# Cationic zinc complexes: a new class of catalyst for living lactide polymerization at ambient temperature†

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*Received 25th August 2010, Accepted 17th September 2010*
**DOI: 10.1039/c0cc03463k**

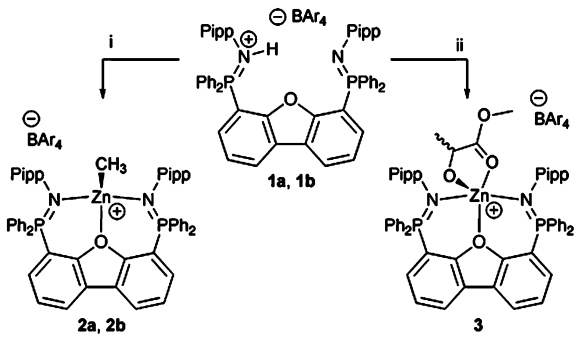
**Cationic zinc complexes of a bis(phosphinimine) pincer ligand have been prepared. Methylzinc and zinc–lactate complexes have been structurally characterized, and the latter is the first cationic metal complex to promote coordination–insertion polymerization of lactide at ambient temperature. This novel catalyst system is remarkably active and also exhibits living character. A detailed investigation of the kinetics and mechanism of the polymerization process has been undertaken.**



Polylactide (PLA), produced primarily by the ring-opening polymerization of lactide (LA), is one of the most commercially relevant biodegradable polymers.[1] A number of well-defined metal alkoxide systems are known to induce the ring-opening polymerization of LA *via* a coordination–insertion mechanism.[2] Specifically, zinc-based systems have been among the most thoroughly studied due to high activity coupled with superior molecular weight control. Of the numerous zinc alkoxide catalysts reported, the vast majority are supported by monoanionic ancillary ligands.[3] The use of neutral ligands is much less common,[2a,4] and there has been virtually no exploration of the LA polymerization properties of cationic systems.[5] This is surprising given the high activity of formally zwitterionic tris(pyrazolyl)borate catalysts.[3b] Cationic, coordinatively unsaturated species should be expected to promote facile coordination of LA, and for this reason we have targeted cationic zinc complexes as homogeneous catalysts for the polymerization of LA.[6]

Our ongoing research has explored neutral mono- and bis-phosphinimine ligands constructed from a dibenzofuran (dbf) backbone, and cationic heteroleptic zinc complexes thereof. It has been demonstrated that cationic alkylzinc complexes can be readily prepared, but these have displayed poor catalytic properties.[6a] More recently, we reported the preparation and crystallographic characterization of a series of coordinatively unsaturated zinc complexes.[6b] Alkylzinc complexes were again mediocre catalysts; however, a zinc–lactate species was found to polymerize *rac*-LA at 60 °C. This represented the first direct observation of coordination–insertion polymerization of LA by a cationic zinc complex.

In this communication we report a variation of the ligand system employed in the preceding study,[6b] whereby the steric demands are reduced by replacing 2,4,6-trimethylphenyl (Mes) with *p*-isopropylphenyl (Pipp) at the phosphinimine *N*-aryl site. Cationic zinc complexes of this ligand have been prepared, including a zinc–lactate complex that exhibits excellent LA polymerization characteristics (Scheme 1). This new generation catalyst promotes the rapid and living ring-opening polymerization of *rac*-LA at ambient temperature, which to our knowledge, has never before been achieved with a cationic metal catalyst.




**Scheme 1** Synthesis of cationic complexes **2a** and **2b**, and the cationic zinc–lactate complex **3** by reaction of (i) **1a** (Ar = *m*-$(CF_3)_2$–$C_6H_3$) or **1b** (Ar = $C_6H_5$) with $ZnMe_2$ and (ii) **1a** with EtZn(methyl-L-lactate).

The bis(phosphinimine) ligand **L** was easily prepared from 4,6-bis(diphenylphosphino)dbf and Pipp-azide under standard Staudinger conditions,[7] and isolated as an analytically pure pale yellow solid in 85% yield. A single resonance appears in the $^{31}P\{^1H\}$ NMR spectrum of **L** at $\delta$ −5.10 ($C_6D_6$). Diagnostic $^1H$ NMR peaks include the isopropyl methine, which resonates as a septet at $\delta$ 2.73, and the corresponding isopropyl methyls, which resonate as a doublet at $\delta$ 1.16.

Using previously described methods,[6a,8] protonation of the ligand was easily carried out generating ion-pairs **1a** and **1b**. Reaction of **1a** with dimethylzinc in toluene afforded the cationic alkylzinc complex **2a** with concomitant loss of methane. This reaction proved exceedingly facile, proceeding to completion within several minutes at ambient temperature. Complex **2a** has apparent $C_{2v}$ symmetry in solution, resonating sharply at $\delta$ 25.4 in the $^{31}P\{^1H\}$ NMR spectrum ($C_6D_5Br$ solvent). In the $^1H$ NMR spectrum, the Zn–Me appears at $\delta$ −0.79, while the diagnostic isopropyl methine and methyl groups shift upfield to $\delta$ 2.53 and $\delta$ 1.00, respectively. Despite repeated attempts, single crystals suitable for an X-ray diffraction experiment remained elusive. However, upon utilization of the more crystalline tetraphenylborate counter-ion, single crystals‡ of **2b** were readily obtained (Fig. 1).[9] No significant interaction exists between the cation and the anion in the solid state, and thus, this can be considered an excellent representation of the cation of **2a**. The geometry at zinc is distorted trigonal pyramidal, with the phosphinimines (Zn(1)–N(1) = 2.044(2) Å, Zn(1)–N(2) = 2.051(3) Å) and the

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† Electronic supplementary information (ESI) available: Additional synthetic and crystallographic details, as well as further information about kinetic experiments and polymer characterization. CCDC 793414–793416. For ESI and crystallographic data in CIF format see DOI: 10.1039/c0cc03463k

 

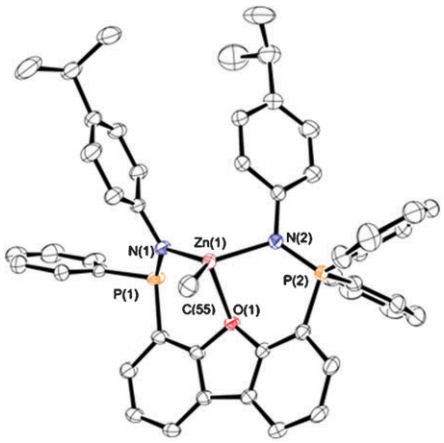


**Fig. 1** X-Ray crystal structure of the cation of **2b**, with ellipsoids shown at the 30% level. Hydrogen atoms, disordered atomic positions, and a phenyl group of P(1) have been omitted for clarity.

methyl group (Zn(1)–C(55) = 2.002 Å) occupying the equatorial positions and the more weakly coordinated dbf oxygen in the apical site (Zn(1)–O(1) = 2.284(2) Å). The phosphinimine bite angle is slightly reduced from ideal (N(1)–Zn–N(2) = 112.5(1)°), and the sum of angles about the equatorial positions is 359.5(5)°. The coordination of the dbf oxygen is of significant interest given that such an interaction was not observed in analogous complexes of the bulkier Mes-substituted ligand.[6b] Presumably, the reduced bulk or donating ability of the Pipp groups renders this bonding mode possible.

Alkylzinc compounds **2a** and **2b** are inactive for polymerization of LA. Thus, complex **3** was prepared by reaction of **1a** with EtZn(methyl-L-lactate) in bromobenzene at 100 °C for 2 h. Characteristic signals for the lactate group of complex **3** were observed in the $^1$H NMR spectrum at $\delta$ 3.19 (O–C$H_3$), 3.76 (C$H$CH$_3$), and 0.94 (CHC$H_3$).[10] Despite the presence of the asymmetric methyl-lactate moiety, **3** exhibits apparent $C_{2v}$ symmetry in solution with a single resonance in the $^{31}$P{$^1$H} NMR spectrum at $\delta$ 28.9, suggesting rapid fluxional behaviour in solution on the NMR timescale.

The solid-state structure of **3**, shown in Fig. 2, reveals a similar bonding mode to **2b**, with strong coordination of both phosphinimine donors (Zn(1)–N(1) = 2.014(6) Å; Zn(1)–N(2) = 2.000(5) Å), and weaker, but significant, coordination of the dbf oxygen (Zn(1)–O(1) = 2.336(5) Å). The geometry at zinc is trigonal bipyramidal, with the phosphinimine nitrogen atoms and the lactate O(2) in the equatorial positions (Zn(1)–O(2) = 1.909(6) Å). The sum of angles about the equatorial sites is 357.3(6)°, with all angles slightly less than 120°. The lactate carbonyl occupies the apical site (Zn(1)–O(3) = 2.120(6) Å) opposite the dbf oxygen, which was vacant in complex **2b**. The angle between these apical sites is 169.8(2)°. The lactate moiety exists as a 50 : 50 mixture of L and D isomers, which was modelled as a two-site positional disorder of the C(55) atom. This observation suggests racemization caused by the harsh reaction conditions used for its synthesis. Notably, however, preliminary experiments using L-LA argue against epimerization during polymerization (*vide infra*).

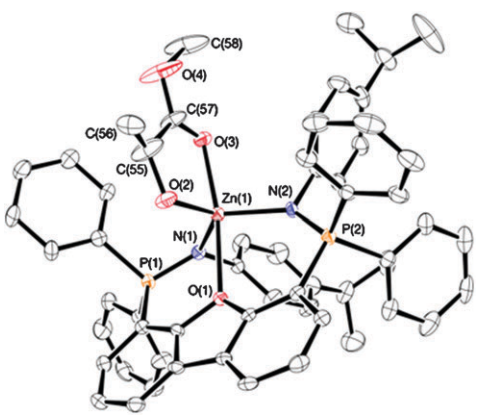


**Fig. 2** X-Ray crystal structure of the cation of **3**, with ellipsoids drawn at the 30% probability level. Hydrogen atoms and disordered atomic positions have been omitted for clarity.

Complex **3** is a highly active catalyst for the polymerization of LA at ambient temperature, giving 90% conversion of 200 equiv. of *rac*-LA in 50 min (25 °C, $CD_2Cl_2$ solvent). The resulting PLA has a slightly hetero-enriched microstructure ($P_r$ = 0.63), likely due to a chain end control process.[11] Such activity is comparable to some of the most highly active zinc-based catalyst systems known.[3] For example, neutral complexes LZnOEt and LMgOEt (L = tris(3-*tert*-butylpyrazolyl)borate) polymerize 500 equiv. of L-LA to 90% in 6 d and 1 h, respectively.[3b] Measurement of the rate under these conditions confirmed the reaction was first order in [monomer], with an observed rate constant of 8.65(4) × 10$^{-4}$ s$^{-1}$. In addition, determination of $k_{obs}$ at various concentrations of **3** established the polymerization to be first order in [catalyst]. Thus, this process has an overall second-order rate law (rate = $k$[**3**][LA]; $k$ = 0.17(1) M$^{-1}$ s$^{-1}$). After complete consumption of monomer, addition of another 200 equiv. of LA demonstrated the living character of the system, which continued polymerization at a similar rate ($k$ = 0.16(2) M$^{-1}$ s$^{-1}$).

Upon exposure of complex **3** to excess *rac*-LA, immediate conversion to a new species with a $^{31}$P{$^1$H} NMR chemical shift (at $\delta$ 29.4) slightly downfield of the initial catalyst ($\delta$ 28.9) was observed. More notably, the lactate end group gives rise to an O–CH$_3$ singlet at $\delta$ 3.64 in the $^1$H NMR spectrum. The methine signal, however, was not observed and is likely obscured beneath the LA/PLA signals. Given these spectroscopic observations, this new species is presumed to be the product of insertion of one or more monomer units, providing strong evidence for a coordination–insertion mechanism. In addition, a low molecular weight polymer sample ([LA]$_0$/[**3**] = 50) was analysed by MALDI-ToF mass spectrometry, and the observed masses of all oligomer fragments were consistent with the presence of a methyl-L-lactate end-group. Unfortunately, the mass peaks are separated by $m/z$ 72, which suggests intermolecular transesterification occurs to a significant degree during polymerization.

Determination of the activation parameters for the polymerization of *rac*-LA by **3** was accomplished by measuring the rate of reaction at temperatures ranging from 37 °C to −7 °C. An Eyring plot of the data revealed $\Delta H^{\ddagger}$ = 47(1) kJ mol$^{-1}$ and $\Delta S^{\ddagger}$ = −147(4) J K$^{-1}$ mol$^{-1}$. These values closely match activation parameters for other known coordination–insertion lactide polymerization catalysts and are indicative of a well-controlled polymerization process.[12]

Several polymer samples have been prepared using a range of catalyst concentrations, with the monomer to catalyst ratio

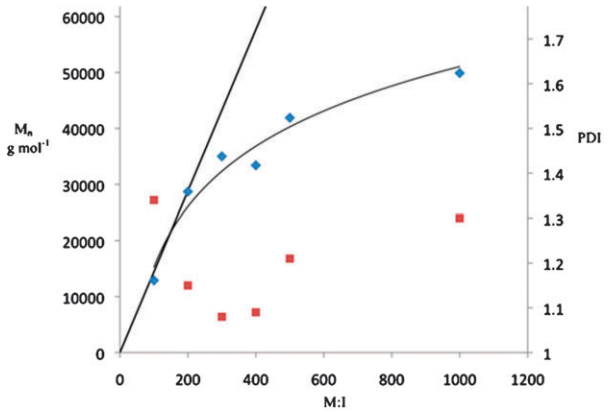


**Fig. 3** Plot of observed $M_n$ (◆) and PDI (■) as a function of the monomer to catalyst ratio. The straight line represents calculated $M_n$ values ($M_n$ = $[LA]_0$ : [**3**] × 144.13), while the curved line shows the general trend for experimental $M_n$ values.

ranging from 100 to 1000, and their molecular weights have been analyzed by gel permeation chromatography (GPC) (Fig. 3). At high concentrations of catalyst **3** ($[LA]_0$/[**3**] = 100 and 200), the molecular weights of the resulting polymer samples closely approximate the calculated values. However, at lower concentrations of **3**, the molecular weights drop off significantly. For example, a number-average molecular weight slightly greater than 50 000 Da, which is only ~35% of the calculated value, was achieved when $[LA]_0$/[**3**] = 1000. This observation is consistent with the presence of monomer impurities acting as chain-transfer agents. The molecular weight distribution is narrow for all samples (PDI = 1.08–1.34), with the most narrow distribution occurring at intermediate catalyst loadings ($[LA]_0$/[**3**] = 300 and 400). A plausible reason for higher PDI's at high catalyst loading is slow initiation relative to propagation, which becomes statistically less relevant at lower catalyst concentrations. Higher PDI values at lower catalyst loading are most likely a result of transesterification, which was observed to be occurring by MALDI-ToF mass spectrometry (*vide supra*). The broadening effect of transesterification on molecular weight distribution should necessarily depend on reaction times for the polymerization experiment, which are longer at lower catalyst loading.

As a further test of the livingness of **3** for LA polymerization, a polymer sample was prepared by sequentially polymerizing two batches of 200 equiv. of *rac*-LA. Analysis of the resulting polymer by GPC showed molecular weights similar to those determined for the single-step polymerization of 400 equiv. of *rac*-LA ($M_n$ = 31.5 × $10^3$ g mol$^{-1}$ *vs.* 33.4 × $10^3$ g mol$^{-1}$). The molecular weight distribution broadened slightly (1.21 *vs.* 1.09), likely as a result of the longer duration of the polymerization experiment.

In summary, we have prepared the first cationic system capable of catalyzing the ring-opening polymerization of lactide at ambient temperature. The mechanism of polymerization has been unambiguously established not to occur *via* a cationic process, but rather, by a well-controlled coordination–insertion mechanism. Future work will involve modification of the steric bulk and electron donating capacity of the phosphinimine donors, as well as installation of chiral functionalities, to inhibit transesterification side reactions and enhance stereocontrol, respectively.

P.G.H. thanks NSERC, CFI, Canada School of Energy and Environment and GreenCentre Canada for financial support. C.A.W. acknowledges NSERC and the Alberta Ingenuity Fund (Alberta Innovates) for student awards. Thanks to Dr. Timothy Clark and Yun Yang of GreenCentre Canada for GPC measurements.

## Notes and references

‡ *Crystal data for* **2b** *and* **3**: **2b**: $C_{85}H_{76.5}BBr_{0.5}N_2OP_2Zn$, $M$ = 1320.09, triclinic, $a$ = 9.878(7), $b$ = 17.43(1), $c$ = 21.93(1) Å, $\alpha$ = 80.235(8)°, $\beta$ = 82.751(8)°, $\gamma$ = 80.160(8)°, $U$ = 3647(4) Å$^3$, $T$ = 173(2) K, space group $P(\bar{1})$ (no. 2), $Z$ = 2, 44 021 reflections, 12 848 unique ($R_{int}$ = 0.0270) were used in all calculations after removing electrons from solvent accessible voids. The final w$R(F_2)$ was 0.1284 (all data); **3**: $C_{90}H_{67}BF_{24}N_2O_4P_2Zn{\cdot}C_6H_6$, $M$ = 1912.68, monoclinic, $a$ = 19.087(2), $b$ = 26.603(2), $c$ = 19.538(2) Å, $\beta$ = 116.133(1)°, $U$ = 8906.6(1) Å$^3$, $T$ = 173(2) K, space group $P2(1)/c$ (no. 14), $Z$ = 4, 72 717 reflections, 9322 unique ($R_{int}$ = 0.0803) were used in all calculations. The final w$R(F_2)$ was 0.1665 (all data).

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