Macromol. Symp. ***175****, 67–79 (2001)*

Synthesis of Polylactides by New Aluminium Schoff's Base Complexes

Dhanjay JHURRY[1], Archana BHAW-LUXIMON[1], Nicolas SPASSKY[2]*

[1]Department of Chemistry, Faculty of Science, University of Mauritius, Réduit, Mauritius
[2]Laboratoire de Chimie des Polymères, UMR 7610, Université Pierre et Marie Curie, 75252 Paris Cedex 05, France
email: djhurry@uom.ac.mu

SUMMARY: The kinetics of DL-lactide polymerization was studied in CH_2Cl_2 and dioxane at 25°C and in toluene at 70°C with different aluminium Schiff's base initiators namely HAPENAlOMe, HAPENAlO^{i}Pr, 5-ClSALENAlO^{i}Pr and 5-ClSALOPHENAlO^{i}Pr. It was observed that HAPEN-type complexes derived from 2-hydroxyacetophenone lead to much faster polymerization as compared to SALEN- or 5-ClSALEN-type initiators derived from salicylaldehyde. Moreover, substitution of the methoxide group coordinated to the central aluminium by an isopropoxide group brings about an increase in the polymerization rate but leads to transesterification reactions at much lower percentage conversion. On the other hand, replacement of the flexible ethylene diamino group by the more rigid phenylenediamino substituent slows down considerably the polymerization reaction. Analysis of the microstructure of all poly(DL-lactides) obtained revealed the presence of isotactic sequences in agreement with a first order Markovian statistics.

INTRODUCTION

The controlled ring-opening polymerization of lactides, cyclic dimers of lactic acid, was shown to occur in the presence of aluminium alkoxide initiators [$Al(OR)_3$, R_2AlOR'] (Ref. 1-4). The living character of the polymerization was verified up to high molar masses (M_n = 90.000). However, these initiators did not lead to stereoselective polymerization such that in the case of DL-lactide, amorphous polymers were obtained.

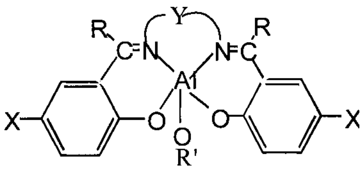
The synthesis of poly(DL-lactides) showing enhanced physical properties such as crystallinity were first reported by Spassky *et al.* (Ref. 5, 6) who introduced Schiff's base aluminium methoxide (SALENAlOMe, **1**) as initiator (Fig. 1). As can be seen, the latter is close in structure to the porphyrin derivatives described by Inoue *et al.* (Ref. 7) but are easier to prepare and can be synthesized with a wide range of ligands. These initiators give rise to controlled and stereoselective polymerization of lactides.

CCC 1022-1360/00/$ 17.50+.50/0

Thus, with the Al- methoxide complex, predominantly isotactic polymers are obtained from DL-lactide (Ref. 6, 8). Spassky *et al.* (Ref. 9, 10) also reported that with a chiral Al-Schiff's complex (*R*-SALBinaphtAlOMe, **2**), there results a stereoelective polymerization of the racemic lactide with preferential addition of the *RR* or D enantiomer. The optical purity at moderate conversion was thus found to be remarkably high. A decrease in optical activity is observed at higher conversion due to polymerization of the excess L-enantiomer leading at the end to the formation of a stereocomplex, which was substantiated by x-ray analysis and DSC (T_m = 187°C). Ovitt and Coates (Ref. 11) described the polymerization of meso-lactide with a similar chiral initiator (*R*-SALBinaphtAlO^{i}Pr, **3**) where the methoxy group has been replaced by an isopropoxy group. An interesting feature of this polymerization is that a highly syndiotactic polymer is formed at high conversion. More recently, the polymerization of DL-lactide was achieved using the racemic form of binaphthyl Al-isopropoxide **(3)** initiator (Ref. 12) leading to an isotactic polymer mixture of L-PLA and D-PLA chains exhibiting also a high melting transition (T_m= 191°C). It is good to note that a much higher T_m (230°C) has been reported before (Ref. 13) by mixing together L-PLA and D-PLA chains synthesized independently. This difference in T_m may be accounted for by the fact that the polymer chains obtained by Baker et al. are not perfectly isotactic.

All polymerization reactions described so far were generally conducted either in DCM or toluene at 70°C. The polymerization rate in the presence of the previously reported Al-Schiff's base complexes were found to be quite low and transesterification reactions occurred significantly in the range 50%-70% extent of conversion. Recently, the polymerization of DL-lactide was shown to occur at ambient temperature in the presence of 5-ClSALENAlOMe **(4)** and HAPENAlOMe **(5)** with enhanced rate (Ref. 14-15). The latter differs from the other Schiff's complexes in that it is derived from 2-hydroxyacetophenone instead of salicylaldehyde. The polymerizations proceeded to quantitative conversion (>90%) without the significant occurrence of tranesterification reactions even in toluene at 70°C.

In this article, we investigate the effect of modifying the ligands of the Al-Schiff's base complexes and the nature of the solvent on the kinetics of DL-lactide polymerization and on the microstructure of the resulting polymers. We also attempt to explain the difference in reactivity of the various initiators.



(1) R=H; Y=$(CH_2)_2$; R'=OMe; X=H	SALENAlOMe
(2) R=H; Y=binaphthyl; R'=OMe; X=H	SALBinaphtAlOMe
(3) R=H; Y=binaphthyl; R'=O^{i}Pr; X=H	SALBinaphtAlO^{i}Pr
(4) R=H; Y=$(CH_2)_2$; R'=OMe; X=Cl	5-Cl-SALENAlOMe
(5) R=CH_3; Y=$(CH_2)_2$; R'=OMe; X=H	HAPENAlOMe
(6) R=CH_3; Y=$(CH_2)_2$; R'=O^{i}Pr; X=H	HAPENAlO^{i}Pr
(7) R=H; Y=$(CH_2)_2$; R'=O^{i}Pr; X=Cl	5-Cl-SALENAlO^{i}Pr
(8) R=H; Y=(C_6H_4); R'=O^{i}Pr; X=Cl	5-Cl-SALOPHENAlO^{i}Pr

Fig. 1: Structure of aluminium Schiff's base complexes

RESULTS AND DISCUSSION

Synthesis and characterization of initiators

The synthesis of the Al-Schiff's base complexes containing a methoxide group was achieved by reacting the corresponding Schiff's base with triethylaluminium and refluxing the Al-Et adduct with methanol as described in Ref. 14. On the other hand, the isopropoxy-derived complexes were prepared by the method reported in Ref. 11 where the Schiff's base is reacted directly with aluminium isopropoxide.

NMR analysis of initiators

The ^1H chemical shifts for the HAPEN Schiff's base and corresponding methoxide and isopropoxide Al-complexes are summarized in Table 1. It is worthy to note that the methyl protons linked to each imino group appears as one singlet in the Schiff's base as well as in HAPENAlO^{i}Pr **(6)** while two distinct singlets are obtained with HAPENAlOMe. A similar observation can be made with the aromatic protons where the multiplicity of the latter complex differs quite markedly from the Schiff base and the isopropoxide derivative. However, an inequivalence of the bridging methylene resonances is noted for both Al-complexes. These data suggest that the Schiff's base presents a square-planar coordination geometry while HAPENAlOMe adopts a rather distorted geometry. It is most probable that the geometry of HAPENAlO^{i}Pr is closer to that of the Schiff base. In all the complexes, the alkoxide group is linked to aluminium in the axial position. The ^1H resonances of the methoxy group and the methine of the isopropoxy group are presented in Table 2.

polymerization in Table 4. This may be accounted for by a greater polarization of the Al-O bond in the isopropoxy-complex due probably to an increased bond length.

It is interesting to note that transesterification reactions occur (Table 5) with HAPENAlO^{i}Pr as early as 35% conversion in DCM though the reaction is carried out at 25°C. In contrast, no side reactions were detected with HAPENAlOMe up to high conversion (about 90%) irrespective of the nature of the solvent and temperature. As can be seen in Fig. 3a, 3b, the correlation between calculated and experimental molar masses is not so good for HAPENAlO^{i}Pr in DCM and the deviation is also even more pronounced for all the initiators in toluene. This result seems to suggest that the temperature might not be a predominant factor leading to transesterification reactions. The reduced selectivity that is observed with HAPENAlO^{i}Pr is according to us closely linked with the enhanced rate of polymerization and most probably with the more planar geometry of the complex.

On the other side, 5-Cl-SALENAlO^{i}Pr gives rise to a higher rate of polymerization in toluene compared with SALENAlOMe although an induction period is observed initially due to the differed solubility of the former in toluene. However, with 5-Cl-SALOPHENAlO^{i}Pr where the flexible diaminoethane has been substituted by the more rigid diaminobenzene, the polymerization reaction is substantially slowed down. The very low reactivity of this initiator is possibly linked to its highly conjugated structure and therefore to the extra stability conferred to it. This actually overrides the inductive effect of the chloro group which would normally enhance the electrophilicity of aluminium thereby leading to a higher rate of polymerization as in 5-Cl-SALENAlO^{i}Pr.

An interesting feature of the polymerization with the latter initiator is that no significant transesterification reactions are observed up to about 95% conversion (Table 5).

All the initiators lead to predominantly isotactic polymers confirming the first-order Markovian statistics.

Table 3. Solubility of the initiators in DCM and in toluene

Initiators	Solubility	
	DCM (25°C)	**Toluene (70°C)**
HAPENAlOMe	soluble	soluble after ~5 min
HAPENAlO^{i}Pr	soluble	soluble after ~5 min
5-Cl-SALENAlO^{i}Pr	insoluble	soluble after ~15 min
5-Cl-SALOPHENAlO^{i}Pr	insoluble	soluble after ~20 min

Kinetics of polymerization

Polymerization of DL-lactide using aluminium Schiff's base initiators proceeds via insertion of the monomer into the aluminium alkoxide bond followed by cleavage of one acyl-oxygen bond of DL-lactide. One end of the polymer remains attached to aluminium through an alkoxide bond while the other end contains a methoxyester group or isopropoxyester group. The signal corresponding to the former can accurately be assigned by ^{1}H NMR by the appearance of a singlet at 3.74 ppm. In the latter case, the methyl groups appear as a triplet centred at 1.17 ppm while the methine proton assignment is more difficult as it is probably overlapped with the methine protons of the polymer chain. In both cases, the ratio of the intensity of the methyl resonances compared with the intensity of the methine protons of the chain as determined by ^{1}H NMR allows calculation of the molar mass of the polymer.

Polymerization in DCM and in toluene

The kinetics of polymerization has been studied only in dichloromethane at 25°C for the HAPEN Al-complexes but not for the 5-Cl-SALEN Al-derivatives due to their insolubility in the solvent as discussed earlier. On the other hand, DL-lactide was successfully polymerized with the latter complexes in toluene at 70°C. Fig 2a, b illustrates the kinetic behaviour of the different initiators under similar experimental conditions. A substantial increase in reactivity was previously reported (Ref. 15) with HAPENAlOMe compared with SALENAlOMe. This trend is confirmed with the isopropoxy-complex which exhibits even a higher reactivity than the methoxy-complex in both solvents (Fig 2a), as also depicted by the apparent rate constants of

Table 1. Comparison of the ^{1}H chemical shifts and multiplicity in HAPEN (Schiff's base), HAPENAlOMe and HAPENAlO^{i}Pr

Group	HAPEN	HAPENAlOMe	HAPENAlO^{i}Pr
2C$\underline{H}_3$	2.38 ppm, 6H, s	2.24 ppm, 3H, s 2.31 ppm, 3H, s	2.44 ppm, 6H, s
C$\underline{H}_2$-C$\underline{H}_2$	3.97 ppm, 4H, s	3.00-3.30 ppm, 2H, m 3.46-3.75 ppm, 2H, m	3.63-3.79 ppm, 2H, m 3.89-4.01 ppm, 2H, m
aromatic $\underline{H}$	6.76-6.82 ppm, 2H, t 6.89-6.93 ppm, 2H, d 7.23-7.32 ppm, 2H, m 7.50-7.54 ppm, 2H, d	6.37-6.80 ppm, 4H, m 7.03-7.24 ppm, 2H, m 7.41-7.52 ppm, 2H, m	6.58-6.64 ppm, 2H, t 7.02-7.05 ppm, 2H, d 7.23-7.00 ppm, 2H, t 7.44-7.47 ppm, 2H, d

Table 2. ^{1}H chemical shifts of methyl- and methine alkoxides in Schiff's base Al-complexes

Initiator	^{1}H NMR (ppm) Al-OC$\underline{H}_3$ / Al-OC$\underline{H}$(CH$_3$)$_2$
SALENAlOC$\underline{H}_3$ **(1)**	2.91, s
HAPENAlOC$\underline{H}_3$ **(4)**	2.70, s
HAPENAlOC$\underline{H}$(CH$_3$)$_2$ **(6)**	3.63-3.73, m
5-Cl-SALENAlOC$\underline{H}$(CH$_3$)$_2$ **(7)**	3.61-3.73, m
5-Cl-SALOPHENAlOC$\underline{H}$(CH$_3$)$_2$ **(8)**	3.61-3.73, m

Solubility characteristics of Al-Schiff's base complexes

The solubility of the Al-Schiff's base complexes has been examined in dichloromethane (DCM) at 25°C and in toluene at 70°C as it is thought to be an important parameter which may affect the kinetics of polymerization. The results are summarized in Table 3. As can be noted, both HAPEN and 5-Cl-SALEN Al-derivatives are soluble in toluene although after different time intervals whereas only the former are soluble in dichloromethane.

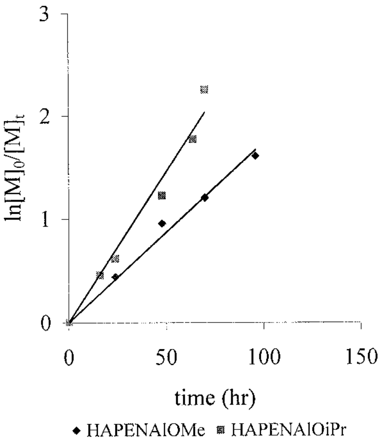


Fig. 2(a)

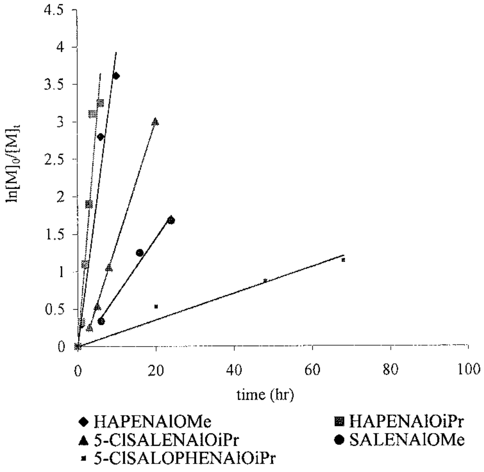


Fig 2: Semi-logarithmic plots of DL-lactide conversion as a function of time for (a) polymerization in DCM at 25°C; (b) polymerization in toluene at 70°C; $[M]_0$ = 1 mol/L; [M]/[I] = 50

Table 4. Comparison of the apparent polymerization rate constants for different initiators in DCM and in toluene. $[M]_0 = 1$ mol/L; $[M]/[I] = 50$

	k_{app}* 10^3 (hr^{-1})	
Initiator	**DCM (25°C)**	**Toluene (70°C)**
SALENAl(OMe)	2.4	73
HAPENAl(OMe)	15	374
HAPENAl(O^{i}Pr)	30	610
5-ClSALENAl(O^{i}Pr)	-	150
5-ClSALOPHENAl(O^{i}Pr)	-	22

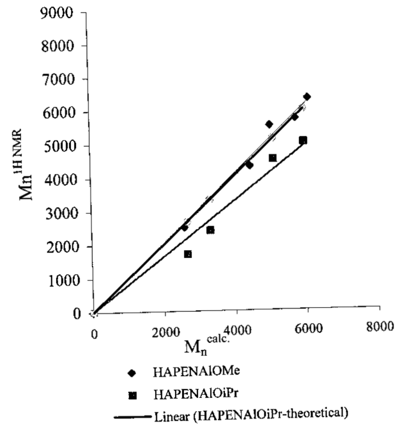


Fig. 3(a)

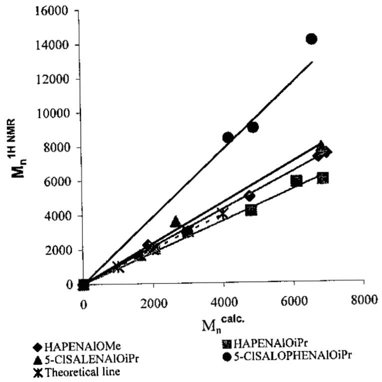


Fig. 3(b)

Fig. 3: Experimental M_n v/s calculated M_n (a) in DCM at 25°C (b) in toluene at 70°C; [M]/[I]=50

Table 5. ^{13}C methine tetrad intensities and percentage transesterification reactions of poly(DL-lactides) obtained with different Al-Schiff's base complexes. [M]=1 M; [I]=0.02M ([M]=2M)

Initiator	Solvent	Time (h)	Conv. (%)	Tetrads				T[1] (%)
				iii-iis-sii-sis-ssi	isi	sss	iss	
SALENAlOMe	Toluene at 70°C	24	81	82	18	0	0	-
HAPENAlOMe		6	94	84	16	0	0	-
HAPENAlOMe		10	97	77	17	2	4	32
HAPENAlO^{i}Pr		1	28	80	14	4	2	16
HAPENAlO^{i}Pr		4	96	73	16	8	3	24
5-ClSALENAlO^{i}Pr		20	95	87	13	0	0	-
5-ClSALENAlO^{i}Pr		22	95	82	15	1	2	16
5-ClSALOPHENAlO^{i}Pr		96	92	79.5	19	0.5	1	8
SALENAlOMe[2]	DCM at 25°C	170	87	86	14	0	0	-
HAPENAlOMe		144	85	82	19	0	0	-
HAPENAlO^{i}Pr		70	90	81	13	3	3	24
Predominantly isotactic[3]				75	25	0	0	-
Disyndiotactic[3]				50	50	0	0	-

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[1] Ref. 16

[2] [M]=2M

[3] Theoretical values (Ref. 17, 18)

Effect of nature of solvent on polymerization

The polymerization of DL-lactide was compared in DCM and dioxane at 25°C with HAPENAlO^{i}Pr under identical experimental conditions. As shown in Fig. 4, a substantial decrease in rate ($k_{app} = 0.008$ hr^{-1} < $k_{app} = 0.030$ hr^{-1}) is observed in the more polar solvent, that is dioxane due probably to a greater degree of solvation of the initiator. Analysis of the polymers by NMR also reveals the presence of transesterfication reactions at low extent of conversion (48%). Therefore, an enhanced rate of polymerization may not necessarily account for the presence of side reactions or for the loss of selectivity as one would tend to think. As invoked earlier, the square planar geometry of the complex might favour the occurrence of such reactions.

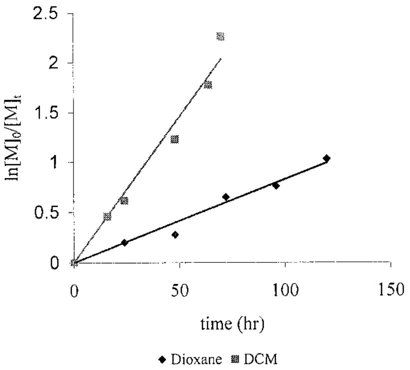

Fig. 4: Semi-logarithmic plots of DL-lactide conversion as a function of time for polymerization with HAPENAlO^{i}Pr in DCM and dioxane at 25°C; $[M]_0$ = 1 mol/L; [M]/[I] = 50

Thermal properties of poly(DL)lactides

Due to the stereoselective character of the Schiff's base aluminium alkoxide initiators, the polymers prepared from DL-lactide exhibit crystalline properties (Ref. 6, 9, 15). As can be seen from table 5, these polymers have a predominantly isotactic structure. The melting point is dependent on the length of enantiomeric sequences in the macromolecular chain. The formation of stereocomplexes between enantiomerically enriched chains of opposite configurations was also established previously (Ref. 8, 10, 19). In the present case, the poly(DL-lactides) prepared with HAPENAlOMe initiator in DCM at 25°C exhibit a melting point of 159°C while that prepared with HAPENAlO^{i}Pr in the same conditions shows a transition at 144°C. However in the latter case, a substantial transesterification was detected (Table 5). The variation of the nature of the Schiff's base and the nature of the Al-OR group as well as the influence of transesterification on the thermal properties of the polymers will be addressed in future publications.

EXPERIMENTAL

Materials: DL-lactide was purchased from Purac-Biochem. It was recyrstallized from dry ethyl acetate, dried under vacuum and finally kept under argon. Dichloromethane was first refluxed and distilled twice over CaH_2 under nitrogen and was stored under argon. Toluene was first refluxed, then distilled with sodium under nitrogen and kept under argon.
$Al(O^iPr)_3$ was used as obtained from Riedel-de-Haën.

Synthesis of initiators: The syntheses of SALENAlOMe and HAPENAlOMe were conducted as described in Ref. 5 and 15 respectively. HAPENAlO^{i}Pr, 5-ClSALENAlO^{i}Pr and 5-ClSALOPHENAlO^{i}Pr were synthesized according to the procedure given in Ref. 11.

Polymerization: Polymerizations in dichloromethane were carried out under stirring in glass tubes at 25°C under argon in a glove box while those in toluene were conducted in Schlenk tubes at 70°C under vacuum. The initiator, solvent and monomer were in both cases introduced in the tubes inside the glove box. After the desired time of polymerization the solvent was removed under vacuum and the percentage conversion was determined by ^1H NMR. Then the reaction mixture was treated three times with 1M aqueous solution acetic acid, washed with water till neutrality and dried on sodium sulphate. After filtration, the polymers were isolated by precipitation in methanol and finally dried under vacuum at 40°C.

Measurements: ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ using an FT Bruker 250 MHz spectrometer at 25°C.

CONCLUSION

We have shown in this article that an enhanced polymerization rate of DL-lactide is observed with the HAPEN-Al type complexes as compared with the SALEN-Al type. An increase is also noted upon substitution of the methoxide group linked to aluminium atom by an isopropoxide group. In both cases, this effect is probably due to a greater polarisation of the Al-O bond. On the other hand, the replacement in the Schiff's base of a flexible ligand in the diamino bridge by a more rigid one, i.e SALOPHEN v/s SALEN, decreases substantially the polymerization rate due to the stabilisation of the structure of the Al-Schiff's base complex. Modifications of structural parameters of the initiator do not only affect the rate of polymerization but they also have an influence on the occurrence of transesterification reactions, on the microstructure of obtained polymers and on their thermal properties. Further studies are currently in progress.

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