

Lactide polymerization by well-defined calcium coordination complexes: comparisons with related magnesium and zinc chemistry†

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Amide and alkoxide coordination complexes of calcium supported by β -diiminato and bulky trispyrazolylborate complexes are reported together with their activity in lactide ring-opening polymerization; some are amongst the most active systems discovered to date.

Well defined coordination complexes¹ have been found to be effective in initiating the ring-opening polymerization (ROP) of lactides to give polylactides, PLAs, which are an important emerging class of environmentally friendly and biocompatible polymers, readily available from an inexpensive renewable resource.² The β -diiminato (BDI) ligand $\text{CH}[\text{CMeN}(\text{2,6-}^i\text{Pr}_2\text{C}_6\text{H}_3)_2]_2$, L, has proved a particularly effective spectator ligand when attached to Mg^{2+} , Zn^{2+} and Sn^{2+} in complexes of the form LMX where X = an amide or alkoxide which acts as an initiator in ring-opening.^{3–7} As with any polymer having commercial interest in the biomedical field, it is important that the metal be biological benign and that any residual catalyst not impart undesired properties such as color to an otherwise colorless polymer. In this regard, calcium is an attractive metal. In comparison to magnesium and zinc, calcium is significantly larger and its organometallic and coordination chemistry is notably different and much less well developed than those of magnesium and zinc. We describe here our initial foray aimed at preparing complexes of the type LCaX where X = an amide or alkoxide capable of initiating ROP of lactide. These initial results are both extremely promising with regard to the potential utility of well-defined calcium coordination complexes for the ROP of lactide and illuminating with respect to the differences in the coordination chemistry of the elements Ca, Mg, and Zn.

The bulky β -diiminato ligand LH reacts with $\text{KN}(\text{SiMe}_3)_2$ (2 equiv.) in THF and subsequently with CaI_2 to yield the complex $\text{LCa}[\text{N}(\text{SiMe}_3)_2]\cdot\text{THF}$, **1** (see Fig. 1).[‡] However, based on variable temperature ¹H NMR data, this compound is either dimeric at low temperatures in toluene-*d*₈ or exists in equilibrium with other calcium species. Compound **1** polymerizes *rac*-lactide (200 : 1 lactide : catalyst) in THF at room temperature to 90% completion in 2 h giving atactic polylactide. When 2 equiv. of LH is used in the above preparation, the bis- β -diiminato complexes, CaL_2 (see Fig. 2)[‡] is obtained.

From reactions employing the more bulky trispyrazolylborate ligands, we have been able to isolate discrete four- and five-coordinate complexes of Ca^{2+} (Scheme 1, Fig. 3 and Fig. 4). The use of the 3-*tert*-butylpyrazole derivative allows the isolation of the four-coordinate amide $[\text{HB}(3\text{-}^i\text{Bupz})_3]\text{CaN}(\text{SiMe}_3)_2$, **2**, and the five-coordinate aryl oxide $[\eta^3\text{-HB}(3\text{-}^i\text{Bupz})_3]\text{Ca}(\text{O-2,6-}^i\text{Pr}_2\text{C}_6\text{H}_3)\cdot\text{THF}$, **3**. There is little doubt that the coordination geometry of the latter compound parallels that of the 3-isopropylpyrazole derivative, $[\eta^3\text{-HB}(3\text{-}^i\text{Prpz})_3]\text{CaN}(\text{SiMe}_3)_2\cdot\text{THF}$, **4**, shown in Fig. 3. Even though the quality of a single crystal X-ray structure of compound **4** is poor, we can state that compound **4** has a five-coordinate Ca^{2+} center with THF at an axial position. A similar five-coordinate structure

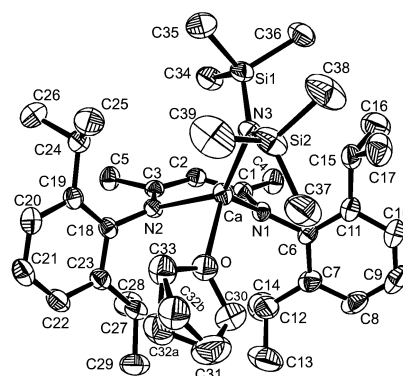


Fig. 1 An ORTEP drawing of $\text{LCa}[\text{N}(\text{SiMe}_3)_2]\cdot\text{THF}$, **1**, with thermal ellipsoids drawn at the 50% probability level. Hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and bond angles (°): Ca–N1 2.352(1), Ca–N2 2.370(1), Ca–N3 2.313(1), Ca–O 2.359(1); N1–Ca–N2 81.14(5), N1–Ca–N3 124.79(5), N1–Ca–O 113.79(5), N2–Ca–N3 136.78(5), N2–Ca–O 91.25(5), N3–Ca–O 104.88(5).

was found for Mg^{2+} in $[\eta^3\text{-HB}(3\text{-}^i\text{Phpz})_3]\text{MgEt}\cdot\text{THF}$.⁵ The THF in compound **3** can be removed by heating at 150 °C under vacuum giving a four-coordinate complex $[\eta^3\text{-HB}(3\text{-}^i\text{Bupz})_3]\text{Ca}(\text{O-2,6-}^i\text{Pr}_2\text{C}_6\text{H}_3)$, **5**,[‡] in quantitative yield (see Fig. 4). The $[\text{HB}(3\text{-}^i\text{Bupz})_3]\text{Ca}$ amide and aryl oxide compounds initiate and sustain the ring-opening polymerization of lactides. Indeed, compounds **2** and **5** are remarkably active for lactide polymerization, and both show stereoselectivity in the polymerization of *rac*-lactide to >90% heterotactic PLA (*isi* + *sis*) in THF at room temperature.^{7,8} The polymerization approaches 90% conversion in 1 min ($[\text{LA}]_0/[\mathbf{2}]_0 = 200$, $M_n = 37.8 \text{ kg mol}^{-1}$, PDI = 1.74 and $[\text{LA}]_0/[\mathbf{5}]_0 = 200$, $M_n = 40.1 \text{ kg mol}^{-1}$, PDI = 1.68) (see Fig. 5). Interestingly, the less bulky $[\eta^3\text{-HB}(3\text{-}^i\text{Prpz})_3]\text{CaN}(\text{SiMe}_3)_2\cdot\text{THF}$ shows no stereoselectivity under the same condition ($[\text{LA}]_0/[\mathbf{4}]_0 = 200$, 97% conversion in 1 min, $M_n = 64.0 \text{ kg mol}^{-1}$, PDI = 1.61).

In examining the relative reactivities of $[\text{HB}(3\text{-}^i\text{Bupz})_3]\text{M}$ complexes we note that under identical conditions 100 equiv. of LA are converted to >90% PLA at room temperature in 1 min

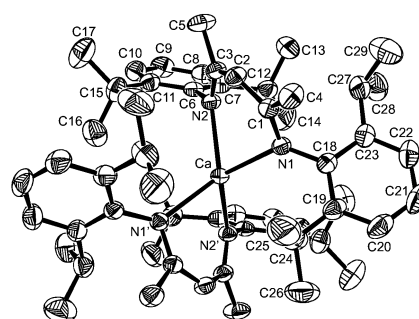
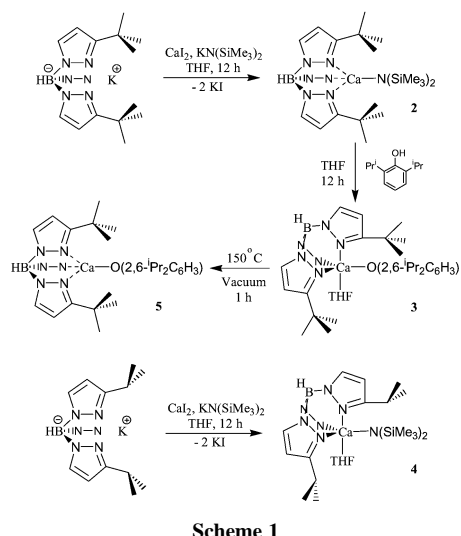


Fig. 2 An ORTEP drawing of CaL_2 with thermal ellipsoids drawn at the 50% probability level. Selected bond lengths (Å) and bond angles (°): Ca–N1 2.384(1), Ca–N2 2.377(1); N1–Ca–N2 83.08(4), N1–Ca–N1' 126.12(6), N1–Ca–N2' 123.26(4), N2–Ca–N1' 123.27(4).

† Electronic supplementary information (ESI) available: syntheses and characterization of compounds **1–5** and CaL_2 . See <http://www.rsc.org/suppdata/cc/b2/b208679d/>



Scheme 1

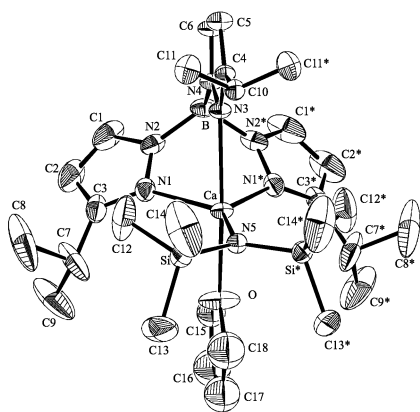


Fig. 3 An ORTEP drawing of $[\eta^3\text{-HB}(3\text{-Prpz})_3]\text{CaN}(\text{SiMe}_3)_2\cdot\text{THF}$, **4**, with thermal ellipsoids drawn at the 30% probability level.

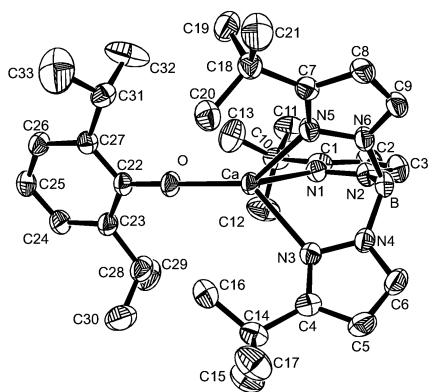


Fig. 4 An ORTEP drawing of $[\eta^3\text{-HB}(3\text{-Bupz})_3]\text{Ca}(\text{O}-2,6\text{-Pr}_2\text{C}_6\text{H}_3)$, **5**, with thermal ellipsoids drawn at the 50% probability level. Selected bond lengths (Å) and bond angles (°): Ca–N1 2.437(1), Ca–N3 2.426(1), Ca–N5 2.412(1), Ca–O 2.106(1); N1–Ca–N3 84.22(4), N1–Ca–N5 85.43(4), N1–Ca–O 120.48(4), N3–Ca–N5 79.84(4), N3–Ca–O 132.31(4), N5–Ca–O 136.79(4), Ca–O–C22 174.4(1).

for $M = \text{Ca}$, 1 h for $M = \text{Mg}$ and 6 days for $M = \text{Zn}$ which clearly defines the reactivity order $\text{Ca} > \text{Mg} > \text{Zn}$. Moreover, in competitive experiments where mixtures of $(\text{BDI})\text{M-N}(\text{SiMe}_3)_2$ were allowed to react with 1 equiv. of LA, we observed the same trend. When calcium and magnesium were both present effectively only the calcium amide reacted while

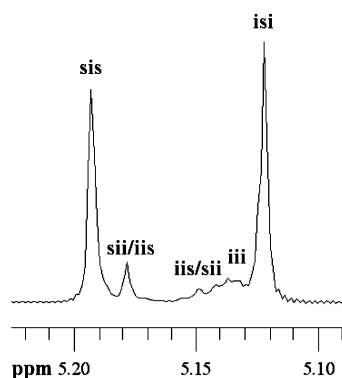


Fig. 5 ^1H NMR spectra (CDCl_3 , 400 MHz) of the homodecoupled CH resonance of poly(*rac*-lactide) prepared in THF using $[\eta^3\text{-HB}(3\text{-}^{13}\text{Bupz})_3](\text{O}-2,6\text{-}^{13}\text{Pr}_2\text{C}_6\text{H}_3)$.

for mixtures of magnesium and zinc, the magnesium reacted to the exclusion of the zinc amide which remained after consumption of LA.

In conclusion, we have discovered some interesting new coordination compounds of calcium and found that some of these are amongst the most active of all known coordination compounds in the ring-opening polymerization of lactides. Some fascinating comparisons within the coordination chemistry of Ca^{2+} , Mg^{2+} and Zn^{2+} are also to be noted. Further studies are in progress.

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Notes and references

‡ Crystal data: $\text{LCa}[\text{N}(\text{SiMe}_3)_2]\cdot\text{THF}$, **1**: $\text{C}_{42}\text{H}_{74}\text{CaN}_3\text{OSi}_2$, $M = 733.30$, triclinic, $P\bar{1}$, $a = 11.912(1)$, $b = 13.222(1)$, $c = 16.888(1)$ Å, $\alpha = 70.150(1)$, $\beta = 80.422(1)$, $\gamma = 63.507(1)^\circ$, $V = 2238.64(3)$ Å³, $T = 200$ K, $Z = 2$, $\mu = 0.226$ mm⁻¹, 47522 collected reflections, 10257 independent reflections, R indices (all data) $R = 0.0633$, $wR = 0.1362$. CCDC 192310.

CaL_2 : $\text{C}_{58}\text{H}_{82}\text{CaN}_4$, $M = 437.68$, monoclinic, $C2/c$, $a = 19.513(2)$, $b = 12.527(1)$, $c = 22.147(1)$ Å, $\beta = 100.280(1)^\circ$, $V = 5326.53(8)$ Å³, $T = 200$ K, $Z = 4$, $\mu = 0.157$ mm⁻¹, 46450 collected reflections, 6114 independent reflections, R indices (all data) $R = 0.0635$, $wR = 0.1317$. CCDC 192311.

$[\eta^3\text{-HB}(3\text{-Bupz})_3]\text{Ca}(\text{O}-2,6\text{-}^{13}\text{Pr}_2\text{C}_6\text{H}_3)$, **5**: $\text{C}_{33}\text{H}_{51}\text{BCaN}_6\text{O}$, $M = 598.69$, monoclinic, $P2_1/c$, $a = 15.177(1)$, $b = 11.737(1)$, $c = 20.885(2)$ Å, $\beta = 110.690(1)^\circ$, $V = 3480.34(5)$ Å³, $T = 200$ K, $Z = 4$, $\mu = 0.214$ mm⁻¹, 60025 collected reflections, 7975 independent reflections, R indices (all data) $R = 0.0542$, $wR = 0.1102$. CCDC 192309.

See <http://www.rsc.org/suppdata/cc/b2/b208679d/> for crystallographic data in CIF or other electronic format.

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