Concerning the relative importance of enantiomorphic site *vs*. chain end control in the stereoselective polymerization of lactides: reactions of (*R*,*R*-salen)- and (*S*,*S*-salen)–aluminium alkoxides LAlOCH$_2$R complexes (R = CH$_3$ and *S*-CHMeCl)†

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The preparations and structures of LAlOCH$_2$C(*S*)HMeCl, where L = (*R*,*R*) or (*S*,*S*)-*N*,*N*′-bis(3,5-di-*tert*-butyl-salicylidene)-1,2-cyclohexenediamino, are reported together with the respective LAlOEt compounds, and their reactivities toward L- and *rac*-lactides in various solvents reveal the surprising complexity of the stereopreference for the ring-opening event.

The control of polymer microstructure is one of the most important goals in the development of single-site catalysis. One recent success story in this field has been in the stereoselective polymerization of propylene by metallocene based catalysts leading to the controlled formation of isotactic, syndiotactic, heterotactic and block polypropylene.[1,2] There is considerable current interest in developing new classes of polymers derived from renewable resources, and the family of polylactides derived from the ring-opening polymerization of lactides (LA), L-, *rac*- or *meso*-LA, represents a prime example.[3,4]

There are now several reports documenting the formation of both heterotactic ($(SSRR)_n$ = *isi*/*sis*) and isotactic stereoblock ($(RR)_n(SS)_n$ = $(i)_n s(i)_n$) polymers formed by the ring-opening polymerization of *rac*-LA.[5–17] However, although the mechanism of the ring opening of LA is generally recognized to proceed *via* the reaction pathway shown in Scheme 1 involving the attack of an alkoxide group on the ketonic group of a coordinated LA molecule,[18] the way in which stereoselectivity is achieved is not well understood. In the case of sterically demanding achiral β-diketonates employed with zinc and magnesium, the formation of heterotactic PLA must arise from chain end control.[9,19] A similar situation would seem to pertain for bulky trispyrazolylborate derivatives of calcium in the presence of donor solvents such as THF.[13] However, the situation when the metal contains chiral chelating ligands is far from clear as the influence of the chiral chain end and the chiral ligand may be either constructive or destructive with respect to the overall stereoselectivity. We describe here a study of the ring opening of one equivalent of lactide (L and *rac*) by chiral-salen aluminium alkoxides in a variety of common solvents, where salen is (*R*,*R*) or (*S*,*S*)-*N*,*N*′-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexenediamino, and the alkoxide initiator is OCH$_2$CH$_3$ or OCH$_2$C(*S*)HMeCl. These studies are particularly relevant to recent reports of the ring-opening polymerization of *rac*-LA by chiral and achiral salen and salan aluminium alkoxides.[10,12,14,17]

The chiral-salen aluminium alkoxides were prepared from the reactions shown in eqns. (1) and (2).

$$\mathrm{AlMe_3} + \mathrm{salen^*H_2} \xrightarrow[\text{r.t.}]{\mathrm{CH_2Cl_2}} (\mathrm{salen^*})\mathrm{AlMe} + 2\mathrm{CH_4} \qquad (1)$$

$$(\mathrm{salen^*})\mathrm{AlMe} + \mathrm{ROH} \xrightarrow[\text{r.t.}]{\text{hexane}} (\mathrm{salen^*})\mathrm{AlOR} + \mathrm{CH_4} \qquad (2)$$
$$^* = (R,R) \text{ or } (S,S);\ \mathrm{R} = \mathrm{CH_2CH_3} \text{ or } \mathrm{CH_2C}(S)\mathrm{HMeCl}$$

The molecular structures of the (salen*)AlOCH$_2$C(*S*)HMeCl complexes are compared in Fig. 1.‡ Here we use (*R*,*R*)-*S*

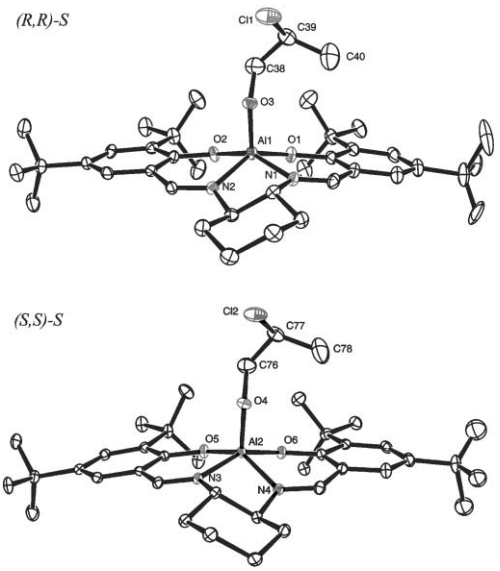
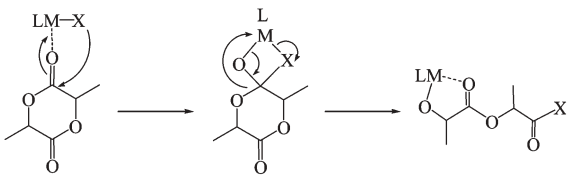


Fig. 1 ORTEP views of (*R*,*R*-salen)AlOCH$_2$C(*S*)HMeCl and (*S*,*S*-salen)AlOCH$_2$C(*S*)HMeCl (at 30% probability level).



Scheme 1 Proposed reaction scheme for the ring-opening polymerization of lactides by a metal alkoxide pathway.

† Electronic supplementary information (ESI) available: Experimental section. See http://www.rsc.org/suppdata/cc/b4/b413266a/

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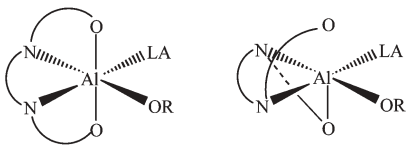
and (*R*,*R*) to represent (*R*,*R*-salen)AlOCH$_2$C(*S*)HMeCl and (*R*,*R*-salen)AlOCH$_2$CH$_3$, respectively. Similarly, (*S*,*S*)-*S* is for (*S*,*S*-salen)AlOCH$_2$C(*S*)HMeCl and (*S*,*S*) is for (*S*,*S*-salen)AlOCH$_2$CH$_3$. In both structures, aluminium is five coordinated and the local AlN$_2$O$_3$ geometry can reasonably be described as square based pyramidal with the Al–OR group in the apical position. It is not unreasonable to believe that a similar five-coordinate geometry is favored in hydrocarbon solvents. The mutual influence of the chiral salen and chiral alkoxide are seen in the conformations of the salen and OR groups as shown in Fig. 1. Little mechanistic information can been gleaned from the ground-state structures as the reactive intermediate leading to the C–O bond formation surely involves a six-coordinate Al(III) center with the Al–OR and Al–O(LA) groups in a *cis* position of a pseudo-octahedral geometry with the salen forming either λ or δ chirality, as shown below.[20]



Thus contributing to the stereoselective C–O bond forming transition state are (i) the chirality of the N–N backbone, (ii) the helicity of the η^4-chelate, λ or δ, and (iii) the chirality of the alkoxide ligand, OR. A further complication arises from the solvent which may or may not hydrogen bond to the substrate (LA) and alkoxide oxygen atom or may coordinate to the [Al] center within the primary or secondary coordination sphere.

In our study we have employed ^{1}H NMR spectroscopy to evaluate the course of the reaction. Recognizing the significant difference in the rate of ring opening of lactide by primary and secondary alkoxide (salen)AlOR complexes,[21] we carried out the reactions at 25 °C to obtain the 1:1 adducts (see ESI† for details). The chain propagation can only proceed slowly at T ⩾ 70 °C. The ring-opened moiety [Al]–OCHMeC(O)OCHMeC(O)OR forms a well defined group of resonances in the methine region (see ESI† details) that can be reasonably assigned from the ring opening of L-LA.[14] In the case of *rac*-LA, the ring-opened L-LA to D-LA ratio may thus be determined. Based on the relative intensities of the methine protons we obtain a measure of the stereoselectivity in the ring-opening step based on the diastereomer excess, de%. The results are collected in Table 1.

The data presented in Table 1 are based upon ^{1}H NMR signal integration of methine proton signals of the –OCHMe group. Each entry is an average of two independent reactions and a reasonable error bar of ±5% can be claimed. Thus for the entries with the OEt initiators we could expect the entries in the columns (*R*,*R*) and (*S*,*S*) to be equal in magnitude and opposite in sign. From the data presented it can be seen that (*R*,*R*-salen)AlOEt shows a modest preference for reaction with L-LA while the (*S*,*S*-salen) complex prefers D-LA. The influence of the chiral donor solvent *S*-propylene oxide (*S*-PO) and *R*-PO has little effect but the influence of the chlorinated solvents CH_2Cl_2 and $CHCl_3$ is more marked. Indeed, for $CHCl_3$, a solvent capable of CH···O bonding, the stereoselectivity is inverted.

Rather interestingly in reactions with the chiral alkoxide initiator [Al]OCH$_2$C(*S*)HMeCl, the (*R*,*R*-salen) ligand leads to the greatest stereoselectivity and now favors reaction with D-LA.

Table 1 Stereoselectivity in 1:1 reactions of (salen*)Al complexes and *rac*-lactide

	L − D (de%)			
Solvent	(*R*,*R*)	(*S*,*S*)	(*R*,*R*)–*S*	(*S*,*S*)–*S*
C_6H_6	20	−18	−31	−40
Toluene	12	−17	−33	−37
$CHCl_3$	−16	14	−30	−3
CH_2Cl_2	6	−6	−22	−4
THF	22	−20	−33	−13
Pyridine	20	−17	−39	−4
S-PO	17	−13	−32	−12
R-PO	14			
rac-PO	17			

For (*S*,*S*-salen)AlOCH$_2$C(*S*)HMeCl in the solvents benzene and toluene this preference is even more pronounced with *de* ∼40% for D-LA, but in other solvents, most notably CH_2Cl_2 and $CHCl_3$ this preference is considerably diminished.

The polymerization reactions of *rac*-LA were carried out in the presence of (salen*)AlOR initiators in toluene at 80 °C for 10 days, yielding polylactide with ∼40% conversion. The microstructure of the resultant polymers was investigated by using ^{1}H homodecoupled NMR and ^{13}C proton decoupled NMR spectroscopies.[22] The PLAs were produced with dominantly isotactic junctions (>90%) (see ESI†). No significant differences in *i:s* junction ratios were observed among the PLAs formed using these initiators, although (*R*,*R*-salen)Al polymerizes L-LA selectively and (*S*,*S*-salen)Al prefers D-LA as reported by Feijen.[12,14] Also Feijen reported that (salen*)AlO^{i}Pr produced PLA in the ring-opening polymerization of *rac*-LA with a similar microstructure to the present work.

From the results presented it is clear that the manner in which the chirality of the ligand bound to the metal, the chirality of the end group of the growing chain and the solvent all play a complex and rather unpredictable role in the preference for the ring opening of L- or D-LA in a racemic mixture. In the polymerization of *rac*-LA, the influence of the chiral end group would surely be greater than for OCH$_2$C(*S*)HMeCl as the stereocenter will be closer in the C–O bond forming step. It is then perhaps not surprising to find that stereoselective polymerizations of *rac*-LA have been observed with up to 90% de. However, to ascribe this to chain-end control or enantiomorphic site control is quite problematic. As Gibson has recently found,[15] we can expect subtle changes in the backbone of a chelating ligand which can adopt λ or δ stereoisomers in response to a chiral end group to greatly influence the outcome of stereoselectivity.

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Notes and references

‡ *Crystal data* for $C_{39}H_{58}AlN_2O_3Cl$, (*R*,*R*)-*S*: M = 665.30, monoclinic, space group $P2_1$, a = 14.923(1), b = 11.021(1), c = 23.440(1) Å, β = 93.397(1)°, V = 3848.6(7) Å^3, T = 200 K, Z = 4, μ = 0.159 mm^{-1}, 60183 reflections collected, 10692 independent (R_{int} = 0.073), $R1$ = 0.0508

for $I > 2\sigma(I)$. (*S*,*S*)-*S*: M = 665.30, monoclinic, space group $P2_1$, a = 14.927(1), b = 10.941(1), c = 23.393(3) Å, β = 93.69(1)°, V = 3812.5(7) Å^3, T = 200 K, Z = 4, μ = 0.160 mm^{-1}, 60079 reflections collected, 13387 independent (R_{int} = 0.058), $R1$ = 0.0555 for $I > 2\sigma(I)$. CCDC 243022 and 246786. See http://www.rsc.org/suppdata/cc/b4/b413266a/ for crystallographic data in .cif or other electronic format.

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