VYSOKÉ UČENÍ TECHNICKÉ V BRNĚ

BRNO UNIVERSITY OF TECHNOLOGY

FAKULTA CHEMICKÁ
ÚSTAV CHEMIE MATERIÁLŮ

FACULTY OF CHEMISTRY
INSTITUTE OF MATERIALS SCIENCE
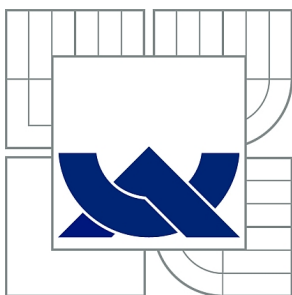
NOVEL "GREEN" CATALYSTS FOR CONTROLLED RING-OPENING
POLYMERIZATION OF LACTIDE
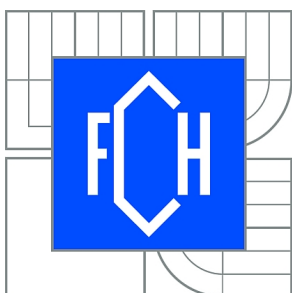
DIPLOMOVÁ PRÁCE
MASTER'S THESIS

AUTOR PRÁCE   Bc. FRANTIŠEK SURMAN
AUTHOR

BRNO 2010

VYSOKÉ UČENÍ TECHNICKÉ V BRNĚ

BRNO UNIVERSITY OF TECHNOLOGY

FAKULTA CHEMICKÁ
ÚSTAV CHEMIE MATERIÁLŮ

FACULTY OF CHEMISTRY
INSTITUTE OF MATERIALS SCIENCE

NOVEL "GREEN" CATALYSTS FOR CONTROLLED RING-OPENING POLYMERIZATION OF LACTIDE

NOVÉ "GREEN" KATALYZÁTORY PRO KONTROLOVANOU RING-OPENING POLYMERACI LAKTIDŮ

DIPLOMOVÁ PRÁCE
MASTER'S THESIS

AUTOR PRÁCE   Bc. FRANTIŠEK SURMAN
AUTHOR

VEDOUCÍ PRÁCE   Mgr. SOŇA HERMANOVÁ, Ph.D.
SUPERVISOR

BRNO 2010

Master's thesis Assignment

Number of master's thesis:	**FCH-DIP0418/2009**	Academic year:	**2009/2010**
Institute:	Institute of Materials Science		
Student:	**Bc. František Surman**		
Study programme:	Chemistry, Technology and Properties of Materials (N2820)		
Study field:	Chemistry, Technology and Properties of Materials (2808T016)		
Head of thesis:	**Mgr. Soňa Hermanová, Ph.D.**		
Supervisors:			

Title of master's thesis:

Novel "green" catalysts for controlled ring-opening polymerization of lactide

Master's thesis assignment:

Advances in the preparation of well-defined polyesters with predicted molecular weight and narrow polydisperzity by ring-opening polymerization of cyclic monomers will be reviewed. Novel organic catalysts as well as the traditional organometallic promoters based on aluminium, tin, zinc, and yttrium metals producing poly(lactide) will be discussed.

The series of polymerization runs of L- and D,L-lactide catalyzed by N-heterocyclic carbene precursor will be carried out with the defined ratios (solvent to monomer, catalyst to Initiator, monomer to initiator).

Prepared polymers will be analyzed, evaluated and compared.

Deadline for master's thesis delivery: 14.5.2010

Master's thesis is necessary to deliver to a secreatry of institute in three copies and in an electronic way to a head of master's thesis. This assignment is enclosure of master's thesis.

-     -   -

Bc. František Surman	Mgr. Soňa Hermanová, Ph.D.	prof. RNDr. Josef Jančář, CSc.
Student	Head of thesis	Head of institute

- -

prof. Ing. Jaromír Havlica, DrSc.

In Brno, 1.12.2009
                                            Dean

ABSTRACT

The synthesis of polylactide (PLA) by ring-opening polymerization (ROP) of cyclic monomer can be realized by different routes. More than 100 catalysts for the synthesis of polylactide and other biodegradable aliphatic polyesters are published in the literature. For example organometallic catalysts based on Sn, Zn, Al etc. after finishing polymerization function became contaminants and using obtained polymer material in human body is controversial. At present, the research is focused on novel *N*-hererocyclic carbene catalysts. These metal-free catalysts are able to produce polymers with controlled molecular weight, narrow polydispersity, end-group fidelity with high reproducibility as well as to synthesize the block copolymers and complex macromolecular architectures, which is characteristic for living polymerization system.

This diploma thesis is focused on study of polymerization of cyclic monomer *D,L*-lactide catalyzed by *N*-hererocyclic carbene. Polymerizations were carried out at the presence of benzylalcohol as initiator at THF. We were focused on the influence of composition of reaction system monomer − initiator − catalyst. Polymers of optically pure *L*-lactide with macroinitiators PEG with M_n of 1000 a 2000 g/mol were prepared as well. Number average molecular weight (M_n) and polydispersity index (PDI) was determined by GPC. ^{1}H NMR was used to prove end-group fidelity.

ABSTRAKT

Syntéza polylaktidu (PLA) polymerací za otevření kruhu cyklického monomeru (ROP) může být uskutečněna různými způsoby. Literatura uvádí více než 100 katalytických systémů, jejichž pomocí lze polylaktid a jiné biodegradabilní alifatické polyestery získat. Například organokovové katalyzátory na bázi Sn, Zn, Al atd. se po splnění své polymerační funkce stávají kontaminanty a pro humánní implantáty je použití takového materiálu diskutabilní. V současné době jsou v centru výzkumné pozornosti nové *N*-heterocyklické karbenové katalyzátory. Tyto „metal-free" katalytické struktury jsou schopné reprodukovatelně řídit syntézu polymerů předem definované molekulové hmotnosti s definovanými koncovými skupinami a nízkou polydisperzitou, která je charakteristická pro živý průběh polymerace. Nabízí se možnost syntézy blokových kopolymerů a různorodých makromolekulárních architektur.

Předložená diplomová práce se zabývá studiem polymerace cyklického monomeru *D,L*-laktidu katalyzované *N*-heterocyklickým karbenem. Polymerace byly vedeny v přítomnosti benzylalkoholu jako iniciátoru v roztoku THF. Byl sledován vliv složení reakčního systému monomer − iniciátor − katalyzátor. Dále byly připraveny polymery opticky čistého *L*-laktidu s makroiniciátory PEG s M_n = 1000 a 2000 g/mol. Střední číselná molekulová hmotnost (M_n) a polydisperzita (PDI) byly stanoveny pomocí GPC. Definovatelnost koncových skupin vybraných polymerů byla prokázána pomocí ^{1}H NMR.

KEYWORDS

Ring-opening polymerization, Lactide, Carbene

KLÍČOVÁ SLOVA

Polymerace za otevření kruhu, laktid, karben

Surman, F. *Novel "green" catalysts for controlled ring-opening polymerization of lactide.* Brno: Brno University of Technology, Faculty of chemistry, 2010. 42 p. Supervisor Mgr. Soňa Hermanová, Ph.D.

DECLARATION

I declare that the diploma thesis has been worked out by myself and that all the quotations from the used literary sources are accurate and complete. The content of diploma thesis is the property of the Faculty of chemistry of Brno University of Technology and all commercial uses are allowed only if approved by both the supervisor and the dean of the Faculty of Chemistry, BUT.

…....…..…......……………….
student's signature

CONTENT

1 INTRODUCTION

Traditional applications of synthetic commodity polymers are mostly based on their inertness to environmental influences such as humidity or microbial attack resulting in their degradations (hydrolysis, oxidation, biodegradation, etc.). Their production exceeds 200 million tons per year.[1] Consequently, the persistence of these polymers in natural environment has been recognized as one of the most serious problems concerning waste disposal process in recent years.

Hence, there is an increasing interest in the development of biodegradable polymers as alternative environmentally friendly materials. The concept of biodegradable synthetic polymers first proposed in the 1960s represents a practical solution of the ecological problems associated with bioresistant plastics waste accumulation.[2]

Among biodegradable and biocompatible polymers some aliphatic polyesters represent promising and important candidates derived from renewable raw materials (RRM). The major representatives; starch blends, polylactic acid (PLA) and aliphatic-aromatic polyesters are now being used in a wide variety of specific applications, particularly for manufacture of rigid and flexible packaging, bags and sacks and foodservice products.

Aliphatic polyesters containing ester linkages, naturally occuring in nature, have been widely investigated. That is an important class of biodegradable macromolecules derived from renewable raw materials (RRM) and provides an alternative to current used industrial and petrochemical based plastics. Current market share of biodegradable plastics is less than 0.1 % of the total plastics market.[3]

The objective of the diploma thesis was the study of the mechanism and kinetics of ring-opening polymerization of lactide catalyzed by novel *N*-heterocyclic carbene precursor at tetrahydrofuran solution. Benzyl alcohol as initiator and polyethylene glycol as macroinitiator were used. The catalytic system under investigation was evaluated according to the polymerization efficiency, conversion of monomer, end group fidelity, polydispersity index and controlled molecular weight of polymer products.

2 THEORETICAL PART

The main objective of this part is to review the recent advances in the area of novel organic catalysts as well as the traditional organometallic promoters based on aluminium and tin metals for the preparation of well-defined polyesters with predicted molecular weight and narrow polydispersity by ring-opening polymerization of cyclic monomers.

2.1 Introduction – Aliphatic polyesters

Of the variety of known biodegradable polymers, the group of linear aliphatic polyesters is particularly attractive and most utilized. The research of aliphatic polyesters began in 1932, when Carothers produced polymers derived from lactic acid. The main members of aliphatic polyester group are presented in Figure 1.[4]
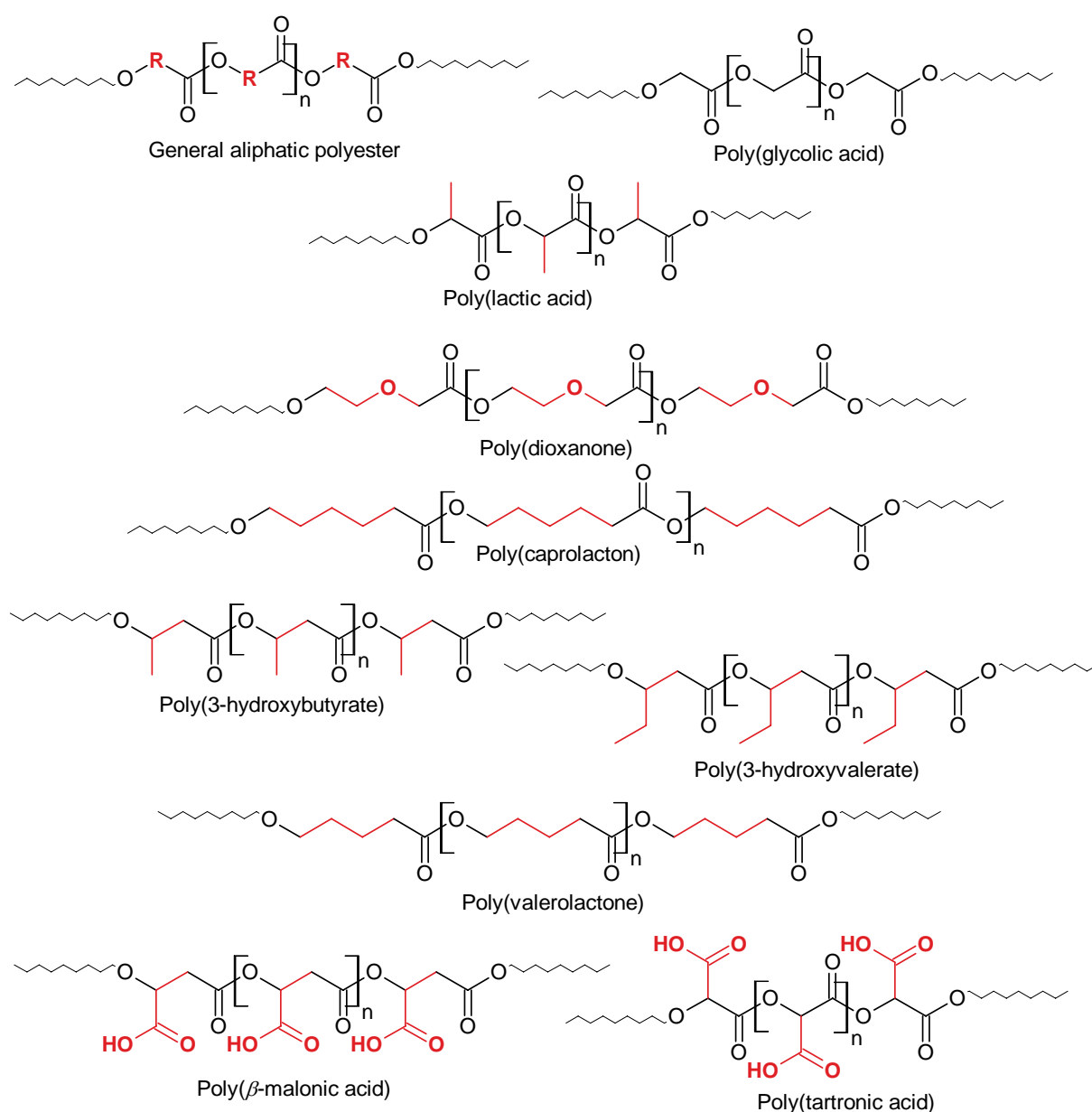

Figure 1 *Summary of some biodegradable polyesters.*

2.2 Monomers

2.2.1 From lactic acid to lactide

Lactic acid belongs to the carboxylic acids, present in certain plant juices, in the blood and muscles of animals and in the soil, is the most widely occurring carboxylic acid in nature.[5] Firstly it was isolated in 1780 by Swedish chemist Carl Wilhelm Scheele as a highly hygroscopic compound.[6] Lactic acid is easily obtained by a biotechnological process (bacterial fermentation usually based on the strain of a *Lactobacillus*) from inexpensive raw materials such as corn, sugar beet, sugar cane, potatoes, and other biomasses.[2] Lactic acid is a chiral molecule, and exists in two enantiomeric forms (*D*-lactic acid *L*-lactic acid). Lactic acid obtained by the chemical process is a racemic mixture of *D*- and *L*-isomers.
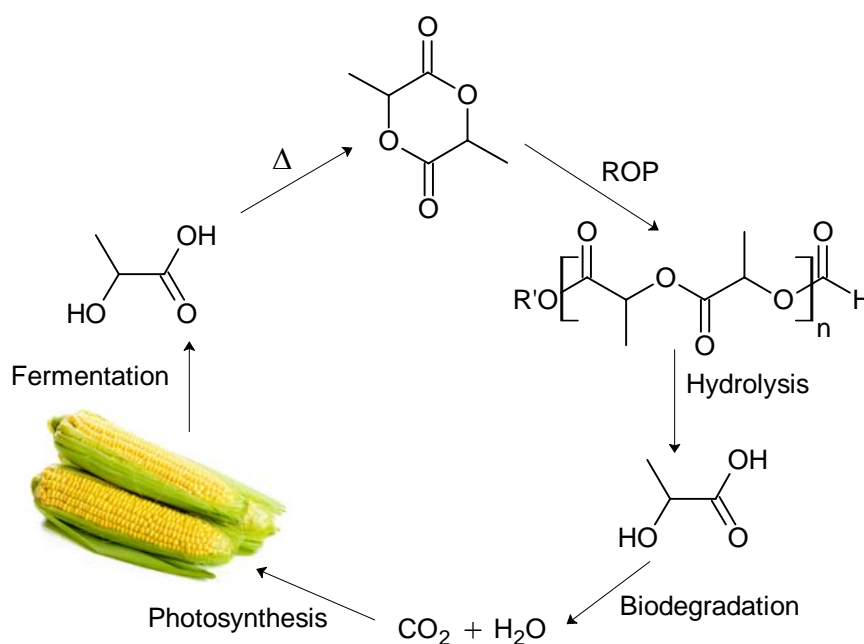

Figure 2 *The life cycle of polylactide (PLA).*[7]

2.3 Poly(lactide)

Poly(lactide) (PLA) is a linear, aliphatic, thermoplastic polyester. PLA can be synthesized primarily by two methods: step-wise polycondensation of lactic acid or chain-grow ring-opening polymerization of lactide (ROP). Polylactide (PLA) is produced from lactide, which is the cyclic dimer of lactic acid. Lactide molecule contains two stereo centers and also exists at three stereo modifications *D,D*-lactide (*D*-lactide), *L,L*-lactide (*L*-lactide) and *D,L*-lactide (*meso*-lactide), *rac*-lactide is synthetic racemic mixture of *D*-lactide and *L*-lactide. Figure 1 represents scheme of PLA formation from various lactide stereoisomers.

PLA homopolymers are semicrystalline with glass-transition and melt temperature of 55 °C and 175 °C, respectively, above 200 °C undergo thermal degradation – loss of molecular weight by hydrolysis, lactide reformation, and oxidative chain scission or inter- or intramolecular transesterification reaction. PLA is a non-volatile, odorless polymer and is classified as GRAS (generally recognized as safe) by the US Food and Drug Administration.

PLA can be processed by injection molding, blow molding, thermoforming, sheet extrusion, film forming or fiber spinning. PLA can be modified specially for fabricating process by copolymerization, branching, isomer content or molecular weight distribution.[8]

R-lactide

d-lactide
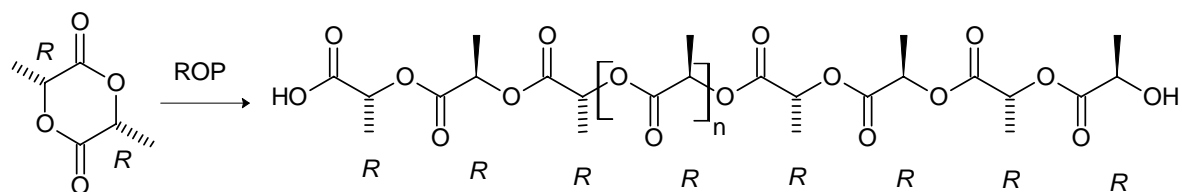
(3R,6R)-3,6-dimethyl-1,4-dioxane-2,5-dione
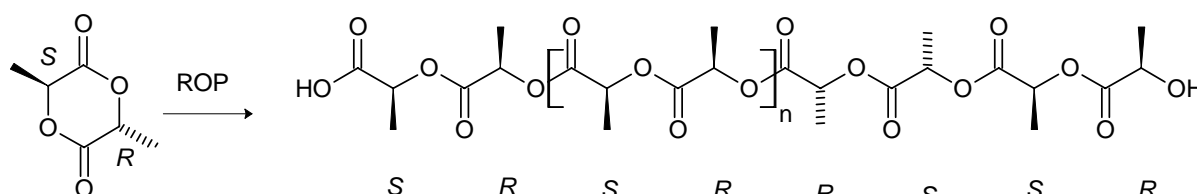
poly(R-lactide) PDLA
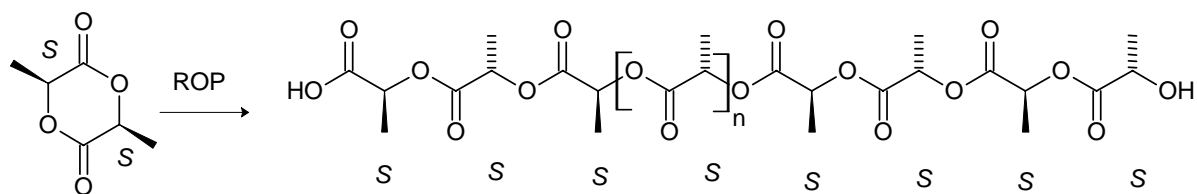
R,S-lactide or meso-lactide

d,l-lactide

(3R,6S)-3,6-dimethyl-1,4-dioxane-2,5-dione

poly(R,S-lactide)   PDLLA

S-lactide

l-lactide

(3S,6S)-3,6-dimethyl-1,4-dioxane-2,5-dione

poly(S-lactide) PLLA
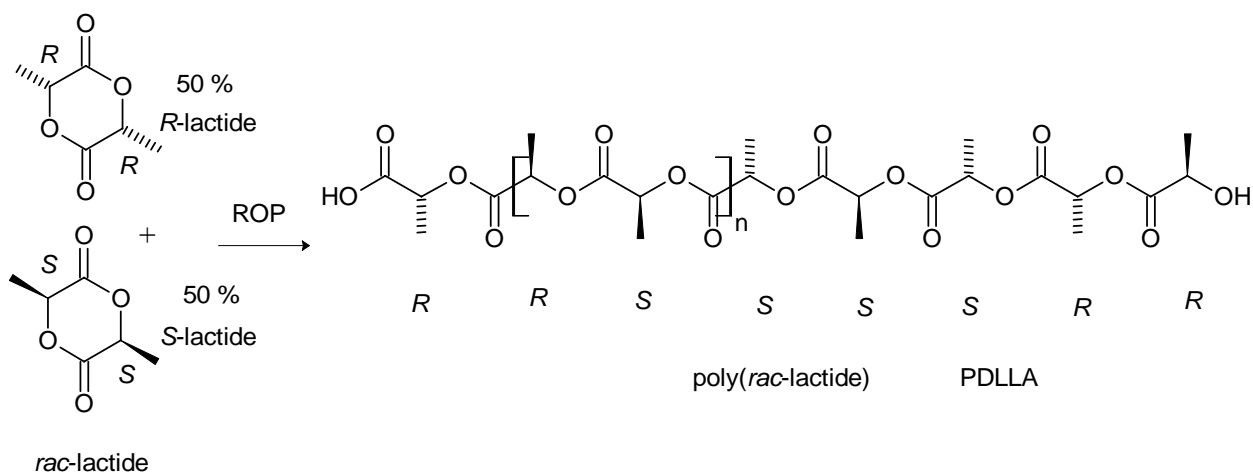
Figure 3 *ROP of lactide stereoisomers.*[9]

2.4 Synthesis of polylactide

Generally, PLA could be synthesized by four different methods (Figure 4). The traditional polycondensation route yields low-molecular weight brittle and glassy PLA. This method has some limitations such as difficulty related to water removal from the highly viscous mixture, to stereoregularity control during the reaction or to "back-biting" reaction giving lactide rings.

Solid state polymerization (SSP) involves heating a semi-crystalline, solid prepolymer (of relatively low molecular weight). Process is carried out at temperature below the melting point with the simultaneous removal of by-products from the solid surface under reduced pressure. Polymerization takes place in the amorphous region of the polymer so temperature has to be above the glass transition temperature of polymer. SSP polymers often have improved properties, because monomer cyclisation and other side reactions are limited.

Azeotropic condensation polymerization overcomes the problem of removal of water using an appropriate organic azeotropic solvent. Water as a by-product is removed azeotropically, whereas solvent is dried and recycled back into the reaction. This method produced highly pure PLA with molecular weight of unto 300 000 g/mol.[2]

Figure 4 *Various routes of synthesis of PLA.*

2.4.1 Ring-opening polymerization

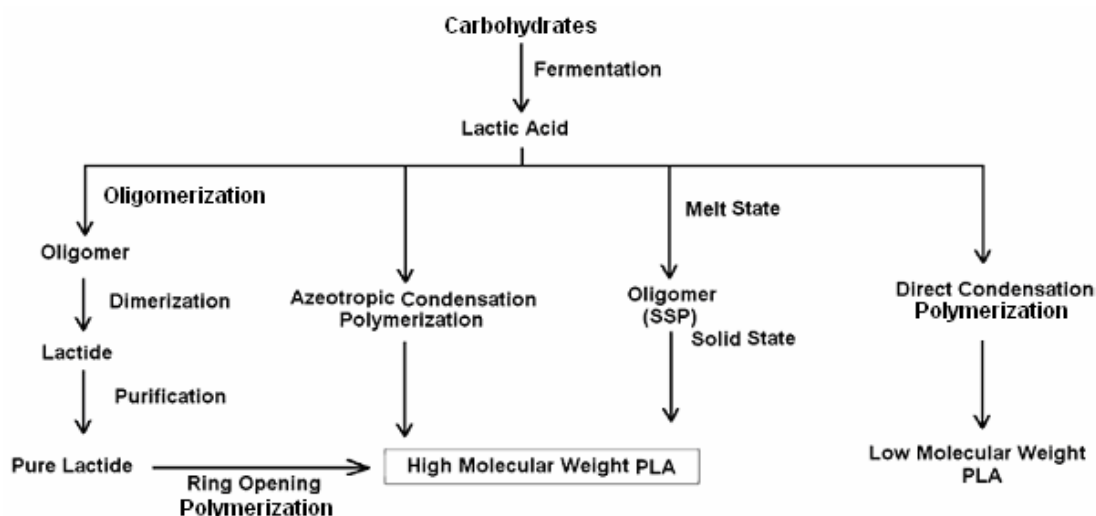Ring-opening polymerization (ROP) of lactide represents by far the most widely utilized route for the synthesis of well-defined and high-molecular weight PLA. The ROP can be performed as a bulk polymerization, or in solution, emulsion or dispersion. A catalyst or initiator is necessary to start the polymerization reaction.

At present, the novel, efficient and selective organometallic and organic catalysts (initiators) allow the polymerization proceeds in a controlled and living way. Under rather mild conditions, high-molecular weight aliphatic polyesters of low polydispersity with definable end-groups, copolymers or advanced macromolecular architectures can be prepared in short periods of time. The general scheme of cyclic monomer ring-opening process is described in Figure 5.[10]
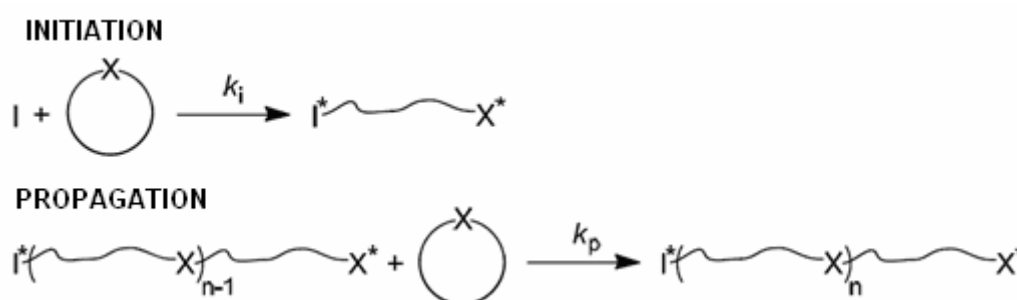
Figure 5 *Ring-opening polymerization process of cyclic monomers*

2.4.1.1 Anionic ring-opening polymerization

Anionic ring-opening polymerization of cyclic ester monomers takes place by the nucleophilic attack of a negatively charged initiator on the carbonyl carbon resulting in the cleavage of the carbonyl carbon and oxygen bond (Figure 6). This oxygen becomes a new anion, which continues the propagation steps. A problem associated with the anionic ROP is the extensive "back-biting", and in some cases only polyesters of low molecular weight are produced.[2]
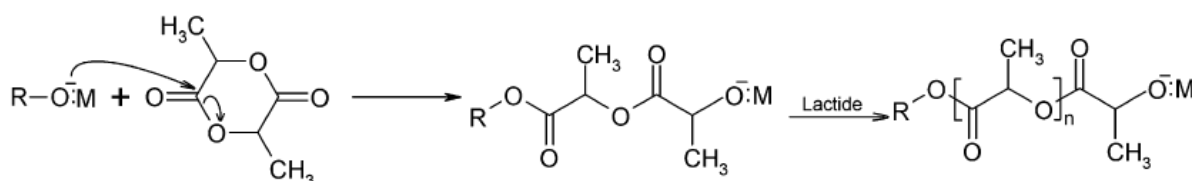
Figure 6 *Scheme of anionic ROP*

2.4.1.2 Cationic ring-opening polymerization

The cationic ROP involves the formation of a positively charged species which is subsequently attacked by a monomer. The attack results in a ring-opening of the positively charged species through an S_N2-type process (See in Fig. 7). The cationic polymerization is difficult to control and often only low-molecular weight polymers are formed.[10]
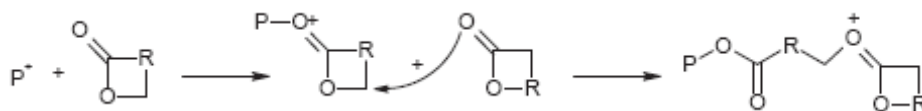
Figure 7 *Scheme of cationic ROP*

2.4.1.3 Coordination-insertion ring-opening polymerization

This approach utilizes (organo)metallic catalysts (initiators) containing vacant *p* or *d* orbitals. The propagation proceeds by coordination of the monomer to active species, followed by its insertion into the metal-oxygen bond accompanied by rearrangement of the electrons. The Figure 8 shows a coordination-insertion mechanism ROP of lactide initiated by aluminium trialkyloxide. At first, the coordination of carbonyl oxygen with metal atom of the initiator occurs. In the second step, the acyl–oxygen bond of the lactide is broken and the lactide chain produced is inserted into the metal–oxygen bond of the initiator. The polymerization continues as additional lactide molecules are opened and inserted into the bond between the metal atom and its adjacent oxygen atom, while the other end, i.e. the alkoxide end of the initiator, becomes a "dead" chain end. The reaction is terminated by hydrolysis forming a hydroxyl-end group. This type of ROP produces well-defined polymers in a living way. [10]
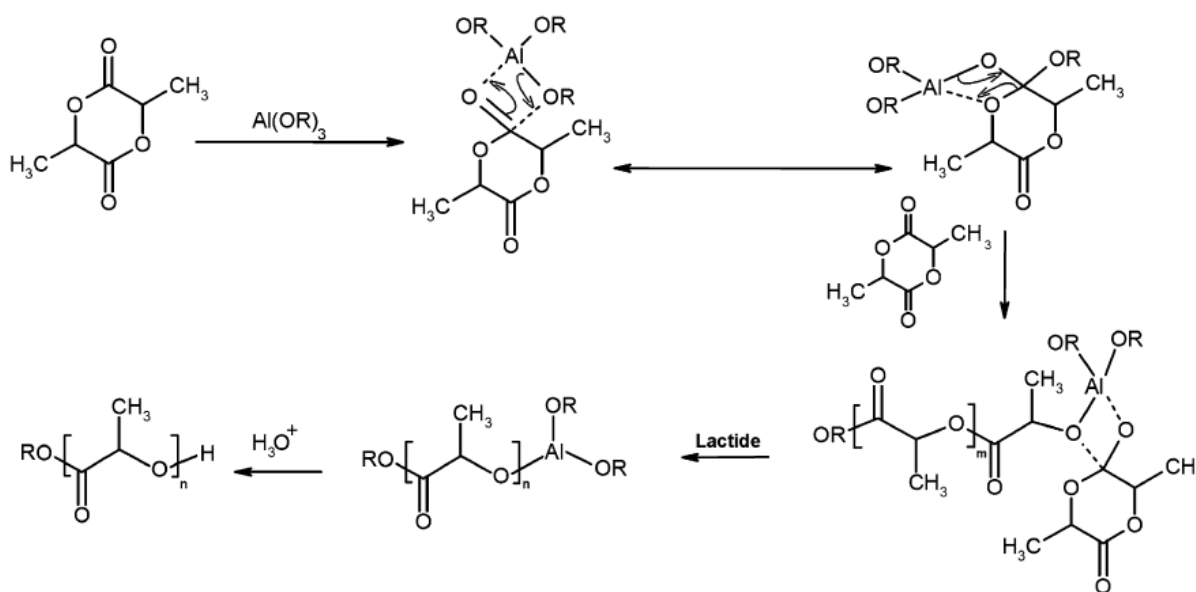
Figure 8 *Coordination-insertion mechanism ROP of lactide.* [2]

2.4.1.4 Transesterification reaction

Transesterification reactions represent the main shortcoming of advanced ROP synthesis of polyesters. These undesirable, competitive side reactions can be referenced as an intermolecular or intramolecular. Intermolecular transesterification reactions modify the homopolymer chain length; in addition change the sequence structure of copolymers. Intramolecular transesterification lead to the formation of cyclic oligomer (See in Fig. 9). Both types broaden the molecular weight distribution. Parameters that influence the number of transesterifications are temperature, reaction time, type and concentration of catalyst or initiator. Distinctly they are taking place at elevated temperatures and long reaction time, respectively at high monomer conversion. [2]

Figure 9 *Competitive side reactions*

2.5 Traditional organometallic catalysts/initiators for ROP of lactide

2.5.1 Tin (II) 2-Ethylhexanoate

Tin (II) 2-ethylhexanoate **I** (See Fig.10), commonly referred as stannous octoate Sn(Oct)$_2$, is a frequently used catalyst in the ROP of lactones and lactides.[10] In addition to defined homopolymers preparation, is also successfully used for advanced macromolecular structures synthesis. Trollsas and Hedrick prepared high molecule weight ($M_n \approx 10^5$ g/mol) dendrimers of poly(ε-caprolactone) with PDI 1.05 – 1.15 using this catalyst.[11] Sn(Oct)$_2$ is a strong transesterification agent, especially at elevated temperatures and long reaction time. The ROP of lactide catalyzed by Sn(Oct)$_2$ is fairly slow, but the addition of an equimolar amount of triphenylphosphine increases the rate and, as an additional advantage, this compound eliminates the occurrence of the undesirable side transesterification reactions.[10]

The last accepted proposal of polymerization mechanism prefers monomer-coordination/insertion mechanism, where Sn(Oct)$_2$ complex is firstly converted into a tin alkoxide before ring-opening the monomer. The Figure 10 shows a formation of stannous alkoxide initiator, subsequent coordination/insertion of first monomer molecule into the stannous alkoxide (initiation) and mechanism of chain extension (propagation).[12]
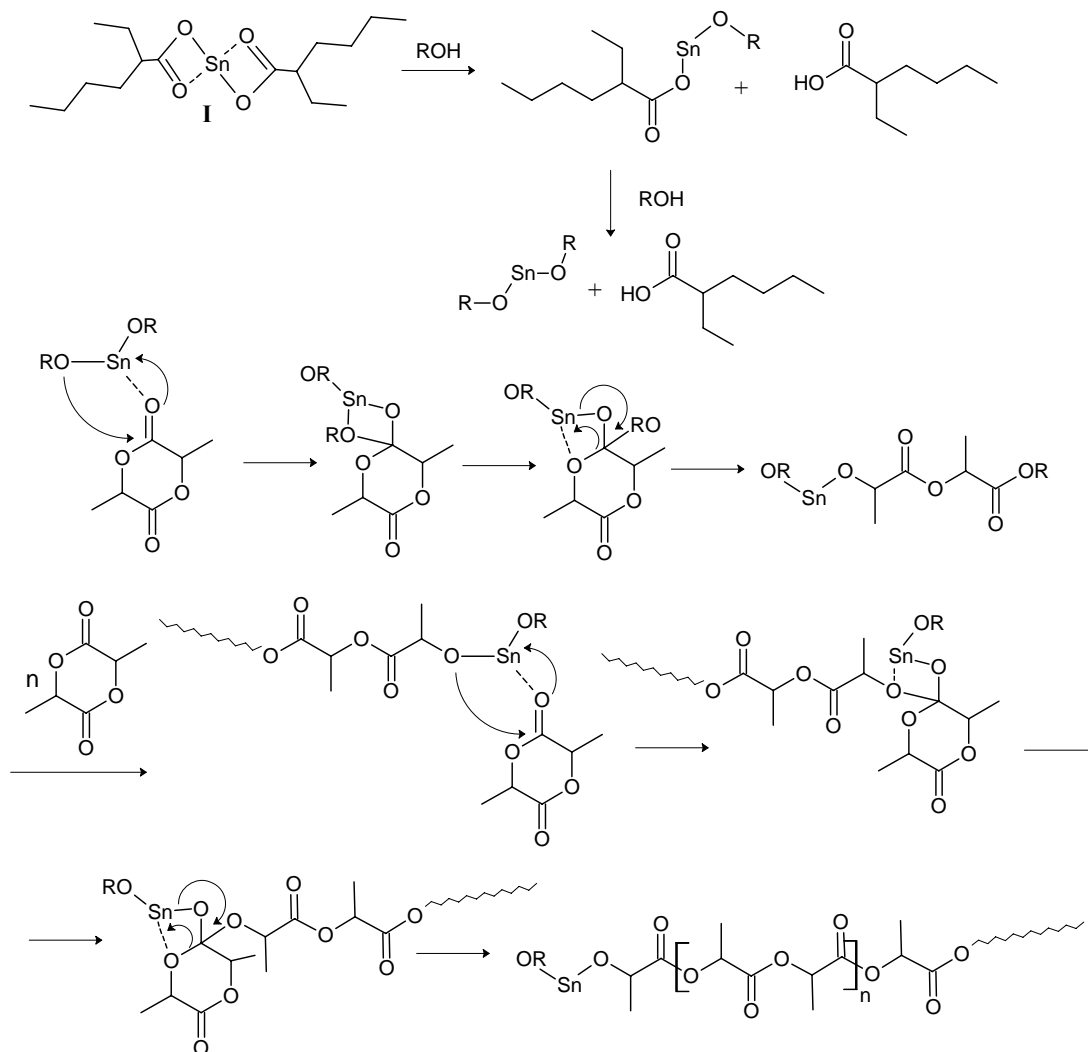

Figure 10 *Stannous octoate Sn(Oct)$_2$ as catalyst in the ROP of lactones and lactides*

2.5.2 Aluminium Tri-Isopropoxide

ROP of lactides by aluminium tri-isopropoxide Al(OiPr)$_3$ yields well defined polymers through living mechanism. Polymerization is assumed to proceed through a coordination-insertion mechanism, which consists of monomer coordination to the active species and insertion by rearrangement of the acyl-oxygen covalent bond of the monomer. The propagation is characterized by almost complete absence of undesirable transesterification reactions. The polymerizations, due to initiator activity, are carried out at low temperatures (0 – 25 °C) usually in solution. Most metal alkoxides typically form aggregates in solution at low temperatures and the groups involved in coordinative aggregation are not available for polymerization process. Due to this fact induction (activation) period could be observed during ROP. The type and size of the aggregates depend on the solvent polarity, the nature of the substituents and presence of coordinative ligands.[10]

2.6 Novel "green" catalysts for ROP of lactide

The main disadvantage of utilization of traditional transition metal based compounds catalyzing/initiating ROP of lactides and lactones consists in the necessity of removal of metal traces, which must be considered for polyester applications in resorbable biomaterials, and in microelectronics.[13] A significant effort to introduce metal-free species as catalysts possible for ROP of lactide and cyclic esters had been developed for last decade. Intensive research of *N*-heterocyclic carbenes as ROP catalysts resulted in well defined aliphatic co/polyester and macromolecular architectures synthesis.[14]

2.6.1 *N*-Heterocyclic carbenes (NHCs)

N-heterocyclic carbenes, introduced by Wanzlick, Arduengo and Bertand, are nucleophilic, metal-free compounds exhibiting catalytic performances for many organic reactions.[14] Nyce and Nolan have demonstrated that NHCs are also potent transesterification and polycondensation polymerization reaction catalysts.[15, 16] Carbenes can be synthesized with considerable diversity by varying the heteroatom in the ring (N or S), the steric arrangement and electronic character of the groups attached to the ring (R$_{2,3}$) and nitrogen(s) (R$_{1,4}$), and ethylene backbone (i.e. saturated or unsaturated) (Figure 11). Thus, nucleophilicity and basicity of NHCs can be tuned by both electronic and steric effects of substituents on NHC ring. The nomenclature of carbene is based on the five member heterocyclic composition (See in Fig. 11). Structure I represents triazolylidene carbene, II with saturated ethylene backbone imidazolinylidene carbene and imidazolylidene carbene with unsaturated ethylene backbone and structure III thiazolylidene carbene.[14] Compounds having this carbene platform are widely studied as catalysts for ROP of cyclic esters.
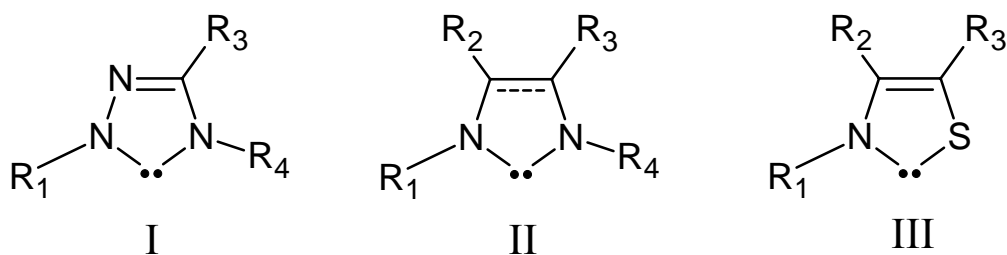
Figure 11 *Structural diversity of N-heterocyclic carbenes.*

2.6.1.1 "In Situ" Generation of NHCs

Generally, the isolation of *N*-heterocyclic carbenes is complicated by their extreme air and moisture sensitivity. Thus, their "in situ" formation and subsequent direct using for polymerization is preferred strategy. NHCs can be generated by deprotonation of their respective salts with appropriate bases. The Figure 12 describes the "in situ" deprotonation of carbene precursor – imidazolylidene salt with stoichiometric amounts of potassium *tert*-butoxide prior to the addition of monomers.[17] However slight excess of carbene precursor is usually used to ensure the complete consumption of potassium *tert*-butoxide as a potential initiator for anionic ROP.
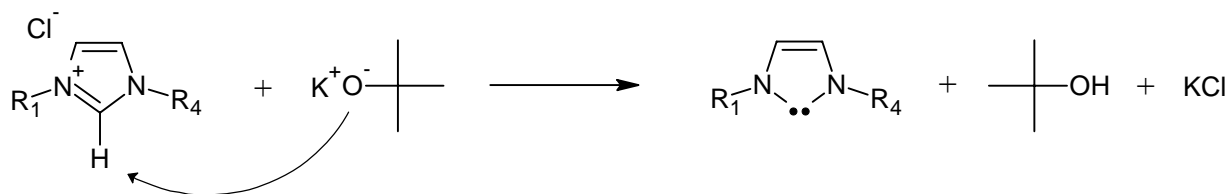
Figure 12 *"In situ"Generation of N-heterocyclic carbene.*

Alcohol adducts of *N*-heterocyclic carbenes which are successfully used as single component catalysts/initiator system for ROP represent another possibility. The elimination of alcohol component (initiator) is thermally controlled and hence in this way the initiation of the polymerization can be reversible command (Figure 13).[18]
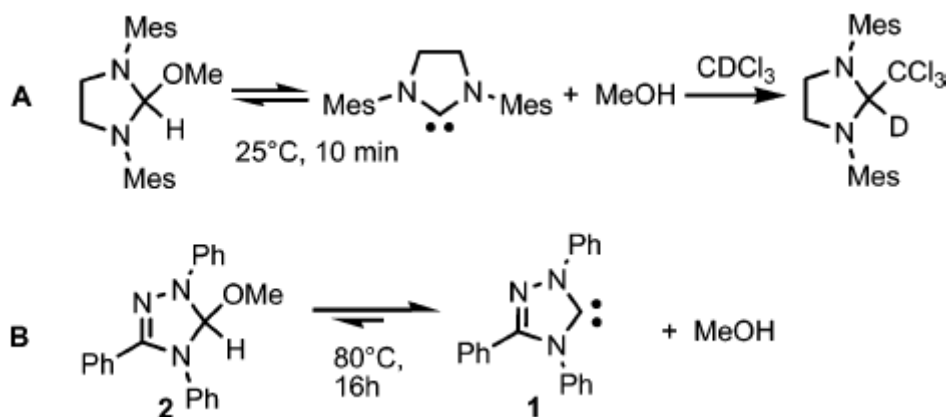
Figure 13 *Elimination of methanol from methoxyimidazolyl-2-yliden (A) and methoxytriazole (B).*

Polymerization reaction can be terminated by deactivation of the carbene centers by the addition of acetic acid, CO_2, or CS_2. Carbene forms with last two compounds a zwitterionic species which is easily removed from the polymer upon precipitation (Figure 14).
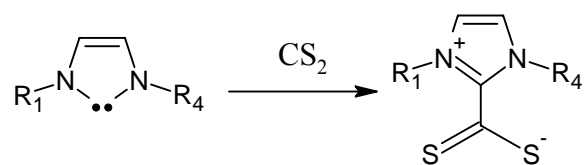
Figure 14 *Formation of the zwitterionic species as termination step.*[13]

2.6.1.2 Mechanism of ROP by NHCs

There are two suggested polymerization mechanisms taking place in ROP catalyzed by carbenes. A monomer activated mechanism (Fig. 15) mediated by the nucleophilic attack of the carbene on the lactide (or other cyclic ester) represents the first possibility. Chain-end activated mechanism during which the carbene activates the alcohol toward nucleophilic attack of monomer in the second route.

At first case, monomer is opened by the carbene (structure **I**) to form an acyl imidazole zwitterion **II**. Protonation of this zwitterion by an alcohol **III**, followed by attack of the resultant alkoxide on the activated acyl imidazolium **IV**, generates a new chain extended alcohol **V**. The α-chain end of the polymer bears the ester from the initiating alcohol, and the ω-chain end is a hydroxyl group serving as the nucleophile for subsequent chain propagation. The second possibility of the propagation step is anionic mechanism, when carbene is protonated with the alcohol, followed by nucleophilic addition of the resultant alkoxide anion to monomer.

The investigations focusing on monomer activated mechanism, which were carried out in the absence of initiator led to possible strategy of cyclic polyesters synthesis (Fig. 16).[19]
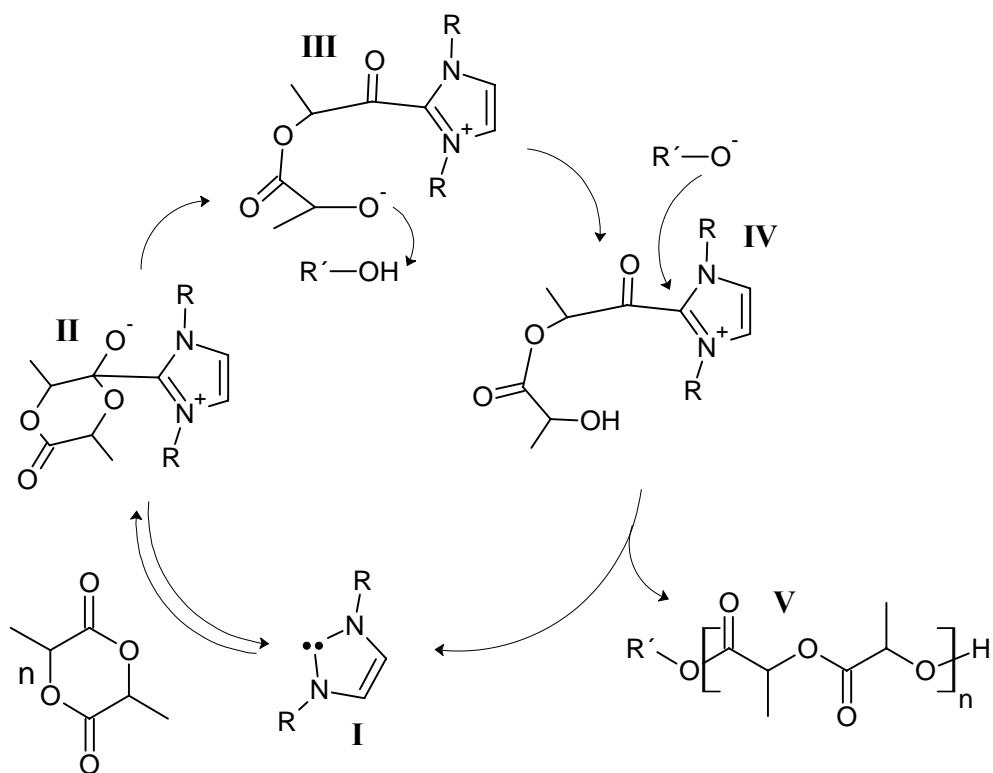
Figure 15 *Nucleophilic monomer-activated mechanism for ROP.*

Figure 16 *Synthesis of cyclic polyesters*

2.6.1.3 Catalytic activity of NHCs

Catalytic activity of NHCs for ROP of lactide (cyclic esters) depends sensitively on their structure respectively on heterocyclic ring composition and diversity of substituents on NHC ring. A wide range of diverse NHCs based on thiazolylidene carbenes, unsaturated imidazolylidene carbene, saturated imidazolinylidene carbene, and triazolylidene carbene have been shown to be effective as polymerization catalysts.[17]

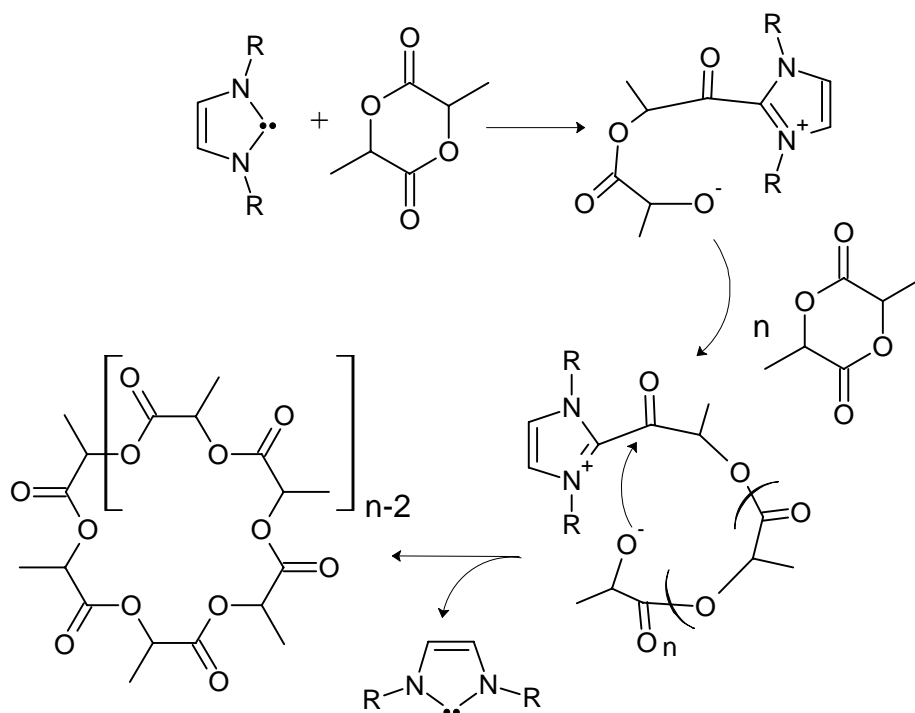Thiazolylidene carbenes **15** and **16** (See in Fig.17) investigated for ROP of lactide produce PLA with narrow polydispersities less than 1.1 for DP about 60. The disadvantages are reaching of conversion about 80 % after 48 hours and obtaining higher molecular weight polylactides after extended polymerization time (even 72 hours). It was found that the utilization of triethylamine as a cocatalyst ensures an optimal catalytic performance.[17, 19]

Imidazolylidene carbenes show significantly higher activity than thiazolylidine carbenes. By using structure **1** (Fig. 17) is possible to synthesize high molecular weight polylactides ($M_n > 25\ 000$ g/mol) within 10 minutes at lab temperature. Ratios catalysts to initiator of 0.25 – 1.50 and 1–2 M lactide solution leads to polylactides with polydispersities less than 1.2 and polymers with predicted molecular weigh. Also carbenes **3** and **5** are extremely active, but controlled polymerization progress requires low catalyst/initiator ratio and low monomer concentration, thus unlike higher consumption of solvent (See Fig 17). Higher monomer concentrations or catalyst/initiator ratios result by broadening polydispersities caused by side reactions.[17]

Imidazolinylidene carbenes with saturated ethylene backbone of NHC ring also exhibit superior catalytic performances with no significant differences in ROP reactivity between **1** and **10**. Typical solvents for these polymerizations are mainly THF, toluene and CH_2Cl_2. Carbenes besides its catalytic activity can readily dimerize if bulky substiuents are not introduced at 1,4 position (See Fig.) to provide kinetic stability. The disadvantage of imidazolinylidene carbenes is tendency to dimerize also in presence of bulky sunstiuents bonded on NHC ring (Fig 18).[17]

imidazolylidene carbenes

imidazolinylidene carbenes

triazolylidene carbene

thiazolylidene carbenes
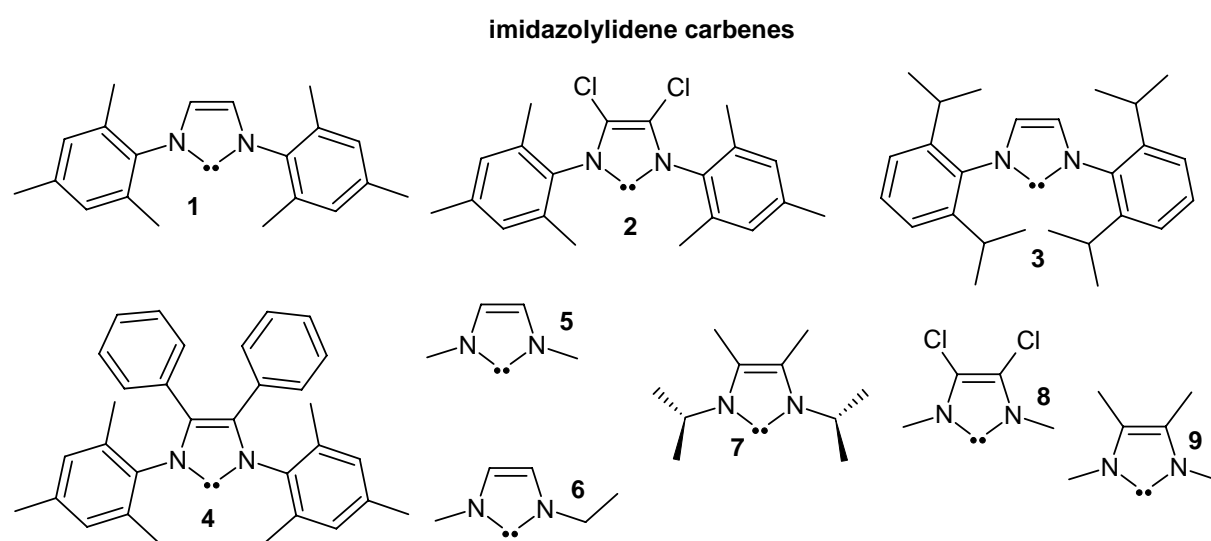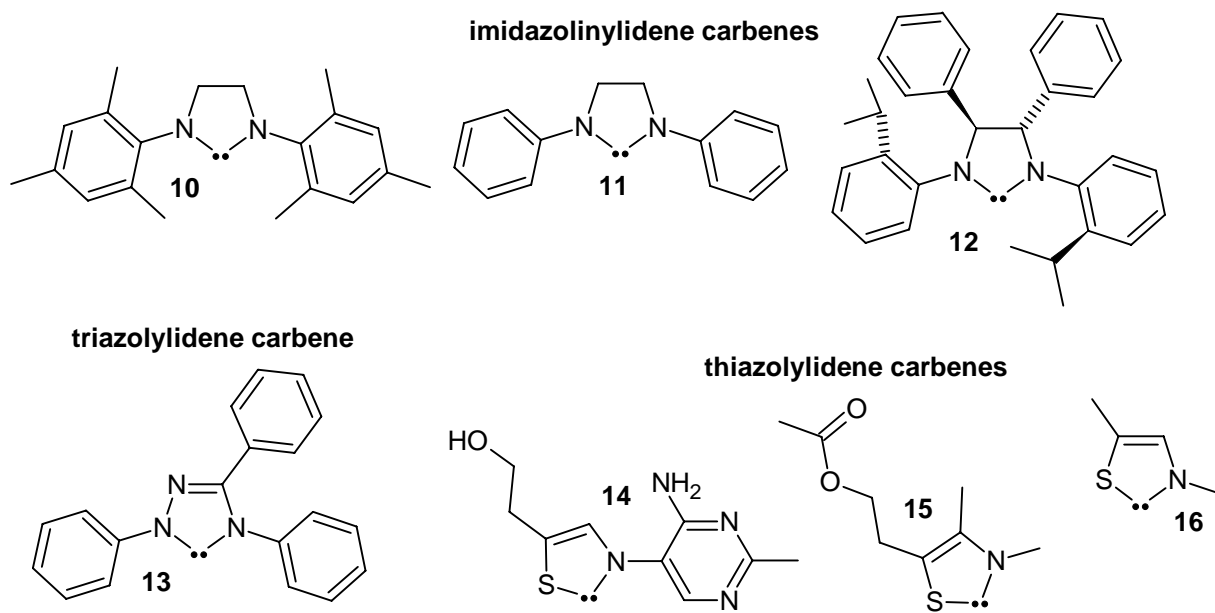
Figure 17 *A wide range of diverse NHCs*
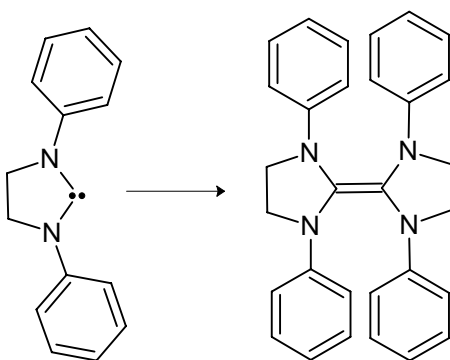
Figure 18 *Dimerization of carbenes*

3 EXPERIMENTAL PART

All manipulations of air and moisture sensitive compounds were performed under inert atmosphere and vacuum using vacuum line (manifold) (Figure 10) and Schlenk techniques.

Figure 19 *Vacuum line- manifold for experiments under inert atmosphere at Polymer Synthesis Laboratory at Faculty of chemistry BUT.*

3.1 Chemicals

- 1,3-di-*tert*-butyl-1*H*-imidazol-3-ium chloride (NHC–1G–F) purchased from Rhodia Company (Lyon, France) and used as received.

- *D,L*-lactide, *L*-lactide ($\geq$ 99.9 %) purchased from Polysciences, Inc., Pennsylvania and was purified by sublimation under vacuum at 75 °C (*D,L*-lactide) and at 60 °C (*L*-lactide).

- Tetrahydrofuran (THF, p.a.) purchased from Lach-Ner s. r. o. (CZ) was dried by metal sodium wire and benzophenone and freshly distilled prior to use.

- Methanol (MeOH, p.a.) purchased from Lach-Ner s. r. o. (CZ) and used as received.

- Benzyl alcohol (BnOH, anhydrous, 99.8 %) purchased from Sigma-Aldrich and used as 0.1 mol·L^{-1} solution at THF.

- Poly(ethylene glycol) monomethyl ether (PEG1000) purchased from Sigma-Aldrich was purified degassing under vacuum for 10 hours and used as 0.1 mol·L^{-1} solution at THF.

- Poly(ethylene glycol) monomethyl ether (PEG2000) purchased from Sigma-Aldrich was purified degassing under vacuum for 10 hours and used as 0.05 mol·L^{-1} solution at THF.

- Potassium *tert*-butoxide (*t*-BuO^{-}K^{+}, 1 mol·L^{-1} solution at THF) purchased from Sigma-Aldrich and used as received.

- Carbon disulphide (CS$_2$, p.a.) purchased from Merck and was used as received.

- Nitrogen gaseous (N$_2$, 99.999 %) purchased from SIAD Czech spol. s. r. o. and was purified passing through the drying columns filled with molecular sieves and Cu catalysts to remove the traces of moisture and oxygen.

3.2 Methods

3.2.1 Polymerization catalyzed by NHC-carbene prepared in situ

Typical procedure of lactide monomer polymerization was performed in a specially designed glass reactor. Initially, the reactor was evacuated for forty minutes, and then the purification cycles (nitrogen flushing/evacuation) were repeated. At first, the NHC-carbene catalytic precursor was introduced to activation part of the reactor equipped with a magnetic stirring bar, than potassium *tert*-butoxide (1 mol·L^{-1} solution at THF, ratio NHC / *t*-BuO^{-}K^{+} = 1/1). Tetrahydrofuran (THF) was then added by Hamilton microsyringe to form 0.1 mol·L^{-1} solution of both NHC-carbene catalytic precursor and potassium *tert*-butoxide. Solution was stirred for 40 minutes to ensure the reaction between the carbene precursor and potassium *tert*-butoxide. A suspension was observed during this carbene formation period. The reaction mixture was then filtered through a sintered glass (S3) to the polymerization part of the reactor to obtain slight yellow solution. The second part of THF calculated to form 1 mol·L^{-1} solution of lactide was then added. Benzyl alcohol (BnOH) was injected by the Hamilton microsyringe (0.1 mol·L^{-1} solution at THF). Solid monomer (*D,L*-lactide) was transferred under nitrogen and the reaction was kept for 2 hours at laboratory temperature (23 °C). Afterwards, the reaction was quenched with a few drops of CS$_2$. The viscous solution was added using a pipette into a cold methanol (−10 °C) the precipitated solids were removed by decantation and dried under vacuum until constant weight.

3.3 Characterization of polymers

3.3.1 Gel permeation chromatography (GPC)

Number average molecular weights (M_n) and polydispersity index (M_w/M_n) of the polymers were determined by gel permeation chromatography (GPC) method. GPC was carried out on an Agilent Technologies 1100 Series instrument equipped with RI and UV-VIS detectors. Polystyrene samples of known molecular weight were used as calibration standards. 5 μm column (300 mm × 7.5 mm) was used with THF as a mobile phase solvent. The samples were prepared by dissolving 5 mg polymer sample at THF.

3.3.2 Nuclear magnetic resonance spectroscopy (^{1}H NMR)

^{1}H NMR spectra were recorded on a Bruker Avance (300 MHz) spectrometer (16 scans) in CDCl$_3$ as a solvent and referenced to the residual signals of solvent proton. Polymer samples before analysis were purified four times by dissolving at THF and precipitating in cold methanol. The samples were prepared by dissolving 25 mg of purified and dried polymer in CDCl$_3$. The spectra obtained were evaluated by programs SpinWorks 3.0 and ACD SpecViewer 4.53.

4 RESULTS AND DISCUSSION

In this work, the screening of polymerization behavior of *N*-heterocyclic carbene with *tert*-butyl substituents on the ring towards ring-opening polymerization (ROP) of lactide was performed. The carbene studied was received as a chloride salt from Rhodia Comp. (Lyon) and its synthesis was carried out by Arduengo et al.[20] For the carbene active centres formation their "in situ" synthesis by the reaction with t-BuO$^-$K$^+$ was chosen (See in Fig. 20). Benzyl alcohol as initiator was examined assuming the function of carbene as catalyst in the ROP. The polymerization experiments were carried out in THF solution at lab temperature.

Particularly, the influence of different reaction composition including ratios between catalyst/initiator/monomer on polymerization process was studied.

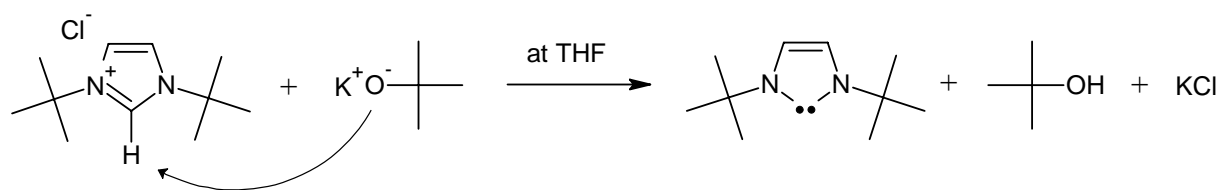**Figure 20** *"In situ" Generation of N-heterocyclic carbene.*

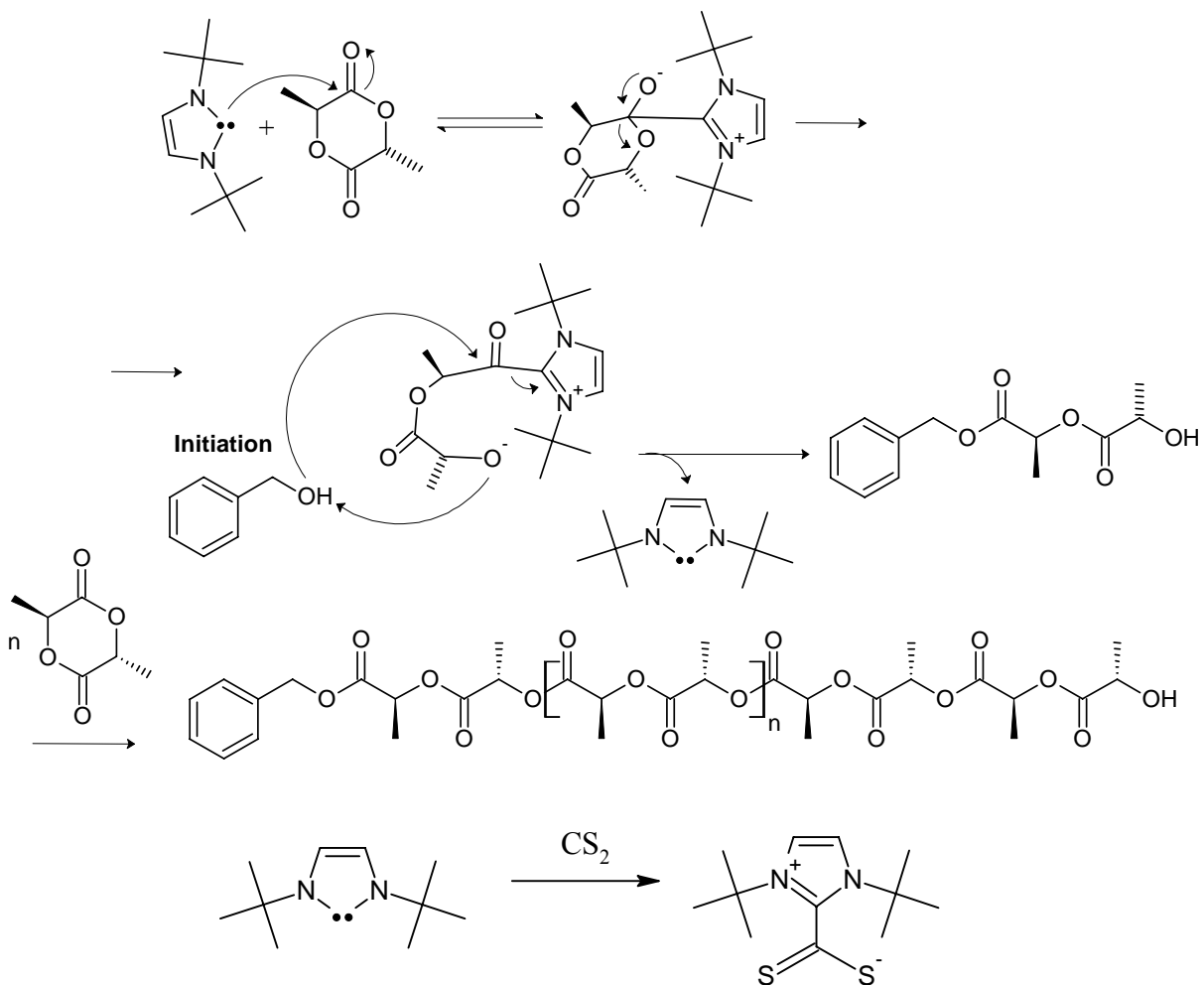**Figure 21** *Detail of carbene generation reaction after 40 minutes activation period.*

Figure 22 Scheme of ROP *D,L*-lactide with *tert*-butyl substituted *N*-heterocyclic carbene and its deactivation by CS_2 forming zwitterionic structure..
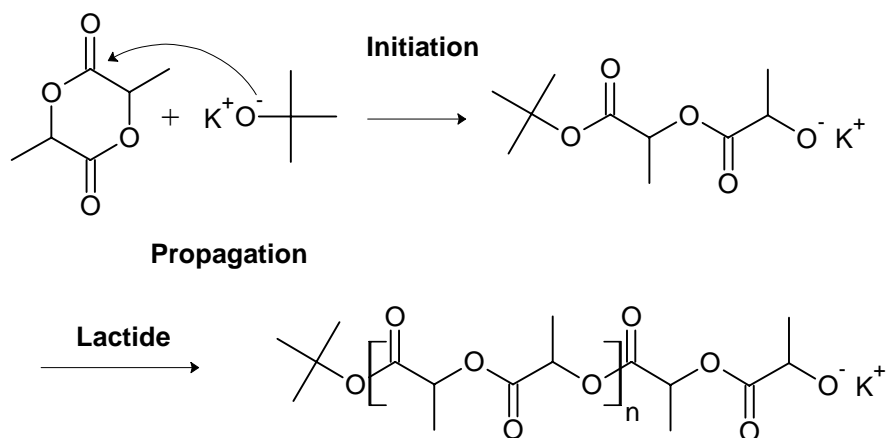

Figure 23 Scheme of competitive anionic polymerization by potassium *tert*-butoxide.

4.1 Influence of molar ratio catalyst/initiator (NHC/BnOH)

Based on literature review discussing similar catalytic systems a few pilot experiments with varying of molar ratios catalyst to initiator (0.9; 1.3; 1.8 and 2.7) were performed. All the experiments were carried out for 2 hours with monomer concentration of 1 M in THF solution (Table 1).

The influence of NHC/BnOH ratio demonstrates Figure 24. Firstly increasing tendency of conversion with increasing molar ratio NHC/BnOH was observed. Maximal conversion reached in range 1 − 1.5 molar ratios NHC/BnOH. More catalysts or lowering initiator concentration affects low conversion obtaining. Molecular weight relationship shows decrease with increasing catalysts/initiator ratio and to obtain high polymers is necessary to reduce catalyst ratios equivalent to initiating alcohol to minimum. This behavior explains very high efficiency of this catalytic process.

Theoretical molecular weight is not in correlation with by GPC obtained one and basically eliminates explaining this process as living. This disorder is probably caused by presence of potassium *tert*-butoxide in reaction mixture as the second capable catalyst/initiator of anionic polymerization. Control experiment without carbene catalyst, but in presence of potassium *tert*-butoxide was performed with 44 % conversion at 30 min, M_n 11 000 g/mol and PDI 1.73. Undiserable presence of *tert*-butoxide initiator at polymerization mixture was caused by incomplete reaction generating the "free carbene" from its imidazolium salt. After activation period solid particles (See Fig. 21) was mostly unchanged and unconsumed *tert*-butoxide molecules were filtrated into polymerization part of the reactor. However literature mention solubility of imidazolium salts at THF, this work used catalytic precursor is not soluble at THF. This fact also causes that the real molar ratio NHC/BnOH is much lower than predicted tabulated number. Optimal conditions obtained from this part of screening were determined as the ratio NHC/BnOH 0.9 − 1.5.

From the other hand, experiment where NHC/BnOH was 2.7, thus the higher amount of "free carbene" was ensured offer high molecular weight polylactide at 78 % and relatively favorable polydispersity 1.45. It's clear that higher presence of "free carbene" at polymerization system narrows polydispersity and reduce effect of *tert*-butoxide initiator.

Table 1 The effect of molar ratio of NHC/BnOH on ROP of *D,L*-lactide [a]

entry	n(C₀)/n(I₀)	n(M₀)/n(I₀)	conversion [b] [%]	$M_{n\,theor}$ [c] [g/mol]	$M_{n\,GPC}$ [d] [g/mol]	M_w/M_n [d]
12		45	48	3 600	17 500	1.22
44	0.9	90	77	9 900	16 300	1.83
34		135	79	15 200	14 600	1.67
42		180	43	11 100	18 700	1.72
39		45	51	3 300	1 500	1.58
45	1.3	90	68	8 800	11 200	1.93
62		135	88	17 200	8 900	1.73
36		180	68	15 500	12 400	1.58
47		45	40	2 600	12 200	1.22
48	1.8	90	52	6 800	13 100	1.79
38		135	82	15 800	13 500	1.98
37		180	81	20 800	18 700	1.83
31		45	33	2 100	4 800	2.13
29	2.7	90	45	5 800	6 300	1.65
30		135	78	15 100	13 400	1.45
28		180	75	19 200	24 200	1.67

[a] THF solution, lab temperature (23-24 °C), BnOH [0.1 M in THF] , [DLLA]₀ = [M]₀ = 1 M, activation period 40 min, polymerization time t_p = 2 hours.

[b] Determined as the gravimetric yield.

[c] $M_{n\,theor} = (M_{wDLLA} \times [DLLA]_0 /[BnOH]_0 \times \text{conversion (\%)})/100 + M_{wBnOH}$

[d] Determined by GPC against PS standards in THF.

Figure 24 Relationship between conversion of *D,L*-lactide ROP and molar ratio catalyst/initiator.

Figure 25 Relationship between number average molecular weight of *D,L*-lactide ROP and molar ratio catalyst/initiator.

4.2 Influence of molar ratio monomer/initiator (DLLA/BnOH)

Examination the influence of monomer resource on ROP was performed by series of experiments varying the DLLA/BnOH molar ratio. This relationship is implicitly influenced by catalyst/initiator ratio, because for ever polymerization period and catalyst amount have to exist optimal amount of monomer, when is at most polymerized. For example monomer/initiator molar ratio 45 requires lower catalysts/initiator molar ratio to obtain high molecular weight polymer of narrow polydispersity. Increasing catalyst concentration resulted in broader dispersed polylactides. The highest conversions 80 − 90 % were observed at DLLA/BnOH ratio 135. M_n determined by GPC was also in good correlation with theoretical value, thus PDI acts about 1.45 − 2. Generally, high conversions and high polylactides (M_n 13 000 g/mol) were reached, when initial ratio monomer/initiator was proposed up to 90. This trend also was confirmed by polymerization runs carried out for 15, 30 and 60 minutes.

Table 2 The effect of molar ratio of DLLA/BnOH of *D,L*-lactide [a]

entry	$n(M_0)/n(I_0)$	$n(C_0)/n(I_0)$	conversion [b] [%]	$M_{n\ theor}$ [c] [g/mol]	$M_{n\ GPC}$ [d] [g/mol]	M_w/M_n
12		0.9	48	3 600	17 500	1.22
39	45	1.3	51	3 300	1 500	1.58
47		1.8	40	2 600	12 200	1.22
31		2.7	33	2 100	4 800	2.13
44		0.9	77	10 000	16 300	1.83
45	90	1.3	68	8 800	11 200	1.93
48		1.8	52	6 800	13 100	1.79
29		2.7	45	5 800	6 300	1.65
34		0.9	79	15 200	14 600	1.67
62	135	1.3	88	17 200	8 900	1.73
38		1.8	82	15 800	13 500	1.98
30		2.7	78	15 100	13 400	1.45
42		0.9	43	11 100	18 700	1.72
36		1.3	68	17 500	12 400	1.58
37	180	1.8	81	20 800	18 700	1.83
28		2.7	75	19 200	24 200	1.67
32		4.4	45	11 400	1 500	1.50

[a] THF solution, lab temperature (23-24 °C), BnOH [0.1 M in THF] , $[DLLA]_0 = [M]_0 = 1$ M, activation period 40 min, polymerization time $t_p = 2$ hours.

[b] Determined as the gravimetric yield.

[c] $M_{n\ theor} = (M_{wDLLA} \times [DLLA]_0 /[BnOH]_0 \times conversion\ (\%))/100 + M_{wBnOH}$

[d] Determined by GPC against PS standards in THF.

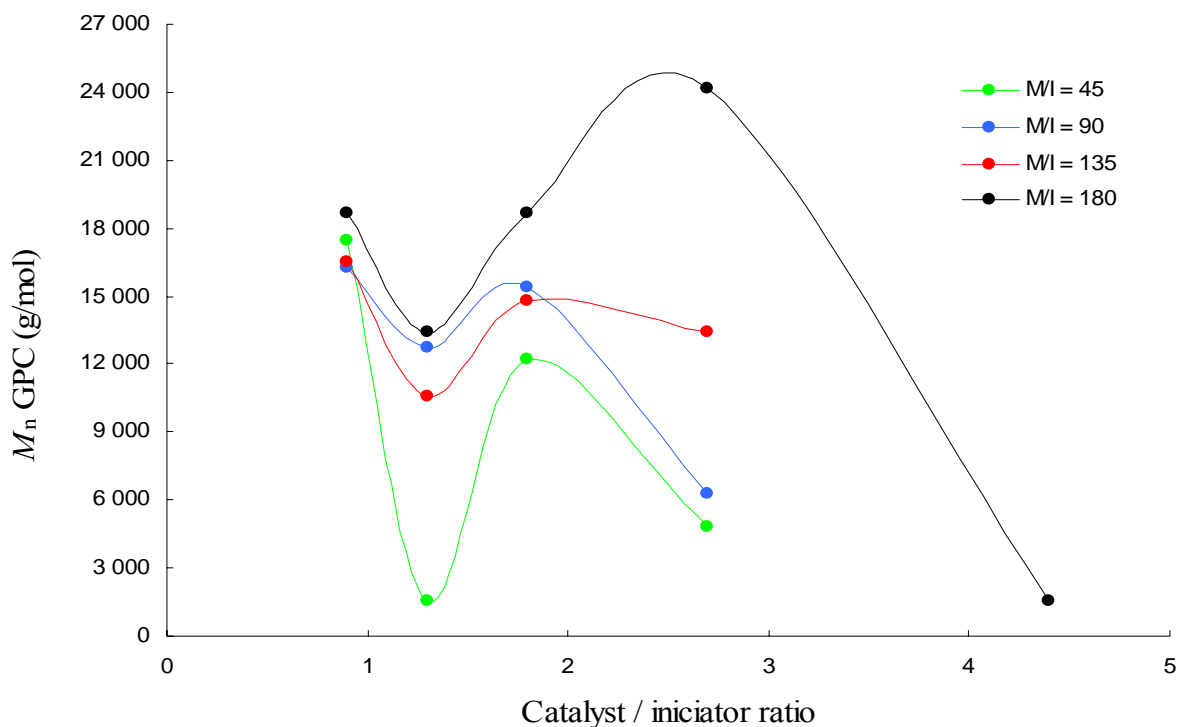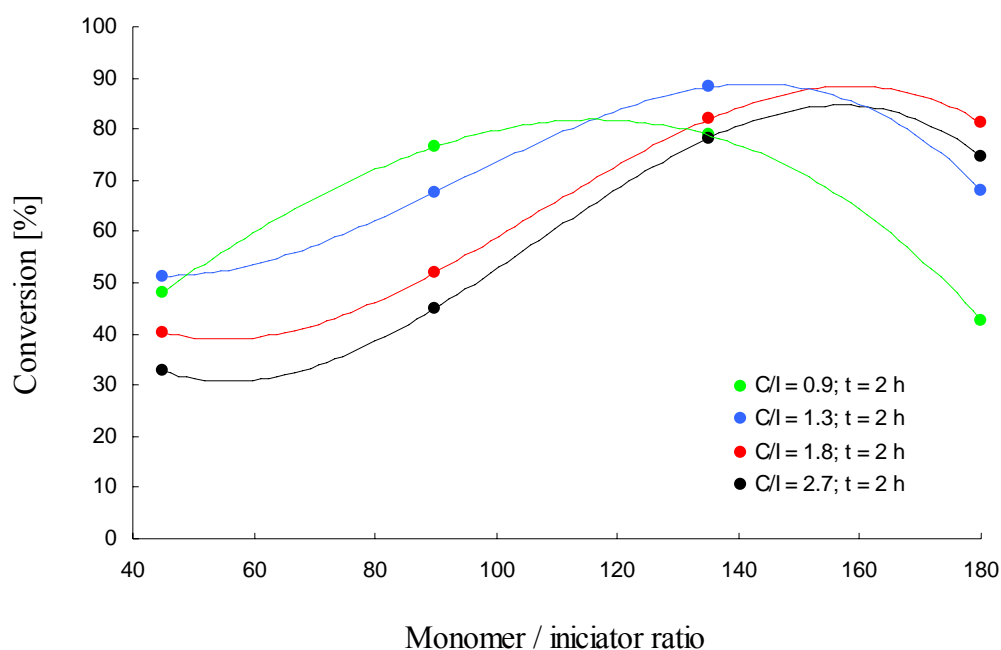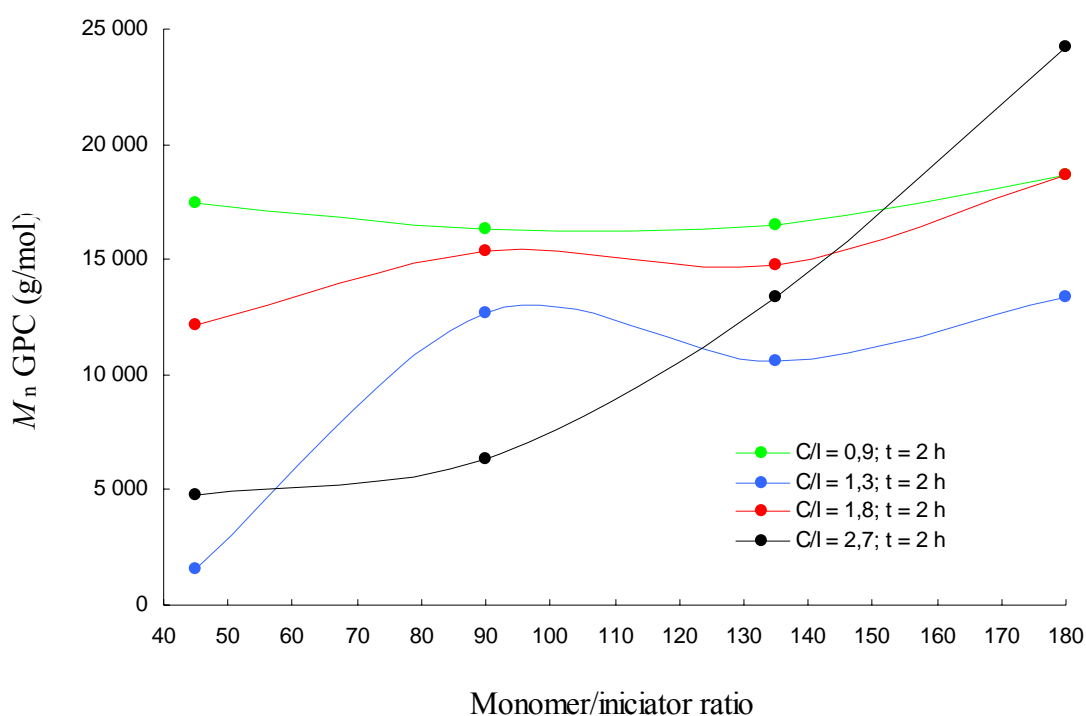**Figure 26** Relationship between conversion of *D,L*-lactide ROP and molar ratio monomer/initiator.

Figure 27 Relationship between number average molecular weight of *D,L*-lactide ROP and molar ratio monomer/initiator.

4.3 Influence of molar ratio monomer/catalyst (DLLA/NHC)

Straight relationship between monomer and catalysts concentration was obtained by mathematical operation, when $n(M_0)/n(I_0)$ ratio is divided by $n(C_0)/n(I_0)$ ratio. Obtained curves shows parabolic progress (Fig 28). High catalysts concentration, low molar ration $n(M_0)/n(C_0)$, causes utilization for side reactions which fractionate polylactide macromolecules to low molecular weight oligomers. These oligomers were soluble at methanol and were not precipitated, thus are not participated in conversion value determined as a gravimetrical yield. Present higher storage of monomer, high $n(M_0)/n(C_0)$ value causes high conversions.

Table 3 The effect of molar ratio of DLLA/NHC of *D,L*-lactide [a]

entry	$n(C_0)/n(I_0)$	$n(M_0)/n(C_0)$	conversion [b] [%]	$M_{n\ theor}$ [c] [g/mol]	$M_{n\ GPC}$ [d] [g/mol]	M_w/M_n
35		50	48	3 600	17 500	1.22
44	0.9	100	77	9 900	16 300	1.83
34		150	79	15 200	14 600	1.67
42		200	43	11 100	18 700	1.72
39		35	51	3 300	1 500	1.58
45	1.3	69	68	8 800	11 200	1.93
62		104	88	17 200	8 900	1.73
36		138	68	15 500	12 400	1.58

47		25	40	2 600	12 200	1.22
48	1.8	50	52	6 800	13 100	1.79
38		75	82	15 800	13 500	1.98
37		100	81	20 800	18 700	1.83
31		17	33	2 100	4 800	2.13
29	2.7	33	45	5 800	6 300	1.65
30		50	78	15 100	13 400	1.45
28		67	75	19 200	24 200	1.67

[a] THF solution, lab temperature (23-24 °C), BnOH [0.1 M in THF] , $[DLLA]_0 = [M]_0 = 1$ M, activation period 40 min, polymerization time $t_p = 2$ hours.

[b] Determined as the gravimetric yield.

[c] $M_{\text{n theor}} = (M_{\text{wDLLA}} \times [DLLA]_0 / [BnOH]_0 \times \text{conversion (\%)}) / 100 + M_{\text{wBnOH}}$

[d] Determined by GPC against PS standards in THF.
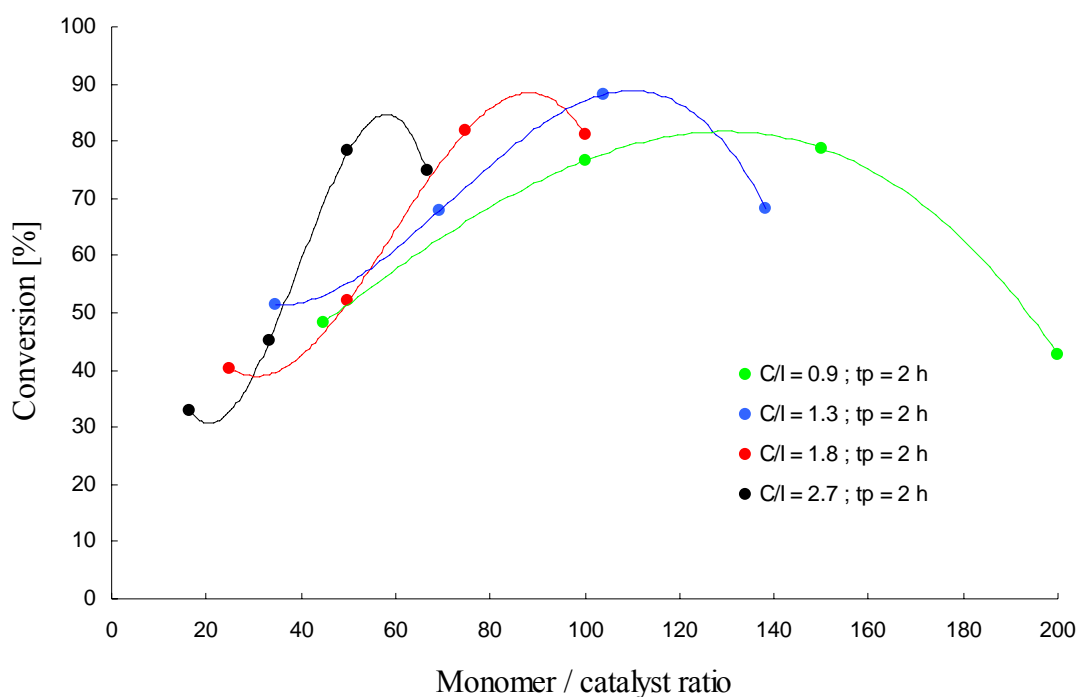

Figure 28 Relationship between conversion of *D,L*-lactide ROP and molar ratio monomer/ catalyst.
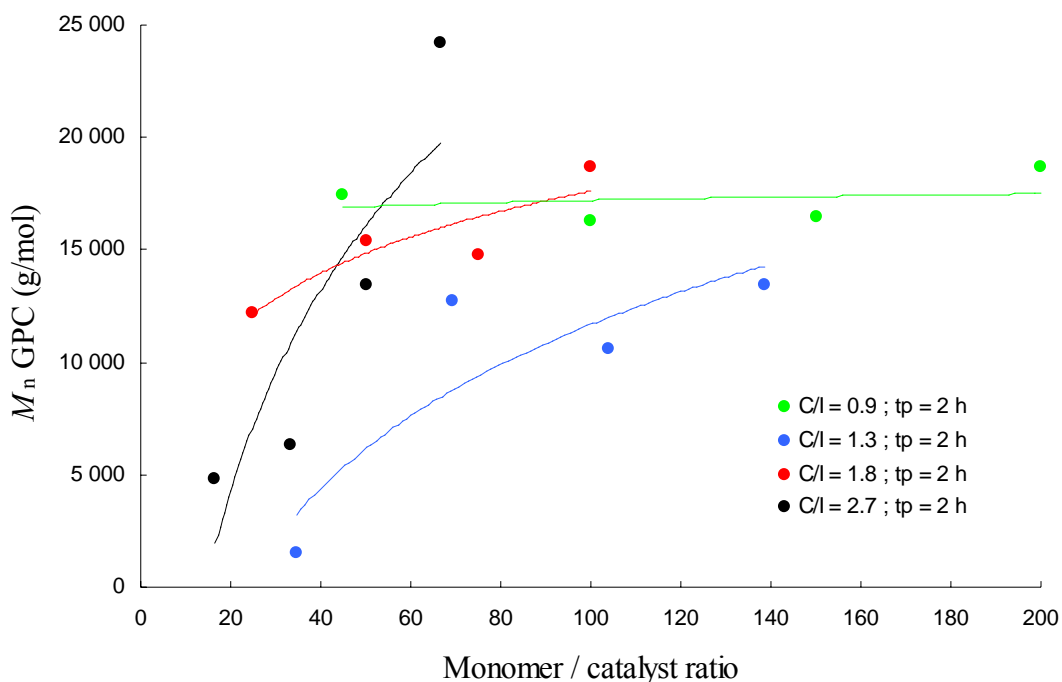
Figure 29 Relationship between number average molecular weight of *D,L*-lactide ROP and molar ratio monomer/catalyst.

4.4 Kinetics study

Kinetics study of ROP of *D,L*-lactide was performed as separately lead identical polymerizations, which was terminated (quenched by CS_2) at various time (0.25; 0.5; 1 and 2 hours). The dependence of the conversion on the time obtained under conditions mentioned at Table 4 is given in Figure 30 and 31. For this kinetic study was chosen higher catalyst/initiator ratio to ensure more "free carbene" presence. Swift increase in conversion was observed during first 30 minutes.

Table 4 Kinetic study of ROP *D,L*-lactide [a]

entry	$n(M_0)/n(I_0)$	$n(C_0)/n(I_0)$	Time [hour]	conversion [b] [%]	$M_{n\ theor}$ [c] [g/mol]	$M_{n\ GPC}$ [d] [g/mol]	M_w/M_n
72			0.25	5	400	1 900	2.20
71	45	1.8	0.50	22	1 500	2 600	1.74
65			1.00	16	1 100	2 100	1.65
47			2.00	40	2 600	12 200	1.22
58			0.25	7	500	2 300	1.43
63	45	2.7	0.50	28	1 800	3000	2.57
64			1.00	35	2 300	5 600	1.44
31			2.00	33	2 100	4 800	2.13
70			0.25	43	5 600	6 400	1.21
83	90	1.8	0.50	53	6 900	14 000	1.48
68			1.00	51	6 600	8 000	1.71
48			2.00	52	6 800	15 400	1.66

			0.25	43	5 600	2 700	1.60
66			0.25	43	5 600	2 700	1.60
41	90	2.7	0.50	49	6 300	5 300	1.51
40			1.00	33	4 300	6 300	1.39
29			2.00	45	5 800	6 300	1.65
81			0.25	56	10 900	18 400	1.47
49	135	1.8	0.50	84	16 300	7 800	1.61
43			1.00	77	15 100	10 000	1.77
38			2.00	82	15 800	14 800	1.91
67			0.25	79	15 400	16 500	1.69
56	135	2.7	0.50	69	13 400	5 700	1.30
55			1.00	71	13 900	5 100	1.33
30			2.00	78	15 100	13 400	1.45
57			0.25	52	13 400	15 500	1.72
50	180	1.8	0.50	47	12 300	14 900	1.37
53			1.00	51	13 300	14 600	1.42
37			2.00	81	20 800	18 700	1.83
61			0.25	64	16 600	21 500	1.45
51	180	2.7	0.50	54	13 900	19 800	1.44
54			1.00	82	21 400	13 600	1.85
28			2.00	75	19 200	24 200	1.67

[a] THF solution, lab temperature (23-24 °C), BnOH [0.1 M in THF] , $[DLLA]_0 = [M]_0 = 1$ M, activation period 40 min.

[b] Determined as the gravimetric yield.

[c] $M_{n\,theor} = (M_{wDLLA} \times [DLLA]_0 / [BnOH]_0 \times \text{conversion}\ (\%)) / 100 + M_{wBnOH}$

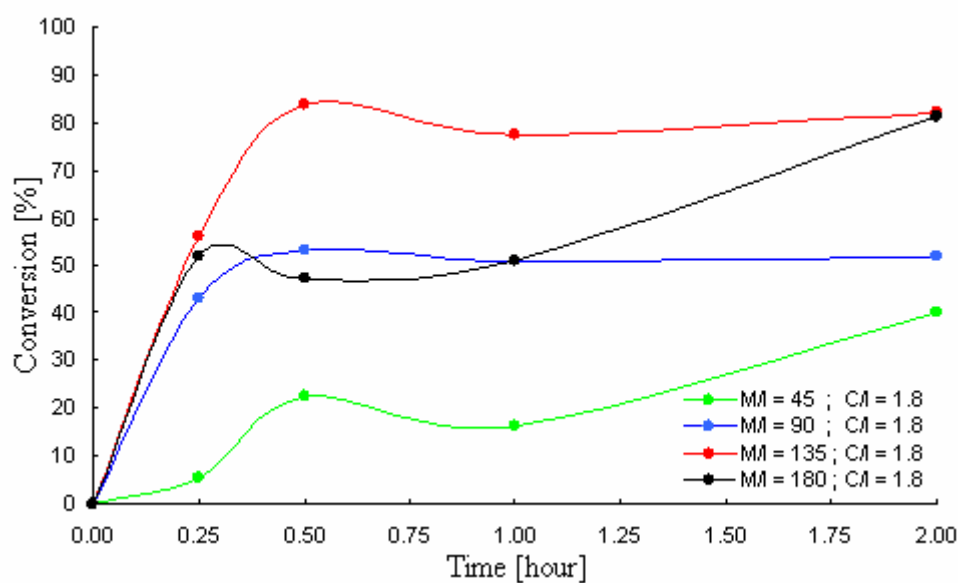[d] Determined by GPC against PS standards in THF.

Figure 30 Time progress of conversion of *D,L*-lactide ROP.
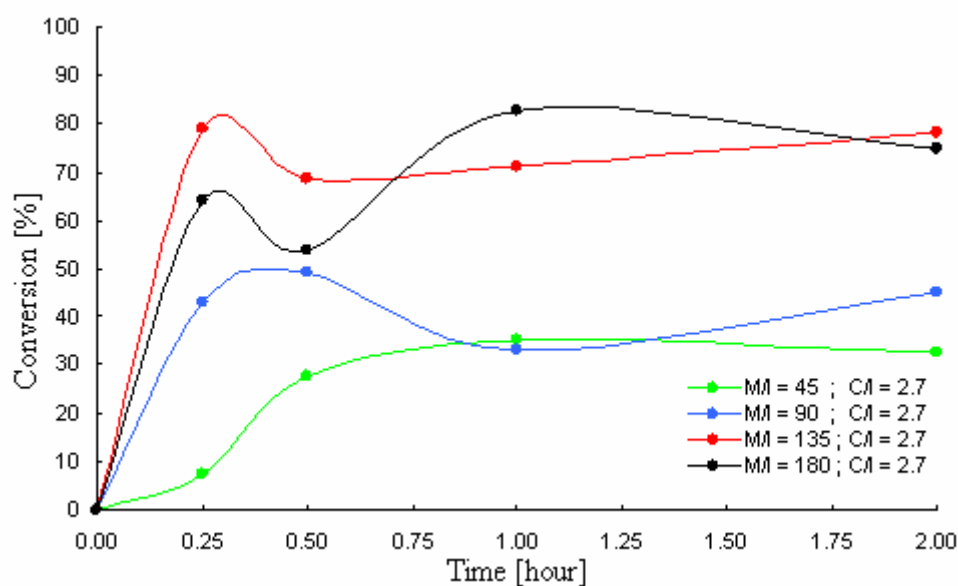
Figure 31 Time progress of conversion of *D,L*-lactide ROP.
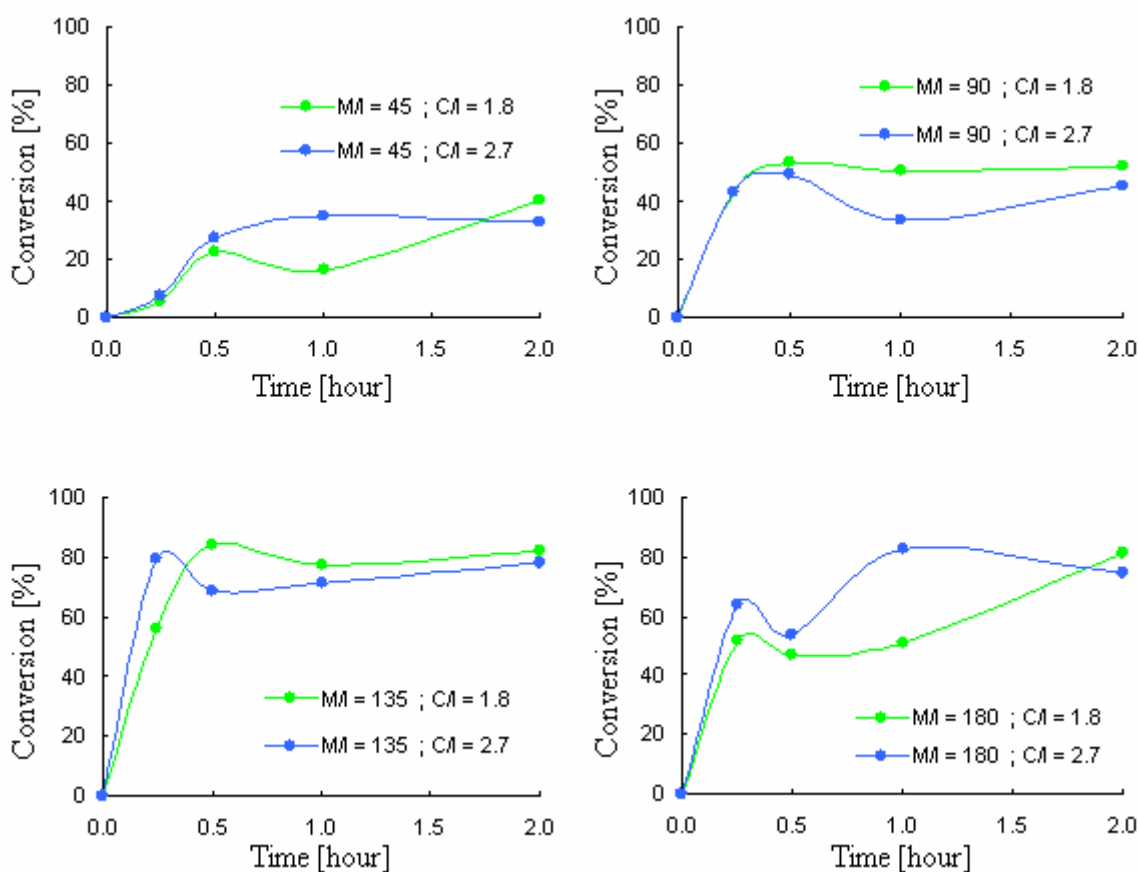

Figure 32 Time progress of conversion of *D,L*-lactide ROP; comparison of $n(M0)/n(I0)$ and $n(C_0)/n(I_0)$ molar ratios

4.5 Study of polymerization efficiency of NHC carbene catalyst in the presence of macroinitiator (PEG) and *L*-lactide monomer

Studied carbene formed in the presence of benzyl alcohol an effective system producing polymers with conversion up to 88 % at lab temperature. To examine the potential of the catalyst a series of runs with macroinitiator-polyethyleneglycol was carried out and *L*-lactide as monomer was used as well. The results are summarized in Table 4. ^{1}H NMR spectroscopic analysis was performed to confirm the character of chain end groups and to calculate M_n.

Table 5 Polymerization Data of Polylactide Using NHC–1G–F as a Catalyst [a]

entry	Monomer	Initiator	conversion [b] [%]	$M_{n\ theor}$ [c] [g/mol]	$M_{n\ GPC}$ [d] [g/mol]	$M_{n\ NMR}$ [e] [g/mol]	M_w/M_n
49	*D,L*-lactide	BnOH	84	16 300	7 800	12 500	1.61
87	*D,L*-lactide	PEG2000	47	11 000	12 100	9 800	1.19
85	*L*-lactide	BnOH	84	16 400	25 000	37 000	1.63
88	*L*-lactide	PEG1000	44	9 600	14 300	12 500	1.20
89	*L*-lactide	PEG2000	60	13 800	11 200	11 100	1.29

[a] THF solution, lab temperature (23-24 °C), t_p = 0.5 hour, BnOH [0.1 M in THF], PEG1000 [0.1 M in THF], PEG2000 [0.05 M in THF], $[LA]_0 = [M]_0 = 1$ M, $n(M_0)/n(I_0) = 135$, $n(C_0)/n(I_0) = 1.8$, activation period 40 min.

[b] Determined as the gravimetric yield.

[c] $M_{n\ theor} = (M_{wLA} \times [LA]_0 / [Initiator]_0 \times conversion\ (\%))/100 + M_{wInitiator}$

[d] Determined by GPC against PS standards in THF.

[e] Determined by integration of signal of polymer protons and tertiary proton H_e ending the polymer chain.
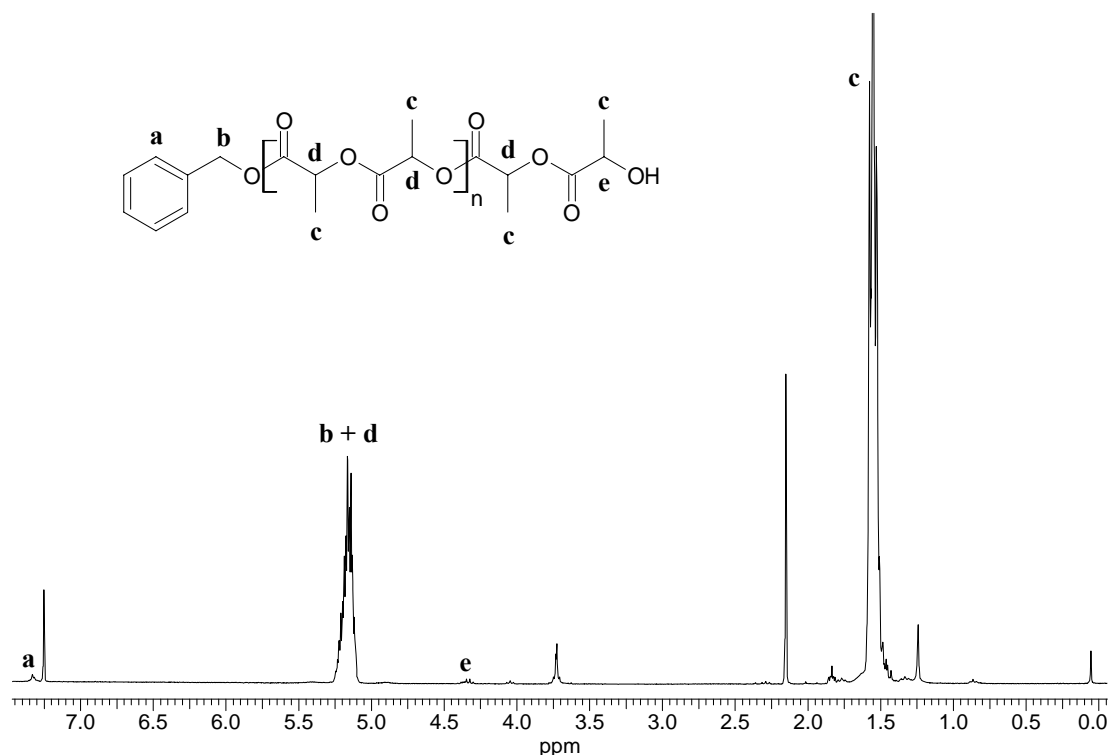

Figure 33 [1]*H NMR spectrum in CDCl₃ of Poly(D,L-lactide) (**sample 49**) obtained by ROP of D,L-lactide initiated by BnOH in the presence of NHC–1G–F as a catalyst.*
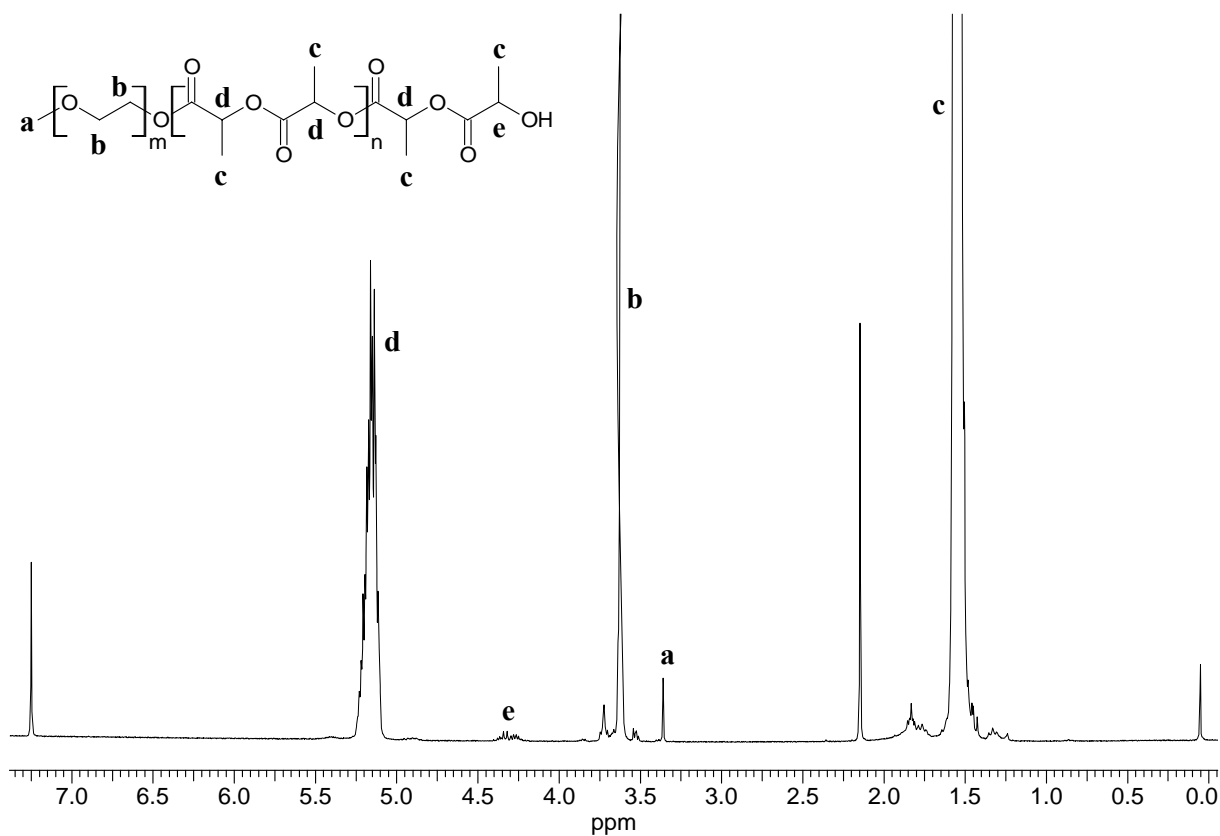
Figure 34 *¹H NMR spectrum in CDCl₃ of Poly(D,L-lactide)* (*sample 87*) *obtained by ROP of D,L-lactide initiated by PEG2000 in the presence of NHC–1G–F as a catalyst.*

Figure 35 *¹H NMR spectrum in CDCl₃ of Poly(L-lactide)* (*sample 85*) *obtained by ROP of*

Figure 36 ^1H *NMR spectrum in CDCl$_3$ of Poly(L-lactide)* (**sample 88**) *obtained by ROP of L-lactide initiated by PEG1000 in the presence of NHC–1G–F as a catalyst.*

Figure 37 ^1H *NMR spectrum in CDCl$_3$ of Poly(L-lactide)* (**sample 89**) *obtained by ROP of L-lactide initiated by PEG2000 in the presence of NHC–1G–F as a catalyst.*
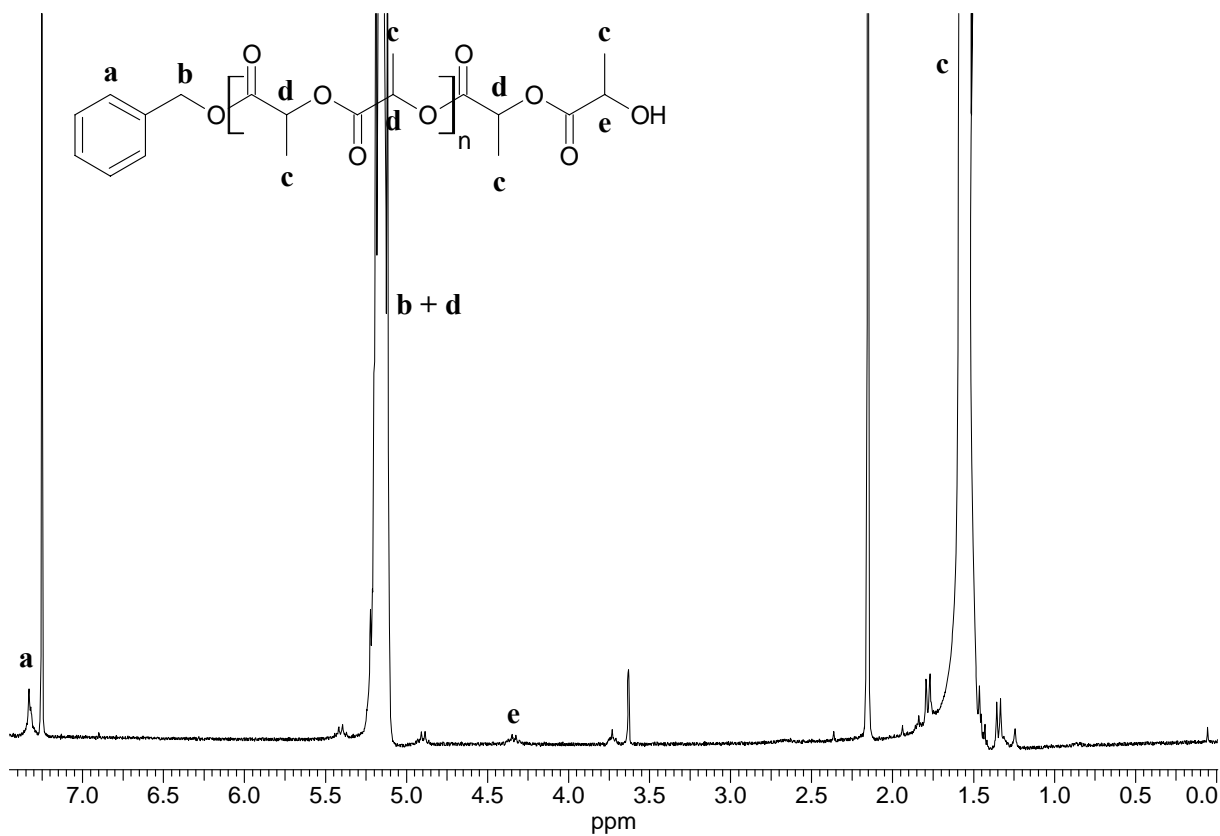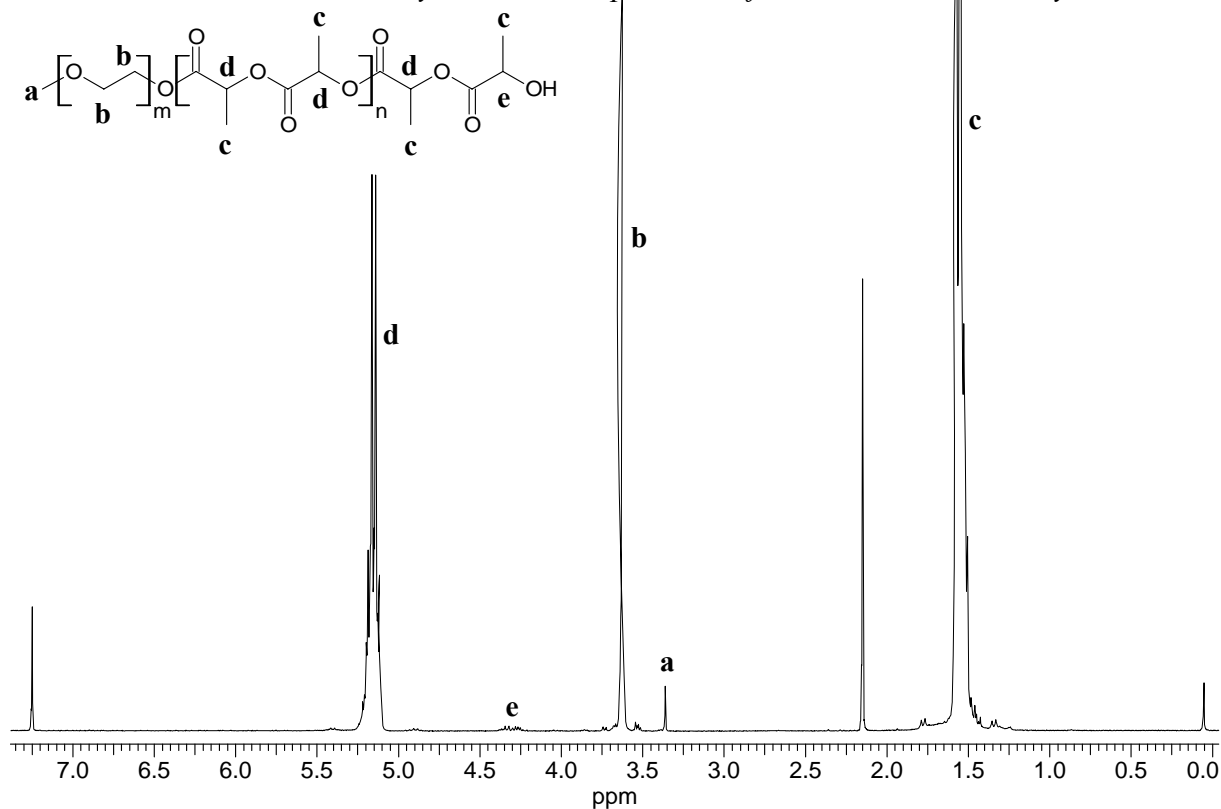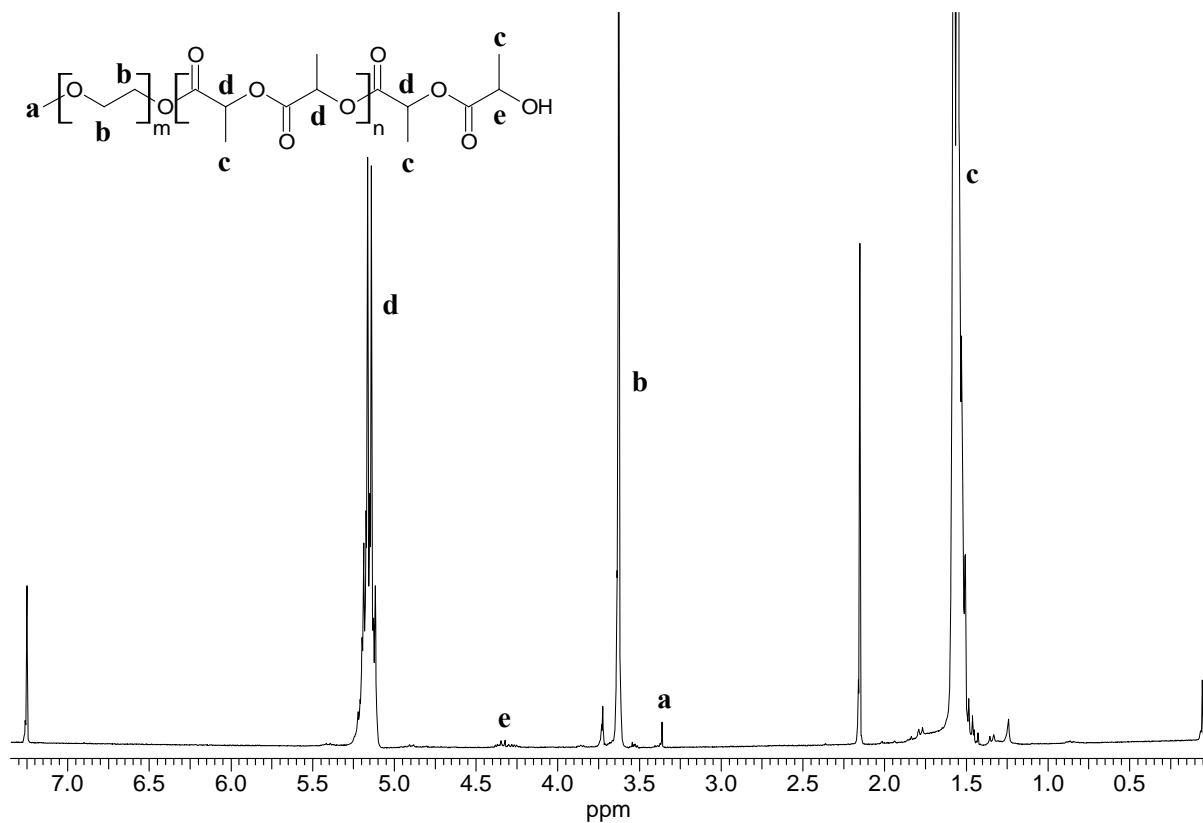
5 CONCLUSION

Based on literature review various carbene platform catalysts have been known as highly active catalysts of ring-opening polymerization (ROP) of cyclic esters. Nowadays, organic catalysis represents an excellent alternative to organometallic approach and proceeds in a control and living way resulting in uniform and defined macromolecules in quantitative yield.

The main aim of the presented work was to find the optimal conditions for ring-opening polymerization of lactide catalyzed by *N*-heterocyclic carbene catalyst with *te*rt-butyl substituents. We were focused on the influence of composition of reaction system i.e. ratios monomer – initiator – catalyst on conversion, molecular weight of polylactides and its polydisperzity.

Polymerizations were carried out at the presence of benzylalcohol as initiator at THF at lab temperature for 2 h. Monofunctional PEG as macroinitiator was examined and optically pure monomer *L*-lactide was used as well.

Molar ratio catalyst/initiator (NHC/BnOH) in the range $0.9 - 1.5$ was found out as optimal for high conversion of polylactide. Higher polydispersity of polymers produced at these ratio values probably resulted from competitive transestefication reactions. Besides, the participation of un-reacted *tert*-butoxide as ionic ROP initiator was expected as well.

High molecular weight, the best define polylactide was obtained, when the ratio monomer concentration equivalent to the initiator is used up to 100.

Polymerizations of *L*-lactide in comparison with its stereomer *D,L*-lactide produces higher molecular weight PLLA with $M_n = 25\ 000$ g/mol. On the contrary, PDLLA was produced with $M_n = 7\ 800$ g/mol. The monomer conversion was 84 % and PDI 1.6.

Conditions for initiator benzylalcohol were not quantitatively proved for PEG macroinitiators. Conversion was around 50 % with PDI $1.2 - 1.3$ showing polylactides uniformity. Rating number average molecular weights M_{ntheor} / M_{nGPC} / M_{nNMR} is in good correlation.

^{1}H NMR spectroscopic analysis of polymers synthesizing in the presence of macroinitiator revealed the signals of respective protons of chain end groups. Even if the polymers were four times purificated before characterization, ^{1}H NMR analysis shows peak in $\delta = 2.15$ ppm. This signal could be related to carbene catalyst protons or, more probably to amino compounds from original imidazolium salt synthesis. Consequently, amino compound could serve as a bifunctional initiator for ROP of lactide.

6 REFERENCES

1   Dubois P., Coulembier O., Raquez J. M., *Handbook of Ring-Opening Polymerization.* WILEY-VCH Verlag GmbH & Co., 2009, ISBN 978-3-527-31953-4.

2   Gupta A.P., Kumar V., *New emerging trends in synthetic biodegradable polymers – Polylactide: A critique.* European Polymer Journal, (43) 2007, p. 4053-4074.

3   Donald G., *A Literature Review of Poly(Lactic Acid).* Journal of Polymers and the Environment. (2) 2001.

4   Scott G., *Polymers and the environment.* The Royal Society of Chemistry, 1999, ISBN 0-85404-578-3.

5   Narayanan N., Roychoudhury P.K., Srivastava A., *L(+) lactic acid fermentation and its product polymerization.* Electronic Journal of Biotechnology, (7) 2004, p. 167.

6   Liška F., *Konstituce, konformace, konfigurace v názvech organických sloučenin.* VŠCHT Praha, 2008, ISBN 978-80-7080-640-1.

7   Williams K. C., *Synthesis of functionalized biodegradable polyesters.* Chem. Soc. Rev., (36) 2007, p.1573-1580.

8   Södergård A., Stolt M., *Properties of lactic acid based polymers and their correlation with composition.* Prog. Polym. Sci., (27) 2002, p. 1123.

9   Jérôme C., Lecomte P., *Recent advances in the synthesis of aliphatic polyesters by ring-opening polymerization.* Advanced Drug Delivery Reviews, (60) 2008, p. 1056-1076.

10   Albertsson A. C., *Degradable Aliphatic Polyesters.* Advanced Polymer Science, (157) 2002, ISBN 3-540-42249-8.

11   Trollsas, M., Hedrick J. L., *Dendrimer-like star polymers.* Journal of the American Chemical Society. 1998, vol. 120, pp. 4644-4651.

12   Storey, R., Sherman, J. *Kinetics and mechanism of the stannous octoate-catalyzed bulk polymerization of ε-caprolactone*. Macromolecules. 2002, vol. 35, pp. 1504-1512.

13   Dove A. P., Pratt R. C., Lohmeijer B. G. G., Culkin D. A., Hagberg E. C., Nyce G. W., Waymouth R. M., Hedrick J. L., *N-Heterocyclic carbenes: Effective organic catalysts for living polymerization.* Polymer, (47) 2006, p. 4018-4025.

14   Connor E. F., Nyce G. W., Myers M., Möck A., Hedrick J. L., *First Example of N-Heterocyclic Carbenes as Catalysts for Living Polymerization: Organocatylytic Ring-Opening Polymerization of Cyclic Esters.* J. Am. Chem. Soc., 124 (6) 2002, p. 914-915.

15 Grasa G. A., Kissling R. M., Nolan S. P., Organic Letters, (4) 2002, p. 3583-3586.

16 Nyce G. W., Lamboy J. A., Connor E. F., Waymouth R. M., Hedrick J. L., Organic Letters, (4) 2002, p. 3587-3590.

17 Nyce G. W., Glauser T., Connor E. F., Möck A., Waymouth R. M., Hedrick J. L., *In Situ Generation of Carbenes: A General and Versatile Platform for Organocatalytic Living Polymerization.* J. Am. Chem. Soc., (125) 2003, p. 3046-3056.

18 Coulembier O., Lohmeijer B. G. G., Dove A. P., Pratt R. C., Mespouille L., Culkin D. A., Benight S. J., Dubois P., Waymouth R. M., Hedrick J. L., *Alcohol Adduct of N-Heterocyclic carbenes: Latent Catalysts for the Thermally-Controlled Living Polymerization of cyclic Esters.* Macromolecules, (39) 2006, p. 5617-5628.

19 Kamber N. E, Jeong W., Waymouth R. M., Pratt R. C., Lohmeijer B. G. G., Hedrick J. L., *Organocatalytic Ring-Opening Polymerization.* Chem. Rev., (107) 2007, p. 5813-5840.

20 Arduengo, A. J., et al. *Photoelectron Spectroscopy of a Carbene/Silylene/Germylene Series*. Journal of the American Chemical Society. 1994, 116, p. 6641–6649.

7 ABBREVIATION LIST

^{1}H NMR	Nuclear Magnetic Resonance spectroscopy of hydrogen nucleus
BnOH	Benzylalcohol
GPC	Gel permeation chromatography
GRAS	Generally recognized as safe
MeOH	Methanol
NHCs	*N*-Heterocyclic Carbenes
NHC–1G–F	*N*-Heterocyclic Carbene 1G (France)
PLA	Poly(lactic acid) or poly(lactide)[1)]
PS	Poly(styrene)
PEG1000	Poly(ethylene glycol) monomethyl ether with number average $M_n \sim 1000$
PEG2000	Poly(ethylene glycol) monomethyl ether with number average $M_n \sim 2000$
RI	Refractive index
ROP	Ring-opening polymerization
RRM	Renewable raw materials
SSP	Solid state polymerization
t-BuO$^-$K$^+$	Potassium *tert*-butoxide
THF	Tetrahydrofuran
T_m	Melting temperature
UV-VIS	Ultraviolet-visible light region

[1)]   The polymers derived from lactic acid by the polycondensation route are generally referred to as poly(lactic acid) and the ones prepared from lactide by ring-opening polymerization as polylactide.