

Zwitterionic Ring Opening Polymerization of Lactide by Metal Free Catalysts: Production of Cyclic Polymers

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ABSTRACT: Tailor made *N*-heterocyclic carbene (NHC) catalyst precursors namely (+) and (–) 1-methyl-3-methoxymethyl imidazolium chloride have been synthesized in high yield with a literature modified procedure. A reaction of catalyst precursor with potassium tert butoxide *in situ* generates the NHC catalyst. The zwitterionic ring opening polymerization of lactide (LA) mediated by a catalytic system composed of NHC catalyst at 25°C under argon atmosphere led to a cyclic poly(lactide) of a high molecular weight with a narrow molecular weight distribution. The cyclic poly(lactide) was characterized by NMR

spectroscopy, Gel Permeation Chromatography (GPC) and Matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS). The NHC catalysts are active for lactide polymerization in the presence of air and elevated temperatures at 55°C. © 2011 Wiley Periodicals, Inc. *J Appl Polym Sci* 123: 1568–1575, 2012

Key words: D-lactide; L-lactide; cyclic poly(lactide); cyclic polymers; Zwitterionic polymerization; ring opening polymerization; *n*-heterocyclic carbene catalyst; organo-catalyst; metal free catalyst

INTRODUCTION

In recent years, biodegradable polymers from renewable resources are attracting much attention because of their biomass origin and their ability to reduce CO₂ emission relative to fossil fuel-based biodegradable polymers. Among the most promising candidates in this class of materials are aliphatic polyesters and, in particular poly(lactic acid) or poly(lactide) (PLA). PLA is highly versatile, biodegradable, aliphatic polyester derived from 100% renewable resources, such as corn, sugar beets, and municipal waste. An interesting aspect of PLA is its availability from a monomer/cyclic dimer (Lactide) produced by fermentation of agricultural crops, mainly corn and sugar beets. PLA is a semicrystalline polymer and it is one of the most important synthetic biodegradable polymers widely used for biomedical and pharmaceutical applications such as controlled drug delivery, resorbable sutures, medical implants, and scaffolds for tissue engineering. Applications of PLA in packaging industry have been lim-

ited due to low strain at break and high modulus of PLA.

A common synthetic route to PLA and other aliphatic polyesters, is the ring opening polymerization (ROP) of cyclic esters. ROP of lactide can be catalyzed by the addition of organometallic compounds such as stannous octanoate^{1–3} and zinc lactate⁴ and high temperatures have to be applied. Such conditions induce side reactions such as transesterification and racemization, which hamper the control over the polymerization process. The scientific interest in well-defined architectures including telechelic-, block-, graft-, and star-shaped polymers has initiated major research efforts toward initiators to yield well-defined poly(lactide)s. The ROP of lactides have been investigated using various metal catalysts, including complexes of Sn,^{5–7} Y,⁸ Ln,^{9–13} Fe,¹⁴ Ca,¹⁵ Ti,¹⁶ Mg,¹⁷ Al,^{18–20} and Zn,^{21–25} which generally proceeds by insertion of monomer into the metal-alkoxide bond. Some of these initiators have proved to be very attractive since they give rise to a controlled polymerization of lactide. On the other hand, the residual metal impurities in the polymer matrix which are in cytotoxic nature will limit the application of PLA in pharmaceutical or biomedical and microelectronics. Removal of these metal impurities from the polymer is a difficult and costly process. As a consequence, a lot of efforts were directed towards the “clean” synthesis of poly(lactide). These requirements have motivated the development of metal free catalysts (nucleophilic^{26–35} or cationic mechanism),³⁶

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bifunctional organo catalysts^{37,38} or enzymes^{39–42} for the ROP of lactide. Among the metal free catalysts, *N*-heterocyclic carbenes (NHC) are very effective for the ROP of lactide^{27,30,32,35} and can afford macrocyclic polylactide through a zwitterionic pathway.⁴³ Low molecular weight cyclic PLA was previously prepared by using lithium alkyls.^{44,45} The synthesis of high molecular weight macrocyclic polymers is a great challenge in polymer chemistry. Cyclic poly(lactide) is a kind of large-ring macromolecule which is a structurally constrained compared with linear PLA. Therefore, it may show unusual physical and solution properties like other cyclic polymers.^{46,47} Cyclic PLA with 3 (20 repeating units) has been found to be an important antitumor agent.^{44,45} In addition, cyclic PLA could be used as macromonomer to prepare high molecular weight linear PLA homopolymers and copolymers by ring opening polymerization. Since these polymers are produced by metal free catalysts they can be used in medical and microelectronic applications.

Within the class of metal free catalysts (organocatalysts), *N*-heterocyclic carbene catalysts (NHC) were used to synthesize high molecular weight cyclic and linear poly(lactide).^{27,30,32,37,43,48} However, NHC catalysts are normally air and moisture sensitive which makes the process inconvenient to scale up. There is a need to develop robust and effective organocatalysts for ROP to produce homo and copolymers of lactide with other cyclic monomers such as ϵ -Caprolactone, δ -Valerolactone etc. In this article, we report the findings on the development of NHC catalysts for the zwitterionic polymerization of D and L-lactide resulting in cyclic poly(lactide)s with high molecular weight (M_w) and narrow molecular weight distributions (MWD). Zwitterionic polymerization is an ionic polymerization where both the anion and cation are attached to the same polymer chain.^{43,49,50}

EXPERIMENTAL

General

All reactions and polymerizations were carried out in a M. Braun Glove box under argon atmosphere or standard Schlenk and vacuum line procedures. D-Lactide (D-LA), L-Lactide (L-LA) were purchased from Purac Biochem and purified by recrystallization from toluene. Recrystallized D and L-lactide were stored in the glove box. 1-Methylimidazole, (+) and (–) Chloromethyl menthyl ether, 1,3-Bis(2,4,6-trimethylphenyl)imidazolium chloride (Catalyst 2), 1-(1-Adamantyl)-3-(2,4,6-trimethylphenyl)-4,5-dihydroimidazolium chloride (Catalyst 3), 1-Butyl-3-methylimidazolium hexafluorophosphate (Catalyst 4) were purchased from ζ -Aldrich chemicals and used as received without further purification. Potassium *tert*-

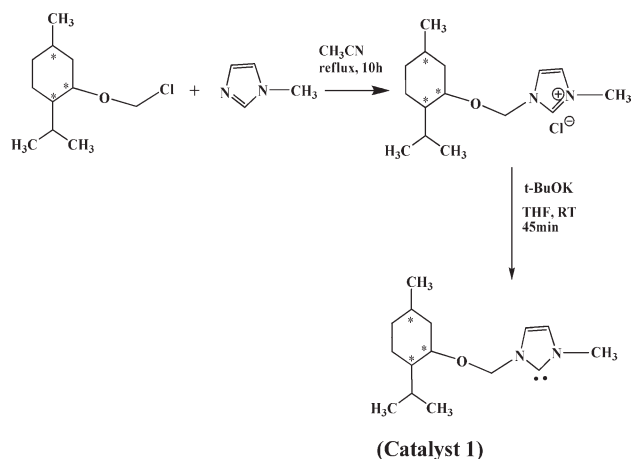
butoxide was purchased from Merck Co. and used as received. Solvents diethyl ether, *n*-hexane, dichloromethane (DCM), tetrahydrofuran (THF) were purchased from JT Baker and purified and dried over molecular sieves using an M. Braun SPS system. Deuterated chloroform (CDCl₃) was purchased from Cambridge Isotope Laboratories, Inc.

Characterization

¹H and ¹³C-nuclear magnetic resonance (NMR) spectra were recorded using a Bruker 400 MHz spectrometer and CDCl₃ as solvent. Chemical shifts were reported in parts per million (ppm) and referenced to tetramethylsilane and chloroform (¹H and ¹³C). Gel permeation chromatography (GPC) was performed in THF (1.0 mL/min) on an Agilent 1200 Chromatograph equipped with a RI detector. A combination of 2 × PLgel 5 μ m Mixed- columns (M_w 200–3 × 10⁶) was used. The molecular weights were calibrated with commercial polystyrene standards. Thermogravimetric analysis (TGA) was performed with a TA Instruments Q500 from 50 to 800°C at a heating rate of 10°C/min under nitrogen atmosphere. Differential scanning calorimetry (DSC) was performed using a Perkin–Elmer Diamond DSC. It was calibrated using high purity indium at a heating rate of 10°C/min. DSC was performed from –50 to 200°C at a heating rate of 10°C/min. Glass transition temperature (T_g) and melting temperature (T_m) were determined from the second heating scan at the rate of 10°C/min. Matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) measurements were obtained using Bruker Daltonics Autoflex TOF/TOF. Cyclic Poly(lactide) was dissolved in THF (5 mg mL^{–1}) and 1 μ L solution, 20 μ L dithranol solution (15mg mL^{–1}) was used as the matrix and 1 μ L sodium iodide (5 mg mL^{–1}) was added as the cation source.

Synthesis of (+)/ (–) 1-methyl-3-menthoxyethyl imidazolium chloride

Totally, 1.0 g of (+)/ (–) Chloromethyl menthyl ether, 2.0 mL of 1-methylimidazole, 5.0 g of activated 4 Å molecular sieves were added to 60 mL anhydrous acetonitrile and refluxed for 10 h under argon atmosphere (Scheme 1).⁵¹ After cooling to room temperature, the molecular sieves were filtered off and washed with 2 × 100 mL anhydrous dichloromethane. The combined organic solutions were dried under reduced pressure to give a sticky residue. The residue was washed with 2 × 50 mL anhydrous diethyl ether to remove any residual starting material, followed by drying in high vacuum to produce 1.3 g of a colorless solid (92%



Scheme 1 Synthesis of 1-methyl-3-menthoxymethyl imidazol-2-ylidene catalyst.

yield). The compound was analyzed by ^1H , ^{13}C NMR (Figs. 1 and 2) and confirmed to be pure.

Synthesis of (+)/ (–) 1-methyl-3-menthoxymethyl imidazol-2-ylidene catalyst from its precursor

In a glove box, (+)/ (–) 1-Methyl-3-menthoxymethyl imidazolium chloride (100 mg, 0.35 mmol) was added to a dry Schlenk flask equipped with a magnetic stirring bar, and 30 mL anhydrous THF was

added. The precursor was sparingly soluble in THF. To this, 81.0 mg (0.69 mmol) of potassium *tert*-butoxide was carefully added. After the addition of potassium *tert*-butoxide the carbene precursor was completely soluble and the reaction mixture was stirred for 45 min to produce a light yellow color catalyst solution. The catalyst solution was filtered through a 45 μm syringe filter to produce a clear carbene solution (Scheme 1). The neat carbene solution was used for the ROP of D and L-lactide.

Synthesis of cyclic poly(D/L-lactide) using (+)/ (–) 1-methyl-3-menthoxymethyl imidazol-2-ylidene

In a glove box, in a Schlenk flask equipped with a magnetic stir bar, 1 g of D- or L-lactide (6.9 mmol) was dissolved in 10 mL of THF at room temperature. To this the carbene catalyst solution was added and reacted for 10 min. Monomer to catalyst [M/C] ratios were 100, 200, 400, and 1000 conducted. The polymerization was terminated by adding a few drops of methanol. Cyclic polymer was obtained by precipitating the polymer solution in excess methanol. The crude polymer was isolated by filtration and dried in a vacuum oven at 50°C for 15 h. The crude polymer was redissolved in dichloromethane and precipitated from a large amount of methanol to remove residual catalyst, filtered, and dried at 55°C

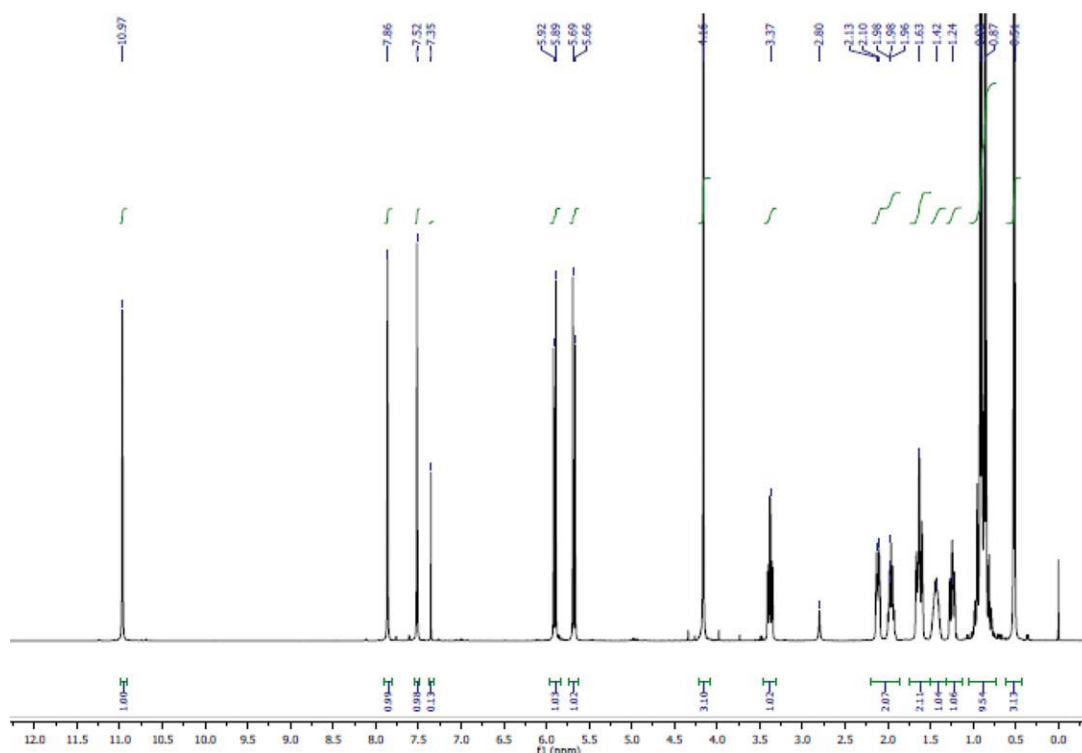


Figure 1 ^1H NMR spectrum of 1-methyl-3-menthoxymethyl imidazolium chloride. ^1H NMR (400 MHz, CDCl_3) δ 10.97 (s, 1H), 7.86 (s, 1H), 7.52 (s, 1H), 5.90 (d, $J = 10.4$ Hz, 1H), 5.68 (d, $J = 10.4$ Hz, 1H), 4.16 (s, 3H), 3.37 (s, 1H), 2.19 - 1.85 (m, 2H), 1.63 (s, 2H), 1.42 (s, 1H), 1.24 (s, 1H), 0.89 (d, $J = 20.7$ Hz, 10H), 0.51 (s, 3H). [Color figure can be viewed in the online issue, which is available at [wileyonlinelibrary.com](http://www.interscience.wiley.com).]

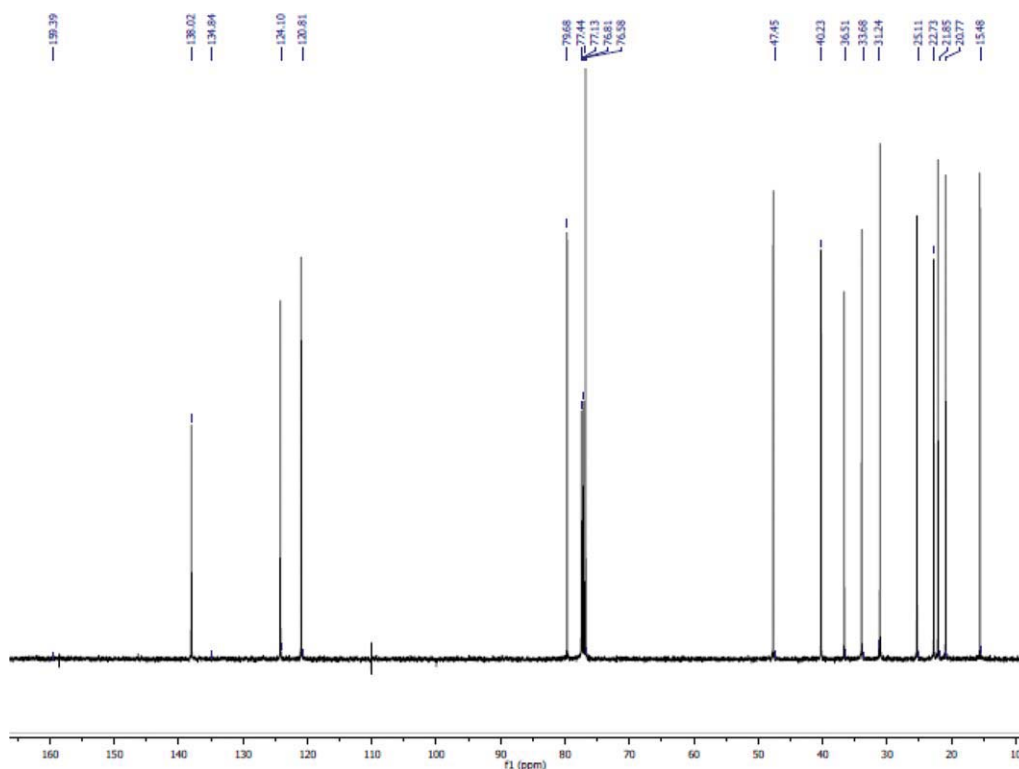


Figure 2 ^{13}C NMR spectrum of 1-methyl-3-menthoxyethyl imidazolium chloride. ^{13}C NMR (101 MHz, CDCl_3) δ 138.02, 124.10, 120.81, 79.68, 77.44, 77.13, 76.81, 76.58, 47.45, 40.23, 36.51, 33.68, 31.24, 25.11, 22.73, 21.85, 20.77, 15.48. [Color figure can be viewed in the online issue, which is available at [wileyonlinelibrary.com](http://www.interscience.wiley.com).]

for 24 h to obtain a constant weight. The polymer was analyzed by ^1H , ^{13}C NMR (Figs. 3 and 4), GPC, TGA, DSC, and MALDI-TOF.

RESULTS AND DISCUSSION

The ROP of D- or L-lactide was conducted under various conditions using (+)/ (–) 1-methyl-3-menthoxyethyl imidazolium chloride as a catalyst precursor. The catalyst precursor was synthesized using literature methods with slight modifications.^{52–55}

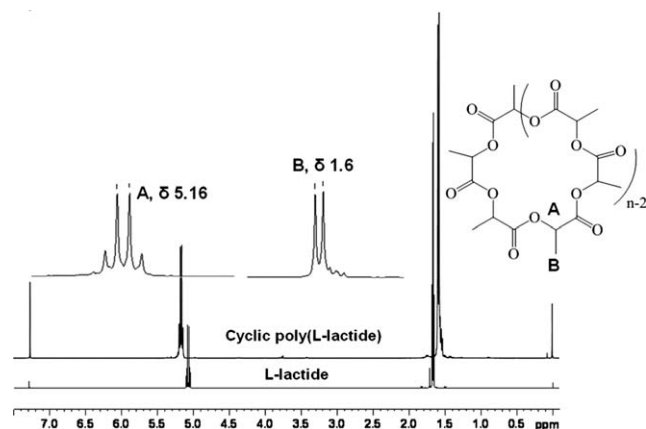


Figure 3 ^1H NMR of cyclic poly(L-lactide) in CDCl_3 (TMS internal reference).

Chloro methyl menthyl ether is commercially available as the (+) and (–) isomers. The enantiomeric carbene catalyst precursors were prepared in acetonitrile by the reaction of (+) and (–) chloro methyl menthyl ether and 1-methyl imidazole (Scheme 2). The carbene precursors were characterized by ^1H and ^{13}C NMR spectroscopy (Figs. 1 and 2). All data show normal functional group absorption peaks. In the presence of potassium tert butoxide both catalyst precursors were soluble in THF and generate a carbene catalyst for the ROP of lactide.

The zwitterionic polymerization of D- and L-lactides in the presence of (+) 1-methyl-3-menthoxyethyl imidazol-2-ylidene catalyst (in the absence of

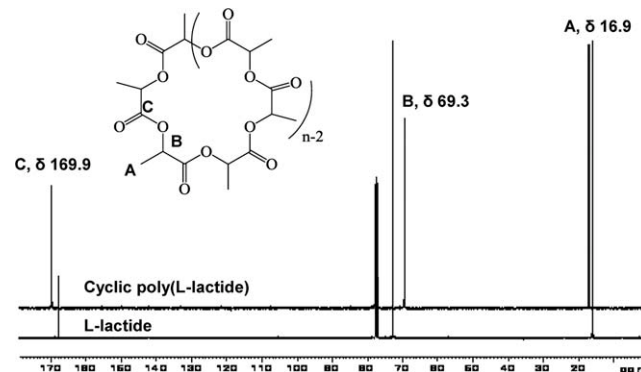
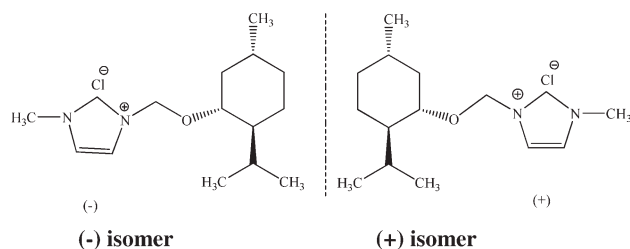


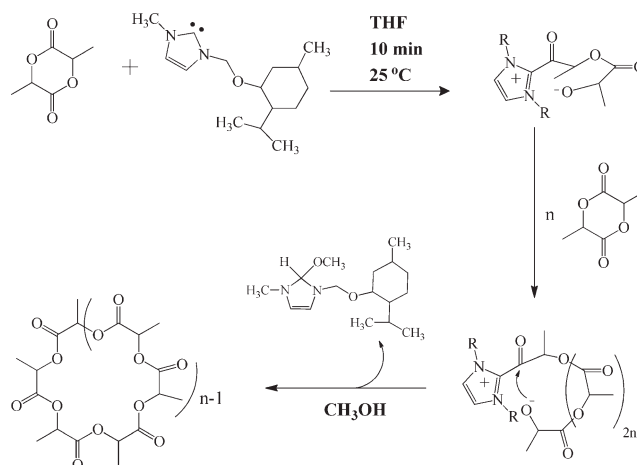
Figure 4 ^{13}C NMR of cyclic poly(L-lactide) in CDCl_3 .



Scheme 2 Enantiomeric forms of (+)/ (–) 1-methyl-3-menthoxy-methyl imidazolium chloride (Catalyst precursor 1).

alcohol initiator) was very fast, resulting in cyclic poly(lactide) within minute time at room temperature. The zwitterionic polymerization was carried out in THF solvent at room temperature under argon atmosphere (glove box). The polymerization reaction was terminated by the addition of methanol. The resulting polymer was isolated by precipitation in methanol and characterized by ^1H , ^{13}C NMR and GPC (Table I). The zwitterionic polymerization mechanism (Scheme 3) was proposed to occur by a nucleophilic attack of the carbene on lactide to generate an alkoxide and acylimidazolium zwitterion which subsequently propagates by the addition of monomer to the alkoxide of the zwitterion intermediate.⁴³

When methanol was added, the NHC could be deactivated by forming an O–H insertion product.⁵⁶ A key factor in the remarkable stability of free carbenes lies in the strong heteroatom stabilization, because of the presence of two heteroatoms, at least one of which is typically a nitrogen in a α position to the carbene carbon. The NHCs are strong σ electron donor through the carbenic carbon. The σ electron donor efficiency depends on the substituents (steric and electronic effects) at the nitrogens on the 1, 3 positions. The electronic and steric properties of ligands can be varied over a wide range by modifying the substituents at the nitrogen atom. In unsymmetrical five-membered NHCs having two different



Scheme 3 Proposed mechanism of zwitterionic polymerization of L-lactide using (+)/ (–) 1-methyl-3-menthoxy-methyl imidazolium chloride.

substituents on the nitrogen atoms adjacent to the carbonic center especially with alkyl and cycloaliphatic functionalities containing heteroatoms like oxygen increases the electron donating ability (due to the electron donating and resonance effect) of NHC.

Our (+)/ (–) NHC catalysts displayed activities which are comparable to the literature reported NHC precatalysts (Catalyst 2) under similar conditions which we consider a benchmark catalyst with a TOF of 12.3 min^{-1} .⁴³ Precatalyst 3 and Catalyst 4 are not active for lactide polymerization at identical conditions due to its steric and electronic effects on the formation of carbene catalyst (Table II). Interestingly, our (+) NHC catalyst displayed a very high activity for the polymerization of L-lactide with TOF of 15.6 min^{-1} at $[\text{L-LA}/\text{Carbene}] = 200$ (Table I entry 2). The polymerization of L-lactide proceeded with $> 90\%$ monomer conversion within 1 min time. From the GPC, the M_w of resulting cyclic poly(L-lactide)s was $M_w 74,000 \text{ g mole}^{-1}$ with a MWD in the range of 2.0 (Table I entry 2). The resulting cyclic

TABLE I
Cyclic Polymerization of D and L-Lactide Using (+) 1-methyl-3-menthoxy-methyl Imidazolium Chloride at 25°C in Glove Box^a

Entry No.	Cat, mmole	Lactide, mmole	[LA]/[cat]	Yield, wt %	$T_g, ^\circ\text{C}$	$T_m, ^\circ\text{C}$	M_w	M_n	MWD
1.	0.0694	L, 6.938	100	81.0	51.5	141.0 146.1	69,404	36,540	1.89
2	0.0348	L, 6.938	200	78.36	50.3	146.4 153.7	74,026	36,515	2.02
3 ^b	0.0159	L, 6.938	433	87.8	0	120.9, 140.5	32,467	18,597	1.74
4 ^b	0.0069	L, 6.938	1000	97.32	ND ^d	ND ^d	25,196	17,598	1.43
5 ^c	0.0485	L, 4.856	100	65.2	45.5	134.4, 141.6	30,151	17,099	1.76
6	0.0694	D, 6.938	100	40	44.0	123.9 130.9	27,224	16,533	1.64
7	0.0173	D, 6.938	400	15	0	105.7	18,517	12,806	1.44

^a Solvent = THF, L = L-lactide, D = D-lactide, Carbene precursor treated with potassium tert butoxide at 25°C for 45min, Polymerization Time = 10 min.

^b Solid was formed upon evaporation of solvent on rotavapor.

^c In air.

^d ND, not detected, GPC in THF at 25°C using PS standards.

TABLE II
ROP of L-lactide Using NHC Catalysts: Comparison in Activity and Molecular Weight

Carbene precursor	Isolated yield, (wt %)	M_w	M_n	MWD
Catalyst precursor 1 (+) isomer	81	69,404	36,540	1.89
Catalyst precursor 1 (-) isomer	68	25,022	15,574	1.6
Catalyst precursor 2	67	26,294	21,291	1.23
Catalyst precursor 3	0	0	0	0
Catalyst precursor 4	0	0	0	0

Solvent = THF, L-Lactide = 6.94 mmol, [L-LA/carbene] = 100, Carbene precursor treated with potassium tert butoxide at 25°C for 45 min, Polymerization time = 10 min GPC in THF at 25°C using PS standards

structure of the poly(L-lactide) was confirmed by a combination of techniques, including ^1H , ^{13}C NMR and mass spectrometry (Figs. 3 and 4). In the ^1H NMR spectra of cyclic poly(L-lactide), no terminal groups were detected and no residual monomer was found. In addition, comparing with monomer (LA), the chemical shift values (δ) of CH, CH₃ and C=O all shifted in ^1H and ^{13}C NMR spectra as shown in Figures 3 and 4.

MALDI-TOF MS is very useful for analyzing the synthetic polymers with absolute molecular weights. It can determine molecular weight independent of polymer structure.^{35,57} The MALDI-TOF spectrum of low molecular weight cyclic poly(lactide)s exhibited molecular ions for the sodium and potassium complexed cyclic poly(L-lactide). As shown in Figure 5 cyclic poly(L-lactide)s molecular ion peaks were separated by 72 mass units, which corresponds to half of the lactide unit. It was revealed that cyclic polymer having equal quantities of even and odd numbered cycles. There is no evidence for linear polymer. Polar polymers having sodium and/or potassium adduct

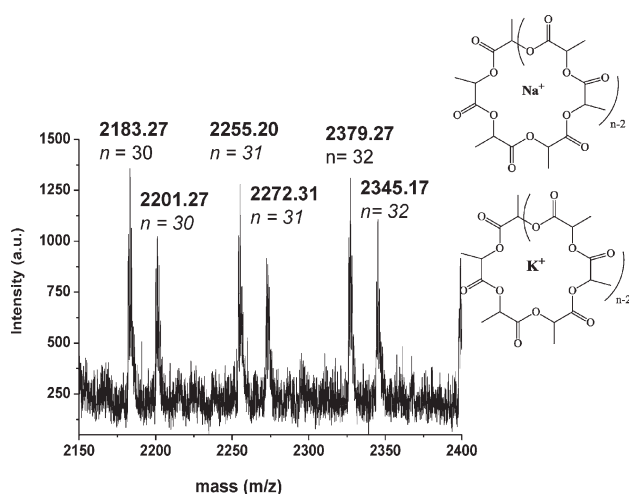


Figure 5 MALDI-TOF spectrum of cyclic poly(L-lactide).

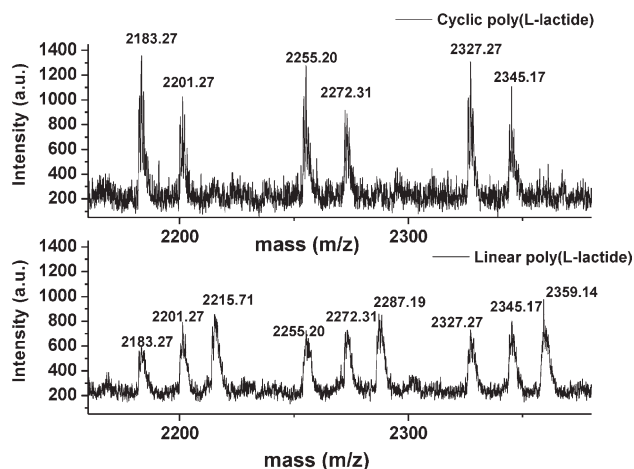


Figure 6 Comparison in linear and cyclic poly(L-lactide) using MALDI-TOF.

ions were observed in the MALDI-TOF spectrum even when they were not intentionally added.^{58,59} These cations present as an impurities in polymer (trapped potassium residue from the catalyst), glassware, solvents, reagents etc., Further investigating on the chain end groups we had prepared linear PLLA using Sn(Octanoate) with methanol as an initiator (Fig. 6). It should be pointed out that in our case both even and odd numbers of mass (m/z) for $[M+\text{Na}^+]$ and $[M+\text{K}^+]$ have been found, which is consistent with literature.⁴³ Gel permeation chromatograms of all cyclic polymers exhibited monomodal molecular mass distribution. Results showed in Tables I and III, the molecular weight (M_w) of cyclic poly(lactide)s were synthesized in the range of 25,000 to 74,000 g mol^{-1} with a molecular weight distribution in between 1.43 and 2.02.

Polymerization of D and L-lactides were carried out using (+) and (-) NHC catalysts under identical conditions showed a difference in activity (Table III). The (-) NHC catalyst displayed similar activity towards D and L-lactide (isolated yield 61 wt % and

TABLE III
ROP of D and L-Lactide Using Catalyst precursor 1 (+) (-) Isomers: Comparison in Activity and Molecular Weight

Carbene precursor	Lactide	Isolated yield, (wt %)	M_w	M_n	MWD
Catalyst 1 (+) isomer	L	81	69,404	36,540	1.89
	D	40	27,224	16,533	1.64
Catalyst 1 (-) isomer	L	68	25,022	15,574	1.6
	D	61	29,362	15,167	1.93

Solvent = THF, L-Lactide = 6.94 mmol, [L-LA/carbene] = 100, Carbene precursor treated with potassium tert butoxide at 25°C for 45min, Polymerization Time = 10 min GPC in THF at 25°C using PS standards.

68 wt %), whereas the (+) NHC catalyst displayed different activities with L-lactide and D-lactide respectively, (isolated yield 81 wt %, 40 wt %). A significant molecular weight difference was observed in the resulting cyclic polymers using the catalysts under identical experimental conditions. As shown GPC data in Table IV, cyclic poly (D-lactide) resulting from the (-) NHC catalyst had $\Delta M_w = 2000$ g mole⁻¹ molecular weight higher compared with the (+) NHC catalyst. Cyclic poly (L-lactide) obtained from the (+) NHC catalyst had M_w 69,000 whereas the (-) NHC catalyst produced M_w 25,000. But when we carried out polymerization with an optically pure (+)/ (-) NHC catalysts and an optically pure (D/L) lactides are resulted in a pure crystalline poly(lactide)s with the original stereochemistry of the lactide used, which indicated the polymerization proceeds with a retention of the stereochemistry of the lactide.

ROP of rac-lactide using the (+) or (-) NHC catalysts were resulted in a low molecular weight linear poly(DL-lactide)s (M_w 2000 to 5000 g mole⁻¹ with a MWD 8.5–11.7). The formation of linear poly(lactide)s were due to the ring opening of low molecular weight cyclic poly(lactide)s in methanol precipitation. D and L-lactides in the presence of an alcoholic initiators with (+) or (-) NHC catalysts were resulted in a linear poly(lactides).

In general, NHC catalysts were very sensitive to temperature, oxygen, and moisture. But our (+)/ (-) NHC catalysts were produced cyclic poly(lactide) in the presence of air. The cyclic polymer produced under this condition had molecular weight (M_w) 30151, MWD 1.76 and 65% yield (Table I entry 5). We had been preparing real (+) NHC catalyst at 25 and 55°C by the treatment of carbene precursor with potassium *tert*-butoxide at different time intervals. The resulting catalyst was used for lactide polymerizations at 0, 25, and 55°C. The generated polymer was in cyclic form (Table IV). We had obtained highest lactide polymerization activity with high molecular weight cyclic poly(lactide) using (+) NHC precatalyst treated with potassium *tert*-butoxide at 25°C

TABLE IV
Effect of Carbene Precursor [Catalyst 1 (+) isomer] with Potassium Tert Butoxide Pretreatment Time, Temperature, and Polymerization Temperature on the Yield and Molecular Weight of Cyclic Poly(L-Lactide)

Entry No	Carbene formation, °C, min	Polymn. Temp, °C	Isolated yield, wt %	M_w	M_n	MWD
1	25, 45	25	78.3	74026	36515	2.02
2	55, 23	55	48.2	55986	39363	1.42
3	55, 23	25	45.7	42385	24228	1.74
4	25, 45	0	54.4	20682	14123	1.46

[L-LA]/[Cat] = 200, Solvent = THF, L-Lactide = 6.94 mmol, GPC in THF at 25°C using PS standards.

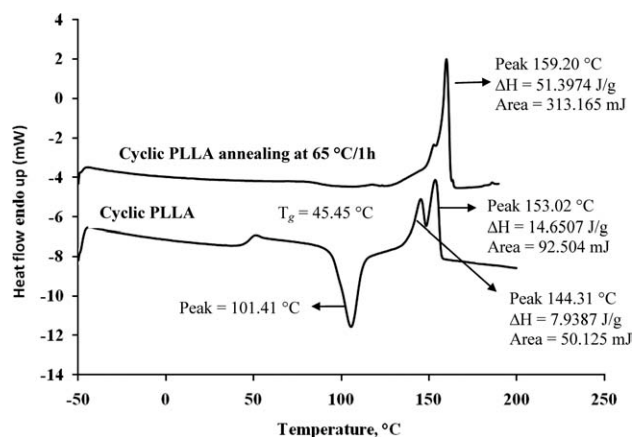


Figure 7 DSC thermogram of cyclic poly(L-lactide).

for 45 min (Table IV, entry 1). In other cases, decreased in polymerization activity and M_w of the cyclic polymer was observed due to the decreases in the concentration of the carbene catalyst.

From the TGA analysis, cyclic poly(lactide) showed thermally stable compared with their linear analogues under isothermal conditions.⁴³ Cyclic poly(L-lactide) showed initial decomposition temperature at 214°C and complete decomposition at 370°C. It is well known that PLA crystallizes slowly compared with other polyesters such as PCL and polyethylene terephthalate because of the rigid segments in its chain.⁶⁰ Linear PLLA exists in three crystalline forms α -, β -, and γ - forms.⁶¹ Figure 7 shows the DSC endothermic graph of cyclic poly(L-lactide)s. The glass transition temperature (T_g) and melting temperature (T_m)s were respectively, observed at 45, 144, and 153°C from the second heating scan. The transitions in α and β crystalline phases results in two melting temperatures in cyclic PLA. Cyclic PLA complete crystallinity change was observed at 104°C due to slow crystallization in the polymer. After annealing at 65°C for 1h and slow cooling (rate 10°C min⁻¹) to -50°C, the sample was reheated, with the subsequent DSC scan demonstrated that one melting peak (T_m) at 159°C was retained. The molecular reordering and thickening in the crystalline phase during the first heating scan resulted in melting peak temperature shifted to high temperature.

CONCLUSIONS

N-Heterocyclic carbene catalysts were synthesized in high yield with a modified literature procedure. These (+)/ (-) NHC catalysts enable rapid lactide polymerization with rapid initiation rate compare to reported catalysts. High molecular weight macro cyclic poly(lactide)s were synthesized by zwitterionic ring opening polymerization method. (+) NHC precatalyst was displayed high activity towards L-lactide

and the resulted polymer had high M_w and narrow MWD. These catalysts were stable in the presence of air and easily polymerized at 55°C. Cyclic poly(lactide)s have two melting temperatures. We are expecting the wide application in industry for both NHC catalysts and cyclic PLA in future.

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