These β-lactones "simply" differ from *rac*-MLA^{R}s by replacement in the pendant (exocyclic) group of a carbonyl by a methylene moiety (Figure 2); however, this proved to have major implications. In fact, application of Y{ONXO^{R1,R2}}(O*i*Pr)(L)$_n$ complexes resulted in two very different outcomes: either a highly syndioselective or an unprecedented, highly isoselective ROP (Scheme 3).[16]

No matter the nature of the alkoxy moiety, syndioselective ROP of *rac*-BPL^{OR} is achieved with yttrium complexes that incorporate bulky *ortho*-substituents on the phenolate rings. The behavior is similar to that observed with *rac*-LA, apart from the fact that complexes with *tert*-butyl and cumyl-substituted ligands lead to much more similar levels of syndiotacticity. Hence, in contrast to the ROP of *rac*-BL, high syndiotacticity towards *rac*-BPL^{OR} can be achieved even with purely aliphatic bulky substituents. This indicates that highly syndioselective ROP of *rac*-BPL^{OR} does not rely on the abovementioned "aryl electronic effects". The dimethyl-substituted yttrium complex gives atactic PHB^{OR}s, demonstrating that syndiotactic ROP is under steric control, following the "regular" CEC model (Figure 1).

On the other hand, use of yttrium complexes bearing ligands with halogens as *o,p*-substituents induced the formation of highly isotactic PHB^{OR}s (as a *racemic* mixture of iso-*R* and iso-*S* macromolecules).[16] To our knowledge, this is the first and still only example of a highly isoselective ROP of a *racemic* chiral β-lactone. For the three *rac*-BPL^{OR} monomers investigated, quite similar isotacticities were observed with either fluoro, chloro or bromo substituents (P_r = < 0.05–0.12; *i.e.*, P_m = 0.88–0.95^{+}); only for *rac*-4-benzyloxymethylene-β-propiolactone, a slightly higher isotacticity was noticed with the *o,p*-difluoro complex. Overall, this indicates that sterics are not the main factor governing the selectivity in isoselective polymerization of this type of β-lactone.

DFT computations were performed for the elementary steps of the ROP of *rac*-BPL^{OAll}. A special focus was placed on the second step of the reaction, which is the formation of the four-membered metallacycle prior to its ring opening, and which determines the stereochemistry of the polymer.[15] Consistent with the experimental observations, modelling of the reaction with a dimethyl-substituted catalyst generated transition states on both iso- and syndio-propagation routes with virtually identical free energies; *i.e.*, an atactic polymer is expected, as indeed experimentally observed. On the other hand, modelling of the reaction with the *o,p*-dichloro complex resulted in a transition state toward the formation of isotactic PHB^{OAll} 4.5 kcal mol^{-1} lower in energy than that for the syndiotactic polymer, also in excellent agreement with experimental findings. The origin of this difference was traced back to strong C–H···Cl interactions between hydrogen from the alkoxymethylene group of the pendant chain in the ring-opened monomer and the chloro substituents of the ligand (Figure 5a). Obviously, this C–H···Cl interaction can exist only because a methylene group in *rac*-BPL^{OR} / PHB^{OR}s (–CHC*H*$_2$OR) has replaced a carbonyl group in *rac*-MLA^{R} / PMLA^{R}



R^1 R^2 / X	CMe$_2$Ph/Me OMe or NMe$_2$	*t*Bu/Me OMe or NMe$_2$	Me/Me OMe or NMe$_2$	Br/Br NMe$_2$	Cl/Cl OMe or NMe$_2$	F/F NMe$_2$
***rac*-PHB^{OBn}** P_r	0.88-0.90	0.85-0.86	0.50	0.09	0.10	< 0.05
***rac*-PHB^{OAll}** P_r	0.82-0.84	0.81-0.83	0.49-0.51	0.09	0.07-0.09	0.09
***rac*-PHB^{OMe}** P_r	0.78-0.81	0.78-0.79	0.49	0.12	0.10	0.11
TOF (h^{-1})	*>100*	*> 80*	*1-10 /7-18*	*20-24*	*1-4/20-30*	*7-12*

Scheme 3. Influence of substituents in the syndioselective ROP of *rac*-BPL^{OR}s (R = Me, All, Bn) promoted by in situ generated Y{ONXO^{R1,R2}}(O*i*Pr) complexes. Values on the bottom line correspond to average TurnOver Frequencies determined for ROP of BPL^{OR}s (R = Me, All, Bn) at 20 °C at 1 M in toluene. Data from ref 16 except with *o,p*-difluoro and -dibromo systems (this work).

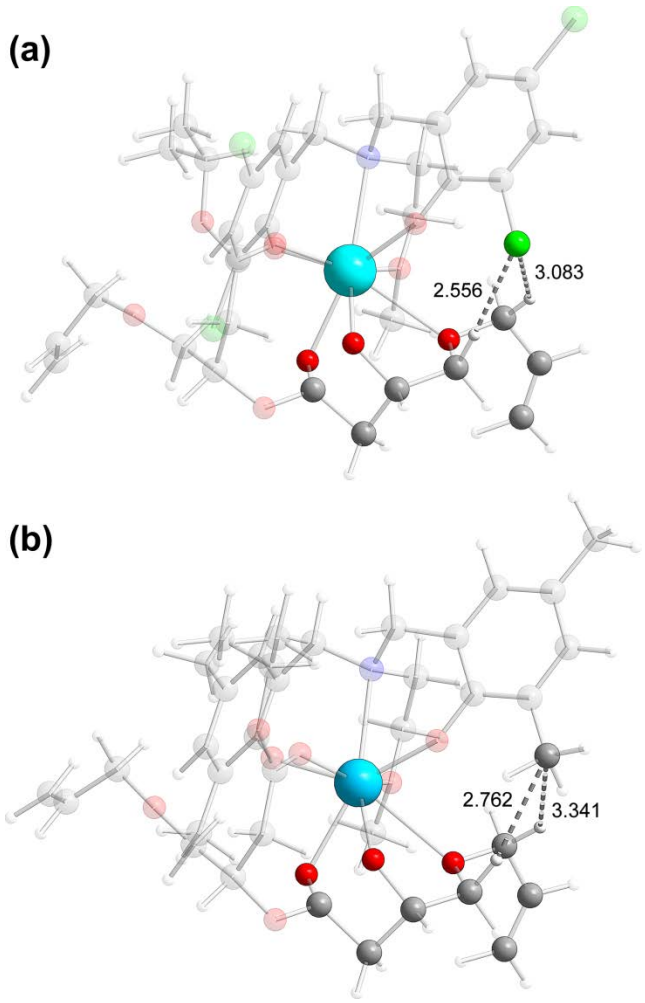


Figure 5. Structures of the transition state at the ring-opening step of *rac*-BPLO^{All} en-route toward isotactic PHB^{OAll}, showing the short contacts between the alkoxymethylene group in the ring-opened monomer and the ligand chloro (a; reprinted from ref 16) or methyl (b) substituents.

(–CHC*(=O)*OR). The attractive C–H···Cl interactions notably stabilize the latter transition state (close to the rate limiting step in energy) en-route to isotactic polymer, thus lowering the overall activation energy for the isotactic propagation.[16] However, with the methyl substituted ligand (Figure 5b), the corresponding interaction (C–H···C and C–H···H), although slightly weaker, is repulsive and the transition state is destabilized. The activation energy for isotactic propagation is in the case of Me substituents virtually identical to the syndioselective polymerization, suggesting formation of atactic PHB^{OAll}, as observed experimentally.

Outlook

The origins of stereocontrol in ROP of *racemic* β-lactones by achiral rare earth catalysts/initiators appear to be of remarkably diverse nature. They do as well impact to an unexpected extent the microstructure of the resulting polyesters since a range of highly syndiotactic to highly isotactic poly(3-hydroxybutyrate)s could be thus prepared. Various secondary interactions of steric and also electronic nature appear to be most likely at work. Possibly a most salient aspect of our latest investigations is that *attractive* interactions between moieties within the propagating polymer chain and substituents on the ancillary ligand nearby appear to take over the repulsive interactions usually invoked in chain-end stereocontrolled polymerizations. Among the four families of chiral cyclic esters we studied so far (*rac*-LA, *rac*-BL, *rac*-MLA^{R}, *rac*-BPL^{OR}) with Y{ONXO^{R1,R2}}(Nu) complexes, each case appears to be almost singular. This may reflect quite a different involvement of secondary interactions, both in nature and intensity. Although this unsuspected diversity has been revealed so far with a single family of rare earth complexes stabilized by a given ligand platform and a limited range of β-lactones, we assume it can be probably a most general feature, as long as chemical functionalities may allow such secondary interactions.

Obviously, it is not possible at this time to provide a fully rationalized picture, and even less to suggest guidelines to be included in the "organometallic toolbox" for specific design of stereoselective ROP (and other) catalysts. However, we shall surely learn more by studying the behavior of similar rare earth catalysts stabilized by different, highly modular ancillary ligands, and applying them in the ROP of new functional chiral cyclic esters. Work along these lines is underway in our laboratories.

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Conflicts of interest

The authors declare no conflicts of interest.

Notes and references

‡ The X donor group in the "capping" moiety of the {ONXO^{R1,R2}} ligand lies also in the immediate metal coordination sphere. This X group actually proved to be a sensitive parameter in the ROP of *rac*-LA, as higher heterotacticities (and activities) were observed for Y{ONXO^{tBu,tBu}}(O*i*Pr) complexes with the $CH_2CH_2NMe_2$ moiety in comparison to CH_2CH_2OMe (see Ref 6b and 7a). Yet, in the ROP of β-lactones such as those discussed in this manuscript, minimal or insignificant differences in terms of stereoselectivity ($\Delta P_r < 0.02$) were noted between families of ligands differing by X = OMe or NMe_2 (see e.g. Schemes 2 and 3). On the other hand, this parameter proved to affect more significantly β-lactones ROP catalytic activities, with systems based on X = $CH_2CH_2NMe_2$ most usually more active than those based on X = CH_2CH_2OMe.

* P_r and P_m are the probabilities of *racemic* and *meso* enchainment, respectively ($P_r = 1 - P_m$). Purely syndiotactic

(heterotactic in the case of PLA) and purely isotactic polymers are obtained when $P_r \rightarrow 1$ and $P_m \rightarrow 1$, respectively.

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Authors Biographies

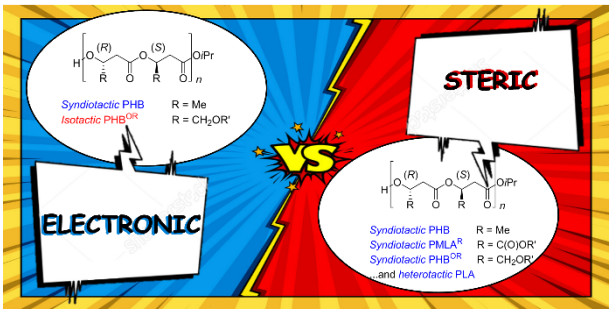
Jean-François Carpentier received his PhD in molecular catalysis from the University of Lille in 1992 with A. Mortreux and was a Postdoctoral Associate at U. Iowa with R. F. Jordan. After a CNRS research fellow position, dedicated to late transition metal catalysis for C–C and C–H bond formation, he moved in 2001 to the University of Rennes as full Professor. His current research interests lie in the organometallic chemistry of oxophilic elements and their use in catalysis for polymer engineering and fine chemicals synthesis. In 2005, he was elected member of the Institut Universitaire de France. In 2014, he was awarded the Silver CNRS medal and the prix Lequeux from the French Academy of Sciences. Besides, since 2016, he acts as vice-president in charge of research of the University of Rennes 1.

Sophie Guillaume received her PhD in Inorganic/Organometallic Chemistry from the University of Syracuse, New York, USA, and afterwards joined the CEA, Saclay, France, for her postdoctoral research. She then joined the CNRS and moved to the LCPO, Bordeaux, France. She now holds a CNRS Directeur de Recherche position at the University of Rennes, France. Her research is mainly focused on polymer chemistry and polymerization catalysis, focusing on the synthesis and structure-property relationships of synthetic polymers (especially polyesters, polycarbonates, polyolefins, polyurethanes). Areas of emphasis include bio-based degradable polymers and functionalized and reactive (co)polymers for advanced industrial and biomedical applications.

Mikko M. Hänninen got his MSc in inorganic chemistry from the University of Jyväskylä, Finland in 2008 and continued to do his PhD still in Jyväskylä under supervision of Profs. Reijo Sillanpää and Heikki Tuononen. He received his PhD in 2013. He then moved to the University of Lethbridge, Canada, to continue his career as postdoc in Prof. Paul Hayes group. In late 2014, Mikko started working as an Academy of Finland postdoctoral researcher at the University of Jyväskylä. His research interests are mainly in reactivity and catalytic properties of base and rare earth metal complexes.

Romain Ligny studied at the University of Le Mans and got his Master of Teaching in 2014 and then his MSc in organometallic chemistry in 2015. For his on-going doctoral studies, he joined the group of Prof. J.-F. Carpentier and Dr. Sophie Guillaume at the University of Rennes 1. His current research is focused on organometallic polymerization catalysis based on yttrium complexes for stereoselective (co)polymerization of functional β-lactones.

Graphical Abstract for ToC



Electronic vs. Steric effects of ligand *ortho*-substituents in (bis)phenolate yttrium-based complexes for preparation of a large scope of stereoregular poly(3-hydroxyalkanoate)s