SYNTHESES AND APPLICATION OF NITROGEN - DONOR ZINC(II) AND COPPER(II) COMPLEXES AS CATALYSTS IN RING OPENING POLYMERIZATION OF LACTIDES AND CAPROLACTONES

BY

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A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS OF THE DEGREE OF MASTER OF SCIENCE IN CHEMISTRY

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ABSTRACT

Petrochemical derived plastics have numerous advantages, however, there are several drawbacks arising from non-renewable sources and their accumulation in the environment due to their non-degradable nature. This has led to the focus on biodegradable polymers obtained from renewable resources. Examples of biodegradable polymers are polylactides and polycaprolactones obtained by catalytic ring-opening polymerization of cyclic lactides and caprolactones obtained from by-products of sugar and corn. Use of these materials would result in increased benefits of the materials, and this could offer a boost to the local producers of the plant materials. Although industrial processes currently employ a tin(II)*bis*-2-ethylhexanoate catalytic system, tin is toxic thus limits the application of tin-derived polymers in biological areas. Design of less toxic and biocompatible metal catalysts is currently attracting much attention. Diaceto{2-(3,5-dimethylpyrazol-1-ylmethyl)pyridine}zinc(II) (**D1**), diaceto{2-(3,5-dimethylpyrazol-1-ylmethyl)pyridine}copper(II) (**D2**), diaceto{2-(3,5-diphenylpyrazol-1-ylmethyl)pyridine}zinc(II) (**D3**) and diaceto{2-(3,5-diphenylpyrazol-1-ylmethyl)pyridine}copper(II) (**D4**) were synthesised and used in catalytic ring-opening polymerization of D,L-lactides and ε-caprolactones. Compounds **D1** and **D3** formed monometallic complexes while **D2** and **D4** were bimetallic. The ligands adopt a bidentate coordination mode in the monometallic complexes **D1** and **D3**, but they are monodentate in the bimetallic complexes **D3** and **D4**. Complexes **D1-D4** were active catalysts in the ring opening polymerization of D,L-lactides and ε-caprolactones to give polylactides and polycaprolactones with low to moderate molecular weights between 1,402-14,568 g/mol. Relatively narrow molecular weight distributions (1.23-1.64) were observed for polylactides whereas broad molecular weight distributions (2.0-3.9) were reported for polycaprolactone. At 110 °C the Zn(II) complexes **D1** and **D3** exhibited higher rate constants of 0.29 h^{-1}(0.044 h^{-1}) and 0.17 h^{-1}(0.096 h^{-1}) respectively compared to 0.06 h^{-1}(0.017 h^{-1}) and 0.04 h^{-1}(0.031 h^{-1}) rates reported for the corresponding Cu(II) complexes **D2** and **D4** respectively for ROP of D,L-lactide (ε-caprolactone). All the polymerization reactions follow pseudo first-order kinetic with respect to monomer. Higher activities were observed using methanol as solvent, elevated temperature and lower monomer/catalyst ratio.

CHAPTER ONE

INTRODUCTION

1.1: Background information

Synthetic polymers are omnipresent in modern society; they can be easily produced, processed and handled and therefore provide a wide variety of applications. Conventional plastics like polyethylene (PE), polypropylene (PP), polyvinylchloride (PVC), polystyrene (PS), and poly(ethylene terephthalate) (PET) possess excellent properties such as lightness, durability, non-degradability and non-corrosive to acids and alkalis (Dechy-Cabaret *et al.*, 2004). However, their high durability, non-degradability has caused a crisis in solid waste management. These properties, together with the dwindling fossil resources, the increasing oil prices and the growing environmental awareness have led to modern approaches towards green and sustainable chemistry which focus on the substitution of petrochemical-based plastics with biorenewable and biodegradable plastics (Dechy-Cabaret *et al.*, 2004; Vert, 2005).

Biorenewable and biodegradable plastics also referred to as bioplastics have found major applications in the packaging (Bastiol, 1997; Lam *et al.*, 2007) and biomedical applications such as drug delivery excipients and absorbable sutures (Chandra and Rustgi, 1998; Ikada and Tsuji, 2000; Sinha *et al.*, 2004). Bioplastics include primarily four polymer types: polysaccharides, polyesters, polyurethanes and polyamides (Table 1) (Wolf *et al.*, 2005).

Two polyseters; polylactide (PLA) and polycaprolactone (PCL) discussed in this thesis are mainly synthesized through catalytic ring-opening polymerization (ROP) of lactides (LA) and

caprolactones (CL) with coordination-insertion (Kurcok *et al.*, 1992) or monomer-activated (Kricheldorf and Krieser, 1990) mechanism involved (Figure 1).

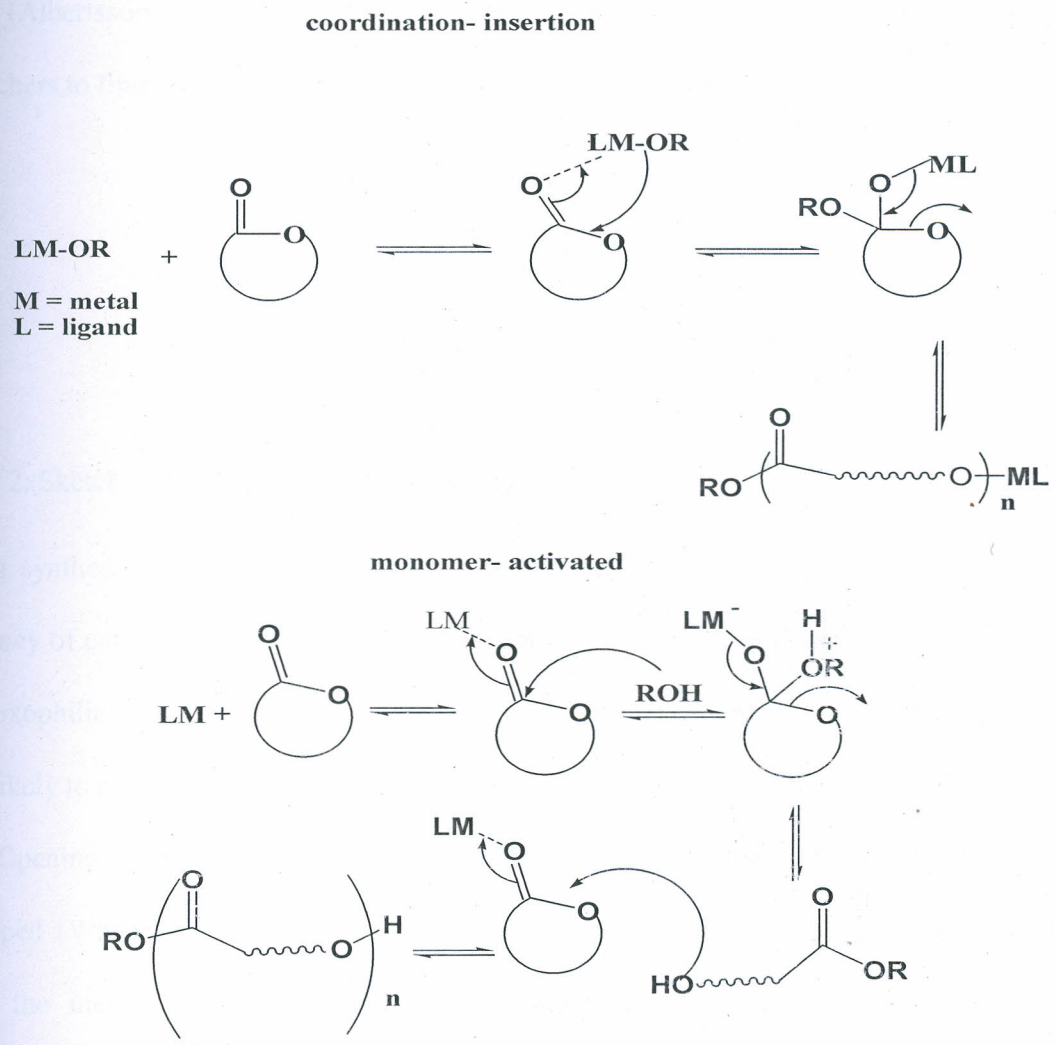


Figure 1: Scheme of Coordination- insertion and monomer- activated mechanisms for ROP of cyclic esters.

The polymerization of LA and CL has been most widely done using Metal alkoxides, such as tin, zinc and aluminum (Albertsson and Varma, 2003) as well as magnesium, calcium, titanium, iron and rare earth metal complexes (Yao *et al.*, 2008) as catalysts.

Industrial systems currently employ tin(II)*bis*(2-ethylhexanoate) catalytic system (Figure 2) to catalyze ring opening due to its good solubility in the LA and CL monomers and other cyclic esters (Albertsson and Varma, 2002) however, toxicity of most tin compounds is pushing researchers to find new catalysts with lower toxicity (Labet and Thielemans, 2009).

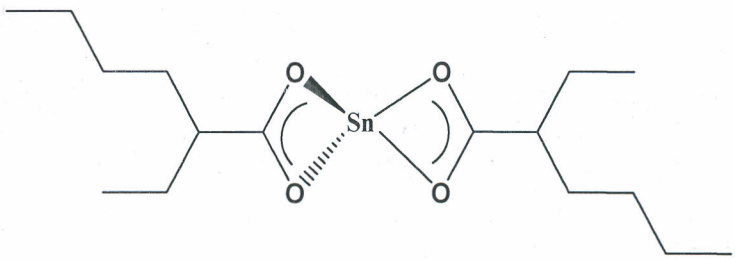


Figure 2: Sketch of tin(II)*bis*(2-ethylhexanoate) structure

During synthesis of PLA and PCL, there are protic impurities like water, which affects the efficiency of catalyst. Zinc(II) and copper(II) catalysts although intrinsically less active than the more oxophilic and electrophilic lanthanide-based complexes, are far more robust and therefore more likely to resist deactivation by these impurities (Albertsson and Varma, 2003).

Ring Opening Polymerization of Lactide using many zinc catalysts has been successfully developed (Wheaton *et al.*, 2009). Two notable families are heteroleptic zinc(II) complexes, where the metal is stabilized by bulky phenolate-based ancillary ligands, and bulky β-diketiminate (BDI) bidentate ligands (Williams *et al.*, 2003).

Copper(II) complexes have also been investigated for ROP of LA and CL(Reger *et al.*, 2012). However, they are efficient catalysts for ring-opening polymerization with moderate molecular weights with narrow molecular weight distributions. Therefore, there is need to develop cheap, less toxic catalysts that enhances the level of control over the polymerization process.

1.2: Statement of the problem

Increased depletion of non-renewable raw materials and disposal of petro-chemicals derived plastics has caused environmental problems, this has led to design and development of biodegradable and renewable polymers from renewable materials such as corn and sugar beets. However, tin(II)*bis*(2-ethylhexanoate) catalyst applied in industrial production of renewable materials is toxic. Therefore there is urgent need for the design and development of less toxic zinc(II) and copper(II) complexes catalysts for the synthesis of degradable polymers on large scale.

1.3: Main objective

To synthesize and characterize zinc(II) and copper(II) pyrazolyl complexes, and investigate their ability as catalyst in ROP of lactides and ε-caprolactones.

The specific objectives were:

i To synthesize and characterize complexes of copper(II) and zinc(II) from acetate salts using pyrazol-1-ylmethylpyridine ligands.

ii To investigate the catalytic activities of the complexes synthesized and characterize the nature of polylactides and polycaprolactones obtained.

iii To investigate kinetics involved in polymerization of lactides and caprolactones.

iv To investigate the effects of varying reaction conditions such as, monomer/catalyst ratio, temperature and solvent on the polymerization reactions.

1.4: Hypotheses

In null hypotheses:-

i Copper(II) and zinc(II) complexes of (pyrazol-1-ylmethyl)pyridine ligands cannot be synthesized nor characterized.

ii Copper(II) and zinc(II) (pyrazol-1-ylmethyl)pyridine complexes cannot catalyze polymerization of lactides and caprolactones and polymers obtained cannot be characterized.

iii Kinetics of ROP of lactides and caprolactones do not follow first order kinetics.

iv Reaction conditions such as time of reaction, monomer/catalyst ratio and type of solvent on the polymerization reactions do not influence polymerization reactions.

1.5: Justification and rationale of study

There is urgent need to design and develop cheap and effective ways for the large scale manufacture of renewable and biodegradable polymers considering; the increasing level of depletion of non-renewable resources. In addition, disposal of non-biodegradable plastics, is major environmental hazard. Moreover, removal of catalysts from the polymers is not absolute thus, polymers used for medical/biological applications require less toxic catalysts. Hence, synthesis of efficient catalysts from Zinc(II) and copper(II) complexes, which are less toxic is of great significance. The use of the by-products from sugar and corn would result in increased benefits of these materials, and this could offer a boost to the local producers of the plant materials.

CHAPTER TWO

LITERATURE REVIEW

2.1: Bioplastics

The term bioplastics in general, includes polymers which are derived from renewable biomass sources and/or are degradable plastics in which the degradation results from the action of naturally occurring micro-organism (ASTM, 1999; Doi and Steinbüchel, 2002a). Biomass sources (also known as Biorenewable resources) are generally recognized as organic materials of recent biological origins, (Brown, 2003) i.e. sustainable natural resources. It is important that bioplastics not to be mistaken with biopolymers which are under the terms of IUPAC defined as macromolecules (including proteins, nucleic acids and polysaccharides) formed by living organisms (Nagel *et al.*, 1992).

The class of bioplastics includes primarily four polymer types: polysaccharides, polyesters, polyurethanes and polyamides (Table 1) (Wolf *et al.*, 2005). Bioplastics derived from renewable biomass sources provide a new source of income for the agricultural sector, as well as a higher independence on fossil resources like crude oil or gas and therefore fulfill the principles of sustainable chemistry. In addition, the biodegradability of plastic materials does not only help to solve the problems of solid waste management but also allows for contributions to environmental protection and new application fields, especially for packaging and for single-use disposal products (Doi and Steinbüchel, 2002b).

Table 1: Types of bioplastics

POLYMER	BIOPLASTIC GROUP
Polyesters	Polylactides (PLA), polycaprolactones (PCL), polyglycolides (PGA), polybuthyleneterephthalate (PBT), polybuthylene succinate (PBS), polyhydroxyalkanoates (PHAs), polytrimethyleneterephthalate (PTT)
Polysaccharides	Starch and cellulose
Polyamides	Nylon
Polyurethanes	Polyurethanes (PURs)

Biodegradation according to a definition by IUPAC in general, means the breakdown of a substance to its building blocks, catalyzed by enzymes or whole microorganisms (Nagel *et al.*, 1992). This process is highly influenced not only by the primary chemical structure of these materials but also by their solid-state morphology and ordering phenomenon such as crystallinity and orientation (Doi and Steinbüchel, 2002a,b).

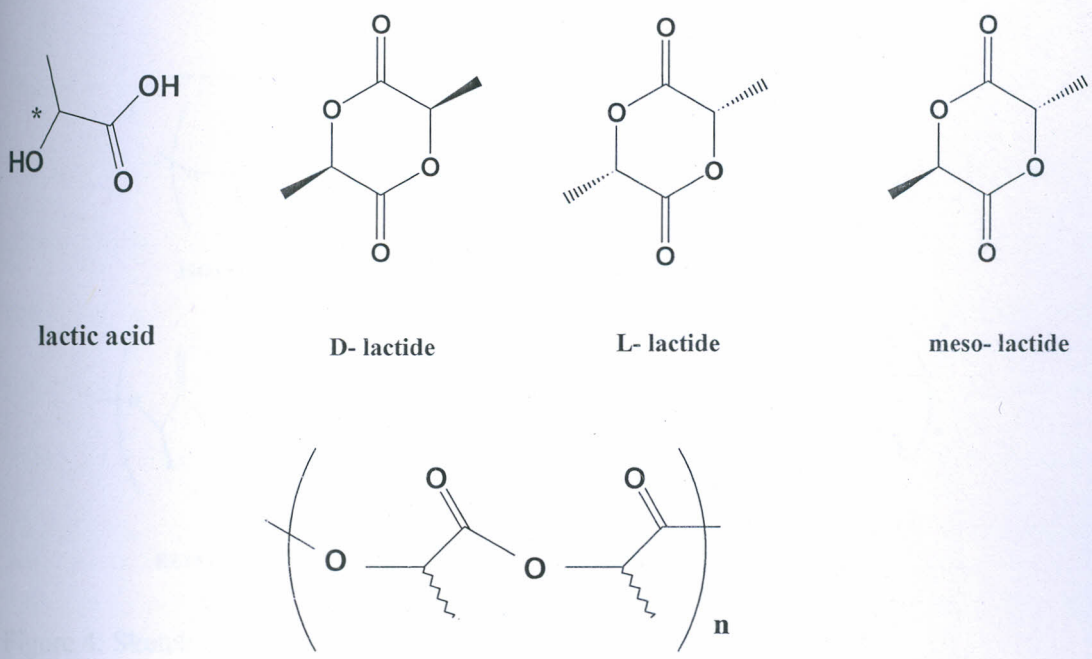
By the year 2017 global production capacity of bioplastics was 2.05 million tonnes while, global consumption estimated to be around 4.00 million tonnes (European Bioplastic Report, 2017). However, the growth rates are double-digit and the capacity of production of 2.05 million tones does not cope with the increasing demand. In the future, improvement of production techniques and material characteristics will allow for the economic production in industrial scale and therefore will lead to a massive reduction in price. Thus, the potential of bioplastic material has by far neither assessed nor utilized. In this research, emphasis is on polyesters and more specifically polylactides and polylactones which are obtained from by products of corn and sugar beets. Utilization of these materials would bring more income to the producers.

2.1.1: Polylactides

Polylactic acid or polylactide (PLA) is an aliphatic polyester derived from lactic acid (Vink *et al.*, 2003; Wasewar, 2005), formally named 2-hydroxycarboxylic acid, possesses a stereogenic center on the methylene carbon. Two lactic acid units combine to form a six-membered-ring dimer called Lactide (LA); which can be found in three stereo isomeric forms (Figure 3). PLA is elastic and flexible above its glass transition temperature (Tg = 50-57 °C for D,L-PLA) (Lu and Mikos, 1999) and can go through melting/freezing cycles repeatedly without alteration of its physical properties (Van De Velde and Kiekens, 2002). Like other thermoplastics, it has low density (1.21-1.25 g/cm^3) and the ability to take on complex shapes relatively easily. Its melting point varies from 150 °C (PLLA) to 170-180 °C (PDLA), and up to 230 °C in the case of stereo complexes formed by blending PLLA and PDLA into melt spun fibers (Furuhashi *et al.*, 2006). Fully amorphous PLA can be obtained by the inclusion of relatively high D-LA content (>20%) whereas highly crystalline material is obtained when the content in D-LA is low (<2%). When compared to other biodegradable polymers (poly(glycolic acid), poly(ε-caprolactone) and polyhydroxbutyrate), PLA seems to gather the best compromise in terms of density which is low, degradation behaviour, mechanical properties, and glass transition temperatures (Van De Velde and Kiekens, 2002).

PLA degrades in the environment through a two-step process. At first high molecular weight polyester chains hydrolyzed to molecular oligomers; the degradation rate depends on temperature and moisture levels and accelerated by acids or bases. Then, under the action of microorganisms, these lower molecular weight chains converted to carbon dioxide, water, and humus (Narayan, 1993). Enzymatic degradation observed with lipases, such as proteinase K, which are efficient at breaking down low-molecular weight and some enzymes, such as the yeast

Cyptococcus, which are able to degrade high-molecular weight PLA. Enzymes show a net preference for degradation of PLLA versus PDLA, with the highest degradation rates observed for amorphous PLA (Reeve *et al.*, 1994).



lactic acid **D- lactide** **L- lactide** **meso- lactide**

polylactide

Figure 3: Sketch of molecular structure of lactic acid, lactides and polylactide

A number of microstructures can be obtained from polymerization of lactide: isotactic PLA formed from either 100% D- or 100% L-lactide, syndiotactic PLA made from meso-lactide, atactic PLA has a random distribution of configurations about the stereocenters. Heterotactic PLA has regions of stereo-homogeneity, and Stereoblock PLA produced by polymerization of *rac*-LA with an enantiopure catalyst (Figure 4) (Ovitt and Coates, 2002).

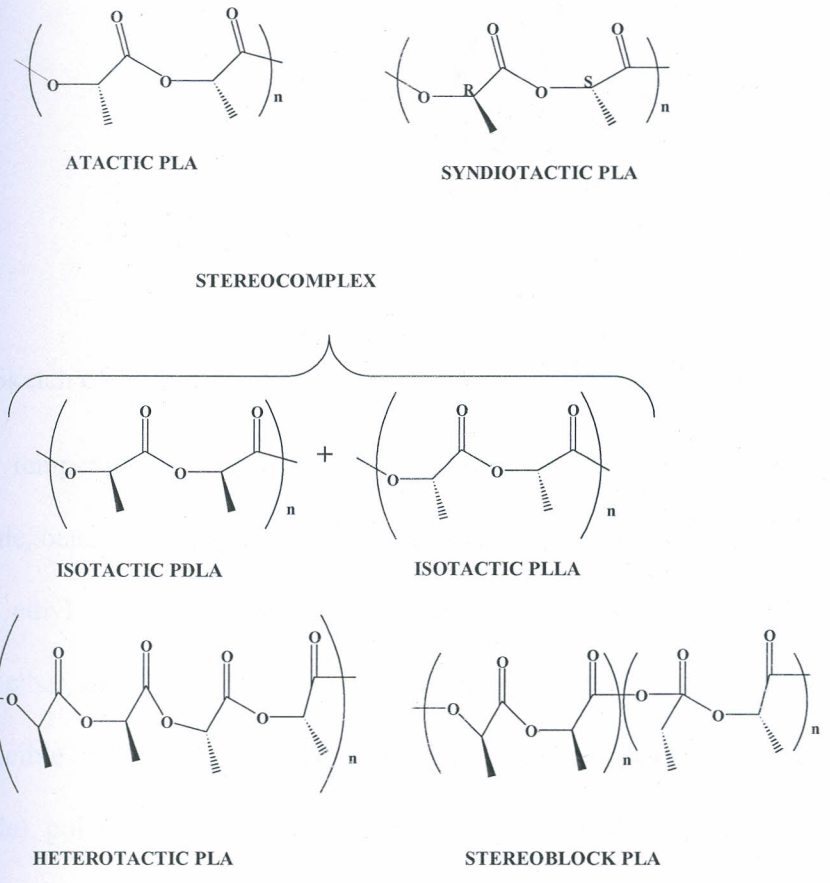


Figure 4: Sketch of polylactide microstructures

2.1.2: Polycaprolactone

Polycaprolactone (PCL) is aliphatic polyester composed of hexanoate (caprolactone) repeat units (Figure 5). It is a semi-crystalline polymer with a degree of crystallinity, which can reach 69% (Iroh, 1999). The unit cell is orthorhombic and the lattice constants are a = 7.496 ± 0.002 A°, b = 4.974 ± 0.001 A° and c = 17.297 ± 0.023 A°, c being the fibre axis (Bittiger *et al.*, 1970). The physical, thermal and mechanical properties of PCL depend on its molecular weight and its degree of crystallinity. Ranges of reported property values shown in Table 2.

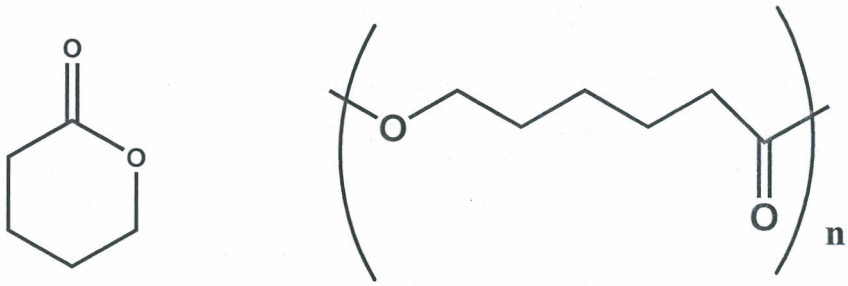


Figure 5: Sketch of structures of ε-caprolactone and polycaprolactone

At room temperature, PCL is highly soluble in chloroform, dichloromethane, carbon tetrachloride, benzene, toluene, cyclohexanone and 2-nitropropane; slightly soluble in acetone, 2-butanone, ethyl acetate, dimethylformamide and acetonitrile; and insoluble in alcohols, petroleum ether, diethyl ether and water (Sinha *et al.*, 2004). PCL displays the rare property of being miscible with many other polymers such as poly(vinyl chloride), poly(styrene–acrylonitrile), poly(acrylonitrile butadiene styrene), poly(bisphenol-A) and other polycarbonates, nitrocellulose and cellulose butyrate, and is also mechanically compatible with others (polyethylene, polypropylene, natural rubber, poly-(vinyl acetate), and poly(ethylene–propylene) rubber) (Sinha *et al.*, 2004).

The molecular weight, degree of crystallinity and the conditions of degradation causes polycaprolactone to biodegrade within several months to several years (Lam *et al.*, 2007; Joshi and Madras, 2008). Many microbes in nature are able to completely biodegrade PCL. The amorphous phase degraded first, resulting in an increase in the degree of crystallinity while the molecular weight remains constant (Lam *et al.*, 2007). Then, cleavage of ester bonds results in mass loss (Pena *et al.*, 2006). The polymer degrades by end chain scission at higher temperatures while it degrades by random chain scission at lower temperatures (Joshi and Madras, 2008). PCL degradation is autocatalysed by the carboxylic acids liberated during hydrolysis (Sinha *et al.*,

2004) but also catalysed by enzymes, resulting in faster decomposition (Chen *et al.*, 2000). While PCL enzymatically degraded in the environment, it is not degraded enzymatically in the body (Ikada and Tsuji, 2000).

Table 2: Property values of PCL

Number average molecular weight (M_n)(g ml^{-1})	530- 630000
Density (ρ) (g/cm^3)	1.071- 1.200
Glass transition temperature (T_g) (^oC)	(-65)- (-60)
Melting temperature (T_m) (^oC)	56- 65
Decomposition temperature (^oC)	350
Inherent viscosity (η_{inh}) (cm^3 g^{-1})	100- 130
Intrinsic viscosity (η) ($/cm^3$ g^{-1})	0.9
Tensile strength (σ) (MPa)	4- 785
Young modulus (E) (GPa)	0.21- 0.44
Elongation at break (ε) (%)	20- 1000

(Iroh, 1999; Van De Velde and Kiekens, 2002; Sinha *et al.*, 2004; Ikada and Tusji, 2000; Lam *et al.*, 2007)

2.1.3: Applications of polylactide and polycaprolactone

The PLA and PCL polymers find major applications in the packaging (Bastiol, 1997; Lam *et al.*, 2007) and biomedical applications such as drug delivery excipients and absorbable sutures (Chandra and Rustgi, 1998; Ikada and Tsuji, 2000; Sinha *et al.*, 2004). Although, polymers have been successfully utilized in a variety of applications that have been traditionally occupied by petroleum based polymers, implementation of these polymers and their-related materials on a

broader scale has been somewhat thwarted due to their high costs of production (Labet and Thielemans, 2009).

2.2: Catalysts used in ring opening polymerization of lactides and caprolactones

A large number of catalysts and catalytic systems, spanning virtually the whole periodic table have been investigated for ring opening polymerization of lactide and caprolactone (Platel *et al.*, 2008; Stanford and Dove, 2010). It is therefore paramount to have a good understanding and overview of these different catalysts and catalytic systems that have been studied to derive new developments in catalysis. They are; metal-free catalysts (Kamber *et al.*, 2007) and metal-based catalysts (Wheaton *et al.*, 2009). Examples of metal-free catalysts are 4-(dimethylamino)pyridine (DMAP) (Satoh *et al.*, 2006), *N*-propylsulfonic acid (Wilson and Jones, 2004), trifluoromethanesulfonic acid (Bourissou *et al.*, 2005), $HCl{\cdot}Et_2O$, *N*-heterocyclic carbenes (Marion *et al.*, 2007), guanidines and amidines (Chuma *et al.*, 2008) and phosphazene bases (Zhang *et al.*, 2007). Metal based catalysts majorly studied, have shown higher level of control in ring opening polymerization of the lactides and caprolactones to yield polymers with higher molecular weights (Platel *et al.*, 2008) however, with respect to biomaterial applications, the biocompatibility of the metal are of importance, as complete catalyst removal from the polymer material is generally not performed (Platel *et al.*, 2008).

Well-known and intensively studied metal-based catalyst used in coordination-insertion polymerization, are metal alkoxides. Multivalent metal alkoxides enable the growth of more than one polymeric chain from a metallic center. Examples are aluminum isopropoxide (Duda and Penczek, 1995) and binolate complexes of zinc and aluminum (Chisholm *et al.*, 2003). Other systems consist of sterically protected catalysts. This protection prevents formation of higher

aggregates, and the metal species are rather inactive or 'dormant', resulting in negligible polymerization. A far more active complex of the metal species and the alkoxide catalyst is formed, upon *in situ* alcoholysis of the protected catalyst, and prevention of aggregation is no longer required due to fast propagation. Examples are the highly active yttrium alkoxides (Stevels *et al.*, 1996) and the widely applied stannous alkoxides, generated *in situ* from stannous octoate ($Sn(Oct)_2$) (Storey and Sherman, 2002).

Single-site catalyst, where metal and ligand are coordinated in such a way that only one initiating moiety is present and thus only one polymeric chain will grow from the metal center. The catalysts (or catalyst complexes) have the general formula L_n-M-R, where L represents a ligand, n number of ligands, M the metal and R the initiating species, which is generally an alkoxide. Alternatively, exchange of an R group by an alkoxide group upon *in situ* alcoholysis is possible, e.g. when R is an alkyl or bis(trimethylsilyl)amide group. The inert ligand L is permanently coordinated to the metal center, and is important in controlling parameters such as polymerization rate and polymer stereochemistry. Over the years, the ROP of lactides and lactones has been explored using varieties of metal-ligand combinations (Dechy- Cabaret *et al.*, 2009; Wheaton *et al.*, 2009). Besides catalytic activity, the stereo selective behaviour of the catalysts in the ROP of especially racemic mixtures of lactides has received great interest.

2.3: Zinc(II) catalysts used in ring opening polymerisation of lactides and caprolactones

In the great majority of known zinc(II) compounds, zinc exists under the ionic form Zn^{2+} with an electron configuration of $3d^{10}4s^0$. Zinc(II) forms a number of complexes which may be linear (*sp hybridization*) e.g. $Zn(CH_3)_2$, tetrahedral (*sp^3 hybridization*) e.g. $[Zn(NH_3)_4]^{2+}$; square pyramidal (*sp^3d*) e.g. $[Zn(acac)_2.H_2O]^0$ and octahedral (*sp^3d^2 hybridization*) e.g. $[Zn(en)_3]^{2+}$. Zinc(II) normally prefers tetrahedral geometry and coordination number four is common owing to its

small ionic and atomic size (Al-Jeboori *et al*, 2009). However, it has been shown that steric properties of the ligand profoundly affect the coordination chemistry of the metal centre as illustrated by the zinc(II) complex that features β-diketiminato and anilido-imine ligands (Figure 6) (Pang *et al*, 2010). Due to the steric bulk of the substituents on the ligand, the zinc(II) centre adopts a three coordinate trigonal planar geometry. Hence, control of the steric requirements of the ligand design can enforce a desired geometry at the metal center.

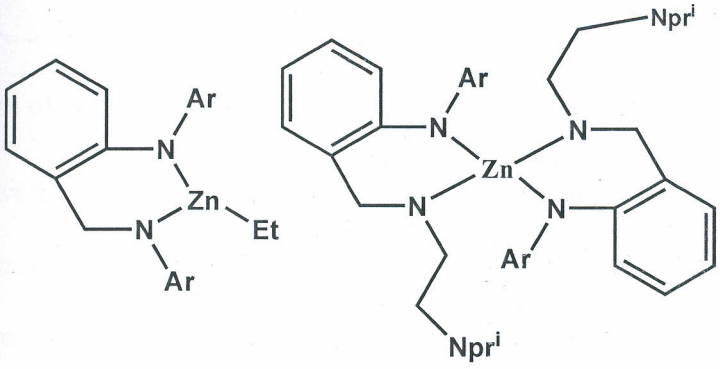


Figure 6:Sketch of zinc(II) complexes that feature anilido-imine ligands, where Ar = 2,6pr^{i}C$_6$H$_3$

In addition, number of donor atoms in the ligands affects the coordination geometry around the zinc(II) center as depicted by zinc(II) complexes of formamidine ligands. Due to the flexibility in the coordination behaviour of benzoate, tetrahedral and octahedral geometries are observed around the zinc(II) center (Figure 7). Moreover, bridging due to bidentate nature of the benzoate ligand leads to more than one metal atom centre (Akpan et al., 2016).

Among the variety of zinc(II)-catalysts, some of the zinc(II) catalysts have demonstrated exceptional activity to polymerize lactide and caprolactone, sometimes with high degree of stereoselectivity (Chamberlain *et al.*, 2001; Chen *et al.*, 2006). These properties combined with low cost and biological tolerance have been major motivations for research to investigate more zinc(II) catalysts in the recent years.

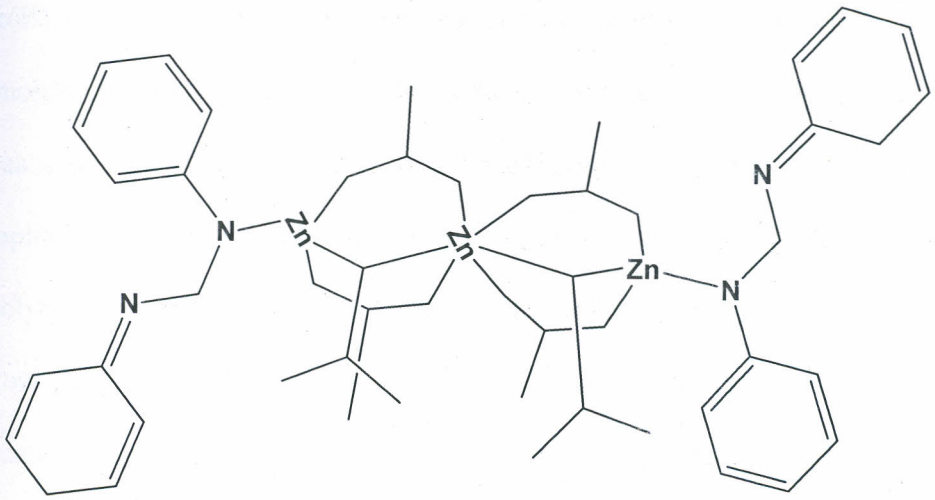
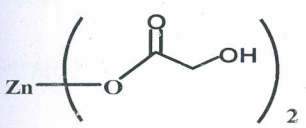
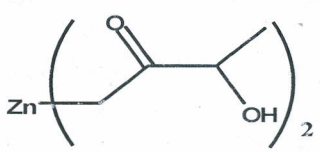


Figure 7: Skecth of zinc(II) complex that feature formamidine ligand

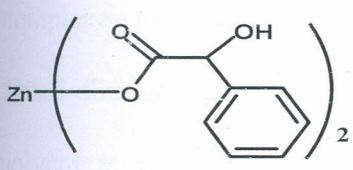
Since 1959, several research groups have been investigating a variety of zinc(II) complexes for ROP of caprolactone and lactide, with the aim of optimizing the activity and stereoselectivity of the catalyst (Bero *et al.*, 1990; Vert *et al.*, 1998). Simple compounds such as zinc(II) oxide or zinc(II) carbonates (Kleine and Kleine, 1959) were found to induce partial racemisation of L-lactide; it was also found that the stable, non-hygroscopic salt zinc(II) stearate (Figure 8) follows the same trend.



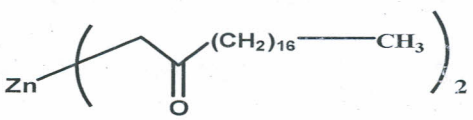
zinc 2-hydroxyacetate



zinc 2-hdroxypropanoate



zinc 2-hydroxy-2-phenylacetate



zinc dioctadecanoate

Figure 8: Skecth of zinc(II) complexes that features hydroxyls and carbonyl

Diethyl zinc(II), despite showing a respectable activity, is not suited for bulk polymerization as it is a highly moisture-sensitive and flammable liquid (Bero *et al.*, 1990). Zinc powder, is however, considered as a good catalyst for polymerization of lactones to the point where it has found industrial applications (Vert *et al.*, 1998); it is easy to handle as starting material, but its removal from the polymer product requires an ultra-filtration process (Chabot *et al.*, 1983), and it promotes slow polymerization (Vert *et al.*, 1998). Zinc(II) 2-hydroxypropanoate (Figure 8), a resorbable catalyst, yields polymers with high conversion, activity, and molecular weight polymers; Vert (1998) proposed Zinc(II) 2-hydroxypropanoate to be the actual initiator of lactide polymerization in presence of zinc metal. A number of zinc(II) salts, such as zinc 2-hydroxy-2-phenylacetate, zinc 2-hydroxyacetate (Kricheldorf and Damrau, 1997), and salts of several amino acids found to catalyze PLA in low molecular weight only. While zinc chloride and zinc(II) iodide were found to polymerize L-lactide to give lower molecular weight poly(L-lactide) even at high temperatures (Kricheldorf and Damrau, 1997), zinc(II) bromide produce high molecular weight polymers (Nijenhuis *et al.*, 1992).

While stereo control induced by chiral metal catalysts in lactide polymerization earlier had demonstrated with some aluminum complexes (Spassky *et al.*, 1996), Coates' group was the first to report a stereoselective achiral zinc(II) catalyst (Cheng *et al.*, 1999). The success of this catalyst (high activity and stereoselectivity) soon generated a number of studies on zinc(II) complexes featuring β-diiminate ligands (Figure 9) (Chen *et al.*, 2005; Chisholm *et al.*, 2005). The β-diiminate complexes reported showed efficient catalysis in ROP of lactide in chlorinated solvent at room temperature. These zinc(II) complexes have been prepared either *via* an exchange reaction from the protonated ligands, or *via* substitution reaction from the lithium or potassium salt of the β-diiminate. Dimeric or monomeric structures obtained, depending on the

steric bulk of the β-diiminate ligand and the initiating group. As the polymerizations were performed on catalysts featuring various co-ligands (amido, alkoxy, silyloxy, methyl lactacte, acetate and ethyl groups), it was found that polymerization initiated from silylalkoxy, acetate and ethyl groups are slower than with alkoxy ligands (Chamberlain, *et al.*, 2001).

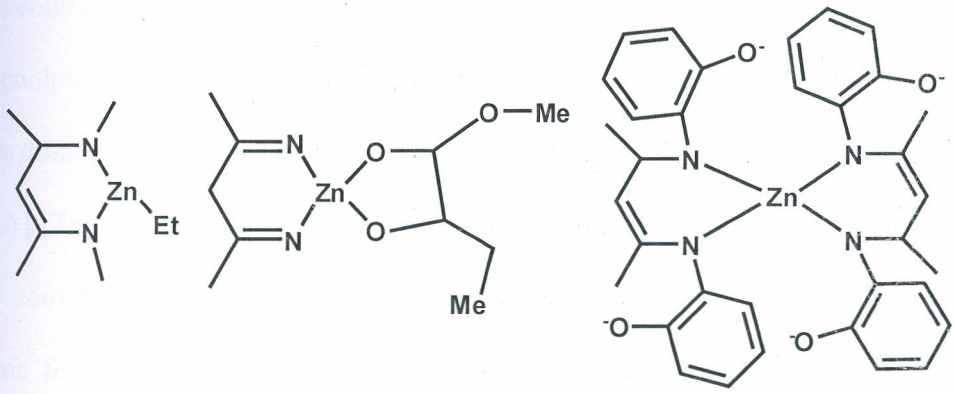


Figure 9: Skect of zinc(II) complexes that features β-diketiminate ligands

Chain-end control, which is usually associated to heterotactic PLA, was greatly influenced by modification of the aryl substituents, as indicated by the decreased heterotacticy observed at 20 °C with (79%) ethyl, (76%) *n*-propyl compared to (90%) isopropyl groups (Chamberlain, *et al.*, 2001). On the other hand, modification of the aryl substituent from isopropyl to *ortho*-methoxyphenyl improved activity of the corresponding zinc complexes (Dowe, *et al.*, 2004). These observations clearly illustrate the difficulties encountered by researchers who try to optimize both stereocontrol and activity of a catalyst.

The other efficient single-site zinc catalysts include; β- diketone Schiff base zinc complex, which forms a macro cycle in solid state; it is capable of polymerizing 100 equivalent *rac*-lactide in dichloromethane at 25 °C in 30 minutes with a polydispersity of 1.09 and a remarkable P_r of 0.73 (Pang *et al.*, 2008). However, it remains unclear if all zinc(II) centers participates in the ring-opening process. Among the zinc(II) *N*-heterocyclic carbenes, the chlorinated dinuclear zinc(II)

complex demonstrates higher catalyttic activity; 130 equivalent *rac*-LA could be polymerized in 4 min at 25 °C in dichloromethane, with a slight preference for racemic linkages between monomer units in the PLA chains (P_r = 0.6) (Jensen *et al.*, 2005). Stereo control of the ROP reactions, in the absence of chiral center in the N-heterocyclic ligand, is presumably induced by chain-end control mechanism. Two other highly active zinc(II) catalysts based on diaminophenolate-based ligands have been developed. The first features two ethylenediamine arms and is dinuclear in solid state and solution (Williams *et al.*, 2003). Polymerization of D,L-lactide ([LA]/[Zn] = 300) in dichoromethane at room temperature was obtained in 30 minutes with 90% conversion and a very narrow molecular weight distribution (PDI ≈ 1.2). The characteristic features of a controlled polymerization and first-order dependency on monomer and catalyst were in agreement with a bimetallic coordination-insertion mechanism were observed from kinetic studies. The second zinc complex, contains only one ethylenediamine arm, therefore it is less prone to accommodate two zinc centers for one ligand unit; X-Ray crystallography and NMR techniques identified the complex as dimeric in solid state and monomeric in solution. Catalyst polymerized lactide with an exceptional rate, in a controlled fashion even at low catalyst yield (1500 equivalent lactide) (Williams *et al.*, 2003).

Investigations on several zinc(II) complexes containing NNO-tridentate Schiff base ligands have been carried (Figure 10). The first study features, achiral zinc(II) complex bearing a mono methylether Salen-type ligand $[(SalenMe)Zn(OBn)]_2$, which was found to be moderately active towards lactide ROP (100 eq. L-lactide polymerized in 4 hours at 60 °C in toluene). Despite producing a polymer with an extremely narrow molecular-weight distribution (PDI = 1.03); polymerization of 50 equivalent *rac*-lactide over a period of 24 hours in dichloromethane at 25 °C produced isotactic polymer with a P_r of 0.75 (Wu *et al.*, 2005).

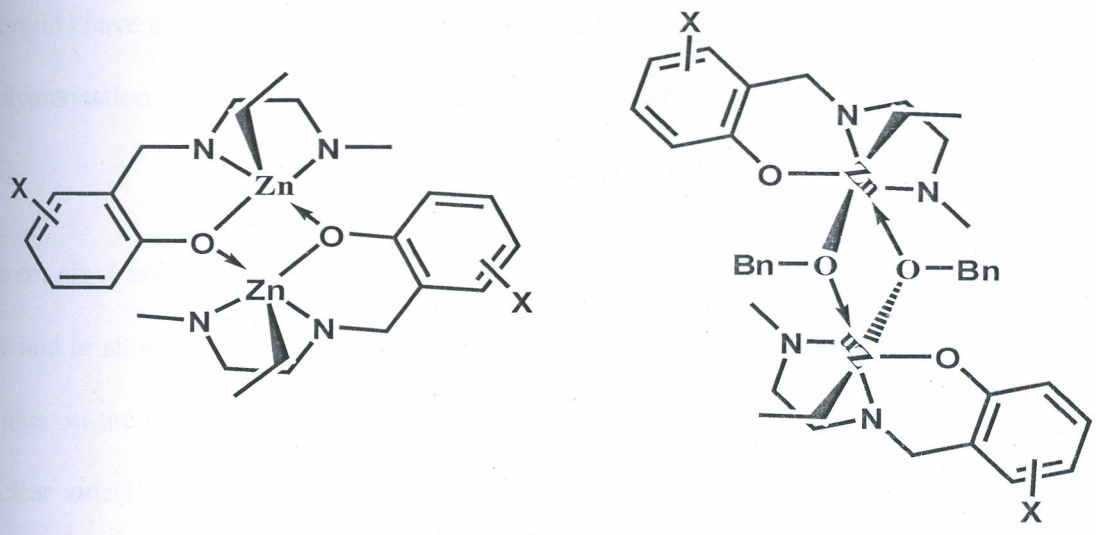


Figure 10: Sketch of zinc(II) complexes that features NNO-tridentate ligands, where X is either Br, Cl, 4,6-di-^{t}Bu, 3,4-naphthalyl

A Schiff base zinc complex studied in 2006 by the same group was found to exist as a dimer in solid state and an equilibrium between dimer and monomer in solution (based on variable temperature NMR analyses (Chen *et. al.* 2006). The protonated version of this achiral complex is a highly active catalytic species (100 equivalent L-lactide converted to polymer in 30 minutes at 25 °C in dicholoromethane) but shows weak stereoselectivity (P_r = 0.59 for 200 equivalent *rac*-lactide polymerized to heterotactic PLA at 25 °C in dicholoromethane). On the other hand, polymerization of the zinc(II) complex bearing tert-butyl substituents at -55 °C in the same solvent allowed to reach great stereocontrol (P_r = 0.91).

The ROP of CL has successfully been catalyzed by zinc(II) oxide in the presence of an ionic liquid 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim][BF_4]) under microwave treatment (Liao *et al.*, 2006). The combination of these two elements (ionic liquid + microwave) increases the efficiency of the ROP. Polymers with average molecular weights between 2,260 g mol^{-1} and 11,060 g mol^{-1} with PDIs between 1.30 and 2.50 were obtained. Zinc(II) mono- and di-alkoxides

(Figure 11) have also been reported to be good catalysts for the ROP of CL resulting in a degree of polymerisation (DP) over 100 being obtained with a PDI between 1.05 and 1.1 (Barakat *et al.*, 1991).

Different alkyl and amide zinc complexes (Figure 12) have been used and reported to be more stable and to show higher activity (Sarazin *et al.,* 2004). Both complexes display high catalytic activities in the range of 50 to 300 kg(mol metal)$^{-1}$ h^{-1}. The ROP of caprolactone employing a trinuclear zinc(II) alkoxide [{(BDI-OMe)Zn(*i*-OBn)}$_2$Zn(*i*-OBn)$_2$] as a catalyst has also been studied and the linear increase in molecular weight average with conversion and the low polydispersity index of PCL shows the level of polymerization control to be high. However, the conversion up to 95% can be achieved within 2 h and PCL obtained with low polydispersity (Chen *et al.*, 2005).

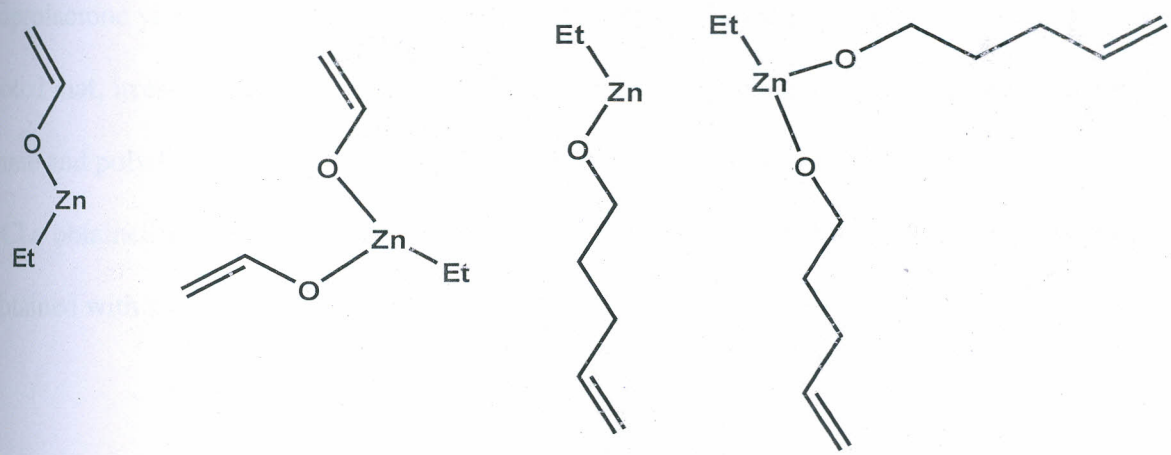


Figure 11: Sketch of zinc(II) complexes that feature mono- and di-alkoxides

Amido-oxazolinate zinc(II) catalysts have shown fast rate and high catalytic activity and isoselectivity for ROP of rac-lactide, producing isotactic PLA with P_m of up to 0.91 at a low temperature of 23 °C (Abbina and Du, 2014). Conversions of over 90% of the rac-lactide at 50 °C in toluene is achieved within 20-30 min for the complexes. Narrow molecular weight

dispersities (1.05-1.37) showed that these complexes have good control of the polymerization of LA. However, use of chiral catalysts does not necessarily ensure stereocontrol in ROP of rac-LA, as a number of chiral zinc catalysts have demonstrated (Darensbourg and Karroonnirun, 2010, Drouin *et al.*, 2010).

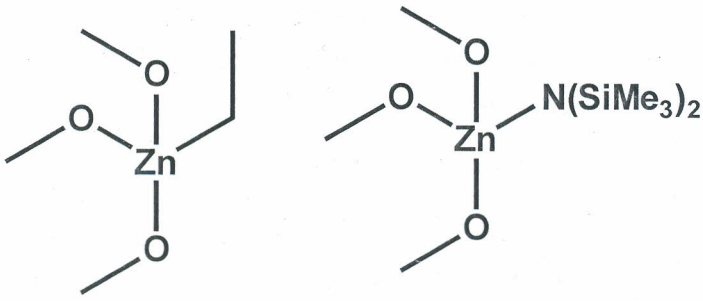


Figure 12: Sketch of zinc(II) complexes that feature alkyl and amido ligands

The (ferrocenylpyrazolyl) zinc(II) complexes (Figure 13) synthesized and used in ROP of caprolactone yielded low molecular weight and narrow to broad PDIs (Obuah *et al.*, 2015). They noted that, irrespective of the [CL]/[Catalyst] used the molecular weights are approximately the same and polydispersity index obtained for the polymers were influenced by the ligand type. The PCLs obtained using amine based ligands have higher polydispersity index compared to PCLs obtained with pyridine-based ligand.

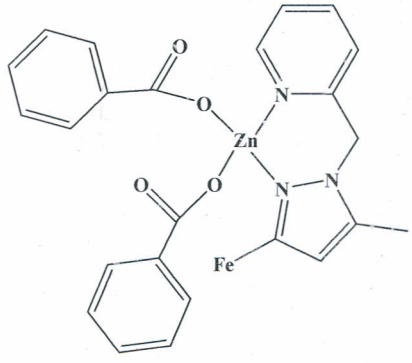


Figure 13: Sketch of (ferrocenylpyrazolyl)zinc(II) benzoate complex

2.4: Copper(II) catalysts used in ring opening polymerisation of lactide and caprolactone

Copper(II) forms a rich variety of compounds with oxidation states +1 and +2, having electronic configuration of $3d^{10}4s^0$ and $3d^94s^0$ respectively (Holleman and Wilburg, 2001). Copper complexes forms varied geometries i.e. tetragonal pyramid $[CuL_2(NO_3)\ (NO_3)(H_2O)]$, L = 2-hydroxymethylbenzimidazole) (Barszcz *et al.*, 2008), square planar (bis-[N(2-pyridylmethyl)-3-thienyl-carboxamido)copper(II)]perchlorate) (Figure 14) (Howell *et al.*, 2007) and octahedral $[Cu(NH_3)_4(H_2O)_2]^{2+}$ (John *et al.*, 2007).

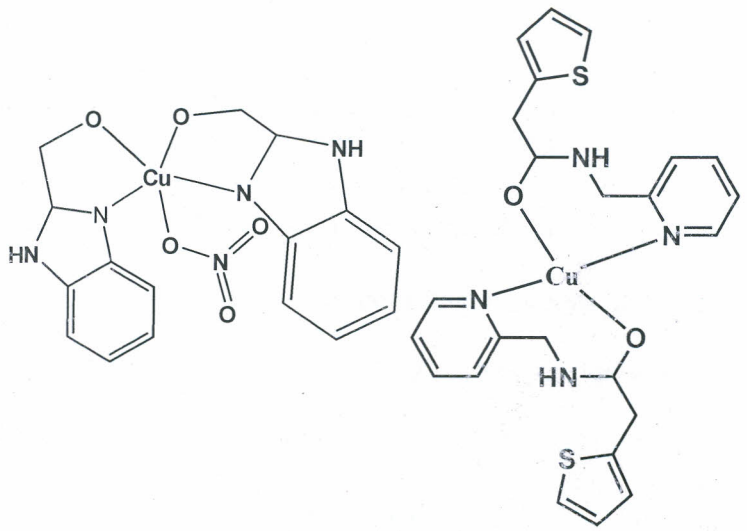


Figure 14: Sketch of copper(II) complexes that feature imidazole and carboxamido ligands

Copper(II) complexes of many nitrogen-containing heterocyclic ligands (Figure 15) form bridged complexes with two or more metal centres. The combinations of the structural and functional properties of bridging ligands have led to interesting advances in the areas of multi-electron catalysis (Steel and Sumby, 2003).

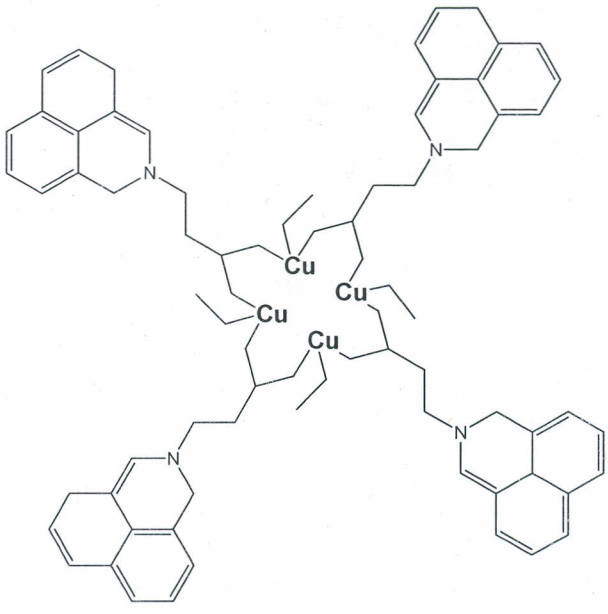


Figure 15: Sketch of copper(II) complex of nitrogen heterocyclic ligand.

Copper(II) carboxylate complexes are an illustration of the bridged complexes. The three complexes form square pyramidal, five-coordinate copper(II) centres with dimeric "paddlewheel" structure. The nonbonding Cu-Cu distances are between 2.60 and 2.64 Å. The alkyl spacers units have effect on orientations, can cause "linear" or "bent" when observed along ligand–Cu··Cu–ligand axis. Paddlewheel dicopper tetracarboxylates exhibit very strong antiferromagnetic interaction between the unpaired electrons of the d^9 copper(II) centres (Reger *et al.*, 2012).

Literature of copper(II) complexes used as catalysts in ROP of LA and CL is limited, however the complexes studied found to be efficient catalysts yielding moderate molecular weights with narrow molecular weight distributions. Copper(II) phenoxy-ketimine ligands complexes with varying steric demands, namely 2-[1-(2,6-diethylphenylimino)ethyl]phenol, 2-[1-(2,6-dimethylphenylimino)ethyl]phenol and 2-[1- (2-methylphenylimino)ethyl]phenol have been synthesized (Figure 16).

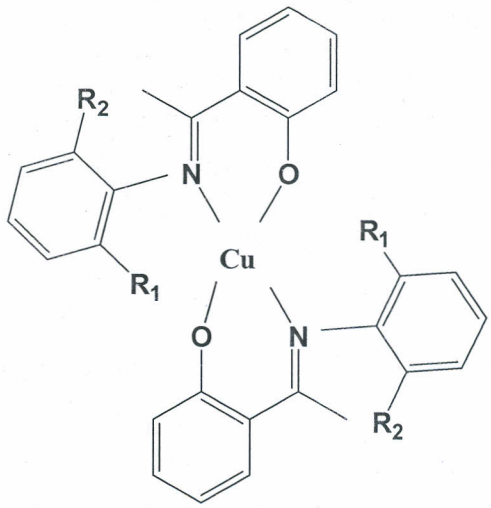


Figure 16: Sketch of copper(II) complexes of phenoxy-ketimine ligands ($R_1 = R_2 = Et$; $R_1 = R_2 = Me$; $R_1 = H$, $R_2 = Me$)

They are efficient catalysts for ring-opening polymerization of L-lactide at elevated temperatures under solvent- free melt conditions, producing polylactide polymers of moderate molecular weights with narrow molecular weight distributions (John *et al.*, 2007).

In the recent past copper(II) complexes of (R,R)-N^1,N^2-dimethyl-bis(naphthalen-1-ylmethyl)cyclohexane-1,2-diamine and (R,R)-N^1,N^2-dimethyl-bis(naphthalen-2-ylmethyl)cyclohexane-1,2-diamine (2-NMCD) ligands (Figure 17) have been synthesized. There use in ring opening polymerization of rac-lactide (rac-LA) showed controlled fashion and displayed high activities of 10 s or 25 s for complete conversion at room temperature (Kwon *et al.*, 2015). The later ligand yields heterotactic PLA with P_r up to 0.90. They noted that homochiral ligand architecture influences the stereoselectivity of the PLA obtained, duration longer than 10 min lowers the degree of heterotacticity, due to factors, such as epimerization and a faster reaction for less crowded initiator (Kwon *et al.*, 2015).

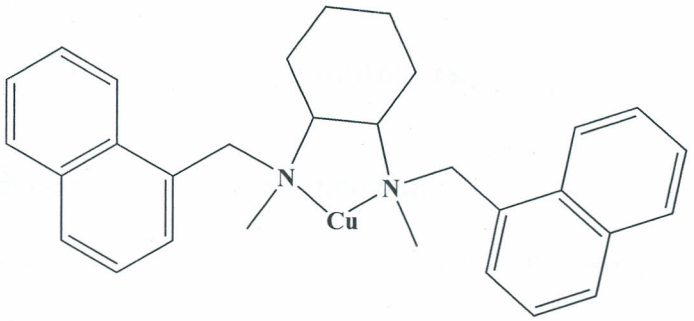


Figure 17: Sketch of copper(II) complex of (R,R)-N^1,N^2-dimethyl-bis(naphthalen-1-ylmethyl)cyclohexane-1,2-diamine ligand.

The examples mentioned here show that very few catalysts capable to polymerize CL and LA with high activity and selectivity discovered so far. Issues such as controlling polymer structure, high activity and selectivity remain a challenge. The design of well-defined catalysts that could produce polyesters with desirable molecular weight and narrow molecular weight distribution remains a desirable goal.

CHAPTER THREE

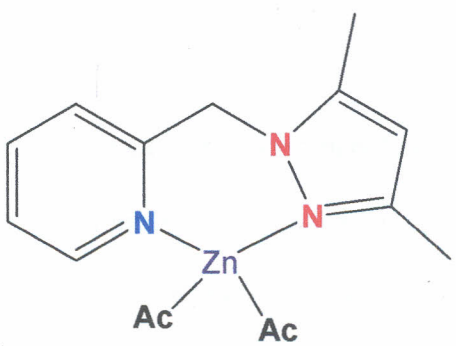
METHODOLOGY

3.1: General materials, methods and instrumentation

The solvents and chemicals: dichloromethane, toluene, methanol, hexane, chloroform, 3,5-dimethylpyrazole, 3,5-diphenylpyrazole, lactic acid, ε-caprolactones, tetrabutylammonium bromide, 2-picolylchloride hydrochloride, sodium hydroxide, zinc(II) acetate and copper(II) acetate were obtained from Sigma–Aldrich (Durban, South Africa) and were used as received. All the solvents were of analytical grade. Nuclear magnetic resonance (NMR) spectra were recorded on a Varian instrument at the University of Nairobi, Kenya and on a Bruker instrument at the University of KwaZulu-Natal, South Africa. Single crystal X-ray crystallography analyses were done on a Bruker APEXII Duo CCD diffractometer. The elemental analyses were performed with Flash 2000 thermoscientific analyser at the University of KwaZulu-Natal, South Africa. ES-MS data were collected on a LC Premier micro-mass spectrometer, University of KwaZulu-Natal.

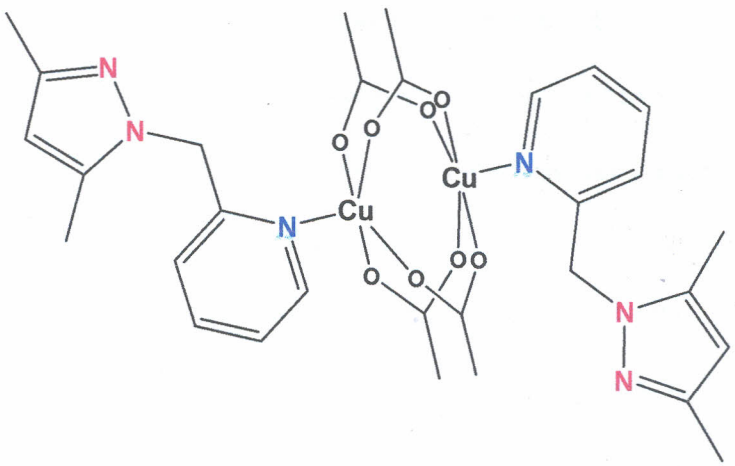
3.2: Syntheses of zinc(II) and copper(II) complexes

3.2.1: *Diaceto{2-(3,5-dimethylpyrazol-1-ylmethyl)pyridine}zinc(II)* (D1)



To a solution of ***2-(3,5-dimethylpyrazol-1-ylmethyl)pyridine*** (**L1**) (0.15 g, 0.80 mmol) in methanol (10 mL) was added a solution of $Zn(Ac)_2$ (0.15 g, 0.82 mmol) in methanol (10 mL) and the solution stirred for 24 h. After the reaction period, the solvent was removed under vacuum to afford a white solid. Recrystallization of the crude product from a dichloromethane/hexane solvent system afforded single-crystals of **D1** suitable for X-ray analysis. Yield: 0.19 g (63%). ^{1}H NMR: (400 MHz, $CDCl_3$): δ, 2.20 (s, 6H, CH_3, Ac); 2.23 (s, 3H, CH_3, pz); 2.54 (s, 3H, CH_3, pz); 5.46 (s, 2H, CH_2); 5.93 (s, 1H, pz); 7.30 (t, 1H, py, ^{3}*J*HH = 7.2 Hz); 7.43 (d, 1H, py, ^{3}*J*HH = 7.2 Hz); 7.94 (t, 1H, py, ^{3}*J*HH = 7.6 Hz); 9.07 (d, 1H, py, ^{3}*J*HH = 7.6 Hz). ^{13}C NMR (CDCl3): d; 12.13; 14.8; 23.6; 54.1; 108.2; 122.8; 125.1; 138.7; 141.1; 152.3; 153.4; 177.1. ES-MS: m/z (%); 309.93 [M^+-Ac, 100]; 251.94 [M^+-2Ac, 20]. Anal. Calc. For $C_{15}H_{19}N_3O_4Zn$: C, 48.60; H, 5.17; N, 11.33. Found: C, 48.31; H, 5.07; N, 11.74.

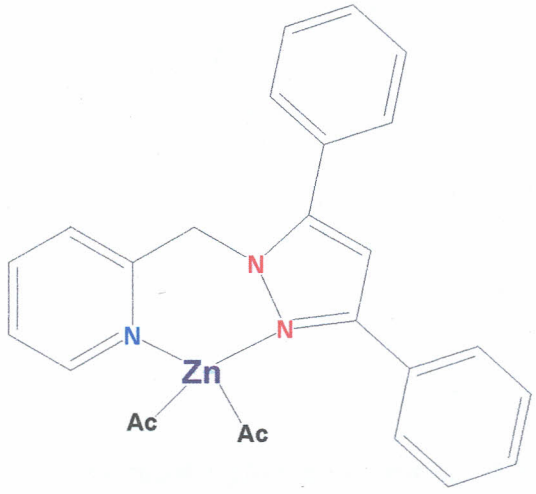
3.2.2: ***Diaceto{2-(3,5-dimethylpyrazol-1-ylmethyl)pyridine}copper(II) (D2)***



To a solution of ***2-(3,5-dimethylpyrazol-1-ylmethyl)pyridine*** (**L1**) (0.15 g, 0.80 mmol) in methanol (10 mL) was added a solution of $Cu(Ac)_2$ (0.15 g, 0.80 mmol) in methanol (10 mL) and the blue solution was stirred for 24 h. Removal of solvent under vacuum gave a deep blue solid material. Recrystallization of the crude product from a dichloromethane/hexane

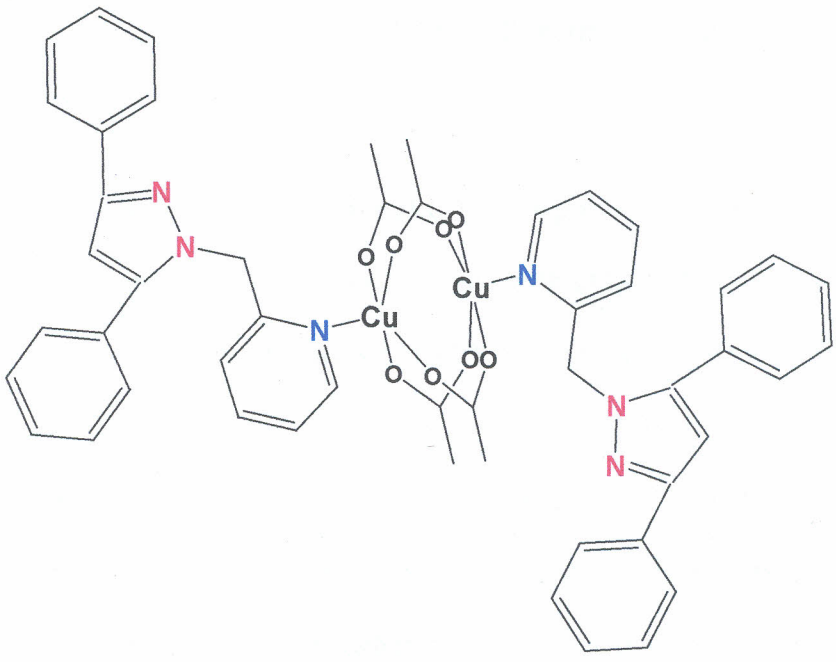
solvent system afforded compound **D2** as pure solid. Yield; 0.18 g (60%), ESI-MS: m/z (%); 308.93 [M^+-Ac, 100]; 249.94 [M^+-2Ac, 20]. Anal. Calc. For $C_{15}H_{19}N_3O_4Cu$: C, 48.84; H, 5.19; N, 11.39. Found: C, 48.61; H, 5.44; N, 11.18.

3.2.3: *Diaceto{2-(3,5-diphenylpyrazol-1-ylmethyl)pyridine}zinc(II) (D3)*



To a solution of ***2-(3,5-diphenylpyrazol-1-ylmethyl)pyridine*** (**L2**) (0.10 g, 0.32 m mol) in methanol (10 mL), was added a solution of $Zn(Ac)_2$ (0.06 g, 0.32 mmol) in methanol (10 mL). After the reaction period, the solvent was removed under vacuum to afford a white solid **D3**. Yield: 0.13 g (81%). ^{1}H NMR: (400 MHz, $CDCl_3$): δ, 2.20 (s, 6H, CH_3, Ac); 5.59 (s, 2H, CH_2); 6.72 (s, 1H, pz); 7.05 (t, 1H, py, ^3JHH = 7.6 Hz); 7.40 (d, 1H, py, ^3JHH = 7.2 Hz); 7.44 (m, 4H, ph); 7.70 (t, 1H, py, ^3JHH = 7.6 Hz); 7.86 (m, 4H, ph); 8.63 (d, 1H, py, ^3JHH = 7.6 Hz) . ^{13}C NMR ($CDCl_3$): d; 24.4; 58.2; 109.2; 122.8; 124.1; 125.6; 138.9; 139.1; 142.1; 151.9; 153.8; 178.3. ES-MS: m/z (%); 433.88 [M^+-Ac, 100]; 373.88 [M^+-2Ac, 20]. Anal. Calc. For $C_{25}H_{23}N_3O_4Zn$: C, 60.68; H, 4.68; N, 8.49. Found: C, 60.52; H, 4.85; N, 8.78.

3.2.4: Diaceto{2-(3,5-diphenylpyrazol-1-ylmethyl)pyridine}copper(II) (D4)



To a solution of ***2-(3,5-diphenylpyrazol-1-ylmethyl)pyridine*** (**L2**) (0.10 g, 0.32 m mol) in methanol (10 mL), was added a solution of $Cu(Ac)_2$ (0.06 g, 0.32 m mol) in methanol (10 mL) and the blue solution stirred for 48 h. Recrystallization of the crude product from a dichloromethane/hexane mixture afforded single-crystals suitable for X-ray analysis. Yield: 0.10 g (63%). ESI-MS: m/z (%); 308.93 [M^+- Ac, 100]; 249.94 [M^+-2Ac, 20]. ESI-MS: m/z (%); 432.88 [M^+-Ac, 100]; 372.88 [M^+-2Ac, 20]. Anal. Calc. For $C_{50}H_{46}N_6O_8Cu_2$: C, 60.90; H, 4.70; N, 8.52. Found: C, 60.62; H, 4.75; N, 8.67.

3.3: Single crystal X-ray crystallography analyses

Crystal evaluation and data collection were collected on a Bruker APEXII Duo CCD diffractometer with MoKα radiation (λ = 0.71073 Å) (Bruker-AXS, 2009). Data reduction and absorption correction were performed with SAINT and SADABS (SAINT, 1995; SADABS, 1996; Sheldrick, 2008). The structures were solved by direct and conventional Fourier

and all non-hydrogen atoms refined anisotropically by full-matrix least squares techniques based on F^2 (Sheldrick, 2008).

3.4: General procedure for D,L-lactide polymerization

A Schlenk tube containing magnetic stirrer was charged with D,L- lactide (1.44 g, 0.01 mol) in toluene (5 mL) and the reaction temperature set at 110 °C. The required amount of the catalyst, depending on the ratio of [monomer]:[catalyst] was weighed (1:100, 1:200, 1:400) and added and to the Schlenk tube and stirring started. After 4, 12, 24, 36, 48, 72 and 96 hours of reaction, the samples were rapidly cooled to room temperature by quenching. The quenched samples were analyzed by ^1H NMR spectroscopy for determination of polymerization. The percentage conversion of the monomer was given by $[PLA]/[LA]_o \times 100$, where $[LA]_o$ is the initial concentration of monomer and [PLA] is the concentration of the polymer at time t, and was evaluated by the formula:

$$\% \text{ Conversion} = \frac{\text{ICH}_{\text{polymer}}}{(\text{ICH}_{\text{monomer}} + \text{ICH}_{\text{polymer}})} \times 100$$

Where, $I_{CH\ polymer}$ is the intensity of CH (methine) protons of the polymer at 5.2 ppm, and $I_{CH\ monomer}$ is the intensity of CH (methine) protons of the monomer at 5.0 ppm of respective spectra. The crude products were purified by dissolving them in CH_2Cl_2 followed by addition of cold methanol that yielded a white precipitate, which was isolated by filtration and dried to constant weight prior to analyses by size exclusion chromatography (Chen *et* al., 2005).

3.5: General procedure for bulk polymerization of ε-caprolactone polymerization

Polymerization reactions were performed by introducing an appropriate amount of the complex, depending on the $[CL]_o/[I]$ ratio (50, 75, 100, 150), in a Schlenk tube equipped with a magnetic stirrer. The monomer, ε-CL (1.14 g, 0.01mol) was then added *via* a gas tight syringe and the temperature set at 110 °C before the reactions were initiated. After 4, 12, 24, 36, 48, 72 and 96 hours of reaction, the mixtures were cooled rapidly to room temperature by quenching. The quenched samples were analyzed by ^1H NMR spectroscopy for determination of polymerization. The percentage conversion of the monomer was given by $[PCL]/[CL]_o \times 100$, where $[CL]_o$ is the initial concentration of monomer and [PCL] is the concentration of the polymer at time t, and was evaluated by the formula:

$$\% \text{ Conversion} = \frac{IOCH_{2polymer}}{(IOCH_{2monomer} + IOCH_{2polymer})} * 100$$

Where, $IOCH_{2polymer}$ is the intensity of OCH_2 protons of the polymer at 4.0 ppm, and

$IOCH_{2monomer}$ is the intensity of OCH_2 protons of the monomer at 4.2 ppm of respective spectra. The polymers were purified by dissolving the crude products in CH_2Cl_2 followed by addition of cold methanol. A white precipitate was formed, which was isolated by filtration and dried to constant weight prior to analyses by size exclusion chromatography (Silvernail *et al.*, 2007).

3.6: Kinetic experiments

Kinetic experiments were carried out by withdrawing polymer samples (approx. 0.2 mL) at regular intervals using a syringe and quickly quenched by rapid cooling into vials which were then analyzed by ^{1}H NMR spectroscopy. The observed rate constants, K_{obs}, were extracted from the slopes of the lines of best-fit to the plots of $\ln[CL]_o/[CL]_t$ vs time (Chen *et* al., 2005).

3.7. Analysis of polymers using size exclusion chromatography (SEC), ^{1}H NMR spectroscopy and mass spectrometry.

The sample solutions were filtered *via* syringe through 0.45 μm nylon filters before analyses. The SEC instrument consists of a Waters 1515 isocratic HPLC pump, a Waters 717plus auto-sampler, Waters 600E system controller (run by Breeze Version 3.30 SPA) and a Waters in-line Degasser AF. A Waters 2414 differential refractometer was used at 30 °C in series with a Waters 2487 dual wavelength absorbance UV/Vis detector operating at variable wavelengths. Tetrahydrofuran (THF, HPLC grade, stabilized with 0.125% BHT) was used as eluent at flow rates of 1 mL min^{-1}. The column oven was kept at 30 °C and the injection volume was 100 μL. Two PLgel (Polymer Laboratories) 5 μm Mixed-C (300x7.5 mm) columns and a pre-column (PLgel 5 μm Guard, 50x7.5 mm) were used. Calibration was done using narrow polystyrene standards ranging from 580 to 2x10^6 g/mol. All molecular weights were reported as polystyrene equivalents (Börner *et al.*, 2009a). The polymers were also characterized by ^{1}H NMR spectroscopy and electron-spray ionization mass spectrometry (ESI-MS) for the determination of the polymer end groups.

CHAPTER FOUR

RESULTS AND DISCUSSION

4.1: Syntheses and characterization of zinc(II) and copper(II) complexes

The complexes were synthesized by the reaction of compounds **L1** and **L2** with either zinc acetate or copper acetate in a 1:1 mole ratio resulting in the formation of the corresponding complexes **D1, D2, D3** and **D4** (Figure 18). The complexes were isolated in moderate to good yields, 62-81%.

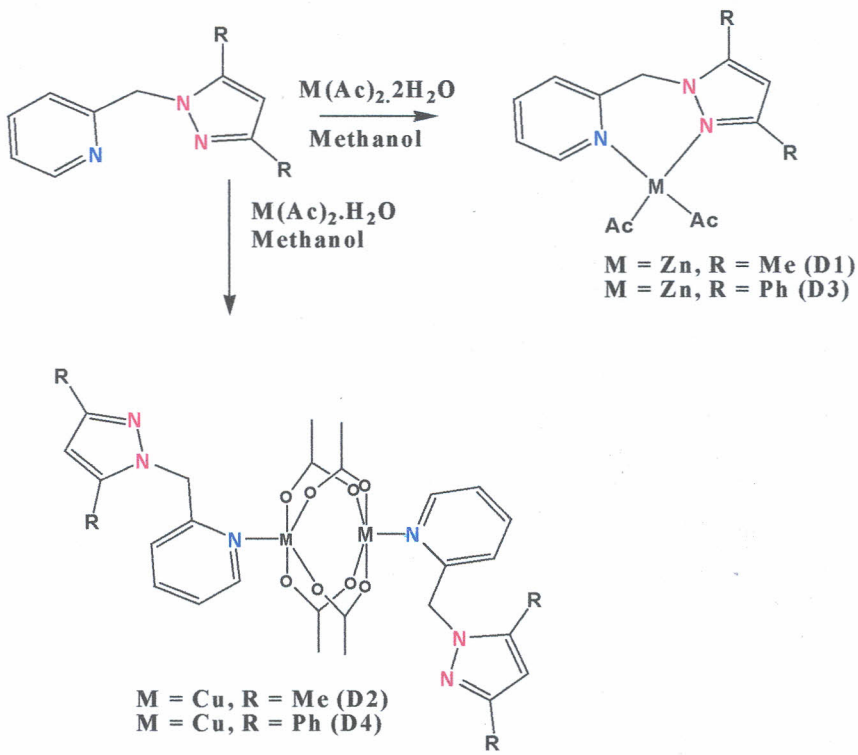


Figure 18: Sythetic protocol of pyrazolyl Zn(II) and Cu(II) complexes **D1-D4**

The ^{1}H NMR was carried for (**D1**) and (**D3**), and the spectra were inspected for complexation. It was done by comparing the signature peaks in the free ligands and the complexes. For example, for the ^{1}H NMR spectrum of **L1** (Figure 19) gave signature peaks of the two methyl groups at 2.16 and 2.24 ppm, the ^{1}H NMR spectrum of the corresponding complex **D1** (Appendix 2) showed a downfield shift in the peaks at 2.31 and 2.36 ppm respectively. These shifts were indicative of ligand coordination to the zinc metal atom that resulted in electron deshielding. As well, the spectra of complexes **D1** and **D3** showed a singlet peak at about 2.10 ppm, diagnostic of the acetate protons. Selected ^{1}H NMR peak frequencies of ligand **L1** and its corresponding complexes **D1** given in Table 3.

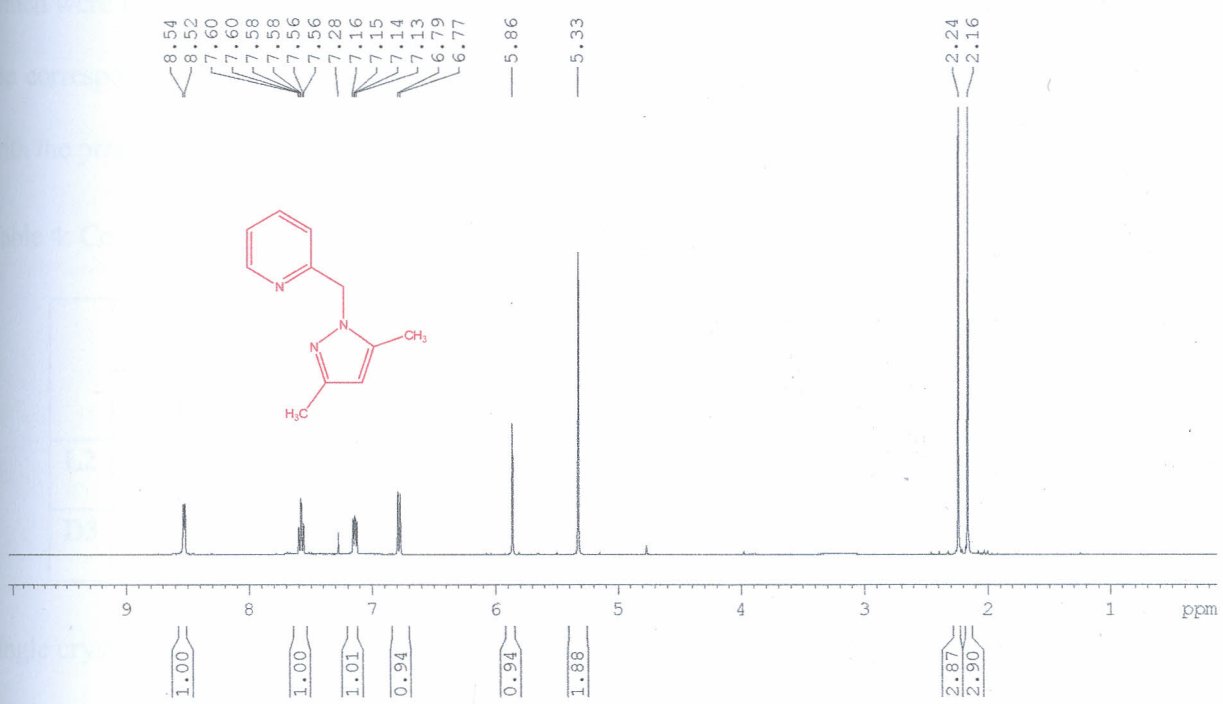


Figure 19: ^{1}H NMR spectrum of ligand **L1**

	Chemical shift (ppm)							
	-CH_2 linker	CH_3-pz	CH_3-pz	1H-pz	1H-py	2H-py	3H-py	4H-py
L1	5.33	2.16	2.24	5.86	6.77	7.15	7.58	8.54
D1	5.46	2.31	2.36	5.93	7.30	7.43	7.94	9.07

The difference in ^{1}H NMR spectra for (**L2**) and (**D3**) proved complexation. Depicted by the peaks of four protons of the phenyl groups of **L2** at 7.40 and 7.64 ppm, while of the corresponding complex **D3** showed a downfield shift of the peaks at 7.44 and 7.86 ppm respectively (Table 4). A similar trend are observed in the four hydrogen peaks of pyridine, which were reported at 6.78, 7.16, 7.58 and 8.54 ppm in **L2** and 7.05, 7.40, 7.70 and 8.63 ppm in the corresponding complex **D3**. Elemental analyses data of all the complexes were consistent with the proposed structures in Figure 18 and also established their purity.

Table 4: Comparative data of chemical shifts for **L2** versus the corresponding complex **D3**

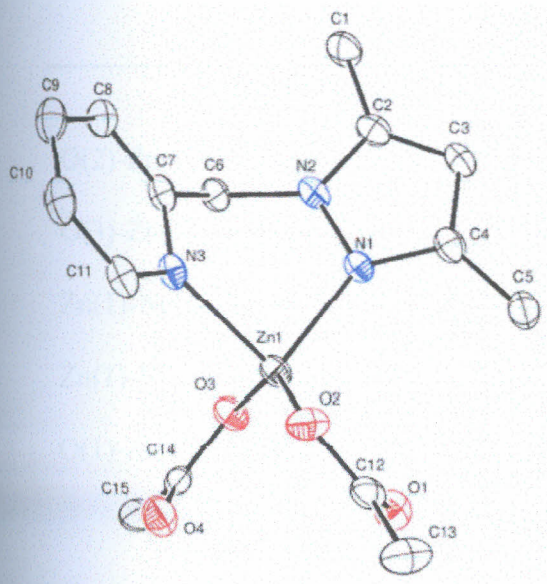
				Chemical shift (ppm)				
	-CH_2 linker	1H-pz	1H-py	2H-py	4H-ph	3H-py	4H-ph	4H-py
L2	5.54	6.70	6.78	7.16	7.40	7.58	7.64	8.54
D3	5.59	6.72	7.05	7.40	7.44	7.70	7.86	8.63

Single crystals of complexes **D1** and **D4** suitable for X-ray crystallography analyses, were grown by slow diffusion of hexane into a dichloromethane solution of the complexes. Data collection and structure refinement parameters given in Appendix 1, Figures 20 and 21 show the molecular structures, while Tables 5 and 6 shows selected bond parameters for **D1** and **D4** respectively.

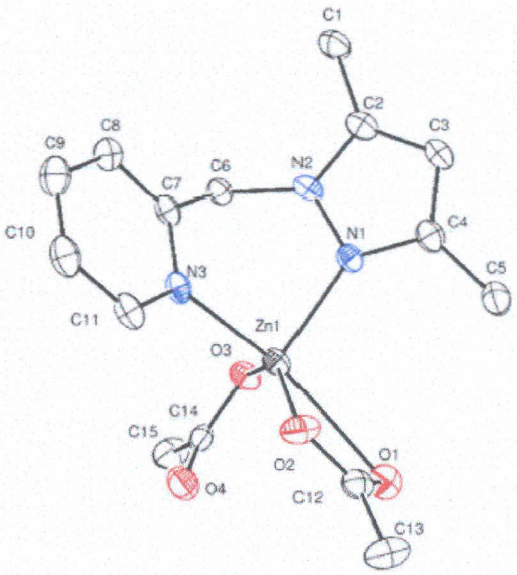
In the solid structure of **D1**, **L1** adopts a bidentate coordination mode. The acetate as a ligand

displays a wide variety of binding modes; monodentate, bidentate and anisodentate. It can be comparable to carbonate and nitrate ligands (Parkin, 2004). Due to this flexibility in its coordination behaviour, therefore we can deduce the various geometries in **D1**. The geometry around the Zinc(II) in **D1** (Figure 20**a**) is fourfold co-ordination, which best described as distorted tetrahedral, due to monodantate behavior of acetate. In **D1** (Figure 20**b**) Five-coordination sphere to give a trigonal bipyramidal geometry, in the case of bidentate coordination of the anisodentate acetate ligand and in **D1** (Figure 20**c**) six-fold coordinated due to two bidentate acetate ligands, generating a distorted octahedral coordination environment. The bond angles around the Zinc(II) of between 89.99(6)° for N(1)-Zn-N(3) to 141.14(6)° for O(3)-Zn-O(2) significantly deviate from 109° expected for a tetrahedral geometry. The distortion could be probably due steric restrictions imposed by **L1** and flexibility of the acetate ligand.

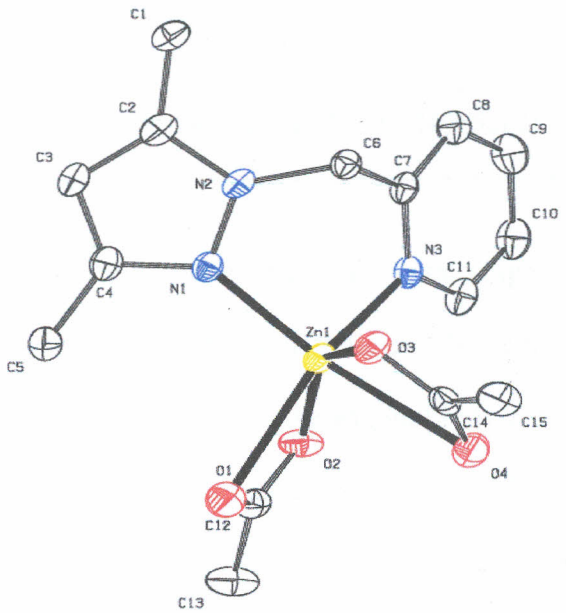
These zinc(II) acetato complexes stabilised by pyrazole-pyridine hybrid ligands are comparable to the already reported bipyridine complex [Zn_2(1,1,2,2-tetrakis(2-pyridyl)-ethane)$(OAc)_4$] (Steel and Sumby, 2003), ferrocenylpyrazolyl (Obuah *et al.,* 2015). The Zn-O distances of this pyrazole-pyridine complexes (1.9653(8) Å), (1.9649(13) Å) lie in the same range as those in pyridyl complex (1.946(2), 1.974(2) Å), however, O(1)-Zn(1), 2.566(2) Å is slightly longer. The zinc(II) pyrazole-pyridine complex bonds of (2.066(2) Å) and (2.102(2) Å) lies in the same range with (2.094(2) Å) and (2.119(2) Å) Zn-Npy bonds of the pyridyl complex (Börner *et al.,* 2009b) as well they are in the same range as ferrocenylpyrazolyl bond lengths of (2.100(3) Å), (2.049(3) (Obuah *et al.,* 2015).



(a)



(b)



(c)

Figure 20: Molecular structure of complex **D1** showing the four-coordinate (a), five coordinate (b) and six coordinate (c) geometries drawn with 50% probability thermal ellipsoids. Hydrogen atoms omitted for clarity.

	Bond lengths [Å]		Bond angles [°]
O(2)-Zn(1)	1.9653(8)	O(3)-Zn(1)-O(2)	141.14(6)
O(3)-Zn(1)	1.9649(13)	O(3)-Zn(1)-N(1)	96.89(7)
Zn(1)-N(1)	2.066(2)	O(2)-Zn(1)-N(1)	115.81(7)
Zn(1)-N(3)	2.102(2)	O(3)-Zn(1)-N(3)	103.52(7)
O(1)-Zn(1)	2.566(2)	O(2)-Zn(1)-N(3)	97.21(7)
		N(1)-Zn(1)-N(3)	89.99(6)
		O(3)-Zn(1)-O(2)	141.14(6)
		O(3)-Zn(1)-N(1)	96.89(7)
		O(2)-Zn(1)-N(1)	115.81(7)
		O(3)-Zn(1)-N(3)	103.52(7)

Complex **D4** is a binuclear species bridged by four acetato ligands. Each Cu(II) centre is coordinated by the four oxygen atoms of four acetato ligands bridging the two copper(II) centres to give two eight-membered rings. To complete the trigonal bipyramidal coordination sphere of each metal atom, a non-bridging Npy-donor of **L2** occupies the fifth coordination site; however, the species is asymmetrical in nature (Figure 21). The bond angles of 90.93(4)° and 91.55(4)° for O(4)-Cu(1)-O(3) and O(1)-Cu(1)-O(2) respectively in **D4** are illustration of distortion from expected bond angle of 90° for an trigonal bipyramidal geometry (Table 6). The molecule has a crystallographic C_2-symmetry axis passing through C24 and C25 rendering many of the atoms symmetrical equivalent.

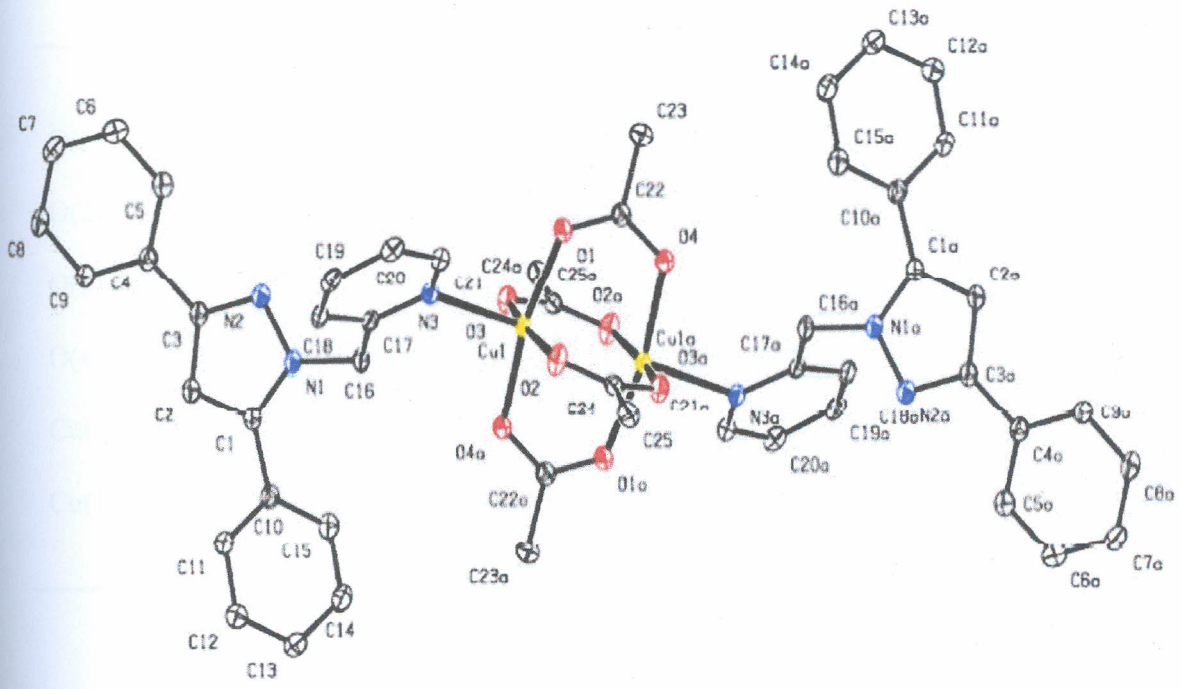


Figure 21: Molecular structure of the paddle wheel copper(II) complex **D4** drawn with 50% probability thermal ellipsoids. Hydrogen atoms are omitted for clarity.

A closer examination of the structure reveals that the bulk part of the ligand resides away from the metal center. The average Cu-Npyridine and Cu-Oacetate bond distances of 2.2138(10) Å and 1.9775(9) Å are comparable to those reported for the 2-amino pyridine Copper(II) complex of 2.0248 (3) Å and 1.991(4) Å respectively (Casarin *et al.*, 2005; Judas, 2005). As well Cu-Oacetate bond distances 1.9775(9) Å are in same range as Cu-O benzoate bond distances 1.9855(15) Å of Bis(3,5-dimethylpyrazole) Copper(II) complex (Appavoo *et al.*, 2014). The Cu-Cu distance of 2.5316(6) Å in **D4** is slightly shorter than the average Cu-Cu lengths of 2.671(2) Å reported in literature (Harding *et al.*, 1991; Casanova *et al.*, 1997; Sarma *et al.*, 2010)

	Bond lengths [Å]		Bond angles [°]
O(1)-Cu(1)	1.9748(9)	O(3)-Cu(1)-O(4)	90.93(4)
O(2)-Cu(1)	1.9875(9)	O(4)-Cu(1)-O(1)	168.06(4)
O(3)-Cu(1)	1.9716(9)	O(3)-Cu(1)-O(1)	87.12(4)
O(4)-Cu(1)	1.9665(9)	O(4)-Cu(1)-(N(3)	98.52(4)
Cu(1) N(3)	2.2138(10)	O(1)-Cu(1)-N(3)	93.34(4)
Cu(1)-Cu(1)#	2.6532(3)	O(2)-Cu(1)-N(3)	89.85(4)

4.2: Kinetics of the ring-opening polymerization of ε-caprolactone

Preliminary investigations of complexes **D1-D4** as catalyst in the ring opening polymerization (ROP) reactions of ε-CL were performed at 110 °C in bulk using [M]/[I] ratio of 100:1. Under these conditions, all the complexes exhibited significant catalytic activities within 24 h for **D1** and **D3** and 48 h for **D2** and **D4** (Figure 22, Table 7). Having established that the complexes form effective catalysts in the ROP of ε-CL, detailed mechanistic and kinetics studies were performed in order to gain insight into the kinetics of the reactions and influence of catalyst structure, and reaction conditions on catalyst activity and polymer properties.

Table 7: Summary of ε-CL polymerization data by complexes **D1-D4**[a]

Catalyst	time (h)	Conversion (%)	Mw(g/mol)[b]	Mn (g/mol)[c]	PDI[c]	IE[d]
D1	24	43	4902	1 982	2.6	0.4
	32	84	9576	2 413	2.58	0.31
	48	94	10716	2 928	3.23	0.27
D2	48	60	6840	n.d	n.d	n.d
	72	82	9348	n.d	n.d	n.d

	96	86	3648	n.d	n.d	n.d
D3	4	33	3762	2 121	3.13	0.56
	8	48	5472	2 454	3.24	0.45
	12	59	6726	2 845	3.48	0.42
	24	92	10488	3 853	3.33	0.37
	36	98	11 172	4 111	3.74	0.37
	48	99	11 286	4 726	3.92	0.42
D4	48	78	8892	2 7 49	2.8 4	0.3 1
	72	93	10602	3 814	3.52	0.36
	96	92	10716	4 652	3.96	0.43
D1[e]	48	32	3648	2 274	3.12	0.63
	72	82	9348	3 413	3.17	0.37
D3[e]	12	45	5130	3 089	3.82	0.61
	24	73	8322	3 338	3.14	0.4
	48	98	11172	4 365	3.27	0.39

[a]Reaction conditions, $[CL]_o$, 0.01 mol, temperature, 110 °C, bulk polymerization.

[b]Molecular weight determined by ^{1}HNMR (mol wt of CL × $[CL]_0/[catalyst]_0$ × % yield).

[c]Molecular weight average and polydispersity index (PDI) determined by GPC relative to polystyrene standards.

[d]Catalyst efficiency = Mwexp/Mwcalc where Mwcalc = Mw(monomer) x $[CL]_0/[I]$ x $[PCL]/[CL]_0$ + Mw(chain-end groups).

[e]Addition of second equivalent of ε-CL without adding the catalyst.

[n.d]Not determined

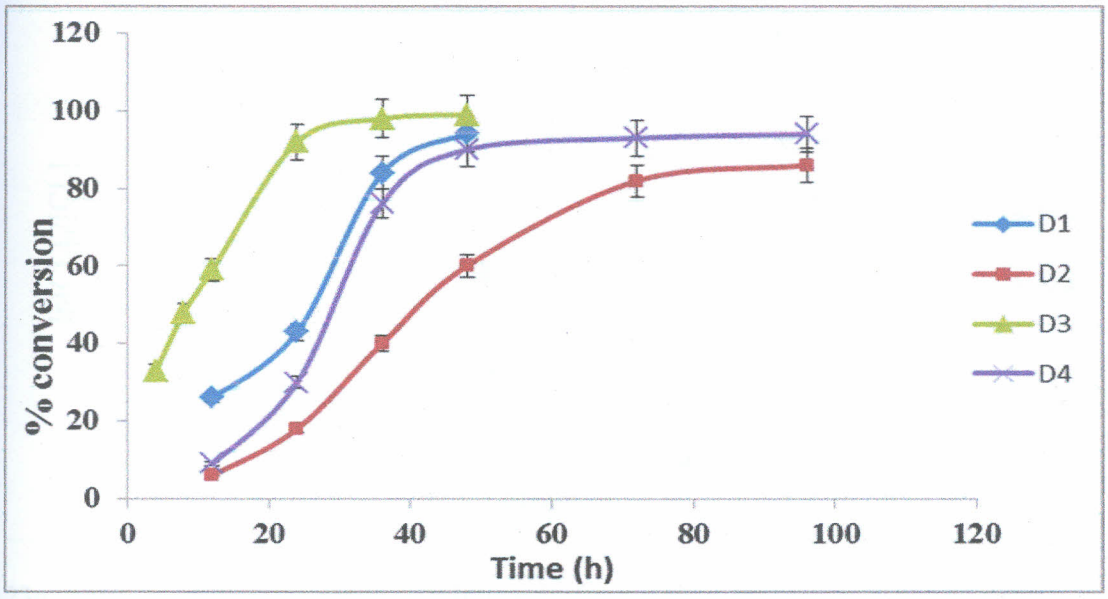


Figure 22: Bulk polymerization of ε-CL to PCL with time for catalyst initiators **D1-D4** at $[CL]_o/[I] = 100$, [CL] = 0.01 mol, [I] = 0.0001 mol.

Kinetics of the ε-CL polymerization was investigated for complexes **D1-D4** by monitoring the reactions using ^1H NMR spectroscopy. Sampling was done at regular intervals and percentage conversions of ε-CL to PCL determined by comparing the intensity of the PCL signals at 4.0 ppm to that of the ε-CL monomer at 4.2 ppm (Appendix 3). A summary of the polymerization data is given in Table 8. A plot of $\ln[CL]_o/[CL]_t$ versus time gave a linear relationship consistent with a pseudo first order kinetics with respect to ε-CL for all the complexes (Figure 23). The kinetics of the ε-CL polymerization reactions thus proceeded according to pseudo first order kinetics with the respect to ε-CL as shown in equation (1).

$$\frac{-d[CL]}{dt} = k[CL]\frac{-d[CL]}{dt} = k_p[CL] \qquad (1)$$

Where $k = k_p[I]^x$, k_p = rate of chain propagation and I = catalyst; x = order of reaction.

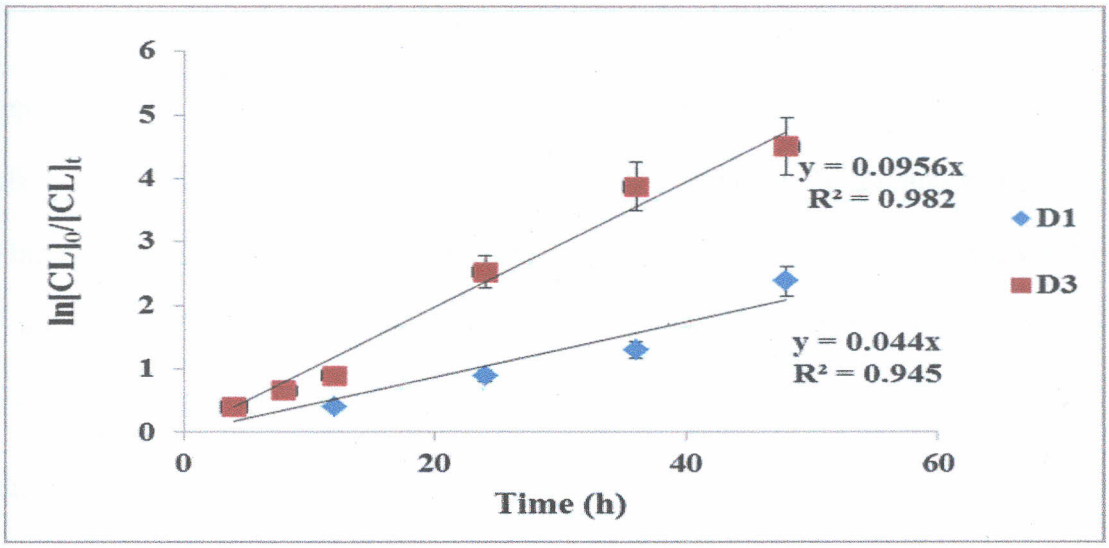


Figure 23a: First order kinetic plots of ln[CL]o/[CL]t vs time for Zn complexes **D1** and **D3** in bulk polymerization of ε-CL at 110 °C, $[CL]_o$, 0.01 mol, $[CL]_o/[I]$ = 100.

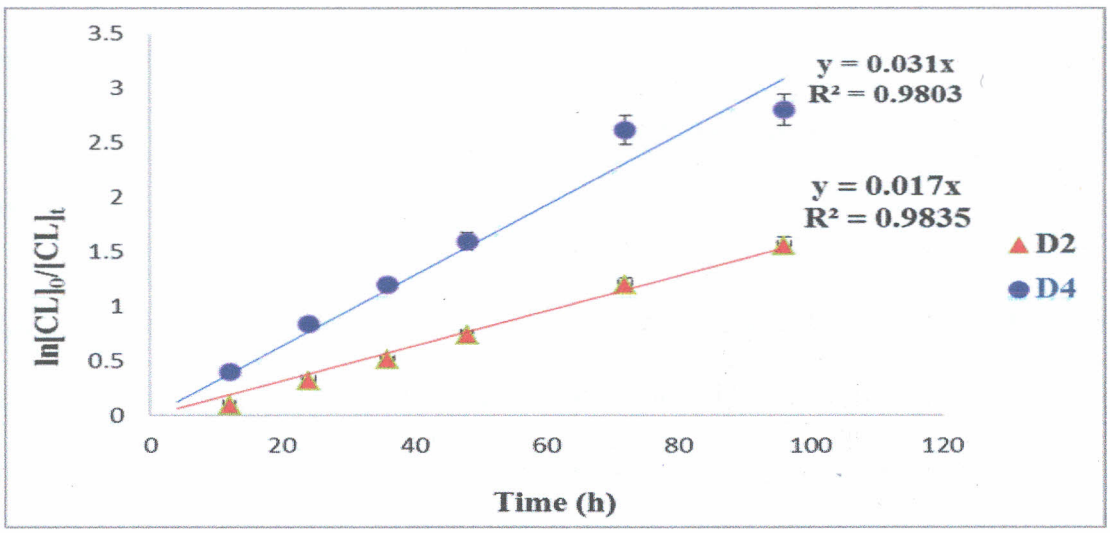


Figure 23b: First order kinetic plots of ln[CL]o/[CL]t vs time for Cu complexes **D2** and **D4** in bulk polymerization of ε-CL at 110 °C, $[CL]_o$, 0.01 mol, $[CL]_o/[I]$ = 100.

The rate constants for catalysts **D1-D4** were extracted from Figure 23a,b and obtained as 0.044 h^{-1} (**D1**), 0.017 h^{-1} (**D2**), 0.096 h^{-1} (**D3**) and 0.031 h^{-1} (**D4**). Catalyst **D3** was thus the most active while **D2** was the least active. Higher activities for Zinc(II) catalysts **D1** and **D3** in comparison to the copper(II) analogues **D2** and **D4** are consistent with literature reports (Labet and Thielemans,

2009, Appavoo *et al*, 2014). More evident was the increase in catalytic activity with increase in steric bulk of the pyrazolyl ligand in **D1- D4**. For instance, replacing the Methyl groups in **D1** with the bulkier Phenyl groups in **D3** resulted in a two-fold increase in the rate of reaction from 0.044 h^{-1} to 0.096 h^{-1} respectively. This observation agrees with reported (Silvernail *et al.*, 2007, Obuah *et al.,* 2015).

Comparatively, the rate constants in the polymerization of ε-CL for **D1-D4** are lower than the active catalysts reported (Williams *et al.*, 2003; Chen *et* al., 2005). A number of very active zinc(II) catalysts are multinuclear and contain alkoxides as the initiating groups. For example, the trinuclear Zinc(II) complex exhibits a rate constant of 0.0508 s^{-1} in the polymerization of ε-CL (Chen, *et al.*, 2005). Despite the relative low activities of **D1-D4**, they were found to be more active than the aluminium alkoxide catalyst reported which displays apparent rate constant of 0.067 day^{-1} (Zhong *et al.*, 2003).

Further kinetics was performed to assess the order of the reaction with respect to **D1** and the overall rates of reactions. This was done by carrying out the polymerizations reactions at different catalyst concentrations at constant concentration of ε-CL (Appendix 4). A plot of $\ln[k_{obs}]$ versus ln[**D1**] gave a linear relationship consistent with a first-order dependency of reaction on **D1** (Figure 24).

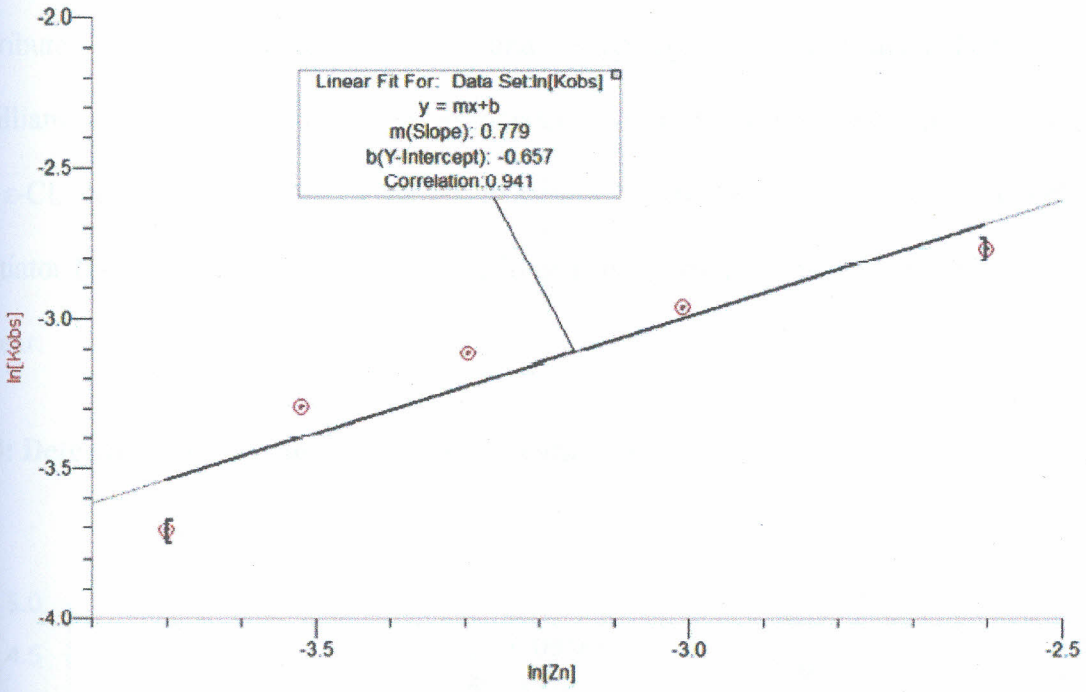


Figure 24: Linear plots of ln[k_{obs}] vs ln[**D1**] polymerization of caprolactone at $[CL]_o$ = 0.01 mol, 110 °C for the determination of order of reaction with respect to **D1**.

The order of the reaction with respect to **D1** was thus extracted from the plot of ln[k_{obs}] versus ln[**D1**] and obtained as 0.8. Fractional order of reaction with respect to the catalyst had been previously observed and is believed to be due to complicated aggregation of the active sites during polymerization reactions (Kowalski *et al.*, 2001). Thus, the overall rate law for ε-CL the ROP by **D1** can be represented by equation (2).

$$\frac{-d[CL]}{dt} = kp\,[CL][D1]^{0.8} \qquad (2)$$

This rate law is consistent with a mechanism involving a coordinative insertion at a single Zn(II) site. It is therefore apparent that only one Zn-$O_{acetate}$ in complex **D1** acts as the initiating group. A closer examination of ln[*kobs*] versus ln[**D2**] showed the presence of an induction period

especially at low catalyst concentrations (Appendix 5). This behaviour has been largely attributed to rearrangement of the coordinative aggregates in the catalyst (Dubois *et al.*, 1991; Williams *et al.*, 2003). This may be associated with dissociation of the Cu-Oacetate bonds prior to ε-CL coordination. Thus, attempts to determine the order of the reaction with respect to initiator **D2** were unsuccessful due to the longer induction periods, which rendered the plots non-linear.

4.3: Determination of the stability of the catalysts

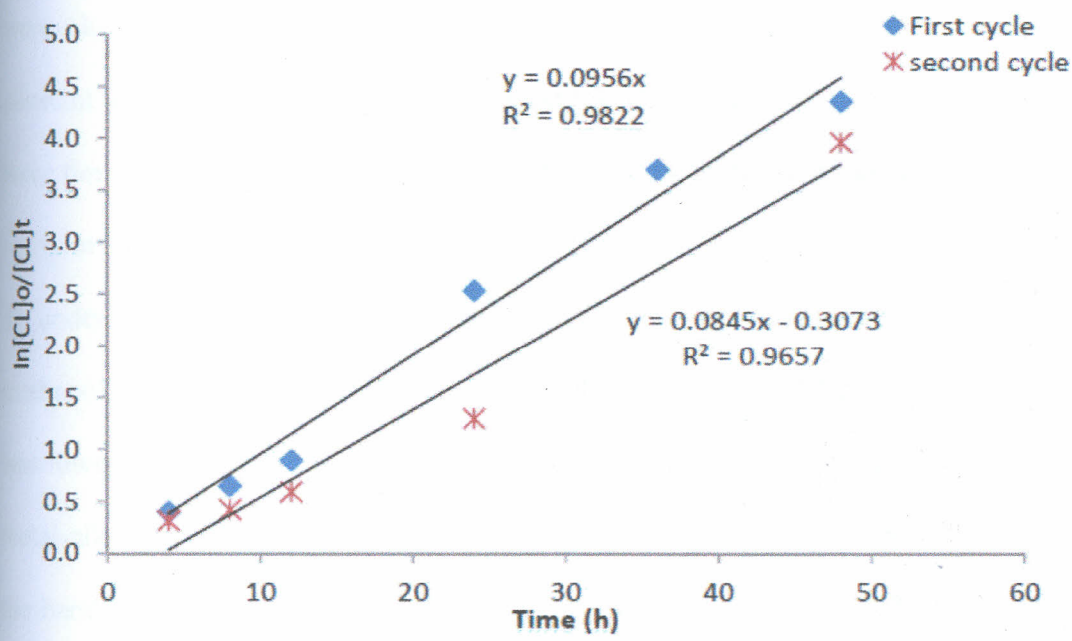


Figure 25: First order kinetic plots of $\ln[CL]_o/[CL]_t$ vs time of the first and second cycle experiments for **D3**, at 110 °C, $[CL]_o$, 0.01 mol, $[CL]_o/[I] = 100$. Equivalent amount of ε-CL monomer was added in the second cycle without adding the catalyst.

To provide the insight into the stability of these systems, a sequential two-stage polymerization of ε-CL was performed using **D1**and **D3** (Table 7, Figure 25). Thus the first cycle ($[CL]_o/[I] = 100$) was allowed to proceed to completion (99%) and another 100 equivalent of ε-CL was added

without adding the catalyst ([CL]0/[I] = 200). For **D3**, rate constants of 0.096 h^{-1} and 0.085 h^{-1} were observed in the first and second cycles respectively (Figure 25). This translates to 12% drop in the catalytic activity of **D3** in the second cycles and therefore confirms its relative stability.

4.4: Effect of temperature and solvent on ε-CL polymerization kinetics

The effect of temperature on the polymerization kinetics of ε-CL by D1 was probed by comparing the activities at 60 °C, 90 °C and 110 °C at $[CL]_o/[D1]$ of 50 (Table 8). At 60 °C, D1 showed very low activity managing a paltry 25% conversion after 48 h. In addition, the reactions were characterized by longer induction periods leading to non-linear plots; hence the rate constant at 60 °C could not be evaluated. At 90 °C, the rate constant was obtained as 0.022 h^{-1}, three times lower than 0.063 h^{-1} recorded at 110 °C. It is therefore apparent that D1-D4 are only active at elevated temperatures.

To understand the influence of solvent on the polymerization reactions, activities of **D1** in bulk, methanol and toluene solvents were compared. The k_{obs} of 0.063 h^{-1} in the bulk polymerization was lower than 0.186 h^{-1} recorded in methanol solvent. This is consistent with the formation of a metal-alkoxide (M-OEt), which is known to give active initiating groups (Chen *et al.,* 2005). On the hand, use of the toluene solvent resulted in a drop in k_{obs} to 0.026 h^{-1}. At this stage, it is unclear why reactions in toluene resulted in decreased activity; however, one hypothesis on the same is that the use of toluene may reduce the concentrations of the reactants hence lower rates of collisions of the molecules as compared to the bulk reactions.

4.5: Molecular weight and molecular weight distribution of polycaprolactone (PCL)

The molecular weight and molecular weight distribution of the polymers were determined by Gel Permeation Chromatography (GPC) and compared to the theoretical values obtained from ^{1}H NMR calculations (Tables 7 and 8). Generally, low to moderate molecular weight polymers between 1,982 g/mol to 14,568 g/mol were obtained. Consistent with living polymerization behaviour, molecular weights increased with percentage conversion (Figure 26). For instance, molecular weights of 2,121 g/mol and 4,726 g/mol were obtained at 33% and 99% conversions respectively for **D1**.

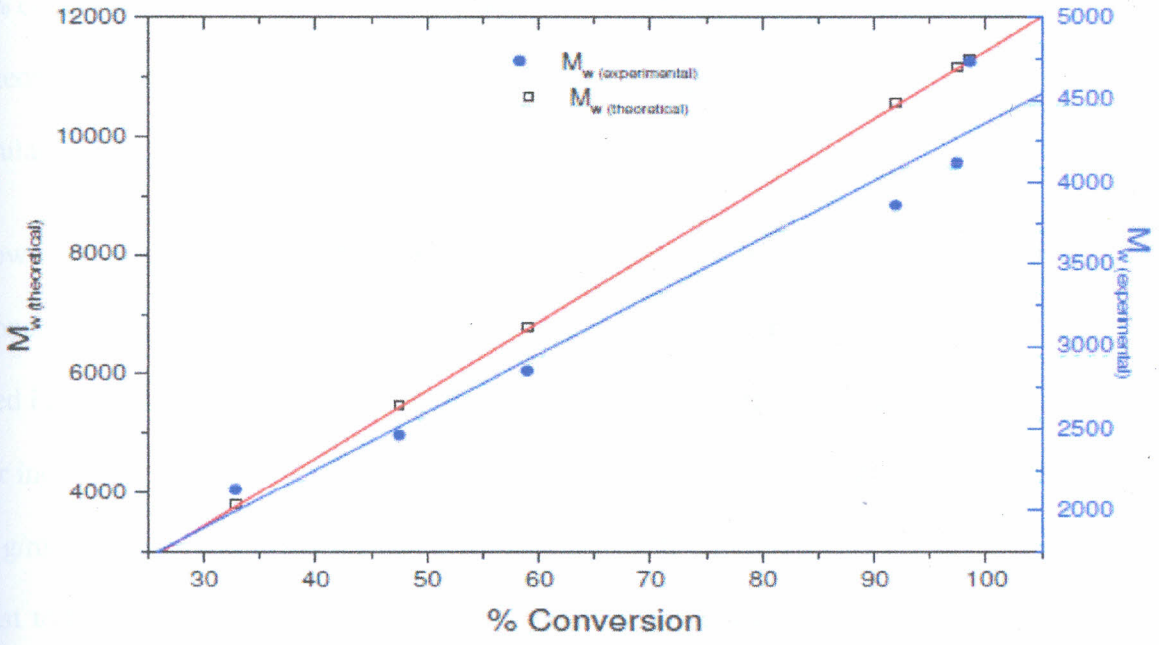


Figure 26: Plot of experimental and calculated Mw of PCL vs % conversion for the bulk polymerization of ε-CL by **D3**. $[CL]_0$ = 0.01 mol, 110 °C, [D3] = 0.0001 mol. The empty rectangles show the theoretical M_w calculated from ^{1}H NMR spectra while the block rectangles show the experimental M_w determined by SEC.

The living polymerization nature (growing a polymer chain to a terminate) using **D1** was further augmented by the observed increase in molecular weights with increase in $[CL]_o/[\mathbf{D1}]$ ratio. For example, an increase in the $[CL]_o/[\mathbf{D1}]$ from 50 to 125 resulted in a concomitant increase in molecular weight from 4,610 g/mol to 10,696 g/mol respectively (Table 8, entries 1-3). The highest catalyst efficiency of 1.1 (110%) was obtained at $[CL]_o/[\mathbf{D1}]$ of 75. Despite the linear dependency of molecular weight on ε-CL conversion, the experimental molecular weights were significantly lower than the theoretically calculated values (Figure 26). This was more evident at higher conversions where lower catalyst efficiencies of 0.42 (42%) were reported. For example, at 99% conversion, the experimental molecular weight of 4,726 g/mol was obtained, compared to the theoretical value of 11,294 g/mol. In addition, the polymers exhibited relatively wide molecular weight distributions (2.00-3.48).

The low catalyst efficiencies of **D1-D4** were further confirmed by the two-stage polymerization reactions. As shown in Table 7, addition of the monomer after completion of the first run resulted in a significant drop of molecular weight from 4,726 g/mol (99%) to 3 089 g/mol (45%); a clear indication of growth of a new polymer chain. Indeed the maximum molecular weight of 4,365 g/mol obtained in the second run is lower than 4,726 g/mol reported in the first. This is in contrast to the expected behavior of living polymerization catalysts. For example, Silvernail *et al.* recorded an increase in molecular weight of PCL from 4,200 g/mol (run 1) to 10,400 g/mol (run 2) (Silvernail *et al.*, 2007). These observations point to lack of controlled ε-CL polymerization by **D1-D4**. A number of factors could be responsible. One, the use of acetate ligand as the initiating group has been reported to give low molecular weight and broad PDI in comparison to the alkoxide initiators (Chamberlain *et al.*, 2001). Indeed polymers obtained in

methanol solvent exhibited relatively narrow PDI of 2.00, indicating the presence of M-OCH_3 initiating group (Table 8, entry 5). The flexibility of the ligand backbone and varied coordination modes of the acetate ligands in **D1-D4** may result in multiple active sites during the polymerization process due to change in the molecular symmetry (Shapiro *et al.*, 1994; Waymouth and Coates 1995). As discussed above, complex **D1** can adopt either a tetrahedral, a trigonal bipyramidal or octahedral geometry depending on the coordination mode of the acetate ligand.

Table 8: Effect of catalyst concentration, temperature and solvent on ROP of ε-CL using catalyst **D1**[a]

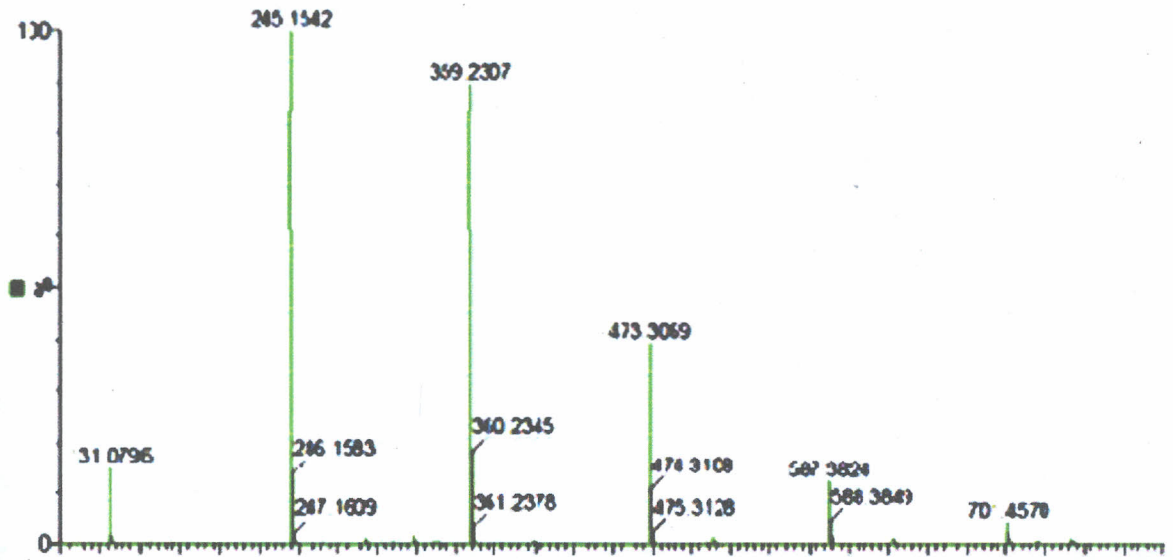
Entry	$[CL]_o/[D1]$	Conversion(%)[b]	K_{obs} (h^{-1})	Mw[c]	PDI[c]	IE[d]
1	50	90	0.063	4 610	2.82	0.9
2	75	85	0.052	8 008	2.96	1.1
3	125	92	0.037	10 696	3.23	0.81
4	150	94	0.01	14 568	3.25	0.91
5	50[e]	99	0.189	2 407	2.00	0.43
6	50[f]	99	0.026	4 193	2.42	0.74
7	50[g]	80	0.022	3 119	2.52	0.68

[a]Reaction conditions, $[CL]_o$, 0.01 mol, temperature, 110 °C, bulk polymerization; [1]Molecular weight determined by [1]HNMR; [b]Maximum conversions achieved; [c]Molecular-weight average and polydispersity index (PDI) determined by GPC relative to polystyrene standards. [d]catalyst efficiency = Mw_{exp}/Mw_{calc} where $Mw_{calc} = Mw_{(monomer)} \times [CL]_o/[I] \times [PCL/[CL]_o + Mw_{(chain\text{-}end\ groups)}$; [e] solvent, methanol; [f] solvent, toluene; [g] temperature, 90 °C.

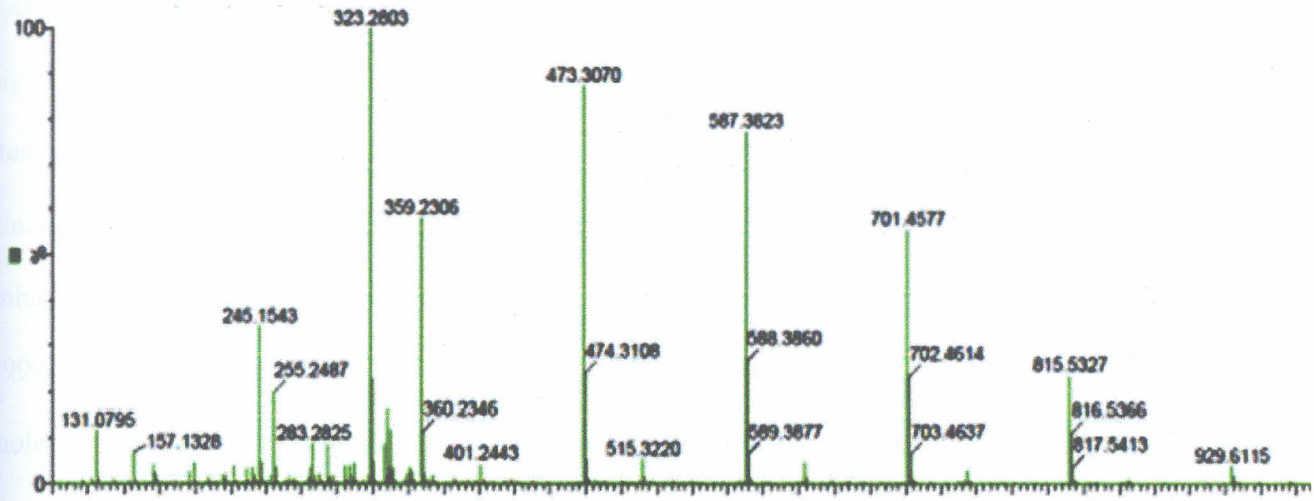
A more possible route to the formation of low molecular weight and broad molecular weight distributions of PCL obtained is *via* the transesterification reactions (Kricheldorf *et al.*, 1985; Dubois *et al.*, 1991; Chamberlain *et al.*, 2000). This competes with ring open polymerization to give wide PDI as observed. The concerted low molecular weight and broad PDI confirm the

presence of both intramolecular (low molecular weights) and intermolecular (broad PDIs) transesterification reactions. At higher retention times, broad distributions observed could originate from the presence of both cyclic and linear oligomers (Appendix 10-12).

In order to confirm the occurrence of transesterification reactions, ESI-MS of the polymers obtained after 4 h and 48 h were recorded (Figure 27). The polymers showed m/z peaks corresponding to the formula {(nCL + 17)} consistent with OH end groups (figure 27a). For example, the m/z peak of 701 corresponds to {(114 x 6) + 17}. Significantly, the spectrum of the crude products obtained after 48 h (Figure 27b) showed smaller peaks corresponding to molecular masses of {(nCL+1/2CL)} repeat units. As an illustration, the m/z peak of 515 corresponds to {(4 x 114) + 57}. This confirms that intermolecular ester-exchange reactions do occur to some extent especially at longer reaction times (Williams *et al.*, 2003). The PDIs of 3.13 and 3.92 reported after 4 h and 48 h respectively reinforces this assumption.



(a)



(b)

Figure 27: ESI-MS of the crude PCL obtained from (a) catalyst **D1**; $[CL]_o/[D1] = 100$, time = 4 h; (b) catalyst D1, [CL]0/[1] = 100, time 48 h. The lager peaks corresponds to (n(CL) + 17) indicating OH as the end group. The smaller peaks in (b) have masses corresponding to (n(CL) + 1/2CL) associated with repeating units from intermolecular transesterification reactions.

The type of solvent used also affected the polymer weight and molecular weight distribution. A higher molecular weight of 4,193 g/mol was obtained in reactions performed in toluene compared 2,407 g/mol when methanol was used as the solvent (Table 8, entries 5 and 6). This is consistent with the lower rate constant observed when toluene was used as the solvent. As reported in literature, reduced catalytic activities would decrease the number of polymer chains, thus increase molecular weight at a fixed conversion (Odian, 1991; Ovitt, and Coates, 2000). At higher temperatures, catalyst activity was lower thus decreasing the number of polymer chains, hence higher molecular weights of the resulted polymers. This observation is in good agreement with lower molecular weight of 3,119 g/mol reported at 90°C compared to 4,610 g/mol at 110°C

Catalysts **D3** and **D4**, bearing the bulky phenyl groups on the pyrazolyl ring, produced relatively higher molecular weight PCL than the corresponding complexes **D1** and **D2** containing the less steric methyl groups (Table 7). For example at 96% conversions, molecular weights of 2,928 g/mol and 4,111 g/mol were obtained for **D1** and **D3** respectively. This could be associated with enhanced chain growth with increase in steric bulk (Temple and Brookhart, 1998; Svejda *et al.*, 1999). However, there was no significant effect of the identity of the metal on polymer molecular weight. For instance, at 99% conversion, **D3** and **D4** produced PCL with molecular weights of 4,726 g/mol and 4,652 g/mol respectively.

4.6: Ring-opening polymerization of D,L-lactide

The solution ring-opening polymerizations of D.L-lactide using the catalysts **D1-D4** were carried at 110 °C in toluene. The amounts of monomer and catalyst were chosen such that the monomer concentration $[M]_o$ = 0.01M and monomer to catalyst ratio [M]:[I] = 100. Polymerization was investigated through inspection of ^{1}H NMR spectrum for monomer (Appendix 6) and ^{1}H NMR spectra for the products (Appendices 7 - 9), the appearance of peaks at 5.1-5.3 ppm in spectra of the products proved polymerization. Conversions were determined by ratio of the integral values of the methine peaks of monomer (δ 5.00) and polymer (δ 5.15). The molecular weight and polydispersity of polylactide (PLA) are measured by gel permeation chromatography (GPC) (Appendices 13 - 16).

Experimental results show low activity in lactide polymerization using **D1-D4**, with **D1** being the most efficient catalyst, having greater than 90 % conversion in 12 h. Generally low molecular weights (1,402 – 4,233 daltons) and relatively narrow PDIs (1.23 – 1.64) were observed from these complexes (Table 9) as compared to previously reported complexes of N-heterocyclic

carbene (Jensen *et al.,* 2005), complexes of β-diiminato (Cheng *et al.,* 1999; Chisholm *et al.,* 2005), complexes of phenoxy-ketimine (Reger et al., 2012), complexes of guanidine-pyridine (Börner *et al.,* 2009b) and complexes of naphthalenyl-aminocyclohexanes (Kwon *et al.,* 2015). This could be due to structural properties (inaccessibility to the metal centre) the strong coordination of the acetate anion, which makes it not to dissociate easily disfavoring coordination of lactide monomer and therefore decelerates the reaction (Börner *et al.,* 2009b). The zinc(II) complexes **D1** and **D3** gave higher molecular weights (4,105 – 4,233 daltons) compared to the corresponding copper(II) catalysts **D2** and **D4** (1,402 – 1,621 daltons). The relatively low polydispersity indices (PDI) of the polymers (Table 9) shows that there is a level of polymerization control with minimal backbiting (chain transfer) reactions (Chen *et al.*, 2005; Grunova *et al.*, 2009, Kwon *et al.,* 2015).

Table 9: Data for the polymerization of D,L- LA by compounds **D1-D4**[a]

Catalyst	Time (h)	%Conv	Mw[b]	Mw[c]	Mn[c]	PDI[c]
D1	4	73	10512	1564	1142	1.36
	12	97	13968	4105	2502	1.64
D2	60	97	13968	1621	1321	1.23
D3	24	95	13680	4233	2664	1.59
D4	60	95	13680	1402	1100	1.27

[a]Reaction conditions, $[LA]_o$, 0.01 mol, temperature, 110 °C, solvent (toluene) polymerization; [b]Molecular weight determined by ^1H NMR (Mol wt of LA × $[LA]_0/[initiator]_0$ × % yield); [c]Molecular weight average and polydispersity index (PDI) determined by GPC relative to polystyrene standards.

The ^1H NMR spectra of the polymers (Appendices 7 - 9), shows peak at 2.4 ppm due to acetate's

The ^{1}H NMR spectra of the polymers (Appendices 7 - 9), shows peak at 2.4 ppm due to acetate's methyl group and peak at 4.4 ppm due to hydroxyl group forming chain end groups, suggesting that the initiation occurs through the insertion of the acetyl alkoxy group from the complexes into lactide, thus the reaction follows the coordination insertion mechanism.

Kinetic studies showed that the polymerization was first-order in monomer regardless of the catalyst used. Generally there were low activities **D1** (0.29 h^{-1}), **D2** (0.06 h^{-1}), **D3** (0.17 h^{-1}) and **D4** (0.04 h^{-1}) with **D1** having highest activity followed by **D3**, **D2** and lastly **D4** (Figure 28).

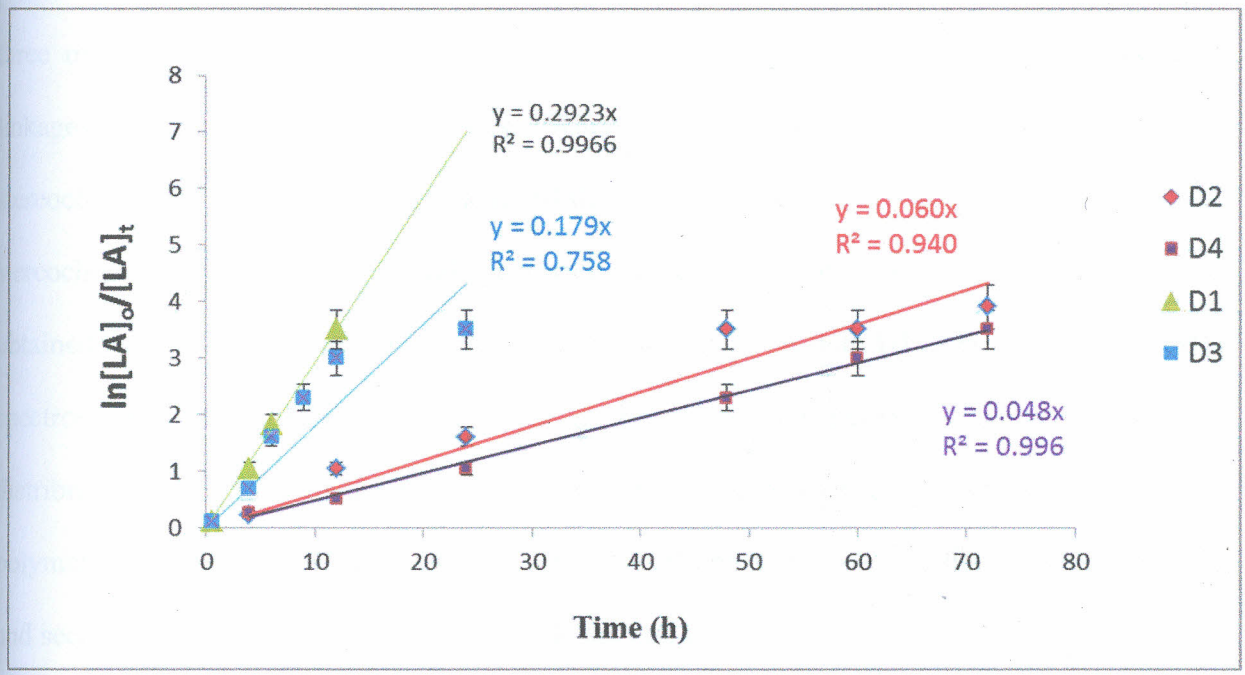


Figure 28: First order kinetic plots of ln[LA]o/[LA]t vs time for compexes **D1**, **D2**, **D3** and **D4** in solvent (toluene) polymerization of LA at 110°C, $[LA]_o$, 0.01 mol, $[CL]_o/[I]$ = 100.

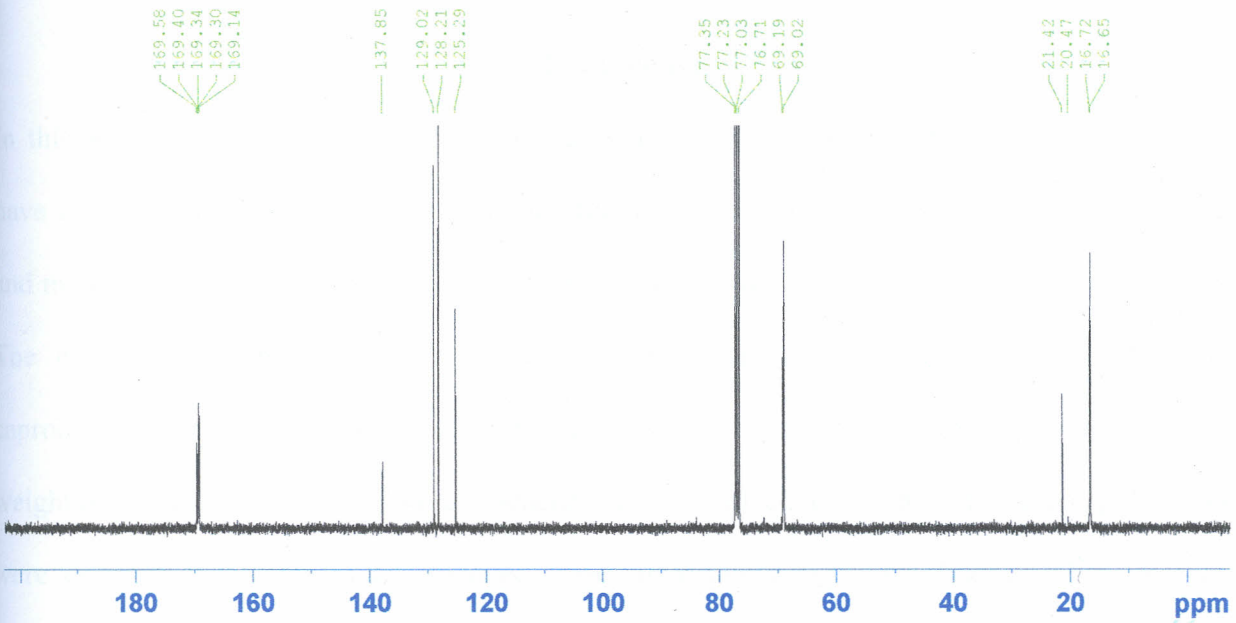
From literature reports, increased ligand bulkiness results in decreased catalyst activity, due to the increased steric shielding of the active metal center (Zhong *et al.*, 2001; Zhong *et al.*, 2002; Albertsson and Varma, 2003, Dechy-Cabaret *et al.*, 2004; Wu *et al.*, 2006, Chen e*t al.*, 2005,

rate constant of 0.17 h^{-1} reported for **D3**, bearing the bulkier phenyl groups. Similary, rate constants of 0.06 h^{-1} and 0.04 h^{-1} were recorded for **D2** and **D4** respectively. The ROP of lactide using complexes **D1**, **D2**, **D3** and **D4** was much faster than ROP of caprolactone contrary to the ROP of the two monomers using zinc and copper complexes of bis-pyrazolyl (Appavoo *et al.*, 2014).

4.7: Tacticity and stereo-regularity of PLAs

Stereo-sequences are sequences of several monomer units of different configuration (triads have three monomer units, tetrads have four units, and so on) labelled according to the type of linkages in the monomer sequences. When two monomers have the same relative stereochemistry, the linkage is isotactic while two consecutive monomers with an opposite stereochemistry give a racemic linkage (syndiotactic). Information on stereo-selectivity was obtained by analysing the product of polymerization of D,L-LA with **D1** after 12 h by ^{13}C NMR spectroscopy. The stereo-sequence are analysed based on tetrad peaks. Tetrad stereo-sequence distribution is sensitive to the methine resonance. Two peaks observed indicate syndiotactic polymerization (Figure 29). First peak (68.90 – 69.10 ppm), includes iii, iis, sis and sii tetrads and second peak (69.10 – 69.30 ppm), include only isi tetrads (Chamberlain *et al.*, 2001; Zhao *et al.*, 2010). Since D,L-lactide monomer was used, we expected heterotactic or stereoblock polymers. However, syndiotactic addition was preferred; this is consistent with the previous works (Thakur *et al.*, 1998; Zhao *et al.*, 2010).

(a)



(b)

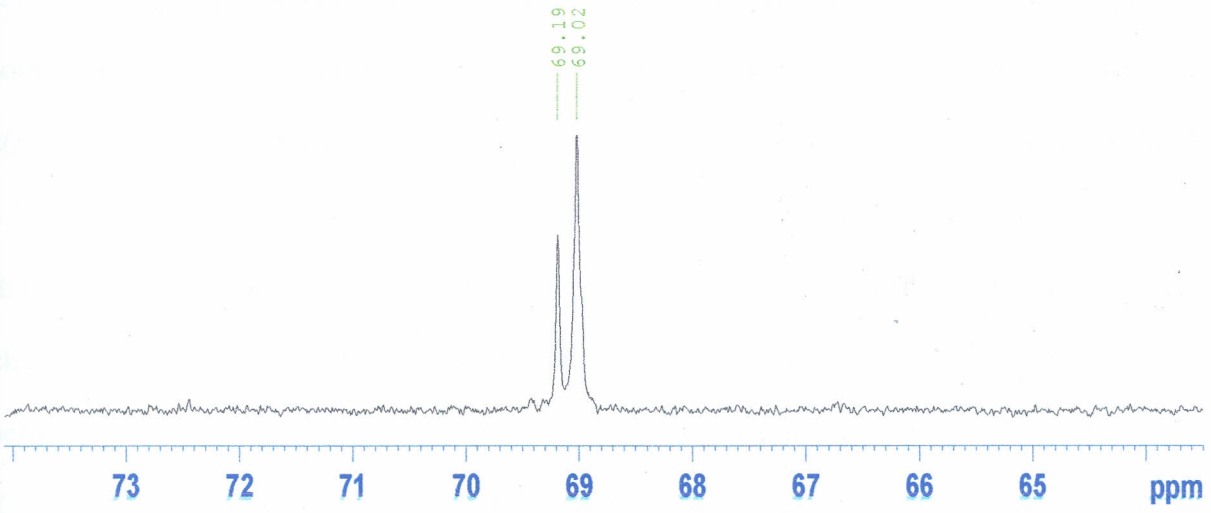


Figure 29: ^{13}C NMR spectrum of (a) PLA catalyzed by **D1**, [M]:[I] ratio 100:1, 12 h (b) is the extrapolation between 65-73 ppm.

CHAPTER FIVE

SUMMARY, CONCLUSIONS AND RECOMMENDATIONS

5.1: Summary

In this work, zinc(II) and copper(II) complexes anchored on (pyrazolylmethy)pyridine ligands have been successfully synthesized and structurally characterized . The ligands adopt bidentate and monodentate coordination modes in the monometallic and bimetallic complexes respectively. The complexes form active catalysts in the ring opening polymerization of lactides and caprolactones. In general, polylactides and polycaprolactone with low to moderate molecular weight of (1,402-14,568 g/mol) were produced. Narrow molecular weight distributions (1.23-1.64) were observed for polylactides whereas, broad molecular weight distributions (2.0-3.9) were observed for polycaprolactones. The kinetics of the polymerization is pseudo-first order in monomer with low rate constants of (0.04-0.29 h^{-1}) for lactides and (0.02-0.09 h^{-1}) caprolactones. Zinc(II) complexes were more active than the corresponding copper(II) complexes in the ROP of both lactides and caprolactones. The nature of ligand influenced the catalytic activities of the resultant complexes with less sterically demanding ligands showing greater activities for lactides. By changing catalyst concentrations, type of solvent and temperature of the reactions, the polymer properties could be regulated; activity of the catalysts increases with elevation of temperature from 60 °C to 110 °C, coordinating solvent increases activity while none coordinating lowers activity.

5.2: Conclusions

In conclusion

i The zinc(II) and copper(II) complexes; diaceto{2-(3,5-dimethylpyrazol-1-ylmethyl)pyridine}zinc(II), diaceto{2-(3,5-dimethylpyrazol-1-ylmethyl)pyridine}copper(II),

diaceto{2-(3,5-diphenylpyrazol-1-ylmethyl)pyridine}zinc(II) and diaceto{2-(3,5-diphenylpyrazol-1-ylmethyl)pyridine}copper(II) were synthesized and characterized.

ii The complexes form active catalysts in the ring-opening polymerization of lactides and caprolactones to give moderate molecular weight polymers. The zinc(II) complexes were more active than the corresponding copper(II) complexes in the ROP of both lactide and caprolactone.

iii Ring-opening polymerization of lactides and caprolactone using the four complexes followed pseudo first order kinetics with respect to the monomer.

iv Higer catalytic activity was observed using methanol as solvent, elevated temperature and lower monomer/catalyst ratio.

5.3: Recommendations

D1, **D2**, **D3** and **D4** are active in ROP of both lactides and caprolactones. From these results, through careful ligand design, more efficient catalyst systems with better control of polymer microstructure could be developed, because they offer a number of advantages: straightforward catalyst synthesis, easy and robust handling. Therefore, it is sufficiently valuable that the following be done for optimization.

i Modify the nature of the ligands size to vary their steric and donor properties in order to fine-tune catalytic performance.

ii Replace the acetate with alkoxide groups. This could result in better control of polymer stereochemistry and chain growth.

iii Extend the catalysis of the synthesised complexes to copolymerization of the lactides with either caprolactones or glycolides.

iv Vary the reaction conditions such as solvents (coordinating), temperature and ratios in order to come up with optimal conditions.

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