Star-shaped PHB-PLA block copolymers: Immortal polymerization with dinuclear indium catalysts

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Complete List of Authors:	Mehrkhodavandi, Parisa; University of British Columbia, Chemistry Yu, Insun; University of British Columbia, Chemistry Ebrahimi, Tannaz; University of British Columbia, Chemistry; University of British Columbia, Chemical and Biological Engineering Hatzikiriakos, Savvas; University of British Columbia, Chemical and Biological Engineering

ARTICLE

Star-shaped PHB-PLA block copolymers: Immortal polymerization with dinuclear indium catalysts

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I. Yu,[a] T. Ebrahimi,[a,b] S. Hatzikiriakos[b] and P. Mehrkhodavandi[a*]

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The first example of a one-component precursor to star-shaped polyesters, and its utilization in the synthesis of previously unknown star-shaped poly(hydroxybutyrate)-poly(lactic acid) block copolymers, is reported. A series of such mono- and bis-benzyl alkoxy-bridged complexes were synthesized, fully characterized, and their solvent dependent solution structure and reactivity examined. These complexes were highly active catalysts for the controlled polymerization of β-butyrolactone to form poly(hydroxybutyrate) at room temperature. Solution studies indicate that a mononuclear propagating species formed in THF and that the dimer-monomer equilibrium affects rates of BBL polymerization. In the presence of linear and branched alcohols, these complexes catalyze well-controlled immortal polymerization and copolymerization of β-butyrolactone and lactide.

Introduction

Recent advances in the synthesis of biodegradable polymers, such as poly (lactic acid) (PLA) and poly(hydroxyalkanoates), have focused on custom design and polymers with tailored properties for use in biomedical applications.[1] In particular poly(β-hydroxybutyrate) (PHB), generated through ring opening polymerization of β-butyrolactone (BBL), is an important biocompatible polymer that has not been studied to the same extent as other polyesters such as PLA.[2] Despite its high ring strain,[3] rapid and highly controlled polymerization of BBL to produce high molecular weight PHB is rare due to the low activity of most catalysts towards β-lactones, as well as the high prevalence of chain termination events with this monomer.[4] These side reactions limit the possibilities for expanding PHB polymer architecture through forming branch points or block copolymers.[5]

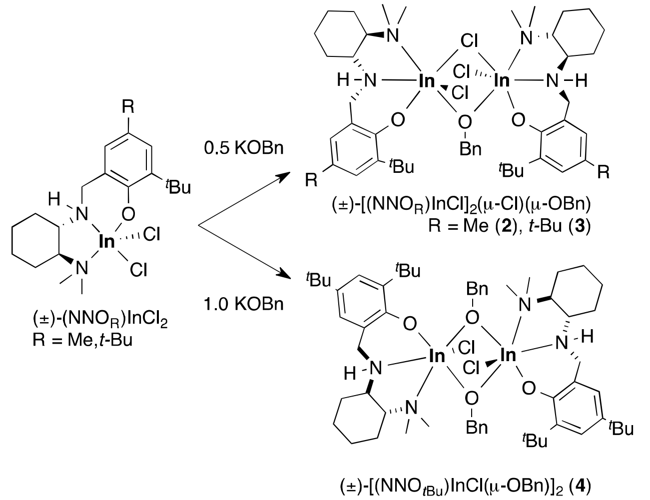
Immortal ring opening polymerization, or living polymerization with reversible transfer, of lactide (LA) in the presence of linear or branched chain transfer agents such as alcohols is a promising route towards reducing metal and ligand contamination and has produced an array of end-functionalized polymers with various architectures.[1a,1b,6] In particular, star-shaped PLAs, synthesized through immortal polymerization with multidentate alcohols, have smaller hydrodynamic radii, lower viscosities, and higher functional group concentration than their linear counterparts and have found applications in drug delivery among other fields.[7] In contrast, immortal polymerization of BBL is difficult due to a paucity of compatible catalytic systems.[8] Reports of star-shaped PHB are rare.[9]

We have reported that dinuclear indium complex, $[(NNO_{tBu})InCl]_2(\mu\text{-}Cl)(\mu\text{-}OEt)$ (**1**),[10] is a highly active and controlled catalyst for the living polymerization of LA[11] and is capable of immortal ring opening polymerization of BBL in the presence of up to 100 equivalents of added alcohol such as ethanol and monomethylated poly(ethylene glycol).[12] In addition to unprecedented stability in the presence of alcohols and high rate of reactivity with BBL, catalyst **1** is also able to form PLA-PHB-PLA triblock polymers through simple sequential addition.[13] Our work in this area has shown that the dinuclear nature of **1** is essential in controlling polymer micro- and macrostructure in lactide polymerization.[11,14] Catalyst nuclearity may also play an important role in BBL polymerization, as reflected in rates of reaction in various solvents. Previously reported zinc[8a] and yttrium[8e] complexes showed faster polymerization rates in non-coordinating solvents, while complex **1** is more active in coordinating solvents such as THF.[12]

In this work, we disclose the first example of an isolated alkoxy-diol bridging two indium centres. This complex is an isolated intermediate in the highly controlled formation of previously unknown star-shaped PLLA-PHB and PHB-PLLA block copolymers.

Results and discussion

SYNTHESIS AND CHARACTERIZATION OF COMPLEXES. Racemic proligands $H(NNO_R)$ (R = Me, *t*-Bu), 2-*t*-butyl-4-R-6-(((2-(dimethylamino)cyclohexyl)amino)methyl)phenol, dichloro complexes $(NNO_R)InCl_2$ (R = Me, *t*-Bu), and $[(NNO_{tBu})InCl]_2(\mu\text{-}Cl)(\mu\text{-}OEt)$ (**1**) can be prepared according to previously published work, and new alkoxy-bridged complexes can be synthesized in a similar manner.[11] Addition of 0.5 equiv KOBn (Bn = CH_2Ph) to (±)-$(NNO_R)InCl_2$ forms alkoxy bridged dinuclear complexes $[(NNO_R)InCl]_2(\mu\text{-}Cl)(\mu\text{-}OBn)$ (R = Me (**2**) and *t*-Bu (**3**)), while addition of one equiv of KOBn forms bis-alkoxy bridged $[(NNO_{tBu})InCl(\mu\text{-}OBn)]_2$ (**4**) (Scheme 1). Importantly, the complexes **2** and **3** are much more readily prepared and isolated in higher yields than their ethoxy analogues due to the greater stability of the mono-alkoxy-bridged complex towards over-alkoxylation. Complex **4** can be synthesized in low yields.



Scheme 1. Synthesis of chiral dinuclear indium complexes [(NNO$_R$)InCl]$_2$(μ-Y)(μ-OBn) (Y = Cl or OBn).

Dinuclear complexes **2**-**4** have been fully characterized by ^{1}H, ^{13}C{^{1}H}, ^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC NMR spectroscopy and have similar solution structures to complex **1** and related compounds (Figures S1-S9).[11,14] In particular, the ^{1}H NMR spectra of **2** and **3** show two doublets, each corresponding to 2 protons, for the diastereotopic ligand NH-CH_2-Ar protons at 3-5 ppm, as well as two doublets, each corresponding to one proton, for O-CH_2Ph at 5-6 ppm. In contrast, the ^{1}H NMR spectrum of **4** shows two sets of doublets, each corresponding to one proton, for In-OCH_2Ph and NH-CH_2-Ar respectively (Figure S13).

Single crystals of complexes **2** and **4**, synthesized from racemic ligand, can be obtained from toluene at room temperature (Figure 1). Single crystal X-ray diffraction analysis shows homo-chiral (*SS*/*SS*)-**2** isolated from its racemic mixture crystalizes in the centrosymmetric orthorhombic space group, *Pca2$_1$*, implying both (*SS*/*SS*) and (*RR*/*RR*) enantiomers exist in the unit cell. The molecular structure of **2** shows two octahedral indium centers asymmetrically bridged with chloro and benzyl alkoxy ligands. The solid structure of **4** shows a bis-benzyl alkoxy bridged dimer with the centrosymmetric heterochiral (*RR*/*SS*) configuration. The heterochiral motif has been observed for all previously reported symmetrically bridged dimers in the series.[11,14]

Reaction of one equiv of 1,3,5-tris(hydroxymethyl)benzene (THMB) with complex **1**, in toluene at room temperature or 70 °C, forms an OTHMB-bridged complex, [(NNO$_{tBu}$)InCl](μ-Cl)(μ-OTHMB) **5** (Scheme 2). The solution structure of **5** can be confirmed by ^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC and ^{1}H-^{13}C HMBC NMR spectroscopies (Figure S10-12). The THMB group is asymmetrically coordinated with no evidence of fluxionality at room temperature. The ^{1}H NMR spectrum (CDCl$_3$, 25 °C) of complex **5** shows two AB doublets at 5.08 and 5.80 ppm belonging to the In-O-CH_2-C$_6$H$_3$(CH$_2$OH)$_2$ protons immediately coordinated to the indium centres and two AB doublets at 4.26 and 4.40 ppm assigned to the distal In-O-CH$_2$-C$_6$H$_3$(CH_2OH)$_2$ protons. Addition of excess THMB does not form a bis-alkoxy bridged dinuclear complex analogous to **4**; there is no evidence of THMB bridged between multiple indium centers.

Although metal-alkoxide complexes with multiple alcohols have been invoked in the proposed mechanisms for star-polymer formation,[9d] complex **5** is the first example of a fully characterized intermediate in these transformations.

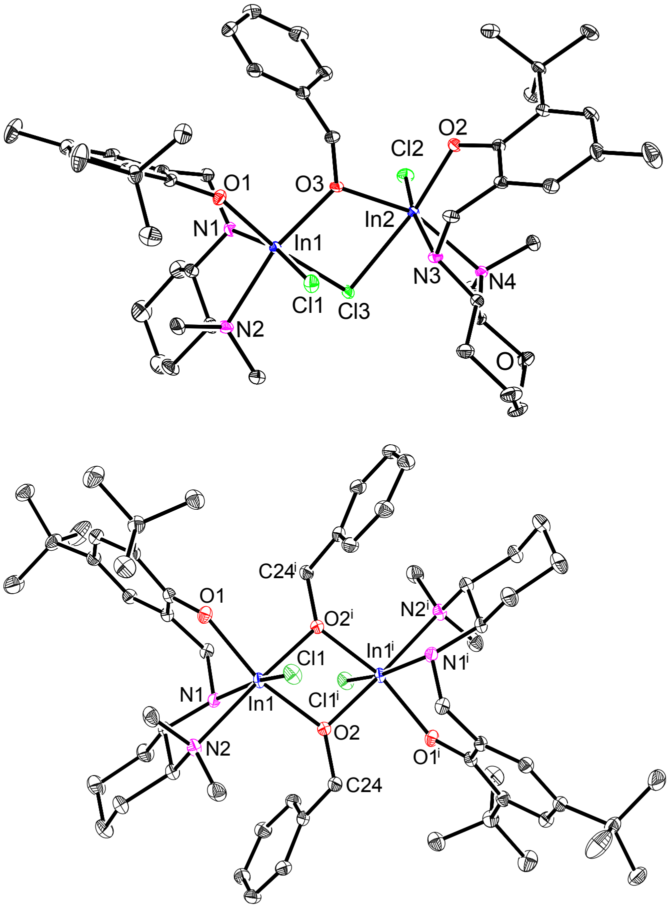
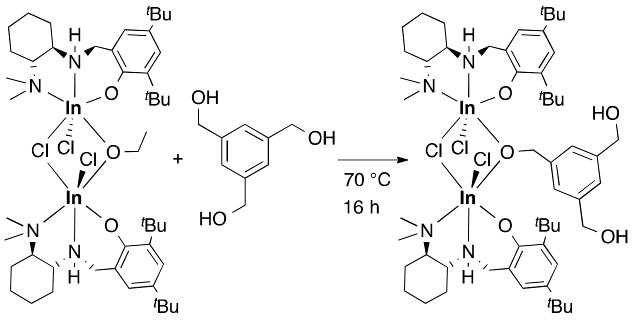
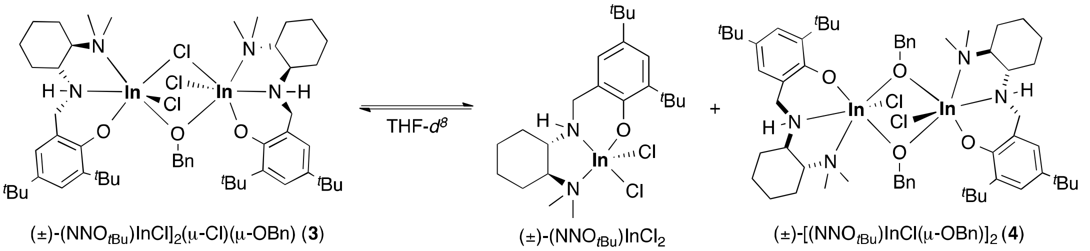


Figure 1. Molecular structure of Top: (*SS*/*SS*)-**2** (depicted with thermal ellipsoids at 50% probability and all H atoms and solvent molecules omitted for clarity); Bottom: (*RR*/*SS*)-**4** (depicted with thermal ellipsoids at 50% probability and all H atoms and solvent molecules omitted for clarity).



(±)-[(NNO$_{tBu}$)InCl]$_2$(μ-Cl)(μ-OEt) (**1**) (±)-[(NNO$_{tBu}$)InCl]$_2$(μ-Cl)(μ-OTMB) (**5**)

Scheme 2. Synthesis of complex **5** [(NNO)InCl]$_2$(μ-Cl)(μ-OTHMB) .



(±)-(NNO$_{tBu}$)InCl]$_2$(μ-Cl)(μ-OBn) (**3**) (±)-(NNO$_{tBu}$)InCl$_2$ (±)-[(NNO$_{tBu}$)InCl(μ-OBn)]$_2$ (**4**)

Scheme 3. Dissociation of complex **4** in THF-d_8.

Crystals of complex **5** suitable for single crystal X-ray structural determination can be obtained from a toluene solution at room temperature. Complex **5** is dinuclear with two octahedral indium centers asymmetrically bridged by chloride and (3,5-bis(hydroxymethyl)phenyl)methoxide, [OTHMB]$^-$, ligands (Figure 2). The bond lengths and angles for homochiral (*SS/SS*)-**5** are similar to those for complex **2** and previously reported asymmetrically-bridged homochiral dimers in the series.[11,14]

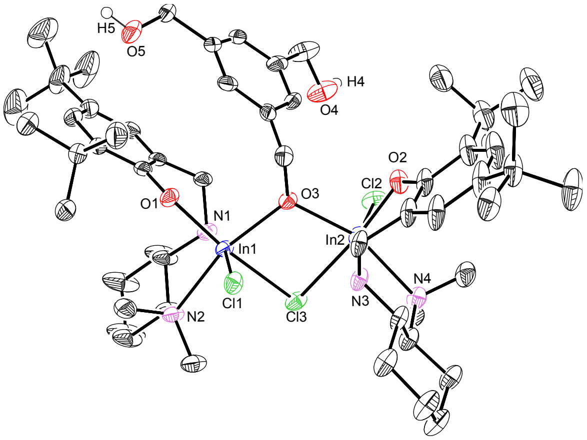


Figure 2. Molecular structure of (*SS/SS*)-**5** (depicted with thermal ellipsoids at 50% probability and most H atoms omitted for clarity).

Benzyl alkoxy bridged dinuclear complexes **3**, **4**, and **5** dissociate in coordinating solvents (Scheme 3). The ^{1}H NMR spectra of **3** are significantly different in $CDCl_3$ and THF-d_8 solutions at room temperature. The new peaks observed in THF-d_8 correspond to (NNO$_{tBu}$)InCl$_2$ and complex **4** and suggest partial dissociation of complex **3** (Figure S14). Importantly, the indium alkoxide complexes in the THF-d_8 solution are dimeric; no monomeric species are observed. Monitoring the dissociation of complex **4** in the presence of two equiv of (NNO)InCl$_2$ (THF-d_8, 16 h) confirms the reverse equilibrium. When the dichloro indium complex (NNO)InCl$_2$ is added to the complex **4**, signals for complex **3** are observed as the major species after only 10 min (Figure S15). No further changes to the relative ratio of complexes **3**, **4** and (NNO)InCl$_2$ are observed after 16 h. These results suggest that asymmetrically bridged complex **3** is more stable than bisalkoxy-bridged complex **4** under these conditions. Complex **5** behaves similarly to complex **3** (Figure S16). These observations highlight the relative stabilities of mono- and bisalkoxy-bridged dinuclear species in a system where catalyst aggregation and solvent effects must be included in all mechanistic considerations.

RING OPENING POLYMERIZATION OF β-BUTYROLACTONE (BBL). Complexes **3**, **4**, and **5** are active catalysts for the ring opening polymerization of BBL to form atactic poly(hydroxyl butyrate) (PHB). The choice of solvent for BBL polymerization is based on the significantly faster reactivity of these systems in THF.[12] *In situ* monitoring of the reactions by ^{1}H NMR spectroscopy (THF-d_8, 25 °C) shows 200 equiv of BBL polymerized to 90% conversion in under 3 h in these conditions (Figure S20). The observed rates of BBL polymerization with complexes **3-5** are in the range of the reported values for **1** (k_{obs} = 2.9 × 10^{-4} s^{-1}) under the same polymerization conditions (Table 1 entries 1-3).

Table 1. Rates of BBL ROP using dinuclear indium initiators.

Entry	Catalyst	k_{obs} (×10^{-4} s^{-1})
1^a	[(NNO$_{tBu}$)InCl]$_2$(μ-Cl)(μ-OBn) (**3**)	3.88(±0.12)
2^b	[(NNO$_{tBu}$)InCl(μ-OBn)]$_2$ (**4**)	2.28(±0.14)
3^a	[(NNO$_{tBu}$)InCl]$_2$(μ-Cl)(μ-OTHMB) (**5**)	4.47(±0.08)
4^a	[(NNO$_{tBu}$)InCl]$_2$(μ-Cl)(μ-OBn) (**3**) + 2 (NNO$_{tBu}$)InCl$_2$	1.00(±0.04)
5^c	[(NNO$_{tBu}$)InCl]$_2$(μ-Cl)(μ-OBn) (**3**)	0.33(±0.03)

All the reaction were carried out in an NMR tube in THF-d_8 at 25 °C and followed to 90% conversion except for the entry 5 carried out in $CDCl_3$. ^{a}[BBL] = 0.91 M. [catalyst] = 0.0091 M ; ^{b}[BBL] = 0.228 M. [catalyst] = 0.00228 M. 1,3,5-trimethoxybenzene (TMB) was used as internal standard. The value of k_{obs} was determined from the slope of the plots of ln([BBL]/[TMB]) vs. time.

The ^{1}H NMR spectra of complex **3** during polymerization of BBL in THF-d_8 show signals for (NNO$_{tBu}$)InCl$_2$ (Figure 3). Similar signals are observed for complex **1** and **5** (Figure S21 and S22, respectively). This dissociation, which is not observed during ROP of BBL with complex **3** in $CDCl_3$ (Figure S23), strongly suggests that the propagating species is monomeric in THF. We have shown that polymerization of lactide with dinuclear complexes such as **1** or **3** in non-coordinating solvents such as $CDCl_3$ does not require catalyst dissociation and similar catalyst activity is obtained in either chloroform or

THF, although all isoselectivity for the polymerization of racemic lactide with **1** in THF is lost.

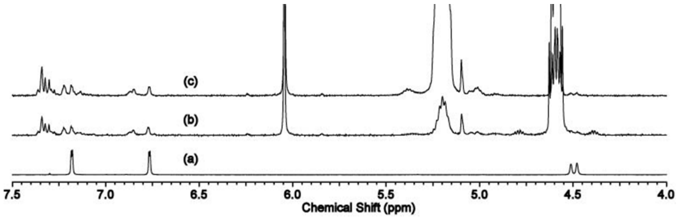


Figure 3. ^{1}H NMR spectra of (a) $(NNO_{tBu})InCl_2$ and polymerization of 200 equivalents of BBL with $[(NNO_{tBu})InCl]_2(\mu\text{-}Cl)(\mu\text{-}OBn)$ (**3**) after (b) 7 minutes and (c) 2 h (THF-d_8, 25 °C).

In contrast to lactide, dissociation of dinuclear indium catalysts is a key factor in the rate of polymerization of BBL. In order to investigate the equilibrium between mononuclear and dinuclear species in this system, we evaluated the effects of excess $(NNO_{tBu})InCl_2$ during polymerization. Our previous work shows that addition of up to five equiv $(NNO_{tBu})InCl_2$ does not affect lactide polymerization rates or polymer molecular weights.[11] We can explore the same reaction for the polymerization of BBL. *In situ* ^{1}H NMR spectroscopy (THF-d_8) of **3** in the presence of 2 equiv of $(NNO_{tBu})InCl_2$ shows that **3** remains unchanged for 16 h (Figure S24). Polymerization of 200 equiv BBL with a mixture of **3** and two equiv of $(NNO_{tBu})InCl_2$ under these conditions shows a depressed rate of BBL polymerization (Figure 4). A similar decrease in rate is observed in $CDCl_3$ where catalyst **3** is expected to remain dinuclear during the polymerization (Figure S25). These similarities between polymerizations carried out in $CDCl_3$ and those carried out in THF-d_8 in the presence of $(NNO_{tBu})InCl_2$ suggest that in both cases polymerization rate is suppressed due to a shift in equilibrium towards a dinuclear species. Thus, in contrast to lactide polymerization, catalyst dissociation is essential to the polymerization of BBL. The mononuclear nature of the catalyst may also contribute to the lack of stereoselectivity in polymerizing rac-BBL; for the polymerization of lactide, we observed a similar decrease in selectivity in complexes that showed dissociation.[14c,14e]

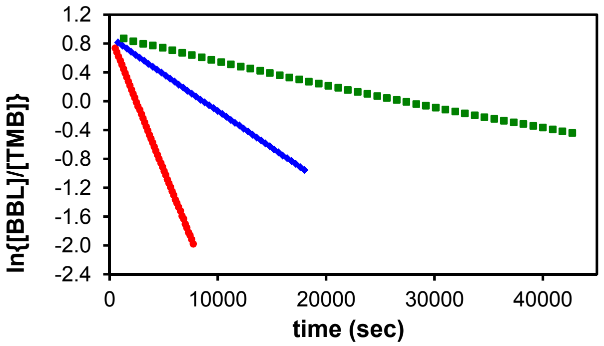


Figure 4. ROP rates for polymerization of BBL by **3** (●) in THF-d_8 ($k_{obs} = 3.9 \times 10^{-4}$ s^{-1}) and (◆) with 2 equiv of $(NNO_{tBu})InCl_2$ in THF-d_8 ($k_{obs} = 1.0 \times 10^{-4}$ s^{-1}) and (■) **3** in $CDCl_3$ ($k_{obs} = 3.3 \times 10^{-5}$ s^{-1}). $[BBL]_o = 0.114$ M, $[\mathbf{3}] = [(NNO_{tBu})InCl_2] = 5.2 \times 10^{-4}$ M, $[BBL]_0/[\mathbf{3}] = 200$ ($CDCl_3$, 25 °C).

Bulk polymerizations of BBL with complexes **1**, **3**, **4** and **5**, as well as with **3** in the presence of two equiv of $(NNO_{tBu})InCl_2$, allow us to assess the efficacy of these catalysts on a larger scale (Table 2). As expected, complexes **1** and **3** show excellent control for the polymerization of BBL, with good agreement between the observed and calculated $M_{n,}$ (Table 2, entries 1-4). The experimental $M_{n,}$ values for PHB obtained from both the bis-alkoxy bridged complex **4**, as well as complex **5**, are somewhat lower than the theoretical values based on the initiator concentration, likely due to trace amounts of BnOH and THMB which can act as chain transfer agents (Table 2, entries 5-8). Addition of two equiv of $(NNO_{tBu})InCl_2$ to complex **3** has no major impact on polymer molecular weight and distribution, indicating that while suppression of catalyst dissociation affects of polymerization rates, it has little influence on polymer properties (Table 2, entries 9-10).

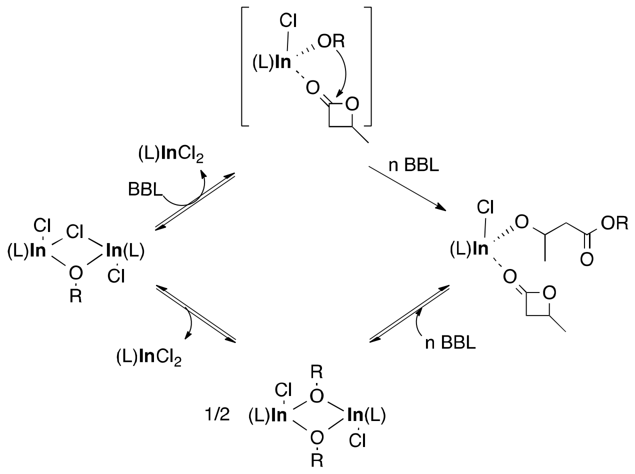
Table 2. Polymerization of BBL by complexes **1**, **3**, **4** and **5,** and **3** + 2 equiv $(NNO_{tBu})InCl_2$.

	I	$[BBL]_o$: [I]	$M_{n,theo}{}^b$/ Da	$M_{n,GPC}{}^c$/ Da	$M_{w,GPC}{}^c$ /Da	$Đ_t{}^c$
1	[**1**]	695/1	59460	60670	62490	1.03
2	[**1**]	1390/1	118790	97330	98750	1.02
3	[**3**]	734/1	62899	62630	65610	1.05
4	[**3**]	1469/1	119331	102600	105200	1.03
5	[**4**]	903/1	77890	64450	65380	1.02
6	[**4**]	1806/1	155629	92780	95950	1.03
7	[**5**]	795/1	67962	53100	55520	1.05
8	[**5**]	1591/1	135756	90360	95620	1.06
9	[**3**] + 2 $(NNO_{tBu})InCl_2]$	800/1	68296	66810	69850	1.05
10	[**3**] + 2 $(NNO_{tBu})InCl_2]$	1600/1	137852	118700	119900	1.01

All reaction carried out in THF at 25 °C over 16h and to >99% conversion. [a] Conversions determined by ^{1}H NMR spectroscopy. [b] $[M]_o$/[initiator] × monomer conversion × $M_M + M_{ROH}$ ($M_{BBL} = 86.09$ g/mol, $M_{EtOH} = 46.07$ g/mol $M_{BnOH} = 108.14$ g/mol, $M_{TMB} = 168.19$ g/mol). Initiator is the dimeric complex. [c] Determined by GPC-LALLS (gel permeation chromatography-low angle laser light scattering) to the polystyrene standard calibration via the Mark–Houwink equation in THF at 25 °C dn/dc = 0.068 mL/g for PHB in THF).

Based on the observations on the structural behavior of the dinuclear indium complexes in the presence of BBL in THF, we propose a mechanism for BBL polymerization with the dinuclear complexes **1, 3**, and **5** which involves the dissociation of the dinuclear complex to yield an active mononuclear propagating species $(NNO_{tBu})In(Cl)(OR)$ (R = Et, Bn, THMB) and an inactive complex $(NNO_{tBu})InCl_2$ (Scheme 4). In the absence of monomer, the mononuclear species dimerizes to form a bis-alkoxy-bridged resting state analogous to complex **4**. As discussed above, the diminished propagation rate with complex **3** in the presence of two equiv of $(NNO_{tBu})InCl_2$ confirms that the preponderance of the dimeric form inhibits BBL polymerization.

IMMORTAL RING OPENING (CO)POLYMERIZATION OF CYCLIC ESTERS WITH COMPLEX 1 IN THE PRESENCE OF THMB AS THE CHAIN TRANSFER AGENT. We have shown that complex **1** is an exceptional catalyst in the presence of high loadings of alcohols over ROP of BBL.[12] We can expand this work to polyols, such as tri(hydroxymethyl)benzene (THMB), to prepare star-shaped PHB as well as star shaped block copolymers (Table 3).



Scheme 4. Proposed mechanism for ring opening polymerization of BBL with dinuclear indium complexes in THF.

Table 3. Polymerization of BBL by complexes **1** and BnOH and THMB as chain transfer agents in THF at room temperature.

	$M_1(M_2)$	I	ROH	$[M_1+M_2]$:[ROH]:[I]	$M_{n,theo}$^{c}/ Da	$M_{n,GPC}$^{d}/ Da	$Đ_t$^{d}
1	BBL	[**1**]	THMB	5000/220/1	2105	2506 (2081^{e})	1.08
2	BBL	[**1**]	THMB	5000/40/1	10822	9823	1.07
3	BBL	[**1**]	THMB	5000/20/1	20830	23200	1.02
4	BBL	[**5**]	-	5000/40/0	9854	9264^{e}	-
5	BBL	[**5**]	-	5000/20/0	20830	18000	1.02
6	BBL	[**5**]	-	5000/5/0	83670	72050	1.04
7	BBL	[**5**]	THMB	5000/4/1	84536	70580	1.04
8$^{a, f}$	BBL (L-LA)	[**1**]	THMB	3125 + 1865/5/1	103433	103000	1.01
9$^{b, f}$	L-LA (BBL)	[**1**]	THMB	1865 + 3125/5/1	98052	96277	1.01

Unless otherwise state, all reaction carried out in THF at 25 °C over 16h to >95% conversion. ^{a}Order of monomer BBL followed by L-LA, conversion BBL:L-LA 99 : 93. ^{b}Order of monomer L-LA followed by BBL, conversion L-LA:BBL 96 : 86. Monomer conversion determined by ^{1}H NMR spectroscopy. ^{c} Calculated from $([M1]_o/([ROH]/[I]) \times$ monomer conversion $\times M_{M1}) + ([M2]_o/([ROH]/[I]) \times$ monomer conversion $\times M_{M2}) + M_{ROH}$ (M_{BBL} = 86.09 g/mol, $M_{L\text{-}LA}$ = 144.13 g/mol, M_{BnOH} = 108.14 g/mol, M_{THMB} = 168.19 g/mol). ^{d} Determined by GPC-LALLS in THF using dn/dc = 0.068 for PHB. ^{e} Molecular weight determined by ^{1}H NMR spectroscopy. ^{f} Block copolymers are not soluble in THF so $CHCl_3$ is used as the GPC solvent (dn/dc = 0.034 for PHB and dn/dc = 0.029 for PLLA).

Catalyst **1** undergoes controlled immortal ring opening polymerization of 5000 equiv BBL with a [ROH] : [**I**] ratios of up to 220, which is unprecedented in BBL synthesis (Table 3, entries 1-3). The resulting polymers have predictable molecular weights and narrow molecular weight distributions. ^{1}H NMR analysis of polymers synthesized with [BBL]/[THMB]/[**1**] ratios of 5000:220:1 shows characteristic resonance signals at 5.1 ppm for the methylene protons and at 7.4 ppm for the aromatic protons of THMB group on 3-arm oligostars of PHB (Figure S26). The ^{1}H NMR spectrum ($CDCl_3$) of this reaction shows approximately 7.2 butyrolactyl units per star arm, which matches the calculated value of 7.5 (based on 5000 monomer units per 660 arms).

Complex **5** is a viable catalyst for the controlled formation of star-shaped PHB in the absence of added alcohol. Decreasing the concentration of **5** with a constant monomer concentration (*i.e.* increasing monomer : initiator ratio) produces higher molecular weight polymers with low dispersity (Table 3, entries 4-6). Polymerizations carried out with 5000 equiv BBL in the presence of 5 equiv of complex **5**, and with one equiv of complex **5** and 4 equiv of THMB yield identical polymers as expected (Table 3, entries 6 and 7 respectively). These observations are in agreement with MALDI-TOF mass spectroscopy results (Figure S27).

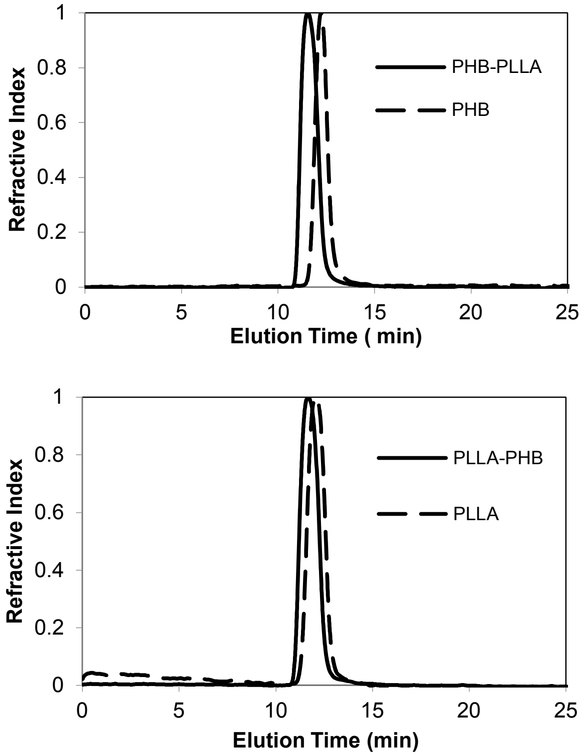
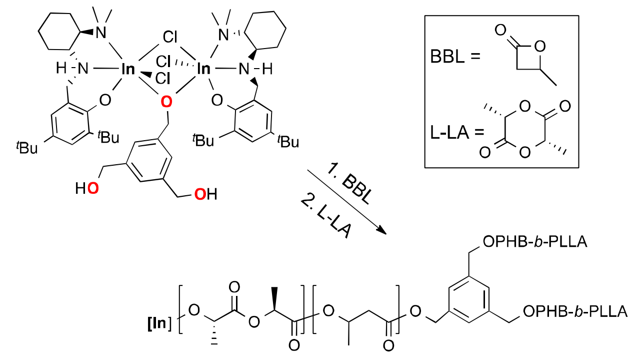


Figure 5. Overlaid GPC traces of 3 arm star block copolymers produced by consecutive additions of (a) 625 equiv. of [BBL]:[THMB] and 373 equiv. of [L-LA]:[THMB] (top) and (b) 373 equiv. of [L-LA]:[THMB] and 625 equiv. of [BBL]:[THMB] (bottom) with complex **1** in THF at 25 °C. (a) right, 1st addition, dashed line (M_n = 49 kDa, PDI =1.01) for BBL; 2nd addition, solid line (M_n = 103 kDa, PDI = 1.01) for PHB-*b*-PLLA (Table 3 entry 8, Figure S50). (b) right, 1st addition, dashed line (M_n = 43 kDa, PDI =1.01) for LLA; 2nd addition, solid line (M_n = 96 kDa, PDI = 1.01) for PLLA-*b*-PHB (Table 3 entry 9, Figure S51).

A unique ability of this system is the immortal block-copolymerization of BBL and LA, regardless of the sequence of addition (Scheme 5). Sequential addition of BBL followed by L-LA, or *vice versa*, to catalyst **5** (prepared in situ with **1** and 5 equiv THMB) forms star block copolymers PHB-*b*-PLLA or PLLA-*b*-PHB, respectively (Table 3, entries 8-9). For example, the first addition of 625 equiv BBL yields 3-arm star PHB homopolymer with an M_n value (46 kDa) close to the calculated value (53 kDa) (Figure 5a dashed line). Monomer conversion can be determined by ^{1}H NMR spectroscopy (Figure S28a).

Next, the addition of 373 equiv L-LA to the reaction mixture containing the 3-arm star PHB forms 3-arm star copolymer PHB-*b*-PLLA with M_n corresponding to 625 BBL and 373 L-LA enchained units (Figures 5a solid line, S28b). Reversing the order of addition also yields a star-shaped block copolymer (Figures 5b, S29). This acceptable agreement between experimental and theoretical molecular weights of the resulting block copolymers, along with very narrow molecular weight distributions, implies that no matter the monomer addition sequence, there is good control in block copolymerization of BBL and LA.



Scheme 5. Star-shaped PHB/PLA copolymers.

Conclusions

A series of benzyl alkoxy bridged complexes were synthesized, fully characterized, and investigated as catalysts for the immortal ring opening polymerization of BBL and LA to form previously unknown star-shaped PHB-*b*-PLA block copolymers. These include mono-THMB alkoxy bridged complex **5**, which is the only example of a one-component system for star-polymer formation and a fully characterized proposed intermediate in star-polymer formation. We have illustrated an important difference in the possible mechanism of polymerization for BBL and LA with these dinuclear systems. Complexes such as **1** and **3** dissociate in coordinating solvents such as THF, while they are dinuclear in solvents such as chloroform. The catalyst nuclearity does not affect the rate of polymerization for LA; however, BBL polymerization is significantly more rapid with the mononuclear systems in THF. Regardless of catalyst nuclearity, these complexes are exceptionally controlled catalysts for the immortal (co)-polymerization of BBL, allowing us to generate previously unknown polymer architectures and macrostructures. We aim to use this capability to explore the range of possibilities in this area in the future.

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Notes and references

[a] Department of Chemistry, University of British Columbia, 2036 Main Mall, Vancouver, British Columbia, Canada. mehr@chem.ubc.ca
[b] Department of Chemical and Biological Engineering, University of British Columbia, 2360 East Mall, Vancouver, British Columbia, Canada.

Electronic Supplementary Information (ESI) available: Full experimental details, full solution and solid state characterization, and polymerization data.

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