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Highly Active Magnesium Initiators for Ring-Opening Polymerization of *rac*-Lactide

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Polylactide (PLA) conveniently prepared by the ring-opening polymerization (ROP) of lactide (LA), a monomer from naturally renewable resources, has been of great interest over the past decades due to its biodegradable and biocompatible properties and the potential as an attractive alternative to petrochemically derived plastics.[1] Thereupon, developing well-defined metal catalysts which possess high activity and stereocontrol for the ROP of lactide has attracted significant attention of many research groups. Discrete complexes of aluminum,[2] rare earth metals,[3] zinc,[4] calcium,[5] magnesium,[6] and so on have been obtained and evaluated as initiators for the ring-opening polymerization of lactide. Among them, aluminum complexes with tetradentate Schiff base ligands display excellent isotactic stereospecificity in the ROP of *rac*-lactide.[2a−e] However, the obvious drawback is that the catalytic activities of these aluminum complexes are generally low.[2] In comparison with them, rare earth metal complexes are highly active for the ROP of *rac*-lactide, in some cases showing significant preference for a heterotactic dyad enchainment.[3b−e] Okuda et al. introduced some yttrium and lutetium complexes supported by 1,ω-dithiaalkanediyl-bridged bis(phenolato) ligands for *rac*-lactide polymerizations at a high initial monomer-to-catalyst ratio of 3000, and high conversions of monomer to PLA up to 93% could be reached within hours at ambient temperature.[3e] Zinc, calcium, and magnesium complexes are also active initiators for the ring-opening polymerization of lactide. The activities of these complexes are dependent on the structure of ligands to some extent. For instance, Hillmyer and Tolman reported the highly active zinc ethoxide complexes bearing amino-phenolate ligands, which initiated rapid polymerizations of *rac*-lactide when 1500 equiv of *rac*-lactide was adopted, yielding PLAs with M_n as large as 130 kg mol^{-1}.[4a] Recently, Carpentier and co-workers reported the complexes of zinc, calcium, and magnesium supported by a bulky bis(morpholinomethyl)phenoxy ligand.[7] Therein, the bis(morpholinomethyl)phenoxymagnesium complex is the first example of a magnesium-based complex capable of promoting an immortal ROP of L-LA ($[LA]_0$:$[Mg]_0$:$[{}^iPrOH]_0$ = 1000:1:10) on such a large scale while maintaining an extremely high catalytic activity (TOF = 18 900 h^{-1}). The corresponding calcium complex nearly quantitatively polymerized 500 equiv of L-LA within 1 min upon addition of 10 equiv of isopropanol with TOF of 28 200 h^{-1}, which becomes one of the most active metal-based catalytic systems known to date for the ROP of lactide.[7] A literature survey indicated that a few cases of PLA obtained by highly active metal catalysts have been reported. With the aim to design and synthesize highly active initiators of biocompatible metals for the ROP of *rac*-lactide, we obtained a series of magnesium silyamido complexes supported by monoanionic aminophenolato ligands, which display extraordinarily high activity for the ring-opening polymerization of *rac*-lactide.

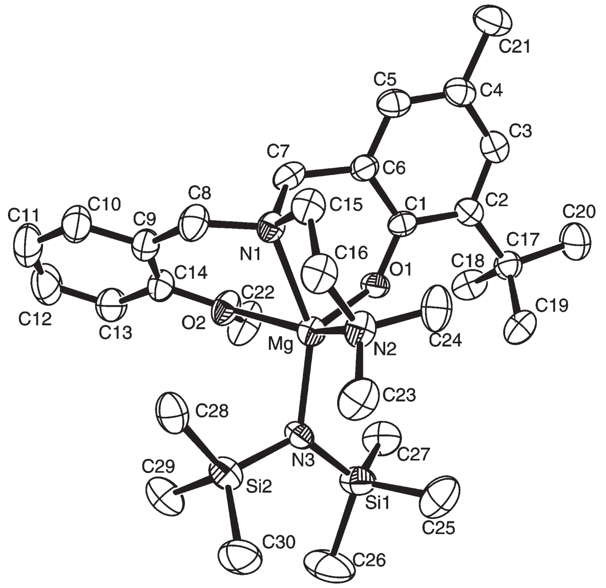
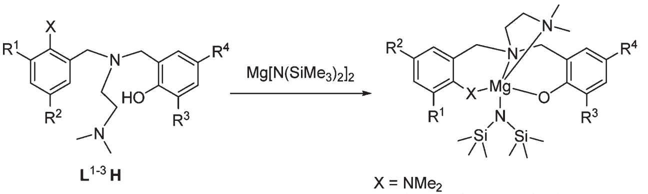


Figure 1. ORTEP diagram of the molecular structure of $[(\mathbf{L^2})MgN(SiMe_3)_2]$ (**2**). Thermal ellipsoids are drawn at the 30% probability level. Hydrogen atoms are omitted for clarity. Selected bond distances (Å) and angles (deg): Mg−N1 2.270(3), Mg−N2 2.293(3), Mg−N3 2.047(2), Mg−O1 1.926(2), Mg−O2 2.253(3); N3−Mg−O1 117.80(10), N3−Mg−O2 91.92(11), N3−Mg−N1 150.10(11), N3−Mg−N2 100.74(12), O1−Mg−N1 90.58(10), O1−Mg−O2 92.19(10), O1−Mg−N2 105.84(11), N1−Mg−N2 78.47(11), N1−Mg−O2 76.85(10), N2−Mg−O2 149.44(10).

Scheme 1



X = NMe_2
1: R^1 = H, R^2 = Me, R^3 = ${}^tBu$, R^4 = Me
X = OMe
2: R^1 = R^2 = H, R^3 = ${}^tBu$, R^4 = Me
3: R^1 = ${}^tBu$, R^2 = Me , R^3 = R^4 = Cumyl

Reactions between an equimolar amount of ligands $\mathbf{L^{1-3}H}$ and $Mg[N(SiMe_3)_2]_2$ in toluene at room temperature afforded magnesium complexes **1**−**3** in 78−87% isolated yields via the elimination of amine (Scheme 1). All the magnesium complexes **1**−**3** are air/moisture-sensitive colorless crystalline solids and show moderate to good solubility in aromatic hydrocarbon solvents.

Single crystals of **2** suitable for X-ray diffraction studies were obtained by slightly cooling the saturated toluene solution. As depicted in Figure 1, complex **2** has a monomeric structure in the solid state, in which the magnesium atom is five-coordinate by four donors of the tetradentate ONNN ligand and one silylamido group adopting a distorted trigonal-bipyramidal geometry around the magnesium center.

To date, a few examples of magnesium amides have been described as successful catalysts for the ROP of lactide.[8] Nevertheless, the magnesium silylamido complexes **1**−**3** exhibit remarkable activities in the ring-opening polymerization of *rac*-lactide. For instance, the

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Table 1. Ring-Opening Polymerization of *rac*-Lactide Initiated by Magnesium Complexes 1−3[a]

run	cat.	$[LA]_0/[Mg]_0/[^iPrOH]_0$	time (min)	conv[b] (%)	TOF (h^{-1})	$M_{n,calcd}$[c] ($\times 10^4$)	M_η[d] ($\times 10^4$)	M_n[e] ($\times 10^4$)	M_w/M_n[e]	P_m[f]
1	**1**	5000:1:0[g]	10	94	28080	67.5	43.3	50.8	1.74	0.59
2		10000:1:0	15	91	36560	131.7	36.6	41.4	1.28	0.58
3		200:1:1	1	91	10920	2.6	2.8	2.3	1.56	0.57
4		2500:1:1[h]	7	91	19392	32.6	35.4	32.5	1.26	0.55
5		5000:1:2[g]	2	91	135750	32.6	18.2	22.3	1.54	0.59
6		10000:1:1	5	84	101040	121.4	37.2	53.1	1.23	0.57
7	**2**	10000:1:0	10	79	47640	114.4	46.2	42.7	1.61	0.55
8		10000:1:0[i]	5	72	86880	104.4	31.2	27.6	1.72	0.54
9		200:1:1	2	90	5400	2.6	2.4	2.4	1.53	0.56
10		10000:1:1	6	95	95200	137.2	39.2	20.5	1.80	0.55
11	**3**	200:1:0[j]	1440	8	1	0.2	*nd.*	*nd.*	*nd.*	0.59
12		10000:1:0	20	95	28470	136.8	26.2	22.34	1.92	0.59
13		200:1:1	2	89	5370	2.6	2.2	2.3	1.65	0.60
14		200:1:1[j]	50	24	57	0.7	*nd.*	*nd.*	*nd.*	0.65
15		10000:1:1	6	69	68700	99.0	15.3	21.30	1.76	0.60
16	**4**[k]	200:1:1	3	15	1740	0.4				
17		200:1:2	3	94	3748	1.4				0.56
18		10000:1:2	5	4	4560	2.9				0.56

[a] In toluene, at 25 ± 1 °C, $[rac\text{-}LA]_0 = 1.0$ M. [b] Determined by ^1H NMR spectroscopy. [c] $M_{n,calcd} = ([rac\text{-}LA]_0/[Mg]_0) \times 144.13 \times$ conv (%); with addition of ^iPrOH, $M_{n,calcd} = ([rac\text{-}LA]_0/[^iPrOH]_0) \times 144.13 \times$ conv (%) + 60. [d] Intrinsic viscosity was determined in chloroform at 25 °C and the molecular weight was calculated using the relation $[\eta] = 2.21 \times 10^{-4} M_\eta^{0.77}$. [e] Determined by GPC. [f] P_m is the probability of forming a new *m*-dyad, determined by homonuclear decoupled ^1H NMR spectroscopy. [g] $[rac\text{-}LA]_0 = 0.5$ M. [h] $[rac\text{-}LA]_0 = 0.25$ M, at 20 °C. [i] Melt polymerization at 110 °C. [j] At −39 °C, no enough sample available for intrinsic viscosity and GPC measurements. [k] **4** = $Mg[(N(SiMe_3)_2]_2$.

ROP of 5000 equiv of *rac*-LA in toluene at ambient temperature was efficiently promoted by **1** within 10 min, and the value of turnover frequency (TOF) reached 28 080 h^{-1} ($[\mathbf{1}]_0 = 0.1$ mM). Complex **1** was able to polymerize up to 10 000 equiv of *rac*-lactide ($[rac\text{-}LA]_0 = 1.0$ M) with corresponding TOF value of 36 560 h^{-1} and produced PLA with M_n as high as 4.14×10^5 g mol^{-1} and a relatively narrow PDI value of 1.28. Upon addition of isopropanol, the activities of magnesium complexes **1**−**3** are increased significantly. Taking complex **1** as an example, a high conversion of monomer to PLA up to 90.5% could be reached just within 2 min when a large molar ratio of $[rac\text{-}LA]_0:[\mathbf{1}]_0:[^iPrOH]_0 = 5000:1:2$ ($[\mathbf{1}]_0 = 0.1$ mM) was adopted. The corresponding TOF value of 135 750 h^{-1} was 5-fold higher than that of the most active metal-based catalytic system reported in the literature by far.[7] For 10 000 equiv of *rac*-lactide ($[rac\text{-}LA]_0 = 1.0$ M), in the presence of 1 equiv of isopropanol, the polymerization initiated by complex **1** still proceeded extremely fast to 84% within 5 min (TOF = 101 040 h^{-1}) in a controlled fashion, affording PLA with $M_n = 5.31 \times 10^5$ g mol^{-1} and a narrow PDI = 1.23 (run 6). Fast polymerization could also be initiated by magnesium silylamido complexes **2** and **3**, when 10 000 equiv of *rac*-lactide was added. In particularly, under melt polymerization condition (110 °C), TOF of 86 880 h^{-1} was obtained when using **2** as an initiator alone. Complex **3** with both bulky cumyl and *tert*-butyl groups exhibits the lowest catalytic activity for the polymerization of *rac*-lactide among them. To exclude the possibility that the high activities of magnesium complexes **1**−**3** might be attributed to "$Mg(O^iPr)_2$" generated possibly by the decomposition reaction of these complexes with isopropanol, controlled polymerizations of *rac*-lactide by $Mg[N(SiMe_3)_2]_2$ in the presence of 1 and 2 equiv of ^iPrOH were carried out, which however only displayed very low activities in comparison with those of complexes **1**−**3** (runs 16−18), giving a strong support for the superiority of these magnesium complexes.

Preliminary kinetic studies of the polymerization of *rac*-lactide initiated by complex **1** in the presence of 1 equiv of isopropanol in toluene indicated a first-order dependence on the monomer concentration with $k_{obs} = 5.74 \times 10^{-3}$ s^{-1} ($[\mathbf{1}]_0 = 0.1$ mM, Figure S1). Meanwhile, as depicted in Figure 2, the molecular weight of the polymer increases linearly with conversion of monomer, indicating a controlled polymerization. To obtain some insight into the active species, less active complex **2** was chose to study the NMR scale polymerization of *rac*-lactide in the presence of isopropanol ($[rac\text{-}LA]_0:[\mathbf{2}]_0:[^iPrOH]_0 = 40:1:1$). The polymerization started instantaneously, and active oligomers end-capped with isopropoxy group could be identified (Figure S2); no free proligand $\mathbf{L^2H}$ was observed, suggesting the *in situ* formation of "$(\mathbf{L^2})Mg(O^iPr)$" species which sequentially initiated the polymerization.

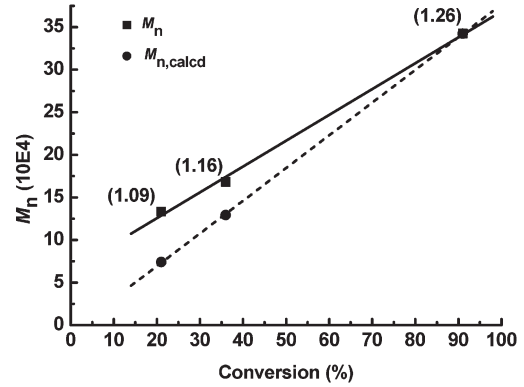

Figure 2. Linear relationship between M_n and monomer conversion of *rac*-lactide polymerization initiated by complex $\mathbf{1}/^iPrOH$ ($[rac\text{-}LA]_0 = 0.25$ M, $[rac\text{-}LA]_0:[\mathbf{1}]_0:[^iPrOH]_0 = 2500:1:1$, 20 °C, in toluene; with PDI values in parentheses).

As shown in Table 1, atactic PLAs with slightly isotactic-enriched microstructure were obtained by magnesium complexes **1**−**3**. Complex **3** with steric demanding cumyl groups showed certain preference for an isotactic dyad enchainment during lactide polymerization when 1 equiv of isopropanol was added ($P_m = 0.60$). Upon cooling the reaction mixture to −39 °C, P_m could be improved to 0.65. Although PLAs with high molecular weight were obtained under the adopted polymerization conditions, the M_n and M_η values deviate from the calculated ones to some extent when large monomer-to-catalyst ratios were adopted; most likely the increased amount of impurities in large molar ratio of lactide acted as chain transfer reagents during the polymerization process and led to the decrease of the molecular weights of resultant PLAs.

In conclusion, monomeric magnesium silylamido complexes **1**−**3** showed excellent catalytic activities for the ring-opening polymerization of *rac*-lactide at ambient temperature. 10 000 equiv of *rac*-lactide could be polymerized to high conversions within minutes using complexes **1**–**3** as initiators and produce high molecular weight polymers. Further study is still ongoing to expand this system and develop new initiators exhibiting higher stereocontrol.

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Supporting Information Available: Crystallographic data for **2** as a cif file, syntheses and characterization of complexes **1**–**3** and ligands ($\mathbf{L^{1-3}H}$), the plot of ln([*rac*-LA]$_0$/[*rac*-LA]$_t$) vs time using complex **1** as initiator for *rac*-lactide polymerization, ^{1}H NMR spectrum of active PLA oligomer by **2**/^{i}PrOH, and homonuclear decoupled ^{1}H NMR spectrum of PLA by complex **3**. This material is available free of charge via the Internet at http://pubs.acs.org.

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