Zirconium complexes of bipyrrrolidine derived salan ligands for the isoselective polymerisation of rac-lactide†

Matthew D. Jones,*a Stuart L. Hancock,a Paul McKeown,ab Pascal M. Schäfer,a Antoine Buchard,a Lynne H. Thomas,a Mary F. Mahon,c and John P. Lowea

Herein we report the synthesis and characterisation of a series of Zr(n) 2,2′-bipyrrrolidine–salan derived complexes and their exploitation for the ring opening polymerisation of rac-lactide to afford highly isotactically enriched polymers.

Poly(lactic acid) is unequivocally a success story in modern sustainable chemistry.1 This is in no small part due to the desirable properties of the resultant polymer—namely biodegradability and the fact that the monomer is sourced from annually renewable raw materials.2 Poly(lactic acid) (PLA) is currently commercially produced using tin(ii) octanoate as the initiator. However, there is a desire to prepare new initiators that are faster and able to control the microstructure of the resultant polymer.3 The stereochemistry of PLA dramatically affects the properties of the material—for example, being easy to prepare, relatively moisture stable and can be trialled under the industrially preferred melt conditions.4

In this paper we report the preparation of three Zr(n) complexes based on a 2,2′-bispyrrrolidine and their exploitation in the ROP of rac-LA. Examples based on such ligands are rare in the literature12 and this is only the second example of the use of this meso-ligand in catalysis13 (Scheme 1).

The ligands were prepared by modified Mannich reactions involving either enantiopure (R,R or S,S) or meso variants of 2,2′-bispyrrrolidine.12c All ligands have been characterised by NMR spectroscopy, HR-MS and the solid-state structure has been

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*a Department of Chemistry, University of Bath, Claverton Down, Bath BA2 7AY, UK. E-mail: mj205@bath.ac.uk; Fax: +44 (0)1225 384908
b Doctoral Training Centre in Sustainable Chemical Technologies, University of Bath, Bath BA2 7AY, UK.
c Bath Chemical Crystallography Unit, Department of Chemistry, University of Bath, Claverton Down, Bath BA2 7AY, UK. E-mail: m.f.mahon@bath.ac.uk
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Scheme 1  Synthesis of the complexes under investigation.
between the five membered rings (relationship of the hydrogen atoms pertaining to the C–C bond the P
S and (in either CDCl3 or d8-THF) was complicated, with clearly more than to the chiral ligands a different coordination mode of the salan D
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Zr(IV)i na
S
fashion with the fac mer isomer,† presumably these enantioners are interconverting in solution at room temperature giving rise to the exchange peaks, which were absent in the chiral complexes Zr(1/2)(OPr)2.

The majority of examples of the polymerisation of rac-LA using group 4 initiators use sublimation methods to purify the monomer. In this study we have simply used recrystallised monomer to mimic more industrially relevant conditions (entries 4 and 11 use sublimed monomer as a comparison). The selectivity and dispersity appear to be relatively similar for the sublimed monomer compared to recrystallised, although similar conversions are achieved in a slightly shorter time frame for the sublimed monomer. The solution polymerisations of rac-LA are incredibly well controlled with low dispersities obtained. For Zr(3)(OPr)2 in the melt (entries 3 and 4) the dispersity of the polymer is slightly higher indicating a degree of transesterification.

Interestingly, the Zr(3)(OPr)2 yielded PLA with a high isotactic bias (Pm = 0.86 in solution), which to the best of our knowledge is the highest reported isotactic initiator in the literature to date utilising a group 4 initiator. Analysis of this highly isotactic polymer prepared in solution via DSC showed there to be a major endothermic peak at 190 °C, indicative of stereoblock isotactic PLA.6 Moreover, in the case of Zr(3)(OPr)2 the sii tetrad is significantly smaller than the sii, isi and isi tetrad indicating isotactic PLA of a blocky nature.5 Furthermore, the MALDI-ToF analysis has a repeat unit of 144 g mol−1, this coupled with the low Mn/Mn (1.05) indicates a controlled polymerisation with little transesterification occurring. The expected H- and OPr end groups from the coordination insertion mechanism were also observed. The solution state kinetics of the polymerisation were investigated with Zr(3)(OPr)2 at room temperature in CDCl3, (100 : 1 LA : Init), for rac-LA kapp = 4.3 × 10−3 min−1 was observed, Zr(3)(OPr)2 polymerises s-LA significantly faster with a kapp = 5.9 × 10−3 min−1, Fig. 2. Both Zr(1−2)(OPr)2 complexes were inactive for the solution state polymerisation of rac-LA in CDCl3 at room temperature. However, the chiral complexes were active at 70 °C in toluene – with ca. 50% conversion being achieved after 4 and 8 hours respectively, with a strong isotactic bias observed and Tm = 178 °C, from DSC (Table 1, entry 5) and Tm = 176 °C, from DSC (Table 1, entry 7). In the case of Zr(1−2)(OPr)2 the mechanism of polymerisation is presumably enantimorphic site control. There does appear to be a slight difference in selectivity with reaction time (entries 5 vs. 7 and 6 vs. 8), at low conversion (ca. 10%) Pm = 0.75 similar to the 4 h run (entries 5 and 6). Only ca. 50% conversion of rac-LA could be achieved in solution with the chiral complexes compared to 85% with the meso complex in the same timeframe [N.B. the Zr(3)(OPr)2 test was at 20 °C cf. 70 °C for Zr(1/2)(OPr)2]. The polymerisation was investigated further with s-LA, where A-Zr(2)(OPr)2 was active (ka = 4.1 × 10−4 min−1 after 37 h, conversion to PLLA = 58% Mw = 6900, Mw/Mn = 1.07) and A-Zr(1)(OPr)2 was slow (ka = 0.97 × 10−4 min−1 after 37 h, conversion to PLLA = 18%) Fig. 3.6

In the solid state Zr(3)(OPr)2 crystallises in the monoclinic P21/c space group, with both enantiomers (the A and A forms) present, arbitrarily the A-form is shown in Fig. 1. Compared to the chiral ligands a different coordination mode of the salan (fac–mer) was observed, this is presumably due to the syn relationship of the hydrogen atoms pertaining to the C–C bond between the five membered rings (cf. antiperiplanar for the chiral complexes). When this complex was recrystallised from toluene, the room temperature solution state NMR spectrum (in either CDCl3 or d6-THF) was complicated, with clearly more than one species present in solution. The ground state energies of various isomers have been studied via DFT methods.† Unsurprisingly the observed structure is the most thermodynamically stable, however the trans isomer is only 8.3 kcal mol−1 higher. Fortunately, when Zr(3)(OPr)2 was recrystallised in hexane the product gave an NMR spectrum that was consistent with the fac–mer isomer, with discrete doublets for the methylene CH2 moieties being observed along with two observed resonances for the methine isopropoxides and four resonances in the aryl region. Room temperature NOESY/EXSY measurements showed the presence of exchange peaks, indicating that in solution an equilibrium exists which potentially is A-isomer ⇔ A-isomer.† Presumably, these enantioners are interconverting in solution at room temperature giving rise to the exchange peaks, which were absent in the chiral complexes Zr(1/2)(OPr)2.
Both Zr(1/2)(O\text{Pr})_2 are “locked”, in solution as single enantiomers (A-Zr(1)(O\text{Pr})_2 and A-Zr(2)(O\text{Pr})_2, respectively). The data clearly show a strong preference for A-Zr(2)(O\text{Pr})_2 to specifically polymerise \(\text{L-LA}\) compared to A-Zr(1)(O\text{Pr})_2. It is thus hypothesised if we consider the polymerisation of rac-LA with the chiral complex A-Zr(1) when an \(\text{L-LA}\) insert a significantly less active catalytic species will form (the same is true when \(\text{D-LA}\) inserts into \(A\text{-Zr(2)}\)). Essentially this is an
eanitomorphic site controlled mechanism. As discussed previously Zr(3)(O\text{Pr})_2 is fluxional in solution, \(A\text{-Zr(3)(O\text{Pr})_2} \leftrightarrow A\text{-Zr(3)(O\text{Pr})_2}^\dagger\) and initially the chirality of \(A\text{-Zr(3)(O\text{Pr})_2}\) controls which monomer is inserted in a site controlled manner (\(A \rightarrow \text{\(\text{L-LA}\)}\), \(A \rightarrow \text{\(\text{D-LA}\)}\)). However, we tentatively suggest that if the “wrong” insertion occurs the complex can convert to the other form and now the chirality of the metal and chain end complement each other again, Scheme 2, and propagation continues leading to stereoblock isotactic PLA. It is also interesting to note that the rate of ROP of \(\text{L-LA}\) with Zr(3)(O\text{Pr})_2 is significantly faster than that of \(A\text{-Zr(2)(O\text{Pr})_2}\), this may well be due to the difference in coordination of the ligand around the Zr(\text{iv}) centre.

Work is currently on-going to investigate the mechanism in more detail, the applicability of the initiators with other cyclic esters and for co-polymer formation. Encouragingly, Zr(3)(O\text{Pr})_2 is active for the ROP of rac-butyro lactone ([M]:[Init] 300:1, \(T = 80 \, ^\circ\text{C}\) solvent free; conversion = 75\%, \(M_w/M_n = 1.10\) after 4 hours to produce atactic polymer).

Zirconium(n) complexes have been prepared and screened for the polymerisation of rac-LA. Stereoblock isotactic PLA is prepared with the meso salan complex Zr(3)(O\text{Pr})_2, which is significantly faster than either of the chiral complexes Zr(1/2)(O\text{Pr})_2. It is hypothesised that this reflects the fluxionality of Zr(3)(O\text{Pr})_2. We wish to thank the EPSRC (EP/G03768X/1), the EPSRC UK National Service for Computational Chemistry Software (CHEM732), Corbion for lactide and support of the CDT at Bath and the University of Bath for funding.

**Notes and references**


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**Fig. 2** Semi-logarithmic plots of the polymerisation of \(\text{L-LA}\) and rac-LA ([LA]_0 = 0.56 mol dm\(^{-3}\)) [LA]: [Init] = 100:1. Init = Zr(3)(O\text{Pr})_2.

**Fig. 3** Semi-logarithmic plots of the polymerisation of \(\text{L-LA}\) ([LA]_0 = 0.56 mol dm\(^{-3}\)) [LA]: [Init] = 100:1. Init = Zr(1 or 2)(O\text{Pr})_2.

**Table 1** Polymerisation data for rac-LA with initiators Zr(1–3)(O\text{Pr})_2

<table>
<thead>
<tr>
<th>Entry</th>
<th>Initiator</th>
<th>Time (h)</th>
<th>Conv. (%)</th>
<th>(M_w/M_n)</th>
<th>(P_w/M_n)</th>
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<tr>
<td>1</td>
<td>Zr(1)(O\text{Pr})_2</td>
<td>15.75</td>
<td>156</td>
<td>1.13</td>
<td>0.70</td>
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<tr>
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<td>Zr(2)(O\text{Pr})_2</td>
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<td>156</td>
<td>1.13</td>
<td>0.70</td>
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<tr>
<td>3</td>
<td>Zr(3)(O\text{Pr})_2</td>
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<td>156</td>
<td>1.13</td>
<td>0.70</td>
</tr>
<tr>
<td>4</td>
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<td>156</td>
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<td>0.70</td>
</tr>
<tr>
<td>5</td>
<td>Zr(3)(O\text{Pr})_2</td>
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<td>156</td>
<td>1.13</td>
<td>0.70</td>
</tr>
<tr>
<td>6</td>
<td>Zr(3)(O\text{Pr})_2</td>
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<td>156</td>
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<tr>
<td>7</td>
<td>Zr(3)(O\text{Pr})_2</td>
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<tr>
<td>8</td>
<td>Zr(3)(O\text{Pr})_2</td>
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<tr>
<td>9</td>
<td>Zr(3)(O\text{Pr})_2</td>
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<tr>
<td>10</td>
<td>Zr(3)(O\text{Pr})_2</td>
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<tr>
<td>11</td>
<td>Zr(3)(O\text{Pr})_2</td>
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<td>1.13</td>
<td>0.70</td>
</tr>
<tr>
<td>12</td>
<td>Zr(3)(O\text{Pr})_2</td>
<td>15.75</td>
<td>156</td>
<td>1.13</td>
<td>0.70</td>
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</tbody>
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**Scheme 2** Proposed mechanism for the polymerisation of rac-LA with Zr(3)(O\text{Pr})_2.
It was found using D-LA it was necessary to sublime the monomer prior to polymerization. For L-LA this was not the case. Using sublimed D-LA for polymerization of Zr(O\textsubscript{2}Pr\textsubscript{2}) gave a much stronger preference for L-LA. Zr(O\textsubscript{2}Pr\textsubscript{2}) has a stronger preference for L-LA than Zr(\textsubscript{1}O\textsubscript{Pr}\textsubscript{2}). These results clearly show that Zr(\textsubscript{1}O\textsubscript{Pr}\textsubscript{2}) has a much stronger preference for L-LA than Zr(\textsubscript{2}O\textsubscript{Pr}\textsubscript{2}).