Polymers

DOI: 10.1002/anie.201310523

From Syndiotactic Homopolymers to Chemically Tunable Alternating Copolymers: Highly Active Yttrium Complexes for Stereoselective Ring-Opening Polymerization of β-Malolactonates**

Cédric G. Jaffredo, Yulia Chapurina, Sophie M. Guillaume, and Jean-François Carpentier**

Abstract: *Alternating copolymers constitute an attractive class of materials. It was shown previously that highly alternated poly(β-hydroxyalkanoate)s (PHAs) can be prepared by ring-opening polymerization (ROP) of mixtures of two different enantiomerically pure 4-alkyl-β-propiolactones. However, the approach could not be extended to PHAs with chemically tunable functional groups, which is highly desirable to access original advanced materials. Reported herein is the first highly syndioselective and controlled ROP of racemic allyl and benzyl β-malolactonates (MLA^R; R = allyl, benzyl) using an yttrium complex supported by a tetradentate dichloro-substituted bis(phenolate) ligand. This highly active catalyst allows the nearly perfect alternating copolymerization of MLA^{Allyl} and MLA^{Benzyl}. Hydrogenolysis of the benzyloxycarbonyl or functionalization of the allyl pendant groups opens a route towards a new class of functional alternating copolymers.*

Nature taught us how vital the sequence is for macromolecules such as DNA and proteins. Controlling the architecture and composition of synthetic macromolecules is also, of course, of paramount importance so as to obtain polymers with optimized properties for applications. Among the broad variety of synthetic materials, regularly alternating copolymers are of special interest, as optimal positioning of functional substituents can induce improved performance over that of copolymers having lower periodicity (block, gradient, random).[1] Major advances have been achieved in this field over the last two decades thanks to the use of coordination polymerization with well-defined metal complexes.[1]

Poly(hydroxyalkanoate)s (PHAs) are a class of aliphatic polyesters having a three-carbon-atom backbone structure, and differ by their substituent on the 4-position. These polymers, which are naturally occurring in different microorganisms in their isotactic form, represent a highly valuable targets as substitutes for nonpetrochemical-based plastics and for use in biomedical applications.[2] PHAs can also be synthetically prepared by ring-opening polymerization (ROP) of β-lactones.[3] However, the stability of the latter monomers makes this process challenging, and even more so if stereoselectivity is simultaneously addressed.[3] Yttrium complexes with tetradentate bis(phenolate) ligands are highly active catalysts for the living ROP of simple β-lactones bearing alkyl substituents at C4; the prototypical example is β-butyrolactone (BL).[4] Additionally, some of these catalysts, when applied to racemic mixtures of these chiral monomers, can achieve high syndioselectivity (P_r, probability of racemic linkage, up to 95%) by a chain-end control mechanism.[4] By taking advantage of this unique syndioselectivity of yttrium catalysts, Coates, Thomas, and co-workers devised a smart, new strategy for making original alternating PHAs by performing ROP on 1:1 mixtures of two different enantiomerically pure 4-substituted-β-propiolactones of opposite absolute configuration.[5] Yet, the demonstration is limited to monomers bearing nonfunctional substituents [(fluoro)alkyls] or substituents that do not allow easy chemical transformations (ethers).

Alkyl β-malolactonates (MLA^R) are monomers that, upon ROP, lead to poly(β-malic acid) derivatives ($PMLA^R$), which are PHAs of high interest because of the potentially accessible pendant functional carboxylate moieties. Although a variety of catalysts/initiators have been disclosed for the ROP of derivatives such as MLA^{Bz} (Bz = benzyl), none of them has shown stereoselectivity towards racemic monomers and thus afford only atactic[6] or slightly isotactic-enriched $PMLA^{Bz}$.[7]

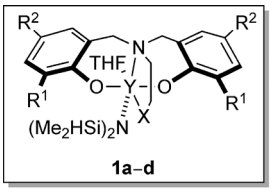
Herein we report on highly active and syndioselective yttrium catalysts for the ROP of *rac*-MLA^R derivatives (R = Bz, All = allyl). Unexpectedly, in light of previous studies on ROP of lactide and more simple β-lactones such as BL,[4] high stereoselectivity has been achieved with an *o*,*p*-dichloro-substituted bis(phenolate) ligand and not with ligands bearing bulky aryl/alkyl substituents.

First, homopolymerization experiments were performed using yttrium isopropoxide initiators generated in situ by using 1 equivalent of *i*PrOH and the compounds **1a–d** (Scheme 1), which were selected based on previous work on the ROP of *rac*-lactide (LA) and *rac*-BL.[4] All four catalytic systems were highly active for the controlled ROP of *rac*-MLA^R at 20 °C in toluene, thus allowing full conversion of 100 equivalents of MLA^R within 2–120 minutes (Table 1). These activities under mild reaction conditions with turnover frequencies (TOF) of at least 3000 h^{-1} using the **1a**/*i*PrOH system (Table 1, entries 1 and 5) are quite remarkable. Although in line with those observed in the ROP of BL with similar systems,[4] these TOF values are the highest ones

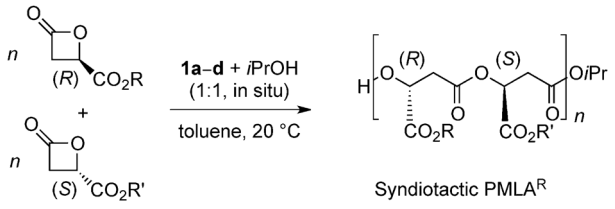
[*] C. G. Jaffredo, Dr. Y. Chapurina, Dr. S. M. Guillaume, Prof. Dr. J.-F. Carpentier
Organometallics: Materials and Catalysis, Institut des Sciences Chimiques de Rennes, UMR 6226 CNRS, Université de Rennes 1
35042 Rennes (France)
E-mail: sophie.guillaume@univ-rennes1.fr
jean-francois.carpentier@univ-rennes1.fr

[**] This research was financially supported in part by the Region Bretagne (Ph.D. grant to C.G.J.).

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201310523.



1a : $R^1 = CMe_2Ph$; R^2 = Me ; X = NMe_2
1b : $R^1 = CMe_2{}^tBu$; R^2 = Me ; X = OMe
1c : $R^1 = CPh_3$; R^2 = Me ; X = OMe
1d : $R^1 = R^2$ = Cl ; X = OMe



rac-MLA^{Bz} R = R' = $-CH_2C_6H_5$ $PMLA^{Bz}$
rac-MLA^{All} R = R' = $-CH_2CH{=}CH_2$ $PMLA^{All}$
R = $-CH_2CH{=}CH_2$ and R' = $-CH_2C_6H_5$ P(MLA^{Bz}-*alt*-MLA^{All})

Scheme 1. Synthesis of syndiotactic and alternating $PMLA^R$.

ever reported for the ROP of any β-malolactonate such as MLA^{Bz} and MLA^{All}.[6,8] Additionally, excellent agreement between theoretical molar mass values and experimental ones, as well as the rather narrow dispersity values ($1.03 \leq Đ_M \leq 1.64$), highlighted the good control of this ROP. The performance in terms of activity and control over the molar mass varied with the nature of the ancillary. Although the CMe_2Ph-substituted ligand in **1a** proved the most active and led to the narrowest dispersities, its stereocontrol abilities turned out to be surprisingly[4] inferior to those of the *o*,*p*-dichloro-substituted ligand (**1d**), as discussed below.

Microstructural analysis of the recovered $PMLA^R$ was performed by $^{13}C\{^1H\}$ NMR spectroscopy. A complete assignment of the methine region was possible, based on previous work describing $PMLA^{Bz}$ having various stereoregularities,[7] and using atactic and isotactic $PMLA^{Bz}$ that were purposely synthesized from the corresponding *rac*-MLA^{Bz} and (*R*)-MLA^{Bz} and the [(BDI)Zn{$N(SiMe_3)_2$}]/*i*PrOH and **1b**/*i*PrOH systems, respectively (see Figures S1–S5 in the Supporting Information). Distinct triads were thus observed in the methine region of the $PMLA^{Bz}$: the *racemic-racemic* triad (*rr*; $\delta = 68.70$ ppm), the *racemic-meso* triads (*rm*, *mr*; $\delta =$ 68.53, 68.61 ppm), and the *meso-meso* triad (*mm*; $\delta =$ 68.42 ppm; Figure 1). A similar distribution was observed for the $PMLA^{All}$ (see Figures S7–S10 in the Supporting Information). The strong contribution of the *rr* triads, compared to the much lower ones of the *mr*, *rm*, and *mm*

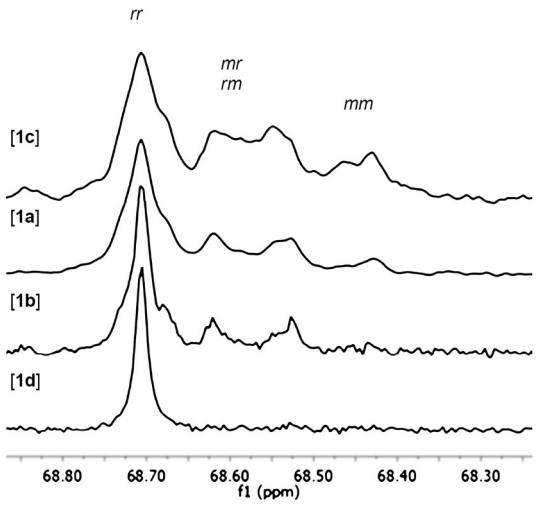


Figure 1. Region of the main-chain methine in the $^{13}C\{^1H\}$ NMR spectra (125 MHz, $CDCl_3$, 25 °C) of $PMLA^{Bz}$ prepared from the complexes **1c** ($P_r = 0.68$; Table 1, entry 3), **1a** ($P_r = 0.79$; entry 1), **1b** ($P_r = 0.85$; entry 2), and.**1d** ($P_r > 0.95$; entry 4).

triads supported the syndiotacticity of the $PMLA^R$ formed. Statistical analysis indicated that the stereocontrol originates from a chain-end mechanism (see the Supporting Information), which is in line with previous observations for the ROP of *rac*- and *meso*-LA and *rac*-BL,[4,9] and allowed extraction of the P_r values (Table 1). A consistent trend was observed for both the β-malolactonates MLA^{Bz} and MLA^{All}, and the syndioselectivity increased in the following order: **1c** ($P_r =$

Table 1: Syndiospecific ROP of *rac*-MLA^R mediated by the **1a**–**d**/*i*PrOH catalyst systems.[a]

Entry	Complex	MLA^R	$[MLA^R]_0/[Y]_0/[iPrOH]_0$	*t* [min][b]	Conv [%][c]	$M_{n,theo}$ [g mol^{-1}][d]	$M_{n,NMR}$ [g mol^{-1}][e]	$M_{n,SEC}$ [g mol^{-1}][f]	$Đ_M$[f]	P_r[g]	T_m [°C][h]
1	**1a**	MLA^{Bz}	100:1:1	2	100	20700	21000	45300	1.06	0.79	71
2	**1b**	MLA^{Bz}	100:1:1	15	91	18800	20300	42100	1.18	0.85	87
3	**1c**	MLA^{Bz}	100:1:1	120	96	19700	19500	39200	1.27	0.68	–[i]
4	**1d**	MLA^{Bz}	100:1:1	120	80	16500	17600	35200	1.54	>0.95	117
5	**1a**	MLA^{All}	100:1:1	2	100	15700	14100	29300	1.03	0.82	51
6	**1b**	MLA^{All}	100:1:1	5	89	14000	14600	20300	1.41	0.87	80
7	**1c**	MLA^{All}	100:1:1	120	100	15700	15300	22100	1.15	0.68	–[i]
8	**1d**	MLA^{All}	100:1:1	10	80	12500	13300	23500	1.64	>0.95	112

[a] All reactions were performed with $[MLA^R]_0 = 1.0$ M in toluene at 20 °C. [b] Reaction times were not necessarily optimized. [c] MLA^R conversion as determined by ^1H NMR spectroscopy on the crude reaction mixture. [d] Theoretical molar mass calculated considering one growing polymer chain per metal center from the relation: $M_{n,theo} = ([MLA^R]_0/[Y]_0 \times M_{MLA^R}) + M_{iPrOH}$, with $M_{MLA^{Bz}} = 206$ g mol^{-1}, $M_{MLA^{All}} = 156$ g mol^{-1} and $M_{iPrOH} = 60$ g mol^{-1}. [e] Molar mass value determined by using the resonances of the terminal isopropoxy group in the ^1H NMR spectra of the isolated polymer in $CDCl_3$ at 25 °C. [f] Number-average molar mass value determined by SEC versus polystyrene standards (uncorrected M_n values) in THF at 30 °C. [g] P_r is the probability of racemic linkages between MLA^R units as determined by $^{13}C\{^1H\}$ NMR spectroscopy. [h] Melting temperature as determined by differential scanning calorimetry (second heating cycle). [i] Not observed.

0.68, Table 1, entries 3 and 7) < **1a** (P_r = 0.79–0.82, Table 1, entries 1 and 5) < **1b** (P_r = 0.85–0.87, Table 1, entries 2 and 6) < **1d** ($P_r \gg 0.95$, Table 1, entries 4 and 8). Most interestingly, this trend is strikingly different from that observed in the ROP of *rac*-LA and *rac*-BL: in these latter polymerizations, only the bulky, aryl-containing CPh_3- (**1a**) and CMe_2Ph-substituted (**1c**) ligands led to high syndioselectivity ($P_{r/rac\text{-}LA} = 0.90$ and 0.96, $P_{r/rac\text{-}BL} = 0.89$ and 0.94, respectively), while the *o,p*-dichloro-substituted ligand in **1d** proved incompetent in controlling the stereoselectivity ($P_{r/rac\text{-}LA} = 0.56$; $P_{r/rac\text{-}BL} = 0.42$).[4,9] Here, even the catalyst based on the ligand bearing a purely aliphatic substituent $R^1 = CMe_2tBu$ (**1b**) proved to be more stereoselective than **1c** and **1a**, yet not as much as with **1d**. Notabbly, Gibson et al. have also reported on the unique stereocontrol of *o*,*p*-dichloro-substituted systems in the ROP of *rac*-LA mediated by aluminum salan and aluminum salen complexes. Although the origin of the dramatically different stereocontrol in these could not be fully rationalized, an electronic contribution was clearly operative.[10]

Thermal analysis by differential scanning calorimetry (DSC) of the $PMLA^{Bz}$ and PML^{All} demonstrated the strong influence of the stereochemistry on the melting temperature (T_m). In both cases, the T_m dramatically increased with the syndiotacticity [up to 117 °C for $PMLA^{Bz}$ (Table 1, entry 4) and 112 °C for $PMLA^{All}$ (Table 1, entry 8); see Figures S6 and S12]. The glass-transition temperature (T_g) remained stable, regardless of the stereochemistry of the polymers (T_g = 12 and 33 °C for $PMLA^{All}$ and $PMLA^{Bz}$, respectively).

Remarkably, original $PMLA^{R}$ were also formed by the simultaneous copolymerization of 50:50 mixtures of MLA^{Bz} and MLA^{All} as enantiopure monomers with opposite absolute configuration (*S* and *R*, respectively; Scheme 1 and Table 2). This synthetic strategy leads to unfunctionalized PHA copolymers with different degrees of alternation when applied to 4-alkyl-substituted β-propiolactones.[5] It is implemented here for the first time for monomers which are prone to chemical transformation of their pendant groups. The use of the yttrium complexes **1a–d** combined with 1 equivalent of *i*PrOH showed the simultaneous conversion of the two monomers (see Figure S13 in the Supporting Information for kinetic monitoring).

The microstructure of the resulting $P(MLA^{Bz}\text{-}alt\text{-}MLA^{All})$ was also elucidated by $^{13}C\{^1H\}$ NMR spectroscopy. The analysis of the methine region of the precipitated copolymers showed the predominance of alternating triad sequences of the type ABA and BAB at δ = 68.77 and 68.83 ppm (A and B stand for MLA^{All} and MLA^{Bz} repeating units, respectively), versus the non-alternating triads sequences AAB, BBA, BBB, and AAA, assigned to the δ = 68.57–68.72 ppm region(Figure 2).[11] As anticipated, the near complete absence of the signals corresponding to non-alternating triads was noted

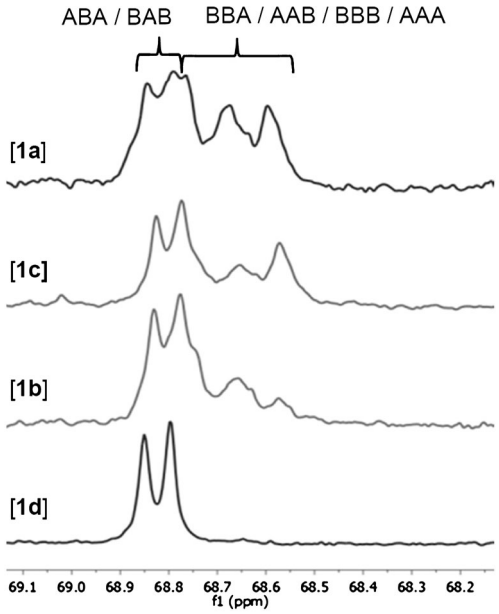


Figure 2. Region of the main-chain methine in the $^{13}C\{^1H\}$ NMR spectra (125 MHz, $CDCl_3$, 25 °C) of $P(MLA^{Bz}\text{-}alt\text{-}MLA^{All})$ prepared from the complexes **1a** (Table 2, entry 1), **1c** (entry 3), **1b** (entry 2), and **1d** (entry 4).

when **1d** was used. This high degree of alternation in $P(MLA^{Bz}\text{-}alt\text{-}MLA^{All})$s prepared from **1d** was further corroborated by MALDI-ToF MS and ESI MS-MS studies. As illustrated in Figure 3, the major signals observed in the MALDI-ToF mass spectrum, in the region corresponding to an overall degree of polymerization of 12 (typically, $6\,MLA^{Bz} + 6\,MLA^{All}$), were assigned to macromolecules with a perfect alternation between MLA^{All} and MLA^{Bz} units (Figure 3; dashed and solid lines), and some signals were also observed to correspond to macromolecules with a single alternation error (dashed/dotted lines).

The control of the alternating copolymerization of (*R*)-MLA^{All} and (*S*)-MLA^{Bz} followed the same trend as the one observed for the syndioselective homopolymerization of these racemic monomers (Table 1). The use of **1c** allowed the preparation of copolymers with 65 % alternation (Table 2, entry 3), a percentage which increased to 75 % with **1b** (Table 2, entry 2), and reached a very high control of alternation with **1d** (> 95 %, Table 2, entry 4). The only

Table 2: Alternating copolymerization of 1:1 mixtures of (*S*)-MLA^{Bz} and (*R*)-MLA^{All} from the **1a-d**/*i*PrOH systems.[a]

Entry	Complex	*t* [min][b]	$M_{n,SEC}$[c] ($g\,mol^{-1}$)	$Đ_M$[c]	$\%_{alt}$[d]	T_m [°C][e]
1	**1a**	5	33 000	1.09	52	–[f]
2	**1b**	15	38 700	1.28	75	54
3	**1c**	120	34 400	1.38	65	–[f]
4	**1d**	15	35 200	1.54	> 95	63

[a] All reactions performed at $[MLA^R]_0/[MLA^{R'}]_0/[Y]_0/[i\text{PrOH}]_0$ = 50:50:1:1, with $[MLA^R]_0$ = 1.0 M in toluene at 20 °C; quantitative conversion of both monomers were observed in all cases, as determined by ^1H NMR spectroscopy on the crude reaction mixture. [b] Reaction times were not necessarily optimized. [c] Number-average molar mass value determined by SEC versus polystyrene standards (uncorrected M_n values) in THF at 30 °C. [d] The percentage of alternation is the probability of alternating linkages between two monomer units of opposite configurations and was determined by $^{13}C\{^1H\}$ NMR spectroscopy. [e] Melting temperature determined by DSC (second heating cycle). [f] Not observed.

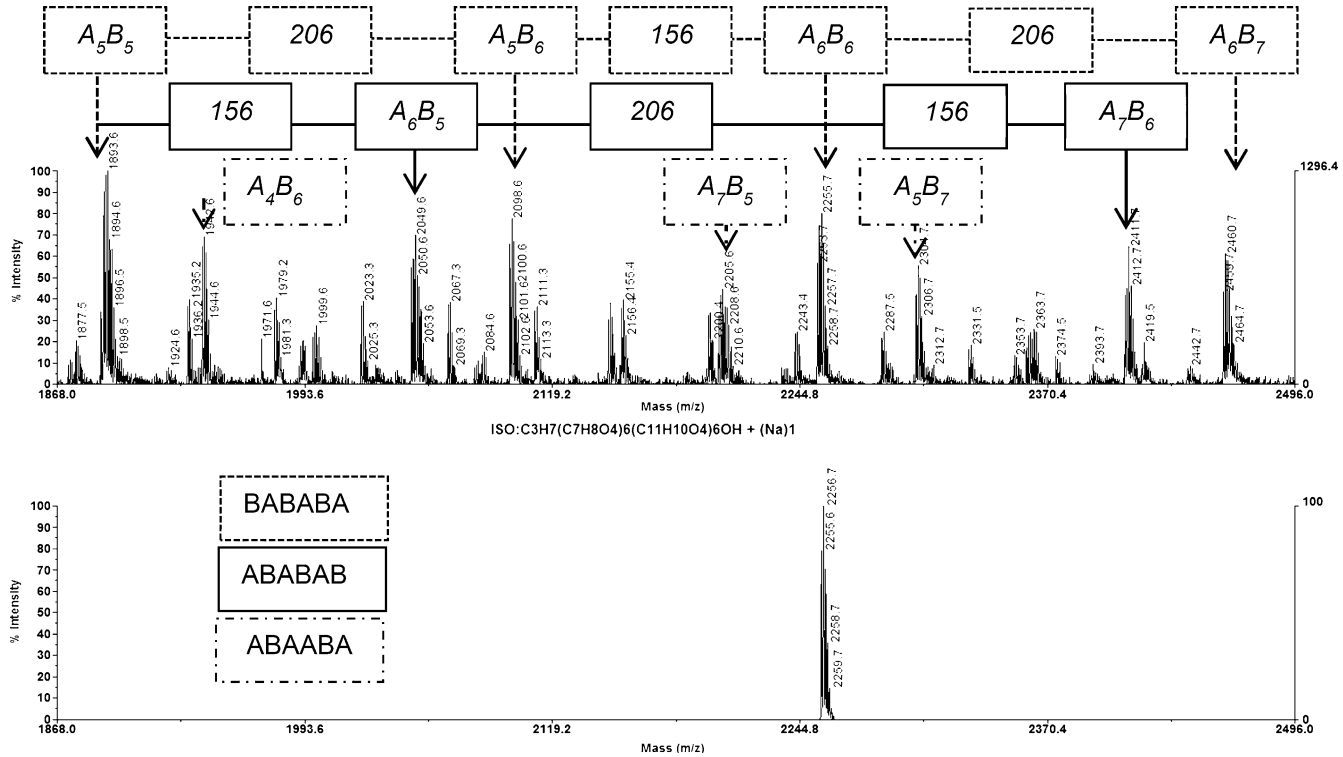
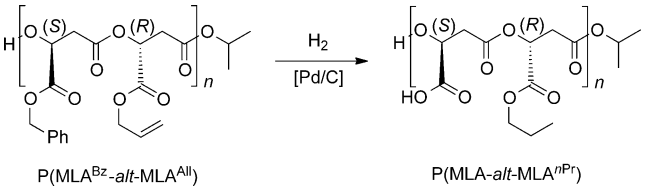


Figure 3. Details of the MALDI-ToF MS of a P(MLA^{Bz}-*alt*-MLA^{All}) prepared by simultaneous ROP of (*S*)-MLA^{Bz} and (*R*)-MLA^{All} with **1d** in presence of 1 equiv of *i*PrOH (Table 2, entry 4) using IAA as matrix. The major populations correspond to macromolecules ionized by Na+ (see the simulated spectrum at the bottom of the figure) and to alternating copolymers with MLA^{Bz} (B) as the first unit (dashed line), alternating copolymers with MLA^{All} (A) as the first unit (solid line), and copolymers with one alternation error (dashes/dotted line).

exception was **1a**, which allowed a fair control of the homopolymerization of MLA^{R} ($P_r = 0.79$–0.82, Table 1, entries 1 and 5), but showed essentially no control in the copolymerization of (*R*)-MLA^{All} and (*S*)-MLA^{Bz} (Table 2, entry 1).

The thermal properties of the P(MLA^{Bz}-*alt*-MLA^{All}) were investigated by DSC (Table 2). Only the copolymers showing a high degree of alternation (i.e. $\geq 75\,\%$; Table 2, entries 2 and 4) featured DSC traces displaying a single broad endotherm assigned to the melting transition. The higher the degree of alternation, the higher the T_m, thus supporting the influence of the monomer sequence on the crystallinity of the copolymer materials. The glass-transition temperature (T_g) was observed at around 22 °C in all cases.

The major advantage of these new alternating PHA copolymers is to readily fine-tune the chemical functionality by post-polymerization modification. The benzyloxycarbonyl moiety of PMLA^{Bz} is well known to be easily cleaved by hydrogenolysis.[2b] Accordingly, totally hydrophobic P(MLA^{Bz}-*alt*-MLA^{All}) copolymers were successfully switched into the corresponding alternating hydrophilic/hydrophobic P(MLA-*alt*-MLA^{nPr}) copolymers by hydrogenation with a heterogeneous Pd/C catalyst under mild reaction conditions (Scheme 2). Hydrogenolysis of the -CO_2Bz moiety proceeded concomitantly with hydrogenation of the allyloxycarbonyl group without altering the copolymer backbone chain. Indeed, the resulting amphiphilic copolymer showed the same degree of polymerization as determined by NMR spectroscopy (see Figure S19 in the Supporting Information).



P(MLA^{Bz}-*alt*-MLA^{All}) P(MLA-*alt*-MLA^{nPr})

Scheme 2. Hydrogenation/hydrogenolysis of P(MLA^{Bz}-*alt*-MLA^{All}) into P(MLA-*alt*-MLA^{nPr}). THF = tetrahydrofuran.

In conclusion, we have developed the first syndioselective polymerization of racemic β-malolactonates. The most stereoselective yttrium catalyst for this purpose, **1d**, unusually relies on an *o*,*p*-dichloro-substituted bis(phenolate) ligand. This unexpected finding leads to new questions about the stereocontrol mechanism(s) operating in the ROP of β-lactones. This catalyst also enables the preparation of highly alternating PHAs with different pendant carboxylate moieties. A simple proof of concept has been described for the easy chemical modification of the carboxylate moieties. This strategy provides a route towards a new class of functionalized alternating copolymers.

Received: December 4, 2013
Published online: February 3, 2014

Keywords: lactones · polymers · ring-opening polymerization · stereoselectivity · yttrium

[1] For recent leading reviews, see: a) N. Badi, J.-F. Lutz, *Chem. Soc. Rev.* **2009**, *38*, 3383 – 3390; b) J.-F. Lutz, M. Ouchi, D. R. Liu, M. Sawamoto, *Science* **2013**, *341*, 1238149; c) E. Brulé, J. Guo, G. W. Coates, C. M. Thomas, *Macromol. Rapid Commun.* **2011**, *32*, 169 – 185.

[2] For leading reviews on PHAs, see: a) G.-Q. Chen, *Chem. Soc. Rev.* **2009**, *38*, 2434 – 2446; b) D. B. Hazer, E. Kılıçay, B. Hazer, *Mater. Sci. Eng. C* **2012**, *32*, 637 – 647; For reviews on PMLA, see: c) O. Coulembier, P. Degée, J. L. Hedrick, P. Dubois, *Prog. Polym. Sci.* **2006**, *31*, 723 – 747; d) J. Y. Ljubimova, M. Fujita, A. V. Ljubimov, V. P. Torchilin, K. L. Black, E. Holler, *Nanomedicine* **2008**, *3*, 247 – 265.

[3] For pioneering work, see: a) L. R. Rieth, D. R. Moore, E. B. Lobkovsky, G. W. Coates, *J. Am. Chem. Soc.* **2002**, *124*, 15239 – 15248; For reviews, see: b) C. M. Thomas, *Chem. Soc. Rev.* **2010**, *39*, 165 – 173; c) J.-F. Carpentier, *Macromol. Rapid Commun.* **2010**, *31*, 1696 – 1705; d) O. Coulembier, P. Dubois, *Handbook of Ring-Opening Polymerization* (Eds.: P. Dubois, O. Coulembier, J.-M. Raquez), Weinheim, Wiley, **2009**; p. 227.

[4] a) A. Amgoune, C. M. Thomas, S. Ilinca, T. Roisnel, J.-F. Carpentier, *Angew. Chem.* **2006**, *118*, 2848 – 2850; *Angew. Chem. Int. Ed.* **2006**, *45*, 2782 – 2784; b) M. Bouyahyi, N. Ajellal, E. Kirillov, C. M. Thomas, J.-F. Carpentier, *Chem. Eur. J.* **2011**, *17*, 1872 – 1883.

[5] a) J. W. Kramer, D. S. Treitler, E. W. Dunn, P. M. Castro, T. Roisnel, C. M. Thomas, G. W. Coates, *J. Am. Chem. Soc.* **2009**, *131*, 16042 – 16044; For an highlight, see: b) J.-F. Carpentier, *Angew. Chem.* **2010**, *122*, 2720 – 2722; *Angew. Chem. Int. Ed.* **2010**, *49*, 2662 – 2663.

[6] a) O. Coulembier, P. Degée, P. Gerbaux, P. Wantier, C. Barbaud, R. Flammang, P. Guérin, P. Dubois, *Macromolecules* **2005**, *38*, 3141 – 3150, and references therein; b) C. G. Jaffredo, J.-F. Carpentier, S. M. Guillaume, *Macromolecules* **2013**, *46*, 6765 – 6776, and references therein.

[7] a) R. A. Gross, Y. Zhang, G. Konrad, R. W. Lenz, *Macromolecules* **1988**, *21*, 2657 – 2668; b) P. Guerin, J. Francillette, C. Braud, M. Vert, *Makromol. Chem. Macromol. Symp.* **1986**, *6*, 305 – 314.

[8] J.-P. Caruelle, D. Barritault, V. Jeanbat-Mimaud, S. Cammas-Marion, V. Langlois, P. Guerin, C. Barbaud, *J. Biomater. Sci. Polym. Ed.* **2000**, *11*, 979 – 991.

[9] a) A. Amgoune, C. M. Thomas, T. Roisnel, J.-F. Carpentier, *Chem. Eur. J.* **2006**, *12*, 169 – 179; b) N. Ajellal, M. Bouyahyi, A. Amgoune, C. M. Thomas, A. Bondon, I. Pillin, Y. Grohens, J.-F. Carpentier, *Macromolecules* **2009**, *42*, 987 – 993.

[10] a) P. Hormnirun, E. L. Marshall, V. C. Gibson, A. J. P. White, D. J. Williams, *J. Am. Chem. Soc.* **2004**, *126*, 2688 – 2689; b) P. Hormnirun, E. L. Marshall, V. C. Gibson, R. I. Pugh, A. J. P. White, *Proc. Natl. Acad. Sci. USA* **2006**, *103*, 15343 – 15348.

[11] Unlike PHB, the study of the carbonyl region of the $^{13}C\{^1H\}$ NMR spectra did not prove fully conclusive about the distribution of diad sequences in P(MLA^{Bz}-*alt*-MLA^{All}) copolymers. Yet, this region in the NMR spectrum of a copolymer prepared from the **1d**/*i*PrOH system showed only four sharp signals of near equal intensity, and were assigned to the two main-chain and the two side-chain carboxylate moieties, which is in line with the high degree of alternation of this polymer (see Figure S15 in the Supporting Information).

