(Pyridyl)benzoazole Copper(II) and Zinc(II) complexes: Synthesis and applications as Catalysts in Polymerization of Lactides and ε-Caprolactones

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DEDICATIONS

To my family

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ABBREVIATIONS

Ar	Aromatic
d	doublet
dd	doublet of doublet
D,L-LA	D,L-lactide/meso-lactide
□-CL	□-caprolactone
ESI-MS	Electron Spray Ionisation Mass Spectrometry
GPC	Gel permeation chromatography
h	hours
I	Initiator
J	Coupling constant
M	monomer
Mn	number average molecular weight
Mw	weight average molecular weight
m	multiplet
MS	Mass spectroscopy
NMR	Nuclear magnetic resonance
OAc	Acetate
Obz	Benzoate
PDI	Polydispersity index
PCL	Poly(□-caprolactone)
PLA	Polylactide
P(D,L-LA)	poly(D,L-lactide)

P(S-LA)	poly(S-lactide)
S-LA	S-lactide
s	singlet
t	triplet

Abstract

This thesis reports the syntheses and characterization of Cu(II) and Zn(II) (pyridyl)benzoazole complexes and their applications in the ring opening polymerization (ROP) of ε-caprolactone and lactides. Reactions of compounds 2-(3-pyridyl)-1*H*-benzimidazole (**L1**), 2-(2-pyridyl)-1*H*-benzothiazole (**L2)** and 2-(2-pyridyl)-1*H*-benzimidazole (**L3**) with Zn(II) and Cu(II) acetates produced the corresponding complexes; [Zn(**L1**)$_2$(OAc)$_4$)] (**C1**), [Cu(**L1**)$_2$(OAc)$_4$] (**C2**), [Zn(**L2**)(OAc)$_2$)] (**C3**), [Cu(**L2**)(OAc)$_2$)] (**C4**), [Zn(**L3**)$_2$(OAc)$_2$)] (**C5)**] and [Cu(**L3**)$_2$(OAc)$_2$)] (**C6**) in quantitative yields. Similarly the reactions of 2-(3-pyridyl)-1*H*-benzimidazole (**L1**) and 2-(2-pyridyl)-1*H*-benzimidazole (**L3**) with benzoic acid and Zn(II) acetate produced complexes: [Zn(**L**1)(Obz)$_2$)] (**C7**) and [Zn(**L3**)(Obz)$_2$)] (**C8**) in high yields. All the complexes were characterized by mass spectrometry, IR spectroscopy, elemental analysis and single crystal X-ray crystallography for complexes **C2** and **C6**. In addition, Zn(II) complexes **C1**, **C3**, **C5**, **C7** and **C8** were characterized by NMR spectroscopy while Cu(II) complexes **C2**, **C4** and **C6** were characterized by magnetic moment measurements due to their paramagnetic nature. The magnetic moments measured for Cu(II) complexes **C2**, **C4** and **C6** were found to be 1.91 BM, 1.89 BM and 1.90 BM respectively. The molecular structure of complex **C2** revealed that ligand **L1** adopts a monodentate binding mode through the pyridyl nitrogen atom while that of **C6** revealed that **L3** binds in a bidentate fashion through the pyridyl and the benzoazole nitrogen atoms.

The catalytic activities of all complexes in the ring opening polymerization of ε-caprolactone and lactides were studied. All the complexes effectively polymerized these cyclic esters to produce low molecular weight polyesters. Generally Zn(II) complexes were more active than the

corresponding Cu(II) complexes. Complexes **C1**, **C2** and **C7** containing the monodentate ligand **L1** showed higher catalytic activities compared to complexes **C5**, **C6** and **C8**, containing the bidentate ligand **L3**.In addition, complexes **C5** and **C6** containing the benzimidazole ligand **L3** showed high activities in ring opening polymerization of ε-CL and LA when compared to complexes **C3** and **C4** bearing the benzothiazole analogue (2-(-2-pyridyl)-1-benzothiozole) **L2**. The benzoate complexes were less active than the corresponding acetate complexes. All the complexes exhibited low initiator efficiencies producing polymers with low molecular weights ranging from 530 g/mol to 21 660 g/mol. Broad molecular weight distributions in the rang p1.39 to 2.38) were reported. The analysis of the methine region in ^{1}H NMR and ^{13}C NMR revealed that the ring opening polymerization of both D,L-LA and S-LA afforded isotactic polylactides. Analysis of polymers by ^{1}H NMR and ESI-MS spectra showed that the polymerization of ε-CL and LA proceeded through coordination insertion mechanism.

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'Before I formed you in the womb I knew you, before you were born I set you apart; appointed you as a prophet to the nations'-Jeremiah 1:5

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Chapter One

Synthesis, properties and application of polylactides and polycaprolactones

1.1 General Introduction

Polymers synthesized from petrochemical based resources have had a remarkable effect in the industry since 1940s.[1] Despite various advantages of these materials two major drawbacks limit their industrial applications. These drawbacks are mainly due to the fact that non-renewable resources are used in their synthetic processes and that they are not biodegradable.[1] Biodegradable and biocompatible polyesters are considered optional environmentally friendly materials replacing petrochemical based materials, mainly because renewable resources are used in their synhthesis.[1,2] Linear aliphatic polyesters are predominantly attractive and the most used type of biodegradable polymers.[1] Polyesters are polymers which contain the ester functional group in the polymer backbone. Polyesters such as polylatide (PLA), polycaprolactone (PCL) and their copolymers have found extensive applications in packaging material, biomedical applications, pharmaceutical, medical implants, medical sutures and drug delivery devices as a result of their biocompatibility, biodegradability and permeable properties in both environmental and *in vivo*.[3]

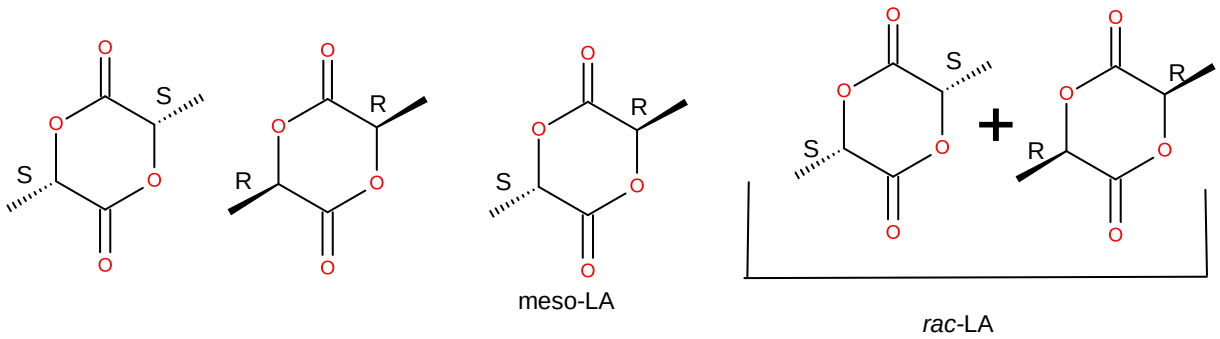
Polyesters are traditionally synthesized by ring opening polymerization (ROP) of cyclic esters *via* coordination-insertion mechanism involving a metal alkoxide catalyst, this method has provided fast and stereoselective conversion to the anticipated polyester with controlled molecular weight and narrow polydispersities.[2] Metal alkoxide are very effective catalysts for the production of aliphatic polyesters by ROP of esters such as lactones.[4] A large number of metal

complexes of different kinds have been widely investigated as initiators for the ROP of heterocyclic monomers, particularly cyclic esters such as lactides (L-LA and rac-LA) and lactones (ε-CL).[5] Extensive investigations were done largely because the polymers of lactides and lactones are biodegradable and biocompatible.[5] These initiators have incorporated organometallics and coordination complexes of main group elements, transition metals and lanthanides for a controlled ROP of lactides and lactones.[5] Kinetic studies have provided detailed mechanistic information concerning the coordination-insertion pathway, effect of ligand and nature of metal on polymerization activity.[2]

The proposed alternative route for ROP of cyclic monomers (esters) is an activated monomer pathway, this route has been recommended for the ROP of lactones with protic alcohol/acid combination that results in low molecular weight polyester with broad molecular weight distribution.[2]

1.2 Polylactides (PLA)

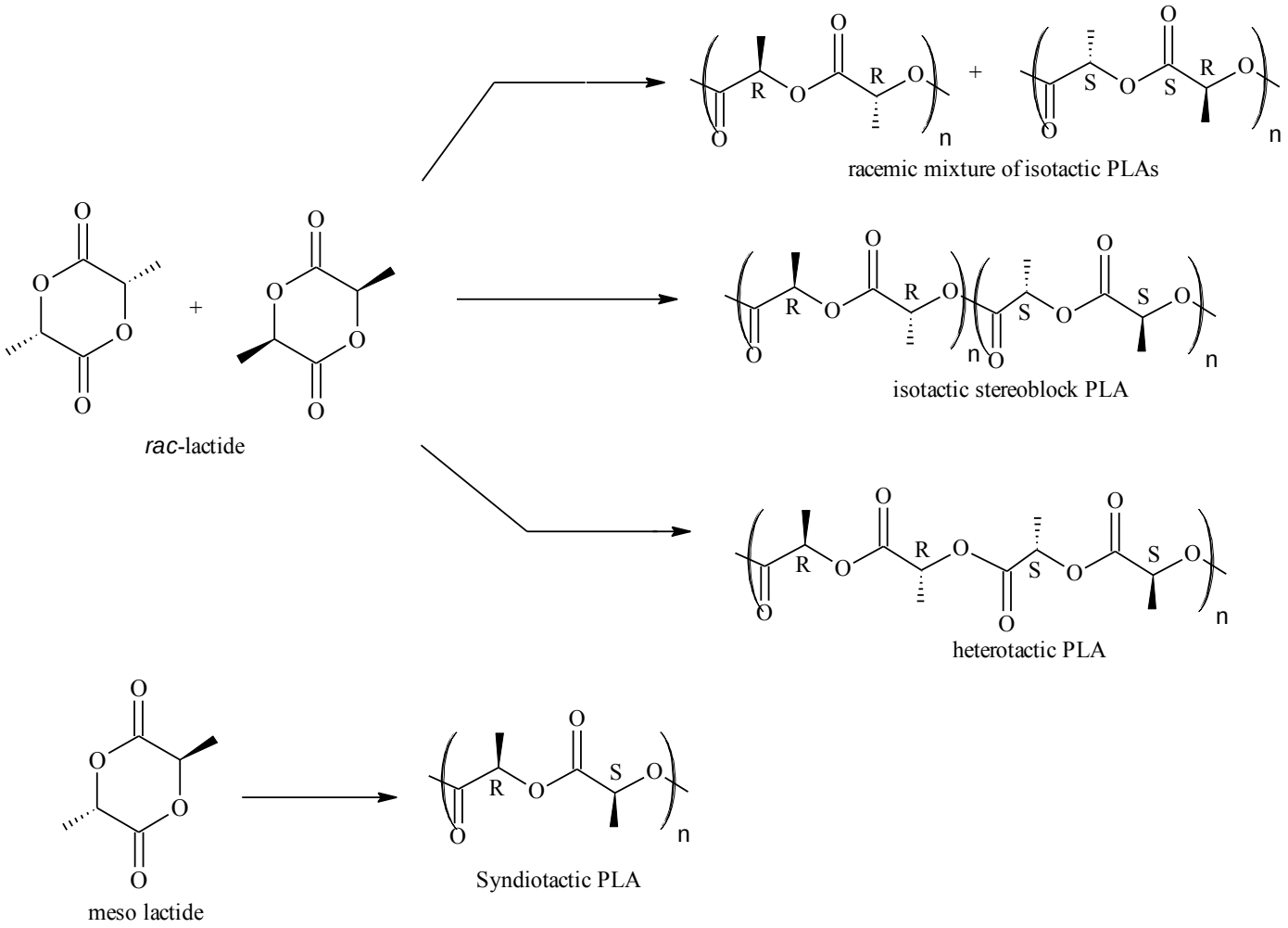
Polylactides (PLA) are biodegradable polymer manufactured by ring opening polymerization (ROP) of the heterocyclic ester lactide (LA).[6] LA can be obtained from the fermented corn and soybeans; therefore synthesis of PLA is independent of the consumption of petrochemical feedstock but is instead dependent on renewable resources.[6] Different forms of lactides stereochemistry are available.[7] Diastereomers (S,)-lactide (L-LA), (R,)-lactide (D-LA) and meso-lictide (D,L-LA) are available in pure form.[7,8] The racemic mixture/rac-LA (50:50) of (L)-LA and (D)-LA is also available.[7]



Scheme 1.1: Stereochemistry of the LA monomer.

Different polymer microstructures such as atactic, isotactic, heterotactic and syndiotactic can be produced from this set of lactide monomers (Scheme 1.2).[7] Polymerization of D-LA with a typical initiator give an isotactic poly(D-LA) which is a crystalline polymer consisting of high transition melting point (Tm = 170-180˚C), on the other hand polymerization of rac-LA with a non-stereoselective metal-based catalyst give an unstructured polymer with a random dissemination of stereocenters along the backbone of the polymer.[7] To synthesize a heterotactic polymer highly active and stereoselective monomeric amide or aryloxide complexes has be used to polymerize rac-LA.[7] Syndiotactic polymers can be produced by ROP of a sequences of D,L-LA in the presence of a chiral aluminium isopropoxide complex (the only known example of an efficient initiator for the stereoselctive preparation of the highly syndiotactic polylactide).[7]

PLA has found global application in food packaging, fibre technology, biomedical and pharmaceutical applications including medical implants, sutures and drug delivery devices.[26,9]

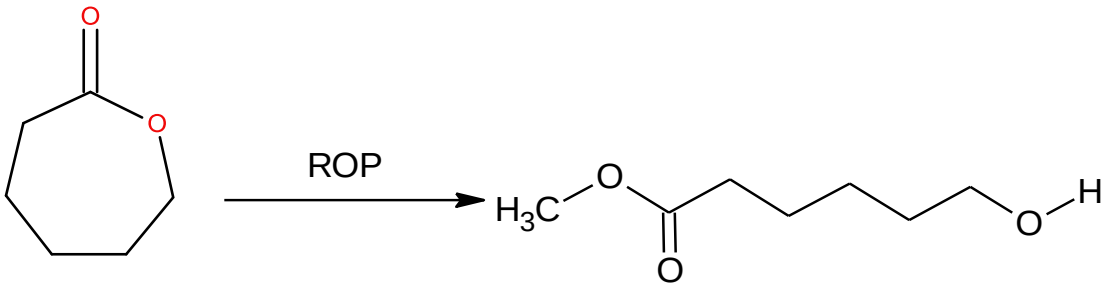


Sheme 1.2: Lactide stereochemistry and typical PLA microstructures from metal-based catalyst.[7]

1.3 Polycaprolactones (PCL)

Another type of aliphatic polyesters that has attracted considerable attention over the last decades are polycaprolactone (PCL), they are also traditionally prepared by ROP of heterocyclic ester known as caprolactones (CL).[10]They are biodegradable and biocompatible with permeable properties both in the environment and *in vivo*.[3] Caprolactone (CL) rich fragments tends to be taken up in the last stage by microphages and massive cells and degraded within the cells, the

degradation is done by the enzymes before yielding ε-hydroxycaproic acid which is either metabolised or excreted from the human body without any hostile toxicological effects.[11] Poly(ε-CL) has been studied thoroughly because of the possibilities of blending it with different commercial polymers such as polyvinyl alcohol (PVA) and bisphenol A polycarbonate for biodegradable packaging material and biomedical application, because its degradation product are non-toxic.[12]



Scheme 1.3: ROP mechanism of ε-CL

PCL is a semicrystalline polymer (T_g = -60˚C) and a has melting point temperature (T_m) in the range 59-64 ˚C.[13] Polycaprolactones with higher molecular weight are strong ductile polymers of excellent mechanical properties.[13] The commonly used method for preparing polymers with high molecular weights is the ROP of ε-CL, this has been performed using many organometallic or transition metal complexes as initiators.[14] Low molecular weight PCLs are known to form sticky liquids or more often hard waxes.[13] The polymer repeating unit consist of five non-polar methylene groups and one relatively polar ester group, this molecular structure of PCL give it unique properties (Scheme 1.3).[13] The higher olefinic content makes it highly compatible with other polymers.[13] PCL is one of the most hydrophobic of commercial biodegradable polymers

because of the impartation of the methylene groups.[13] The properties of PCL may be altered by controlling it crystallinity.[13]

1.4 Synthesis of PLAs and PCLs

Polylactides and polylactones can be prepared by two well defined approaches, polycondensation of hydroxycarboxylic acids or by ROP of cyclic esters.[7,12] The polycondensation approach is cheaper than ROP but it makes it very difficult to obtain high molecular weight polymers with specific end groups and making well defined polyesters.[12]

1.4.1 Condensation polymerization of esters

Condensation polymerization is the process where monomers join together losing molecules (usually water) as by-products.[15] The product of condensation polymerization depends on the number of functional groups in the monomer that can react because condensation polymers are formed from monomers bearing two or more reactive groups.[15] The monomers that are known to undergo condensation polymerization are amides, acetals and esters. Polyester formed from this type of reaction consist of a molecular formula with no integral multiplies of the formula of the monomer.[15] Employment of condensation polymerization certainly allows access to broad range of polymer structures than ROP through a higher accessibility of the monomer involved.[7,15] The alpha-hydroxy acids can be directly converted into linear polymers by intermolecular esterification.[8] The benefit of direct condensation is ease of process but it is difficult to get polyesters with high molecular weight.[16] Only low molecular weight polymers can be formed because reaction conditions necessary to form higher-molecular weight polymers by water

removal lies in the range where the unzipped and ring closure reactions become the main reaction.[8] To get high molecular weight polymers when using direct condensation mechanism, there are three important factors: dynamic control, removal of water and control of degradation.[16]

The condensation polymerization can be performed in the absence of a catalyst and some initiators previously used in this type of polymerization have been described.[8] One successful procedure for polycondensation of lactide consisted of heating the lactide under reduced pressure and temperature of 130˚C for 2 to3 hours, an initiator can be added in the presence of diphenyl ether, water is removed continuously by Soxhlet extraction using molecular sieves for extra 30 to 40 hours at 130˚C.[17] Depending on obtained molecular weight, condensation polymers can liquid or solid.[8] Applications have been described in drug delivery devices, to alter the release rate of active components. The alteration of molecular weight distribution has to be possible for any given polymer.[8]

1.4.2 Ring Opening Polymerization

Ring opening of cyclic esters requires the use of a metallic catalyst which allows the manufacture of polymers with high molecular weight and also allows the reduction of secondary reactions taking place during polymerization.[8,18] ROP process include enzymatic, anionic, cationic, organocatalytic and coordination insertion.[7] Whether the polymerization reaction is executed as bulk or in solution a catalyst is always required to initiate the polymerization.[8] The thermodynamic driving force of the ROP process is the ring strain relief that allows the entropy unfavourable to all polymerizations to be overcomed.[7,17] Whilst the polymerization reaction is determined thermodynamically, the rate, stereoselectivity and control are determined by the choice of the catalyst.[17] Metal complexes are preferred initiators because they affords controlled

polymerization and are known to yield polymers with narrow polydispersity index (PDI), well-defined M_n and are compatible with the production of block copolymers.[17]

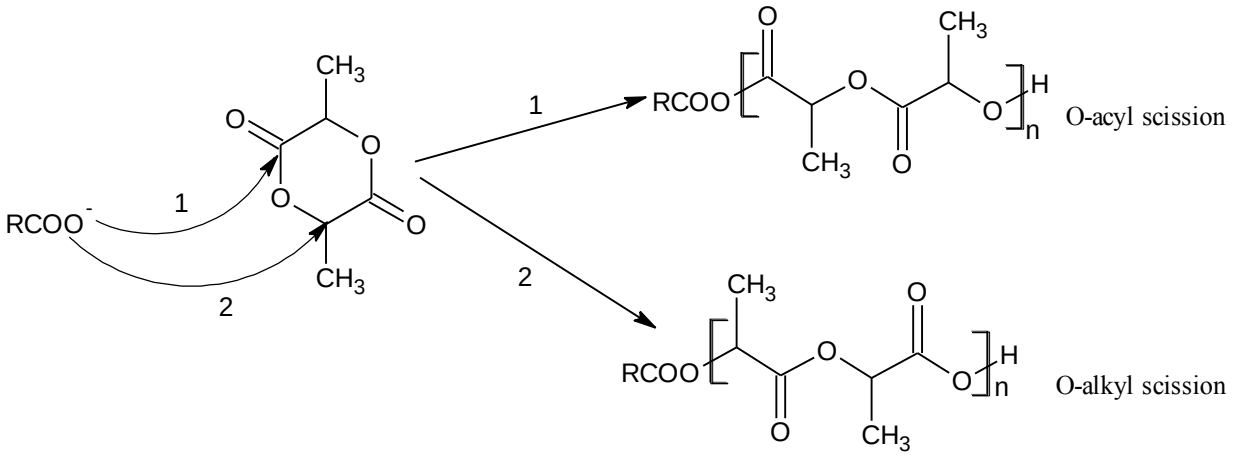
Metal alkoxide or amide coordination compounds are useful due to their tolerance, selectivity, rate and lack of side reactions. On the other hand, for some biomedical applications metal residues are undesirable and in these cases low toxicity organocatalytic or enzyme initiators are favourable.[17]

1.4.2.1 Anionic ROP

Countless studies have been performed on the anionic polymerization of lactones.[19] Initial papers have reported that β-lactone polymerization by weak bases proceeds via alkyl-oxygen bond cleavage of monomers and that carboxylate anions are species activating propagation in the presence of an organic ligand.[19] The anionic polymerization of *β*-lactones with the strong base (e.g. alkali metal-alkoxide) is reported to be one of most complex ROP mechanism.[19] The initiator alkoxide anions attacks the carbonyl carbon atom of the *β*-lactone to make the monomer acyl-oxygen bond cleavage producing an unstable intermediate responsible for further polymer growth (1 in Scheme 1.4).[19] An alternative route to initiate this type of polymerization involves the anionic initiator attacking the carbon atom next to the oxygen of the ether resulting in linear polyester (2 in Scheme 1.4).[20]

Sodium and potassium alkoxide are well known to promote anionic type polymerization, however significant side reactions occur.[4] Metal alkoxide containing free p-, d-, or f-orbitals

bring about lactone polymerization *via* "coordination insertion" mechanism; this type of polymerization is commonly referred to as pseudo anionic polymerization.[4]

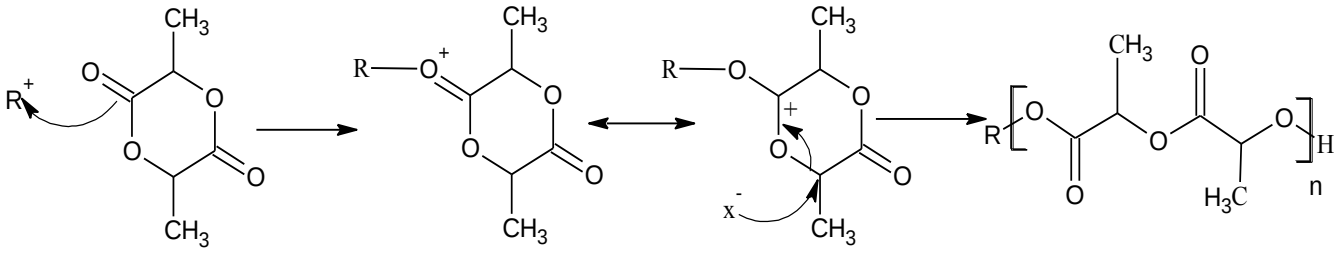


Scheme 1.4: Reaction pathway for ROP of cyclic esters by anionic initiation.

1.4.2.2 Cationic and activated monomer ROP of cyclic esters

One of the most powerful methods for controlling cationic ROP is activated monomer cationic polymerization.[21] Penczek *et al*. reported that activated monomer cationic polymerization can suppress unfavourable reactions such as backbiting and deproportionation.[21] This method is also known for producing linear polymers free from cyclic oligomers.[21] The activated monomer mechanism is proposed for organocatalytic and cationic initiation systems.[17] In this mechanism a nucleophilic substrate activates the monomer to attack by exogenous alcohol.[17] According to this mechanism a monomer is activated by either a Bronsted acid, a nucleophile such as N-heterocyclic carbene or H-bond donor.[17] For LA the initiation involves coordination of the LA molecule by it ketonic oxygen.[22] Initiation occurs when the alcohol reacts with activated monomer e.g. Lactide to form a ring open adduct, the α-end chain of the polymer thus bear the

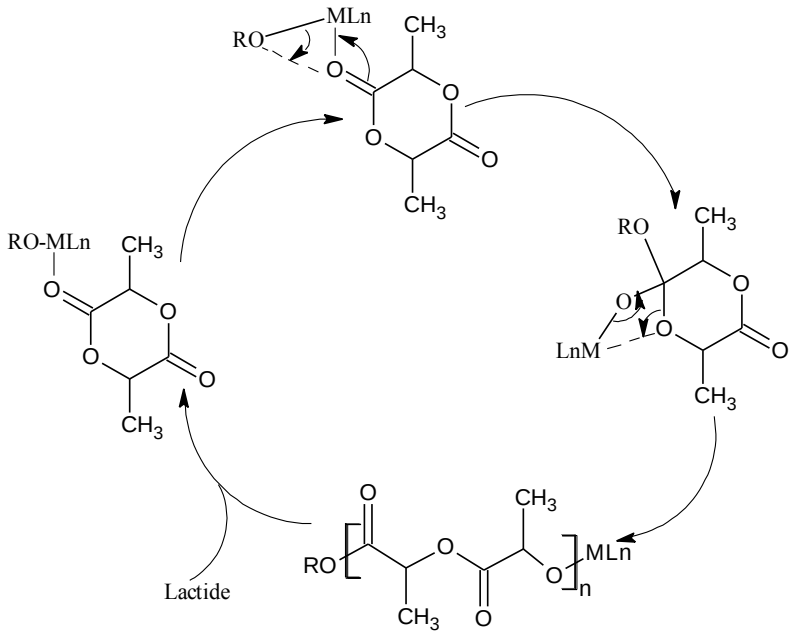
ester from the initiating alcohol and the ω-chain end is a secondary alcohol that serves as the alcohol to propagate the chain (Scheme 1.7).[17] The Propagation involves the repeat enchainment of the monomer and the regeneration of the metal-alkoxide bond.[22]



Scheme1.5: Reaction pathway for ROP of cyclic esters by cationic initiation.

1.4.2.3 Coordination insertion ROP

The coordination insertion is now widely accepted and supported experimentally and theoretically.[17] According to the mechanism, the Lewis acidic metal centre loosely binds and activates cyclic ester to attack by metal alkoxide group.[17] The intermediate undergoes the acyl bond cleavage of the ring to generate a new metal alkoxide species and a growing chain end capped with an ester or amide group (Scheme 1.7).[17] ML_n represent the metal centre and its set of ligands.[22] A range of different metal complexes have been tested, these includes ionic and covalent alkoxides/amides, the most useful are covalent metal alkoxides which do not suffer from side reactions such as the epimerization.[17]



Scheme 1.6: The coordination insertion mechanism for ROP of the lactide.

1.4.2.4 Enzymatic Polymerization

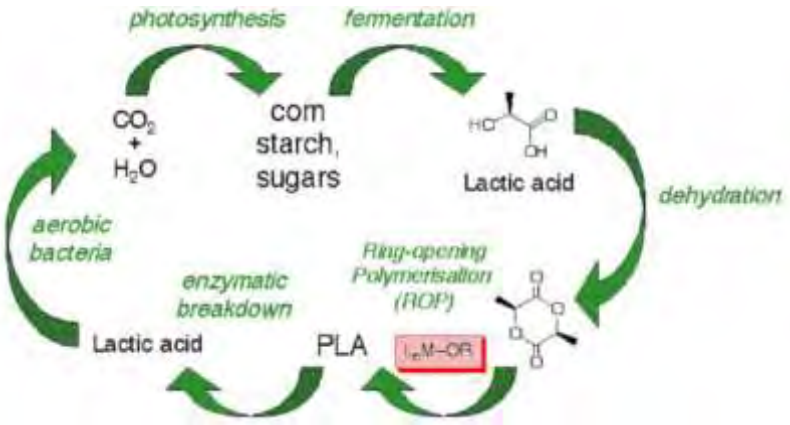
In vitro polyester synthesis using an enzyme as a catalysts started in 1993 when lipase catalysed-ring opening polymerization was found by two independent groups. These groups discovered that a lipase enzyme can induce ROP of ε-caprolactones and δ-valerolactones.[18] ROP of lactones and macrolides of several sizes using lipase have been reported.[23] Copolymerization of β-propiolactone and ε-caprolactone using *Pseudomonas fluorescens* lipase produces a copolymer with a random monomer distribution within the polymer chain and a molecular weight of 520 g/mol. In these cases the reaction rate and molecular weight build up were found to be slow, to enhance the reaction rate and reduce the incubation period, initiators like methanol and butanol were used.[23]

Also a number of other cyclic monomers have been polymerized by enzyme catalysts.[18] Lipase catalysed synthesis of polylactic acid have been investigated where three different lipases (*Porcine pancreas lipase/PPL, Lipozyme IM20 and Chirazyme*) have been used.[23] Other lipases like lipase CC and Lipase PPL were also active for ROP of monomers.[18] Enzymatic polymerization methods suffer from many disadvantages such as a use of derivatives to activate the ester monomers, low conversion yields, longer reaction periods and use of large enzyme (initiator) amounts.[23]

1.5 Applications of PLAs and PCLs

Due to their unique properties biodegradable polymers have long been considered as environmentally friendly polymers, and the remarkable advances achieved over the past three decades in the synthesis, manufacturing and processing of these materials have given rise to a range of practical application.[1] For the past decades, in view of their biodegradable, biocompatible and permeable properties both in environment and in vivo, polyesters such as polylactide (PLA), polycaprolactone (PCL) and their copolymers, have found wide applications as packaging materials, devices in more sophisticated pharmaceutical and medical industries.[3,24] They can be used for controlled drugs release, antibody and gene delivery in pharmaceutical and medical industries, scaffolds in tissue engineering and as alternatives of synthetic petrochemical-based plastics for packaging materials.[3] Polylactides and their copolymers are also bioassimilable and their hydrolysis gives non-toxic components that are eliminated through Krebs cycle as water and carbon dioxide.[1,8] Degradation of ε-CL within the cells yields ε-hydroxycaproic acid which is either metabolised or excreted from the human body without any adverse toxicological effects.[11]

Tissue repairing and engineering biodegradable implants has been used for a fixation of fractured bones and joints.[1] Several orthopaedic devices such as ligating screws,[8] clips and bone pins produce from 70% lactic acid and 30% glycolic acid are commercially available, with these biodegradable and bioassimilable devices there are no specific precaution required for their use and no need for removal operations and this is highly advantageous compared to metal implants.[1] Beside the surgery related applications, numerous efforts have been devoted to pharmacological applications over the last two decades, for example on the controlled delivery by drug-loaded biodegradable devices.[1] The encapsulation of a drug in a polymeric matrix allows the drug level to be maintained within the desired range, increasing therapeutic activities, decreasing side effects and reduce the number of administrations necessary.[1]



Scheme 1.7: Life cycle of PLA. It is biodegradable and derived from renewable recourses.[22]

Other experimental applications are scaffolds for auto grafted new skin, wound covers, anastomose systems and stents, a growing field also is dental applications (membranes).[22]

Chapter Two

Literature review of metal catalyzed ROP of Lactide and ε-caprolactone

2.1 Introduction

Until now, there is still a need for the design of well-defined initiators that can be used in the manufacturing of polyesters with controllable molecular weight and narrow PDI values.[25] The work by Kleine *et al*. that was done in the 1950s initiated the focus on the study of the metal based initiators for ROP of cyclic monomers, metal-based catalytic systems have been the focus of considerable attention for the polymerization of esters.[26] In the past two decade, a broad variety of metal complexes have been evaluated as catalysts for the ring opening polymerization (ROP) of lactones and di-lactones.[27] Metal complexes of different kinds have been widely explored as initiators in polymerization reactions of heterocyclic monomers (cyclic esters) such as ε-caprolactones (ε-CL) and lactides (LA).[28]

Well-defined complexes combining an ancillary ligand and an initiating group have allowed for remarkable improvements in terms of activity and control, on the other hand great progress has also been achieved over the past few years in organo-catalyzed ROP.[27] These catalysts/initiators have encompassed organometallic or coordination complexes of main group elements, transition metals and lanthanides for controlled ROP of lactides and lactones.[28,29] The metal coordinated initiators are the most efficient method for the ROP production of well controlled polyesters in terms of molecular weight, composition and microstructure as a result many studies have been directed toward synthesizing efficient metal-based initiators and studying their reactivity.[30]

The first generations of active catalysts used in ROP reactions were mostly made of simple homoleptic metal complexes such as Sn(II) *bis*(2-ethylhexanoate), zinc(II) lactate and aluminum(III) isopropoxide (AlO^iPr_3).[6] Catalysts including homoleptic group four alkoxide (Ti and Zr), acetylacetonate (Zr) complexes and titanium-organic framework derived from $Ti(O^iPr)_4$ and 1,4-butanediol have been used for ROP of $_L$-LA and ε-CL.[28] A variety of metal alkoxides have been used as catalysts/initiators in ROP of LA.[31] In addition to alkoxides *bis*(amido)tatinium complexes supported by chelating diaryloxy ligands have also been used for ROP of L-LA and ε-CL.[28]

Other reports have discussed the ring opening polymerization of ε-CL by group four metallocene complexes such as zirconocene and titanocene alkyl complexes, the bimetallic congeners of these complexes formed with $^iBu_2AlH$ were found to be active in ROP of ε-CL.[28] Homoleptic rare-earth derivatives of the general formula $Ln[N(SiHMe_2)_2]_3(THF)_X$ proved to be very active for polymerization of rac-LA at room temperature.[31] Lactide is prepared from lactic acid, it can be found in two diastereomeric and two enantiomerically pure forms.[26] As a result polylactide (PLA) produced can be of different microstructures, but this depends on the type of monomer used in polymerization and mechanism of polymerization reaction, also different initiating systems have been tested for production of stereocontrolled PLAs and the results showed that this depends on retention of configuration.[26] Stereoselective chiral ligands can be used to obtain stereoselective catalyst. According to kinetic measurements, a given homochiral catalyst exhibit a 28:1 preference for the polymerization of one enantiomeric monomer over the other.[26]

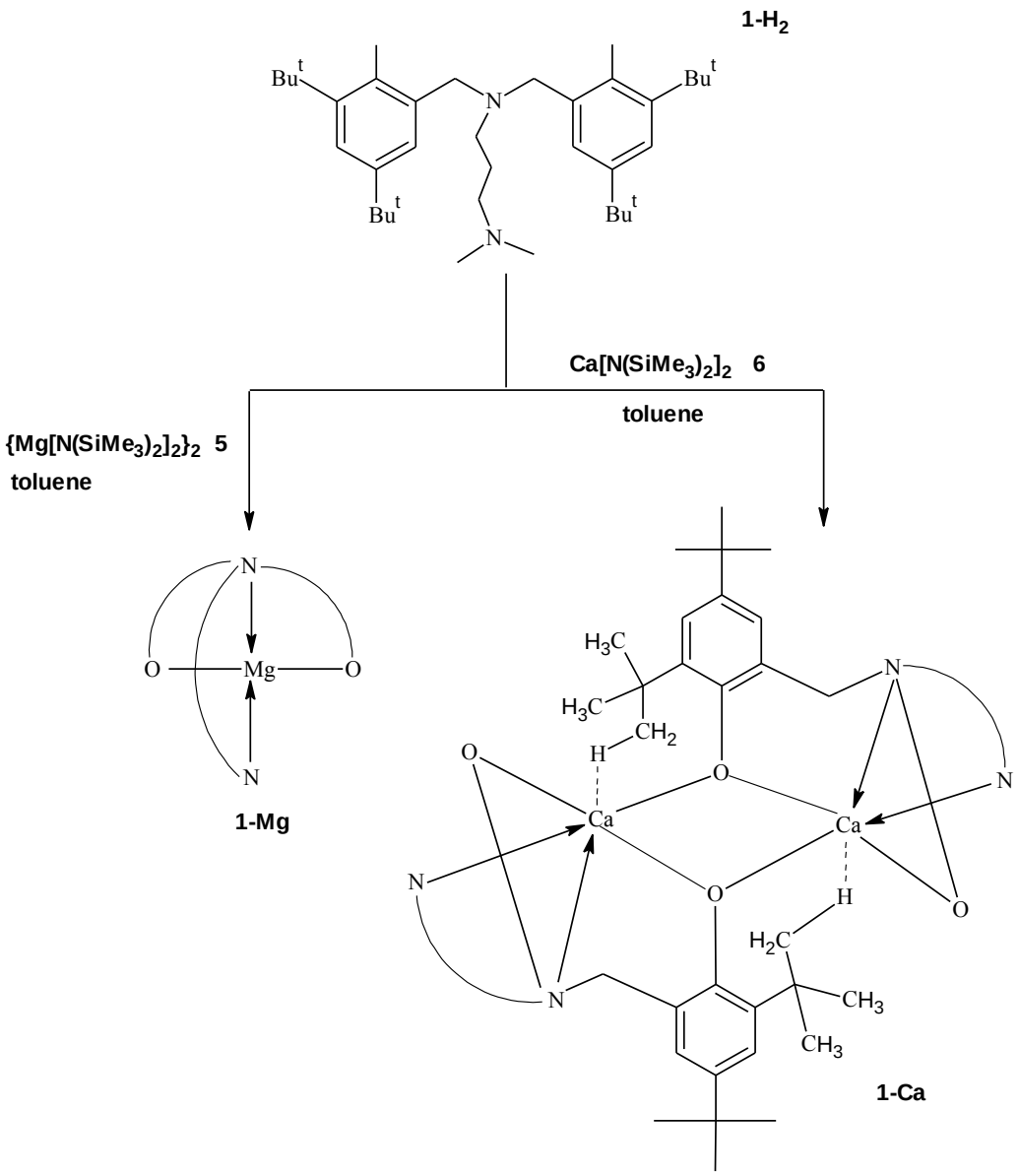
Important initiator parameters for controlled polymerization are reaction rate and stereocontrol (for LA).[31] Controlled polymers are desirable due to the ability to predict and allowing the tuning of their physical properties by quantity and the nature of the initiator used.[31] Other desirable features for the catalyst are low cost, tolerance, abundance, lack of colour and low toxicity.[31] In the next section we review some of the transition metal complexes that have been employed as catalysts in the ROP of cyclic esters.

2.1.1 Alkali and alkaline earth complexes as ROP initiators

Complexes of the large alkali-earth (Ae) metals such as calcium, strontium and barium have now found a new application as effective and versatile catalyst for a variety of transformation involving σ-bond metathesis.[32] Well defined heteroleptic alkali-earth metal complexes have displayed remarkable activities in ROP of cyclic esters, however the suitable [L_nX^-] ancillary ligands able to stabilize [L_nX^-]Ae-Nu heteroleptic complexes are still very rare and the selection is restricted to tris(pyrazolyl)borate, aminotrop(on)iminates, *β*-diketiminates and *bis* or *tris*(imidazazolin-2-ylidene-1-ly)borate.[32] Calcium (Ca) initiators that are used in PLA synthesis have appeared in several publications but not even one of them has employed discrete well-defined complexes before a report by Chisholm *et al*. which discussed well-defined Ca complexes of type LCaX for the synthesis of PLAs.[33] The introduction of the ligand *β*-diiminate $CH[CMeNC_6H_4\text{-}2\text{-}OMe]_2$ (BDI-OMe) affords additional coordination to the large calcium metal through the ether groups.[33]

Use of a chiral Tp ligand with calcium metal affords the stereoselectivity LA polymerization *via* enantiomorphic site control.[33] Synthesis of most calcium complexes (e.g. *tris*(pyrazolyl)borate

calcium complexes) are found to be challenging and difficult.[33] Another Alkali metal that can used for polymerization of LA is magnesium (Mg). The complexes (BDI)-$MgN(SiMe_3)_2$ and (BDI)-$ZnN(SiMe_3)_2$ are used at a ratio of 1:1 to react with one equivalent of L-LA in a competition experiment.[33] The same competition reaction was employed where Mg and Ca complexes were mixed at 1:1 and this time only the Ca complex was consumed, thus the reactivity of the M-N toward competition ring opening polymerization of lactides is established to be Ca> Mg.[33]



Scheme 2.1: Mg complex (**5**) and dimeric Ca complex (**6**) supported by a bidentical ligand found to be an efficient initiator of ROP of CL.[34]

When the complex ((BDI)-CaN(SiMe$_3$)$_2$).THF was used independently for ring opening polymerization of *rac*-LA equivalent at ratio 200:1 at 25 ˚C temperature, a 90 percentage

conversion was obtained in two hours affording atactic PLA.[33] On the other hand ((BDI)-$MgN(SiMe_3)_2$ independently polymerized 200 equivalent of *rac*-LA at room temperature yielding 90% of heterotactic PLA within five minutes.[33] This reactivity order of Mg in the polymerization of LA is the opposite of that reported in the experiment described above.[33] Calcium complexes are also reported to initiate ROP of CL effectively, Sarazin *et.al*. reported the dimeric calcium amino bis(phenolate) $[Ca\{Me_2NC_2H_4N(CH_2\text{-}3,5\text{-}Bu^t{}_2C_6H_2O\text{-}2)_2\}]_2$ which have acted as a very efficient initiator for CL polymerization.[34] Polymerizations with this complex are well controlled with narrow molecular weight distribution and a linear increase of the peak molecular weight with conversion.[34] Complexes supported by the bidentate ligand described the activity of the polymerization of ε-CL to be of the order Ca >> Mg (Scheme 2.1).[34]

2.1.2 Group 13 and 14 metal-based catalyst

The most widely use complex for industrial PLA preparation is Sn(II) bis(2-ethylhexanoate) which is usually referred to as tin(II) octanoate $Sn(Oct)_2$ (Figure 2.2).[26] $Sn(Oct)_2$ is readily available, easy to handle and highly soluble in most organic solvents and monomers melt.[26] $Sn(Oct)_2$ is highly active and allow the production of high molecular weight polymers but the toxicity associated with most tin compounds is a considerable disadvantage in the case of biomedical applications.[26] Cyclic tin(IV) bisalkoxide such as $Bu_2Sn(\text{-}OCH_2CH_2O)$ have also been evaluated for lactide polymerization and they were found to be less active than tin(II) oxide but the molecular weight-distribution remained narrow like in tin(II) oxide when this complex was used in ROP of LA.[26]

Aluminium alkoxides have also proved to be efficient initiators/catalysts for ROP of cyclic esters, example being $Al(O\textit{i}\text{-}Pr)_3$ which has been widely used in mechanistic studies (Figure

2.1).[26] Aluminium alkoxides with supporting salen-type ligands have shown good control of tacticity in the production of PLA from D,L-LA but require high temperatures and long reaction time for adequate conversion.[35] The relatively low activity of aluminium alkoxide in LA ROP resulted in further investigations. In these investigations other metals were studied for a purpose of obtaining more active metal alkoxide complexes, metals such as especially yttrium and lanthanum were given special attention.[26] It has been revealed that Al(O*i*-Pr)$_3$ is significantly less active than Sn(Oct)$_2$, also with Al(O*i*-Pr)$_3$ the induction period of three minutes is systematically being observed during polymerization reactions.[26] Aluminium ions do not belong to human metabolism and they are suspected of supporting Alzheimer's disease, for all these reasons Al(O*i*-Pr)$_3$ is less used for preparation of biodegradable polyesters.[26]

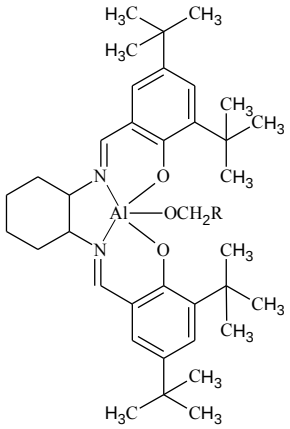


Figure 2.1: Al(O*i*-Pr)$_3$, one of the aluminium initiators used in ROP studies.[26]

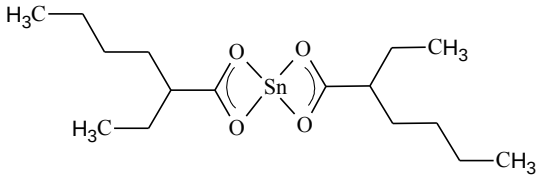


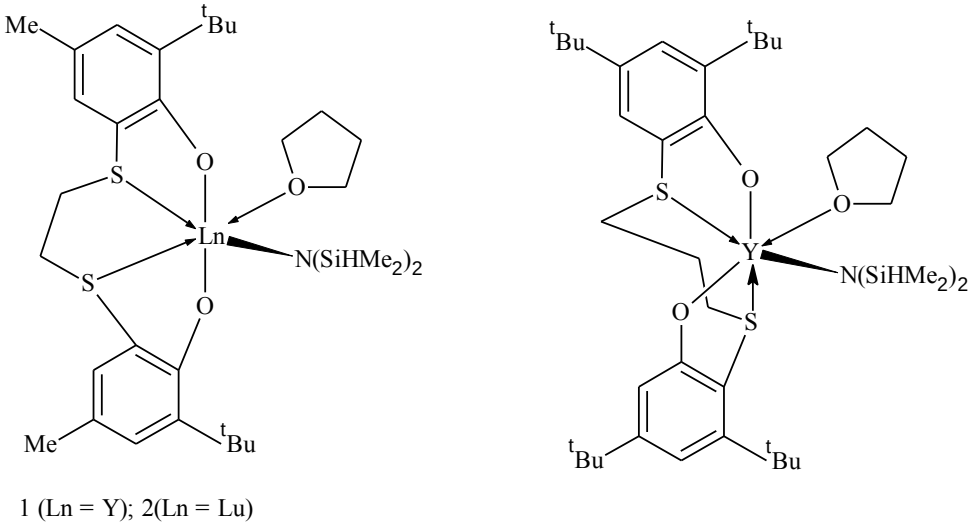
Figure 2.2: Sn(Oct)$_2$, most widely used complex for production of PLa.[33]

2.1.3 Rare earth metal based catalysts

Recently alkyl and amide metal complexes have been discovered as initiating groups replacing alkoxy ligand.[36] In the chemistry of rare-earth metals, an increase in number of complexes with alkyl group and silylamide that are structurally well characterized, synthesized and tested for the polymerization lactide and lactone has been observed (Figure 2.3).[36] Alkyl metal complexes of rare earth metals have also attracted lot of attention as initiators in polymerization processes and have been widely used in polymerization of cyclic ester monomers.[37] Sequential ROP of two cyclic esters for the production of poly(CL)-block-poly(CL) and poly(LA) using the rare earth complexes of cyclopentadienyl ($LnCp_3$) has been reported and the possible reaction mechanism was also proposed (Ln is Sm, Er, Pr, Gd and Ce).[38] Trivalent lanthanum and yttrium alkoxide $Ln(OR)_3$ (Ln = La or Y, R = *i*-Pr or *n*-Bu) prepared by employment of ligand exchange from already available bulky phenoxides succesfully polymerized LA within several minutes in dichloromethane, at 25 ˚C for [monomer]/[$Ln(OR)_3$] ≈ 150 and monomer concentration ≈ 02. M.[26] Other alkoxides metal complexes that have been investigated for ROP are oxoalkoxide clusters of general formula $Ln_5(\mu_5\text{-O})\text{-}(O\textit{i}\text{-Pr})_{13}$.[26]

In the past decades, the most studied rare-earth metal alkyl complexes were stabilized by cyclopentadienyl (CP) ligands.[37] Agarwal *et al*. in 2002 reported that irrespective of their size the rare earth cyclopentadienyl complexes ($LnCp_3$) of Sm, Pr, Ce, Gd and Er acts as ROP initiators of ε-CL at room temperature giving high molecular weights polycaprolactone (PCL) with moderate poly-dispersity indexes.[38b] The size of the meatal ion in the $LnCp_3$ complexes had an effect in catalytic activity and the order of reactivity was found to be Er ~ Gd > Sm > Pr > Ce.[32] When using the $LnCp_3$ complexes as initiator the gel formation was observed and prolonged

reaction time resulted with high yield and moderate poly-dispersity index.[38] Coordination of an oxygen atom of the polymer chain with the rare earth metal may form a loose network structure resulting in the formation of gel, this type of gelling behaviour was also reported for ROP of CL by Okuda *et. al*. using heterobimetallic lanthocene complexes.[38]



1 (Ln = Y); 2(Ln = Lu)

Figure 2.3: Rare earth metal silylamido complexes used in polymerization of L-LA.[36]

Non-Cp ligands based on O, P and N heteroatoms have recently gained increasing attention because of their strong ligand-metal bonds and outstanding tuneable electronic and steric features essential for compensating coordinative unsaturation of metal centre and catalytic activity toward polymerization.[37] Formation of solvent and salt adducts, ligand distribution and dimerization hinder the separation of alkyl complexes containing rare-earth metal. Especially *bis*(alkyl) complexes supported by O, P and N ancillary ligands.[37] As a result development of ligands with bulky substitutes and multi-coordination sites become a major strategy for stabilizing the rare-earth metal bis(alkyl) complexes (Figure 2.4).[37] Complexes $LY(CH_2SiMe_3)_2$-$(THF)_1$ and $LLu(CH_2SiMe_3)_2$-$(THF)_0$ were applied to initiate the polymerization (ROP) of ε-CL, they

exhibited high activities at room temperature and gave full conversion of ε-CL within five minute when used as initiators.[37]

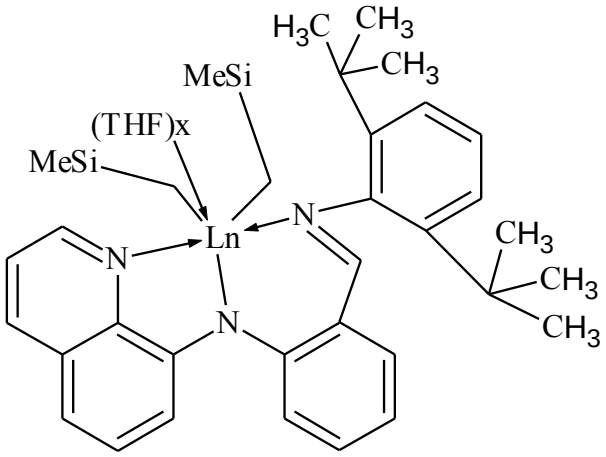
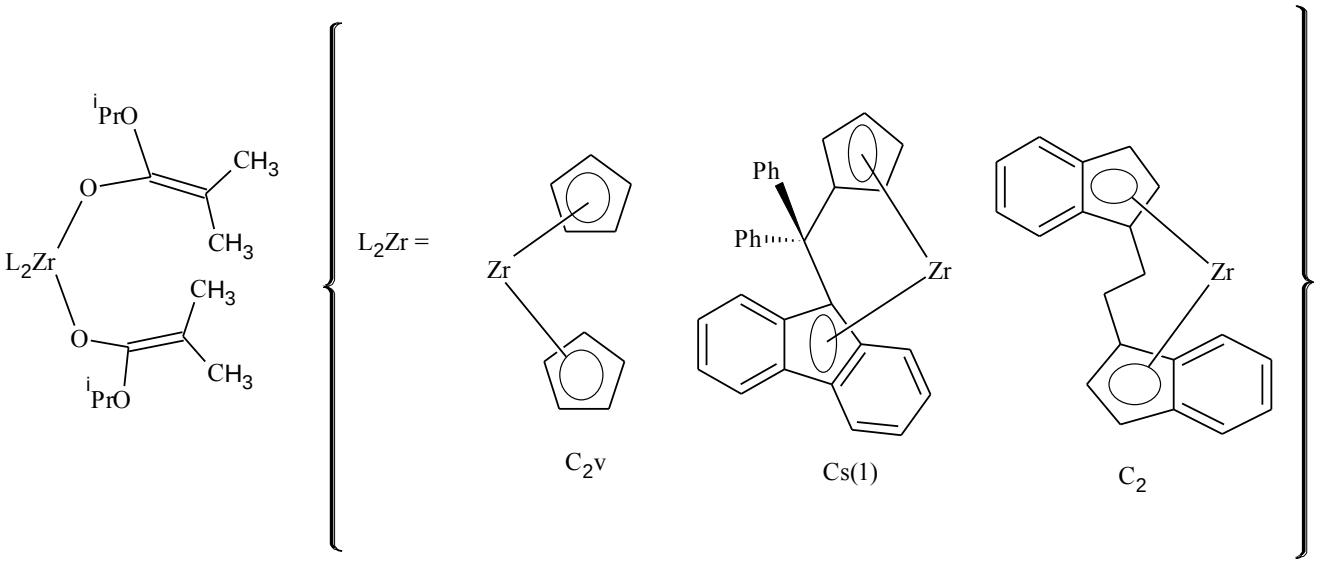


Figure 2.4 Ln bis(alkyl), a complex stabilized by a bulky bis(alkylligand.[37]

2.14 Early transition metal-based catalysts

ROP of cyclic esters through coordination-anionic ROP using complexes of group four non-metallocenes is well known.[35] Several reports have defined the use of the group four metallocene complexes in ring opening polymerization of ε-CL, titanocene and zirconocene alkyne complexes and their bimetallic congeners formed with $^{i}Bu_2AlH$ were found to be active initiators in ROP of ε-CL.[28] Species of titanocene alkoxide derived from the Cp_2TiCl initiated radical ring opening polymerization of epoxides have been reported as potential catalysts for controlled polymerization of cyclic monomers like ε-CL.[28] Other group four metallocene complexes that have been reported to polymerize ε-CL are the cationic zirconocene complexes, for example $[Cp_2ZrMe]^{+}[B(C_6F_5)_4]^{-}$ and $Cp_2ZrMe^{+}MeB(C_6F_5)_3^{-}$. These complexes are known to promote living polymerization through the non-coordinative cationic mechanism.[28] Ning *et al*. reported

the initial effective lactide ROP initiated by group four metallocene complex $Ph_2C(Cp)(Flu)Zr[OC(O^iPr)=CMe_2]_2$ (**1** in Scheme 2.2) and non-zirconocene bis(alkoxy) complexes $(BAIP)Zr(O^iPr)_2[O=C(NMe_2)CHMe_2]$.[28] Titanium-organic frame works make use of polyfunctional aryloxides instead of ligands to impact structural stability.[39] Chuck *et al*. proposed and proved that the air stable metal-organic frame works based on titanium oxide are useful initiators for ring opening polymerization of esters like ε-CL and *rac*/L-LA. Their study was motivated by the fact that great interest has been paid in the ring opening polymerization of cyclic ester catalysed by a variety of metal alkoxides.[39] $[Ti_2L_3(LH_2)]_2$ (LH_2 = 1,4-butanediol) have been used as an initiators in both polymerization of esters such as ε-CL and *rac*/L-LA, it activity were similar to those previously reported of molecular titanium metal alkoxide ROP initiators and it also yielded reasonable low PDIs indicating that polymerization is well-controlled.[39]



Scheme 2.2: Group four metallocene complex known to promote living polymerizations.[28]

2.1.5 Metal alkoxides in ROP

Other known highly effective initiators for the ring opening polymerization of lactides and lactones are metal alkoxides [$M(OR)_m$].[36] Metal alkoxides are not structurally simple and mostly aggregated via μ-alkoxo bridges in both solution and the crystalline state.[36] A perfect well defined single site structure for a initiator [$L_nM(OR)$] appropriate for mechanistic and kinetics studies would have at least one active alkoxy group joined to a metal centre.[29] A steric polydentate ligand (L_n) vacates most of the coordination sphere also stop intermolecular reactions, especially aggregation when used in metal alkoxide complexes.[36] Transition metal alkoxides have been used previously as initiators of ring opening polymerization (ROP) of cyclic esters.[40] Recently a conformational flexible diketiminate copper isopropoxide catalyst (Figure 2.5) has been reported by Whitehorne *et al*..[41] This complex showed very high catalytic activities yielding 56% of polylactide with low PDI values within 1 minute of polymerization.[40,42] In this report they also revealed that the polymerization of *rac*-lactide was initiated with no induction period and that in all studies the kinetics of polymerization were established as first order with respect to the lactide.[41]

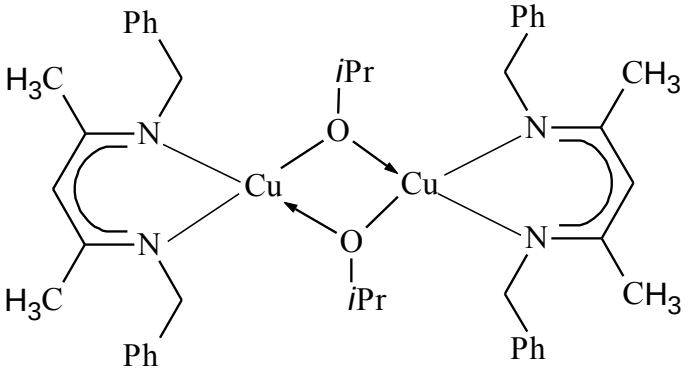
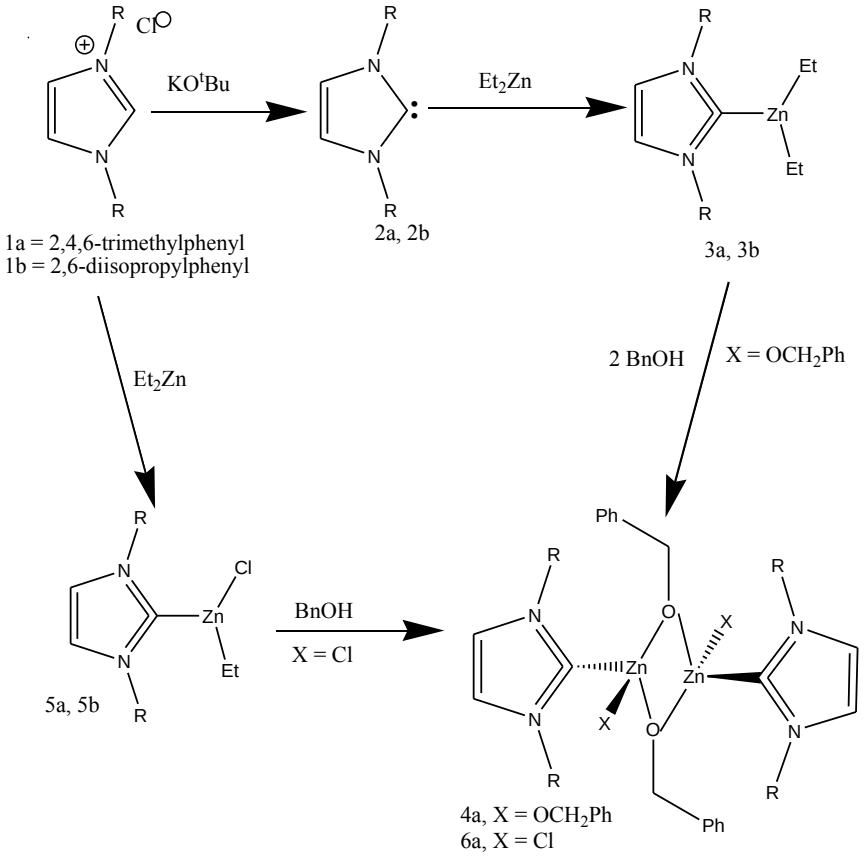


Figure 2.5: The diketiminate copper isopropoxide catalyst. [41]

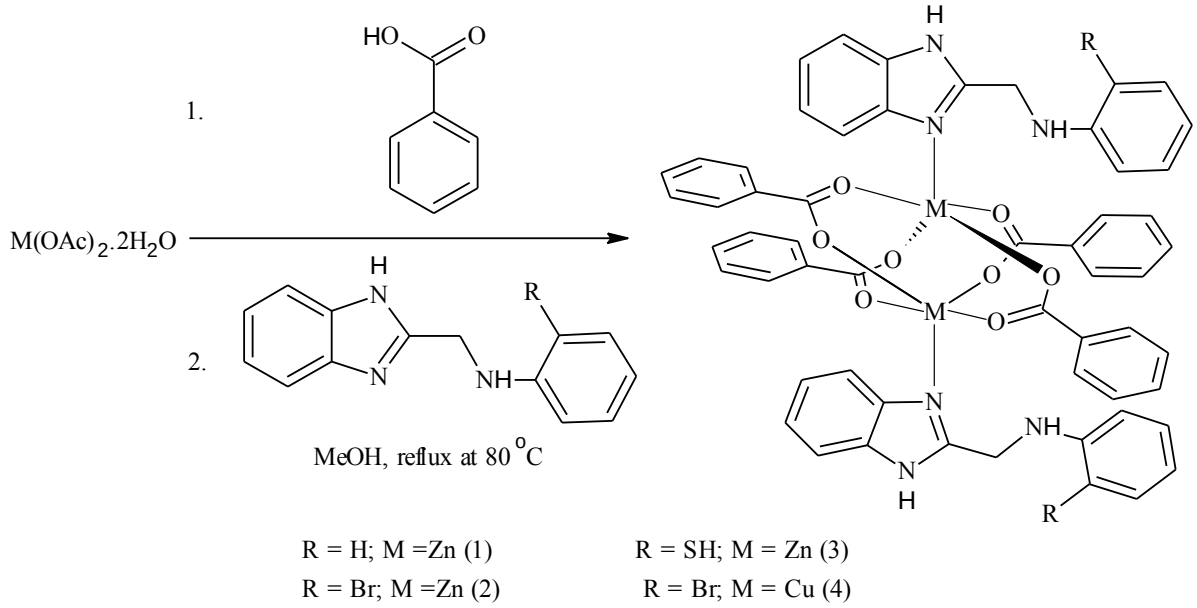
2.1.6 Zn(II) and Cu(II) metal-based catalysts in ROP of cyclic esters

The use of biocompatible metals that display comparable activity to the commercial used Sn-based catalysts is gaining attention.[40,43] Biocompatible metal complexes that are receiving numerous interest are that of Zn and Cu,[40] and they have been reported to possess the propetency to produce active catalysts for ring opening polymerization of cyclic esters.[25] A lot of attention has already been devoted to Zn derivatives as potential non-toxic catalyst and Zn powder alone is reported to be a good polymerization initiator that is used industrially.[26] NHC complexes of Zn are reported to be highly active for the polymerization of LA, also reported to perform the polymerization with good control of molecular weight, and moderate stereoselectivity.[26,35] One of the best results regarding LA polymerization was observed with zinc lactate ($Zn(Lact)_2$) which is a commercially available complex and can be synthesized from ethyl lactate and ZnO. [26] Studies in ring opening polymerization of D,L-LA catalysed by **4a** and **6a** (Scheme 2.3) in CH_2Cl_2 showed good control of molecular weight that grew linearly with lactide conversion.[35]



Scheme 2.3: NHC Zn complexes with good molecular weight control. [35]

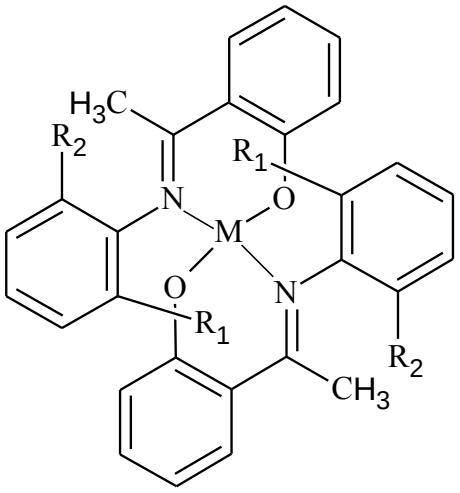
Attandoh *et al*. recently reported the coordination chemistry of Zn(II) and Cu(II) carboxylate complexes and their application in ring opening polymerization of ε-caprolactones (ε-CL) (Scheme 2.4). [40] In this report, detailed structural, mechanistic and kinetics studies of ROP of ε-CL were discussed. These carboxylate Zn(II) and Cu(II) complexes exhibited significant catalytic activities for the ROP of ε-CL. [40]



Scheme 2.4: Zn(II) and Cu(II) carboxylate complexes used in ROP of ε-CL. [40]

Only few publications are available in the use of copper complexes as initiators in the polymerization of LA and other cyclic esters due to their low activities and their tendency to produce poorly controlled polymers.[42,44] Synthesis, characterization and catalytic studies of the series phenoxy-ketamine copper complexes with varying steric demand were reported by John *et al*., these copper complexes revealed to be efficient initiators for ROP of L-LA at very high temperatures and when used in the absence of solvent.[45] Each of the copper complexes was heated together with L-LA for a certain period of time. During heating the reactants will form a monomer (LA) melt in which the polymerization was allowed to occur.[45] For the copper complex **3a** and **3b** (Figure 2.6) the temperature dependence study done at ratio 50:1 revealed that polymer molecular weight increased when the temperature was increased but for complex **3c** (Figure 2.6) a decrease in polymer molecular weight was observed when temperatures was increased. [45]

The molecular weights obtained from ROP of L-LA melt initiated by the copper complexes were comparable to the molecular weights obtained when catalysts such as [3-mesityl-1-picolylimazol-2-ylidene]Zn(Et)I and [(1-i-propyl-3-{N-phenylacetamido}imidazole-2-ylidene)$_2$Ag]$^+$Cl$^-$ were used, however several other initiators which produces molecular weight that are higher than those obtained by copper complexes have been report.[45] Detailed comparison of copper complexes (**3a-3c,** Figure 2.6) with other defined catalyst revealed that these copper catalysts are reasonably active for ring opening polymerization of lactide. [45]



$R_1 = R_2 =$ Et; M = Ni(**2a**), Cu(**3a**)
$R_1 = R_2 =$ Me; M = Ni(**2b**), Cu(**3b**)
$R_1 =$ H, $R_2 =$ Me; M = Cu(**3c**)

Figure 2.6: Structure of metal complexes used in polymerization. [45]

2.2 Rationale and justification of this study

Synthetic petrochemical-based polymers use non-renewable resources[1], even though there is an increase in popularity of plastic recycling, removal of these non-degradable materials has led to

severe environmental problems.[30] Catalysts that have been used in the production of biodegradable polyesters are derived from toxic metals such as aluminium.[26]

The problem of petrochemical-base polymers can be solved by the synthesis of biodegradable PLA and PCL using renewable, biodegradable materials such as fermented corn, beets and soybeans. Environmentally friendly and non-toxic metals and metal complexes such as zinc, copper and calcium can be used to substitute for toxic metals as catalysts. The transition metal complex suitable for ROP is one which allows control of molecular weight, stable with respect ligand dissociation. We thus envisage that the benzoazole zinc and copper metal complexes would not be only less toxic but also form stable catalyst for polymerization of lactides and ε-caprolactones.

2.3 Objectives

The aim of the project is to synthesise benzoazole transition metal complexes and use them as catalysts in the ring opening polymerization of lactides and ε-caprolactones to form biodegradable PLA and PCL.

2.3.1 Specific objectives

1. To synthesise and characterize benzoazole ligands and their corresponding Cu(II) and Zn(II) metal complexes.

2. To investigate the ability of the isolated Cu(II) and Zn(II) complexes to catalyze ring opening polymerization of lactides and ε-caprolactones.

3. To investigate the mechanism and kinetics of polymerization of both lactides and ε-caprolactone.

4. To study the effects of temperature, solvent and catalyst concentration on the polymerization kinetics of these reactions.

Chapter Three

Synthesis and Structural Characterization of Pyridyl(Benzoazole) Copper(II) and Zinc(II) Carboxylate Complexes

3.1 Introduction

A wide range of different metal complexes have been broadly investigated as initiators for ring opening polymerization of cyclic esters such as lactides and ε-caprolactone (ε-CL).[46] These catalysts includes organometallic and the coordination complexes of main group elements, transition metals, and lanthanides.[46a] The most common method for synthesizing polyesters with well-controlled molecular weights arrangement and microstructure is the ROP using metal complexes as catalysts.[46b,47] A number of reactions initiated by these metal complexes are very specific and a careful selection of ligand and metal centre allow the catalyst properties to be fine-tuned to give the preferred polymer structure.[48]

For the catalyst/initiator to be used in polymerization, metal centre choice is as important as that of the ligand. Some interesting initiators contain Zn(II) in combine high activity with low toxicity,[49] catalysts based on Zn(II) have been receiving an increase in attention due to the fact that they can be metabolized in the body.[50] More recently Zn(II) and Cu(II) metals have received considerable attention as catalysts in ring opening polymerization of lactides and lactones because they have toxicity, cheap and easy of synthesis.[51] Zn(II) and Cu(II) complexes are known to make effective catalysts for ring opening polymerization of cyclic esters like lactides and ε-caprolactones.[52] Also complexes of these metals are known to be stable and significantly biocompatible.[52] Furthermore for more controlled, rapid and in some cases stereoselective monomer conversion these complexes should be supported by steric/bulky achiral, ancillary

ligands.[53] Recently, Attandoh *et al*. reported (benzimidazolymethyl)amine Zn(II) and Cu(II) based carboxylate complexes that successfully catalyzed ε-cparolctones.[51] Other reports on active Zn(II) and Cu(II) based catlysts for ROP of lactides and ε-caprolactones were by Garces *et al*.[54] and Bhunora *et al*.[50]

Our research group has reported several literatures in ring opening polymerization of lactides and caprolactones. The most recent reports are by Ojwach *et al*. and Attandoh *et. al*. In Ojwach *et al*. the structutral and kinetics studies of polymerization reactions of cyclic esters initiated by (pyrazol-1-ylmethyl)pyridine Zn(II) and Cu(II) complexes are disucced. Their reports also highlights that steric factors control bimetallic or monometallic formation of (pyrazol-1-ylmethyl)pyridine Zn(II) and Cu(II) complexes, they mentioned that the complexes were active initiators in ROP polymerization processes.[52] On the other hand the report by Atthandoh et al. was about benzimidazolymethyl)amine Zn(II) and Cu(II) based carboxylate complexes used in ROP of ε-CL, this discussed how the activities of the initiators is affected by the nature of the metal centre and nature of the carboxylate ligand.[51] In this chapter, we will be describing the coordination chemistry of (Pyridyl)Benzimidazoles and Pyridyl)Benzothiazole Cu(II) and Zn(II) carboxylate complexes.

3.2 Experimental sections

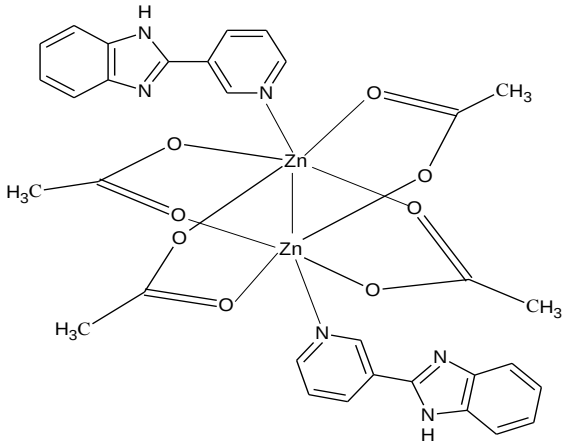
3. 2.1 Materials and instrumentation

The ligands, 2-(3-pyridyl)-1H-benzimidazole (**L1**), and 2-(2-pyridyl)-1H-benzimidazole (**L3**), zinc acetate, cupric acetate, toluene, DMSO, deuterated chloroform ($CDCl_3$), benzoic acid. Compound 2-(2-pyridyl)-1-benzothiazole (**L2**) was prepared following literature procedures.[41]

^{1}H NMR measurements was recorded on a Bruker 400 UltraShield equipment (^{1}H at 400 MHz) using DMSO-d_6 and $CDCl_3$. IR spectroscopic measurements were recorded on Perkin-Elmer spectrum 100 series FT-IR spectrometer. Magnetic susceptibility measurements were performed on an Evans balance. Elemental analyses and mass spectrometry were recorded on Flash 2000 thermoscientific analyser and micromass LCT premier mass spectrometer respectively. Crystallographic data were collected on a Bruker APEXII diffractometer with Mo Kα radiation (λ = 0.71073 Å).

3.2.2 Synthesis of zinc(II) and copper(II) complexes

3.2.2.1 Synthesis of $[Zn_2(\mathbf{L1})_2(OAc)_4]$ (C1)

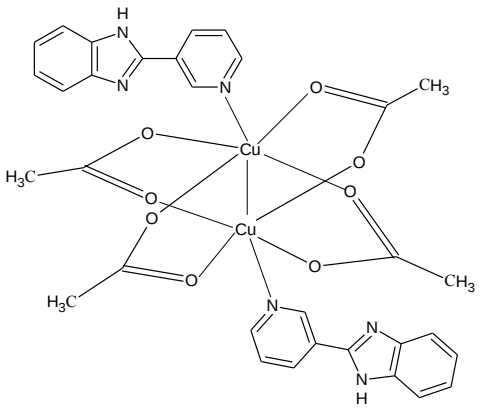


A solution of 2-(3-pyridyl)-1H-benzimiadazole, **L1**, (0.34 g, 1.79 mmol) in methanol (4 ml) was added to a solution of $Zn(OAc)_2.2H_2O$ (0.39 g, 1.79 mmol) in methanol (6 ml). The mixture was stirred for 24 h at room temperature to give a white precipitate. After the reaction period, the white precipitate was filtered and dried to afford complex **C1**. Yield = 0.39 g (58%). ^{1}H NMR

(400 MHz, DMSO-d_6): δ(ppm) 13.15 (s, 1H, NH), δ(ppm) 9.45 (d, 1H, J_{HH}=7.19 Hz, ArH), δ(ppm) 8.76 (d, 1H, J_{HH}=7.29 Hz, ArH), δ(ppm) 8.54 (d, 1H, J_{HH}=7.29 Hz, ArH), δ(ppm) 7.61 (d, 2H, J_{HH}=7.19 Hz, ArH), δ(ppm) 7.21 (d, 2H, J_{HH}=7.30 Hz, ArH), δ(ppm) 1.80 (d, 6H, J_{HH}=7.29 Hz, CH_3). IR ν (cm^{-1}): 3074.87 (weak, N-H), 1625.40 (strong, C=O), 1601.75 (medium, C=N), 1445.30 (weak, ArH). (ESI-MS) m/z (%): 194 (M^+-$Zn_2C_8H_{13}O_8$**L1**, 100%); 314 (M^+-$ZnC_6H_{13}O_6$**L1**, 8.0%), 501 (M+-$ZnC_7H_{12}O_6$, 8.2%), 701(M+-C_4H_{12}, 8.2%). Anal. Calcd. for $C_{16}H_{15}N_3O_4Zn$: C, 43.50; H, 3.99; N, 9.36.. Found: C, 43.60; H, 3.70; N, 9.0.

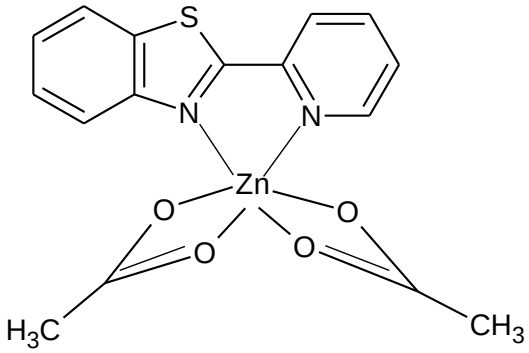
Complexes **C2-C6** were prepared by following the procedure used to prepare complex **C1** using the corresponding metal carboxylate and appropriate ligand (**L1** - **L3**). The crystals obtained for **C2** and **C6** were grown by slow evaporation of their methanol solution.

3.2.2.2 Synthesis of $[Cu_2(\mathbf{L1})_2(OAc)_4]$ (**C2**):



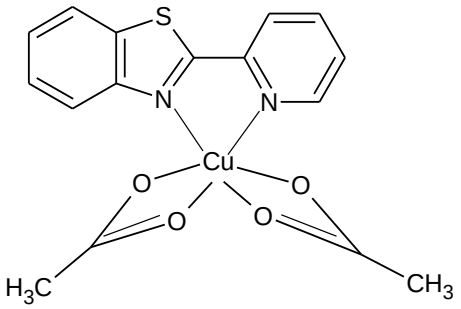
Compound **L1** (0.35 g, 1.80 mmol) and $Cu(OAc)_2.H_2O$ (0.35 g, 1.80 mmol). Product: light blue powder. Yield = 0.59 g (86%). μ_{eff} = 1.91 BM. IR ν (cm^{-1}): 3075.24 (weak, N-H), 1621.60 (strong, C=O), 1600 (medium, C=N), 1500 (weak, ArH). (ESI-MS) m/z (%): 194 (M^+-$Cu_2C_8H_{13}O_8$**L1**, 100%); 317 (M^+- $CuC_6H_{10}O_6$**L1**, 9.0%); 453 (M^+- $C_4H_{10}O_3$**L1**, 8.4%). Anal. Calcd for $C_{16}H_{15}N_3O_4Cu$: C, 48.68; H, 4.34; N, 10.64. Found: C, 48.37; H, 3.85; N, 10.76.

3.2.2.3 [Zn(**L2**)$(OAc)_2$)] (**C3**):



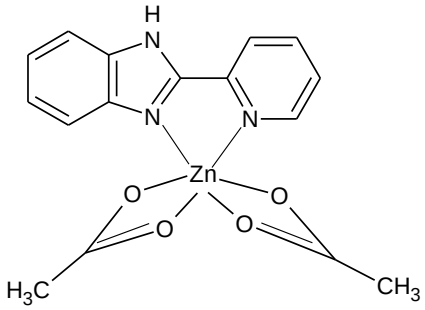
Compound **L2** (0.50 g, 2.4 mmol) and $Zn(OAc)_2.2H_2O$ (0.52 g, 2.4 mmol). Product: light green solid. Yield = 0.47 g (53%).^{1}H NMR (400 MHz, DMSO-d_6): δ 8.73 (s, 1H, Bz), δ(ppm) 8.32 (d, 1H, J_{HH}=7.30 Hz, Py), δ 8.09 (d, 1H, J_{HH}=6.09 Hz, Py), δ 8.05 (d, 1H, J_{HH}=7.30 Hz, Bz), δ 8.04 (t, 1H, J_{HH}=6.09 Hz, Py), δ 7.55 (m, 2H, Bz), δ 7.47 (t, 1H, J_{HH}=7.30 Hz, Py), δ 1.79 (s, 6H, CH_3). IR ν (cm^{-1}): 3199.63 (weak, N-H), 1625 (weak, C=O), 1601.91 (medium, C=N), 1450 (weak, ArH). (ESI-MS) m/z (%): 323 (M^+-$C_3H_6O_2$**L2**, 23.0%); 336 (M^+- $C_2H_3O_2$**L2**, 58.5%); 489 (M^+-C_9H_8N, 9.7%). Anal. Calcd for $C_{16}H_{14}N_2O_4SZn$: C, 42.42; H, 4.48; N, 6.23. Found: C, 42.38; H, 4.44; N, 6.19

3.2.2.4 [Cu(**L2**)$(OAc)_2$)] (**C4**):



Compound **L2** (0.50 g, 2.4 mmol) and $Cu(OAc)_2.H_2O$ (0.46 g, 2.4 mmol). Product: pale blue powder. Yield = 0.27 g (29%). μ_{eff} = 1.89 BM. IR ν (cm^{-1}): 3072.76 (weak, N-H), 1558.77 (medium, C=N), 1490.69 (medium, ArH). (ESI-MS) m/z (%): 334 (M+- $C_2H_4O_2L_2$, 100%); 364 (M+- CH_3OL_2, 5.0%); 489 (M+-C_9H_8N, 23%). Anal. Calcd. for $C_{16}H_{14}N_2O_4SCu$: C, 44.79; H, 3.60; N, 7.75. Found: C, 44.31; H, 3.13; N, 8.13.

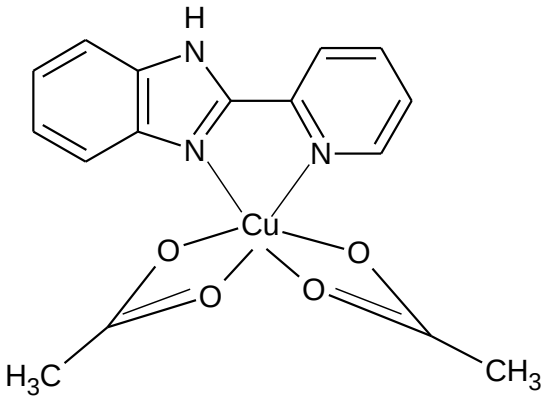
3.2.2.5 [Zn(**L3**)$(OAc)_2$)] (**C5**):



Compound **L3** (0.50 g, 2.6 mmol) and $Zn(OAc)_2.2H_2O$ (0.56 g, 2.6 mmol). Product: cream white solid. Yield = 0.33 g (34%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.16 (s, 1H, Py), δ 8.11 (d, 1H, J_{HH}=7.29 Hz, Py), δ 8.09 (t, 1H, J_{HH}=7.30 Hz, Bz), δ 8.06 (t, 1H, J_{HH}=7.30 Hz, Py), δ 8.04 (t, 1H, J_{HH}=7.30 Hz, Bz), δ 8.02 (m, 2H, Py), δ 7.61 (t, 1H, J_{HH}=7.28 Hz, Py), δ 1.82 (s, 6H, CH_3). IR ν

(cm^{-1}): 3074.27 (weak, N-H), 1623.25 (medium, C=O), 1603.25 (medium, C=N), 1500.81 (weak, ArH). (ESI-MS) m/z (%):194 (M^+-$Zn_2C_8H_{13}O_8$**L1**, 100%); 289 (M^+-$C_3H_7O_3$**L3**, 8.0%); 376 (M^+- H_2**L3**, 43.0%); 575 (M^+, 1.5%). Anal. Calcd. for $C_{16}H_{15}N_3O_4Zn$: C, 45.56; H, 3.15; N, 8.18. Found: C, 45.50; H, 3.60; N, 8.30.

3.2.2.6 [Cu(**L3**)$(OAc)_2$)] (**C6**):



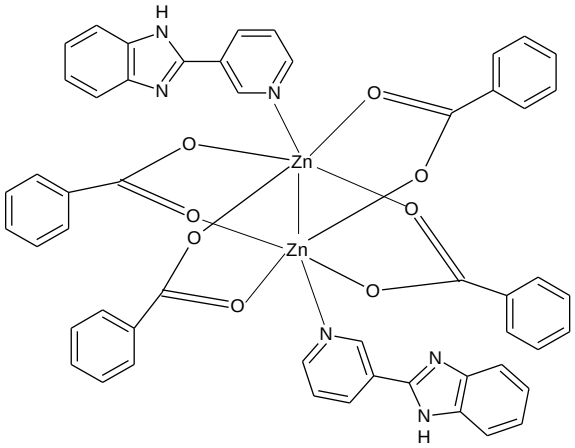
Compound **L3** (0.50 g, 2.6mmol) and $Cu(OAc)_2.H_2O$ (0.51 g, 2.6 mmol). Product: blue-green solid. Yield = 0.80g (65%). μ_{eff}=1.90 BM. IR ν (cm^{-1}): 3078.1 7 (weak, N-H), 1601.44 (medium, C=N. (ESI-MS) m/z (%): 194 (M^+-$Cu(C_2H_3O_2)_2$**L3**, 100%); 258 (M^+-$C_4H_6O_4$**L3**, 4.0%); 377 (M^+-**L3**, 37.0%); 455 (M^+- $C_7H_5N_2$**L3**, 12.0%); 575 (M^+, 9.0%). Anal. Calcd. for $C_{16}H_{15}N_3O_4Cu$: C, 48.60; H, 4.34; N, 10.94. Found: C, 48.08; H, 3.88; N, 11.87.

Complexes **C7** was prepared by addition of $Zn(OAc)_{2\cdot2}H_2O$ (1.09, 4.56mmol) and the benzoic acid (1.1g, 9.11 mmol) at ratio 2:1 in the presence of 20 ml methanol. The mixture was then stirred and heated at 70˚C for four hours. The ligand 2-(3-pyridyl)-1H-benzimiadazole, **L1**, (0.90

g, 4.56 mmol) was then added and the reaction was left for 24 hours. Product **C7** was obtained as white precipitate which was filtered and dried at room temperature.

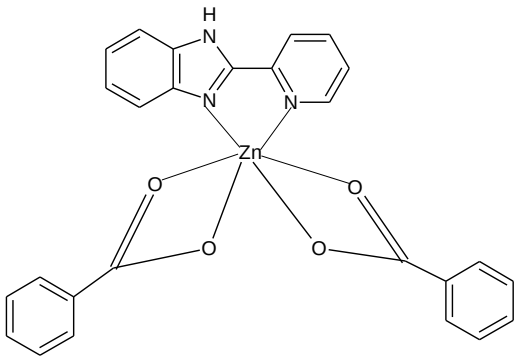
Complexes **C8** was prepared by following the procedure used to prepare complex **C7** using the corresponding of $Zn(OAc)_2.2H_2O$, benzoic acid and ligand **L3**.

3.2.2.7 [Zn(**L1**)(Benzoate)$_2$)] **(C7):**



Compound **L1**(0.89 g, 4.6mmol), $Zn(OAc)_2.2H_2O$ (1.0 g, 4.6 mmol) and benzoic acid (1.11 g, 9.11mmol). Product: White powder. Yield =1.716g (74%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.34 (s, 1H, Bz), δ 8.66 (s, 2H, Py), δ 8.48 (s, 2H, Bz), δ 7.70 (d, 5H, J_{HH}=7.29 Hz, ArH), δ 7.45 (t, 3H, J_{HH}=6.68 Hz, Bz), δ 7.40 (t, 5H, J_{HH}=7.29 Hz, ArH). IR ν (cm^{-1}): 3062.71, 2756.33 (weak, N-H), 1582.22 (strong, C=N), 1429.60 (weak, ArH). (ESI-MS) m/z (%): 196 (M^+-$ZnC_{17}H_{17}N_3O_4$, 100%); 332 (M^+-$C_{15}H1_7O$, 21.0%); 347 (M^+- H_2, 12.0%); 575(M^+-CH_3, 11.5%). Anal. Calcd. for $C_{29}H_{26}N_6O_4Zn$: C, 56.28; H, 4.18; N, 9.57. Found: C, 56.02; H, 3.68; N, 9.15.

3.2.2.8 [Zn(**L3**)(Benzoate)$_2$)] (**C8**):



Compound **L3**(0.44 g, 2.8mmol), $Zn(OAc)_2.2H_2O$ (0.50 g, 2.8 mmol) and benzoic acid (0.92 g, 4.56mmol). Product: White powder. Yield =1.14g (98%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.40 (d, 1H, J_{HH}=7.29 Hz, Py), δ 8.10 (t, 1H, J_{HH}=8.10 Hz, Py), δ 7.96 (d, 5H, J_{HH}=6.48 Hz, ArH), δ 7.55 (m, 4H, Bz), δ 7.45 (t, 5H, J_{HH}=6.48 Hz, ArH), δ 7.12 (m, 2H, Py). IR ν (cm^{-1}): 3007.55 (weak, N-H), 1679.33 (medium, C=O), 1633.28 (medium, C=N), 1470.92 (medium, ArH). (ESI-MS) m/z (%): 502 (M^+, 62.0%); 453 (M^+-C_4H_2, 100%); 427(M^+-C_6H_2, 41.5%); 380 (M^+-$C_7H_5O_2$, 62.5%); 196 (M^+-$ZnC_{14}H_{10}O_4$, 19.2%). Anal. Calcd. for $C_{26}H_{19}N_3O_4Zn$: C, 59.75; H, 3.06; N, 8.07. Found: C, 59.31; H, 2.98; N, 7.48.

3.2.3 Magnetic susceptibility measurements

The magnetic moment measurements were recorded at 24 ºC. The constant of the machine C was 1.0137, R_0 which was the reading for an empty tube was -28, mass of the empty tubes were 0.6293 g, 0.6227g and 0.6293 g. The samples were grinded, weighed, inserted in the small tubes and the R measurements of tube and sample were done. The calculations were done using the equations 3.1 and 3.2:

$$X_g = \frac{C \times L\,(R\text{-}Ro)}{10^9 \times mass} \qquad (3.1)$$

$$\mu_{obs} = 2.84\,[(X_m \times T)^{1/2}] \qquad (3.2)$$

Where $X_m = X_g \times$ Molecular weight.

3.2.4 Crystallography section

Single crystals suitable for X-ray analysis for complex **C2** and **C6** were grown by slow evaporation of the methanol solution and were used to determine their solid state structures.

3.2.4.1 Data Collection

Crystals of dimensions 0.20 x 0.20 x 0.07 mm^3 (**C2**) and 0.12 x 0.10 x 0.06 mm^3 (**C6**) were selected and glued on to the tip of a glass fibre. Crystals were then mounted in a stream of cold nitrogen at 296(2) K (**C2**) and at 100(2) K (**C6**), they were then centred in the X-ray beam by video camera. The crystal evaluation and data collections were performed on a Bruker Smart APEXII diffractometer with Mo Kα radiation (λ = 0.71073 Å). The diffractometer to crystal distance was set at 4.00 cm. The initial cell matrix was obtained from three series of scans at different starting angles. Each series consisted of 12 frames collected at intervals of 3.13 to 26.05˚ for **C2** and 1.31 to 26.12° for **C6,** to range about with the exposure time of 10 seconds per frame. The reflections were successfully indexed by an automated indexing routine built in the

APEXII program suite. The final cell constants were calculated from a set of 3539 (**C2**) and set of 4871 (**C6**) strong reflections from the actual data collection and set of 4871 strong.

Data collection method involved ω scans of width 3.13 to 26.05 ˚ for **C2** and 1.31 26.12° for **C6**. Data reduction was carried using the program *SAINT*+. The structure was solved by direct methods using SHELXS and refined. Non-H atoms were first refined isotropically and then by anisotropic refinement with full-matrix least-squares calculations based on F^2 using SHELXS. All H atoms were positioned geometrically and allowed to ride on their respective parent atoms. All H atoms were refined isotropically. The absorption correction was based on fitting a function to the empirical transmission surface as sampled by multiple equivalent measurements (Bruker, 2008).

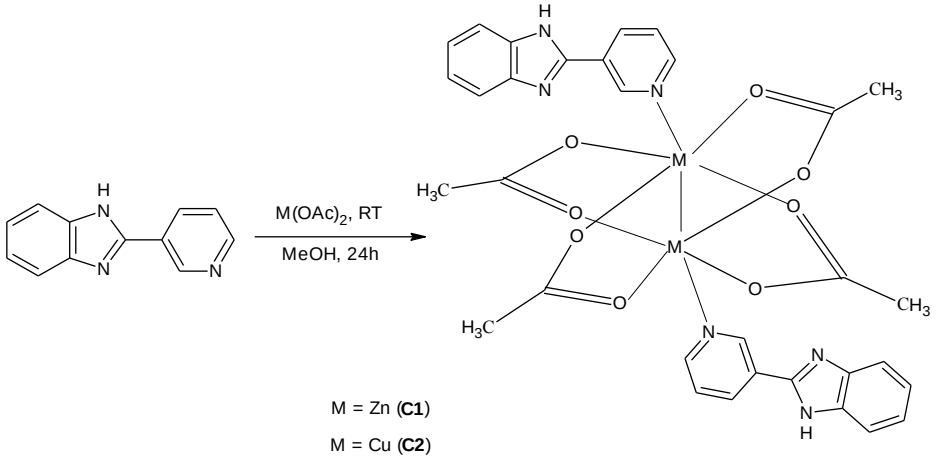
For **C2** the final least-squares refinement of 258 parameters against 3539 data resulted in residuals *R* (based on *F*2 for $I>2\sigma$) and *wR*(based on F^2 for all data) of 0.0794 and 0.2089 respectively. For **C6** the final least-squares refinement of 379 parameters against 4871 data resulted in residuals *R* (based on *F*2 for $I>2\sigma$) and *wR*(based on F^2 for all data) of 0.0466 and 0.1170. The final difference Fourier map was featureless.

3.3 Results and discussion

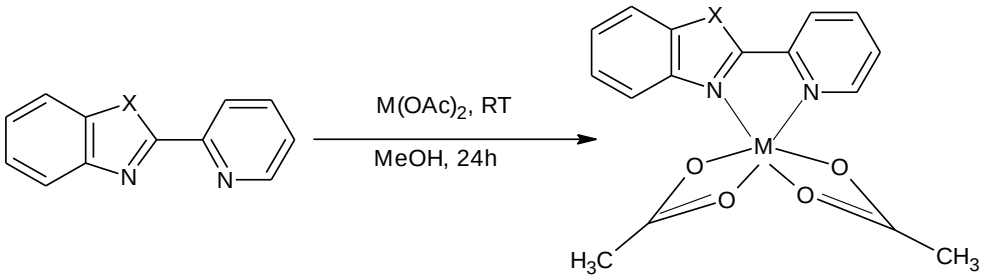
3.3.1 Syntheses and characterization of Cu(II) and Zn(II) complexes

The compound 2-(2-pyridyl)-1-benzothiazole (**L2**) was synthesized from *o*-aminothiophenol and 2-pyridinecarbaldehyde according to a known literature procedure.[55]

The Cu(II) and Zn (II) complexes, **C1-C6**, were synthesized by a one-step reaction. Cu(II) and Zn(II) acetates with the respective benzoazole ligands (**L1**-**L3**) in a stoichiometry ratio1:1 to produce the corresponding complexes **C1**-**C6** in low to high yields (Schemes 3.1 and 3.2). Zin(II) complexes were isolated as white/cream white and light green solids while the Cu(II) complexes were obtained as blue/green solids.



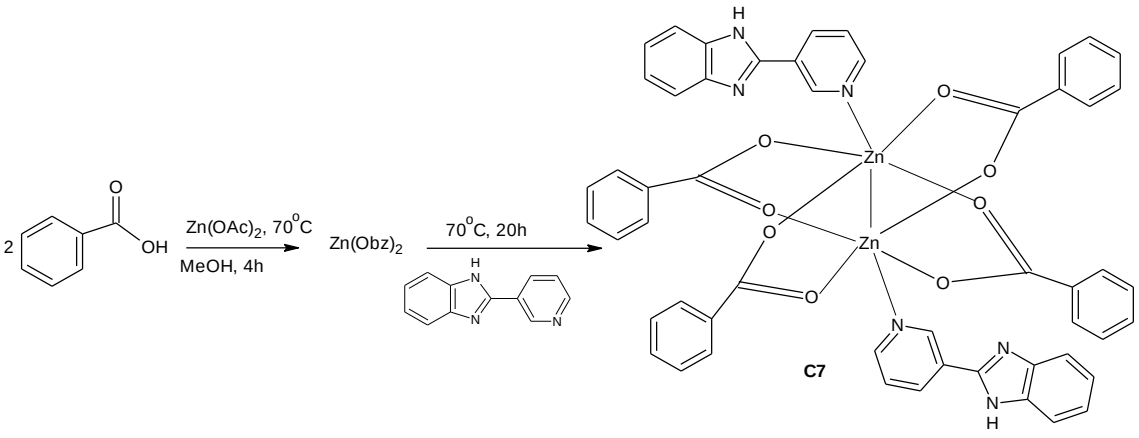
Scheme 3.1: Syntheses of Zn(II) and Cu(II) complexes **C1** and **C2**.



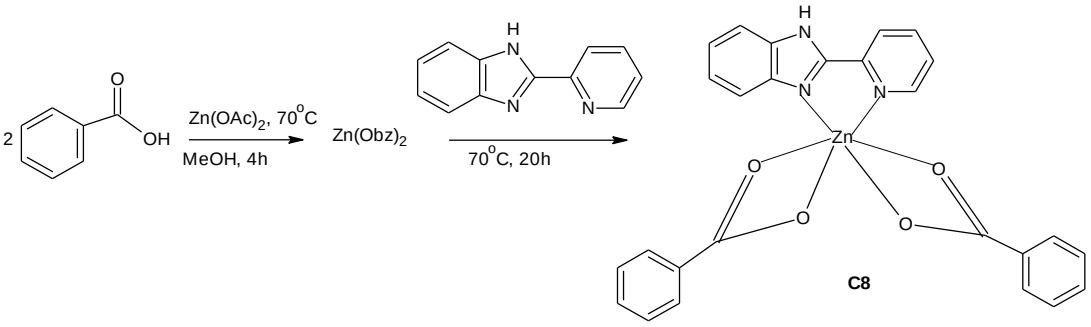
M = Zn, X= S (**C3**),
M = Cu, X= S (**C4**)
M = Zn, X= NH (**C5**),
M = Cu, X= NH (**C6**)

Scheme 3.2: Syntheses of Zn(II) and Cu(II) complexes **C3-C6.**

In another synthetic route, the Zn(II) benzoate salt was generated in situ by reaction of zinc acetate with benzoic acid in a 1: 2 ratio. This was followed by addition of ligands **L1** and **L3** to give complexes **C7** and **C8** as white solids in high yields of 98% and 74% respectively (Scheme 3.3 and 3.4).



Scheme 3.3: Synthesis of the Zn(II) complex **C7.**



Scheme 3.4: Synthesis of the Zn(II) complex **C8.**

The identity and formation of the Zn(II) complexes were confirmed by analysing the chemical shifts in ^{1}H NMR spectra of the of the benzoazole ligands relative to their corresponding complexes. As it can be seen, in ligand **L3**, pyridyl protons appeared as triplets at 7.27 and 7.72 ppm, doublet 8.32 ppm and singlet at 8.74 ppm compared to upfield signals at at 7.50 and 7.60 ppm, 8.16 ppm and 8.34 ppm respectively complex **C5** (Figure 3.1). Similarly, a singlet peak assigned to the acetate group was observed at 1.82 ppm which is upfield compared to the Zn(II) acetate signal usually observed at 1.91 ppm.[56] Both the shift in ligand peaks and the presence of the acetate CH_3 signals confirmed the formation of the complexes (Fig. 3.1). Another noticeable difference was the absence of the N-H peak at 13.10 ppm from the complex spectra, this peak is known to be weak and it disappearance might be due to appearance of more intense CH_3 peaks of the acetate. The N-H functional group is still part of the complexes but it peak cannot be identified in the 1H NMR spectra due to weak and low intensity compared to other peaks. This was the case for all Zn(II) complexes.

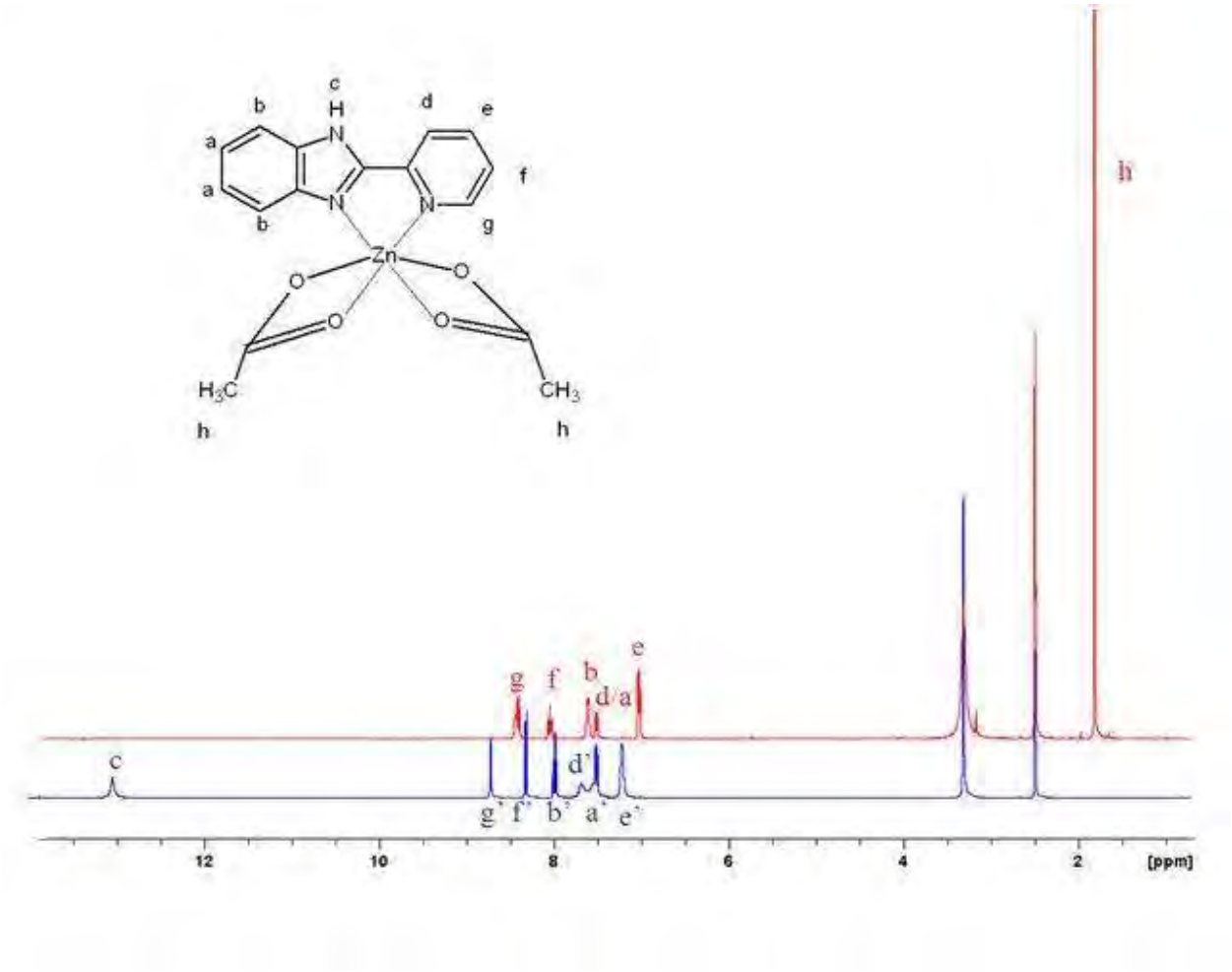


Figure 3.1: An overlay of ^{1}H NMR spectra of **L3** (blue) and **C5** (red) showing peaks due to coordination.

The measured room temperature magnetic moments for complex **C2**, **C4** and **C6** were obtained as 1.91, 1.89 and 1.90 BM respectively. These observed magnetic moments are within the range of 1.85-2.12 BM typical for Cu(II) complexes.[51,57] Another indication of complex formation, was evident from the difference in magnetic moments values of $CuAC_{2.2}H_2O$ of 1.40 BM (294.5 K) and 1.43(295 K) to those of complexes formed by coordination of ligands (**L1-L3**) to $CuAC_{2.2}H_2O$ to give complexes **C2**, **C4** and **C6**.[58]

The distinctive absorption of the ligands and complexes in the infrared (IR) region of the electromagnetic spectrum was used to study the chemical environment of the N-H and C=N functional groups and used to establish the formation and identity of the complexes. Typical IR spectra of complexes **C1**-**C8** showed that coordination of metal atom to ligands resulted in shifts in stretching bands from lower frequencies to higher frequencies (Fig. 3.2 and Table 3.1).

Table 3.1: C=N stretching bands ($\nu_{C=N}$) for complexes **C1**-**C8** (ligands)[a]

Complex	$\nu_{C=N}$ (cm^{-1})	Complex	$\nu_{C=N}$ (cm^{-1})
C1	1601 (1570)	**C5**	1603 (1595)
C2	1600 (1570)	**C6**	1601 (1595)
C3	1602(1575)	**C7**	1633 (1595)
C4	1559 (1575)	**C8**	1582 (1570)

[a]$\nu_{C=N}$ of ligand in brackets

The $\nu_{C=N}$ band of a ligand **L1** appeared at 1570.0 cm^{-1} and shifted to 1601.75 cm^{-1}, both these values fall within 1633.28-1558.77 cm^{-1} which is the range of literature reported C=N frequencies.[45] This is due to the coordination of the metal atom to the nitrogen atoms of the benzimidazolyl and pyridyl of the ligand.[51,55a,59] All ligands and some complexes (**C1**-**C6**) contained weak bands between 3199.63-3062.71 cm^{-1} and these can be attributed to the N-H stretching vibrations.[46] The bands of all complexes were similar, followed the same trend as the complex **C1** and agreed with the values reported in literature.[59]

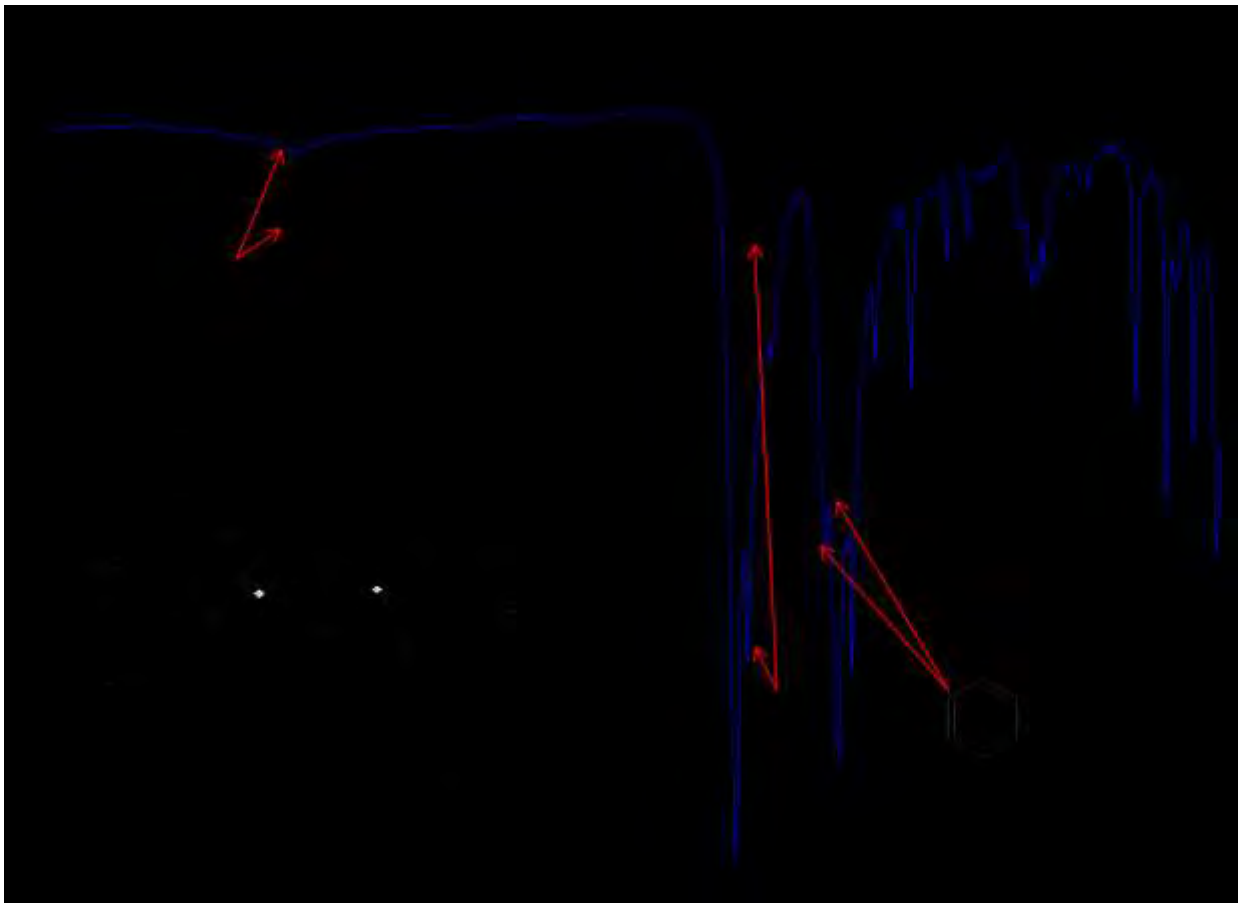


Figure 3.2: IR spectrum of **L1** (black) and **C1** (blue) highlighting shift in bands of functional groups of complexes when compared to the bands of the ligand.

The complexes were also characterised by mass spectroscopy. As an illustration, ESI-MS spectrum of complex **C6** showed a peak *m/z* at 573 and a base peak at 194 (Figure 3.3) corresponding to $[C_{28}H_{24}CuN_6O_4]^+$ and ligand **L3** fragments respectively. This indicates that the metal is coordinated to two **L3** ligand units and two acetate anions. Scheme 3.5 represents a typical fragmentation pattern of the complexes.

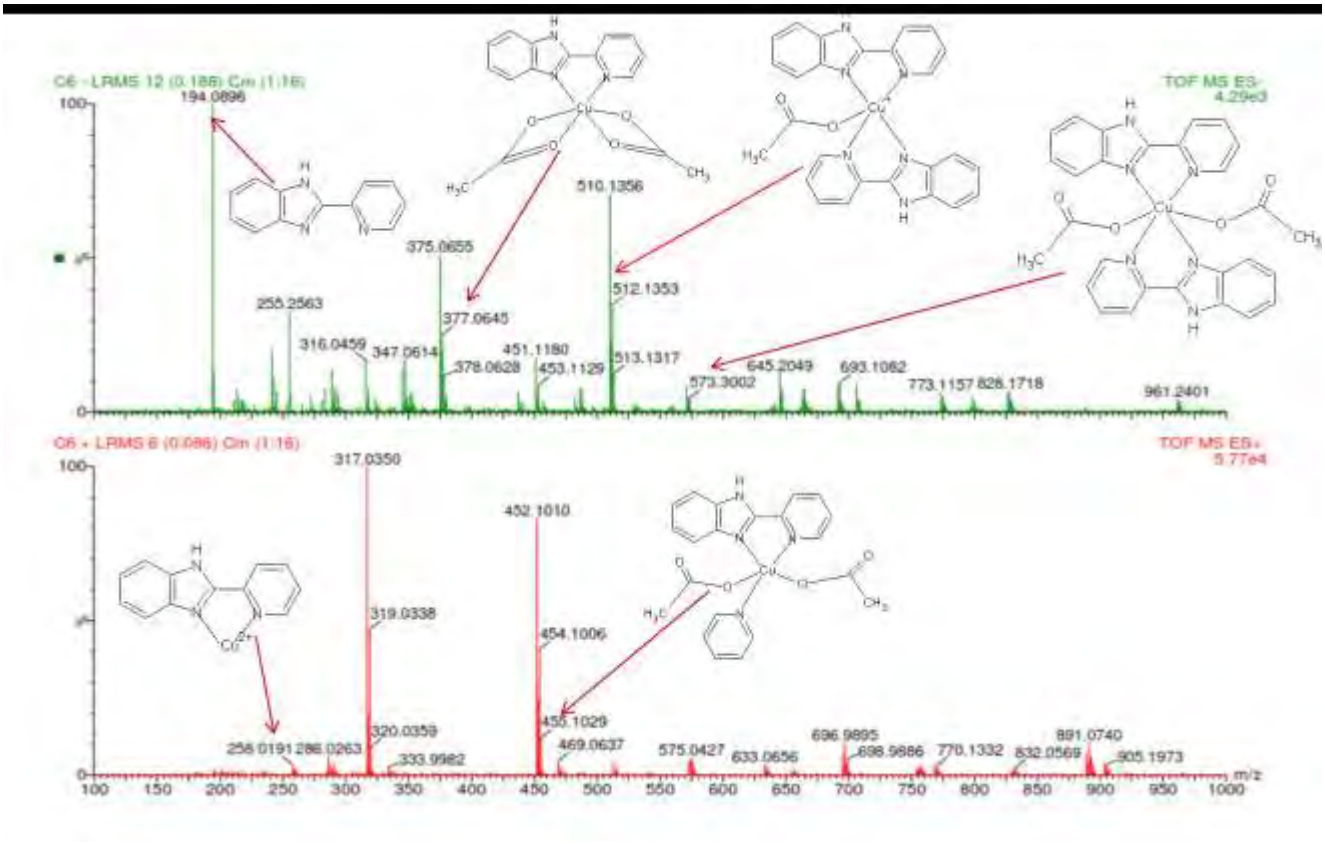
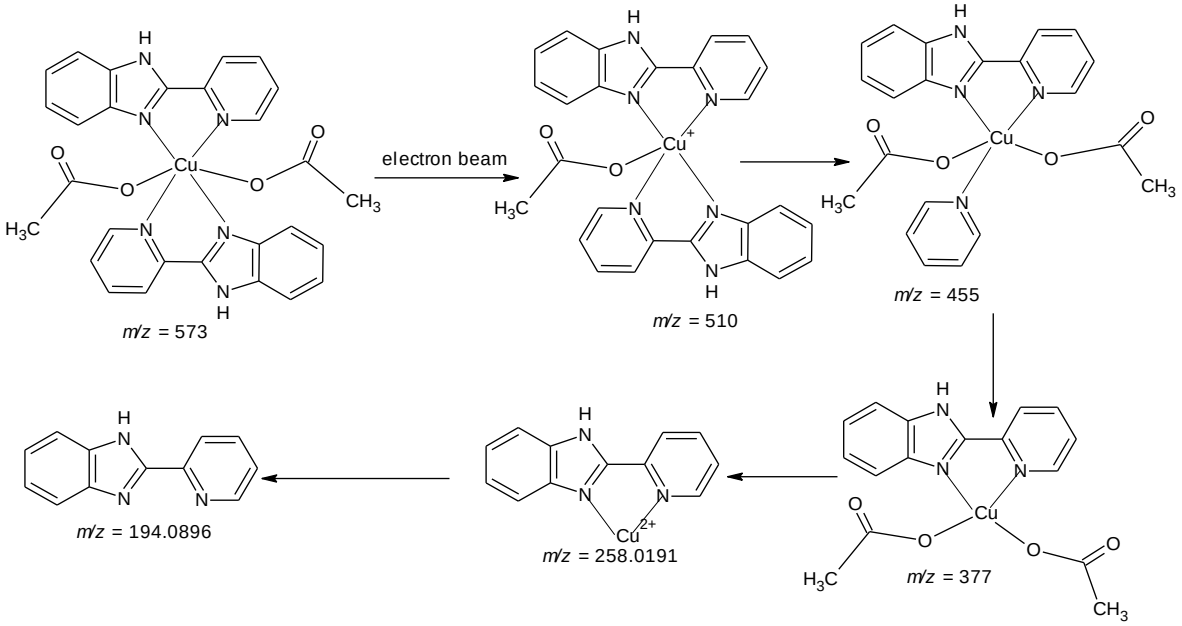


Figure 3.3: The Mass spectra showing complex **C6** and it fragments



Scheme 3.5: The fragmentation pattern of the Cu(II) complex **C6**.

Elemental analyses data were in good agreement with the proposed structures and empirical formulae of the compounds as shown in Schemes 3.1-3.4. In addition, the elemental analysis data confirmed the purity of the isolated complexes except for the reasonable observed minor deviations (~0.5) from the expected values.

3.3.2 Solid state structures of complexes C2 and C6a

Single crystals of complexes **C2** and **C6** were grown by slow evaporation of their methanol solutions at room temperature and used to determine their solid state structures by X-ray crystallography. A summary of X-ray crystallographic data collected and refinement parameters are given in Table 3.2 while Table 3.3 and 3.4 contain selected bond lengths and bond angles for the complexes. The molecular structures of complexes **C2** and **C6a** are shown in Figure. 3.4 and 3.5 respectively.

The solid state structure of **C2** is binuclear, with each asymmetric unit of the complex consisting of one metal centre, two bidentate acetate anion, one monodentate pyridyl(benzimidazole) ligand (**L1**) and one Cu-Cu metal bond to give a six coordinate geometry around the Cu(II) atom. There are two uncoordinated water molecules in the crystal lattice. The two Cu(II) atoms are bridged by two pairs of acetate anions. Ligand **L1** coordinates through the pyridyl nitrogen possibly due to the unfavourable seven-membered ring that would be formed when bidentate coordination mode was to be adopted (Figure 3.4).

Table 3.2: X-ray Crystallographic data for complexes **C2** and **C6a**

Parameters	**C2**	**C6a**
Empirical formula	C16 H19 Cu N3 O6	C28 H26 Cu N6 O5
Formula weight (g mol^{-1})	412.88	573.17
Temperature (K)	296(2)	100(2)
λ (Å)	0.71073	0.71073
Crystal system	Monoclinic	Triclinic
Space group	P 21/c	P-1
α, β, γ (°)	90, 96.538(14), 90	75.399(5), 77.672(5), 83.638(5)
Volume ($Å^3$)	1796.3(5)	1251.4(11)
Z	4	2
ρ (calculated, Mg/m^3)	1.527	1.566
Absorption coefficient	1.254 mm^{-1}	0.927 mm-1
F(000)	852	610
Crystal size (mm^3)	0.20 x 0.20 x 0.07	0.12 x 0.10 x 0.06
Theta range for data collection	3.13 to 26.05°.	1.31 to 26.12°.
Reflections collected	12765	20911
Independent reflections	3539 [R(int) = 0.0926]	4871 [R(int) = 0.0280]
Completeness to theta = 25.00°	99.8 %	98.2 %
Goodness-of-fit on F^2	1.066	1.063
Final R indices [I>2sigma(I)]	R_1 = 0.0794, wR_2 = 0.2089	R_1 = 0.0466, wR_2 = 0.1170
R indices (all data)	R_1 = 0.1211, wR_2 = 0.2207	R_1 = 0.0527, wR_2 = 0.1212
Largest diff. peak and hole	1.370 and -0.821 e.Å-	1.484 and -0.817 e.Å-3

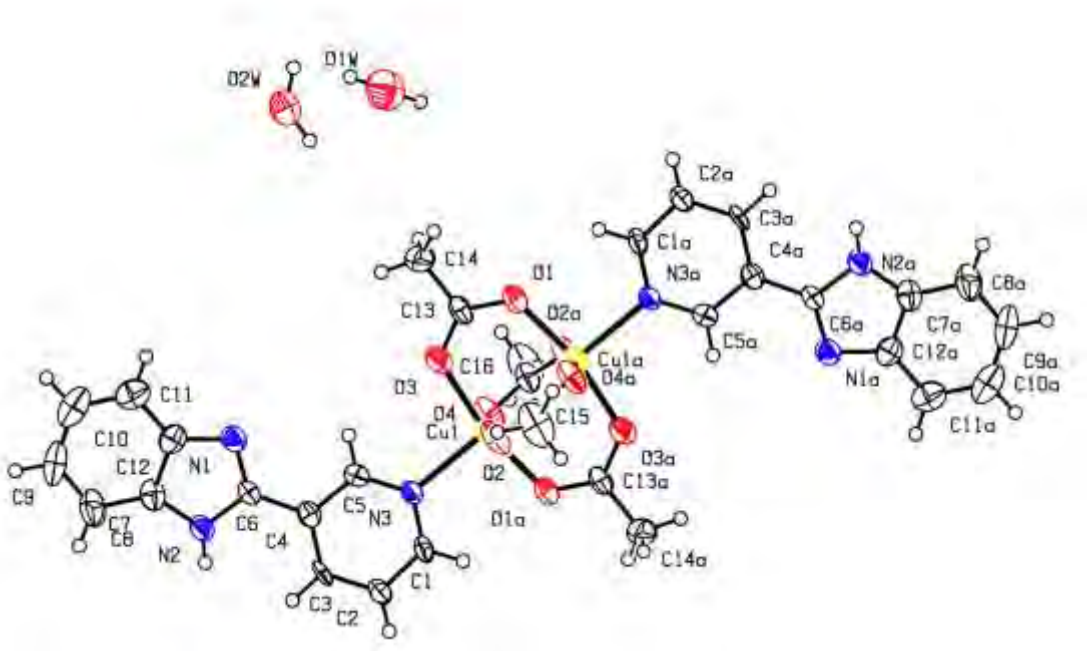
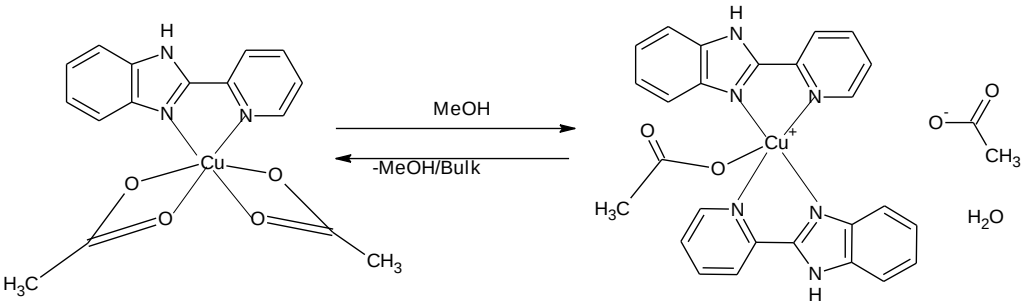


Figure 3.4: Molecular structure of the copper complex **C2,** showing the six coordinates geometry drawn with 50% probability thermal ellipsoid.

On the other hand, complex **C6a** is mononuclear in which the metal coordination sphere consists of two bidentate ligands (**L3**) and one monodentate acetate anion to give a five-coordination number around the copper atom. In the crystal lattice, there exists an acetate counter anion. This transformation from the expected **C6** (one **L3** unit) to **C6a** containing two **L3** units during crystallization (Scheme 3.6) infers that **C6** is not thermodynamically stable. This might originate from insufficient shielding of the Cu metal by one **L3** unit and two bidentate acetates in an octahedral environment. Thus incorporating of more bulky secondary unit is plausible. The displacement of an acetate anion from the metal coordination sphere could be possibly due to steric restrictions upon inclusion of another **L3** unit. The acetate was displaced because it coordinates with a hard oxygen atom and according to HSAB theory Cu(II) is an intermediated acid (not hard or soft). Nitrogen on the other hand is also intermediate when compared to the

oxygen atom; therefore Cu prefers coordinating to the nitrogen donor atom.



Scheme 3.6: Behaviour of Cu(II) complex **C6** in bulk and in solvent.

Table 3.3: Selected bond lengths and angles for **C2**

Bond lengths (Å)		**Bond angles (°)**	
O(3)-Cu(1)	1.960(5)	O(3)-Cu(1)-O(4)	88.0(2)
O(4)-Cu(1)	2.009(5)	O(1)#1-Cu(1)-O(4)	89.2(2)
O(1)-Cu(1)#1	1.960(5)	O(1)#1-Cu(1)-N(3)	95.5(2)
O(2)-Cu(1)	1.991(5)	O(2)-Cu(1)-Cu(1)#1	82.17(14)
Cu(1)-Cu(1)#1	2.6496(16)	N(3)-Cu(1)-Cu(1)#1	178.37(15)
N(3)-Cu(1)	2.184(5)	C(5)-N(3)-Cu(1)	122.9(4)
C(4)-C(6)	1.459(9)	N(1)-C(6)-C(4)	125.2(6)

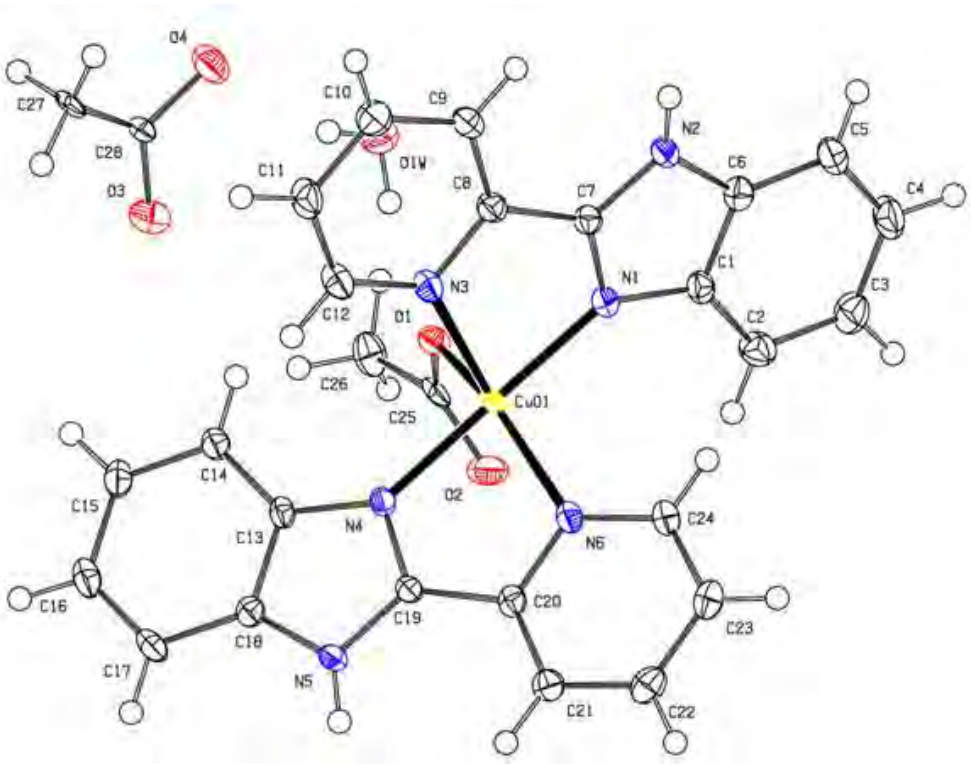


Figure 3.5: Molecular structure of the copper complex **C6,** showing the five coordinates geometry drawn with 50% probability thermal ellipsoid.

The average Cu-$O_{acetate}$ bond lengths of 1.985(5) Å and 1.994(2) Å for complexes **C2** and **C6** respectively are comparable indicating similar strengths of ligands **L1** and **L3** and fall within the range of bond lengths observed for similar complexes reported by literature.[60] For example, Li *et al*. reported a binuclear Cu(II) complex of 2-(3-pyridyl)-1H-benzimiadazole ligand with Cu-$O_{acetate}$ bond lengths ranging from 1.9584(17) –1.9983(16) Å.[42,55a] The Cu-N bonds of **C2** (2.184(5) Å) and that of **C6** (1.970(3)-2.214(3) Å) are also statistically similar and compared well with values reported in literature (2.0031(16) – 2.1755(19) Å and 1.997(2) Å). [55a,61] In the solid state structure of **C2,** Cu-Cu bond length of 2.6496(16) Å is similar to typical bond distance of 2.6432 Å[62] for related binuclear Cu(II) complexes.

Table 3.4: Selected bond lengths and angles for **C6**

Bond lengths (Å)		Bond angles (°)	
N(6)-Cu(01)	2.071(3)	N(4)-Cu(01)-N(1)	173.76(11)
O(1)-Cu(01)	1.994(2)	N(4)-Cu(01)-N(6)	80.48(10)
N(1)-Cu(01)	1.975(3)	N(1)-Cu(01)-N(6)	96.04(10)
N(3)-Cu(01)	2.214(3)	N(4)-Cu(01)-N(3)	97.45(11)
N(4)-Cu(01)	1.970(3)	N(1)-Cu(01)-N(3)	79.11(11)
N(1)-C(6)-C(4)	125.2(6)	N(1)-C(7)-C(8)	121.1(3)

The O-Cu-O bond angles for **C2** range from 88.0(2) – 89.2(2) ˚, O-Cu-N bond angles are 95.5(2)˚ and the angle for N-Cu-Cu is 178.4(15)˚. These values deviate slightly from the regular octahedral geometry resulting in a distorted octahedral. The bond angles obtained for complex **C6** are very similar to those reported in the literature for (pyridyl)benzoazoles complexes, For example the bond angles 80.4(10)˚, 96.0(10)˚and 173.8(11)˚for N(4)-Cu-N(6), N(1)-Cu-N(6) and N(4)-Cu-N(1) agree well to the N-Cu-N bond angles reported by Beloglazkina *et. al*. (81.6(3), 86.0(2) and 172.0(5)).[55a,60b] The geometry around the Cu(II) atom can be said to be a distorted square pyramidal with the acetate anion residing on the axial position and the two ligand units sitting on the basal plane.[41a]

3.4 Conclusions

In conclusion eight (Pyridyl)Benzoazole Cu(II) and Zn(II) complexes were synthesized. These complexes were characterized fully with IR spectroscopy, mass spectrometry and elemental analysis. In addition all the Zn(II) complexes (**C1**, **C3**, **C5**, **C7** and **C8)** were characterised by ^{1}H NMR while the paramagnetic Cu(II) complexes **C2**, **C4** and **C6** were characterised by magnetic moment measurements. Cu(II) and Zn(II) complexes of 2-(-3-pyridyl)-1*H*-benzimidazole (**L1**) are binuclear complexes in which the ligand coordinated through the pyridyl nitrogen in a monodentate fashion. The complexes of 2-(-2-pyridyl)-1*H*-benzimidazole (**L3**) and 2-(-2-pyridyl)-1-benzothiozole (**L2**) are mononuclear and the ligands coordinated in a bidentate mode using pyridyl and benzimidazole/benzothiozole nitrogen atoms. The coordination modes of complexes were confirmed by single crystal x-ray crystallography while their formation was confirmed by NMR, IR, elemental analysis and mass spectrometry.

Chapter Four

Ring opening Polymerization of ε-Caprolactone and Lactides Catalyzed by Pyridyl(benzoazole) Cu(II) and Zn(II) complexes.

4.1 Introduction

Plastics are inexpensive, light weight and durable material which can be moulded into a variety of product that find use in a wide range of applications.[63] They are used in a vast and expanding range of products and have already replaced many tradition materials such as wood, stones, bones, glass and ceramics in their former usage. In developed countries approximately a third of plastic is used in packaging, another third in building such as piping used in plumbing or vinyl siding.[64] Plastic has high chemical and light resistance, it is very strong and tough, can be easily worked as hot melt and it can be used in a wide range of temperatures, all these properties and it low cost has increased its worldwide annual demand.[63,64] The production of plastic has increased over the last 60 years.[63] The current levels of plastic usage and disposal generate several environmental problems. [64] Plastic has been produced from petrochemicals produced from fossil fuel and gas. [63] Most plastics from fossil fuel and gas are not biodegradable and extremely durable. [64] As a result the majority of polymers produced today will persist for at least a decade or probably a century.[64] To solve the problems caused by polymers produced from non-renewable resources such as fossil fuel and gas, most research has focused on synthesis of biodegradable polymers.[65] A variety of biodegradable polymers known, linear aliphatic polyesters are the most well-known because their enzymatic and hydrolysis chain cleavage gives ω-hydroxy acids which in most cases are metabolized into carbon dioxide and water.[65,66] The biocompatible and biodegradable polymers that's been receiving excellent attention over the past decade are polylactide (PLA) and polycaprolactone (PCL).[67] These polyesters (PLA and PCL)

have found applications as packaging materials,[68] sophisticated devices in pharmaceutical and medical industries.[67]

Polyesters are commonly produced by ring opening polymerization (ROP) of the cyclic monomers.[66] Metal-based complexes have been used as catalysts/initiators in ROP of both lactide (LA) and ε-caprolactone (ε-CL).[67] To date, a large number of metal complexes including potassium, lithium, zinc, magnesium, calcium, iron, aluminum, stannous, yttrium and lanthanide have been designed and their catalytic activities has been investigated.[67] However, some of the most active systems such as tin-based are toxic hence not suitable for the production of biocompatible polymers.[5] Thus zinc, copper, magnesium and calcium metal complexes are attractive due to their non-toxicity.[69] Herein, we report the polymerization of LA and ε-CL using the (pyridyl)benzoazole Cu(II) and Zn(II) complexes synthesized in Chapter three.

4.2 Experimental section

4.2.1 Materials and methods

All reactions were carried out under dry nitrogen gas using by a standard Schlenk line techniques. Glassware used in the polymerization was oven-dried at 120 ˚C. The monomers, ε-caprolactone (ε-CL) and lactides (LA) were purchased from Sigma Aldrich Co. ε-CL was dried over CaH_2, vacuum distilled and stored under inert conditions prior to use while the lactides were purified by crystallization from dry toluene in the refrigerator. $CDCl_3$ was also bought from Sigma Aldrich and dried over activated alumina. Toluene and methanol were purchased from Merck chemicals. Toluene was distilled from sodium while methanol was purified by distilling from magnesium. The zinc and copper complexes used in the polymerization were prepared in Chapter three.

NMR spectra were recorded on Bruker 400 UltraShield NMR (400 MHz for ^{1}H and 100 MHz for ^{13}C) spectrometer. All the chemical shifts were recorded in δ units relative to tetramethylsilane. The ^{1}H and ^{13}C spectra are referenced using residual CDCl3 solvent peaks. The mass spectra of the polymers were obtained using a micromass LCT premier mass spectrometer while the number average Molecular mass (Mn) and the molecular weight distribution of the polymers were determined using Gel Permeation Chromatography (GPC) at the University of Stellenbosch.

4.2.2 General procedure for ε-caprolactone and lactide polymerization

Polymerization of ε-caprolactone was carried out in bulk at 110 ˚C. In a typical bulk polymerization, 0.038 g of the complex was weighed into a pre-heated Schlenk tube equipped with a magnetic stirrer and ε-CL (1.10 mL, [M]/[I] = 100/1) was added. The Schlenk tube was immersed in silicon oil bath at the desired temperature and the reaction mixture stirred until completion of polymerization. The extent of monomer conversions was monitored by taking aliquots at regular intervals and percentage conversions determined by ^{1}H NMR spectroscopy. In the case of lactides, (1.44 g, [M]/[I] = 100/1) were added to a rapidly stirring solution of 0.038 mol complex in toluene (2.5 mL) and the reaction mixture stirred at 110 ˚C. The reactions were monitored to completions as in ε-CL by ^{1}H NMR spectroscopy.

4.2.3 Polymerization Kinetics

Kinetic studies were carried out by taking aliquots of the polymer at regular time intervals and quenching the reaction by freezing in liquid nitrogen. The quenched aliquots were dissolved in $CDCl_3$ and analyzed by ^{1}H NMR spectroscopy. For ε-CL polymerization, the ratio of initial

monomer concentration to monomer concentration at time t, $[CL]_0/[CL]_t$, was determined based on the peak intensities of ε-CL and PCL from the ^1H NMR spectrum. The signal around 4.2 ppm and 4.0 ppm corresponds to ε-CL and PCL respectively.[67,68] The ratio $[\varepsilon\text{-CL}]_0/[\varepsilon\text{-CL}]_t$ was calculated according to equation 4.1.

$$\frac{[CL]_0}{[CL]_t} = \frac{I_{4.2}+I_{4.0}}{I_{4.2}} \qquad (4.1)$$

$I_{4.2}$ = Integral of monomer (ε-CL).

$I_{4.0}$ = Integral of polymer (PCL).

For LA polymerization, the peak intensities around 4.8 ppm and 5.4 ppm correspond to monomer LA and polymer PLA respectively.[67] The ratio $[LA]_0/[LA]_t$ was calculated according to the equation 4.2.

$$\frac{[LA]_0}{[LA]_t} = \frac{I_{4.8}+I_{5.4}}{I_{4.8}} \qquad (4.2)$$

$I_{4.8}$ = Integral of monomer (D,L-LA and L-LA).

$I_{5.4}$ = Integral of polymer (PLA).

The apparent rate constant (K_{Obs}) of all polymerization reactions were obtained from the gradient of the line of best-fit of the plot of $In[M]_0/[M]_t$ versus time.

4.2.4 Polymer characterization

The molecular weight (Mw) and number average molecular mass (Mn) of the polymers were determined by Size Exclusion Chromatography (SEC) at Stellenbosch University. The SEC instrument consist of Waters 1515 isocratic HPLC pump, Waters 717plus auto-sampler, Waters 600E system controller (run by Breeze version 3.30 SPA), a Waters in-line Degasser AF and a Waters 2414 differential refractometer (operated at 30 ˚C) in series with a Waters 2487 dual wavelength absorbance UV/Vis detector operating at variable wavelength. The polymers were dissolved in a BHT stabilized THF (2 mg/ ml), filtered through a 0.45 μm nylon filters and eluted through two sets PLgel (Polymer laboratories) 5 μm Mixed-C (300x7.5 mm) column and a precolumn (PLgel 5 μm Guard, 50x7.5 mm) at a flow rate of 1 ml/min. The column oven was kept at 30 ˚C and injection volume was 100 μl. THF (HPLC grade stabilized with 0.125% BHT) was used as the eluent. Narrow polystyrene standards ranging from 580 to 2 x 106 g/mol was used for calibration hence molecular weights were measured as polystyrene equivalents.

4.3 Results and discussion

4.3.1 Polymerization of ε-CL and LA

The ring opening polymerization of ε-caprolactone (ε-CL), D, L-lactide (D, L-LA) and L-lactide (L-LA) were investigated using Zn(II) and selected Cu(II) complexes synthesized in chapter 3 (Figure 4.1). The polymerization of ε-CL and LA were carried out in bulk and in toluene at 110 ˚C using initial Monomer/Initiator ratio of 100:1 (Scheme 4.1).

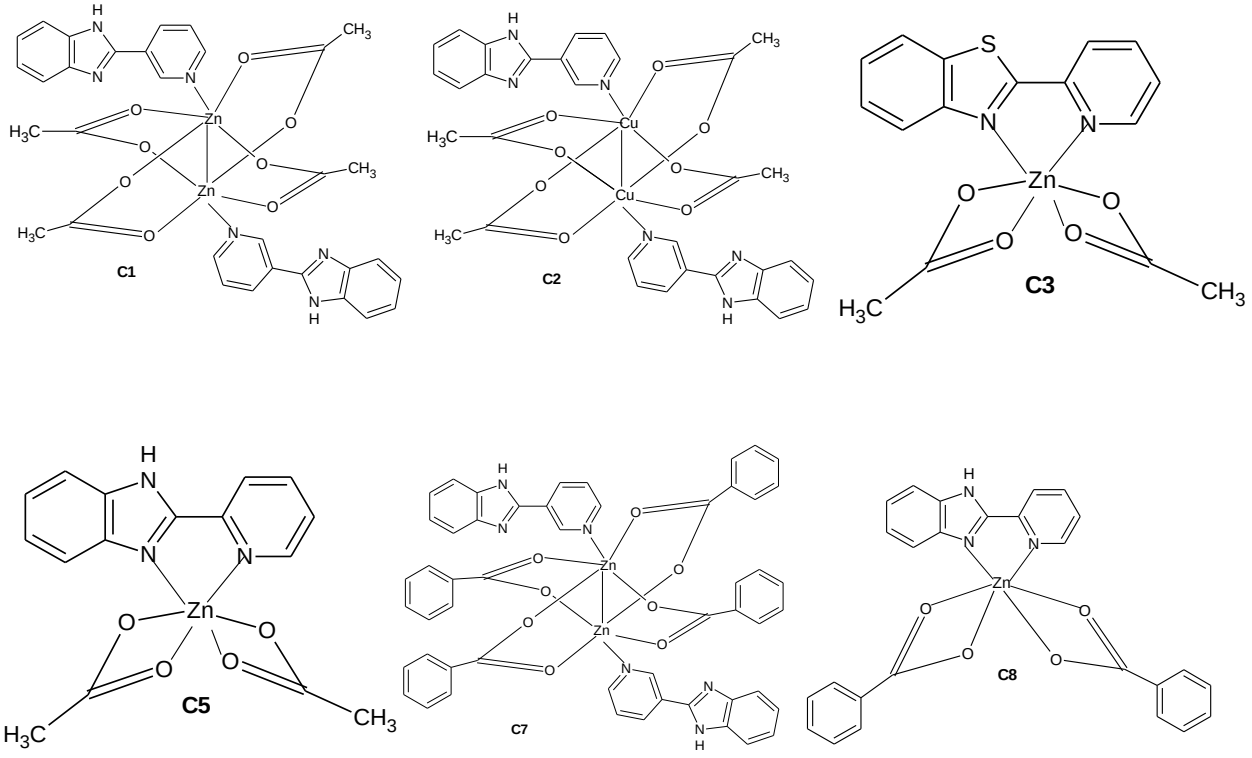
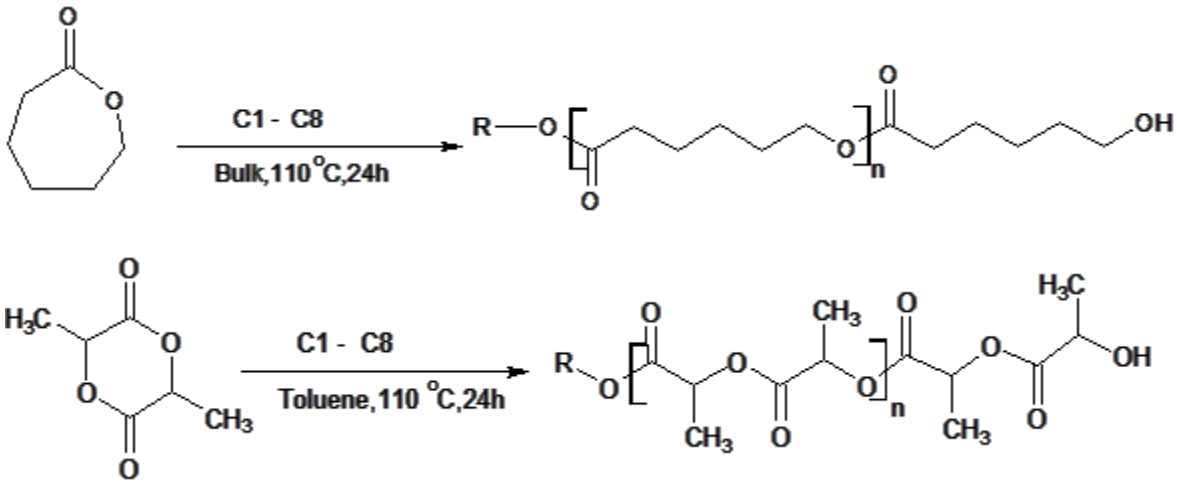


Figure 4.1: Complexes tested as initiators for ROP of ε-CL and LA.

The results of the polymerization under these conditions are reported in Table 4.1. The initial results showed that the complexes exhibited significant catalytic activities toward ROP of ε-CL and LA giving maximum 98% conversion between 24-72 hours (Figures 4.2-4.5, Table 4.1).

Further mechanistic and kinetics of polymerization reactions were thus investigated to determine the effect of reaction conditions, catalyst structure, catalyst concentration and nature of monomer on the kinetics of polymerization reactions.



Scheme 4.1: ROP reactions conditions of ε-CL and LA.

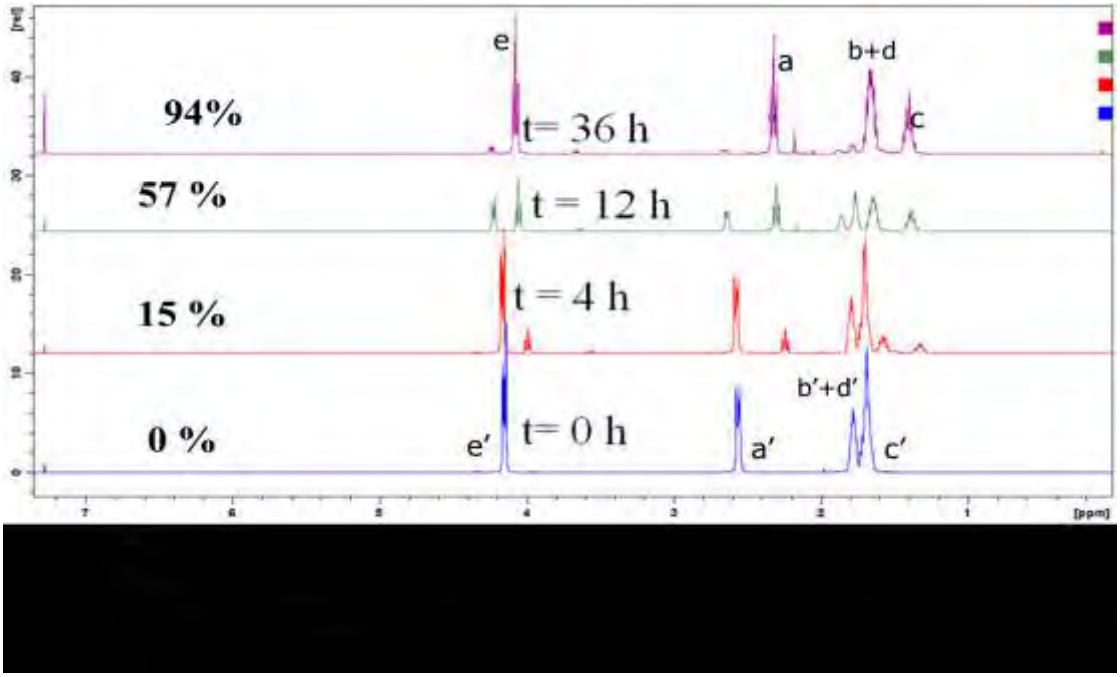


Figure 4.2: The ^{1}H NMR showing conversion of ε-CL to PCL as the ROP of ε-CL proceeds.

Table 4.1: ROP of ε-CL, D,L-LA and L-LA catalyzed by synthesized metal complexes[a]

Entry	Catalyst	Monomer	t (h)	Conv (%)	Mn_{GPC}[b]	MW_{GPC}[b]
1	**C1**	ε-CL	24	97	1478	6254
2	**C2**	ε-CL	72	98	1259	5108
3	**C3**	ε-CL	28	92	2007	5521
4	**C4**	ε-CL	24	8	-	-
5	**C5**	ε-CL	24	43	811	2458
6	**C6**	ε-CL	24	7	-	-
7	**C7**	ε-CL	42	96	-	-
8	**C8**	ε-CL	48	90	-	-
9	**C1**	D,L-LA	24	95	994	6954
10	**C2**	D,L-LA	24	29	340	530
11	**C3**	D,L-LA	24	42	386	620
12	**C5**	D,L-LA	24	44	-	-
13	**C7**	D,L-LA	48.5	97	3048	6127
14	**C8**	D,L-LA	34	87	1881	2909
15	**C1**	S-LA	60	98	4067	8430
16	**C3**	S-LA	59	92	1279	1762
17	**C5**	S-LA	59	96	1453	1942
18	**C7**	S-LA	60	90	2258	3161
19	**C8**	S-LA	60	84	1245	1603

[a] Conditions: 110 ˚ C, continuous stirring. [M]:[I]=100, [ε-CL]=0.01 mol, [LA]=0.01mol, polymerization of ε-CL in bulk and LA in toluene. [b] Measured by GPC.

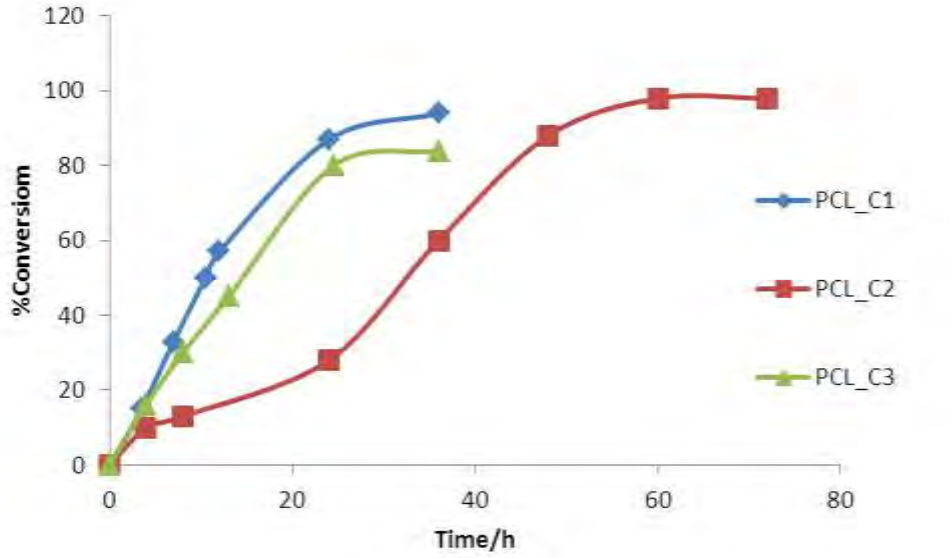


Figure 4.3: The plot of conversion (%) against time (h) for PCL.

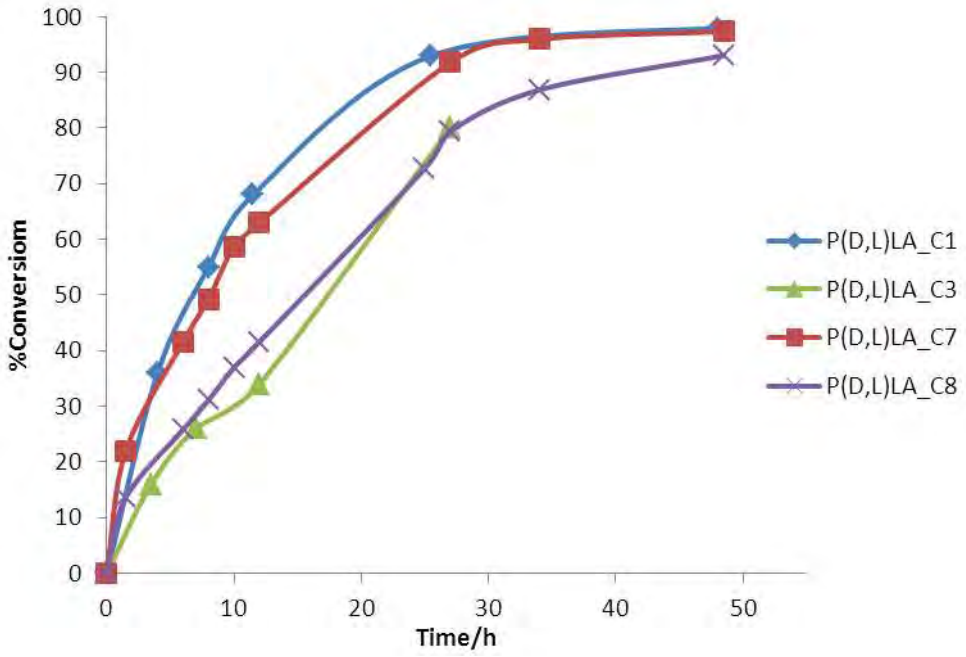


Figure 4.4: Plot of conversion (%) against time (h) for P(D,L)-LA.

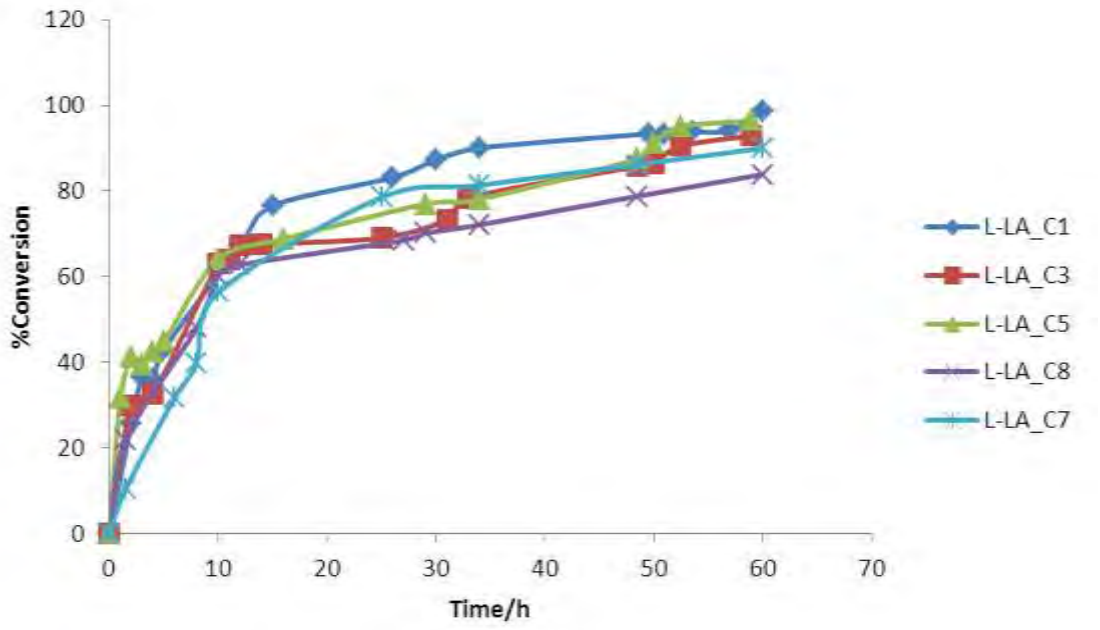


Figure 4.5: Plot of conversion (%) against time (h) for P(L)-LA

4.3.2 Kinetics of polymerization

The kinetics of ε-CL and LA were investigated using complexes **C1, C2, C3, C4, C5, C6, C7** and **C8** in bulk and in toluene respectively at 110 ˚C. Kinetics of polymerization reactions were was monitored by ^{1}H NMR spectroscopy as described in the experimental section. The rate constants of the reactions were extracted from the graphs of $\ln[M]_0/[M]_t$ against time ((Figures4.6-4.8). In the following sections, we present systematic investigations of the respective kinetic parameters for the complexes.

4.3.2.1 Order of reaction with respect to monomer

To determine the dependency of the reactions kinetics on each monomer, plots of $\ln[M]_0/[M]_t$ vs time were constructed for the complexes and the respective monomers. The linear plots were

consistence with pseudo-first order of reactions with respect to ε-CL and LA monomers (Figures 4.6-4.8). Thus the rate equations for the ROP reaction can be written as given in equation 4.3. These results are in agreement with those previously reported in literature.[69] For example, Ojwach *et al.* reported that the kinetics of polymerization of ε-CL proceed according to pseudo first-order kinetics.[70]

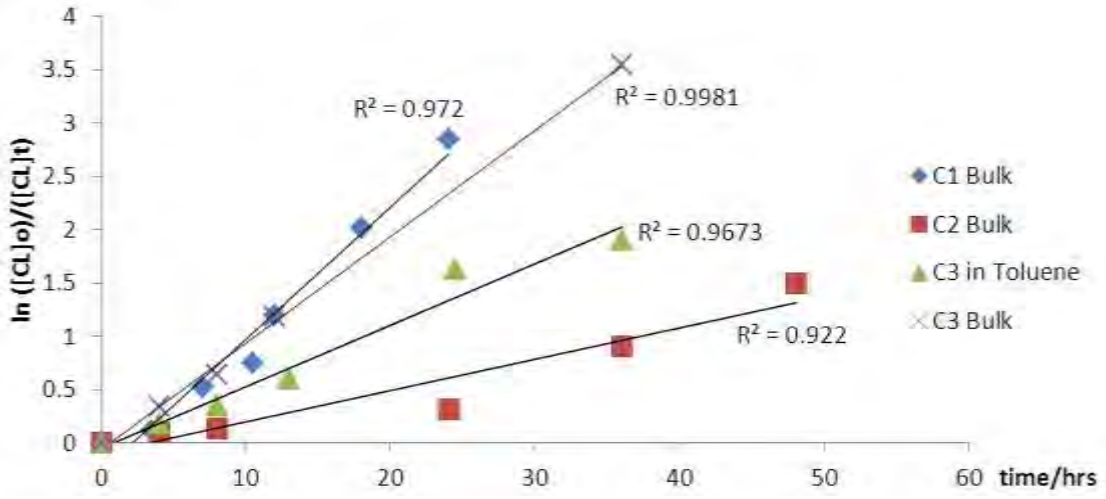


Figure 4.6: Plots showing linear relationship of $\ln[\varepsilon\text{-CL}]_0/[\varepsilon\text{-CL}]_t$ and time.

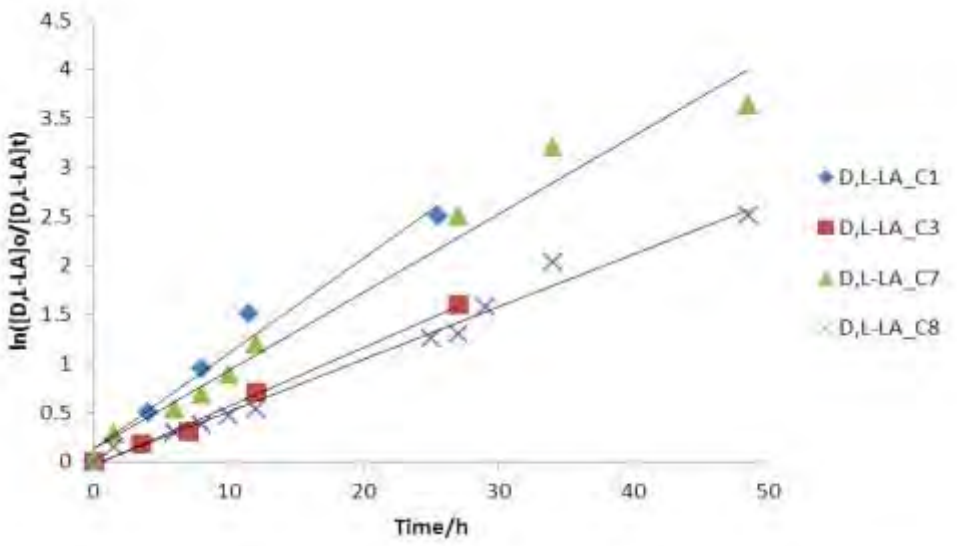


Figure 4.7: Plots of $\ln[LA]_0/[LA]_t$ against time for D,L-LA.

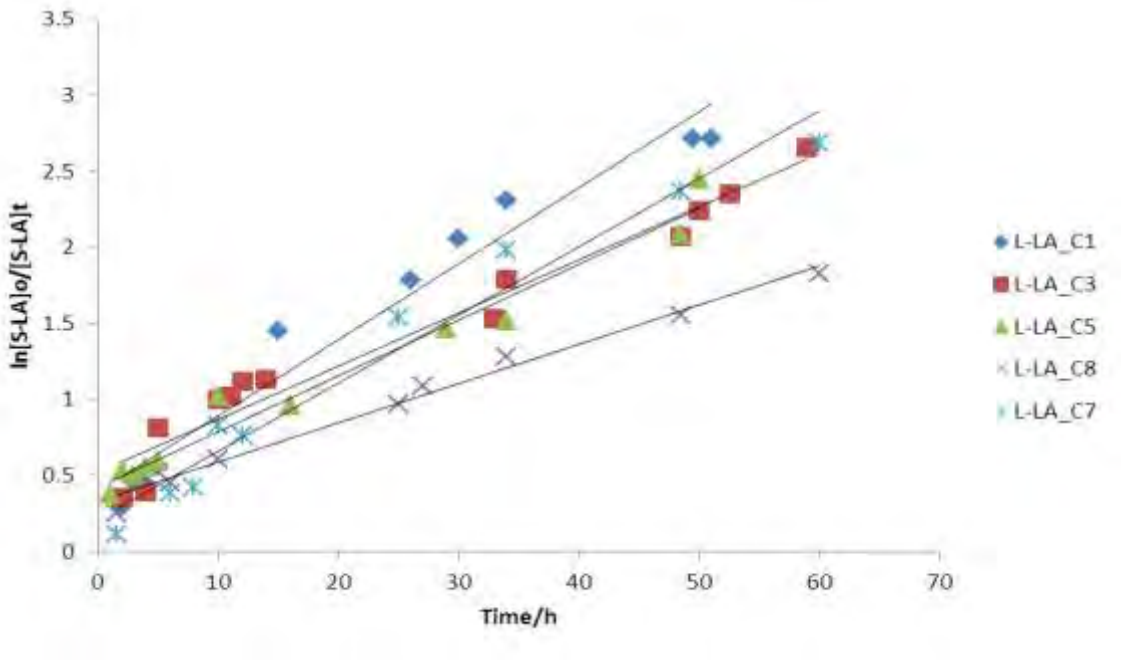


Figure 4.8: Plots of $\ln[LA]_0/[LA]_t$ against time for L-LA .

$$\frac{d[M]}{dt} = K_{app}[M], \text{ where M = Monomer} \qquad (4.3)$$

It is important to not the absence of induction periods in the kinetocs plots for these complexes in the ROP or both ε-CL and LA. This contrasts the findings of Attandoh *et al*. using similar Zn(II) and Cu(II) complexes of (benzoimidazolylmethyl)amine complexes.[69] The absence of induction period in this case demonstrates lack of structural rearrangement or aggregation of the reacting species usually responsible for longer induction periods.[71]

From these linear plots of $\ln[M]_0/[M]_t$ vs time, the apparent rate constants of the complexes for each monomer was obtained and summarized in Table 4.2. These results reveals that generally all complexes polymerized the ε-CL monomer faster than both D,L-LA and L-LA monomers.

This might be due to the fact that ε-CL polymerization was performed in bulk while LA reactions were carried out in solvent. Bulk polymerization is simple, it allows production of pure polymers and direct conversion of monomer to polymer without side reactions.[80] It has been reported in literature that bulk polymerizations are preferred to polymerizations performed in toluene.[72] Also ε-CL monomer is a seven membered ring while LA is a six membered ring, therefore ε-CL is less stable than LA and as a result more reactive.[73] When comparing rate of polymerization of D,L-LA to that of L-LA, it was observed that D,L-LA displayed faster reaction kinetics than L-LA (Table 4.2). D,L-LA have both R and S CH_3 groups next to the reactive region of the monomer while L-LA contain of two R CH_3 groups. In D,L-LA the catalyst will choose the most reactive region while in L-LA both regions are the same.

Table 4.2: The observed apparent rate contsants of polymerization of monomers by complexes

Entry	Catalyst	K_{obs} (h^{-1}) ε-CL	K_{obs} (h^{-1}), D,L_LA	K_{obs} (h^{-1}), L-LA
1	**C1**	0.139	0.087	0.0499
2	**C2**	0.071	0.019	-
3	**C3**	0.134	0.059	0.0348
4	**C3**[c]	0.057	-	-
5	**C5**	0.135	0.053	0.0366
6	**C7**	0.132	0.0791	0.0447
7	**C8**	0.079	0.0486	0.0257

[C]Solvent, toluene used in polymerization of ε-CL.

We also observed the dependency of reaction rates/polymerization kinetics on the catalyst structure. From Table 4.2, it is apparent that Zn(II) complexes were more active compared to the corresponding Cu(II) complexes. For example, zinc complex **C1** (0.139 h^{-1}) showed higher catalytic activity in polymerization of ε-CL than the corresponding copper complex **C2** (0.071 h^{-1}) (Table 4.1 and 4.2). This trend was observed for all copper complexes including D,L-LA **C1** (0.087 h^{-1}) and **C2** (0.019 h^{-1}). These observed high catalytic activities of zinc-based complexes over copper-based complexes in polymerization of ε-CL and D,L-LA has been reported by Ojwach *et al.*[70] and Attandoh *et al.* [69] In the reports of Ojwach *et al.* the zinc complexes exhibited

the rates that were about twice those of their corresponding copper complexes and is in good agreement with our observations. High activities of the Zn(II) complexes when compared to the corresponding Cu(II) complexes has been attributed to the high electrophilicity of Zn(II) metal making them better Lewis acids.[74]

The nature of the ligand in the complexes was also observed to influence the catalytic activities of the respective catalysts. Generally complexes of 2-(3-pyridyl)-1*H*-benzimidazole (**L1**) were more active in ROP of ε-CL, D,L-LA and L-LA than the corresponding complexes of 2-(2-pyridyl)-1*H*-benzimidazole (**L3**), Table 4.2. This could be attributed to the binuclear/bimetallic nature of **L1** complexes as shown in the solid state structure of complex **C2**. In addition, ligand **L1** bind to the metal in a monodentate fashion using the pyridyl nitrogen, this leaves enough space for monomer coordination compared to **L2** and **L3** that adopt bidentate coordination modes thus creating steric hindrance around the metal atoms. Indeed, complexes **C3** and **C4** of **L2** showed similar activities in ROP of ε-CL, D,L-LA and L-LA when compared to the complexes **C5** and **C6** of **L3** (Table 4.1). This showed that the coordination in the complexes played a crucial role in regulating their catalytic activities. In addition, considering the comparable activities of complexes **C3** and C**5** bearing benzothiazole and benzimidazole ligands, it is conceivable that the identity of the heteroatom on the ligand motif does not play a major role in the reaction kinetics of the complexes. This contrast the benzothiozole complexes are expected to be more basic and as a result more active than the benzimidazole complexes because they have pKa values that are higher than the benzimidazole.[75] We also observed higher rates of reactions in ROP with acetate complexes compared to corresponding benzoate complexes. For example the acetate complex **C5** (0.135 h^{-1}) showed high activities compared to corresponding

benzoate complex **C8** (0.079 h^{-1}) in ROP of ε-CL. This effect was also observed for D,L-LA and L-LA. Similar observations have been reported in literature, and can be explained using steric factors introduced by bulky benzoate groups.[76]

When compared to some of the most active systems in literature these complexes showed relatively lower activities. For example the zinc complexes prepared by Sung *et al*. polymerized L-LA affording 97-99% conversion after 3 h of reaction at 30 ˚C.[77] In contrast to our systems which achieved similar conversions within 48-72h. Similarly, Chisholm *et al*. reported active zinc catalysts that polymerized 93% of lactide within 1 h at 25 ˚C and Wang *et al*. reports included zinc catalyst that were able to afford 92% conversion at 25 ˚C, after 9 hour at low catalyst ratios.[68,74,78] However these catalysts were also more active than some of the literature reported initiators, for example we observed the apparent rate constants of the Zn(II) complexes in polymerization of ε-CL to be in the range 0.057-0.139 h^{-1} and Attandoh *et al*. reported that the apparent rate constants of their Zn(II) complexes were between 0.054-0.092 h^{-1}.[69]

4.3.2.2 Order of reaction with respect to catalyst

To further gain insight into the order of reaction with respect to the catalyst, further kinetic studies were performed using catalyst **C1**. This was done by varying the monomer to catalyst ratio, at constant monomer concentration. The kinetics of the different concentrations was studied and the respective apparent rate constants, $K_{app,}$ used to derive the order of reaction with respect to catalyst. The graph of $\ln K_{app}$ versus ln[**C1**] was plotted to obtain the order of reaction with respect to the catalyst which was extracted from the gradient of the line of the best fit (Figure 4.9). The order of reaction with respect to catalyst **C1** was obtained as 1.2282≈1

(Figure 4.9).

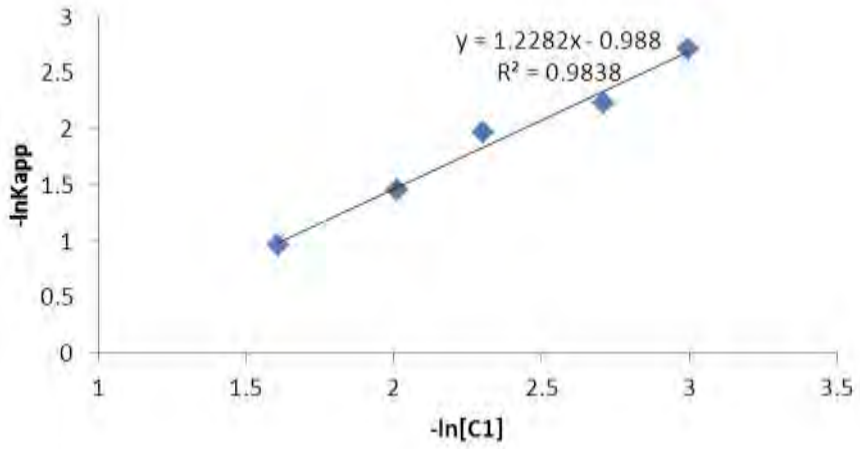


Figure 4.9: Plot of $-\ln K_{app}$ vs -ln[**C1**] to determine the order of reaction using the complex **C1**.

Similar polymerization reaction orders with respect to the catalyst have been previously observed.[70] The rate equation of polymerization can thus be represented as shown in equation 4.4.

$$\frac{d[\varepsilon\text{-CL}]}{dt} = k_p[\varepsilon\text{-CL}][\mathbf{C1}]^x \quad \text{become} \quad \frac{d[\varepsilon\text{-CL}]}{dt} = k_p[\varepsilon\text{-CL}][\mathbf{C1}] \tag{4.4}$$

4.3.3 Number of active sites

To determine the number of active sites in initiator **C1**, the degree of polymerization (X_n) was plotted against monomer to initiator ratio ([ε-CL]/[**C1**]) using the data in Table 4.3 and the number of initiating site in **C1** was determined from the slope of the line (0.8987).[79] The number of active sites was determined from the inverse of the slope, to give an average of 1.1 active initiating sites out of the possible two in **C1** (Figure 410). This data is in agreement with first

order dependency of the polymerization kinetics (Figure 4.9). Similar behavior of Zn(II) complexes in ring opening polymerization of ε-CL has been reported by Ojwach *et al*.[70] The findings indicates that out of the two possible sites (two M-$O_{acetate}$ bonds) only one is used to initiate the polymerization, and is consistent with a number of literature reports in which the initiators do not utilize all the available initiating sites.[80]

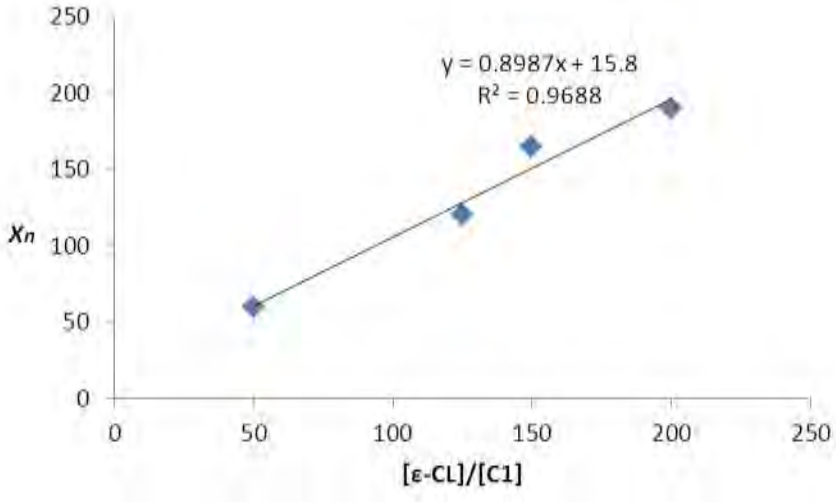


Figure 4.10: Plot of degree of polymerization (X_n) of ε-CL vs [ε-CL]/[**C1**].

Table 4.3: Effect of catalyst concentration in polymerization of ε-CL

Entry	Ratio	t (h)	Conv (%)	Mn	MW_{GPC}	MW_{NMR}	PDI	IE	X_n
1	50:1	9	96	6043	11025	32738	1.82	0.21	60
2	125:1	32	97	6417	11970	16042	1.86	0.75	105
3	150:1	36	96	9932	18850	20855	1.89	0.90	165
4	200:1	72	98	11728	22660	28389	1.93	0.76	190

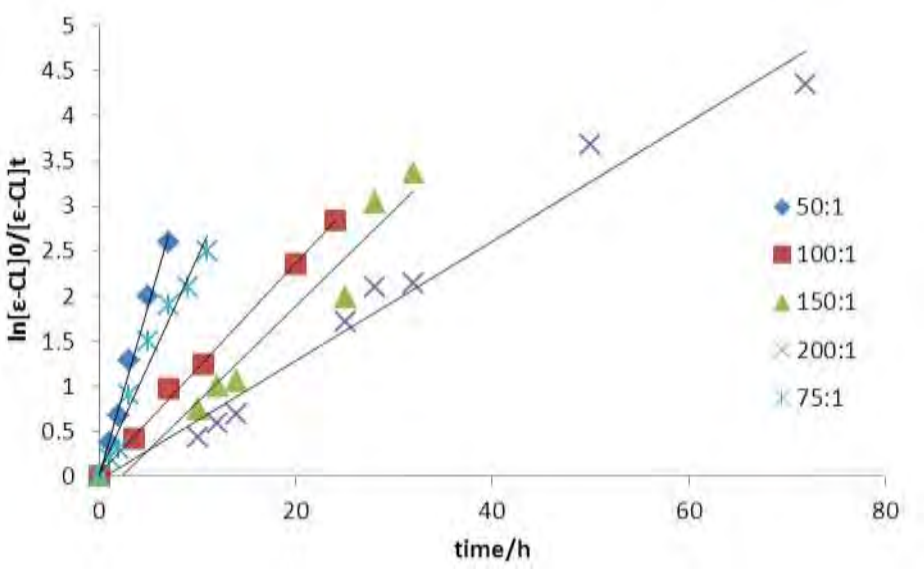


Figure 4.11: Plots of $\ln[\varepsilon\text{-CL}]_0/[\varepsilon\text{-CL}]_t$ against time for varied [ε-CL]/[I] ratios.

4.3.4 Effect of temperature and solvent on kinetics of ROP reactions

The effect of temperature on the polymerization kinetics of ε-caprolactone was evaluated by comparing the activities at 80 ˚C, 110 ˚C and 150 ˚C at 50:1 of [ε-CL]/[**C1**]. At reaction temperature of, 80 ˚C, very low activities (conversions of less than 5% after 13 h) were observed. The rate constant at 80 ˚C was found to be 0.0013 h^{-1} which was much lower compared to 0.381 h^{-1} obtained at 110 ˚C (Figure 4.11). An increase reaction temperature from 110 ^{o}C to 140 ˚C was marked decrease in the rate constant from 0.381 h^{-1} to 0.228 h^{-1}, The decrease in activity at elevated temperatures of 140 ˚C indicates that there is an optimum temperature for the activity of the complexes and that they might be assigned to catalyst decomposition at high temperatures. Cheng et al. reported a similar trend in which the zinc complexes that showed decreased activity with increase in temperature.[81] In this report the zinc catalyst showed higher activity at temperatures 100 ˚C giving 95% conversion while the conversion of 87% was observed at 80 ˚C the conversion.[81]

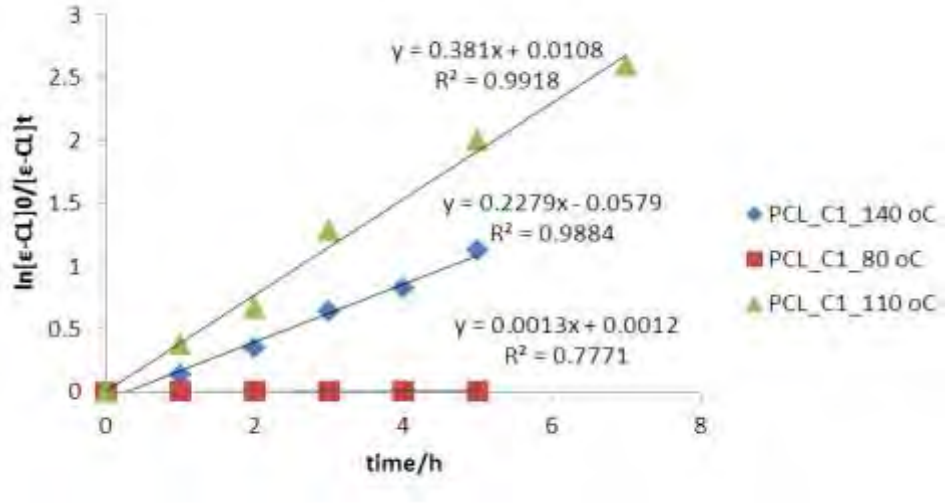


Figure 4.12: Kinetic plot of polymerization of ε-CL at 80, 110 and 140 ˚C, [ε-CL]/[I] = 50.

The effect of solvent was also studied for polymerization reactions of both ε-CL and D,L-LA. For D,L-LA reactions, use of methanol solvent instead of toluene resulted in very fast kinetics such that 100% conversion was obtained within 30 minutes. The polymerizations in methanol were performed at 60 ˚C. Methanol was previously reported to increase the polymerization reactions of lactide by Attandoh *et al*. where it decrease reaction hours from 60 h to 16 h.[69] We also investigated the effect of toluene in the polymerization kinetics of ε-CL using catalyst **C3** (Figure 4.13). In toluene solvent, we observed a lower rate of polymerization compared to bulk polymerizations (Figure 4.13). For example, rate constants of 0.134 to 0.057 h^{-1} were reported in bulk and toluene solvent respectively (Table 4.2).

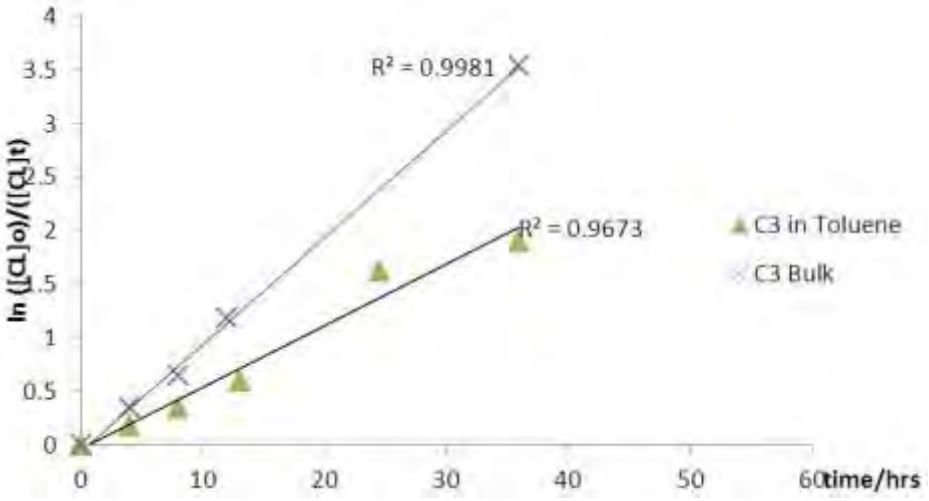


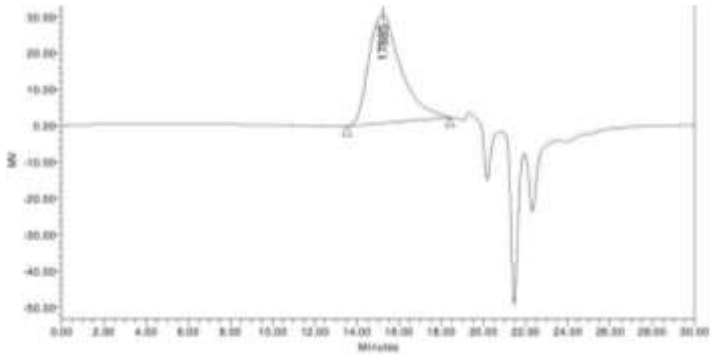
Figure 4.13: Plots of $\ln[\varepsilon\text{-CL}]_0/[\varepsilon\text{-CL}]_t$ for the effect of toluene in polymerization of ε-CL.

4.3.5 Polymer molecular weight

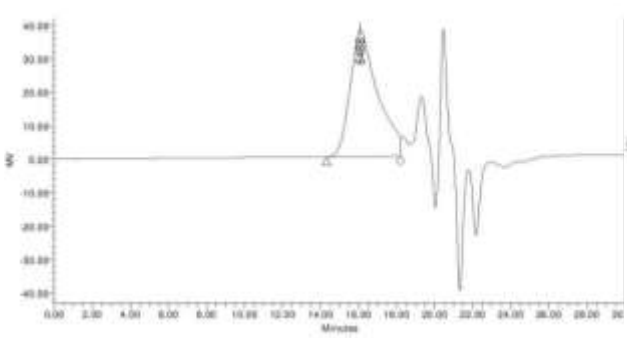
4.3.5.1 Effect on catalyst structure on polymer Mw and Mw distribution

The molecular weights (MW) and molecular weight distributions (PDIs) of the polycaprolactone (PCL) and polylactide (PLA) were determined by GPC and compared to theoretical values obtained from ^{1}H NMR calculations (Table 4.1 and 4.3). Figure 4.14 shows typical GPC traces obtained for PCL, P(D,L-LA) and P(L-LA). The molecular weights obtained ranged from 53 0 g/mol to 21 660g/mol.

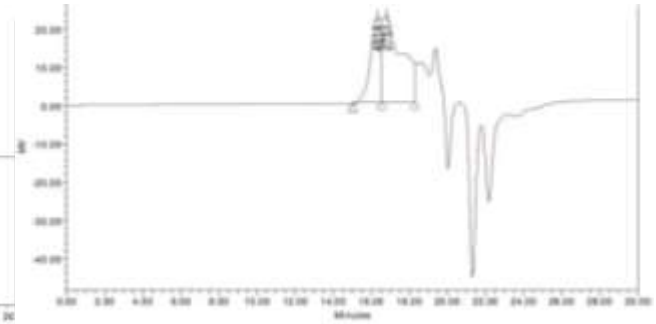
These values were much lower than the expected theoretical values, for example the observed molecular weight for polymer PCL at 96% conversion ([M][I] = 50) was 6840 g/mol which is very low when compared to 32738 g/mol value obtained from ^{1}H NMR calculations. Similarly lower molecular weights were observed for polymers of L-LAand D,L-LA compared to expected molecular weights.



(a)Chromatogram of [ε-CL]/[**C1**]=200:1



(b)Chromatogram of [D,L-LA]/[**C8**]=100:1



(c)Chromatogram of [L-LA]/[**C5**]=100:1

Figure 4.14: Typical GPC trace for PCL and PLA

Even though there was no specific trend in effect of catalyst structure on molecular weight, bulky complexes appeared to yield polymer with high molecular weights. For example, polylactide obtained from the reaction of D,L-LA and complex **C7** afforded polymer with MW of 3040 g/mol at 97% conversion while **C1** only afforded 1478 g/mol at 97%.

Polymers exhibited broad molecular weight distribution (PDI) values in the range 1.82 to 1.93. The broadening of PDI values and low observed polymer molecular weight could be due to the transesterification reaction taking place during polymerization as reported in other literature.[82]

Transesterification compete with ring opening polymerization (ROP) to give wide PDIs and indicate the lack of control in polymerization leading to random breakage of polymer chains.[82,83] To confirm the occurrence of transesterification reactions, ES-MS of polymers was studied. The ES-MS spectra of the poly-ε-caprolactone (PCL, [ε-CL]/[**C1**]) showed the mass distribution corresponding to (nCL+23), for example *m/z* peak at 593 corresponding to ((5 x 114.14)+23) (Figure 4.16). This does not include the -OH capping end group, therefore might be due to formation of cyclic oligomers with loss of water.[84] In addition, the presence of oligomers and high PDIs confirmed occurrence of transesterification reactions during polymerization process. Similar results and observations has been reported in the literature by Ojwach *et al*. and Attandoh *et al*. [69,70] In these reports the PDI values of the range 1.29 to 3.97, which are moderate to broad values indicating the lack of control in ROP and the presence of transesterification.

4.3.5.2 Living polymerization nature

Molecular weights increased with increase in percent conversion, this is consistent with living polymerization behavior (Figure 4.15).[85] For example the observed increase in molecular weight with increase in monomer to initiator ratio [**ε-CL**]/[**C1**] (Table 4.3) indicated living polymerization nature of complex **C1**. An increase in [**ε-CL**]/[**C1**] from 50 to 150 resulted in increase in observed molecular weight from 6840 g/mol to 18850 g/mol.

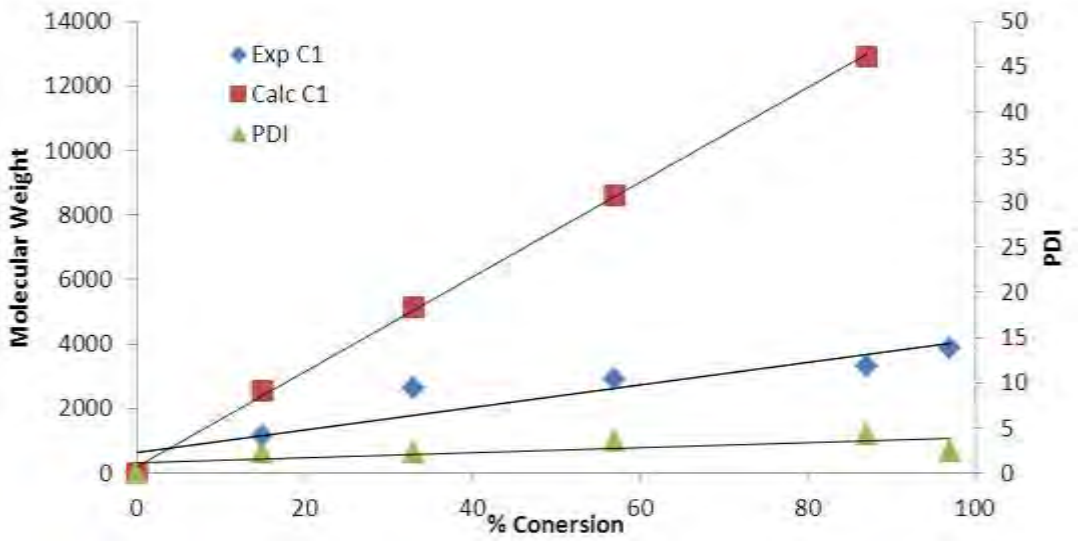


Figure 4.15: Plots of PCL experimental and theoretical molecular weight vs % conversion showing the living polymerization nature of catalyst **C1**.

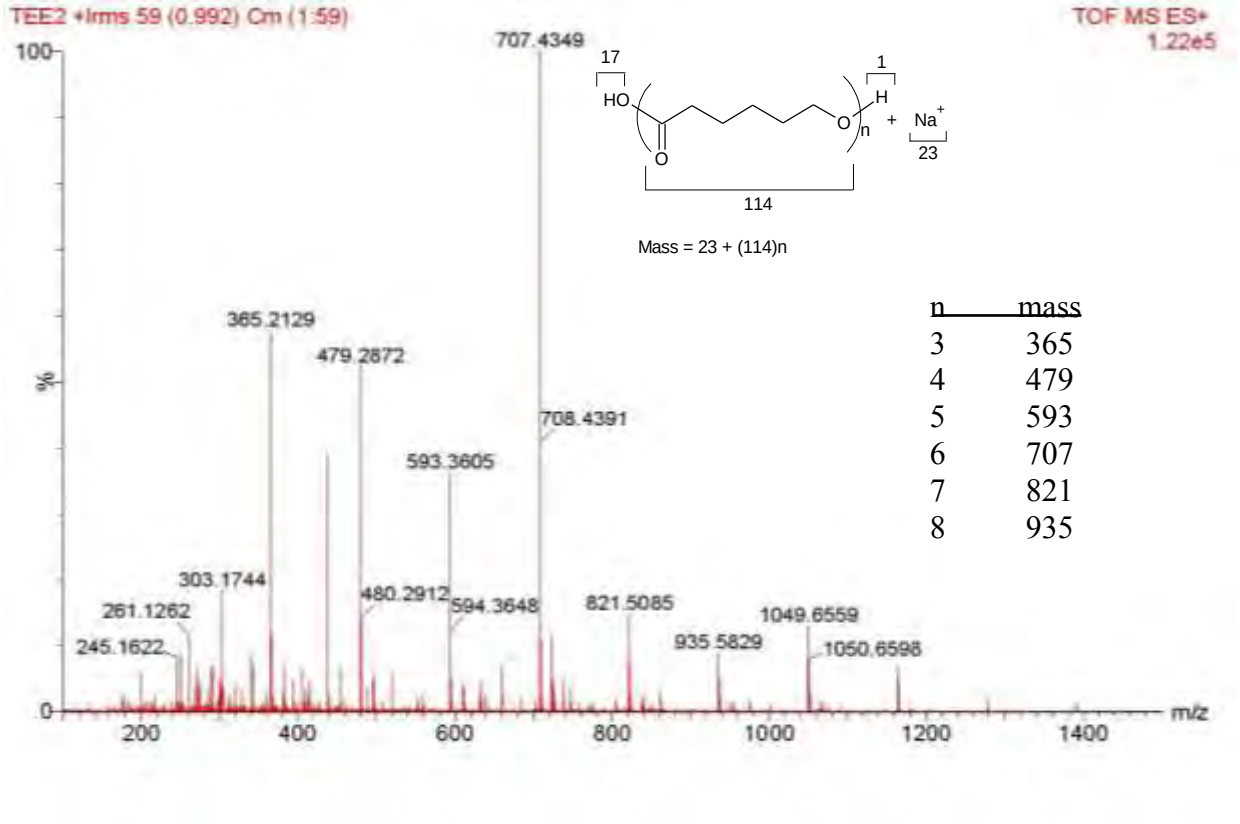


Figure 4.16: The ES-MS of crude PCL [ε-CL]/[**C1**]= 100:1 after 24h.

4.3.6 Polylactide tacticity

Homonuclear decoupled ^{1}H NMR spectroscopy is usually employed in determination of the stereochemistry and tacticity of polylactides.[68,86] This is achieved by examination of the methine protons in the polymer backbone.[68] The tacticity of produced polylactides was determined by homonuclear decoupled ^{1}H NMR and ^{13}C NMR spetroscopy. The comparison of ^{1}H NMR and homonuclear decoupled ^{1}H NMR spectra of the methane region of both D,L-LA and L-LA are presented in Figure 4.17. The decoupled methane resonance in the spectra of poly(L-LA) shows primarily the iii tetrad (Figure 4.17, D). [86,87] The methane region of poly(D,L-LA) consists of several superimposed tetrads (Figure 4.17, A) corresponding to different stereoisequences. The iii tetrad is the dominant peak in both homonuclear decoupled spectra of poly(D,L-LA) (Figure 4.17 B).[88] Analysis of tetrads intensities indicated the production of isotactic enriched polylactide from polymerization of both D,L-LA and L-LA. The sequences observe in the decoupled spectra of poly(D,L-LA) matches those reported by Kricheldorf *et al*. in 2001, also matches several literature reports.[88,89] Also in 2004 Jensen et al. reported similar observation where the tacticity of poly(D,L-lactide) was found to be isotactic.

Similarly ^{13}C NMR was used to determine the tacticity of poly(D,L-LA), the spectra displayed the isi (69.2 ppm) and sis (60.o ppm) peak of comparable intensities, the ratio of the isi/sis peaks indicated that the polylactide synthesized from D,L-LA is predominantly isotactic (Figure 4.18). This is in agreement with the observations from the ^{1}H NMR and these observations are in agreement with those reported by Zell *et al*.[90]

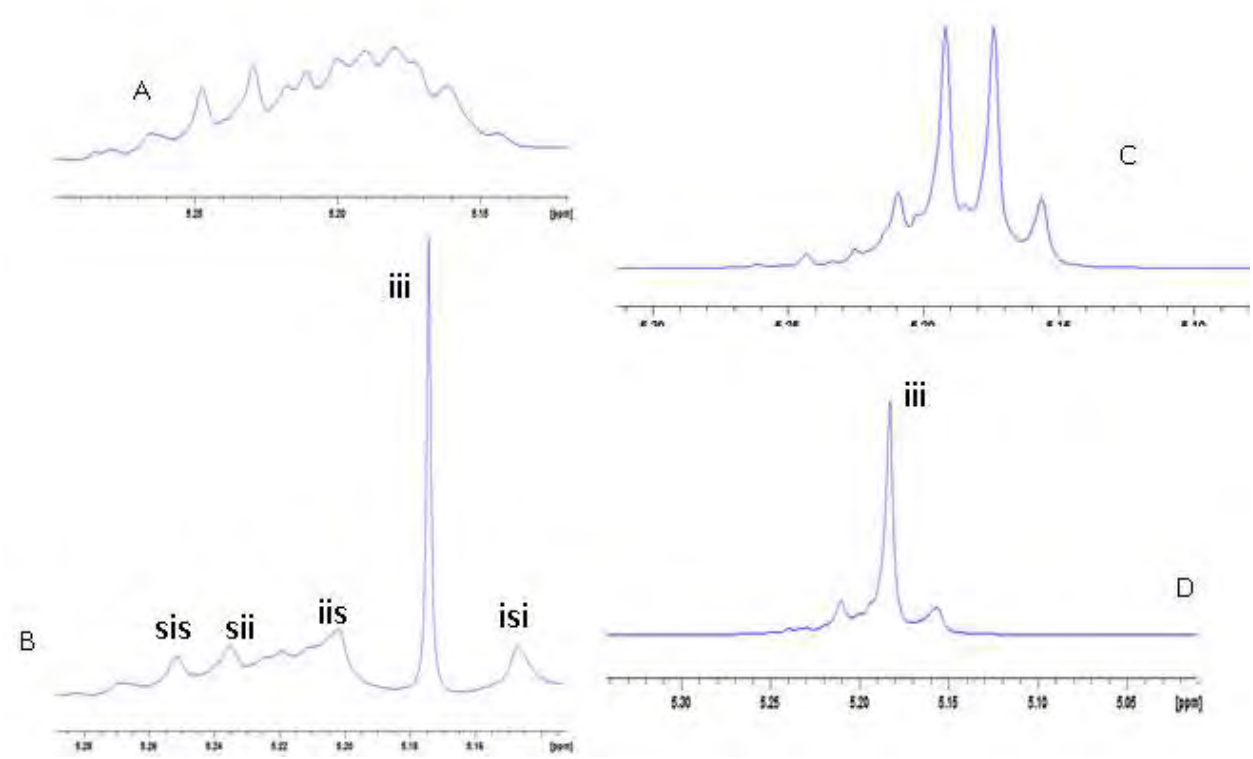


Figure 4.17: Normal and homonuclear decoupled ^{1}H NMR spectra of PLA. **A**: normal poly(D,L-LA), **B**: homonuclear decoupled poly(D,L-LA), **C**: normal poly(L-LA), **D**: homonuclear decoupled poly(L-LA).

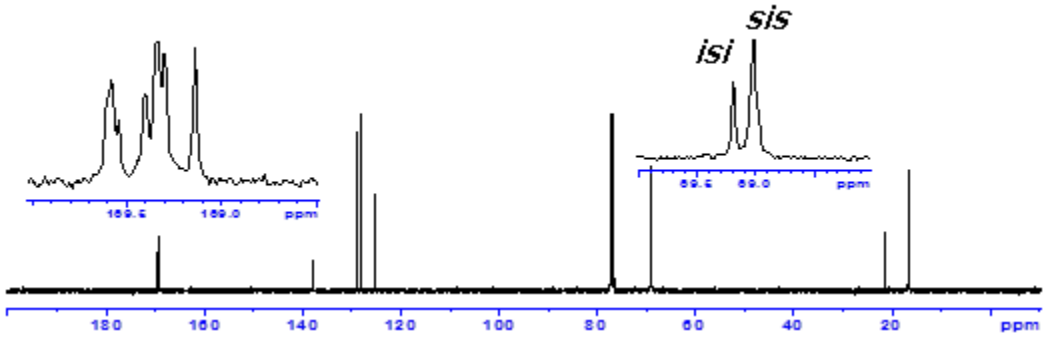


Figure 4.18: ^{13}C NMR spectra of poly(D,L-LA)

4.3.7 Mechanisms of ROP reactions

The ring opening polymerization (ROP of ε-CL, D,L-A and L-LA using heteroleptic Zn(II) and Cu(II) complexes is most likely to proceed *via* the coordination-insertion mechanism or the activated-monomer mechanism.[65,78] In the coordination-insertion mechanism the polymer end chain the OR groups (in this case, acetate or benzoates) are incorporated within the polymer backbone and serves as the end groups. However, the presence of the chain transfer agents such as water or alcohols might promote hydrolysis of the metal end to form OH end groups.[91] To determine the mechanism of polymerization of ε-CL and LAs by our complexes, ^{1}H NMR and ESI-MS spectra's of synthesized polymer were acquired.

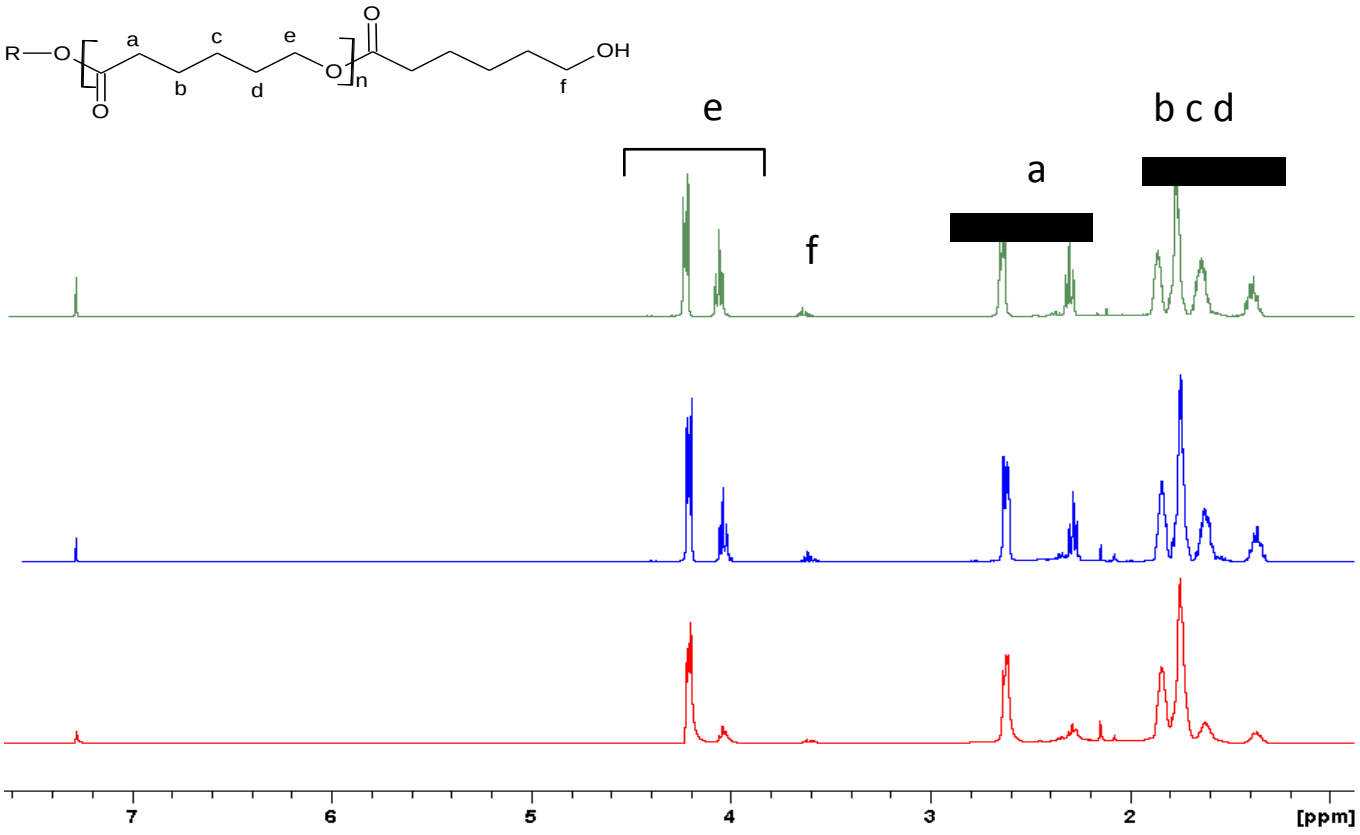


Figure 4.19: ^{1}H NMR spectrum of polycaprolactone ([ε-CL]/[C1]) at 140 ˚C after 1, 2 and 3 h.

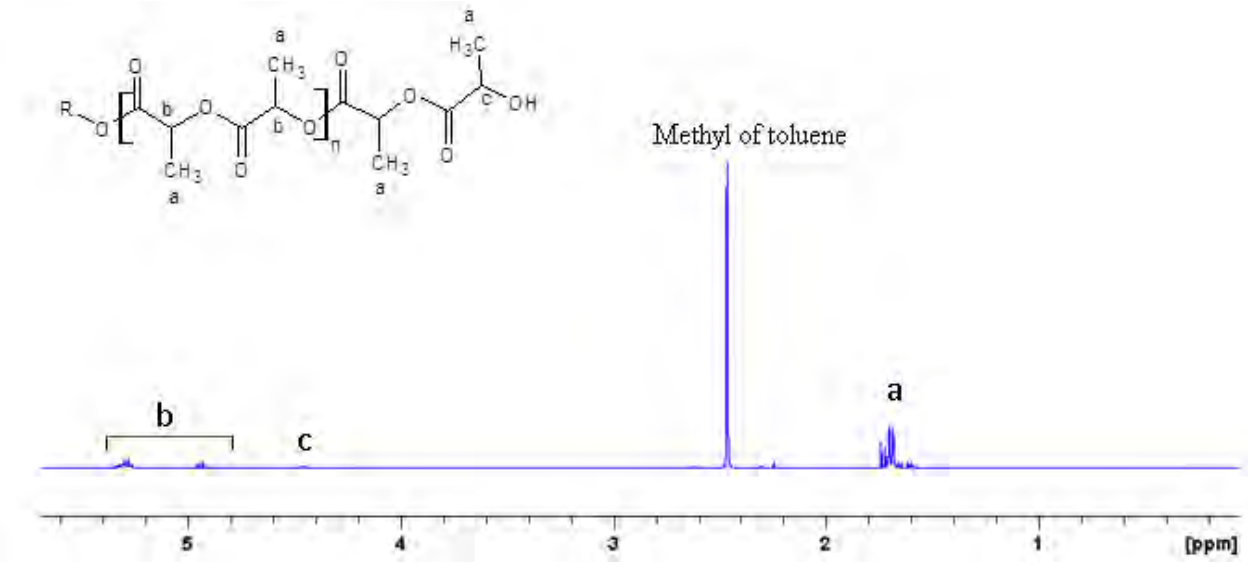


Figure 4.20: ^{1}H NMR spectrum of poly(D,L-LA), ([D,L-LA]/[C8]) after 48 h.

Analysis of the ESI-MS spectra was in agreement with the results obtained from the ^{1}H NMR spectra analyses which indicated that the monomer was converted to polymer using synthesised complexes (Figure 19-Figure 20). The ESI-MS spectra of the poly(ε-caprolactone), poly(D,L-lactide) and poly(L-lactide) displayed signals corresponding to $HO(C_6H_{10}O_2)_nH{\cdot}Na^+$ for poly(ε-CL) and $HO(C_6H_8O_4)_nH{\cdot}Na^+$ for both polylactides (Figure 4.21 and 4.22). The ^{1}H NMR (Figures 4.18 and 4.19) of all polymers did not contain the methyl/benzyl protons characteristic of the acetate/benzoate as the initiating groups in coordination-insertion mechanism and this might be due to the hydrolysis reaction taking place.

The ESI-MS spectra also show that the end group of the polymer consists of the OH group which could arise from hydrolysis of the complexes by the adventitious water molecule.[92] This phenomenon has been reported previously by Pilone *et al.* and Bourissou *et al.*[84,93] From the data of both ^{1}H NMR and ESI-MS the of ring opening polymerization of ε-caprolactone, D,L-

lactide and L-lactide can thus be said be said to proceed via the coordination insertion mechanism.

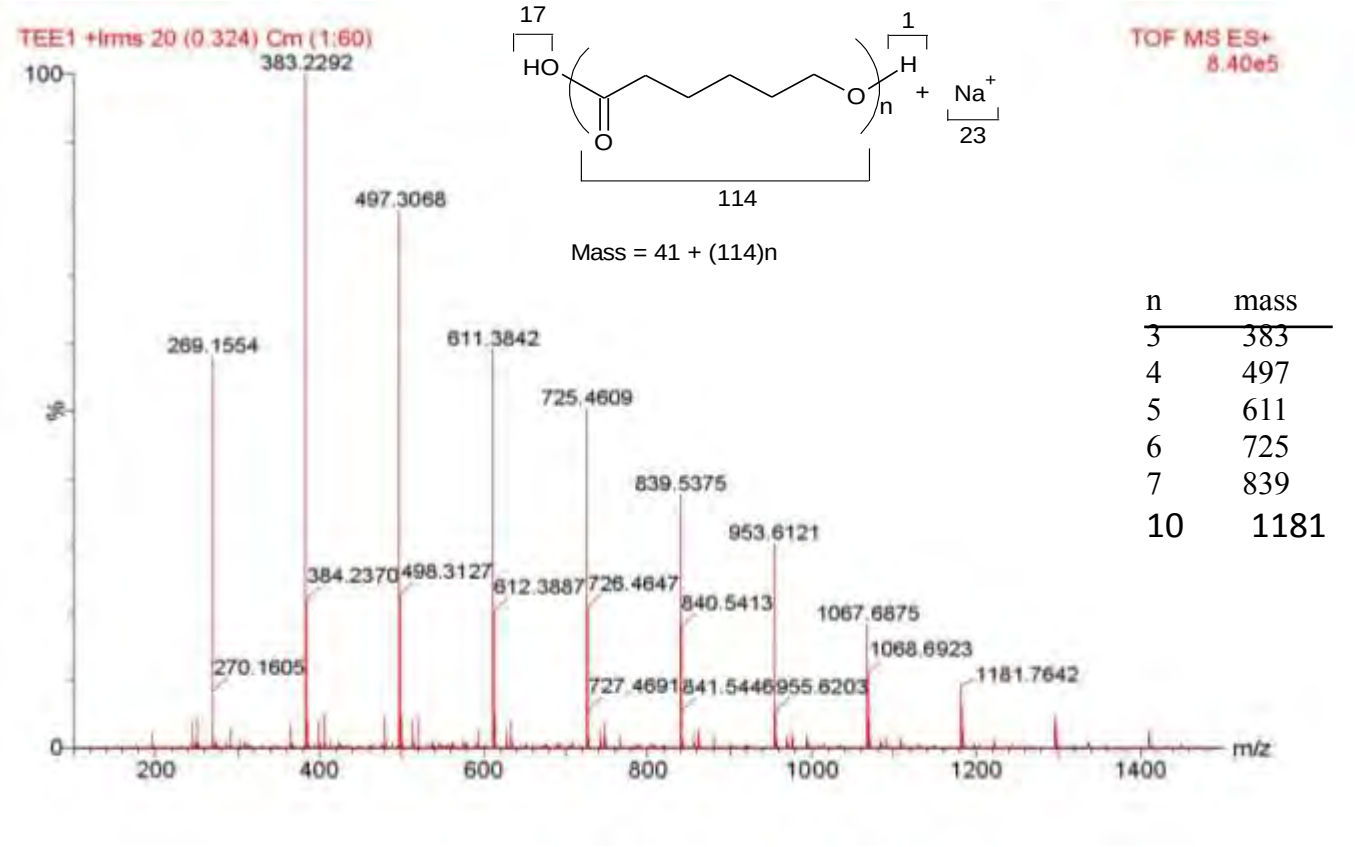


Figure 4.21: ESI-MS spectra of crude PCL after 7.5 h, at ([ε-CL]/[C1] = 100:1).

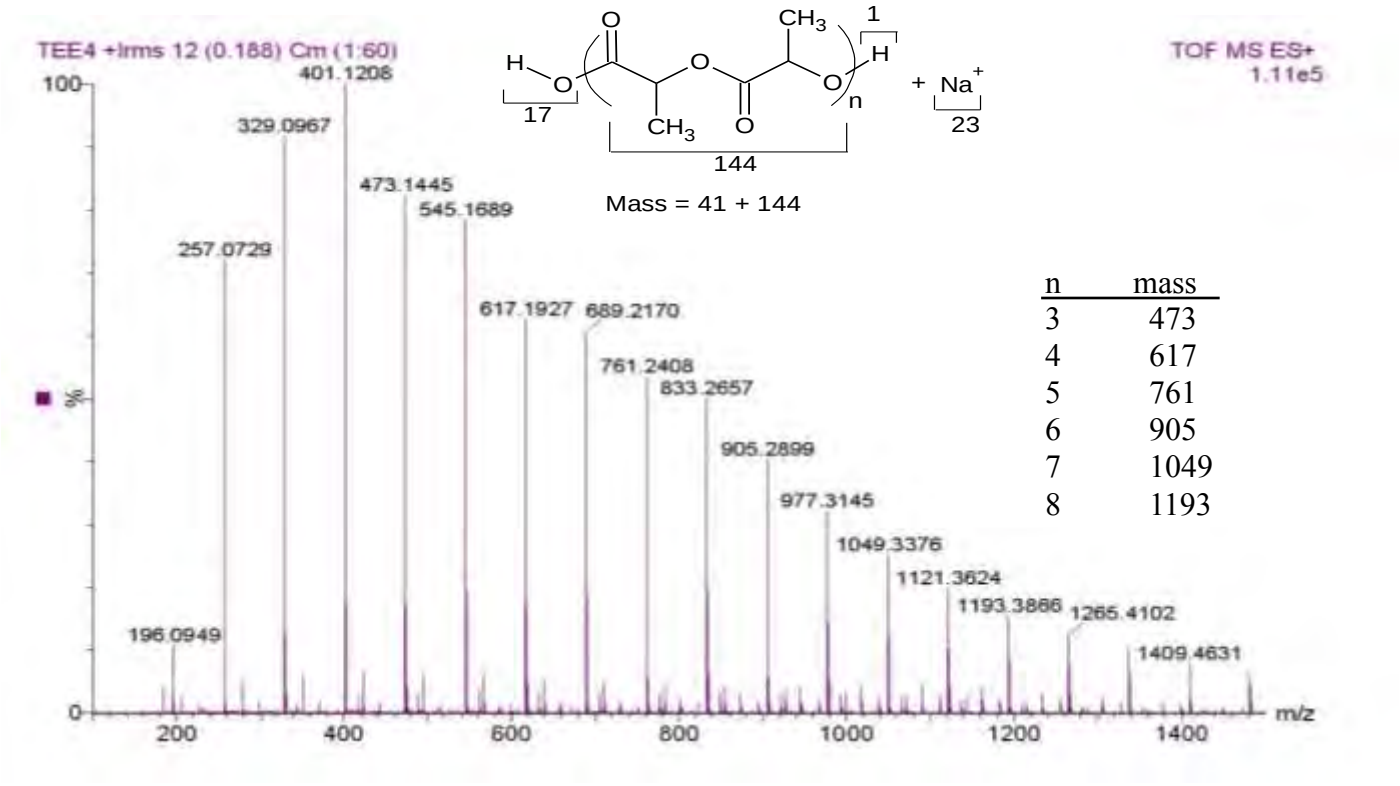


Figure 4.22: ESI-MS spectra of crude P(D,L-LA) after 24 h of reaction between D,L-LA and C1 at ([D,L-LA]/[C1] = 100:1).

4.4 Conclusions

In summary, the synthesized complexes revealed good catalytic activities toward ROP of ε-CL, D,L-LA and L-LA. In these complexes the zinc-based complexes exhibited higher activities compare to their corresponding copper-based complexes. The ligand type was also found to have influence in the catalytic activities of the complexes in polymerization of ε-CL, D,L-LA and L-LA. Complexes of the monodentate 2-(3-pyridyl)-1H-benzimidazole (**L1**) exhibited higher activities when compared to the bidentate 2-(2-pyridyl)-1H-benzimidazole (**L3**). We have also showed that the complexes of benzoate were less active than the corresponding complexes of acetate. This suggests that the less crowding around the metal centre by the less bulk acetate group enhances the monomer coordination to the metal centre resulting increased activity.

The nature of monomers also affected the activity of the complexes. ε-CL monomer showed high reactivity compared to both LA. The polymerization processes of ε-CL and LA proceeded through pseudo-first order kinetics with respect to the monomers. The polymerization of D,L-LA and L-LA afforded isotactic polylactides. The polymerization mechanism was found to be through the coordination insertion mechanism. The rate of polymerization was affected by solvent and temperature variation. The polymers produced had molecular weights ranging between 530 g/mol to 21660 g/mol and these values were lower than theoretical/expected molecular weights. Polymer PDIs ranged from 1.82 to 1.89. The observed low molecular weights and broad PDI values confirmed the lack of control in the ROP reactions of lactides and ε-caprolactones and the presence of the *trans*-esterification side reaction competing with the ROP reactions.

Chapter Five

Conclusions and future work

5.1 Conclusion

This work reports the syntheses and characterization of (Pyridyl)Benzoazole Cu(II) and Zn(II) complexes. Cu(II) and Zn(II) complexes bearing 2-(-3-pyridyl)-1*H*-benzimidazole were binuclear complexes in which the ligand coordinated through the pyridyl nitrogen in a monodentate fashion. On the other hand, complexes containing 2-(-2-pyridyl)-1*H*-benzimidazole and 2-(-2-pyridyl)-1-benzothiozole were mononuclear and the ligands coordinated in a bidentated mode using pyridyl and benzimidazole/benzothiazole nitrogen atoms. The coordination modes of complexes were confirmed by single crystal x-ray crystallography while their formation was confirmed by NMR, IR, elemental analysis and the mass spectrometry.

All the complexes were investigated as initiators in the ring opening polymerization of ε-caprolactones and lactides, the observations revealed that they were active in initiating the polymerization reactions of these cyclic esters. The activities of the complexes were affected by the type of metal centre as zinc-base complexes were very active in ROP when compared to copper-based complexes. The type of ligand also influenced the activities of the complexes in initiating ROP polymerization reactions with the complexes of the monodentate ligand (2-(-3-pyridyl)-1*H*-benzimidazole) showing higher catalytic activities compared to bidentate ligand (2-(-2-pyridyl)-1*H*-benzimidazole). Also the complexes of the benzimidazole (2-(-2-pyridyl)-1*H*-benzimidazole) showed high activities in polymerization of ε-CL and LA when compared to the benzithiazole (2-(-2-pyridyl)-1-benzothiazole) complexes. The complexes containing the bulky benzoate in them were less active than those bearing the acetate. The complexes exhibited low

initiator efficiencies and low molecular weights ranging 530 g/mol to 21660 g/mol of polymers were produced. The lack of control in ring opening polymerization of ε-CL and LA and the presence of *trans*-esterification reactions resulted in polymer with broad PDI value (1.82 to 1.89). The analysis of the methane region in ^{1}H NMR and ^{13}C NMR revealed that the ring opening polymerization of both D,L-LA and L-LA afforded isotactic polylactides. Analysis of polymers by ^{1}H NMR and ESI-MS spectra revealed that the polymerization of ε-CL and LA proceeded through coordination insertion mechanism.

5.2 Recommendation for future works

This study has shown that Cu(II) and Zn(II) complexes were active initiators of ring opening polymerization of ε-caprolactones, D,L-lactide and L-lactide. However the activities of the Cu(II) complexes were very low, in future we plan to replace the Cu(II) metal centre with more active metals such as Ca(II) and Mg(II) metals which are reported to give active initiators. The catalytic activities increased in the presence of alcohol, the design of complexes with an alkoxide initiating group will improve the catalytic efficiencies of our complexes, so we plan to design complexes with alkoxide initiating group as part of our future work and test their abilities in ring opening polymerizations of ε-caprolactones, D,L-lactide and L-lactide.

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