Efficient Bulky Organo-Zinc Scorpionates for the Stereoselective Production of Poly(rac-lactide)s

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Abstract: The direct reaction of the highly sterically demanding acetamidinate-based NNN’-scorpionate protioligand Hphpb’amd [Hphpb’amd = N,N’-di-p-tolylbis(3,5-di-tertbutylpyrazole-1-yl)acetamidine] with one equiv. of ZnMe₂ proceeds in high yield to the mononuclear alkyl zinc complex [ZnMe(κ³-phpb’amd)] (1). Alternatively, the treatment of the corresponding lithium precursor [Li(phpb’amd) (THF)] with ZnCl₂ yielded the halide complex [ZnCl(κ³-phbptamd)] (2). The X-ray crystal structure of 1 confirmed unambiguously a mononuclear entity in these complexes, with the zinc centre arranged with a pseudotetrahedral environment and the scorpionate ligand in a κ³-coordination mode. Interestingly, the inexpensive, low-toxic and easily prepared complexes 1 and 2 resulted in highly efficient catalysts for the ring-opening polymerisation of lactides, a sustainable bio-resourced process industrially demanded. Thus, complex 1 behaved as a single-component robust initiator for the living and immortal ROP of rac-lactide under very mild conditions after a few hours, reaching a TOF value up to 5520 h⁻¹ under bulk conditions. Preliminary kinetic studies revealed apparent zero-order dependence on monomer concentration in the absence of a cocatalyst. The PLA materials produced exhibited narrow dispersity values, good agreement between the experimental M₀ values and monomer/benzyl alcohol ratios, as well as enhanced levels of heteroselectivity, reaching Pₙ values up to 0.74.

Keywords: homogenous catalysis; zinc scorpionates; rac-lactide; heterotactic poly(rac-lactide)

1. Introduction

The rational use of natural resources and the efficient management of waste materials represent two of the most important challenges in this century [1,2] for the sustainability of our planet, in accordance with the “Twelve Principles of Green Chemistry” [3].

Poly(lactide) (PLA) [4–6] is an annually biorenewable material that has attracted great attention [7–14] as a result of the important concerns about the depletion of fossil-fuel feedstocks along with the environment waste-derived problems. PLAs can be obtained through the ring-opening polymerisation (ROP) of the biosourced cyclic ester of lactide (LA), by employing efficient metal-based initiators. This process offers excellent control of molecular weight, molecular-weight distribution and stereoselectivity in the growing polymer chains (see Chart 1). Particularly, the production of this top commercial material is annually increasing, and it now represents close to 7% of the total bioplastics produced worldwide [15], since PLAs find multiple biomedical and pharmaceutical applications, including the controlled release of drugs [16,17], regenerative medicine [18] and wound healing [19], as well as in packaging and agriculture as a real alternative to conventional commodity thermoplastics [20,21].
Representative achiral zinc-based catalysts for the synthesis of hetero-enriched poly(lactide)s via the ROP of rac-lactide mediated by steroselective metal-based catalysts.

In this context, biologically benign metal-based catalysts are of great interest for the production of this bioassimilable material, with calcium [22–25], magnesium [26–29] and zinc [30–35] (see Chart 2), as the most representative centres, although other metals from group 13 (aluminium [36] and indium [37]), group 4 [38], as well as rare earth [39] metals, have been also successfully described, all of them supported by a wide variety of ancillary ligands. These examples constitute a much greener alternative to the toxic industrially employed tin(II) 2-ethylhexanoate, which, despite its robustness, offers poor control of polymer parameters [40].

![Chart 1. Preparation of hetero- and isotactic poly(lactide)s via the ROP of rac-lactide mediated by steroselective metal-based catalysts.](image)

**Previous works**

- 1 mol%, 60°C, 2 min., Conv. = 99%, P_i = 0.54
  - Macromolecules 2020
- 0.1 mol%, 25°C, 29 s, Conv. = 97%, P_i = n.d.
  - Angew. Chem., Int. Ed. 2016
- 0.15 mol%, 25°C, 5 min., Conv. = 96%, P_i = n.d.
  - J. Am. Chem. Soc. 2003
- 0.5 mol%, 20°C, 20 min., Conv. = 97%, P_i = 0.94
  - J. Am. Chem. Soc. 2001

**This work**

- 1 mol%, 50°C, 3.75 h, Conv. = 95%, P_i = 0.74
- 1 mol%, 125°C, TOF = 5.520 h⁻¹, P_i = 0.68

![Chart 2. Representative achiral zinc-based catalysts for the synthesis of hetero-enriched poly(rac-lactide)s.](image)

Particularly, our research group has successfully reported over the last few years a series of well-defined mono- and multinuclear organo-zinc [41–46] scorpionate complexes as efficient one-component initiators for the living ROP of cyclic esters [47], and significant levels of isotacticity (P_i = 0.77 [44,45]–0.88 [41]) have been successfully attained.

On the bases of our previous expertise [41–46], now we endeavour to develop a series of inexpensive, low-toxic and easy-to-prepare zinc-based catalysts that are very efficient and selective in this industrially-demanded process. For this propose, a very successful sterically hindered acetamidinate-based NNN'-scorpionate [48] from our extended ligand library [48–50] has been employed.
Hereby the preparation of novel mononuclear zinc complexes supported by a sterically hindered scorpionate is reported. These complexes behave as single-component initiators for the living and immortal ROP of rac-lactide to produce stereoselectively poly(rac-lactide)s with enhanced degrees of heterotacticity.

2. Materials and Methods

2.1. Materials

All manipulations were carried out under a nitrogen atmosphere using standard Schlenk techniques or a glovebox. Solvents were predried over sodium wire and distilled under nitrogen from sodium (toluene and n-hexane) or sodium-benzophenone (THF and diethyl ether). Deuterated solvents were stored over activated 4 Å molecular sieves and degassed by several freeze–thaw cycles. The protioligand Hphbptamd was prepared according to the procedures in the literature [48]. ZnMe$_2$ (Sigma-Aldrich, Munich, Germany) was used as purchased and ZnCl$_2$ (Sigma-Aldrich, Munich, Germany) was predried by several heat toluene suspension-vacuo cycles before use. rac-lactide (Sigma-Aldrich, Munich, Germany) was sublimed twice, recrystallised from THF, and finally sublimed again prior to use.

2.2. Experimental

2.2.1. Nuclear Magnetic Resonance Spectroscopy (NMR)

The NMR spectra of complexes were recorded on a Varian Inova FT-500 spectrometer and were referenced to the residual deuterated solvent signal. $^1$H NMR homodecoupled and NOESY-1D spectra were recorded on the same instrument with the following acquisition parameters: irradiation time 2 s and 256 scans, using standard VARIAN-FT software. Furthermore, 2D NMR spectra were acquired using the same software and processed using an IPC-Sun computer.

The microstructures of PLA samples were determined by examination of the methine region in the homodecoupled $^1$H NMR spectrum of the polymers recorded at room temperature in CDCl$_3$ with concentrations in the range 1.0 to 2.0 mg/mL.

2.2.2. Elemental Analysis

Microanalyses were performed with a Perkin-Elmer 2400 CHN analyser (Perkin Elmer, Inc., Waltham, MA, USA).

2.2.3. Gel Permeation Chromatography (GPC)

The molecular weights ($M_n$) and the molecular-mass distributions ($M_w/M_n$) of polymer samples were measured by gel permeation chromatography (GPC) performed on a Shimadzu LC-20AD GPC equipped with a TSK-GEL G3000Hxl column and an ELSD-LTII light-scattering detector (Shimadzu Corporation, Kyoto, Japan). The GPC column was eluted with THF at 40 °C at 1 mL/min and was calibrated using eight monodisperse polystyrene standards in the range 580–483,000 Da.

2.2.4. MALDI-TOF Mass Spectrometry

MALDI-ToF MS data were acquired with a Bruker ULTRAFLEX III ToF/ToF spectrometer (Bruker, Billerica, MA, USA), using a Nd:YAG laser source (355 nm) in reflector mode with a positive acceleration voltage of 25 kV. Samples were prepared as follows: PLA was dissolved in dichloromethane 1.5 mg/mL and mixed with matrix (DCTB 10 mg/mL in dichloromethane) and NaI (2 mg/mL in acetone) in a 20:5:0.5 ratio (matrix:sample:NaI). Before evaporation, 0.5 mL of the mixture solution was deposited on the sample plate. External calibration was performed using Peptide Calibration Standard II + ACTH clip 7–38, ACTH clip 1–39 + INSULINE (covered mass range: 1000–7000 Da).
2.2.5. Crystallographic Refinement and Structure Solution

Crystals suitable for X-ray diffraction were obtained for 1. The crystals were selected under oil and attached to the tip of a nylon loop. The crystals were mounted in a stream of cold nitrogen at 240–250 K and centred in the X-ray beam. A single crystal of 1 was measured at 100 K with a Bruker Kappa Apex II system, with graphite-monochromated Mo Kα radiation (λ = 0.71073 Å) from conventional sealed tubes. The initial cell constants were obtained from three series of scans at different starting angles. The reflections were successfully indexed by an automated indexing routine built into the SAINT program [51]. The absorption correction was based on fitting a function to the empirical transmission surface as sampled by multiple equivalent measurements [52]. A successful solution using the direct methods [53] provided most non-hydrogen atoms from the E-map. The remaining non-hydrogen atoms were located in an alternating series of least-squares cycles and difference Fourier maps. All non-hydrogen atoms were refined with anisotropic displacement coefficients unless specified otherwise. All hydrogen atoms were included in the structure factor calculation at idealised positions and were allowed to ride on the neighbouring atoms with relative isotropic displacement coefficients.

Final R(F), wR(F2), and goodness-of-fit agreement factors, details on the data collection, and analysis for 1 can be found in Table S1 in the Supporting Information.

2.3. General Procedures

2.3.1. Preparation of Compounds 1–2

Synthesis of [ZnCl(κ3-phbpamd)] (1). In a 100 mL Schlenk tube, pbp5amd-H (1.00 g, 1.68 mmol) was dissolved in dry n-hexane (25 mL) and cooled to −70 °C. A solution of ZnMe2 (1.2 M in toluene) (1.40 mL, 1.68 mmol) was added and the mixture was allowed to warm up to room temperature and stirred for 2 h. After concentration and being cooled at −26 °C, compound 1 was obtained as colorless crystals. Yield: 0.91 g, 80%. Anal. Calcd. for C39H56N6Zn: C, 69.47; H, 8.37; N, 12.10. Found: C, 69.50; H, 8.39; N, 12.51.

Synthesis of [ZnCl(k3-phbpamd)] (2). In a 100 mL Schlenk tube, Hpbp5amd (1.00 g, 1.68 mmol) was dissolved in dry tetrahydrofuran (25 mL) and cooled to −70 °C. A solution of n-BuLi (2.5 M in hexane) (0.67 mL, 1.68 mmol) was added to the mixture, and it was allowed to warm up to room temperature and stirred for 30 min. A solution of ZnCl2 (0.23 g, 1.68 mmol) in dry tetrahydrofuran (25 mL) was added dropwise to the previous cooled mixture, and the reaction mixture was stirred for 2 h. The solvent was removed in vacuo and extracted with toluene (25 mL), and the resulting solution was concentrated ca. 10 mL and was cooled at −26 °C to give compound 2 as a white semicrystalline solid. Yield: 0.94 g, 80%. Anal. Calcd. for C38H53ClN6Zn: C, 65.70; H, 7.69; N, 12.10. Found: C, 65.81; H, 7.75; N, 12.15. 1H-NMR (CDCl3, 297 K), δ 7.66 (s, 1 H, CH), 6.53 (d, 3)H-H = 8 Hz, 6 H, Ar-H), 6.24 (d, 3)H-H = 8.2 Hz, 2 H, Ar-H), 6.08 (s, 2H, H-H), 2.04 (s, 3 H, N’C6H4Me), 2.01 (s, 3 H, N’C6H4Me), 1.56 (s, 1 H, CBu3), 1.43 (s, 1 H, CBu3), 1.33–0.66 (m, 9 H, CBu3), 13C{1H}-NMR (CDCl3, 297 K), δ 164.4 (C6), 159.5, 154.4 (C5, C5′, C5′′), 147.6–121.9 (N’C6H4Me), 103.4 (C4), 77.1 (C3), 32.6 (tBu3), 32.5 (tBu3), 31.05 (tBu5), 30.30 (tBu5), 20.8 (N’C6H4Me), 20.7 (N’C6H4Me).

2.3.2. Typical Polymerisation Procedures

The polymerisation of rac-lactide (LA) was performed on a Schlenk line in a flame-dried Schlenk tube equipped with a magnetic stirrer. The Schlenk tubes were charged in a glovebox with the required amount of LA and initiator, separately, and then attached to the vacuum line. The initiator and LA were dissolved in the appropriate amount of solvent and temperature equilibration was ensured in both Schlenk tubes by stirring the
solutions for 15 min in a bath. Under immortal conditions, the corresponding equiv of 
BnOH (benzyl alcohol as cocatalyst, stock solution) were also included in the LA Schlenk 
flask solution. Next, the appropriate amount of initiator was added by using a syringe, and 
polymerisation times were measured from that point. Polymerisations were stopped by 
injecting a solution of acetic acid in water (0.35 M). Polymers were precipitated in methanol, 
filtered off, redissolved, and reprecipitated in methanol, and dried in vacuo to a constant 
weight. All kinetics experiments were repeated at least twice and were mutually consistent.

3. Results

3.1. Synthesis and Characterisation of NNN'-Scorpionate Alkyl and Chloride Zinc Complexes 1 and 2

The high sterically demanding acetamidinate-based scorpionate protioligand 
Hphbp'amd [48] \([Hphbp'amd = N,N''-di-p-tolylbis(3,5-di-tertbutylpyrazole-1-yl)acetamidine]\) was initially reacted with one equivalent of ZnMe₂ in toluene at room temperature. This 
reaction cleanly afforded the mononuclear amidinate-based scorpionate zinc complex 
\([\text{ZnMe}(\kappa^3\text{-phbp'amd})] \) 1, a white solid in good yield (ca. 80%) (see Scheme 1a).

Scheme 1. Preparation of the acetamidinate-based NNN'-scorpionate zinc complexes 1 and 2.
Alternatively, we considered it very interesting to prepare a halide derivative analog to 1, since diverse M-halide species have been also described as efficient catalysts for the ROP of lactides [54–57]. Thus, the treatment of the protioligand Hphbp'amd with nBuLi in thf at 0 °C afforded the scorpionate lithium salt [Li(phbp'amd)(THF)] [58] [phbp'amd = N,N'-di-p-tolylbis(3,5-di-tert-butylpyrazole-1-yl)acetamidinate], and subsequent reaction with ZnCl$_2$ yielded the halide complex [ZnCl($\kappa^3$-phbp'amd)]$_2$, a yellow pale solid in good yield (ca. 80%) (see Scheme 1b). Compounds 1 and 2 are stable to the air and moisture for 5 h and 24 h, respectively, but complex 1 readily decomposed when dissolved in dichloromethane, possibly through a protonolysis reaction.

Interestingly, attempts to activate the bridging C–H group by the addition to complex 1 of a second equivalent of ZnMe$_2$ to prepare potentially more active bimetallic catalysts through an intramolecular cooperative mechanism were fruitless, in contrast to the behaviour previously observed in our group for the preparation of homobimetallic complexes containing other metals and bearing lower sterically demanded scorpionates [58,59].

The $^1$H and $^{13}$C ($^1$H) NMR spectra of 1 and 2 in benzene-d$_6$ at room temperature show similar patterns. The spectra show one sets of resonances for the $^1$Bu$^{3,5}$ and H$^4$ in the sterically hindered pyrazole rings, one signal for the CH group and two different signals for the acetamidinate fragment, which are in agreement with a monodentate binding for the acetamidinate moiety (see Scheme 1). Additionally, one signal at negative chemical shift appears for the Zn-alkyl group in complex 1 (see Figures S1 and S2 in the SI). In addition, the signals for C$^4$, $^1$Bu$^{1,2}$ in the pyrazole rings, as well as for the 4-MePh amidinate substituents were assigned by $^1$H–$^{13}$C heteronuclear correlations (g-HSQC). The proposed structures for the acetamidinate complexes 1 and 2 were further confirmed by the X-ray molecular analysis (see below Figure 1).

Figure 1. ORTEP view of [ZnMe($\kappa^3$-phbp'amd)] 1. Hydrogen atoms have been omitted for clarity. Thermal ellipsoids are drawn at the 30% probability level.
Single crystals of complex 1 suitable for X-ray diffraction were easily grown from a toluene solution at –26 °C. The molecular structure is depicted in Figure 1. Selected bond lengths and angles are collected in Table 1, and the crystallographic details are reported in Table S1 in the SI. The molecular structure of 1 consists of a monomeric arrangement in the solid state. The zinc metal exhibits a distorted tetrahedral geometry, with the scorpionate ligand in a $κ^3$-NNN’ coordination mode. The N(1)–Zn and N(3)–Zn bond lengths [2.167(5) Å and 2.135(5) Å] are well balanced and compare well with that observed in the analog acetamidinate-based scorpionate zinc alkyls [48] but are considerably longer than the N(5)–Zn bond length [2.034(5) Å]. The solid-state structure also confirms that the acetamidinate is coordinated in a monodentate fashion with the Zn atom, and delocalisation is also evidenced in the N–C–N moiety of the acetamidinate, with the bond lengths C(24)–N(6) and C(24)–N(5) ranging from 1.351(8) Å to 1.295(8) Å. An analog crystal structure of complex 2 has been previously reported by our group [48].

### Table 1. Selected bond lengths (Å) and angles (°) for 1.

| Distances (Å)       | Angles (°)       |
|--------------------|-----------------|
| N(1)-Zn(1)         | 1.970 (7)       |
| C(39)-Zn(1)-N(5)   | 128.2 (2)       |
| N(3)-Zn(1)        | 2.135 (5)       |
| C(39)-Zn(1)-N(3)   | 125.8 (2)       |
| N(5)-Zn(1)        | 2.034 (5)       |
| C(39)-Zn(1)-N(1)   | 90.8 (2)        |
| C(39)-Zn(1)-N(5)   | 124.2 (2)       |
| N(5)-Zn(1)-N(1)    | 91.76 (18)      |
| C(24)-N(6)        | 1.295 (8)       |
| N(5)-Zn(1)-N(5)    | 83.00 (18)      |
| C(24)-N(5)        | 1.351 (8)       |
| C(23)-C(24)       | 1.540 (8)       |
| N(6)-C(24)-N(5)   | 135.5 (6)       |
| N(6)-C(24)-C(23)  | 110.3 (5)       |
| N(5)-C(24)-C(23)  | 114.1 (5)       |
| N(2)-C(23)-N(4)   | 110.6 (4)       |
| N(2)-C(23)-C(24)  | 114.9 (5)       |
| N(4)-C(23)-C(24)  | 106.7 (4)       |

### 3.2. Catalytic Studies on the ROP of rac-LA for the Production of Poly(rac-lactide) 3

These first studies were aimed at comparing the activity and stereoselectivity of these new mononuclear high sterically hindered acetamidinate-based initiators 1 and 2 with analog scorpionate zinc alkyls [41–46] and other remarkable dinuclear [30–35] and mononuclear [60–64] organo-zinc initiators reported to date in the ROP of rac-LA.

Thus, complexes 1 and 2 were systematically assessed in the ring-opening polymerisation (ROP) of the polar monomer rac-lactide (rac-LA) at 40–60 °C in tetrahydrofuran, toluene, and dichoromethane as solvents and, in bulk conditions (125 °C), under a nitrogen atmosphere for the production of poly(rac-lactide) (PLA) 3 (see Scheme 2 and Table 2). The experimental medium-low $M_n$ values of the PLAs produced were determined by size exclusion chromatography (SEC) using the Mark–Houwink corrections [65,66] and showed good agreement with the expected theoretical calculated values considering one growing polymer chain per zinc centre (see Table 2). In addition, examination of the resulting polyesters revealed a monomodal weight distribution, with narrow dispersity values ranging from 1.05 to 1.35 (see Figure S3 in the SI).

![Scheme 2. ROP of rac-lactide for the production of poly(rac-lactide) 3 catalysed by complexes [ZnMe($κ^3$-phbp'amd)] 1 and [ZnCl($κ^3$-phbp'amd)] 2.](image-url)
Table 2. Polymerisation of rac-lactide catalysed by initiators 1 and 2.

| Entry | Initiator | Temp (°C) | Time (h) | Yield (g) | Conv (%) | \(M_n\) (Da) | \(M_n\) (Da) | \(M_w/M_n\) | \(P_0^*\) |
|-------|-----------|-----------|----------|-----------|-----------|----------------|----------------|----------------|----------|
| 1     | 1         | 50        | 1        | 0.17      | 13        | 1900           | 2500            | 1.05           | 0.74     |
| 2     | 1         | 50        | 2        | 0.35      | 27        | 3900           | 4800            | 1.09           | 0.73     |
| 3     | 1         | 50        | 3        | 0.90      | 70        | 10,100         | 10,400          | 1.12           | 0.74     |
| 4     | 1         | 50        | 3.75     | 1.23      | 95        | 13,700         | 13,000          | 1.13           | 0.74     |
| 5     | 2         | 60        | 6        | 0.67      | 52        | 7500           | 7200            | 1.12           | 0.72     |
| 6     | 1 + HOBN (1:5) | 50 | 1      | 0.78      | 60        | 1700           | 1900            | 1.08           | ND       |
| 7     | 1 \(^{\text{i}}\) | 50 | 7.5     | 2.41      | 93        | 26,800         | 25,200          | 1.12           | ND       |
| 8     | 1 \(^{\text{g}}\) | 40 | 24      | —         | traces    | —              | —               | —              | —        |
| 9     | 1 \(^{\text{g}}\) | 50 | 8      | 0.25      | 19        | 2700           | 3100            | 1.06           | ND       |
| 10    | 1 \(^{\text{h}}\) | 125 | 1 min | 1.19      | 92        | 13,200         | 12,600          | 1.28           | 0.68     |
| 11    | 2 \(^{\text{h}}\) | 125 | 2 min | 0.76      | 59        | 8500           | 9100            | 1.29           | 0.67     |
| 12    | 1 \(^{\text{i}}\) | 125 | 5 min  | 0.54      | 42        | 6000           | 6400            | 1.35           | —        |
| 13    | [Zn(Et)(tbptamd)] \(^{\text{i}}\), [46] | 110 | 48 | 0.81 | 63 | 9100 | 8700 | 1.11 | 0.68 |
| 14    | [Zn(Me)(bpzampe)] \(^{\text{i}}\), [42] | 20 | 4 | 1.10 | 85 | 12,200 | 12,300 | 1.15 | 0.62 |
| 15    | [Zn(CH\(3\)SiMe\(3\))(R,R)-bpzmm)] \(^{\text{i}}\), [46] | 50 | 3.5 | 0.94 | 73 | 10,500 | 10,600 | 1.08 | 0.77 |

\(a\) Polymerisation conditions: (a) 90 \(\mu\)mol of initiator, [rac-LA]_0/[Zn] = 100 and 10 mL of tetrahydrofuran as solvent. \(b\) Percentage conversion of the monomer ([weight of polymer recovered/weight of monomer] × 100). \(c\) Theoretical \(M_n\) = (monomer/initiator) × (% conversion) × \(M_n\) of lactide. \(d\) Determined by GPC relative to polystyrene standards in tetrahydrofuran. Experimental \(M_n\) was calculated considering Mark–Houwink’s corrections [65,66] for \(M_n\) (obsd.) = 0.58 × \(M_n\) (GPC). \(e\) \(P_0^*\) is the probability of racemic linkages between monomer units and is determined from the relative intensity in the tetrads obtained in the decoupled 1H NMR by \(P_0 = 2I_1/(I_1 + I_2)\), with \(I_1 = \delta 5.20–5.25\) ppm (\(\text{iii, iii, ii}^\prime\) and \(I_2 = \delta 5.13–5.20\) ppm (\(\text{ii}^\prime, \text{ii, iii}\)) [68]. \(f\) Double-feed experiment; additional injection of 100 equiv after 3.75 h. \(g\) 25 mL of toluene as solvent. \(h\) Melt rac-LA monomer at 125 °C in the absence of solvent. \(i\) Melt twice-sublimed rac-LA monomer at 125 °C in the absence of solvent. These data have been included for comparison in the ROP with mononuclear NNN-amidate-based [67], and mononuclear [42] and binuclear [46] alkoxide-based scorpionate zinc alkyl analogs. \(\text{ND}^\text{e}\) Not determined.

Complexes 1 and 2 were initially evaluated in the polymerisation of rac-LA employing 100 equiv. of monomer at mild conditions to demonstrate their catalytic activity. Thus, the alkyl complex 1 behaved as a very active single-component living initiator, reaching almost complete conversion (95%) in tetrahydrofuran in less than 4 h at 50 °C (see Table 2, entry 4). Interestingly, the halide complex 2 transformed 52% of the initial monomer in 6 h at 60 °C (see Table 2, entry 5), whilst analog halide zinc-based initiators have been described to operate in this process under much more harsher conditions (i.e., 150 °C [55] and 130 °C [57]) and have been reported to need up to 5 days at room temperature [56] to reach high conversions of 3.

It is worth noting that the presence of this high sterically hindered ligand that additionally incorporates phenyl substituents in the acetamidinate fragment very efficiently prevents the possible formation of the homoleptic six-coordinate sandwich-like \([\text{Zn(phbp}^\text{a}^\text{amd})_2]\) that disfavour catalytic performance, as previously observed for low sterically hindered zinc-based scorpionate analogs [67].

Interestingly, catalyst 1 presents an induction period, since limited catalytic activity was observed during the first 2 h (Table 2, entries 1 and 2), similarly to the bis(imino)diphenylamido-zinc-based catalyst previously reported by Williams et al. (Chart 2 [31]) and other zinc-based catalysts [34,35] This induction period is possible due to the delay in the formation of the essential catalyst active species in the monomer pool, which are highly influenced by both the steric and electronic effects of the scorpionate ligand. Similarly to this previous work, preliminary kinetic studies on catalyst 1 revealed zero dependence to the monomer concentration, which means that the transformation of the monomer with time remains constant (see Figure S4 in the SI). Very interestingly, in the presence of an excess of benzyl alcohol (5 equiv) as a cocatalyst, 1 efficiently mediated the immortal ROP of this monomer at 50 °C, as evidenced by the very narrow dispersity value and the good agreement between the experimental \(M_n\) values and monomer/benzyl alcohol ratios (see Table 2, entry 6). Under this immortal behaviour, 60% of the monomer was transformed in only 1 h and no induction period was observed.

Moreover, the well-controlled living performance of 1 was confirmed through a double-feed experiment, resulting in a polymer chain extension of 3 with comparable...
polymer features, which confirms the existence of a single type of reaction site (see Table 2, entries 4 and 7).

The effect of temperature and solvent was also examined. Thus, initiator 1 dramatically reduced conversion level at 40 °C, and only traces of 3 were observed after 24 h of reaction. In addition, a significant reduction in catalytic performance was observed on using toluene as solvent, reaching a poor 19% of conversion after 8 h at 50 °C, possibly as a result of the complexation of the zinc ions when using the tetrahydrofuran coordinating solvent, thus leading to an increase in the nucleophilicity of the alkyl initiating group and the alkoxide propagating chains (Table 2, entries 8 and 9). Not unexpectedly, initiator 2 did not transform any monomer either in toluene at 60–90 °C and in dichloromethane at 40 °C, after 48 h of reaction in both cases.

Very interestingly, complex 1 displayed near-complete conversion of 100 equiv of rac-LA into 3 under bulk conditions (125 °C) after just 1 min, reaching a TOF value of 5520 h⁻¹, whilst complex 2 needed 2 min to transform 59% of the monomer (TOF = 1770 h⁻¹). In view of these promising results, we were encouraged to carry out a further experiment employing partially purified (twice-sublimed) monomer, which confirmed the lower moisture sensitivity of complex 1 in comparison with analog zinc(II)-based scorpionate initiators [42,46,67], reaching 42% of conversion in 5 min (TOF = 504 h⁻¹) (see Table 2, entries 10–12, respectively).

This initiator offered activities much higher than mononuclear sterically demanding NNN' amidinate-based zinc scorpionate analogs [67] and similar activity to the NNO alkoxide-based zinc scorpionate counterparts previously described in our group [46]. However, complex 1 needs more temperature to initiate efficiently the ROP of rac-LA than the recently reported amine-functionalised NNO-scorpionate analogs [42] (Table 2, entries 13–15, respectively). Moreover, these activity values had lower results than the dinuclear species described above (Chart 2, [30–33]) or the mononuclear complexes recently reported by Ma employing zinc complexes bearing benzoimidazolyl-[60], pyridyl-[61] or [NNNO]-type tetradentate-[62] based aminophenolate ligands, which efficiently operate at room temperature for a few minutes; however, in the last case, the presence of 1PrOH as a cocatalyst was necessary [61,62].

In addition, low-molecular-weight materials of 3 prepared with initiator 1 were inspected by MALDIToF MS (see Figure S5 in the SI). Moreover, end-group analyses by 1H NMR of poly(rac-lactide) oligomers were also examined (see Figure S6 in the SI). These two results provide evidence that the ring-opening of rac-LA occurs by the initial addition of the alkyl fragment to the monomer in the PLA materials, with the cleavage of the acyl-oxygen bond [69] followed by further monomer additions to the (macro)alcohols.

More importantly, 1H-NMR microstructure analysis in the poly(rac-lactide) 3 produced in tetrahydrofuran revealed enhanced levels of heteroactivity imparted by 1, reaching a Ps of 0.74, probably through a chain end control mechanism [59] (Table 2, entry 4, see Figure S7 in the SI).

Very interestingly, this value is close to the highest data previously reported for the heteroactivity displayed by zinc-based scorpionate initiators prepared in our group in the stereoselective ROP of rac-LA [41–46,50,67] For instance, complex 1 exerted much higher heteroactivity than the amine-functionalised NNO-scorpionate zinc analogs [42] (Ps = 0.62) than the sterically demanded NNN' amidinate-based zinc scorpionates (Ps = 0.68) [67], close to the value reported for the NNO alkoxide-based zinc scorpionates (Ps = 0.77) [46] (Table 2, entries 13–15, respectively). Moreover, this value has results that were significantly higher than those reported for racemic pyridyl- (Ps = 0.49) [61] and [NNNO]-type tetradentate (Ps = 0.54–0.60)-based [62] aminophenolate zinc complexes. This is certainly attributed to the more sterically demanding environment produced by all bulkier substituents in the phbp'and scorpionate ligand. Furthermore, under bulk conditions, initiator 1 exerted moderate values of heterotacticity (Ps = 0.68) (Table 2, entry 10, see Figure S8 in the SI).
4. Conclusions

Hereby, the easy preparation of zinc-based complexes \([\text{ZnR(κ³-phbptamd)}] (R = \text{Me, Cl})\) supported by a high sterically hindered NNN'-acetamidinate scorpionate is described. X-ray diffraction analysis for \([\text{ZnMe(κ³-phbptamd)}]\) evidenced a mononuclear species and the zinc centre in a pseudotetrahedral disposition with the scorpionate ligand in a κ³-fashion.

Very interestingly, these complexes behaved as highly efficient catalysts for the ROP of \(\text{rac-lactide}\). Thus, \(\text{1}\) can act as an effective and robust single-component initiator for the living ROP of \(\text{rac-LA}\) under very mild conditions with a \(2\ h\) induction period, as shown by the narrow dispersity values of the PLAs prepared. As evidence, this initiator is capable of reaching a TOF value up to \(5520\ h^{-1}\) under bulk conditions. Preliminary kinetic studies confirmed apparent zero-order dependence on monomer concentration in the absence of a cocatalyst, whereas in the presence of \(\text{HOBn}\), catalyst \(\text{1}\) displayed an immortal performance, with nice agreement between the \(\text{Mn}\) observed and monomer/benzyl alcohol ratios. More importantly, the degree of steric hindrance of the scorpionate ligand in \(\text{1}\) exerts enhanced levels of hetero-activity during polymerisation to produce steroselective poly(\(\text{rac-lactide}\)), reaching a \(P_s\) value of 0.74.

We consider these results to represent an important further step forward in the search of inexpensive, low-toxic, and easy-to-prepare metal-based catalysts that are interesting for industrial applicability and which are capable of operating efficiently in the sustainable bioresourced ROP of lactides.

**Supplementary Materials:** Details of spectroscopy details for complexes \(1\) and \(2\), X-ray diffraction studies for \(1\) and experimental details for the ring-opening polymerisation of \(\text{rac-lactide}\). CCDC 2092631. For ESI and crystallographic data in CIF or other electronic format, see https://www.mdpi.com/article/10.3390/polym13142356/s1.

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