Bis(pyrazolyl)pyridine Cu(II) and Zn(II) complexes: Syntheses, Molecular Structures and Polymerization Reactions of *ε*–Caprolactone and Lactides

By

Mnqobi Zikode

(208524167)

Submitted in partial fulfillment of the requirements for the award of Master of Science degree in the School of Chemistry and Physics

College of Agriculture, Engineering and Science

Pietermaritzburg

Supervisor: Dr Stephen. O. Ojwach

Declaration

I, Mnqobi Zikode, declare that the work based on **"Bis(pyrazolyl)pyridine Cu(II) and Zn(II) complexes: Syntheses, Molecular Structures and Polymerization Reactions of ε–Caprolactone and Lactides"** is original work carried out in the school of Chemistry and Physics, university of KwaZulu-Natal, Pietermaritzburg and has not been submitted for the award of a degree or diploma at any university and that all sources used, quoted and referenced have been accredited, indicated and duly acknowledged by complete physical referencing.

……

M. Zikode

As the candidate's supervisor I have/have not approved this thesis/dissertation for submission.

Signed:……. Name:……..... Date: ……

Dedication

Dedicated to Zikode family

Abstract

Reactions of 2,6-bis((3,5-dimethyl-1H-pyrazol-1-ylmethyl)pyridine (**L1**) and 2,6-bis(3,5-dimethyl-***N***-pyrazolyl)pyridine (**L2**) ligands with Zn(II) and Cu(II), acetates and carboxylates (benzoates, 2-chlorobenzoate, & 2-bromobenzoate) in a single pot afforded seven Zn(II) and Cu(II) carboxylate complexes. The complexes [Zn(**L1**)($C_6H_5COO)_2$] (**1**), [Zn(**L1**)(2-Br-$C_6H_4COO)_2$] (**2**), [Cu(**L1**)($C_6H_5COO)_2$] (**3**), [Cu(**L1**)(2-Br-$C_6H_4COO)_2$] (**4**), [Zn(**L2**)($C_6H_5COO)_2$] (**5**), Zn(**L2**)(2-Cl-$C_6H_4COO)_2$ (**6**) and Cu(**L2**)(2-Cl-$C_6H_4COO)_2$ (**7**) were obtained in excellent yields. On the other hand, reactions of 2,6-bis(3,5-dimethyl-***N***-pyrazolyl)pyridine (**L2**) with Zn(II) and Cu(II) acetates afforded complexes Zn(**L2**)$(OAc)_2$ (**8**) and Cu(**L2**)$(OAc)_2$ (**9**) in moderate to good yields. The complexes were characterized by employing a combination of ^{1}H NMR and IR spectroscopies, microanalyses, mass spectrometry and single crystal X-ray crystallography for **1, 2** and **5-9** complexes. Complexes **1-6** and **8-9** were employed as catalysts/initiators in the ring-opening polymerization (ROP) of ε-caprolacone (ε-CL) and they produced active initiators at 110 ^{o}C. Compounds **1** and **8** were screened in the ROP of lactide and were found to be active. Detailed kinetics and mechanistic studies were performed for polymerization reaction of ε-CL using complexes **1-8** and revealed that the reactions follow *pseudo*-first-order in regards to monomer and second order overall rates. Polymerization reactions using these complexes proceeded in a controlled manner to afford polymers with moderate molecular weights and narrow polydispersities (PDIs). The polymerization reactions occurred through coordination insertion mechanism.

Acknowledgements

I understand words can never be sufficient to express my sincere and heart-felt gratitude and appreciation to Dr Stephen. O. Ojwach my supervisor for his prolific guidance and encouragement during the duration of my research. It has been the privilege to have him as my mentor and a teacher. He is indeed one of the distinguished scientists; it has been an honour to work under such guidance. I would like to also thank the following individuals who have also contributed so much in this research:

- Dr akerman for solving X-ray crystal structures
- Mrs C. Janse van Rensburg for CHN and LC-MS
- Dr Xulu for EPR studies
- Craig Grimmer for NMR related issues
- Mr S. Ball and Mr F. Shaik for their technical assistance
- Mr B. Dlamini for IR assistance
- Last but not list I thank the Catalysis research group for guidance and fruitful discussions

I would like to thank my grandmother Thokozile Virginia Zikode. She never had too much but from the little that she had, she made sure that I benefit something from it. I couldn't have asked for any better guidance, you are an amazing woman I know on earth. I thank you for raising me. I would like to further thank my family members, extended family members and friends for their endless support and words of wisdom.

I acknowledge NRF for financial assistance

Most importantly I would like to thank God almighty for blessing, loving and guiding me throughout everything.

Table of contents

List of abbreviations

^{1}H NMR	Proton Nuclear Magnetic Resonance
IR	Infrared Spectroscopy
LA	Lactides
ε-CL	ε-caprolactone
PLA	Polylactide
PCL	Polycaprolactone
ROP	Ring-opening polymerization
FDA	Food and Drug Administration
THF	Tetrahydrofuran
PDI	Polydispersity
m/z	Mass to charge ratio
mL	Millilitre
mmol	Millimole
h	Hours
Calc.	Calculated
s	Sharp
Br	Broad
s	Singlet
m	Multiplet
g	Grams

List of figures

List of schemes

Chapter 1

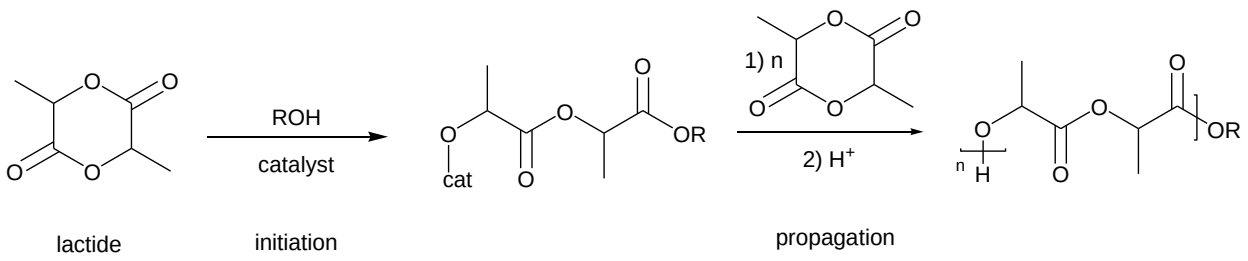
Introduction

1.1 Introductory remarks

Lactides (LA) and ε-caprolactones (ε–CL) are monomers derived from renewable resources which includes; wheat, sugar beets, and corn.[1] For the past few decades much attention has been devoted to the study of polymerization of these monomers since they provide an alternative route to petrochemically derived polymers. Poly(lactide) (PLA) and poly(ε–caprolactone) (PCL) are polymers derived from the ring-opening polymerization (ROP) of aliphatic esters.[1] The development of aliphatic polyesters (PLA and PCL) has managed to deal with the challenges of replacing natural resources, woods, natural fibres, etc., they have also dealt with the difficulties associated with the environmental pollution.[2]

1.2 Synthesis of aliphatic polyesters by ring-opening polymerization (ROP)

Higher-molecular weight polyesters can be directly synthesised by ring-opening polymerization of cyclic esters catalysed by a number of initiators including metal complexes to nucleophilic organocatalysts and enzymes.[3,4] In general alcohols acts as catalysts precursors in the ROP of aliphatic esters , hence the formation of polymer chains with an ester group and an alkoxy group to which the catalyst is coordinated (Scheme 1.1).[5,6]



Scheme 1.1: ROP of lactides; initiation and propagation steps.[7]

This type of polymerization is also known as "living" or "controlled" polymerization. "Living" or "controlled" polymerization leads to great control over molecular weights and polydispersities (PDIs) of the polymers. ROP method has numerous advantages over other methods of polymerization, these advantages includes; good control over polymerization reactions and access to advanced architectures.[8] ROP of cyclic esters is found to be thermodynamically favourable, due to relief of a ring strain of lactone and caprolactone monomers.[9]

In addition, the choice of the initiator and other setting of reaction conditions allows for a good control of polymerization which then provides tailoring of the properties such as microstructure and the molecular architecture of the polymer.[10] Other advantages of ROP are that it requires low concentration of catalyst and relatively low temperatures to obtain complete conversion of the monomers. Normally temperature ranges between 100–150 ^{o}C for bulk polymerization and it ranges between 0–25 ^{o}C in the solution.[11] Polymerization reactions are carried in solvent-free medium or in solutions (THF, Dioxane or Toluene) preferably emulsion.[11] ROP is one of the most powerful tools for the production of well-defined polyesters.[10]

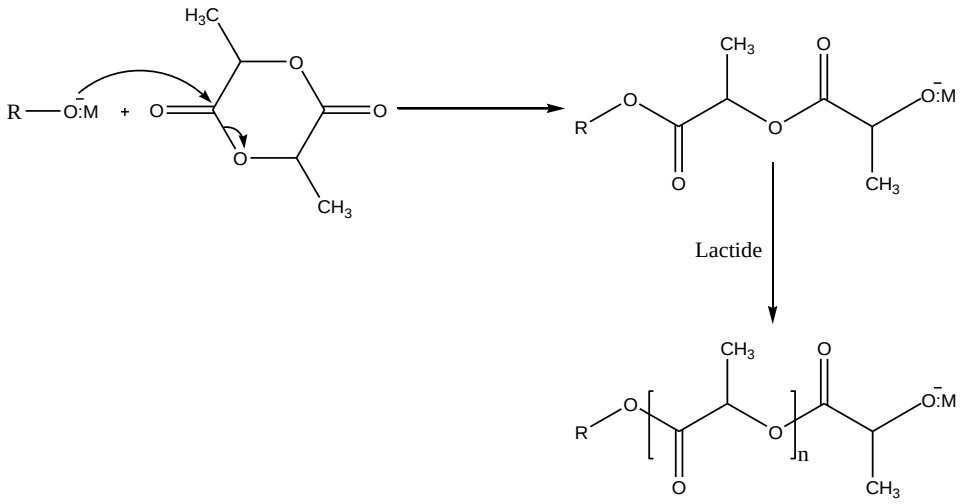
1.3 Types of mechanisms of the ROP of cyclic esters

A number of techniques have been employed towards the ROP of cyclic esters.[2] The most well-known/established mechanisms includes; anionic polymerization mechanism, cationic polymerization mechanism and coordination-insertion mechanism.

1.3.1 Anionic polymerization mechanism

Alkali metals, alkali metal oxides and alkali metals naphthelinide complexes with crown ethers are the well-known effective initiators that are generally employed for anionic ROP of lactones,.[11] This process may proceed via living or non-living manner. However this depends on the nature of reaction conditions and catalyst initiation.

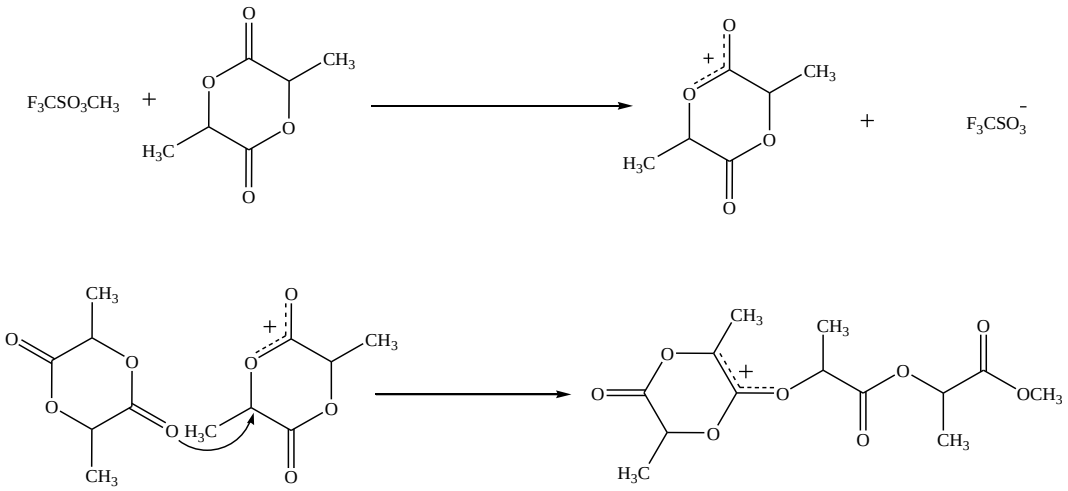
Anionic ROP involves nucleophilic attack of carbonyl carbon of the monomer, resulting in the C-O single bond cleavage (Scheme 1.2). This results in the formation of an alkoxide which proceeds to generate new anion. Anionic polymerization mechanism gives higher conversion rates compared to cationic mechanism. However anionic ROP has risks of partial racemization if the monomer is deprotonated by the initiator or the active chain end.[12]



Scheme1.2: Summary of the anionic ring opening polymerization of LA monomer.[7]

1.3.2 Cationic polymerization mechanism

Cationic ROP has found comparatively little success when compared to other types of ROP mechanisms discussed. Dittrich and Schulz made attempts to polymerize LA using cationic initiators in 1971, unfortunately this was unsuccessful.[12] However, in the late 1980's Krichedorf *et al*. demonstrated the feasibility of this mechanism.[13] To date cationic ROP of lactones have been reported for a number of cyclic esters.[14] The most well established compounds that have been employed in cationic ROP of lactones are: alkylating agents, acylating agents, Lewis acids, and protic acids.[15]

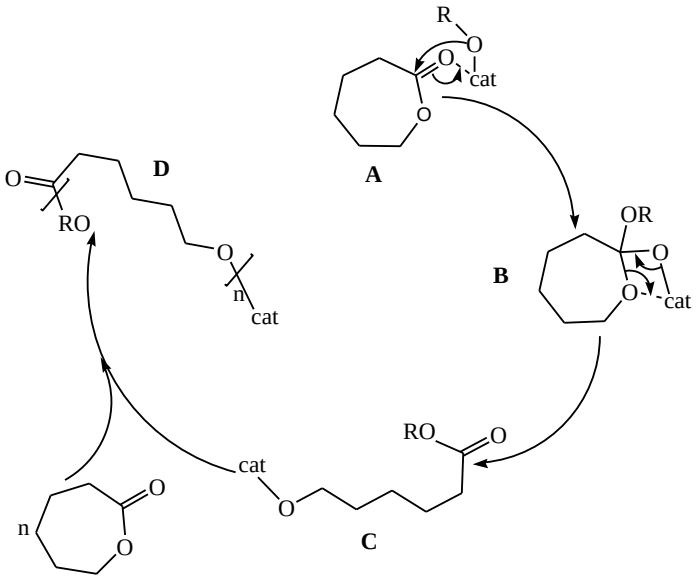


Scheme1.3: Cationic ring opening polymerization of LA monomers.[9]

Krichedorf and co-workers reported on several papers in the 1980's that alkylating agents such methyl triflate catalyse the cationic ROP polymerization of CL, LA, glycolide, etc.[14,17,18] The mechanism is initiated when the exocyclic oxygen of the monomeric carbonyl is either alkylated or protonated by the initiator, causing the resulting O–CH bond to be positively charged (Scheme 1.3). The second monomer nucleophillically attacks this bond and thereby creating another electrophilic carbenium ion. Further addition of monomers propagates polymerization, this continues until such time that monofunctional nucleophile water is added to terminate the reaction. In cationic ROP, reaction conditions such as higher temperature results in racemization. Nevertheless this can be reduced by using lower temperatures <50 ^{o}C but this also affect the rate of the reaction and yields low molecular weight polymers.

1.3.3 Coordination-insertion polymerization mechanism

A number of metal catalysts used to date employ coordination-insertion mechanism for ROP (Scheme 1.4) because of its ability to produce well-controlled polyesters with high molecular weight, this mechanism is widely used for ROP and it is well-known. Research studies have been devoted towards synthesizing potentially efficient metal-based initiators, study their reactivity and their activity towards cyclic esters. The first two researchers to have been able to define a three step coordination-insertion mechanism for the ROP of cyclic esters were Dittrich and Schulz.[13] Kricheldorf *et al*. and Teyssieet *et al*. further studied the involvement of this mechanism in the ROP of various cyclic esters using $Al(OiPr)_3$ as an initiating species.[19]



Scheme 1.4: Mechanism of coordination-insertion of ROP for *ε*–CL.[7]

The coordination-insertion mechanism proceeds via coordination of a monomer to the metal center of the initiator, followed by the insertion into the metal-alkoxide species through the acyl-oxygen bond.[20] Coordination between the metal alkoxide catalytic species and carbonyl oxygen occurs. This is followed by nucleophilic acyl substitution to initiate the ring opening of the

monomer to yield **C** (Scheme 1.4)**.**[7] The intermediate **C** then further reacts with the monomers, chain propagation yields **D**. This approach can help eliminate or suppress the side-reactions (intra- or intermolecular transesterification, chain termination and epimerization). While suppressing these side-reactions the mechanism also controls the molecular weight, stereochemistry and polydispersity (PDI) of the polyesters.[7] By altering the polymerization reaction conditions this mechanism can control the polymerization rate and streoselectivity hence regulating the chemical and physical properties of the polymeric material (polymer microstructure).[21,22]

1.3.4 Enzymatic ROP mechanism

Enzymes have gained much interest as biocatalysts, this could be attributed to their excellent activity and high selectivity. In addition to these attributes, enzymes are environmentally friendly and they are more acceptable as compared to some conventional catalysts.[23]

Enzymes provides an exclusive synthetic strategy for a number of useful polymers.[24,25] In comparison to conventional catalysts, enzyme catalysed polymerization reactions have several advantages namely; mild reaction conditions i.e. temperature, pH, absence of organic solvents, high enantio and regioselectivity, as well as catalyst recycling.[11]

Lipase is an example of an enzyme that has been used in ROP of cyclic esters. Lipase have demonstrated extraordinary activity in the enzymatic ring opening polymerization (eROP) of caprolactones[26-33] and co-polymerization of lactones.[34-40]

1.4 Properties of aliphatic polyesters

Aliphatic polyesters are biodegradable, bioassimilable, biocompatible and thus serve as an alternative route to the petrochemical derived plastics.[2] Aliphatic polyesters displays incredible mechanical features/properties as well as hydrolyzability. They also lack toxicity and also their monomeric market price is relatively low. Some other important properties and mechanistic features of PCL are given in Table 1.1.

Table 1.1: Properties of PCL.[41]

Number average molecular weight (M_n/ g ml^{-1})	530- 630000
Density (p / 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

The properties that these aliphatic polyesters display allow them to have a wide variety of applications. Amongst other advantages that these polymers have over other material is their ability to mould mechanical features and properties as well as degradation kinetics so it could suite various applications.[42]

1.5 Applications of aliphatic polyesters

PLA and PCL have become leading candidates in biomedical, pharmaceutical as well as plastic industries. Since the early 1970s these erodible polymers have been used as vehicles for controlled drug delivery.[11,43] They are applied in pharmaceutical applications e.g. resorbable implants materials as well as plastic packaging material in food and container industry.[43] These polymers are aimed to develop surgical implants and tissue engineering.[11] In addition these polymers have been used in artificial skin, dental implants, vascular grafts, pins, bone screws, prosthetics, and they are also used as plates during temporal fracture fixation.[11]

References

1. a) Stanford, C. A.; Dove, A. P. *Chem. Soc. Rev*., **2010,** 39, 486.; b) Wheaton, C. A.; Hayes, P. G.; Ireland, B. J. *Dalton Trans*., **2009**, 4832.; c) Dove, A. P. *Chem. Commun*., **2008**, 6446.; d) Dechy-Cabaret, O.; Martin-Vaca, B.; Bourissou, D. *Chem. Rev*., **2004**, 104, 6147.; e) Chisholm, M. H.; Zhou, Z. J. *Mater. Chem*., **2004**, 14, 3081.; f) Drumright, R. E.; Gruber, P. R.; Henton, D. E. *Adv. Mater*., **2000**, 12, 1814.; g) Cushion, M. G.; Mountford, P. *Chem. Commun*., **2011**, 47, 2276.; h) Sarazin, Y.; Howard, R. H.; Hughes, D. L.; Humphrey, S. M.; Bochmann, M. *Dalton Trans*., **2006**, 340.
2. Silvernail, C. M.; Yao, L. J.; Hill, L. M. R.; Hillmyer, M. A.; Tolman, W. B. *Inorg. Chem*., **2007**, 46, 6565.
3. Wu, J.; Yu, T. L.; Chen, C.T.; Lin, C.C. *Coord. Chem. Rev*., **2006**, 250, 602.
4. Kowalski, A.; Libiszowski, J.; Biela, T.; Cypryk, M.; Duda, A.; Penczek, S. *Macromolecules*, **2005**, 38, 8170.
5. Sobczak, M.; Oledzka, E; Kolodziejski, W. L. *Macromolecules, J. Sci. Pure Appl. Chem*., **2008**, 45, 872.
6. Kamber, N. E.; Jeong, W.; Waymouth, R. M. *Chem. Rev*., **2007**, 107, 5813.
7. Ten Breteler, M. R. Stereoselectivity polymerization of lactones proteins of streocomplexed PLA building blocks: *Enschede, the Netherlands.*, **2010**, pp 9-33.
8. Dechy-Cabaret, O.; Martin-Vaca, B.; Bourissou, D. Handbook of ring-opening polymerization, Dubois, P.; Coulembier, O.; Raquez, J.M. *Wiley VCHveriag GmbH and co. KGA Weinheim*, **2009**, 255.
9. Duda, A.; Penczek, S. *Thermodynamics, kinetics and mechanisms of cyclic esters polymerisation. In Polymers from Renewable Resources: Biopolyesters and Biocatalysis*; Scholz, C.; Gross, R. A., Eds.; ACS Symposium Series; Oxford University Press: Washington, DC, **1996**,; Vol. 5, pp 317-343.
10. a) *Biopolymers - Polyesters I Biological Systems and Biotechnological Production* (Eds.: Y. Doi, A. Steinbüchel), Wiley-VCH,Weinheim, **2002**.; b) *Biopolymers - Polyesters II Properties and Chemical Synthesis* (Eds.: Y. Doi, A. Steinbüchel), Wiley-VCH,Weinheim, **2002**; c) *Biopolymers - Polyesters III Application and Commercial Products* (Eds.: Y. Doi, A. Steinbüchel), Wiley-VCH,Weinheim, **2002**.
11. Albertsson, A.-C.; Varma, I. K. *Biomacromolecules*, **2003**, 4, 1466.

12. Kricheldorf, H,R.; Saunders, I. K. *Die Makromo.l Chem.*, **1990**; 191(5): 1057.
13. Dittrich, W.; Schulz, R. C. *Angew. Makromol. Chem.*, **1971**, 15, 109.
14. a) Kricheldorf, H. R.; Dunsing, R. *Makromol. Chem*., **1986**, 187, 1611.; b) Kricheldorf, H. R.; Kreiser, I. *Makromol. Chem*., **1987**,188, 1861.
15. Penczek, S. *J. Polym. Sci., Part A: Polym. Chem*., **2000**, 38, 1919.
16. a) Tang, Z.; Chen, X.; Liang, Q.; Bian, X.;Yang, L.; Piao, L. et al. *J Polym Sci Part A Polym Chem.*, **2003**; 41,1934; b) Stridsberg, K. M.; Albertsson, M.R. and A. C. *Adv. Polym. Sci*., **2002**, 157, 41-.
17. Kricheldorf, H. R.; Jonte, J. M.; Dunsing, R. *Makromol. Chem*., **1986**, 187, 771.
18. Kricheldorf, H. R.; Dunsing, R.; Serra, A. *Macromolecules,* **1987**, 20, 2050.
19. a) Kricheldorf, H. R.; Berl, M.; Scharnagl, N. *Macromolcules,* **1988,** 21, 286.; b) Dubois, P.; Jerome, R.; Teyssie, P. *Makromol. Chem, Macromol. Symp.,* **1991**, 42/43, 103.; c) Dubois, P.; Jacobs, C.; Jerome, R.; Teyssie, P. *Macromolecules*, **1991**, 24, 2266.
20. Thomas, C. M. *Chem. Soc. Rev*., **2010**, 39, 165.
21. Platel, R. H.; Hodgson, L. M.; Williams, C. K. *Polym Rev.*, **2008**, 48, 11.
22. Abdessamad, A.; Redshaw, C. *Polym Chem.*, **2010**, 1, 801.
23. Schmid, A.; Dordick, J. S.; Hauer, B.; Kiener, A.; Wubbolts, M.; Witholt, B. *Nature.*, **2001**, 409, 258.
24. Kobayashi, S.; Uyama, H.; Kimura, S. *Chem. ReV*., **2001**, 101, 3793.
25. Gross, R. A.; Kumar, A.; Kalra, B. *Chem. ReV*., **2001**, 101, 2097.
26. Uyama, H.; Kobayashi, S. *Chem. Lett*., **1993**, 1149.
27. MacDonald, R. T.; Pulapura, S. K.; Svirkin, Y. Y.; Gross, R. A.; Kaplan, D. L.; Akkara, J.; Swift, G.; Wolk, S. *Macromolecules,* **1995**, 28, 73.
28. Uyama, H.; Suda, S.; Kikuchi, H.; Kobayashi, S. *Chem. Lett*., **1997**, 1109.
29. Bisht, K. S.; Henderson, L. A.; Gross, R. A.; Kaplan, D. L.; Swift, G. *Macromolecules*, **1997**, 30, 2705.
30. Kobayashi, S.; Uyama, H.; Namekawa, S.; Hayakawa, H. *Macromolecules,* **1998**, 31, 5655.
31. Kumar, A.; Kalra, B.; Dekhterman, A.; Gross, R. A. *Macromolecules,* **2000**, 33, 6303.
32. Namekawa, S.; Uyama, H.; Kobayashi, S. *Macromol. Chem. Phys*., **2001**, 202, 801.
33. Uyama, H.; Kobayashi, S.; Morita, M.; Habaue, S.; Okamoto, Y. *Macromolecules,* **2001**, 34, 6554.

34. Meyer, U.; Palmans, A. R. A.; Loontjens, T.; Heise, A. *Macromolecules*, **2002**, 35, 2873.
35. van As, B. A. C.; Thomassen, P.; Kalra, B.; Gross, R. A.; Meijer, E. W.; Palmans, A. R. A.; Heise, A. *Macromolecules.*, **2004**, 37, 8973.
36. Wahlberg, J.; Persson, P. V.; Olsson, T.; Hedenstrom, E.; Iversen, T. *Biomacromolecules*, 2003, 4, 1068.
37. de Geus, M.; Peeters, J.; Wolffs, M.; Hermans, T.; Palmans, A. R. A.; Koning, C. E.; Heise, A. *Macromolecules*, **2005**, 38, 4220.
38. Sha, K.; Li, D. S.; Wang, S. W.; Qin, L.; Wang, J. Y. *Polym. Bull.*, **2005**, 55, 349.
39. Skaria, S.; Smet, M.; Frey, H. *Macromol. Rapid Commun*., **2002**, 23, 292.
40. Peeters, J. W.; Palmans, A. R. A.; Meijer, E. W.; Koning, C. E.; Heise, A. *Macromol. Rapid Commun*., **2005**, 26, 684.
41. a) Van de Velde, K.; Kiekens, P. *Polymer Testing*., **2002**, 21, 436; b) Ikada, Y.; Tsuji, H. *Macromol. Rapid Commun*., **2000**, 21, 117.
42. a) Vanhoorne, P.; Dubois, Ph.; Jerome, R.; Teyssie, Ph. *Macromolecules*, **1992**, 25, 37.; b) Shen, Y.; Zhun, K. J.; She, Z.; Yao, K.-M. *J. Polym. Sci., Part A: Polym. Chem*., **1996**, 34, 1799–1805.; c) Bero, M.; Kasperczyk, J. *Macromol. Chem. Phys*., **1996**, 197, 3251.; d) Hiljanen-Vainio, M. P.; Orava, P. A.; Seppala, J. V. J. *Biomater. Mater. Res.* **1997**, 34, 39.; e) Kister, G.; Cassanas, G.; Bergounhon, M.; Hoarau, D.; Vert, M. *Polymer.*, **2000**, 41, 925.; f) Baimark,Y.; Molloy, R. *Science Asia.*, **2004**, 30, 327.; g) Fay, F.; Renard, E.; Langlois, V.; Linossier, I.; Vallee-Rhel, K. Eur. *Polym. J*., **2007**, 43, 4800.; h) Calandrelli, L.; Calarco, A.; Laurienzo, P.; Malinconico, M.; Petillo, O.; Peluso, G. *Biomacromolecules*, **2008**, 9, 1527.
43. Del Rosal, I.; Poteau, R.; Maron, L. *Dalton Trans*., **2011**, 40, 11228.

Chapter 2

Literature Review

2.1 Catalysts used in ring-opening polymerization for LA and *ε*–CL

Ring-opening polymerization (ROP) of LA and *ε*–CL requires the use of appropriate catalysts also known as initiators. In the past two decades, one of the most widely used group of initiators for the ROP of cyclic esters in both industrial and academic arenas are aluminium and tin based catalysts.[1] Interests have been directed towards less toxic and biologically compatible initiators such as organocatalysts,[1] iron,[2] magnesium,[3-5] zinc,[4,5] calcium,[5,6] titanium,[7] and bismuth.[8]

A number of catalysts have been developed over the decade for ROP of LA and *ε*–CL. These includes metal-free catalysts[9] and metal-based catalysts.[10] The most widely used metal-free catalysts are N-heterocyclic carbenes,[11,12,13] N-propylsulfonic acid,[14] trifluoromethanesulfonic acid,[14] 4-(dimethylamino)pyridine (DMAP),[15] guanidines and aminides[16] and HCL-Et_2O.[17] Nevertheless, many catalysts that have been employed for ROP of LA and *ε*–CL are metal based catalysts. The next section reviews the scope of metal-based catalysts that have been employed as initiators in the ring-opening polymerization of LA and *ε*–CL.

2.1.1 Alkali metal based catalysts in ROP of LA and ε–CL

A number of alkali metal-based compounds have been studied extensively for ROP of LA and *ε*–CL, most of them were reported as being successful initiators/catalysts in the polymerization of aliphatic esters over the past few decades. However, the challenges such as improving the activity

of the catalyst, isotactic selectivity, decreasing sensitivity of the catalyst to moisture still remains in this field.[18]

Alkali metal based compounds have drawn much interest as initiators in the ROP of LA and *ε*–CL, due to their non-toxicity, ease of synthesis and stability. Kricheldorf and kasperczyk *et al*. reported the use of alkali metals (Li and K) supported by oxygen donor alkoxide ligands as catalysts in the ROP of LAs.[19] However, these compounds show low activity and produce polymers with broad polydispersities (PDIs), which occur as a result poor control over polymerization process and the presence of side reactions.[19] In another related work, Lithium chloride is also reported as an active and biocompatible catalyst that has been employed in ROP of LA.[19d] Polymerization reaction is carried in the presence of ethylene glycol or methyl α-D-glucopyranoside solvents with 1% (w/w) of LiCl at 128 ^{o}C to give PLA with high polydispersities (PDIs >2.2), which also indicates poor control over polymerization. In addition, lithium alkoxides and aryloxides complexes have displayed higher catalytic activities in the ROP of LA and *ε*–CL.[20-28]

The catalytic investigation of alkali metal complexes bearing bis(phenolate) phosphine ligand (Fig. 2.1) in the ROP of lactides has been reported by Chang and Liang.[29] These complexes produce exceptionally higher molecular weight polylactides of about 1×10^6 g/mol in comparison to typical living polymerization catalysts (ca Mw = 1×10^4 g/mol).[30] The high molecular weights observed in addition to the low polydispersity indices (<1.6) points to controlled polymerization process with minimum transesterification reactions.[31]

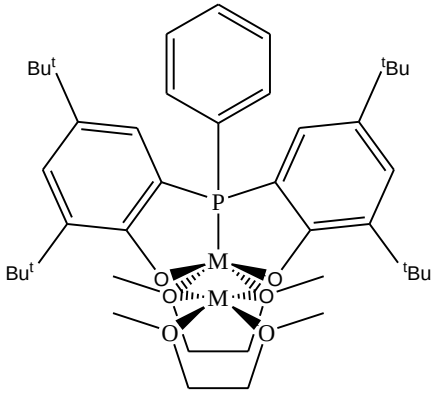


Fig. 2.1 Alkali metal bis(phenolate) phosphine complexes; M = Li, Na, K.

On the other hand, alkali metal complexes bearing tridentate amine-bis(phenolate) ligands (Fig. 2.2) form active initiators/catalysts in the ROP of rac-lactide at 27 ^{o}C with substantial inter and intra-molecular transesterifications, and yield polymers with moderate PDI values (>1.92).[32] This could be attributed to the solvent effect, for example toluene have tendencies to reduce the reactants concentrations thus lowering the rates of collisions of the molecules, hence resulting in occurrence of polymer back biting.

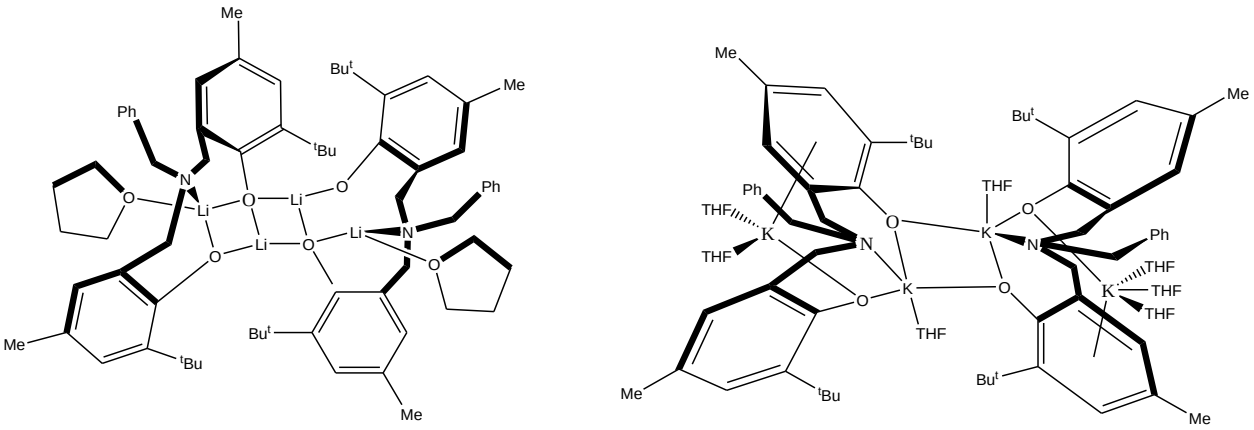


Fig. 2.2 Bis phenolate amine alkali metal complexes

A series of alkali-metal aryloxo compounds (Fig. 2.3) have been investigated as potential catalysts in the ROP of L-LA in the absence of alcohol, the reported compounds form efficient catalysts.[33] High molecular weight polymers with narrow polydispersities (PDIs of 1.39-1.60) are produced.

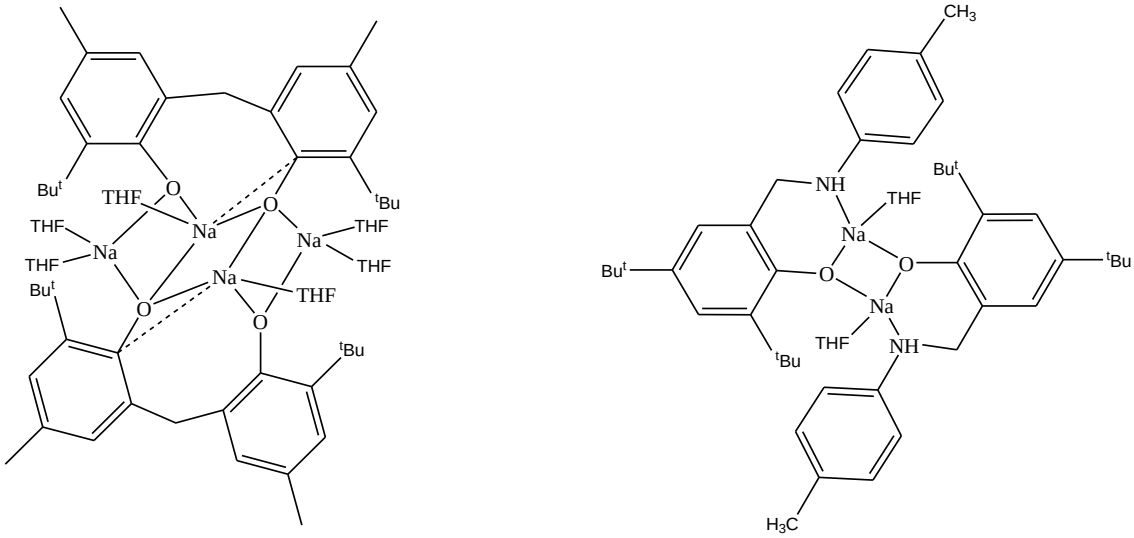


Fig. 2.3 Aryloxo ligands supported sodium complexes.

Sodium complexes supported by bisphenol ligand system (Fig. 2.4) were synthesized and employed towards the ROP of L-LA.[34] These complexes form effective catalysts for the ROP of

L-LA at low temperature (0-25 ^{o}C) affording polymers with narrow polydispersities (PDIs =1.38-1.44). In addition, the linearity between Mn versus $[M]_o/[I]_o$ indicate controlled polymerization process. This could be attributed to the ligand framework and architecture which plays a very crucial role in modifying the polymer properties and controlling the polymerization process.[35]

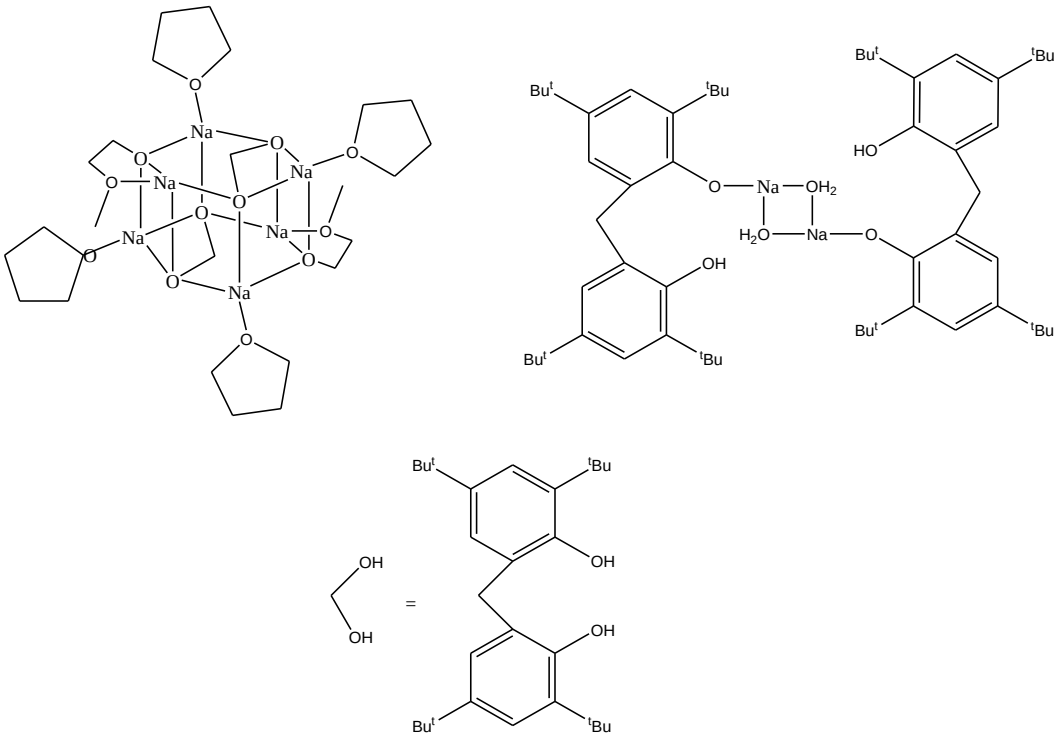
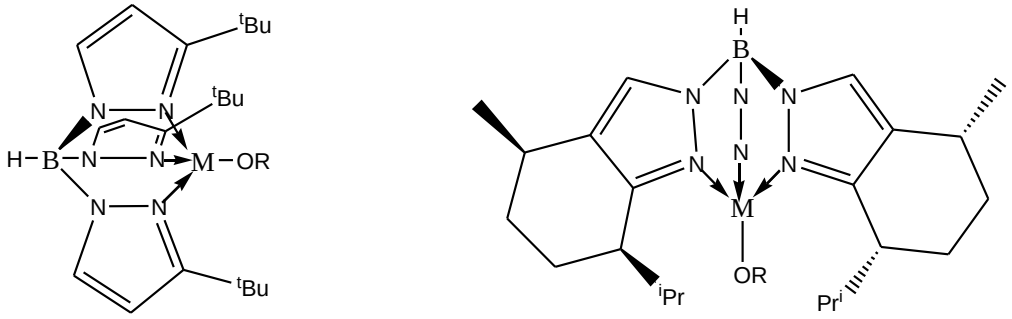


Fig. 2.4 Bisphenol sodium complexes.

2.1.2 Alkali earth metal based compounds in ROP of cyclic esters (Mg, Ca, Sr)

Previous developments show that alkali earth metals are the emerging catalysts in the ROP of cyclic esters due to their low toxicity and low cost.[36] A number of well-defined alkali earth compounds have been reported in ROP of aliphatic esters in the past decade.[5,31]The catalytic behaviour of magnesium complexes supported by sterically bulky trispyrazolyl and trisindazolyl-hydroborate ligands (Fig. 2.5) have been investigated.[37] The reported complexes form active

catalysts in the ROP of L-LA with great linearity of M_n vs %conversion and low PDIs 1.10-1.35. Moreover, investigation of kinetics studies show 1st order with respect to the both monomer and metal complexes at room temperature.



M = Mg R = Ph

M = Mg R = Et

Fig. 2.5 Trispyrazolyl- and trisindazolyl-hydroborate ligands supported magnesium complexes.

Bochman and co-workers reported the catalytic screening of calcium and magnesium complexes bearing nitrogen donor arm bis(phenolate) amine ligands (Fig. 2.6) in the ROP of ε–CL.[38] Interestingly, magnesium complex suffers from poor activity compared to its calcium complex counterpart, this is influenced by lewis acidity. In addition, even though the authors didn't mention the reason why dimeric complex is more active, we believe calcium complex exist in monomeric form in bulk solution hence become more active. Polymers were obtained with low PDIs<1.4..

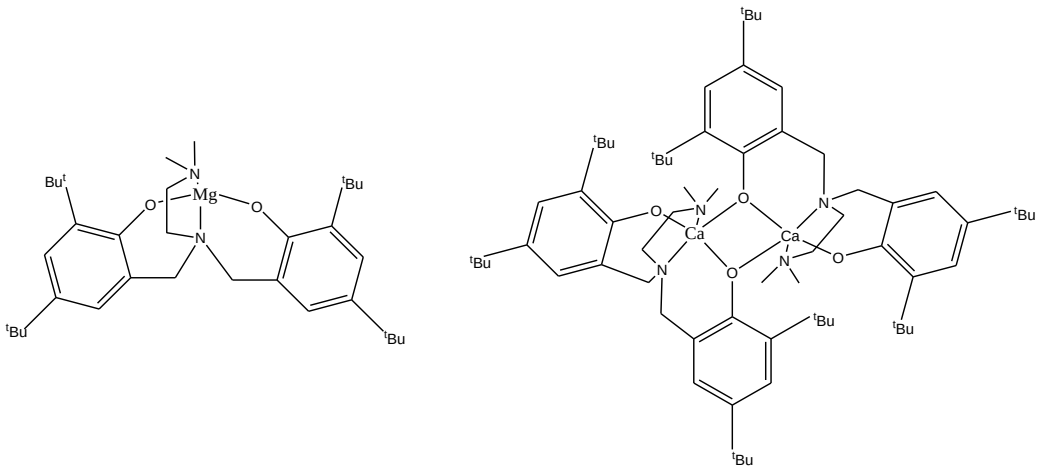


Fig. 2.6 Alkali earth metal amine bis(phebnolate) calcium and magnesium complexes.

Magnesium complexes supported by ketiminate ligand (Fig. 2.7) form inactive catalysts in the ROP of ε–CL at room temperature, however, the catalysts are active at moderate temperatures i.e. 70 ^{o}C.[39] Giving polymers with high PDIs (> 3) in combination with higher polymer molecular weight observed than expected (e.g. $M_{n(measured)}$ 32 310 against $M_{n(calculated)}$ 22 370 g/mol). This is attributed to the ligand exchange at 70 ^{o}C.

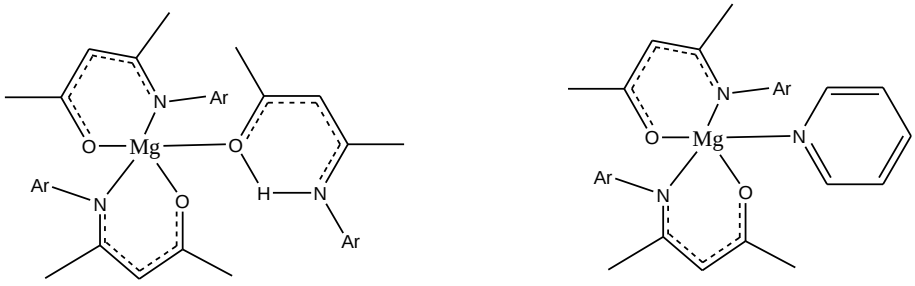


Fig. 2.7 Ketiminate ligands supported magnesium complexes.

Monomeric THF adducts rather than dimers of β-dikeminate (BDI) complexes (Fig. 2.8 (a)), are reported to be active in the ROP of lactides in methylene chloride solvent,[40] the results matches those obtained by Coates *et al.*[41] A range of initiating groups have been explored and the polymerization rates were: $O^{t}Bu > N(SiMe_3)_2 > OSiPh_3$. Even though the complex containing the

initiating group O^{t}Bu displays much higher activity, it suffers from poor molecular weight control and no stereoselectivity. On the other hand, [(BDI-1)Ca N(SiMe$_3$)$_2$] complex afforded atactic PLA.

In another related work, magnesium β-diketiminate complexes have been investigated for their ability to initiate ROP *ε*–CL (Fig. 2.8(b)), these complexes are active as catalysts towards ROP of *ε*–CL.[42] Monomeric magnesium complexes show excellent activity at ambient temperature. On the other hand, dimeric magnesium complex is inactive at room temperature. This is attributed to dimeric disruption which occur steadily at room temperature.[35a] Magnesium complex (Fig. 2.8(c)) displayed exceptional activity even at very low catalyst loadings.[43] In the field of polymer chemistry this is a very significant attribute for the catalyst as this offers access to high molecular weight polymers. Despite excellent activity at low catalyst loadings, the recorded molecular weight is extremely low ($M_{n(corrected)}$ = 3 360 g mol^{-1}) in comparison to the expected molecular weight at this conversion ($M_{n(calculated)}$ = 37 210 g mol^{-1}) with low PDI values (1.6). Unfortunately the authors of the paper did not account for this descrepency. However, we believe that THF solvent attached to the metal center inhibits the activity of this complex.

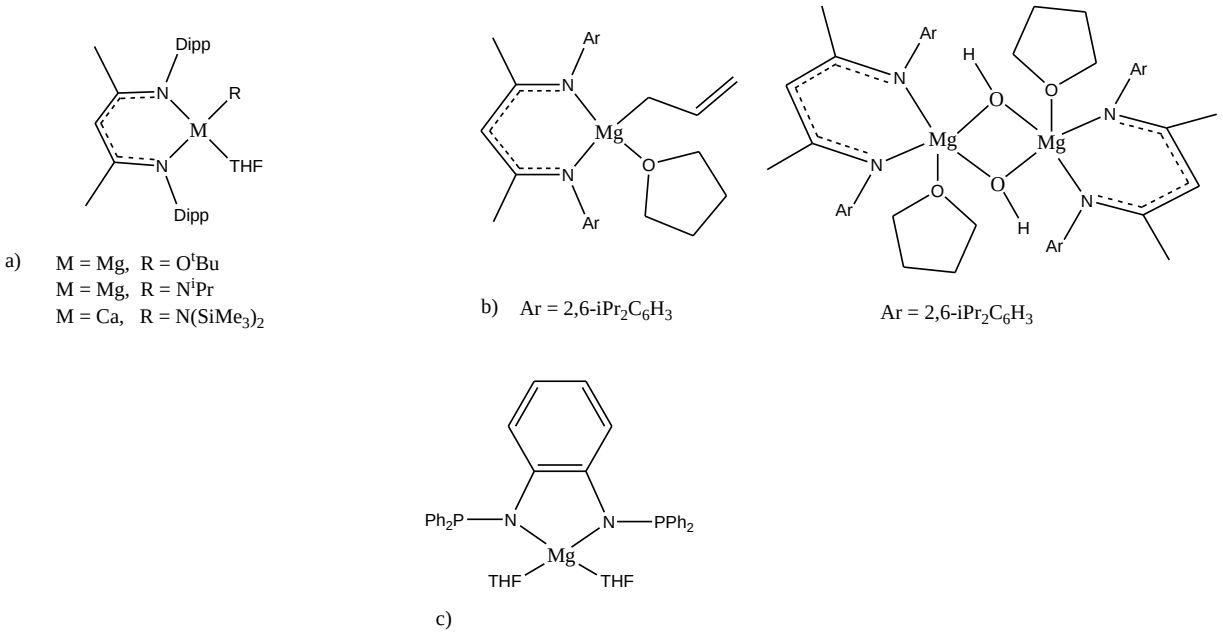
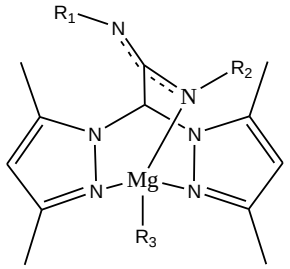


Fig. 2.8 Magnesium and calcium complexes.

Heteroscopionate ligands were also employed to support alkyl magnesium complexes (Fig. 2.9), these complexes have led from moderate to excellent activity in the ROP of *ε*–CL.[44] The complexes afforded polymers with low PDI values (up to 1.5), and low molecular weight of polymer than expected was observed.



R$_1$ = R$_2$ = iPr, R$_3$ = nPr, tBu and CH$_2$SiMe$_3$

Fig. 2.9 Heteroscopionate magnesium complexes.

Since the success of magnesium catalyst systems in the ROP of aliphatic esters, Chisholm *et al.* synthesized calcium complexes bearing tris(pyrazolyl)borate and β-ketiminate ligand framework

(Fig. 2.10).[37] Interestingly, the reported calcium complexes are even more active than the corresponding magnesium analogues (Fig. 2.5) in the ROP of LA.

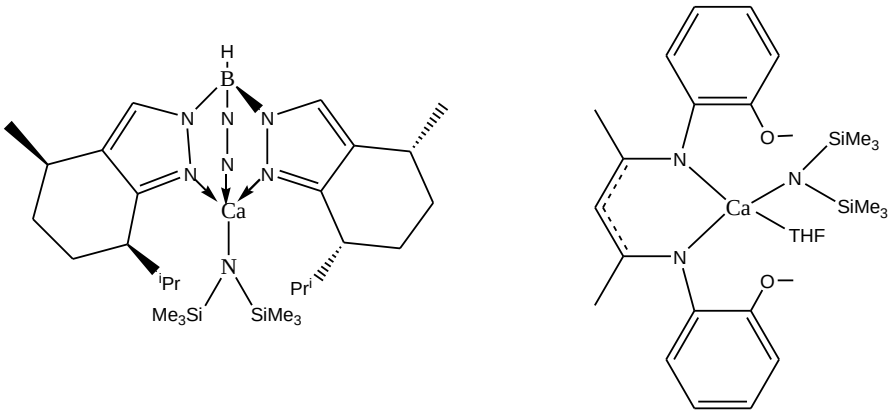


Fig. 2.10 Calcium complexes.

Current trends in the catalyst design involve the use of dinuclear complexes which is aimed to minimize and mimic mechanistic behaviour of hydrolases.[12] Thus dinuclear magnesium complexes supported by diimino or diamino ligand framework,[45] monoaninic bis(phenolate) ligand frameworks[46] as well as ketimate ligand framework (Fig. 2.11)[47] have been reported as potential candidates to achieve this goal.

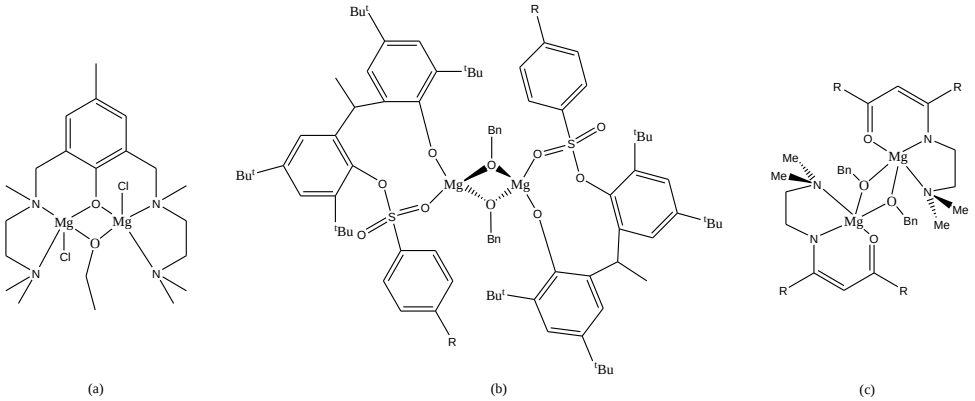


Fig. 2.11 Dinucleic magnesium complexes.

Even though magnesium and calcium catalysts/initiators have dominated and gained interests in ROP of cyclic esters, not many strontium complexes have been employed to catalyse the ROP of cyclic esters. The reaction between propylene oxide and liquid strontium ammoniate solution yield amino isopropoxyl strontium (Sr-Po) which is used as a catalyst in ROP of cyclic esters.[48] This initiator displayed effective initiating ability for the ROP of *ε*–CL and L-LA.

2.1.3 Tin carboxylates and oxides in ROP of cyclic esters

Tin(II) 2-ethylhexanoate also known as stannous octate (Fig. 2.12) with the formula $Sn(oct)_2$ is one of the most commonly used catalyst/initiator for ROP of LA and *ε*–CL for both industrial production and academic research.[49] $Sn(oct)_2$ is a versatile and effective catalyst that was approved by FDA. The ROP reactions initiated by $Sn(oct)_2$ needs to be carried out under the active hydrogen-containing compounds, or else impurities of hydrogen-containing compounds may result if no active hydrogen species is supplied.[50]

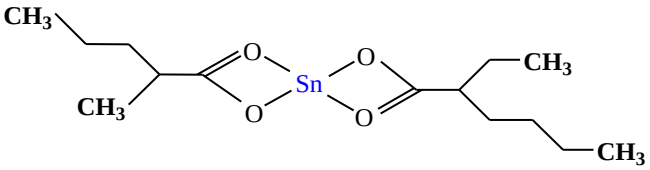


Fig. 2.12 Structure of Tin(II) 2-ethylhexanoate ($Sn(oct)_2$).

Tin(II) butoxide, $Sn(oBu)_2$ is one of the tin(II)-based catalysts used in the ROP of LA and *ε*–CL. This catalyst is an example of tin-based initiator that exists in both monomeric and dimeric forms. When using the tin-based catalysts the mechanism for ROP of LA and *ε*–CL is believed to proceed via coordination-insertion also known as pseudo-anionic. Nevertheless, there are other

tin based compounds i.e. tin (IV) alkoxides that have been investigated in the ROP of cyclic esters.[51] Even though tin based catalysts are excellent initiators for ROP of cyclic esters, these compounds suffers from toxicity and complete removal of the catalyst/initiator after ROP of cyclic ester is complete is generally not achieved.

2.1.4 Group 13 metal complexes in ROP of cyclic esters

Very few complexes of Ga(III) have been reported in the ROP of cyclic esters, Chisholm's group synthesized Ga(III) complexes which demonstrate poor activity as catalysts in ROP of cyclic esters.[52]

On the other hand, good catalytic activity of aluminium based complexes in ROP of LA and cyclic esters has led to aluminium based compounds to be studied extensively in this field. The synthesized aluminium complexes range from: aluminium alkoxides, alkyl aluminium complexes, porphyrin aluminium complexes, diamidoamino aluminium, amine bisphenolate aluminium complexes, aluminium thiolates, etc. Yu *et al*.,[53] Radano *et al*.,[54] Huang *et al*.,[55] Chakraborty and Chen,[56] Chen *et al*.,[57] and Hormnirun *et al*.[58] have synthesized and investigated the catalytic behaviour of aluminium based compounds in the ROP of cyclic esters. However, in this study we are going to limit ourselves to discussion of few aluminium based compounds.

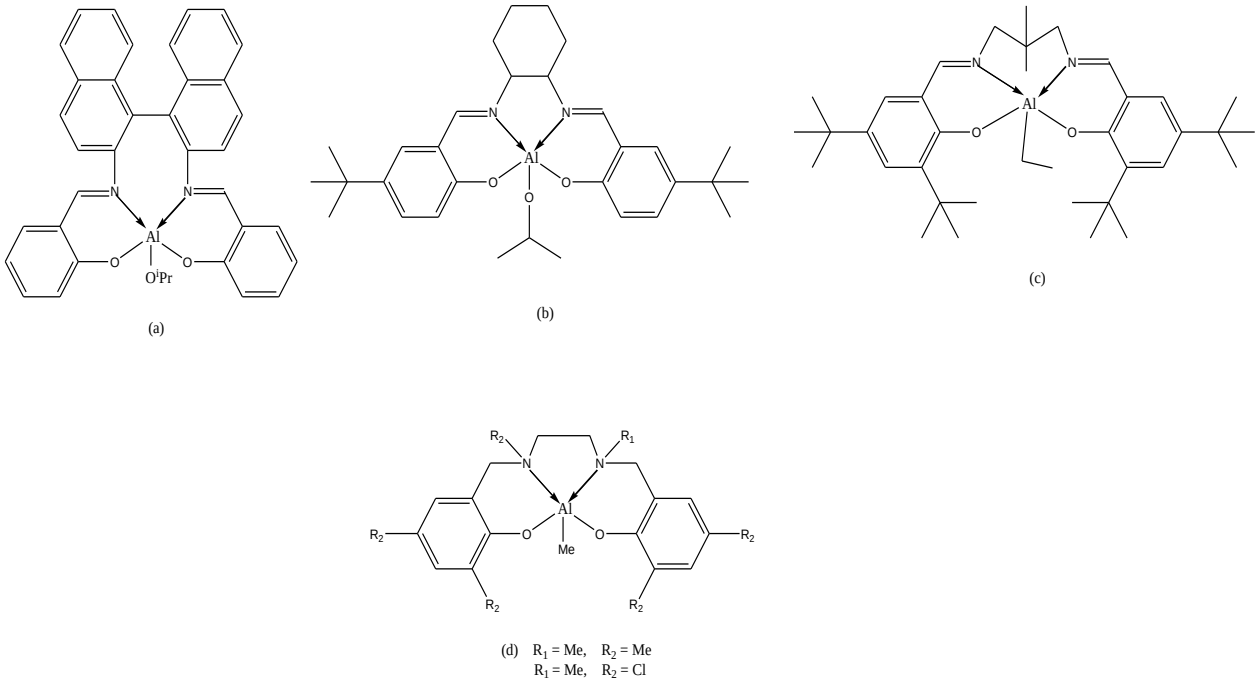


Fig. 2.13 Salen supported aluminium complexes.

Salen aluminium complexes have low activities i.e. convincing monomer conversions are obtained only at harsh conditions e.g. at higher temperatures (>70 ^{0}C). However, these complexes have great selectivity attributes in polymerization of rac-LA. Salen ligands are not only easy to synthesize but they also have easily adjustable groups, and they are prepared from condensation of salicylic carbonyl derivatives and diamines. Alcoholysis of aluminium alkyl complexes or ligand exchange with trialkoxy aluminium precursors gives aluminium alkoxides. Coate's group synthesized aluminium complexes (Fig. 2.13) that are employed to synthesize syndiotactic PLA from meso-LA.[59,60] The results show that these complexes are very selective giving Pr = 0.96 in the presence of toluene. Some of these complexes i.e. aluminium complex (Fig. 2. 13(b)) demonstrate outstanding control over molecular weight in combination with stereochemical control for LA polymerization in bulk.[61] Furthermore, aluminium complex (Fig. 2.13(c)) demonstrate highly effective isotactic selectivity for rac-LA polymerization in bulk with Pm =

0.90.[62] This could be attributed to the ligand architecture. Quite remarkably, Gibson *et al*. reported excellent stereocontrol of aluminium complexes bearing tetradentate aminophenoxide ligands as catalysts in the ROP of rac-LA, the complexes afforded highly isotactic and heterotactic PLA with Pr = 0.96 and Pm = 0.79 respetively at 70 ^{o}C in toluene.[58] Even though this was not highlited, it is well known from the literature that the ligand architecture and framework play a major role not only in controlling the polymerization process but also in the selectivity of the lactide polymerization reactions.[35]

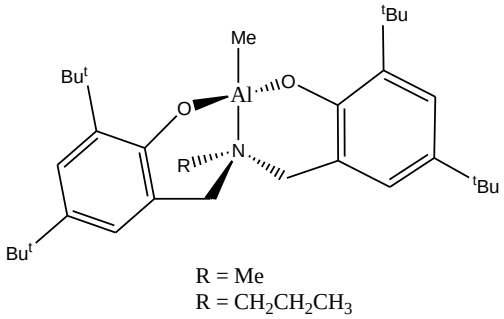


Fig. 2.14 Bisphenolate amine aluminium complexes.

Aluminium complexes bearing bisphenolate amine ligands have been reported (Fig 2.14)[63,64] in the catalytic polymerization of *ε*–CL in the presence of benzyl alcohol and they form active initiators.[57] Furthermore, the synthesis and catalytic screening of aluminium complexes (Fig. 2.15) have been reported in ROP of *ε*–CL.[53] The complexes form active catalysts with narrow PDIs of 1.07-1.31.

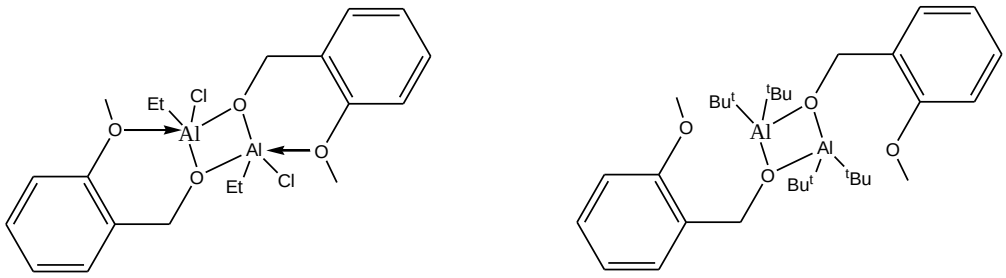
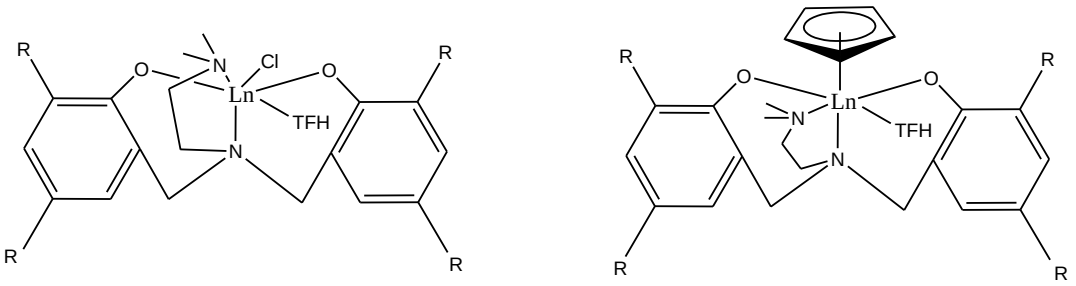


Fig. 2.15 Aluminium alkoxide complexes**.**

2.1.5 Rare earth metal complexes in ROP of cyclic esters

Generally, rare earth metal alkoxides are found to be the most active catalysts in the ROP of cyclic esters. To afford polymers with narrow PDIs and reduced transesterification reactions the use of bulky ligand system with rare earth metal is essential.[65,66] Thus, rare earth yttirium, scandium and lutetium complexes bearing tridentate ligand framework have been screened for catalytic activity of *ε*–CL and L-LA.[67-69] These complexes exhibit notably high activity with PDIs of 1.1-1.2 for both *ε*–CL and L-LA.[70]

Recently, much attention has been received by lanthanide (III) complexes compared to lanthanide (II) complexes. Willans *et al*. [71] reported lanthanide (III) chloride complexes bearing amino bis(phenolate) ligand (Fig. 2.16). Interestingly, the lanthanide (III) chloride complexes show poor activities in ROP of cyclic esters. Notably, organolanthanide (III) complexes (Fig. 2.16) also form poor to moderate active catalysts.[72]

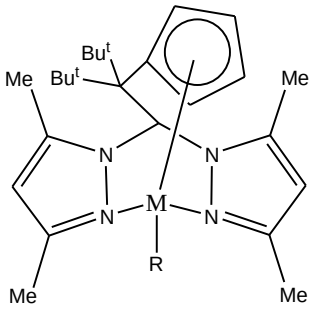


$R = C(CH)_3Et$, Ln = Y, La , Sm, Pr, Gd, Ho, Yb

Ln = La , Sm

Fig. 2.16 Lanthanide(III) chloride and organolanthanide(III) complexes.

Rare earth heteroscopionate complexes (Fig. 2.17) form catalytically active initiators in ROP of *ε*–CL, compared to magnesium complexes bearing heteroscopionate ligands (Fig. 2.9), these complexes showed good activity.[73]

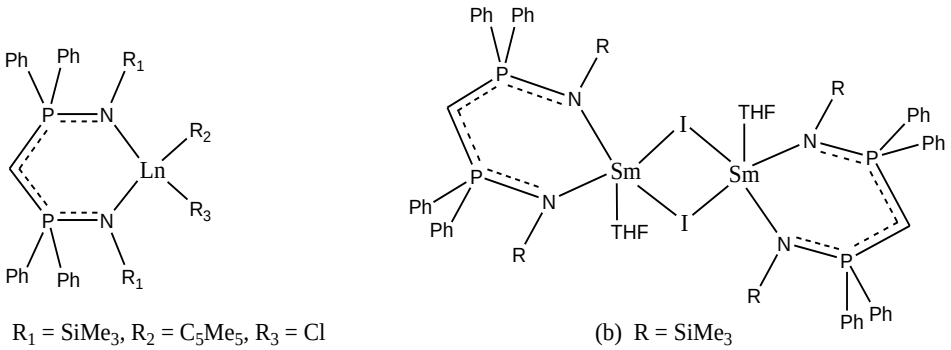


$R = CH_2SiMe_3$, M = Sc, Y

Fig. 2.17 Heteroscopionate lanthanide complexes.

Roesky and co-workers reported rare earth metal complexes bearing bulky phosphiniminomethanide ligands (Fig. 2.18) as catalysts in ROP of *ε*–CL, affording PCL with narrow PDIs.[74,75] Surprisingly, Samarian (III) complex (Fig. 2.18(b)) is the most active catalyst ever reported in the ROP of *ε*–CL giving complete conversion even at very low catalyst loadings 10 000:1 at room temperature. However, this complex affords polymers with high molecular weight distribution (PDI up to 2.75).[76] It should be noted that these findings are very interesting

since this complex is expected to be sluggish due to its bimetallic nature. However, this activity could be attributed to the electron withdrawing iodide group which is a bridging ligand. The iodide bridging ligand has ability to withdraw electrons from the metal center causing it to be more electropositive as a result becomes more susceptible to the monomer insertion.



(a) $R_1 = SiMe_3$, $R_2 = C_5Me_5$, $R_3 = Cl$
Ln = Y, Sm, Yb

(b) $R = SiMe_3$

Fig. 2.18 Rare earth metal complexes bearing bis(phosphinimino)methanide.

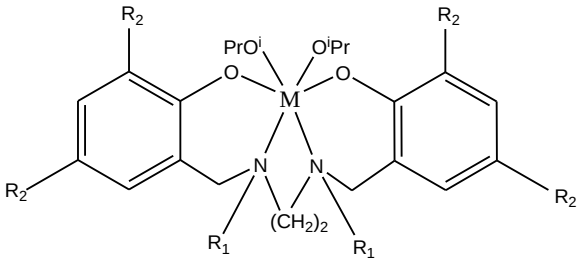
2.1.6 Early transition metal complexes in ROP of cyclic esters

Early transition metal compounds especially those in group IV have received much interests over the years as potential catalysts in the ROP of cyclic esters.

Aryloxide and alkoxide of group IV metals have attracted attention as catalysts in the ROP of cyclic esters. The influence of alkoxo or aryloxo groups on the polymerization process i.e. titanium tetra-n-propoxide ($Ti(OnPr)_4$) and tetra-phenoxide ($Ti(OPh)_4$) have been studied and investigated for ability to polymerise cyclic esters by Bounor-Legare and co-workers.[77] $Ti(OnPr)_4$ is more active than $Ti(OPh)_4$, this activity could be related to the disparity in polymer molecular weight amongst the two systems. Additionally, del Hierro and co-workers reported

$Ti(OR)_2(OiPr)_2$ and $Ti(OR)_2Cl_2$ complexes as initiators in ROP of cyclic esters and show low activity.[78] Alkoxide complexes are more active than their dichloro counterparts.

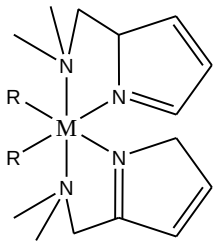
Another catalytic system of titanium and zirconium complexes bearing amino bis(phenolate) have been reported (Fig. 2.19).[79] Titanium complex display low activity for polymerization of ε–CL and afford polymers with large PDIs (2.60) at room temperature. In a similar report, zirconium complex is found to be poorly active.



R_1 = Me, R_2 = tBu, M = Ti, Zr
M = Zr, R_1 = R_2 = Me

Fig. 2.19 Titanium and zirconium complexes.

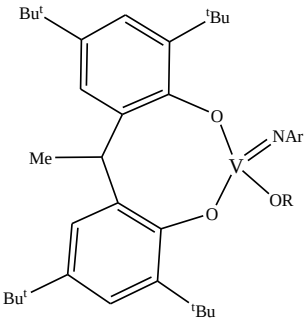
The success of halide and alkoxide zirconium catalysts have led to Huang and co-workers to synthesize and investigate the catalytic behaviour of zirconium and hafnium complexes bearing substituted pyrrolyl ligands (Fig. 2.20),[80] all the complexes are active for ROP of ε–CL.



R = C_4H_4N, M = Zr, Hf
R = 2,6-$Me_2C_6H_3O$, M = Zr, Hf
R = 2,6-$iPr_2C_6H_3O$, M = Zr, Hf

Fig. 2.20 Zirconium and hafnium complexes.

On the other hand, vanadium and other group V metals have received relatively little attention in ROP of cyclic esters. Atlamsani, Bregault and co-workers reported heteropolyacids of vanadium, $VOSO_4$ and $VO(acac)_2$ for the oligomerization of ε–CL under atmosphere of dioxygen.[81] These vanadium based compounds were catalytically active giving low molecular weight (M_w = 4 900 g mol^{-1}) oligo(ε–CL). In another related study Arbaoui's group synthesized and investigated the catalytic behaviour of organoimido vanadium (V) complexes (Fig. 2.21) in ROP of ε–CL.[82] Interestingly, the fluorinated vanadium complex is found to be inactive, this could be attributed to fluorinated alkoxide group (electron withdrawing) which is counter balanced by the loss of nucleophilicity of the alkoxide group.



Ar = 4-$CH_3C_6H_4$, R = tBu, $C(CF_3)_2CH_3$
Ar = 4-ClC_6H_4; R = tBu

Fig. 2.21 Vanadium complexes.

2.1.7 Late transition metal complexes in ROP of cyclic esters

Late transition metals have displayed promising catalytic activities. This is why they caught increased interests in regards to biodegradable polymer production

Hillmyer, Tolman and co-workers reported the catalytic screening of dinuclear cobalt complex (Fig. 2.22) which is the analogue of magnesium complex(Fig. 2.11(a)).[45] This complex is found to be less active than its magnesium counterpart.

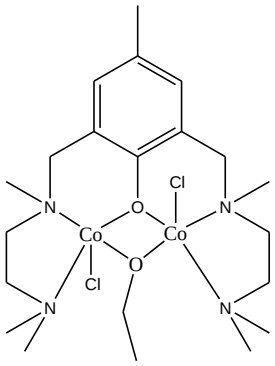


Fig. 2.22 Dinuclear cobalt complex.

Synthesis of N-heterocyclic carbenes supported iron (II) complex (Fig. 2.23) was reported by Shen and co-workers. The complex is screened as catalyst in the ROP of ε–CL, the catalyst is

found to be moderately active.[83] Polymer molecular weight decrease as the monomer conversion increases leading to high PDIs (1.9-3.1), this suggests that polymerization process proceeds in an uncontrolled manner.

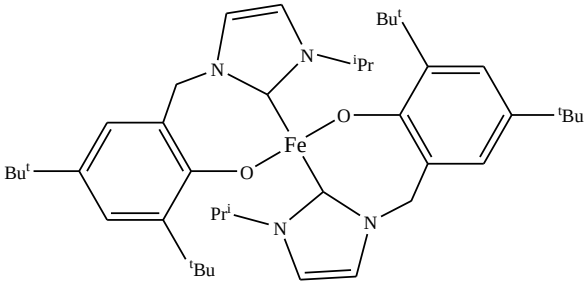


Fig. 2.23 N-heterocyclic carbene iron complex.

Gowda and Chakraborty reported the catalytic activity of commercially available metal halides such as iron (II), iron (III) and ruthenium chloride.[84] At room temperature $FeCl_3.6H_2O$ give quantitative monomer conversion and for monomer to initiator ratio of 200:1. Surprisingly, these metal halides seemed to have good control over polymerization process affording polymers of predictable molecular weights.

2.1.7.1 Zn(II) and Cu(II) metal complexes in ROP of cyclic esters

Zn(II) and Cu(II) containing initiators/catalysts have been studied extensively in the ROP of cyclic esters; it is for that reason that we would like to highlight different ligand systems employed with these metals in order for them to be able to catalyse ROP of cyclic esters. Copper metal compounds have not received much attention as catalysts/initiators for ROP of cyclic ester, due to copper metal being considered as non-environmentally friendly. Thus, researchers haven't explored copper metal based compounds extensively.

Despite copper metal being suspected to be non-environmental friendly Gowda and Chakraborty assessed $Cu(OAc)_2$ to be a good catalyst for the bulk polymerization of LAs.[85] The results obtained indicate that the bulk polymerization of LAs were highly controlled leading to the formation of polymers with expected molecular weights and narrow polydispersties.

Here in this contribution, we are going to limit our discussion to the Zn(II) and Cu(II) complexes bearing nitrogen and oxygen donor atoms. In the early 1990's Parkin reported bulky tripodal ligands based on tris(pyrazolyl) (TPB) skeleton to be useful ligands that can stabilize both magnesium and zinc alkyl and hydroxide species.[86] Chisholm *et al*. further reported that these ligands could be considered as useful ligands combined with metals in ROP of LA catalysts (Fig. 2.24).[4] The synthesized complexes displayed exceptionally high activities exhibiting narrow to moderate polydispersity indices (PDI = 1.1-2.25).

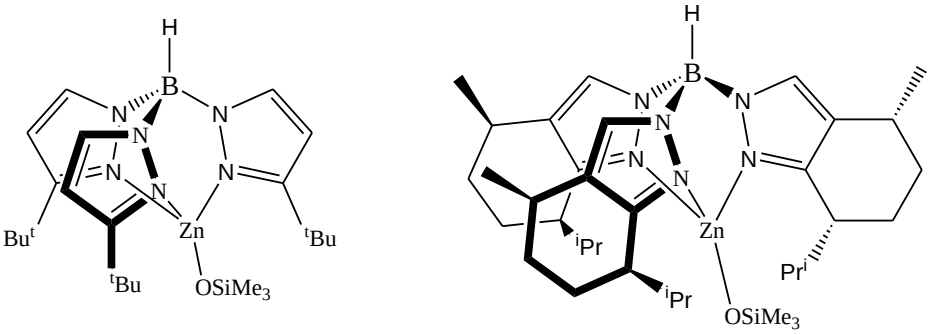


Fig. 2.24 Trispyrazolyl- and trisindazolyl-hydroborate ligands supported zinc complexes.

Bis(pyrazolyl)amide Zn(II) complexes catalyse the ring-opening polymerization of lactides and form active catalysts (Fig. 2.25).[87] These complexes are very effective and they afford polymers with low PDIs(1.23-1.71). Binuclear zinc complex bearing the bridging ethoxide initiating group is extremely active at room temperature even at very low catalyst loading of 0.25%. It is not quite clear what could lead to this phenomenal behaviour, however, we suspect this could be due to the tetrahedral geometry nature of the complex in conjunction with the ligand architecture.

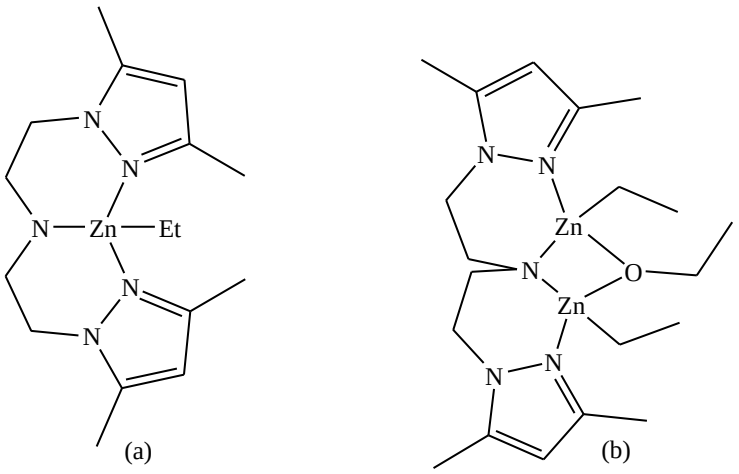


Fig. 2.25 Bis(pyrazolyl)amide supported mononuclear zinc ethyl complex (a) and binuclear zinc alkoxide (b).

The synthesis and catalytic behaviour of Schiff base Zn(II) complexes have been investigated in the ROP of LAs (Fig. 2.26).[88] The complexes were catalytically active for ROP of LAs at ambient temperature and afforded polymers with controlled and narrow polydispersities. However the synthesized complexes show no selectivity towards either L- or D-Lactides. Interestingly, Zn(II) complex (fig. 2.26 (b)) is the most active catalyst in ROP of LA, this could be attributed to steric hindarance imposed by the benzyl group.

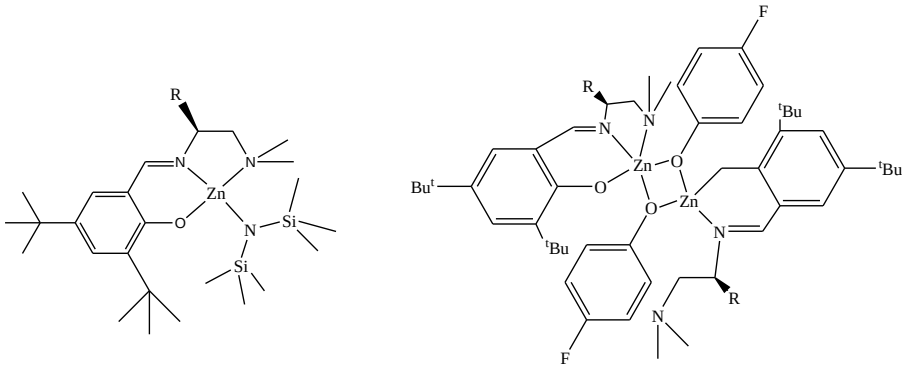
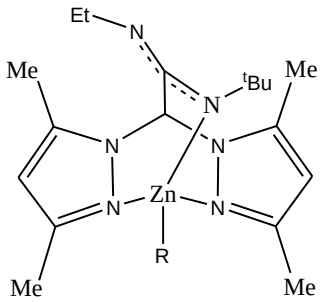


Fig. 2.26 Natural amino-acid based zinc complexes.

The investigation heteroscopionate Zn(II) complexes as initiators in the ROP of *ε*–CL was successful, the complexes catalyse ROP of *ε*–CL effectively (Fig. 2.27).[89] Notably, compared to their magnesium analogues (Fig. 2.9) zinc complexes are much less active, this could be attributed to the nature of lewis acidity between the two metals.



R =Me, Et, CH_2SiMe_3

Fig. 2.27 Heteroscopionate Zn(II) complexes.

Pyridine based ligands were used to support Zn(II) complexes (Fig. 2.28),[90] it should be noted complexes bearing these ligands form active initiators in ROP of *ε*–CL.

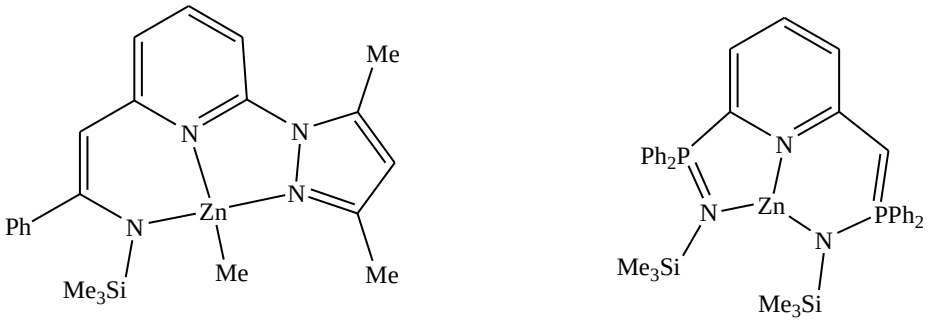
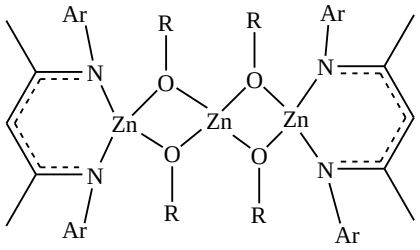


Fig. 2.28 Zn(II) complexes supported by pyridine based ligands.

In another related work catalytic behaviour of trinuclear β-diketiminate Zn(II) complex was investigated in ROP of *ε*–CL (Fig. 2.29).[91] The complex form active catalyst, quite interestingly this complex is more active for LA than for *ε*–CL polymerization.



Ar = 2-$MeOC_6H_4$, R = $CH_2C_6H_5$

Fig. 2.29 β-diketiminate Zn(II) complex

More recently, the synthesis and catalytic screening of bis(3,5-dimethylpyrazole) Cu(II) and Zn(II) complexes (Fig. 2.30) have been reported.[92] The complexes are found to be catalytically active in the ROP of *ε*–CL and D,L-LA. However, the Cu(II) complexes are less active than their Zn(II) analogues and complexes produce PCL and PLA of moderate molecular weights (ca 4 757 Da PCL and 2484 Da PLA) with PDIs = 1.36-1.42 for both PCL and PLA and heterotactic PLA.

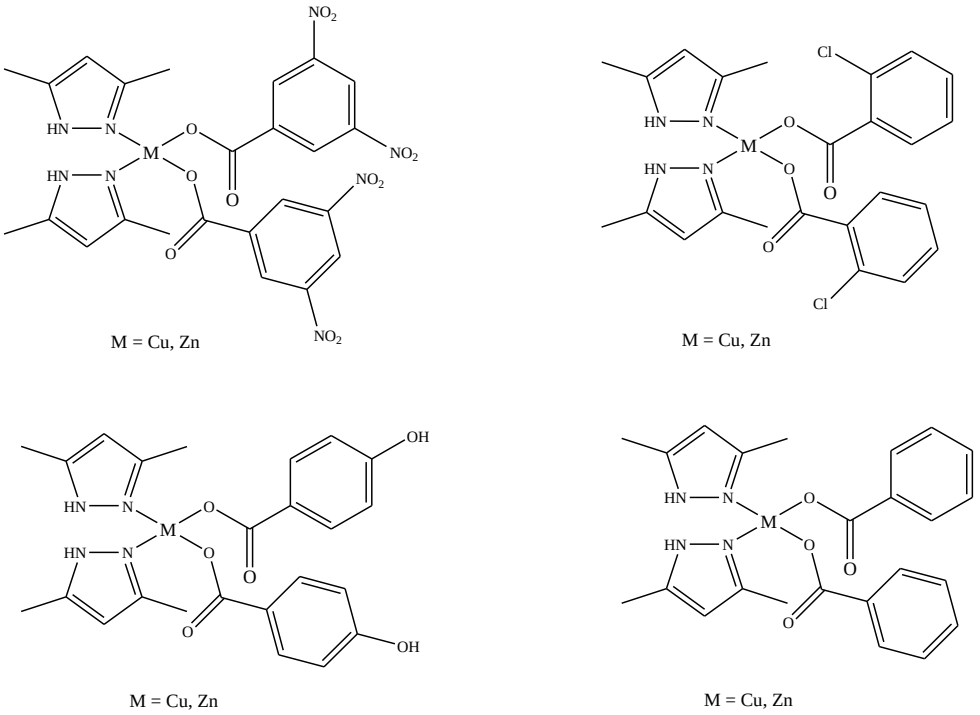


Fig. 2.30 Pyrazole Cu(II) and Zn(II) complexes.

Complementary to these findings, our research group reported the synthesis of Cu(II) and Zn(II) complexes bearing (pyrazol-1-ylmethyl)pyridine ligands (Fig. 2.31), and the use as initiators in ROP of ε–CL at 110 ^{o}C.[93] All the synthesised complexes form active initiators with Zn(II) complexes being more active than their Cu(II) counterparts. Kinetic studies reveal that polymerization process follow 1st order kinetics, and the polymers exhibit broad molecular weight distributions.

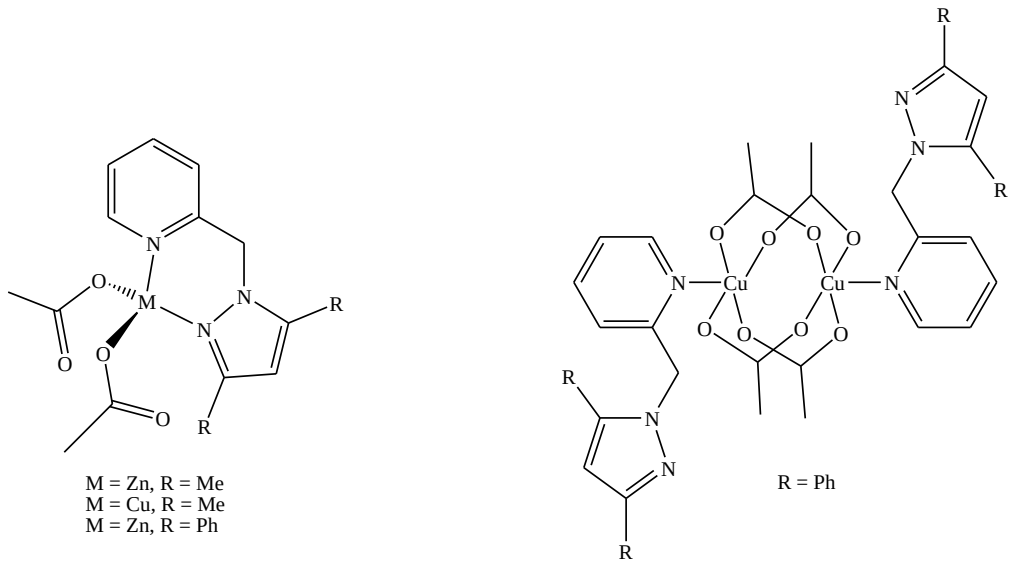


Fig. 2.31 (Pyrazol-1-ylmethyTHFl)pyridine supported Cu(II) and Zn(II) complexes.

2.2 Statement of the problem

There have been concerns associated with the biodegradability, biocompatibility and bioassimilability of PLA and PCL. Another concern is the use of toxic tin-based catalysts as initiators in the ROP of LA and *ε*–CL. It has been reported in numerous cases that tin catalyst is not completely removed during purification of polymers, so this has brought concerns for the use of tin-based catalysts as initiators in ROP of cyclic esters. Moreover, most catalysts employed for ROP of cyclic esters suffer from low activities and poor control over polymerization process.

2.3 Rationale of the study

This study therefore focuses on the design of catalysts that are based on pyrazolyl ligands with transition metals Zn(II) and Cu(II). Zn(II) and Cu(II) complexes are less toxic and it is believed that the polymers produced by these complexes could be used in biomedical, pharmaceutical as

well as plastic packaging industries. Furthermore, the Zn(II) and Cu(II) complexes are relatively cheap, stable and easy to synthesis.

2.4 Aims of the study

The overall objective of the study is to synthesize well-defined catalysts that could be potentially employed in ROP of LA and ε–CL. Thus the specific objectives are formulated as follows:

i. To synthesize and characterize the Zn(II) and Cu(II) carboxylate complexes.
ii. Investigate complexes as catalysts in the ROP of *ε*–CL and LA.
iii. To perform detailed kinetics and mechanistic studies of the ROP to gain insights of the mechanistic pathways of the polymerization reactions.

References

1. Kiesewetter, M. K.; Shin, E. J.; Hendrick, J. L.; Waymouth, R. M. *Macromolecules*, **2010**, 43, 2093.
2. O'Keefe, B. J.; Breyfogle, L. E.; Hillmyer, M. A.; Tolman, W. B. *J. Am. Chem. Soc.*, **2002**, 124, 4384.
3. Chisholm, M. H.; Eilerts, N. W. *Chem. Commun*., **1996**,853.
4. Chisholm, M. H.; Eilerts, N. W.; Huffman, J. C.; Iyer, S. S.; Pacold, M.; Phomphrai, K.; Ireland, B. J. *J. Am. Chem. Soc*., **2000**, 122, 11845.
5. Wheaton, C. A.; Hayes, P. G.; Ireland, B. J. *Dalton Trans*., **2009**, 4832.
6. Dias, M. L.;Palermo, L. C.; Silvino, A. C. *Macromol. Symp*., **2011**, 299-300, 156.
7. Parssinen, A.; Kohlmayr, M.; Leskela, M.; Lahcini, M.; Repo, T. *Polym. Chem*., **2010**, 1, 834.
8. Kricheldorf, H. R. *Chem. Rev*., **2009**, 109, 5579
9. Kamber, N. E.; Jeong, W.; Waymouth, R. M. *Chem. Rev*., **2007**, 107, 5813.
10. Coetes, G. W. *J. Soc. Chem*., *Dalton Trans.*, **2002**, 467-475.
11. Connor, E. F.; Nyce, G. W.; Myers, M.; Mock, A.; Hedrick, J. L. *J. A. Chem. Soc*., **2002**, 124, 914.
12. Jensen, T. R.; Brefogle, L. E.; Hillmyer, M. A.; Tolman, W. B. *Chem. Commun.,* **2004**, 21, 2504.
13. Jensen, T. R.; Schaller, C. P.; Hillmyer, M. A.; Tolman, W. B. *Org. Chem*., **2005**, 690, 5881.
14. Wilson, B. C.; Jones, C. W. *Macromolecules*, **2004**, 37, 9709.
15. Nederberg, F.; Connor, E. F.; Moller, M.; Glauser, T.; Hedrick, J. L. *Angew. Chem-Int. Edit*, **2001**, 40, 2712.
16. Ten Breteler, M. R. Stereoselectivity polymerization of lactones proteins of streocomplexed PLA building blocks: *Enschede, the Netherlands.*, **2010**, pp 9-33.
17. Kim, M. S.; Seo, K. S.; Khang, g.; Lee, H. B. *Macromolecules, Rapid. Commun*, **2005**, 26, 643.
18. a) Du, H.; Pang, X.; Yu, H.; Zhuang, C. X.; D. Cui, D. *Macromolecules*, **2007**, 40, 1904; b) Tang, Z. H; Chen, X. S.; Pang, X.; Yang, Y. K. ; Zhang, X.F.; Jing, X.B. *Biomacromolecules*, **2004**, 5, 965.
19. a) Kasperczyk, J.E.; Bero, M. *Polymer.,* **2000**, 41, 391; b) Kricheldorf, H.R.; Kreiser-Saunders, I. *Makromol. Chem.,* **1990**, 191, 1057; c) Kasperczyk, J.E. *Macromolecules*, **1995**,

28, 3937; d) Xie, W.; Chen, D. Fan, X.; Li, J.; Wang, P.G. ; Cheng, H.N.; Nickol, R.G. *J. Polym. Sci., Part A: Polym. Chem.*, **1999**, 37, 3486; e) C.A. Huang, C.T. Chen, *J. Chem. Soc., Dalton Trans.*, **2007**, 5561.

20. Sutar, A.K.; Maharana, T.; Dutta, S.; Chen, C.-T.; Lin, C.-C. *Chem. Soc. Rev.*, **2010**, 39, 1724.
21. Ko, B.-T.; Lin, C.-C. *J. Am. Chem. Soc.*, **2001**, 123, 7973.
22. Huang, B.-H.; Ko, B.-T.; Athar, T.; Lin, C.-C. *Inorg. Chem.*, **2006**, 45, 7348.
23. Chisholm, M.H.; Lin, C.-C.; Gallucci, J.C.; Ko, B.-T. *Dalton Trans.*, **2003**, 406.
24. Yu, T.-L.; Huang, B.-H.; Hung, W.-C.; Lin, C.-C.; Wang, T.-C.; Ho, R.-M. *Polyme*r., **2007**, 48, 4401.
25. Huang, Y.; Tsai, Y.-H.; Hung, W.-C.; Lin, C.-S.; Wang, W.; Huang, J.-H.; Dutta, S.; Lin, C.-C. *Inorg. Chem.*, **2010**, 49, 9416.
26. Hsueh, M.-L.; Huang, B.-H.; Wu, J.-C.; Lin, C.-C. *Macromolecules*, **2005**, 38, 9482.
27. Huang, C.-A.; Chen, C.-T. *Dalton Trans.*, **2007**, 5561.
28. Huang, C.-A.; Ho, C.-L. Chen, C.-T. *Dalton Trans*., **2008**, 3502.
29. Chang, Y.-N.; Liang, L.-C. *Iorg. Chim. Acta.*, **2007**, 360, 136.
30. Darensbourg, D. J.; Choi, W.; Karroonnirun, O.; Bhuvanesh, N. *Macromolecules*, **2008**, 41 (10), 3493.
31. Wu, J.; Yu, T.-L.; Chen, C.-T.; Lin, C.-C. *Coord. Chem. Rev*., **2006**, 250, 602.
32. Saunders, L. N.; Dawe, L. N.; Kozak, C. M. *J. Organomet. Chem.*, **2014**, 749, 34.
33. Zhang, J. Wang, C.; Lu, M.; Yao, Y.-M.; Zhang, Y.; Shen, Q. *Polyhedron*, **2011**, 30, 1876.
34. Xu, X.; Pan, X.; Tang, S.; Lv, X.; Li, L. Wu, J.; Zhao, X. *Inorg. Chem. Commun.*, **2013**, 29, 89-93.
35. a) Chen, H.-Y.; Huang, B.-H.; Lin, C.-C. *Macromolecules*, **2005**, *38*, 5400; b) Cheng, M.; Moore, D. R.; Reczek, J. J.; Chamberlain, B. M.; Lobkovsky, E. B.; Coates, G.W. *J. Am. Chem. Soc.*, **2001**, *123*, 8738; c) Williams, C. K.; Breyfogle, L. E.; Choi, S. K.; Nam, W.; Young, Jr., V. G.; Hillmyer, M. A.; Tolman, W. B. *J. Am. Chem. Soc.*, **2003**, *125*, 11350; d) Azor, L.; Bailly, C.; Brelot, L.; Henry, M.; Mobian, P.; Dagorne, S. *Inorg. Chem.*, **2012**, *51*,

10876-10883; e) Jensen, T. R.; Schaller, C. P.; Hillmyer, M. A.; Tolman, W. B. *J. Organomet. Chem.*, **2005**, *690*, 5881.

36. Ejfler, J.; Kobylka, M.; Jerzykiewicz, L. B.; Sobota, P. *Dalton Trans*., **2005**, 2047
37. a) Chisholm, M. H.; Eilerts, N.W. *Chem. Commun*., 1**996**, 853: b) Chisholm, M. H. Galluci, J.; Phomphrai, K. J. *Chem. Commun*., **2003**, 48.
38. Sarazin, Y.; Howard, R. H.; Hughes, D. L.; Humphrey, S. M.; Bochman, M. *Dalton Trans*., **2006**, 340.
39. Lee, W.-C.; Hsieh, H.-H.; Hsieh, C.-C.; Lee, M. H.; Huang, J.-H.; Wu, T.-C.; Chuang, S.-H. *J. Organomet. Chem*., **2007**, 692, 1131.
40. a) Chisholm, M. H.; Huffman, J. C.; Phomphrai, K. *J. Am. Chem. Soc. Dalton Trans*., **2001**, 48-49; b) Chisholm, M. H. Galluci, J.; Phomphrai, K. *Inorg. Chem*., **2002**, 41, 2785.
41. Chamberlain, M. H.; Cheng, M.; Moore, D. R.; Ovitt, T. M.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc*., **2001**, 123, 3229.
42. Sanchez-Barba, L. F.; Hughes, D. L.; Humphrey, S. M.; Bochmann, M. *Organometallics*, **2006**, 25, 1012.
43. Amgoune, A.; Lavanant, L.; Thomas, C. M.; Chi, Y.; Welter, R.; Dagorne, S.; Carpentier, J.-F. *Organometallics*, **2005**, 24, 6279.
44. Sanchez-Barba, L. F.; Garces, A.; Fajardo, M.; Alonso-Moreno, C.; Fernandez-Baeza, J.; Otero, A.; Antinolo, A.; Tejeda, J.; Lara-Sanchez, A.; Lopez-Solera, M. I. *Organometallics*, **2007**, 26, 6403.
45. Brefogle, L. E.; Williams, C. K.; Young, V. G.; Hillmyer, M. A.; Tolman, W. B. *Dalton Trans*., **2006**, 928.
46. a) Shuch, M.-L.; Wang, Y.-S.; Huang, B.-H.; Kuo, C.-Y.; Lin, C.-C. *Macromolecules*, **2004**, 37, 5155-5162; b) Yu, T.-L.; Wu, C.-C.; Chen, C.-C.; Huang, B.-H.; Wu, J.; Lin, C.-C. *Polymer*, **2005**, 46, 5909.
47. Tang, H.-Y.; Chen, H.–Y.; Huang, J.-Y.; Lin, C.-C. *Macromolecules*, **2007**, 40, 8855.
48. Tang, Z. H.; Chen, X. S.; Liang, Q. Z.; Bian, X. C.; Yang, L. X.; Piao, L. H.; Jing, X. B. J. *Polym. Sci. Part A: Polym. Chem*., **2003**, 41, 1934.
49. Albertson, A. C.; Varma, I. K. *Adv. Polym. Sci*., **2002**, 157, 1.
50. Jerome, C.; Lecomte, P. *Adv. Drug Delivery Rev*., **2008**, 60, 1056.
51. Del Rosal, I.; Poteau, R.; Maron, L. *Dalton Trans*., **2011**, 40, 11228.

52. Chisholm, M. H.; Llobet, D. N.; Galluci, J. *Inorg. Chem*., 40, **2001**, 6506.
53. Yu, T.-L.; Huang, C. H.; Yang, L. F.; Ko, B. T.; Lin, C.-C.; Chin, J. *Chem. Soc*., 47, **2000**, 1185.
54. Radano, C. P.; Baker, G. L.; Smith, M. R. *J. Am. Chem. Soc*. 122, **2000**, 1552.
55. Huang, C. H.; Wang, F.C.; Ko, B. T.; Yu, T.-L. Lin, C.-C. *Macromolecules*, 34, **2001**, 356.
56. Chakraborty, D.; Chen, E. Y.-C. *Organometallics*, 21, **2002**, 1438.
57. Chen, C.-T.; Huang, C. A.; Huang. B. H. *Macromolecular*, 37, **2004**, 7968.
58. Hormnirum, P.; Marshall, E. L.; Gibson, V. C.; White, A. J. P.; Williams, D. J. *J. Am. Chem. Soc*. 126, **2004**, 2688.
59. Ovitt, T. M.; Coates, G. W. *J. Am. Chem. Soc*. 121, **1999**, 4072.
60. Ovitt, T. M.; Coates, G. W. *J. Am. Chem. Soc*. 121, **2002**, 1316.
61. Zhong, Z.; Dijkstra, P. J.; Feijen, J. *Angew Chem. Int. Ed*. 41, **2002**, 4510.
62. Tang, Z.; Chen, X.; Pang, X.; Yang, Y.; Zhang, X.; Jing, X. *Biomacromolecules*, 5, **2004**, 965.
63. Chen, C.-T.; Huang, C.A.; Huang, B. H. *Dalton Trans*., **2003**, 3799.
64. Alcazar-Roman, L. M.; O'Keefe, B. J.; Hillmyer, M. A.; Tolman, W. B. *Dalton Trans*., **2003**, 3082.
65. Albertsson, A.-C.; Varma, I. K. *Biomacromolecules*, **2003**, 4, 1466.
66. Shen, Y.; Shen, Z.; Zhang, Y.; Yao, K. *Macromolecules*, **1996**, 29, 8289.
67. Allan, L. E. N.; Belanger, J. A.; Callaghan, L. M.; Cameron, D. J. A.; Decken, A.; Shaver, M. P. *J. Organomet. Chem.*, **2012**, 706, 106.
68. Shang, X.; Liu, X.; Cui, D. *J. Polym. Sci. Part A: Polym. Chem*., **2007**, 45, 5662.
69. Gao, W.;Cui, D.; Liu, X.; Zhang, Y.; Mu, Y. *Organometallics*, **2008**, 27, 5889.
70. Tsai, Y.-H.; Lin, C.-H.; Lin, C.-C.; Ko, B.-T. *J. Polym. Sci. Part A: Polym. Chem.* **2009**, 47, 4927.
71. Willans, C. E.; Sinenkov, M.A.; Fukin, G. K.; Sheridan, K.; Lynam, J. M.; Trifonov, A. A.; Kerton, F. M. *Dalton Trans*., **2008**, 3592.
72. Zhou, L. Z.; Wang, Y. M.; Yao, Y. M.; Zharing, Y.; Shen, Q. *J. Rare Earths*, **2007**, 25, 544.
73. Otero, A.; Fernandez-Baeza, J.; Antinolo, A.; Lara-Sanchez, A.; Martinez-Caballero, E.; Tejeda, J.; Sanchez-Barba, L. F.; Alonso-Moreno, C.; Lopez-Solera, M. I. *Organometallics*, **2008**, 27, 976.

74. Gamer, M. T.; Rastater, M.; Roesky, P. W.; Steffens, A.; Glanz, M. *Chem. – Eur. J.*, **2005**, 11, 3165.
75. Gamer, M. T.; Roesky, P. W.; Palard, I.; Le Hellaye, M. Guillaume, S. M. *Organometallics*, **2007**, 26, 651.
76. Wiecko, M.; Roesky, P. W.; Bularkov, V. V.; Spannenberg, A. *Eur. J. Inorg. Chem*., **2007**, 876.
77. Cauyela, J.; Bounor-Legare, V.; Cassagnau, P.; Michel, A. *Macromolecules*, **2006**, 39, 1338.
78. Perez, Y.; del Hierro, I.; Sierra, I.; Gomez-Sal, P.; Farjado, M.; Otero, A. *J. Organomet. Chem.*, **2006**, 691, 3053.
79. Chmura, A. J.; Davison, M. G.; Jones, M. D.; Lunn, M. D.; Mahon, M. F.; Johnson, A. F.; Khunkamchoo, P.; Roberts, S. L.; Wong, S. S. F. *Macromolecules*, **2006**, 39, 7250
80. Hsieh, K.-C; Lee, W.-Y.; Hsueh, L.-F.; Lee, M. H.; Huang, J.-H. *Eur. J. Inorg. Chem.*, **2006**, 2306
81. Mahha, Y.; Atlamsani, A.; Blais, J.-C.; Tessier, M.; Bregault, J.-M.; Salles, L. *J. Mol. Catal. A: Chem.*, **2005**, 234, 63.
82. Arbaoui, A.; Redsahw, C.; Homden, D. M.; Wright, J. A.; Elsegood, R. J. *Datlton Trans*., **2009**, 8911.
83. Chen, M.-Z.; Sun, H.-M.; Li, W.-F.; Wang, Z. G.; shen, Q.; Zhang, Y. *J. Organomet. Chem*., **2006**, 691, 2489.
84. Gowda, R. R.; Chakraborty, D. *J. Mol. Catal. A: Chem*., **2009**, 301, 84.
85. Gowda, R. R.; Chakraborty, D. *J. Mol. Cat. A: Chem*., **2011**, 349, 86.
86. a) Han, R.; Parkin, G. *Organometallics*, **1991**, 10, 1010-1020; b) Han, R.; Parkin, G. *J. Am. Chem. Soc*., **1992**, 114, 748.
87. Lian, B.; Thomas, C. M.; Casagrande, O. L.; Lehmann, Jr., C. W.; Roisnel, T. Carpentier, J.-F. *Inorg. Chem*., **2007**, 46, 328.
88. Darensbourg, D. J.; Karroonnirun, O. *Inorg. Chem*., **2010**, 49, 2360.
89. Alonso-Moreno, C.; Garces, A.; Sanchez-Barba, L. F.; Fajardo, M.; Fernandez-Baeza, J.; Otero, A. .; Lara-Sanchez, A.; Antinolo, A.; Broomfield, L.; Lopez-Solera, M. I.; Rodriguez, A. M. *Organometallics*, **2008**, 27, 1310.
90. Chai, Z.-Y.; Zhang, C.; Wang, Z.-X. *Organometallics*, **2008**, 27, 1626.
91. Chen, H.-Y.; Huang, B.-H.; Lin, C.-C. *Macromolecules*, **2005**, 38, 5400.

92. Appavoo, D.; Omondi, B.; Guzei, I. A.; van Wyk, J. L.; Zinyemba, O. Darkwa, J. *Polyhedron*, **2014**, 69, 55.
93. Ojwach, S. O.; Okenwa, T. T.; Attandoh, N. W.; Omondi, B. *Dalton Trans.*, **2013**, 42, 10735.

Chapter 3

Synthesis and Structural Characterization of Pyrazolyl-pyridine Cu(II) and Zn(II) Carboxylate Complexes

3.1 Introduction

In the past decade, a number of ligands bearing pyrazole and pyrazolyl backbone have gained much attention mostly in the fields of coordination chemistry and biology.[1] The most important feature of these heterocyclic compounds is that they behave as excellent σ-donor and π-acceptor ligands, thus showing versatility in coordination modes towards the metals.[2] Hence, the reported compounds offer highly electropositive metal centers.

Pyrazolyl ligands can act as tridentate, bidentate as well as bridging ligands. Sarma *et al.* reported that pyrazolato ligand is a precursor for the preparation of binuclear or polynuclear metal complexes.[2] The 2,6-bis(3,5-dimethyl-***N***-pyrazolyl)pyridine ligands coordinated to late transition metals are monomeric. The reports by Wu *et al*. show that steric hindrance around the metal center reduces aggregation.[3] The synthesis, characterization and molecular structures of pyrazole and pyrazolyl complexes with late transition metals have been studied extensively.[4] Bis(pyrazol-1-ylmethyl)pyridine ligands have been used to construct Co(II),[5] Fe(II),[5] and Ni(II)[5,6] complexes that form active catalysts for polymerization reactions.

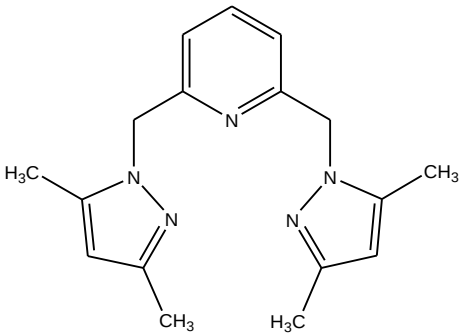
Pyrazolyl ligand systems possess the ability to effect the metal complex's ability to catalyse ring-opening polymerization of the cyclic esters. This is largely due to the fact that pyrazole and pyrazolyl ligands coordinated to transition metals form compounds that are actively and

potentially developed as nitrogen-donor catalysts.[7] Their electronic properties influence the efficiency of the catalysts. In addition, bulky nature of pyrazolyl ligands provides the metal center with steric hindrance thus preventing the growing polymer chain from accessing the active catalyst site, and hence preventing transesterification reactions.[8] Pyrazolyl zinc compounds reported by Yu *et al*.,[7b] Kang *et al*.,[7c] and Lian *et al*.,[7d] formed active catalysts in the ROP of D,L-Lactide. More recently, appavoo *et al*.,[9] Ojwach *et al*.[10] reported pyarazole and pyrazolyl Zn(II) and Cu(II) complexes to be the active catalysts in ROP of *ε*–CL and D,L-Lactide.

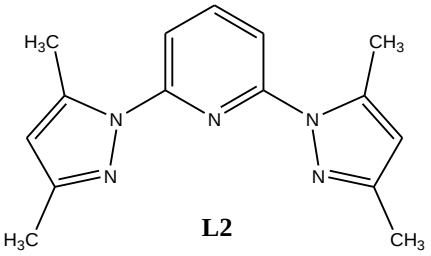
In this contribution, we explore the coordination behavior of pyrazolyl pyridine ligands with Cu(II) and Zn(II) metal ions. The ligands utilized in this work are shown on Scheme 3.1. These ligands have been used to explore their coordination chemistry with Cu(II) and Zn(II) metal ions. To the best of our knowledge not many studies have been conducted to explore ROP of cyclic esters using these Zn(II) and Cu(II) complexes supported by pyrazolyl pyridine ligands as initiators. Most catalysts employed for ring opening polymerization of cyclic esters result in transesterification reactions, poor control of polymerization process, non-biocompatibility, low activity, and toxicity. For instance, even the commercialized and promising tin-based compounds[11] are not prospering in biomedical and pharmaceutical industries due to their toxicity.[12] It should be noted that the choice of the metal is equally significant as the ligand design. Thus, the design of Zn(II) and Cu(II) metal complexes have been motivated by their low toxicity[13] and their good Lewis acidity[14] which aids in their good activity towards ROP of cyclic monomers. For instance, Williams *et al*.,[15] Drouin *et al.*,[16] reported zinc-based catalysts to form active initiators in the ROP of ε-CL and LAs. On the other hand, John *et al.*,[17] Bhunora *et al.*[18] reported the catalytic screening of copper complexes in the polymerization of these cyclic monomers and found them to be the active initiators. Zn(II) and Cu(II) acetates have also

been reported to possess excellent activities as catalysts for bulk ring-opening polymerization of cyclic esters.[14,19] In addition, the design of pyrazolyl pyridine Zn(II) and Cu(II) complexes is also largely motivated by their ease of synthesis, low costs, relatively easy to handle, stability, and importantly their biocompatibility.

In the current chapter we report and discuss the synthesis and characterization of pyrazolyl pyridine Zn(II) and Cu(II) carboxylate complexes. In chapter four we will discuss the ability of these complexes to initiate the ROP of ε-CL and LAs.



L1



L2

Scheme 3.1 2,6-bis(3,5-dimethyl-pyrazol-1-ylmethyl)pyridine (**L1**) and 2,6-bis(3,5-dimethyl-***N***-pyrazolyl)pyridine (**L2**) ligands.

3.2 Experimental section

3.2.1 Materials and instrumentation

All solvents and reagents were purchased from commercial vendors and were used as received unless otherwise stated. For instance, benzoic acid (99.5%), 2-bromobenzoic acid, 2-chlorobenzoic acid, 3,5-dimethylpyrazole, 2,6-bis(dichloromethyl)pyridine and 2-bromopyridine were purchased from Sigma Aldrich. While $Zn(CH_3COO)_2 \cdot 2H_2O$ (≥99.5%) and $Cu(CH_3COO)_2 \cdot 2H_2O$ (≥99.5%) were purchased from Saarchem. Dichloromethane, Acetonitrile, Hexane, Toluene and Methanol (~99.5%$^{V}/_{V}$) solvents were sourced from Merck. Deuterated chloroform ($CDCl_3$) on the other hand was sourced from Sigma Aldrich.

Pyrazolyl ligands 2,6-bis(3,5-dimethyl-1-ylmethyl)pyridine **(L1)** and 2,6-bis(3,5-dimethyl-***N***-pyrazolyl)pyridine (**L2**) were prepared using literature procedures.[20,21] NMR spectra were recorded on a Bruker 400 UltraShield instrument (400 MHz for ^{1}H NMR) at ambient temperature using chloroform-d ($CDCl_3$). All the ^{1}H NMR chemical shifts were referenced to the signals of the protons of the ^{1}H NMR solvent and are reported in δ (ppm): $CDCl_3$ at 7.28 ppm for ^{1}H NMR. Elemental analyses were performed on a Flash 2000 thermoscientific analyser. All the IR spectra were recorded with the aid of Perkin-Elmer spectrum 100 (IR spectrometer) whereas the mass spectra were recorded by micromass LCT premier mass spectrometer. Magnetic moments of paramagnetic copper complexes were studied with the aid of the Evans balance with the constant C = 1.031 while electron paramagnetic resonance (EPR) studies were performed on a Bruker EMX/Premium-240 653 instrument operating at X-band (9 GHz) frequency. All coupling constants are reported in Hertz.

The X-Ray crystal evaluation and data collection were carried on a Bruker APEXII diffractometer with Mo Kα (λ = 0.71073 Å) radiation and diffractometer to crystal distance 4.9 cm. With the aid of an automated indexing routine built in the APEXII program suit, all the reflections were indexed successfully.[22] Full-matrix least-squares procedures against F^2 using SHELXS97 was used for structural refinement from a direct method of solving structures. Refinement of all non-hydrogen atoms was achieved by using anisotropic displacement coefficient.[23]

3.2.2 Synthesis of Zn(II) and Cu(II) pyrazolyl carboxylate complexes

3.2.2.1 [2,6-((3,5-Me_2pz)CH_2)$_2$py-Zn(II)(C_6H_5COO)$_2$] (1)

This complex was prepared by a one pot synthesis by refluxing $ZnOAc_2 \cdot 2H_2O$ (0.20 g, 0.90 mmol) and C_6H_5COOH (0.25 g, 2.0 mmol) in methanol (20 mL) in a 1:2 ratio for 5 h. After 5 h, a solution of 2,6-[(3,5-Me_2pz)CH_2]$_2$py (**L1**) (0.26 g, 0.90 mmol) in methanol (4 mL) was added drop wise and the reaction was refluxed further for 24 h. After 24h, the solvent was removed in *vacuo* to give a white solid; this was recrystallized from CH_2Cl_2-hexane mixture and afforded colorless single-crystals suitable for X-ray analysis. Yield = 0.26 g, (49%). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 2.09 (s, 3H, free acetic acid) 2.19 (s, 6H, CH_3-Pz) 2.31 (s, 6H, CH_3-Pz) 5.54 (s, 4H, CH_2) 5.90 (s, 2H, CH-Pz) 6.87 (d, $^3J_{HH}$ = 7.77 Hz, 2H, CH-Py) 7.37 (t, 1H, C_6H_5COO) 7.41-7.51 (m, 3H, C_6H_5COO) 7.55-7.66 (m, 1H, CH-Py) 8.08 (dd, $^3J_{HH}$ = 8.44 Hz, 6H, C_6H_5COO). IR (cm^{-1}): 2987w (C-H), 1642s (C=O), 1399s (C=N), 714s (monosubstituted aromatic ring). Anal. Calc. for $ZnC_{31}N_5O_4H_{31}$: C, 61.74; H, 5.18; N, 11.62. Found: C, 61.22; H, 5.11; N, 11.24.

3.2.2.2 [2,6-((3,5-Me_2pz)CH_2)$_2$py-Zn(II)(2-Br-$C_6H_5COO)_2$] (2)

Using a procedure similar to the preparation of **1**, $ZnOAc_2 \cdot 2H_2O$ (0.10g, 0.47 mmol), 2-Br-C_6H_4COOH (0.20g, 1.0 mmol) with a solution of **L1** (0.14g, 0.47 mmol). The crude product was recrystallized from CH_2Cl_2-hexane mixture and gave single-crystals of compound **2** worthy for X-ray analysis. . Yield = 0.25 g, (68%). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 2.06 (s, 3H, free acetic acid) 2.24 (s, 6H, CH_3-Pz) 2.33 (s, 6H, CH_3-Pz) 5.52-5.77 (s, 4H, CH_2) 5.89 (s, 2H, CH-Pz) 6.96-7.05 (s, 2H, CH-Pz) 7.14-7.22 (s, 2H, CH-Py) 7.22-7.37 (m, 3H, 2-Br-C_6H_5COO) 7.41-7.51 (m, 3H, 2-Br-C_6H_5COO) 7.50-7.59 (m, 2H, 2-Br-C_6H_5COO) 7.72.08 (t, $^3J_{HH}$=7.81 Hz, 1H, CH-Py) 7.76-7.87 (m, 2H, 2-Br-C_6H_5COO). IR (cm^{-1}): 2880w (C-H), 1587s (C=O), 1387s (C=N), 749s (orthosubstituted aromatic ring). Anal. Calc. for $ZnC_{31}N_5O_4H_{29}Br_2$: C, 48.94; H, 3.84; N, 9.21. Found: C, 49.08; H, 4.01; N, 8.70.

3.2.2.3 [2,6-((3,5-Me_2 pz)CH_2)$_2$py-Cu(II)($C_6H_5COO)_2$] (3)

This complex was prepared using the same procedure employed for the preparation of **1**, $CuOAc_2 \cdot 2H_2O$ (0.21 g, 1.0 mmol), C_6H_5COOH (0.25 g, 2.1 mmol), and a solution of **L1** (0.31 g, 1.0 mmol) afforded a deep blue solid. Yield = 0.41 g, (51%). IR (cm^{-1}): 2880w (C-H), 1600s (C=O), 1373s (C=N), 715s (monosubstituted aromatic ring). Magnetic moment: μ_{eff} = 1.86 BM. Anal. Calc. for $CuC_{31}N_5O_4H_{31}$: C, 61.93; H, 5.20; N, 11.65. Found: C, 61.51; H, 4.81; N, 11.59.

3.2.2.4 [2,6-((3,5-Me_2 pz)CH_2)$_2$py-Cu(II)(2-Br- $C_6H_5COO)_2$] (4)

This complex was prepared using the same procedure employed for the preparation of compound **1**, $CuAc_2 \cdot 2H_2O$ (0.10 g, 0.51 mmol), 2-Br-C_6H_2COOH (0.21 g, 1.0 mmol) and a solution of **L1** (0.15g, 0.51 mmol) gave blue solid. Yield = 0.18 g, (46%). IR (cm^{-1}): 2881w (C-H), 1575s (C=O), 1387s (C=N), 750s (orthosubstituted aromatic ring). Magnetic moment: μ_{eff} = 1.89 BM. Anal. Calc. for $CuC_{31}N_5O_4H_{29}Br_2$: C, 49.06; H, 3.85; N, 9.23. Found: C, 48.67; H, 4.06; N, 9.15

3.2.2.5 [2,6-bis(3,5-Me_2-N-pz)py-Zn(II)($C_6H_5COO)_2$] (5)

To a solution of $ZnOAc_2 \cdot 2H_2O$ (0.086 g, 0.39 mmol) in methanol (30 mL) C_6H_5COOH (0.094g, 0.77 mmol) was added. After stirring this reaction for 5h at reflux, bis(3,5-dimethyl-***N***-pyrazolyl)pyridine (**L2**) (0.10 g, 0.38 mmol) was added and the reaction was then stirred at reflux for further 15h. After 15h the reaction was allowed to cool at ambient temperature, 5 mL toluene was added and the reaction was stirred at room temperature for 30 minutes. The solvents were removed in *vaccuo* and white solid was obtained. Recrystallization of crude product from CH_2Cl_2-hexane mixtures after 1 to 2 days gave single-crystals of compound **5** commendable for X-ray analysis. Yield = 0.19g, (87%).^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 2.43 (*s*, 6H, CH_3-Pz) 2,63 (*s*, 6H, CH_3-Pz) 6.09 (*s*, 2H, CH-Pz) 7.35-7.37 (t, 4H, $^3J_{HH}$=7.6 Hz, C_6H_6COO) 7.40-7.44 (d, $^3J_{HH}$=7.20 Hz, 2H, C_6H_6COO) 7.44-7.46 (d, $^3J_{HH}$=7.20 Hz, 2H, CH-Py) 8.09 (d, $^3J_{HH}$=7.60 Hz, 1H, CH-Py) 8.09-8.11 (t, $^3J_{HH}$=8.0 Hz, 4H, C_6H_6COO). IR (cm^{-1}): 2881w (C-H), 1609s (C=O), 1362s (C=N), 720s (monosubstituted aromatic ring). Anal. Calc. for $C_{29}H_{27}N_5O_4Zn$: C, 60.58; H, 4.73; N, 12.18. Found: C, 60.45; H, 4.81; N, 12.30.

3.2.2.6 [2,6-bis(3,5-Me_2-N-pz)py-Zn(II)(2-Cl-$C_6H_5COO)_2$] (6)

Complex **6** was synthesized by following the procedure adopted for the synthesis of **5** using $ZnOAc_2 \cdot 2H_2O$ (0.083g, 0.38 mmol), 2-Cl-C_6H_5COOH (0.12g, 1.00 mmol) and **L2** (0.10 g, mmol) gave white solid. The crude product was then recrystallized from acetonitrile overnight and afforded single-crystals for compound **6** suitable for X-ray analysis. Yield = 0.18 g, (73%). ^1H NMR (400 MHz, $CDCl_3$) δ ppm 2.52 (*s*, 6H, CH_3-Pz) 2,67 (*s*, 6H, CH_3-Pz) 6.19 (*s*, 2H, CH-Pz) 7.15-7.18 (m, 4H, CH-Pz) 7.26-7.28 (d, $^3J_{HH}$=7.20 Hz, 2H, 2-Cl-C_6H_5COO) 7.44-7.46 (d, $^3J_{HH}$=8.0 Hz, 2H, 2-Cl-C_6H_5COO) 7.61-7.63 (d, $^3J_{HH}$=8.8 Hz, 2H, CH-Py) 8.02-8.06 (t, $^3J_{HH}$=8.0 Hz, 1H, CH-Py). IR (cm^{-1}): 2881w (C-H), 1611s (C=O), 1461m (C=N), 743s (orthosubstituted aromatic ring). Anal. Calc. for $C_{29}H_{25}Cl_2N_5O_4Zn$: C, 54.10; H, 3.91; N, 10.88. Found: C, 54.43; H, 3.95; N, 11.02.

3.2.2.7 [2,6-bis(3,5-Me_2-N-pz)py-Cu(II)(2-Cl-$C_6H_5COO)_2$] (7)

This compound was prepared in accordance with the procedure described for **5** using $CuOAc_2 \cdot 2H_2O$ (0.075g, 0.38 mmol), 2-Cl-C_6H_5COOH (0.11g, 0.76mmol) and **L2** (0.10 g, 0.37 mmol) yielded dark green solid. The crude product was recrystallized from acetonitrile after 1 to 2 days and gave green single crystals for compound **7** worthy for X-ray analysis. Yield = 0.16 g, (65%). IR (cm^{-1}): 2881w (C-H), 1609s (C=O), 1462.5m (C=N), 720s (orthosubstituted aromatic ring). Magnetic moment: μ_{eff} = 1.92 BM. Anal. Calc. for $C_{29}H_{25}Cl_2N_5O_4Cu \cdot H_2O$: C, 52.77; H, 3.82; N, 10.61. Found: C, 52.50; H, 4.10; N, 10.72.

3.2.2.8 [2,6-bis(3,5-Me_2-N-pz)py-Zn(II)$(OAc)_2$] (8)

To a solution of $ZnOAc_2 \cdot 2H_2O$ (0.083 g, 0.18 mmol) in methanol (30 mL), **L2** (0.11 g, 0.41 mmol) in methanol (2 mL) was added and the reaction was refluxed for 24h. After 24h, 5 mL toluene was added and the reaction was stirred at ambient temperature for 30 minutes. Solvents were removed in *vaccuo* and white solid was obtained. The crude product was recrystallized from CH_2Cl_2-hexane mixture after 1 to 2 days and gave single-crystals for compound **8** worthy for X-ray analysis. Yield = 0.11 g, (60%). ^1H NMR. IR (cm^{-1}): 2888w (C-H), 1594s (C=O), 1456m (C=N). Anal.Cal for $C_{19}H_{23}N_5O_4Zn \cdot 3H_2O$: C, 45.20; H, 5.79; N, 13.88. Found: C, 45.26; H, 5.27; N, 13.41.

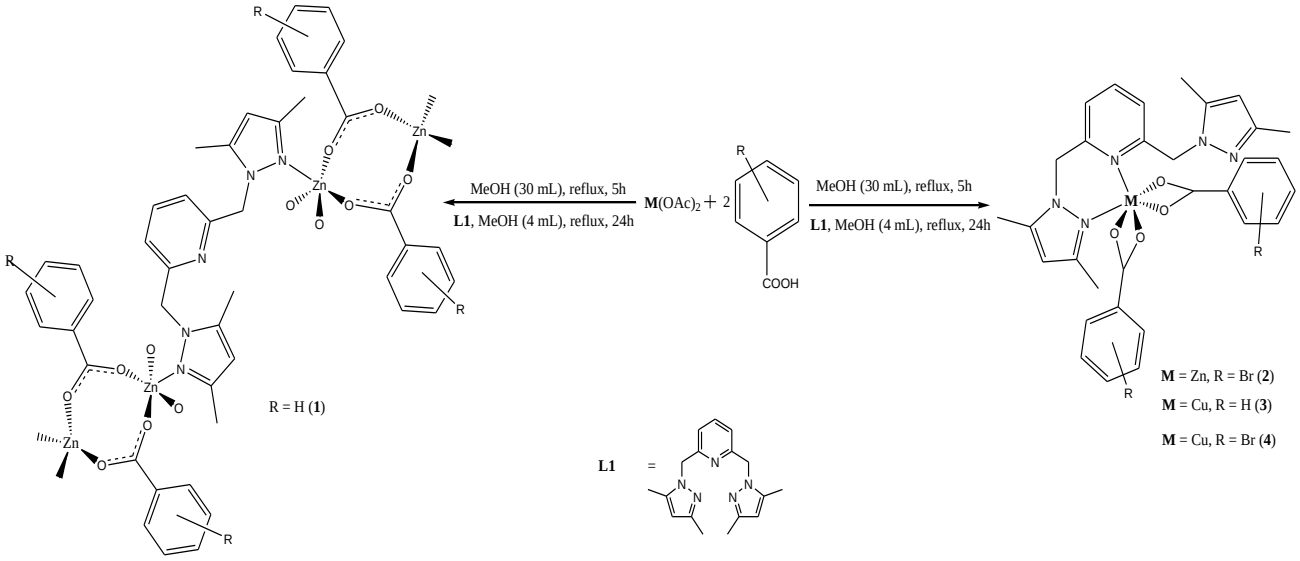
3.2.2.9 [2,6-bis(3,5-Me_2-N-pz)py-Cu(II)$(OAc)_2$] (9)

Using a procedure identical to the preparation of **8**, $CuOAc_2 \cdot 2H_2O$ (0.076 g, 0.38 mmol) and **L2** (0.10 g, 0.37 mmol) yielded green solid. The crude product was then recrystallized from CH_2Cl_2-hexane mixtures after 1 to 2 days and afforded blue single-crystals of compound **9** worthy for X-ray analysis. Yield = 67 mg, (38%). IR (cm^{-1}): 2881w (C-H), 1565s (C=O), 1394s (C=N). Magnetic moment: μ_{eff} = 1.85 BM.

3.3 Results and discussion

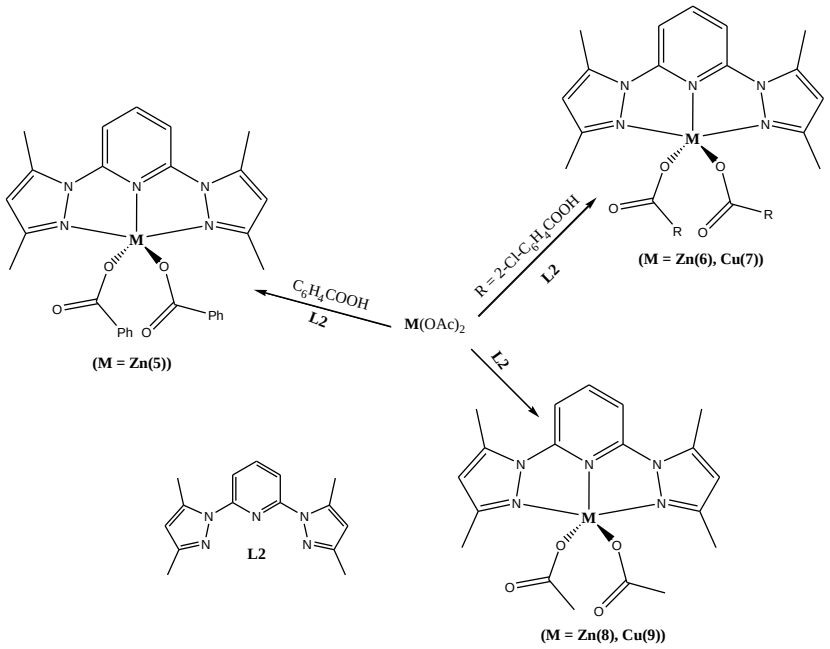
3.3.1 Synthesis and structural characterization of Zn(II) and Cu(II) Carboxylate complexes

The ligands, 2,6-bis(3,5-dimethyl-1-ylmethyl)pyridine **(L1)** and 2,6-bis(3,5-dimethyl-***N***-pyrazolyl)pyridine (**L2**) were prepared following previously published procedures.[20,21] The corresponding Zn(II) and Cu(II) benzoate complexes (**1**-**7**) were prepared by a single pot two step reaction process which involved reaction of the metal(II) acetates with the respective carboxylates in a 1:2 ratio followed by *insitu* addition of a methanolic solution of **L1** or **L2** in 1:1 ratio (Schemes 3.2 and 3.3). The elimination of acetic acid from the metal acetates followed by reaction with the ligands to afford the corresponding metal benzoates which was the driving force for the formation of the benzoate complexes.[9] The Zn(II) complexes were isolated as white solids while the Cu(II) complexes were isolated as blue solids. The benzoate compounds were isolated in low to excellent yields (46% and 87%). Generally, relatively higher yields were observed for complexes bearing the rigid ligand **L2** compared to those supported on **L1**. For example, the Zn(II) complexes **1** (with **L1**) and **7** (with **L2**) were obtained in 49% and 87% yields respectively. The observed low conversions for **L1** complexes could be attributed to the unhindered rotation around the CH_2 linker carbon and flexibility of the complexes which might hinder complex formation as opposed to the more rigid framework of ligand **L2**.



Scheme 3.2: Synthesis (pyrazolyl)pyridine Zn(II) and Cu(II) carboxylate complexes **1-4**.

Another synthetic strategy employed involved the reactions of compound **L2** with Zn(II) and Cu(II) metal acetates to produce the corresponding Zn(II) and Cu(II) acetate complexes **8** and **9** in 60% and 38% yields respectively (Scheme 3.3). All the synthesized complexes were soluble in most organic solvents.



Scheme 3.3: Synthesis of (pyrazolyl)pyridine Zn(II) and Cu(II) carboxylate complexes **5-9**.

The Zn(II) complexes **1**, **2**, **5**, **6** and **8** were characterized by ^{1}H NMR spectroscopy to establish their identity and confirm the coordination of the ligand **L1** and **L2** to Zn salts to form the respective complexes. This was conducted by comparing the ^{1}H NMR spectra of the ligands **L1** or **L2** with those of their corresponding complexes. For instance, the methylene protons (-CH_2- linker) of **L1** recorded at 5.32(**a**) ppm shifted downfield to 5.65 and 5.54(**a'**) ppm in complexes **1** and **2** respectively (Fig 3.1**)**. Similarly the methine protons (-CH-) of the pyrazole in **L1** were observed at 6.66 ppm in comparison to downfield signals at 7.01 and 6.87 ppm in **1** and **2** respectively.

In contrast to complexes **1** and **2**, doublet methine proton (-CH-) of pyridine in **L2** recorded at 7.71 ppm shifted upfield to 7.39 and 7.45 ppm in the respective complexes **5** and **6** (Fig. 3.2).

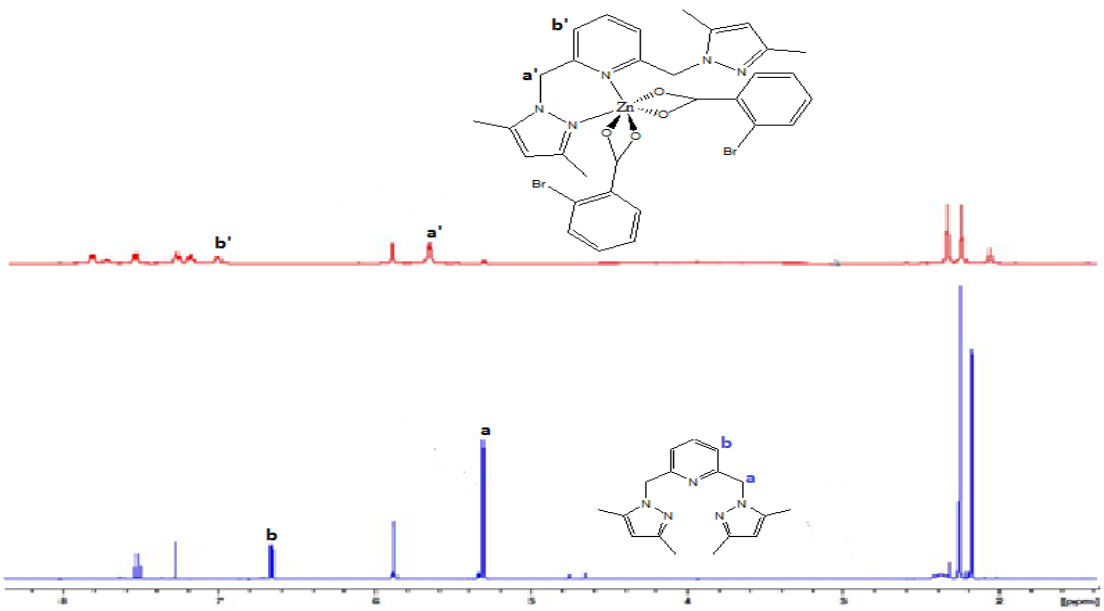


Figure 3.1: ^{1}H NMR spectra of the ligand **L1** (below) and its corresponding complex **2** (above) interlay.

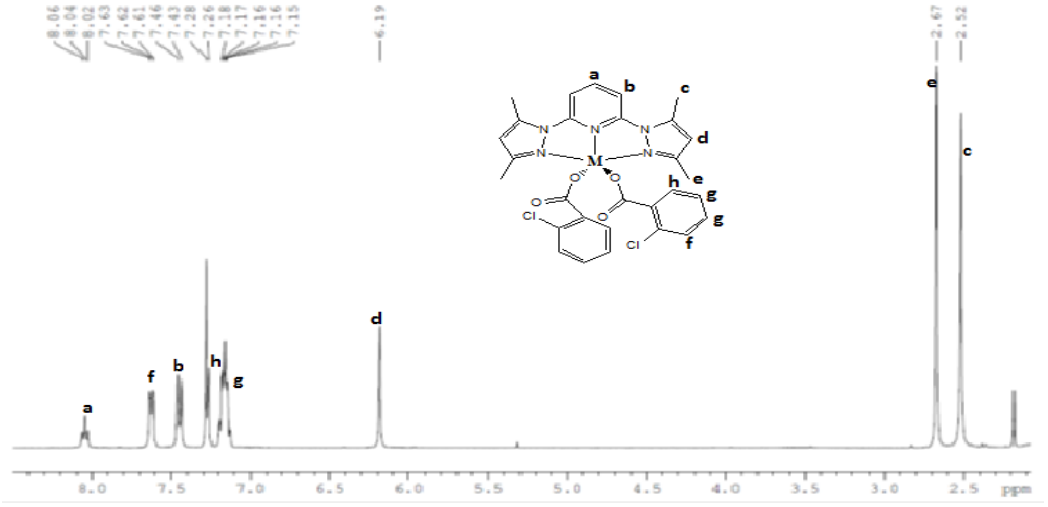


Figure 3.2: ^{1}H NMR spectrum of complex **6**

All the Cu(II) complexes were paramagnetic. Hence, ^{1}H NMR spectroscopy was not useful in their structural elucidation. Thus we used magnetic moment measurements to characterize these Cu(II) complexes. Room temperature magnetic moment measurements for **3**, **4**, **7** and **9** were found as 1.86, 1.89, 1.92, and 1.85 BM respectively, suggesting the presence of one unpaired electron. The observed, magnetic moments are comparable to the other Cu(II) compounds reported in literature[9] and fall within the range of 1.7–2.2 BM for a free Cu^{2+} ion. However, these values are relatively lower than 3.00 BM which is expected value for the spin only and spin-orbital coupling[24] pointing to the role played by the ligand in the observed magnetic moments of Cu(II) complexes.

IR spectroscopy was also employed to characterize the complexes and confirm ligand coordination. Table 3.1 shows selected IR frequencies for the C=O and C=N functional groups of the corresponding complexes, while Figure 3.3 and 3.4 represent the IR spectra for complexes **1** and **7** respectively. Due to conjugation, the carbonyl stretching frequencies were observed at slightly lower wavenumbers in the range of 1555.4 to 1642.1 cm^{-1} (Table 3.1) instead of 1700 cm^{-1} for all the complexes. This is in agreement with the results obtained by Appavoo *et al.*,[9] Ye *et al.*[25] The IR spectra of complexes **1-9** showed some slight differences from their corresponding ligands especially the C-N stretching frequencies, with the general shifts towards lower frequencies in the complexes when compared to their corresponding ligands. For example, **L1** with its corresponding complex **1**, the C-N stretching frequencies were observed at 1420.4 cm^{-1} and 1399.4 cm^{-1} respectively. On the other hand, the C-N stretching frequencies of **L2** and its corresponding complex **7** were observed at 1435.2 cm^{-1} and 1362.3 cm^{-1} respectively.

Table 3.1 Selected IR stretching frequencies of **1-9**.

Complex	$\upsilon_{(C=O)}$ cm^{-1}	$\upsilon_{(C=N)}$ cm^{-1}
1	1642.1	1399.4
2	1586.9	1387.1
3	1555.4	1373.2
4	1574.7	1386.7
5	1608.5	1362.3
6	1611.3	1461.4
7	1564.4	1362.3
8	1594.1	1381.7
9	1565.3	1393.9

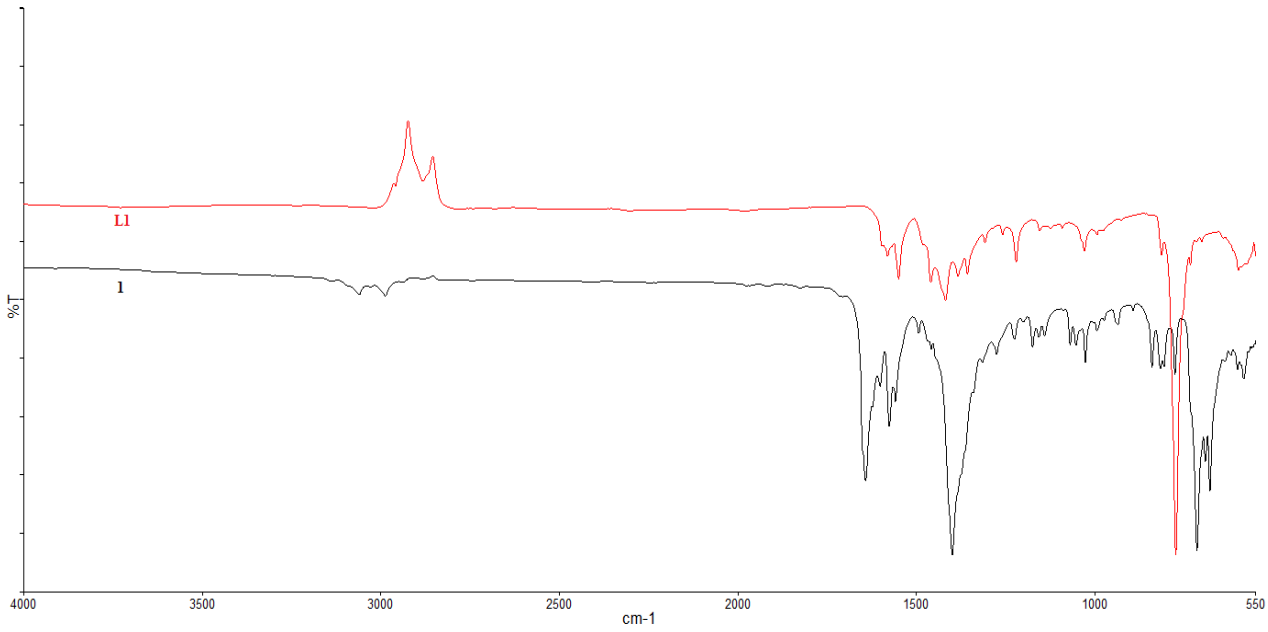


Figure 3.3: IR spectra of **L1** and its corresponding complex **1**.

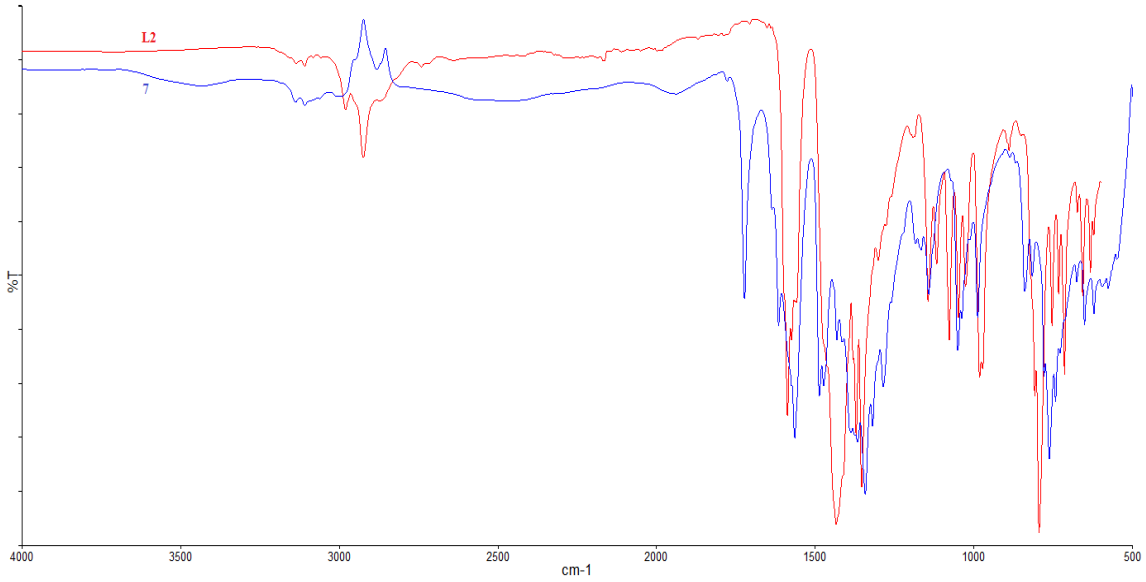


Figure 3.4: IR spectra of **L2** and its corresponding complex **7**.

Mass spectrometry was employed to further characterize and establish the proposed structures of complexes **1-9**. Fig. 3.5 represents the fragmentation pattern of complex **8**, and shows *m/z* = 268 peak which correspond to the ligand **L2** (Mw = 267.34). Notably, complexes **7** and **8** exhibited similar fragmentation patterns. For instance, the mass spectra of **7** and **8** exhibited base peaks at *m/z* = 268, which is a result of the loss of metal acetate [M^+ - $M(OAc)_2$], where M = Zn (**8**), Cu (**7**). The absence of molecular ion peaks could be attributed to lower stability of the compounds under the extreme temperatures and ionization conditions.[26]

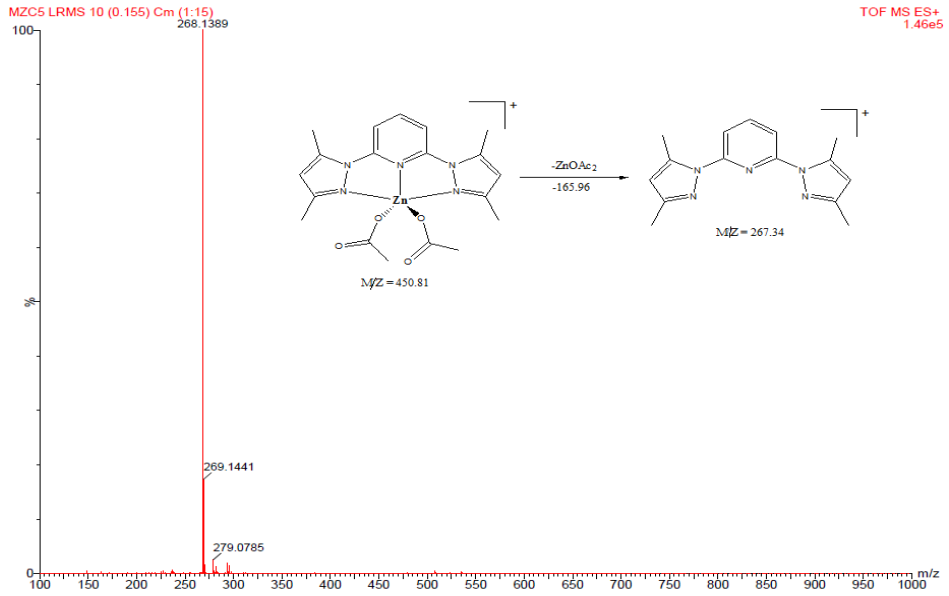


Figure 3.5: Mass spectrum of compound **8**.

To confirm the purity and empirical formulae of compounds **1**–**9** microanalyses was performed. The obtained data showed that all the proposed complexes were consistent with a single metal center, a single ligand unit and two acetate or benzoate units to give the general formula of $[ML(OR)_2]$. The Micro-analyses data for compounds **1-5**, **7** and **8** were within the acceptable range and confirmed the purity of these compounds. However, the data for complexes **6** and **9** did not meet the expected standards and hence require further purification and analyses. We are still investigating a possible explanation for this deviation.

3.3.2 Solid state structures of complexes 1-2 and 5-9

Single crystals suitable for X-ray analyses for complexes **1-2** and **5-9** were grown and used to further confirm their solid state and molecular structures. Table 3.2 contains the crystal data as well as the structure refinement for compounds **1** and **2** while Figures 3.6 and 3.7 contain the X-ray crystal structures and selected bond parameters for **1** and **2** respectively.

Table 3.2 Crystal data for complexes **1** and **2.**

Crystal data	**1**	**2**
Chemical formula	$C_{46}H_{43}Cl_2N_5O_8Zn_2$	$C_{31}H_{29}Br_2N_5O_4Zn$
Mr	995.49	760.78
Crystal system	Monoclinic	Monoclinic
space group	$P2_1/n$	$P2_1/C$
Temperature (K)	100(2)	100(2)
a, b, c (Å)	10.8399 (8), 20.9390 (16), 19.9943 (14)	8.3996 (3), 14.3622 (5), 27. 7214 (10)
α, β, γ (^{o})	90, 92.269 (4), 90	90, 90.681 (2), 90
V (Å3)	4534.7 (6)	3344.0 (2)
Z	4	4
Radiation type	M_o K_α	M_o K_α
μ (mm^{-1})	1.234	3.165
Crystal size (mm)	0.42×0.20×0.13	0.12×0.10×0.08
Data collection		
Diffractometer	Bruker Apex II Duo diffractometer	Bruker Apex II Duo diffractometer
Absorbtion correction	Multi-scan Bruker SADABS	Multi-scan Bruker SADABS
T_{min}, T_{max}	0.744, 0.852	0.691, 0.776
No of measured, independent and observed [I> 2σ(I) reflections	39016, 8839, 2048	27211, 6548, 1528
R_{int}	0.0316	0.0332
Refinement		
$R[F^2>2\sigma(F^2)]$, $wR(F^2)$, *S*	0.0289, 0.0708, 1.012	0.0331, 0.0748, 1.088
No. of reflections	8839	6548
No. of parameters	572	392
No. of restraints	0	0

Complex **1** is polymeric in which **L1** is bridging two Zn metal centres and four bidentate carboxylate ligands to give a five coordinate geometry around each Zn metal centre (Fig. 3.6). On the other hand, complex **2** is monomeric containing one bidentate **L1** and two bidentate carboxylate anions resulting in a six coordinate geometry around the Zn metal centre (Fig. 3.7). The bond angles around the zinc atoms in **1** of 156.77(6)^o and 90.52 (6)^o, and for O(5)-Zn(1)-O(9) and O(3)-Zn-O(4)respectively. In **2** the bond angles around zinc atom are 89.96 (7)^o for O(2)-Zn(1)-O(3) and 165.20 (7)^o for N(5)-Zn(1)-O(3). The geometries around zinc atoms in **1** and **2** can thus be described as distorted square pyramidal and distorted octahedral respectively,

with compound **2** having slightly greater distortions compared to compound **1**. For instance, in **1** bond angles of 90.52 (6)^{o} and 156.77 (6)^{o} instead of 90 and 180 ^{o} were observed respectively, while on the other hand, bond angles of 89.96 (7)^{o} and 165.20 (7)^{o} instead of 90 and 180 ^{o} were observed respectively in **2**. In compound **1,** the distortion could be attributed to the reduced crowding to the zinc atoms as a result of monodentate coordination of of **L1**, while geometric distortions in **2** could be due to steric crowding imposed by **L1**.

The bond distances of Zn-N_{pz} of 2.0352 (16), 2.0576 (16) and 2.072 (16) Å in **1** and **2** respectively are comparable to bond lengths of similar zinc compounds reported in literature.[2, 6, 27] Interestingly, the Zn-O bond lengths (2.0367 (15)-2.0577 (14) Å, Fig. 3.6) in **1** are shorter that the bond lengths of Zn-O in **2** (2.0680 (18)-2.3010 (19) Å, Fig. 3.7) owing to the significant contribution from the bromide substituent in the phenyl rings. The reported Zn-O bond lengths for both compounds falls within the expected range compared to other zinc carboxylate complexes.[6, 28] The average Zn⋯Zn bond distance in **1** is 3.0498 Å and is in good agreement with previously reported values for similar bimetallic zinc complexes containing carboxylate bridges.[29, 30, 31]

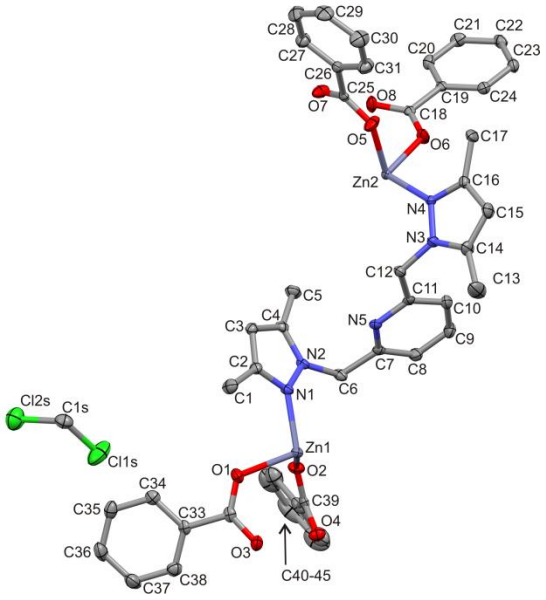


Figure 3.6: Molecular structure for complex $Zn_2L2(\mu\text{-}C_6H_5COO)_2(\mu\text{-}C_6H_5COO)_2$, **1** with 50% probability thermal Selected bond lengths (Å) and bond angles (º): Zn(1)-O(5), 2.0367(15); Zn(1)-O(9), 2.0387(14); Zn(1)-O(6), 2.0456(14); Zn(1)-N(4), 2.0576(16); Zn(1)-O(10), 2.0574(14); Zn(2)-N(1), 2.0352(16); Zn(2)-O(4), 2.0458(15); Zn(2)-O(2), 2.0483(14); Zn(2)-$O(1)^i$, 2.0534(14); Zn(2)-O(3), 2.0608(14); Zn(1)-$Zn(1)^i$, 3.0574(5); Zn(2)-Zn(2)i, 3.0422(5). O(5)-Zn(1)-O(9), 156.77(6); O(5)-Zn(1)-O(6), 89.26(7); O(4)-Zn(2)-$O(1)^i$, 157.17(6); N(1)-Zn(2)-O(3), 100.42(6); O(4)-Zn(2)-O(3), 90.52(6); O(2)-Zn(2)-O(3), 157.23(6). (^{i} Symmetry transformations used to generate equivalent atoms: 1 -x,y,-z+3/2)

Single crystals suitable for X-ray analyses of complexes **5-9** were also grown and used to determine their solid state structures. Crystal data and structural refinement parameters are given in Table 3.5, while selected bond lengths and angles for **5-8** are represented in Figures 3.8, 3.9, 3.10, and 3.11 respectively. The Zn(II) and Cu(II) carboxylate complexes **5-9** are monomeric with **L2** tridentately binding to the metal centers. While compounds **5-8** consists of two *anti* monodentate terminal carboxylate anions (Fig. 3.8, 3.9, 3.10, and 3.11), compound **9** on the other hand contains one *anti* monodentate terminal acetate anion and one water ligand (Fig 3.12). All five complexes (**5-9**) display five-coordinate number around the metal center.

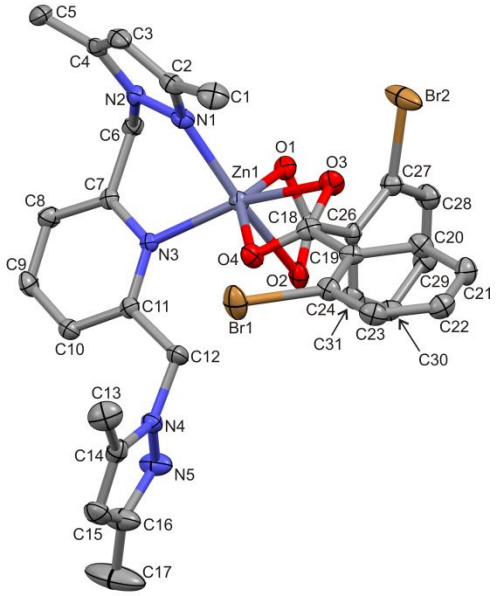


Figure 3.7: ORTEP drawing of compound **2** showing six coordinate geometry drawn with 50% probability levels of thermal ellipsoids. Selected bond lengths (Å) and bond angles (º): Zn(1)-O(1), 2.0912(18); Zn(1)-O(2), 2.3010(19); Zn(1)-O(3), 2.260(2); Zn(1)-O(4), 2.0680(18); Zn(1)-N(5), 2.166(2); Zn(1)-N(9), 2.072(2). O(4)-Zn(1)-N(9), 104.48(8); O(4)-Zn(1)-O(1), 144.94(8); O(1)-Zn(1)-N(5), 97.56(8); N(5)-Zn(1)-O(3), 165.20(7); N(9)-Zn(1)-O(2), 160.98(7); O(3)-Zn(1)-O(2), 89.96(7).

The bond angles of complex **5** around zinc atom are 146.32(18) for N(2)i-Zn(1)-N(2) 73.16(9) for $N(2)^{i}$-Zn(1)-N(3), while compound **6** bond angles are 146.66(12) for N(1)-Zn(1)-N(5) and 73.49(11) for N(3)-Zn(1)-N(5) also suggests distortion from the desired geometry. In addition, compound **5** possesses crystallographic symmetry axis passing through C9, N3 and Zn.

Table 3.3 Crystal data for complexes **5-9.**

Crystal Data	**5**	**6**	**7**	**8**	**9**
Chemical formula	$C_{29}H_{27}N_5O_4Zn$	$C_{29}H_{25}Cl_2N_5O_4Zn$	$C_{29}H_{24}Cl_2CuN_5O_4$	$C_{19}H_{27}N_5O_6Zn$	$C_{17}H_{22}CuN_6O_6$
Mr	574.95	643.81	640.98	486.83	469.95
Crystal system	Orthorhombic	Triclinic	Monoclinic	Monoclinic	Triclinic
space group	Pbcn	P-1	$P2_1/n$	Cc	P-1
Temperature (K)	100 (2)	100 (2)	100	100 (2)	100
a, b, c (Å)	19.482 (14), 18.758 (13), 8.9857 (8)	8.2326 (4), 11.5701 (7), 15.2943 (9)	5.8133 (5), 10.0366 (10), 17.3281 (16)	15.245 (20, 15.548 (2), 9.6063 (12)	8.2705 (4), 10.8236 (5), 11.7411 (6)
α, β, γ (°)	90, 90, 90	80.198 (3), 88.270 (2), 81.942 (2)	90, 91.804 (5), 90	90, 104.798 (2), 90	66.896 (2), 87.634 (3), 83. 008 (2)
V (Å3)	3283.8 (4)	1421. 34 (14)	2744 (5)	2201.5 (5)	959.51 (8)
Z	8	2	4	4	2
Radiation type	$M_o K_\alpha$	$M_o K_\alpha$	$M_o K_\alpha$	$M_o K_\alpha$	$M_o K_\alpha$
μ (mm^{-1})	0.784	1.097	1.037	1.161	1.19
Crystal size (mm)	0.60×0.09×0.08	0.60×0.16×0.09	-	0.50×0.18×0.12	0.2×0.2×0.2
Data collection					
Diffractometer	Bruker Apex II Duo diffractometer	Bruker Apex II Duo diffractometer	Bruker Apex II Duo diffractometer	Bruker Apex II Duo diffractometer	Bruker Apex II Duo diffractometer
Absorbtion correction	Multi-scan Bruker SADABS	Multi-scan Bruker SADABS	Multi-scan Bruker SADABS	Multi-scan Bruker SADABS	Multi-scan Bruker SADABS
T_{min}, T_{max}	0.919, 0.939	0.810, 0.906	-	0.778, 0.870	0.697, 0.745
No of measured, independent and observed [I> 2σ(I) reflections	11472, 2955, 1192	23903, 5486, 660		9396, 3573, 1016	12872, 3611, 3429
R_{int}	0.0319	0.0241	-	0.0179	0.014
Refinement					
$R[F^2>2\sigma(F^2)]$, $wR(F^2)$, *S*	0.0626, 0.1458, 1.093	0.0585, 0.1553, 1.062	-	0.0250, 0.0588, 1.081	0.025, 0.068, 1.06
No. of reflections	2955	5486	-	3573	3611
No. of parameters	180	374	-	302	359
No. of restraints	0	0	-		

While bond angles around zinc atom in **8** are 74.1(3)^{o} for N(3)-Zn(1)-N(5), 93.7(2)^{o} for O(1)-Zn(1)-N(5), and 148.44(6)^{o} for N(1)-Zn(1)-N(5), the bond angles around copper(II) atom in **9** are 95.07 (6)^{o} for N3-Cu1-O1, 157.34 (6)^{o} for N5-Cu1-N1, and 163.83 (6)^{o} for O2-Cu1-N3. These bond angles are indicative of distortion within the complexes. The coordination geometry for the zinc compounds **5**, **6** and **8** can be described as distorted trigonal bipyramidal with N-atoms of **L2** occupying the axial sites and O-atoms of the carboxylates occupying the equatorial positions. On the other hand, compounds **7** and **9** adopt distorted square pyramidal geometries with N-atoms and one carboxylate O-atom occupying the basal plane and one carboxylate anion and the water ligand residing on the apical position for 7 and **9** respectively. The observed distortions in all compounds could be assigned to ligand strain, steric restrictions as well as the flexibility of the carboxylate ligands.[10] Bhattacharyya *et al*. reported a distorted trigonal bipyramidal compound which has comparable bond angles with zinc complexes **5**, **6**, and **8**.[32]

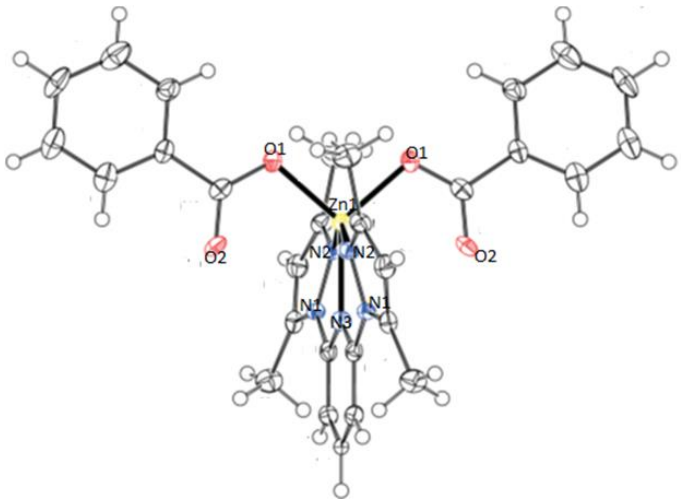


Figure 3.8: An ORTEP drawing of **5**, with thermal ellipsoids drawn at the 50 % probability level. Selected bond lengths (Å) and bond angles (^{o}): Zn(1)-O(1)^{i}, 1.991(3); Zn(1)-O(1), 1.991(3); Zn(1)-N(2)^{I}, 2.138(4); Zn(1)-N(2), 2.138(4); Zn(1)-N(3), 2.142(4); O(1)^{i}-Zn(1)-O(1), 97.59(17); O(1)-Zn(1)-N(2), 103.31(13); O(1)^{i}-Zn(1)-N(3), 131.20(8); N(2)^{i}-Zn(1)-N(3), 73.16(9). (^{i} Symmetry transformations used to generate equivalent atoms: 1 -x,y,-z+3/2)

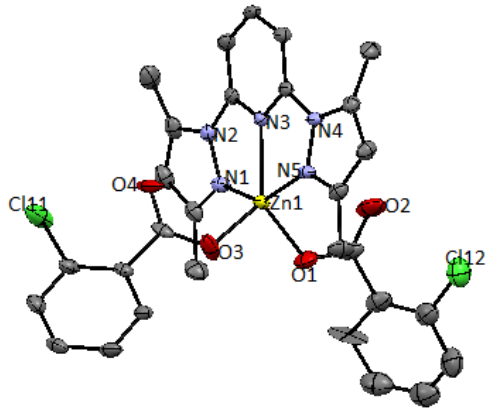


Figure 3.9: An ORTEP drawing of **6**, with thermal ellipsoids drawn at the 50 % probability level and hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and bond angles (º): Zn(1)-O(1), 1.955(3); Zn(1)-O(3), 1.957(3), Zn(1)-N(3), 2.129(3); Zn(1)-N(1), 2.139(3); Zn(1)-N(5), 2.151(3). O(1)-Zn(1)-O(3), 95.38(15); O(1)-Zn(1)-N(3), 136.25(13); O(3)-Zn(1)-N(5), 102.65(13); N(3)-Zn(1)-N(5), 73.49(11); N(1)-Zn(1)-N(5), 146.66(12).

For compounds **5**, **6** and **8** the bond distance of Zn-N_{py} of 2.1208 (15), 2.142(4), and 2.129(3) Å are similar to Zn-N_{py} bond distances for (pyrazolyl-methyl)pyridine Zn(II) reported by Ojwach et al.[6] The Zn-N_{pz} bond distances of 2.129(3) Å for **5**, 2.151(3) Å for **6** and 2.122 (6) and 2.128 (6) Å for **8**, and falls within the range of the related compounds in the literature.[2, 6, 27] The Zn-$O_{benzoate}$ bond distance in **5** is 1.991(3) Å whereas Zn-$O_{benzoate}$ bond distances in **6** are 1.955(3) and 1.957(3) are comparable and consistent to those found in [Zn($C_6H_5COO)_2$(3.5-dimethlypyarazole)$_2$].[2] On the other hand the Zn-$O_{acetate}$ bond lengths distances of 1.975 (5) and 1.995 Å in **8** are within the range expected for Zn-$O_{acetate}$ lengths in the literature.[6, 32]

In Copper(II) compound **9** on the other hand, the bond lengths of 2.0131 (14), 2.0072 (14) and 1.9564 (14) Å for Cu(1)-N(1), Cu(1)-N(3), and Cu(1)-N(5) respectively are very much comparable with corresponding compounds in the literature.[8, 33] The Cu-$O_{acetate}$ bond distance of 1.9243 Å for compound **9** is consistent with the bond distances of Cu-$O_{acetate}$ in the literature.[33]

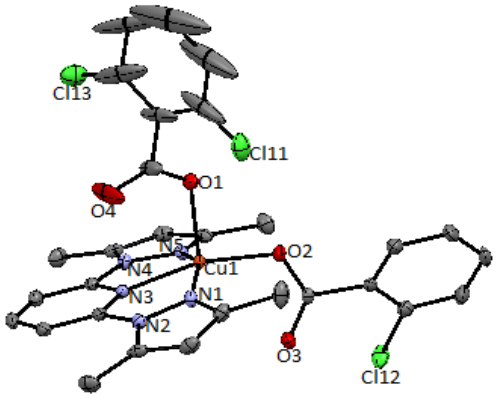


Figure 3.10: ORTEP drawing of **7**, with thermal ellipsoids drawn at the 50 % probability level and hydrogen atoms are omitted for clarity.

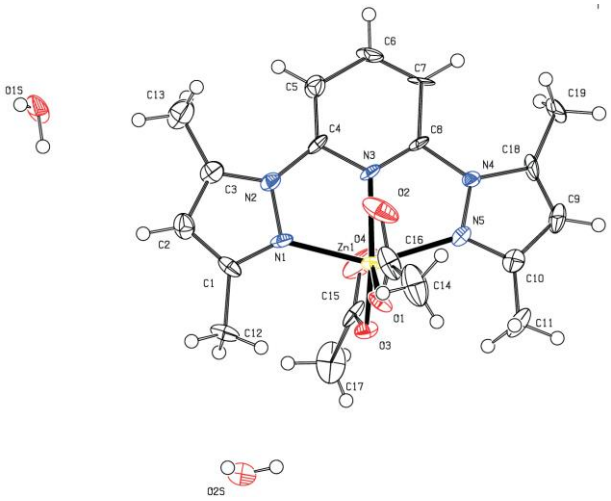


Figure 3.11: ORTEP drawing of **8**, with thermal ellipsoids drawn at the 50 % probability level. Selected bond lengths (Å) and bond angles (º): Zn(1)-O(3), 1.975(5); Zn(1)-O(1), 1.995(5); Zn(1)-N(3), 2.1208(15); Zn(1)-N(1), 2.122(6); Zn(1)-N(5), 2.128(6). O(1)-Zn(1)-N(3), 128.4(3); O(3)-Zn(1)-N(1), 94.7(2); O(1)-Zn(1)-N(5), 93.7(2); N(3)-Zn(1)-N(5), 74.1(3); N(1)-Zn(1)-N(5), 148.44(6).

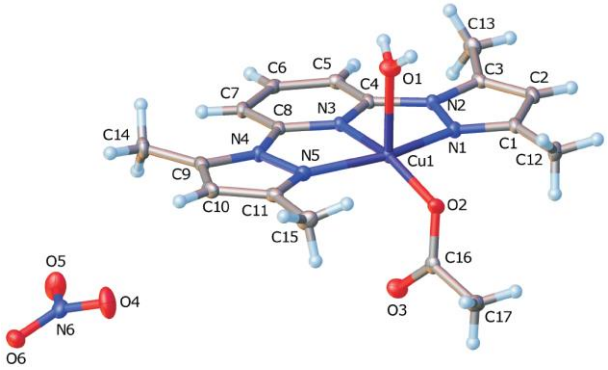


Figure 3.12: Molecular structure for **9** showing five coordinate geometry with thermal ellipsoids drawn at the 50% probability level. Selected bond lengths (Å) and bond angles (º): Cu1-O1, 2.2011 (14); Cu1-O2, 1.9243 (13); Cu1-N3, 1.9564 (14); Cu1-N1, 2.0131 (14); Cu1-N5, 2.0072 (14). O2-Cu1-N3, 163.83 (6); N3-Cu1-O1, 95.07 (6); N3-Cu1-N5, 78.73 (6); N5-Cu1-O1, 91.63 (6); N5-Cu1-N1, 157.34 (6).

Even though the crystal data collected and structure refinement parameters for complex **7**, were of low quality for discussion of bond parameters due to disorder on one of the phenyl rings, the atom connectivity and geometry of compound **7** is not in doubt. Thus complex **7** adopts distorted square pyramid geometry. However due to this disorder we couldn't get crystallographic parameters, bond angles and bond distances. For that reason it will be wrong of us to discuss the bond lengths and bond angles for this compound.

3.3.3 Electron Paramagnetic Resonance (EPR) Analysis

To further understand the nature of coordination environment on the Cu(II) complexes **3** and **4** both in the solid and in solution EPR studies were employed. X-band EPR spectra of the Cu(II) complexes were recorded in DCM at room temperature. Typically the spectra of **3** and **4** in both solid and solution (Fig. 3.13), indicates a dx^2-y^2 ground state ($g_{\parallel} > g_{\perp} > 2.0023$) and this is consistent with monomeric Cu(II) complexes.[29, 34, 35] Both complexes in the solid and solution

showed axial (tetragonal) symmetry with g-tensor values ($g_{\parallel}$ = 2.1556/2.1350, $g_{\perp}$ = 2.0941/2.0722, and $A_{\parallel}$ = 150/158 for **3**/**4** respectively). The $g_{\parallel}$ values for both complexes in the solid state are greater than $g_{\perp}$ values suggesting distortions. The distortion of coordination geometry is also reflected by $g_{\parallel}/A_{\parallel}$ factor. Greater distortions correspond to the higher values of $g_{\parallel}/A_{\parallel}$ factor.

Generally the $g_{\parallel}/A_{\parallel}$ factor value of less than 135 is expected for octahedral Cu(II) complexes and this value increases with increasing octahedral distortion. The $g_{\parallel}/A_{\parallel}$ values were obtained as 144 and 135 for **3** and **4** respectively. This indicates slight distorted octahedral geometry. Based on these findings compound **3** exhibited larger distortions than **4**. Axial symmetry parameter G = ($g_{\parallel}$ - 2.0023)/($g_{\perp}$ - 2.0023), which measures the exchange interaction between the metal centers in a polycrystalline solid was also calculated. Ideally, if G>4 the exchange interaction is so little such that it is negligible, however, if its less than 4 it indicates considerable exchange interaction in the solid.[36] The reported G values of <4 for complexes **3** and **4** suggests a considerable exchange interaction in the respective complexes.

The $g_{\parallel}$ values between 2.1556-2.1350 which were less than 2.3 indicates a significant degree of covalency in the metal-ligand bond, and confirms the presence of Cu-N and Cu-O bonds in these chelate complexes.[37] This is further confirmed by α^2 values which range from 0.57-0.59 for **4** and **3** respectively. These values indicate considerably strong degree of covalency.

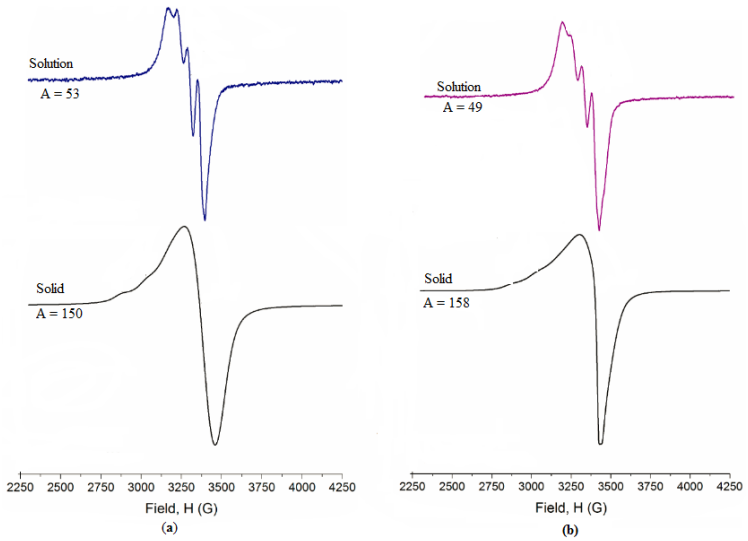


Figure. 3.13: X-band EPR spectra of (a) complex 3 and (b) complex 4 in the solid state and in dichloromethane solution at 298 K. **3** in solid state: g∥ = 2.1556; g⊥ = 2.0941; A∥ (G) = 150; g∥/A∥ $\times 10^{-4}$ = 144; G = 1.65; α^2 = 0.59. **4** in solid state: g∥ = 2.1350; g⊥ = 2.0722; A∥ (G) = 158; g∥/A∥ $\times 10^{-4}$ = 135; G = 1.87; α^2 = 0.57.

Moreover in the solution state, it is evident from the g-tensor signals that complexes **3** and **4** display hyperfine coupling of the single electron to the Cu(II) nucleus, whereas in the solid state the copper complexes did not show hyperfine structure (Fig. 3.13). In addition, the A values are greater in solid state than in the solution for both complexes, these values decrease because the lines sharpen up due to loss of line broadening induced by spin-lattice relaxation in the solid state. The bigger the A values as in the solid state, suggests that the unpaired electron is more localized in the $3dx^2$-y^2 orbital of the metal for an octahedral Cu(II) ion. It should be noted that, from these findings we proposed the geometry of Cu(II) complexes **3** and **4** to be distorted octahedral (Scheme 3.1). This is supported by the coordination geometry in complexes **1** and **2**, the molecular structures of **1** and **2** suggested that **L1** cannot tridentately bind to the metal centers due to the steric hindrance.

3.4. Concluding Remarks

A series of bis(pyrazolyl)pyridine Zn(II) and Cu(II) complexes were successfully synthesized and obtained in moderate to excellent yields. The compounds have been characterized using a combination of analytical techniques including ^{1}H NMR spectroscopy, IR spectroscopy, mass spectrometry, magnetic susceptibility measurements, and single crystal X-ray crystallography. X-ray analyses of compound **1** confirmed that **L1** is bridging the two metal centers whereas in **2**, **L1** is bidentate with one pyrazolyl unit non-coordinating. Molecular structures of compounds **5-9** confirmed the presence of one tridentate bis(pyrazolyl)pyridine ligand (**L2)** in the metal coordination sphere. EPR studies confirmed the geometry of complexes **3** and **4** to be distorted octahedral both in the solid and solution state.

References

1. a) Trofimenko, S. *Prog. Inorg. Chem*., **1986**, 34, 115; b) Ardizzoia, G.A.; La Monica, G.; Cenini, S.; Moret, M.; Masciocchi, N. *J. Chem. Soc*., *Dalton Trans*., **1996**, 1351; c) Mondal, R.; Bhunia, M. K.; Dhara, K. *CrystEngComm.*, **2008**, 10, 1167; d) Seredyuk, M.; Haukka, M.; Fritsky, I. O.; Kozłowski, H.; Kramer, R.; Pavlenko, V. A.; G¨ utlich, P. *Dalton Trans*., **2007**, 3183; e) Klingele, J.; - Prikhod'ko, A. I.; Leibeling, G.; Demeshko, S.; Dechert, S.; Meyer, F. *Dalton Trans*., **2007**, 2003; f) Zhang, J. X.; He, J.; Yin, Y. G.; Hu, M. H.; Li, D. Huang, X. C. *Inorg. Chem.*, **2008**, 47, 3471; g) Li, H.-X.; Wu, H.-Z.; Zhang, W.-H.; Ren, Z.-G.; Zhang, Y. Lang, J.-P. *Chem. Commun*., **2007**, 5052; h) Chandrasekhar, V.; Boomishankara, R.; Sasikumara, P.; Nagarajan, L.; Cordes, A. C.; *Anorg. Allg. Chem*., **2005**, 631, 2727; i) Das, M. K.; Ghosh, S.; *Indian J. Chem*., **1997**, 36A, 324; j) Ghose, C.; Poddar, S.N. *Indian J. Chem*., **1977**, 15, 248; k) Walz, R.; Ruf, M. Vahrenkamp, H. *Eur. J. Inorg. Chem.*, **2001**, 139; l) Looney, A.; Han, R.; McNeill, K.; Parkin, G. *J. Am. Chem. Soc*., **1993**, 115, 4690; m) Lipscomb, W. N.; Strater, N. *Chem. Rev.,* **1996**, 96, 2375.
2. Sarma, R.; Kalita, D.; Baruah, J. B. *Dalton Trans*., **2009**, 7428.
3. Wu, J.; Yu, T.-L.; Chen, C.-T.; Lin, C.-C. *Coord. Chem. Rev*., **2006**, 250, 602
4. Mukherjee, R. *Coord. Chem. Rev*., **2000**, 203, 166.
5. Abbo, H. S.; Titinchi, S. J. *J. Catal Lett.*, **2010**, 139, 90.
6. Ojwach, S. O.; Guzei, L. A.; Benade, L. L.; Mapolie, S. F.; Darkwa, J. *Organometallics*, **2009**, 28, 2127.
7. a) Ojwach, S.O.; Darkwa, J. *Inorg. Chim. Acta*., **2010**, 363, 1947; b) Yu, X.F.; Zhang, C.; Wang, Z.X. *Organometallics*, **2013**, 32, 3262; c) Kang, Y.K.; Jeong, J. H.; Lee, N. Y.; Lee, Y. T.; Lee, H. *Polyhedron*., **2010**, 29, 2404; d) Lian, B.; Thomas, C.M.; Casangrande Jr., O.L.; Lehmann, C.W.; Roisnel, T.; Carpentier, J.-F. *Inorg. Chem.*, **2007**, 47, 328.
8. a) Chen, H.-Y.; Huang, B.-H.; Lin, C.-C. *Macromolecules*, **2005**, *38*, 5400; b) Cheng, M.; Moore, D. R.; Reczek, J. J.; Chamberlain, B. M.; Lobkovsky, E. B.; Coates, G.W. *J. Am. Chem. Soc.*, **2001**, *123*, 8738; c) Williams, C. K.; Breyfogle, L. E.; Choi, S. K.; Nam, W.; Young, Jr., V. G.; Hillmyer, M. A.; Tolman, W. B. *J. Am. Chem. Soc.*, **2003**, *125*, 11350; d) Azor, L.; Bailly, C.; Brelot, L.; Henry, M.; Mobian, P.; Dagorne, S. *Inorg. Chem.*, **2012**, *51*,

10876; e) Jensen, T. R.; Schaller, C. P.; Hillmyer, M. A.; Tolman, W. B. J. *Organomet. Chem.*, **2005**, *690*, 5881.

9. Appavoo, D.; Omondi, B.; Guzei, I. A.; van Wyk, J. L.; Zinyemba, O. Darkwa, J. *Polyhedron*., 69, **2014**, 55.
10. Ojwach, S. O.; Okemwa, T. T.; Attandoh, N. W.; Omondi, B. *Dalton Trans.*, **2013**, 42, 10735.
11. Albertson, A. C.; Varma, I. K. *Adv. Polym. Sci*., **2002**, 157, 1.
12. a) Oshimura, M.; Tang, T.; Takasu, A. *J. Polym. Sci. , Part A: Polym. Chem*., **2001**, 49, 1210; b) Liu, Y.-C.; Ko. B.-T.; Lin C.-C. *Macromolecules*, **2001**, 34, 6196.
13. Arrowsmith, R.L.; Pascu, S.I.; Smugowski, H. *Organomet. Chem.*, **2012**, *38*, 1.
14. Gowda, R.R.; Chakraborty, D. *J. Mol. Catal. A: Chem.*, **2010**, *333*, 167.
15. Williams, C.K.; Brooks, N.R.; Hillmyer, M. A.; Tolman, W. B. *Chem. Commun.*, **2002**, 2132.
16. Drouin, F.; Oguadinma, P.O.; Whitehorne, T. J. J.; Prud'homme, R. E.; Schaper, F.; *Organometallics*, **2010**, *29*, 2139.
17. John, A.; Katiyar, V.; Pang, K.; Shaikh, M.M.; Nanavati, H.; Ghosh, P. *Polyhedron.*, **2007,** *26*, 4033.
18. Bhunora, S.; Mugo, J.; Bhaw-Luximon, A.; Mapolie, S.;Van Wyk, J.; Darkwa, J.; Nordlander, E. *Appl. Organometal. Chem.*, **2011**, *25*, 133.
19. Gowda, R. R.; Chakraborty, D. *J. Mol. Cat. A: Chem*., **2011**, 349, 86.
20. Watson, A. A.; House, D. A.; Steel, P. J. *Inorg Chim Acta.*, **1987**, 130, 167.
21. Jameson, D.L.; Goldsby, K. A. *J. Org. Chem*., **1990**, 55, 4992.
22. Bruker-AXS, Madison, Wisconsin, USA, **2009.**
23. a) Sheldrick, *Acta Cryst*. **2008**, *A64*, 112; b) SADABS Area-Detector Absorption Correction; Siemens Industrial Automation, Inc.: Madison,WI, **1996**; c) SAINT Area-Detector integration Softeware. Siemens Industrial Automation, Inc.: Madison,WI, **1995**.
24. Heslop, R. B.; Jones, K. *Inorganic Chemistry (A guide to advanced study)*. Elsevier Scientific Publishing company. **1976**, page 72
25. Ye, B.-H.; Li, X.-Y.; Williams, I. D.; Chen, X.-M. *Inorg. Chem*., **2002**, 41, 6426.
26. a) Ojwach, S. O.; Letitia, B.; Guzei, I. A.; Darkwa, J.; Mapolie, S. F. *Organometallics*, **2009**, 28, 2127; b) Ojwach, S. O.; Guzei, I. A.; Darkwa, J. *Organomet. Chem*., **2009**, 694, 1393.

27. a) Börner, J.; Flörke, U.; Huber, K.; Döring, A.; Kuckling, D.; Herres-Pawlis, S. *Chem,-Eur. J.*, **2009**, 15, 2362; b) Ojwach, S. O.; Nyamato, G. S.; Omondi, B.; Darkwa, J.; Okoth, A. O. *J. Coord. Chem.*, **2012**, 65, 298.
28. Allen, F. A. *Acta Crystallogr*., **2002**, B58, 380.
29. Huang, B.-H.; Lin, C.-H.; Hsueh, M.-L.; Athar, T.; Lin, C.-C. *Polymer*., **2006**, 47, 6622.
30. a) Darensbourg, D. J.; Rainey, P.; Yarbrough, J. *Inorg. Chem*., **2001**, 40, 986; b) Kunert, M.; Brauer, M.; Klobes, O.; Gorls, H.; Dinjus, E.; Anders, E. *Euro. J. Chem*., **2000**, 1803; c) Hlavinka, M. L.; McNevin, M. J.; Shoemaker, R.; Hagadorn, J. R. *Inorg. Chem*., **2006**, 45, 1815.
31. Silvernail, C. M.; Yao, L. J.; Hill, L. M. R.; Hillmyer, M. A.; Tolman, W. B. *Inorg. Chem*., **2007**, 46, 6565.
32. Bhattacharyya, S.; Kumar, S. B.; Dutta, S. K.; Tiekink, E. R. T.; Chaudhury, M. *Inorg. Chem*., **1996**, 35, 1967.
33. Deverex, M.; O'Shea, D.; O'Connor, M.; Grehan, H.; Connor, G.; McCann, M.; Rosair, G.; Lyng, F.; Kellet, A.; Walsh, M.; Egan, D.; Thati, B. *Polyhedron*., **2007**, 26, 4073.
34. Singh, O.I.; Damayanti, M.; Singh, N. R.; Singh, R. K. H.; Mohapatra, M.; Kadam, R. M. *Polyhedron.*, **2005**, 24, 909.
35. Barik, A.; Mishra, B.; Kunwar, A.; Kadam, R. M.; Shen, L.; Dutta, S.; Padhye, S.; Satpati, A. K.; Zhang, H.-Y.; Priyadarsini, K. I. *Eur. J. Med. Chem*., **2007**, 42, 431.
36. Neiman, R.; Kivelson, D. J. *Chem. Phys*., **1961**, 35, 149.
37. a) Ozarowski, A.; Szymanska, I. B.; Muziol, T.; Jezierska, J. *J. Am. Chem. Soc*., **2009**, 131, 10279.; b) Ozarowski, A. *Inorg. Chem*., **2008**, 47, 9760.

Chapter 4

ROP of ε–Caprolactone and Lactides initiated by bis(pyrazolyl)pyridine Cu(II) and Zn(II) complexes: Kinetics, Polymer Properties and Mechanistic Studies

---

4.1 Introduction

The synthesis of polycaprolactones (PCLs) and polylactides (PLAs) has been the subject of investigation by researchers in the past decades. These polymers have a wide range of applications, including biomedical, pharmaceutical, agricultural, environmental as well as plastic packaging industries.[1] These aliphatic polyesters are synthesized from cyclic esters by ring-opening polymerization catalyzed by, transition metal-based initiators and organocatalysts. The use of metal-based catalysts in the ROP of cyclic esters have been the subject for several reviews.[2,3,4] Ideally, this route has potential to offer great control over molecular weight as well as stereo-selectivity of the polymers produced.[5] In addition, kinetics studies plays a very crucial role in giving mechanistic insight with regards to this pathway.[6,7]

To meet the above mentioned purposes it is of great significance to develop catalysts that are inexpensive, less toxic, and biologically benign towards biodegradable polyesters. Generally, metal-based catalysts in combination with a variety of coordinating ligands have been explored for these purposes. However, finding well-defined catalysts that could incorporate the requirements of the polymers such as great control over ring-opening polymerization with narrow polydispersities polymers still remains a major challenge to date. Despite tin-based catalysts showing great control of polymer molecular weight with narrow molecular distribution and

excellent activity, their toxicity have limited their industrial application in the production biocompatible products.[8,9] More recently, growing scientific interests have been received by organocatalysts[10] as well as metal complexes of Ca,[11,12] Mg,[11,13, 14] Fe,[15] Ti,[16] and Bi[17] as catalysts in the ROP of aliphatic esters. Even though these catalysts show promising results in the ROP of aliphatic esters, challenges such as catalyst stability, poor control of polymer microstructure and catalysts high costs are still prohibiting their commercialization. Moreover, Zn(II) and Cu(II) complexes continue to draw considerable attention as initiators in the ROP of aliphatic esters due to their ease of synthesis, stability, biocompatibility and low costs. More recently, Darensbourg *et al.* reported a series of Zn(II) complexes bearing Schiff base ligands as catalysts in the ROP of lactides, reported complexes displayed good activity, with excellent control over molecular weight, and good stereocontrol for ROP of LAs.[18]

The main core focus of our research group is centered around designing and developing novel catalysts in the ring-opening polymerization of aliphatic esters, in regards to these objectives we have recently reported Zn(II) and Cu(II) carboxylate complexes of (pyrazol-1-ylmethyl)pyridine[19] and (benzimidazolylmethyl)amine[20] ligands as catalysts for ROP of lactides and *ε*–caprolactone. Hence, our contribution reported in this study is the continuation of our current research focus.

In this contribution, the ability of bis(pyrazol)pyridine Zn(II) and Cu(II) carboxylate complexes synthesized in Chapter 3 (Fig. 4.1) to act as catalysts in the ROP of LA and *ε*–CL was investigated. The activity, kinetics and mechanistic studies were explored to understand some features of our catalysts.

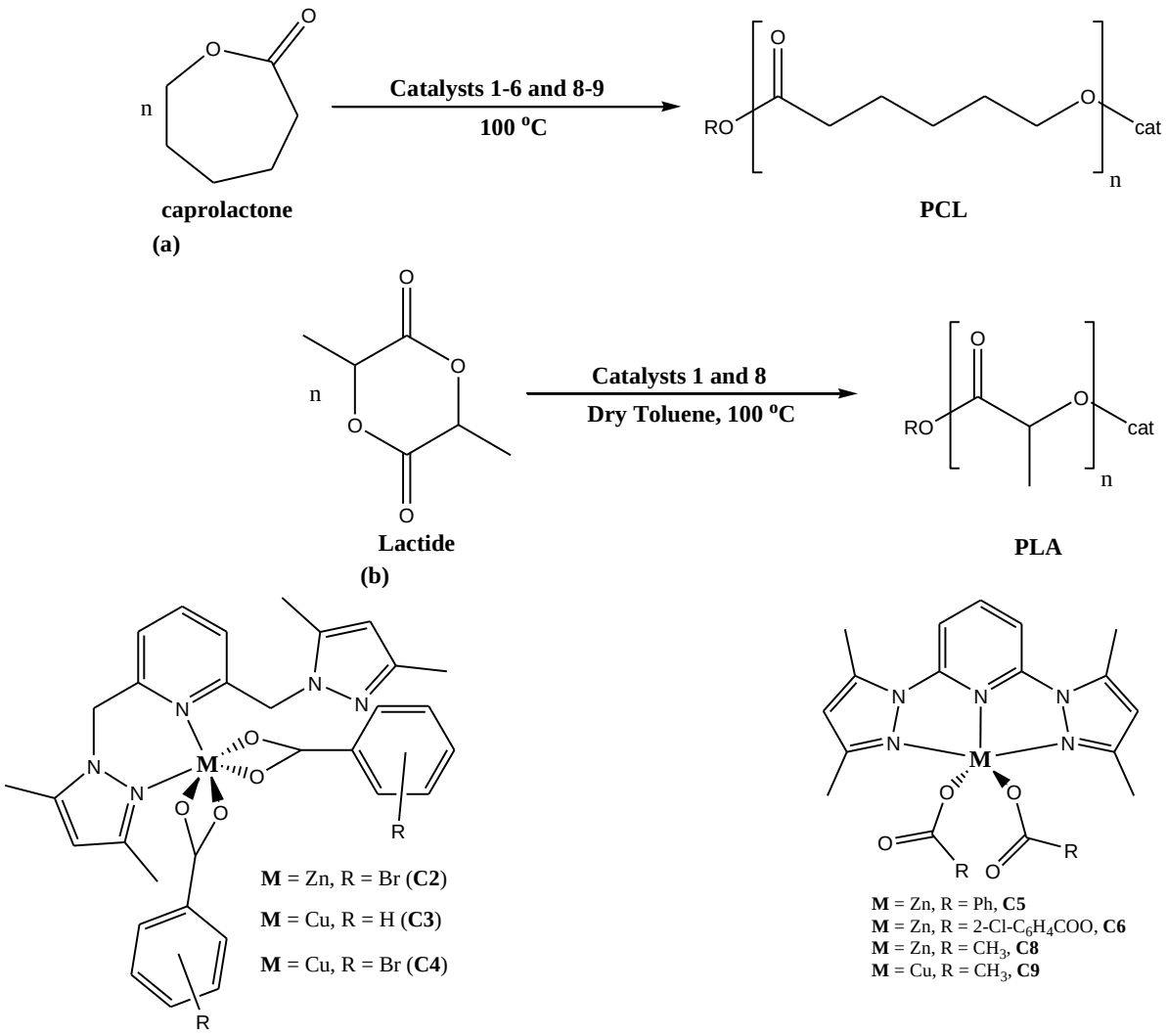


Fig. 4.1: Ring-opening polymerization of (a) *ε*–caprolactone using **1-6** and **8-9** as catalysts (b) and lactides employing **1** and **8** as catalysts.

4.2 Experimental section

4.2.1. Materials and methods and instrumentation

Unless otherwise stated, all experiments were carried under nitrogen using Schlenk techniques. Monomers, D,L-LA, s-LA and *ε*–CL were sourced from Sigma Aldrich and used as received. Deuterated chloroform ($CDCl_3$) was sourced from Sigma Aldrich, while toluene solvent was purchased from Merck and dried according to standard procedures prior to use. Polymerization catalysts **1-6** and **8-9** were synthesized as reported in chapter 3 and were used with no further purification. NMR spectra were recorded on a Bruker 400 UltraShield instrument (400 MHz for ^{1}H NMR) at ambient temperature using chloroform-d ($CDCl_3$). All the ^{1}H NMR chemical shifts were referenced to the signals of the protons of the ^{1}H NMR solvent and are reported in δ (ppm): $CDCL_3$ at 7.28 ppm for ^{1}H NMR. Size exclusion chromatography (SEC) analyses were conducted on a gel permeation chromatograph (GPC) fitted with a refractive index detector.

4.2.2. Ring opening polymerization reactions and kinetic studies

4.2.2.1.Polymerization procedure of ε–caprolactone

The ring-opening polymerizations of *ε*–caprolactone using Zn(II) and Cu(II) carboxylate complexes **1-6** and **8-9** were performed in bulk at 110 ^{o}C under nitrogen atmosphere. Generally, polymerization reactions were carried by introducing an appropriate amount catalyst in a Schlenk tube charged with magnetic stirrer bar. An appropriate amount of *ε*–CL monomer (1.14 g, 9.99 mmol) was then introduced in a Schlenk tube *via* a syringe. In general, most polymerization reactions were performed for [M]:[I] = 100:1. However, using initiator **1**, the monomer-to-

catalyst ratios were varied from 50:1, 75:1, 125:1 and 150:1. All the polymerization reactions and the percentage conversions were monitored by taking aliquots at regular time intervals using ^{1}H NMR spectroscopy to record the spectra. The percentage conversion is defined by $[PCL]/[CL]_o \times 100$, where $[CL]_o$ represents the initial concentration of the monomer, while [PCL] represents the polymer concentration at a given time. Percentage conversion was assessed by the integration of the peaks for ε–CL (4.2 ppm, OCH_2 signal) and PCL (4.0 ppm, OCH_2 signal), and was given by equation $[PCL]/[CL]_o \times 100 = I_{4.0}/ (I_{4.2} + I_{4.0})$, where intensities $I_{4.2}$ and $I_{4.0}$ correspond to CL monomer signal at 4.2 ppm and PCL signal at 4.0 ppm respectively for the OCH_2.

4.2.2.2. Polymerization procedure of lactides

Using a procedure identical to the preparation of PCL, ring-opening polymerizations of D,L-Lactide and s-Lactide were performed in presence of dry toluene (2 mL) using Zn(II) carboxylate complexes **1** and **8** as initiators for [M]:[I] = 100:1 at a temperature of 110 ^oC.. To the appropriate amount the catalyst in a Schlenk tube the monomer (D,L-LA or s-LA) (0.96 g, 6.66 mmol) was then added The percentage conversions were evaluated by the integration of the peaks for D,L-LA or s-LA (4.99 ppm, OCH_2 signal) and PCL (5.27 ppm, OCH_2 signal), and was given by equation $[PCL]/[CL]_o \times 100 = I_{5.27}/ (I_{4.99} + I_{5.27})$, where $I_{5.27}$ is the PCL intensity signal at 5.27 ppm and $I_{4.99}$ is the D,L-LA or s-LA intensity of the monomer signal at 4.99 ppm for the OCH_2 protons.

4.2.2.3. Kinetics experiments and rate constants

Kinetics studies of *ε*–caprolactone and lactides were conducted by the removal of ~ 0.2 mL aliquots at appropriate time intervals using a syringe, the aliquots were quenched into the vials containing $CDCl_3$ solvent. To assay the polymerization of monomer to polymer, ^1H NMR spectroscopy was employed to analyse and determine the kinetics of the quenched samples at appropriate time intervals. The rate constants (k_{obs}) were extracted from the slopes of semilogarithmic plots of *ε*–caprolactone and lactides monomer consumption ($\ln[M]_o/[M]_t$) with time.

4.2.3. Molecular weight determination, using GPC

Size Exclusion Chromatography (SEC) from Stellenbotsch University was used to determine the molecular weight (M_w) and average molecular mass (M_n) of the polymers. The SEC instrument consist of a Waters 1515 isocratic HPLC pump, Waters 717 plus autosampler, Waters 600E system controller (run by Breeze version 3.30 SPA), a Waters in-line Degasser AF and a Waters 2414 differential refractometer (operated at 30 °C) in series with a Waters 2487 dual wavelength absorbance UV/Vis detector operating at variable wavelength. Samples were dissolved in BHT stabilized THF (2mg/ml). Sample solutions were filtered via syringe through 0.45 μm nylon filters before subjected to analysis. Tetrahydrofuran (THF, HPLC grade, stabilized with 0.125% BHT) was used as eluent at flow rates of 1ml min^{-1}. The column oven was kept at 30 ^oC 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 2x106 g mol^{-1}. All molecular weights were reported as polystyrene equivalents.

4.3. Results and discussion

4.3.1 Polymerization of *ε*–CL and LA initiated by complexes 1-6 and 8-9

Ring-opening polymerization of LA and *ε*–CL employing bis(pyrazolyl)pyridine Cu(II) and Zn(II) complexes **1-6** and **8-9** respectively as catalysts was systematically examined. In general, polymerization reactions of both LA and *ε*–CL were carried out at 110 ^{o}C. While the polymerization reactions of *ε*–CL was performed in bulk, the reactions of LA were performed in toluene. The conversion of LA and *ε*–CL to PLA and PCL respectively were monitored by ^{1}H NMR spectroscopic studies. Preliminary data for the polymerization reactions indicated all the complexes **1-6** and **8-9** form active catalysts in the ROP of both LA and ε- CL achieving near complete monomer conversions within 60-70 h (Figures 4.2 and 4.3). As a result, detailed mechanistic and kinetics studies were carried in order to further understand the role played by the catalyst structure, reaction conditions, nature of monomer and polymer properties in the polymerization kinetics and possible mechanistic pathways.

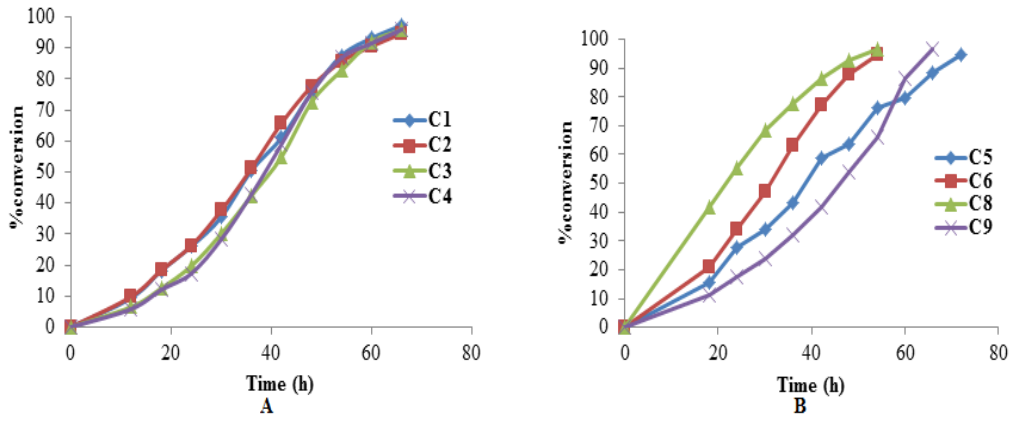


Fig. 4.2: ROP of *ε*–CL using complexes (a) **1-4** and (b) **5-6** and **8-9** at 110 ^{o}C and for [M]:[I] = 100:1.

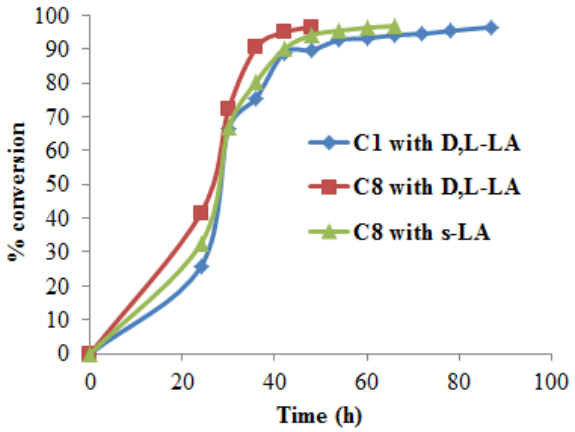


Fig. 4.3: ROP of lactides (D,L-LA and s-LA) using complexes **1** and **8** 110 ^{o}C and for [M]:[I] = 100:1.

4.3.2 Kinetics of ring-opening polymerization reactions of LA and *ε*–CL by complexes 1-8

4.3.2.1 Order of reaction of with respect to monomer

Upon establishing that the complexes **1-6** and **8-9** form active catalysts in the ROP reactions of *ε* –caprolactone and lactides, we carried out kinetic studies in order to determine the dependency of reaction rates on monomer and initiator. This was performed at 110 ^{o}C with [M]:[I] ratio of 100:1. All the reactions were monitored by ^{1}H NMR spectroscopy from which monomer consumptions were calculated. Table 4.1 contains a summary of the polymerization and rate constants obtained for complexes **1-6** and **8-9**. In order to establish the kinetics and the overall order of the polymerizations reactions, a semilogarithmic plot of ln[CL]/[CL]t vs time was constructed (Figure 4.4). The linearity observed in Figures 4.4(a) and (b) indicates that, *ε*–CL polymerizations with **1-6** and **8-9** as initiators proceeded *via* pseudo-first order kinetics with respect to *ε*–CL monomer. Previously reported studies by our research group supports these findings.[19] Thus, we propose that the polymerization of *ε*–CL by complexes **1-6** and **8-9** proceeds according to equation (1):

$$-\frac{d[Cl]}{dt} = k[Cl]^1 \quad (1)$$

Where $k = k_{app}[I]^m$, and where k_{app} is the rate of chain propagation, I is the initiator and *m* is the order of the reaction. This also implies that during the polymerization, the concentration of catalytic active species was not affected.

4.3.2.2 Effect of catalyst structure on polymerization kinetics

To assess the effect of catalyst structure on catalytic activity and reaction rates, rates constants for the complexes were obtained from the slopes of the plots in Figure 4.4. A summary of the rate constants (k_{obs}) for initiators **1-6** and **8-9** is given in Table 4.1, entries 1-8. For complexes **1-4**, rate constants were extracted from Fig. 4.4(a). Complex **1** (Table 4.1, entry 1) was found to be more active with rate constant of 0.0312 h^{-1}, while complex **3** (Table 4.1, entry 3) was the least active with rate constant of 0.0276 h^{-1}. Complex **8** was the most active initiator for the ROP of ε–CL compared to all tested initiators giving a rate constant of 0.0415 h^{-1} (Table 4.1, entry 5).

Table 4.1 Summary of LA and *ε*–CL polymerization data by complexes **1-6** and **8-9** [a]

Entry	Cat.	Conv. (%)[b]	Time (h)	K_{obs} (h^{-1})	M_n[c] (g mol^{-1})	M_w[c] (g mol^{-1})	PDI[d]	IE[e]
1	**1**	97	66	0.0312	7291	11036	1.51	0.99
2	**2**	95	66	0.0301	8553	12696	1.48	1.15
3	**3**	96	66	0.0275	6784	9881	1.46	0.89
4	**4**	96	66	0.0290	7732	12133	1.57	1.09
5	**5**	96	72	0.0221	8168	11114	1.36	1.00
6	**6**	95	54	0.0281	5622	7977	1.42	0.74
7	**8**	97	54	0.0415	5363	7954	1.48	0.71
8	**9**	95	72	0.0146	5124	7130	1.39	0.65
9[f]	**1**	96	87	0.0426	-	-	-	-
10[f]	**8**	72	54	0.0726	1004	1154	1.15	0.11
11[g]	**8**	97	72	0.0616	2011	4053	2.02	0.29

[a] All polymerization reactions were carried at 110 ^oC for *ε*–CL monomer in bulk for different [M]:[I] ratio. [b] Maximum conversions achieved from ^1H NMR spectroscopy. [c] GPC M_n and M_w values. [e] Polydispersity indices (PDI = M_w/M_n) from GPC. [e] Initiator efficiency (IE) = Mw_{exp}/Mw_{cal} = (M/I) × (% conversion) × $Mw_{(monomer)}$ + $Mw_{(chain\text{-}end\ groups)}$. . [f] D,L-LA and [g] s-LA polymerization reactions in dry toluene 110 ^oC with GPC Mn and Mw values.

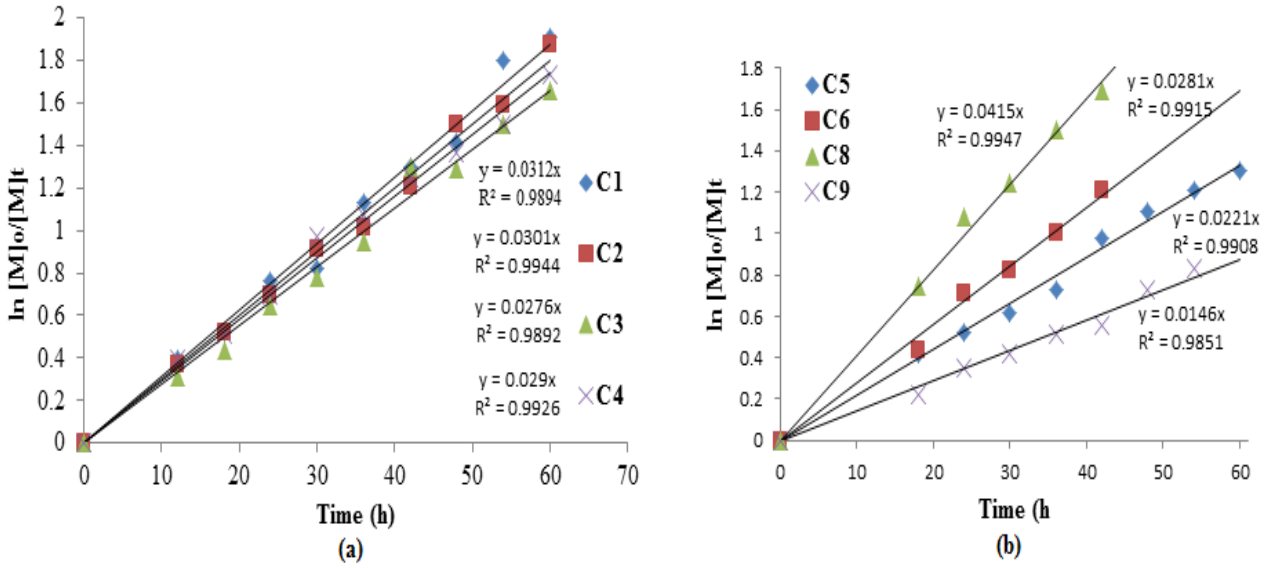


Fig. 4.4: Semilogarithmic plots of ε–CL conversion with time in bulk at 110 ^{o}C and for [M]:[I] = 100:1 (a) complexes **1-4** and (b) complexes **5**, **6**, **8** and **9**.

The ligand design played a crucial role in determining the catalytic activity and stability of the complexes.[21-23] For example, bis(pyrazol-1-ylmethyl)pyridine (**L1**) complexes (Table 4.1, entries 1-4) were found to be more active than their respective bis(3,5-dimethyl-***N***-pyrazolyl)pyridine (**L2**) complexes **5**, **6** and **9** (Table 4.1, entries 5, 6 and 8) counterparts. For instance, bis(pyrazol-1-ylmethyl)pyridine Zn(II) complex **1** exhibited a rate constant of 0.0312 h^{-1} compared to a rate constant of 0.0281 h^{-1} exhibited by bis(3,5-dimethyl-***N***-pyrazolyl)pyridine complex **6**. Hence, higher activities of complexes **1-4** could be due to the flexible character of **L1** ligand induced by the methylene linker (-CH_2-)**,** thus allowing easy monomer insertion. On the other hand, the more rigid ligand **L2** architecture in complexes **5**, **6** and **9** may crowd the metal centers, thus hindering monomer insertion resulting in less active catalysts.

To fully understand the effect of the carboxylates in the polymerization process, we used different carboxylates such as acetate, benzoate, 2-Bromobenzoate, and 2-Chlorobenzoate anions. In general, carboxylates containing electron withdrawing groups formed more active ROP initiators. For an example, complex **6** with electron withdrawing substituent (-Cl) was more active giving 95% conversion in 54 h and exhibited a rate constant of 0.0281 h^{-1} (Table 4.1, entry 6) On the other hand, complex **5** containing no electron withdrawing substituent reached 96% conversion in 72 h translating to a rate constant of 0.0221 h^{-1} (Table 4.1, entry 5). However, this did not hold true for some of complexes of the bis(pyrazolylmethyl)pyridine ligand **L1**. For example complex **1** (k_{obs} = 0.0312 h^{-1}) showed comparable activity to complex **2**, (k_{obs} = 0.0312 h^{-1}) bearing electron withdrawing groups on the benzoate ring. The greater catalytic activity of complex **1** could be attributed to the number of active Zn(II) sites in the initiation process as discussed in section 4.3.3.4. The higher catalytic activity displayed by complex **8** could be attributed to the reduced steric crowding due to the acetate carboxylate anions, thus allowing facile monomer coordination. Complexes **1-4** showed induction periods within the first 30 h, but activity increased linearly thereafter under the investigated polymerization conditions (Fig. 4.2A)

In comparison to their Cu(II) analogues, Zn(II) complexes were found to be more active in the ROP of *ε*–CL, Figure. 4.4(a) and 4.4(b), These findings matches well with the previously reported studies.[24,25] For instance in Figure. 4.2, **1** and **2** were more active for ROP of *ε*–CL compared to the corresponding Cu(II) complexes **3** and **4**. Similar trend was observed for Zn(II) complexes **8**, **5** and **6** when compared to the analogous Cu(II) complex **9**. This could be attributed to Zn(II) metal center being more electropositive than Cu(II) metal center, hence resulting in zinc compounds being more active and better Lewis acids than copper compounds.[26] Even though initiators **1-6** and **8-9** were active in the ROP of *ε*–CL, nevertheless, it should be noted that the

rate constants observed using our complexes are slower than some of the most active polymerization catalysts reported in the literature.[27,28] Our research group have previously reported (pyrazolyl-1-ylmethyl)pyridine Cu(II) and Zn(II) complexes[19] exhibiting rate constants ranging from 0.017 to 0.096 h^{-1} for polymerization of *ε*–CL which are slightly higher compared with those of the present study. Appavoo *et al*.[24] also reported bis(3,5-dimethylpyrazole) Cu(II) and Zn(II) complexes that exhibited rate constants of 0.090 to 0.286 h^{-1} for polymerization of *ε*–CL which is approximately seven times more efficient compared to our catalysts. However, more interestingly the very catalysts reported by Appavoo *et al*.[24] were less active compared to our catalysts for polymerization of D,L-LA exhibiting the rate constants of 0.018 to 0.039 h^{-1}, while our initiator **1** exhibited rate constant of 0.0426 h^{-1}.

4.3.2.3 Effect of monomer on ring-opening polymerization

Our promising *ε*–CL polymerization results encouraged us to study the activities of complexes **1** and **8** in the ring-opening polymerization of D,L- and s-lactides (Table 4.1, entries 9-11 and Fig. 4.3). The polymerization reactions of D,L-LA and s-LA were carried out in toluene at 110 ^{o}C and for [M]:[I] = 100:1. Notably, ring-opening polymerization reactions of D,L-LA and s-LA were slightly faster than those of *ε*–CL reactions (Table 4.1). For instance, using complex **1**, complete conversion of CL to PCL with rate constant of 0.0312 h^{-1} (Table 4.1, entry 1) was obtained, while complete conversion of D,L-LA to PLA displaying a rate constant of 0.0426 h^{-1} was recorded (Table 4.1, entry 9). This is not surprising due to the electronic effects corresponding to lactide monomers compared to *ε*–CL as reported by Chen *et al*.[28]

Interestingly, the reactivity of D,L-LA was higher than those observed for s-LA polymerization reactions. For example, rate constant of 0.0726 h^{-1}(Table 4.1, entry 10) was observed for the D,L-LA polymerization using complex **8** as initiator, compared to a rate constant of 0.0616 h^{-1} reported for s-LA (Table 4.1, entry 11) under similar conditions. This could be attributed to the monomer stereochemistry.

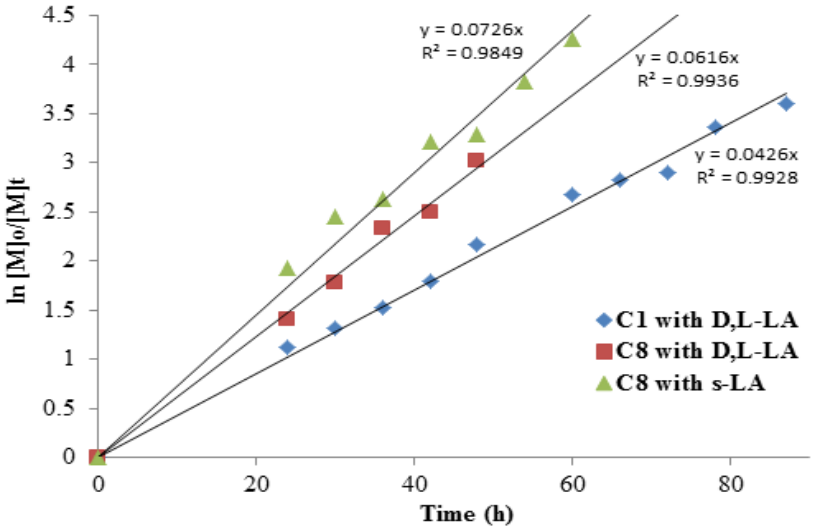


Fig. 4.5: Kinetics for the ROP of lactides using complexes **1** and **8**.

4.3.2.4 Dependency of reaction kinetics on catalyst concentration

Further studies were carried in order to determine the kinetic order in [**1**] by performing the polymerization reactions at different catalyst concentrations corresponding to [M]:[I] ratio of 50:1, 75:1, 125:1 and 150:1 (Fig. 4.6) at constant *ε*–CL concentration (Table 4.2). The linearity of the plot of –ln k_{obs} vs –ln [**1**] at 110 ^{o}C, with non-integer slope of 0.64 which is consistent with first order dependency of the polymerization kinetics on [**1**] was observed.

Table 4.2 Summarized data of ROP of *ε*–CL showing effect of catalyst (**1**) concentration and polymerization kinetics for **1**[a]

Entry	$[M]_o/[I]$	Conv. (%)[b]	Time (h)	K_{obs} (h^{-1})	M_n[c] (g mol^{-1})	M_w[c] (g mol^{-1})	PDI[d]	IE[e]
1	50	97	38	0.0592	4789	6500	1.36	1.15
2	75	97	38	0.0568	4987	6617	1.33	0.79
3	100	97	66	0.0312	7291	11036	1.51	0.99
4	125	97	72	0.0227	8203	11193	1.36	0.80
5	150	97	85	0.0192	9268	11965	1.29	0.72

[a] All polymerization reactions were carried at 110 ^oC for *ε*–CL monomer in bulk for different [M]:[I] ratio. [b] Maximum conversions achieved from ^1H NMR spectroscopy. [c] GPC M_n and M_w values. [e] Polydispersity indexes (PDI = M_w/M_n) from GPC. [e] Initiator efficiency (IE) = Mw_{exp}/Mw_{cal} = (M/I) × (% conversion) × $Mw_{(monomer)}$ + $Mw_{(chain\text{-}end\ groups)}$.

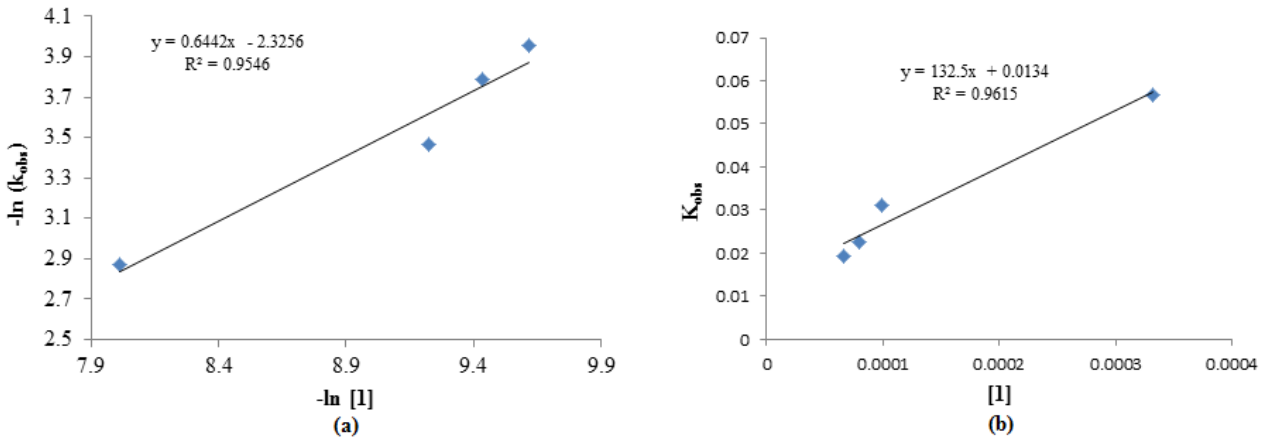


Fig. 4.6:(a) Linear plots of $-\ln[k_{obs}]$ vs $-\ln[\mathbf{1}]$ polymerization of ε-caprolactone at 110 ^oC and for [M]:[I] = 100:1 for the determination of order of reaction with respect to **1**. Fig. 4.6:(b) Plot of k_{obs}vs [1], to determine the threshold catalyst concentration (x-intercept) required to initiate the polymerization reaction

Non-integer order of reactions in catalyst is difficult to interpret mechanistically. Fractional dependencies upon the catalyst are well established for ring-opening polymerization of lactones with alkoxides.[29-31] This is associated with complicated aggregation phenomenon which occur during the generation of the active species prior to the polymerization.[32,33] The overall kinetic rate law for ε–CL polymerization by **1** can therefore be expressed as shown in eqn. 2. The rate law is consistent with a coordination-insertion mechanism involving single zinc site.

$$-\frac{\mathrm{d[Cl]}}{dt} = k[Cl]^1[\mathbf{1}]^{0.64} \qquad (2)$$

4.3.3 Molecular weight and molecular weight distribution of PCL and PLA

4.3.3.1 Effect of catalyst structure on polymer weight and molecular weight distributions

To determine the molecular weights and polydispersities (PDIs) of polymers, the polymers obtained were analyzed by gel permeation chromatography (GPC) and the experimental results compared with the theoretical data calculated from ^{1}H NMR spectra (Tables 4.1, 4.2 and 4.3). The plots of Mw vs % conversion (Fig. 4.7) showed great linearity (increase in Mw with percentage conversion) typifying living polymerization behaviour.[34] For instance, a typical increase in molecular weight of the polymer from 1372 to 7291 g mol^{-1} was observed at 18% to 97% respectively for complex **1**. Similarly, an increase in percentage conversion from 64% to 96% was accompanied by an increase in molecular weights from 7 558 to 11 114 g mol^{-1} for complex **5** (Table 4.3, entries 1-5 and 12-15). Narrow polydispersities (PDI) ranging from 1.33-1.73 and 1.29-1.43 (Table 4.3, entries 1-5 and 12-15) were obtained for both complex **1** and **5** respectively. This indicates some degree of good control of the polymerization reactions. Our research group have previously reported PCL polymers with moderate to wide molecular weight

distribution (PDIs = 2-4), indicating little control over molecular weight.[19,20] Better control over molecular weight observed from these systems could be attributed to the nature of ancillary ligands coordinated to the metals. In addition, the bulky nature of **L1** and **L2** may prevent the growing polymer chain from accessing the active catalyst site, hence limiting backbiting/transesterification reactions.[35]

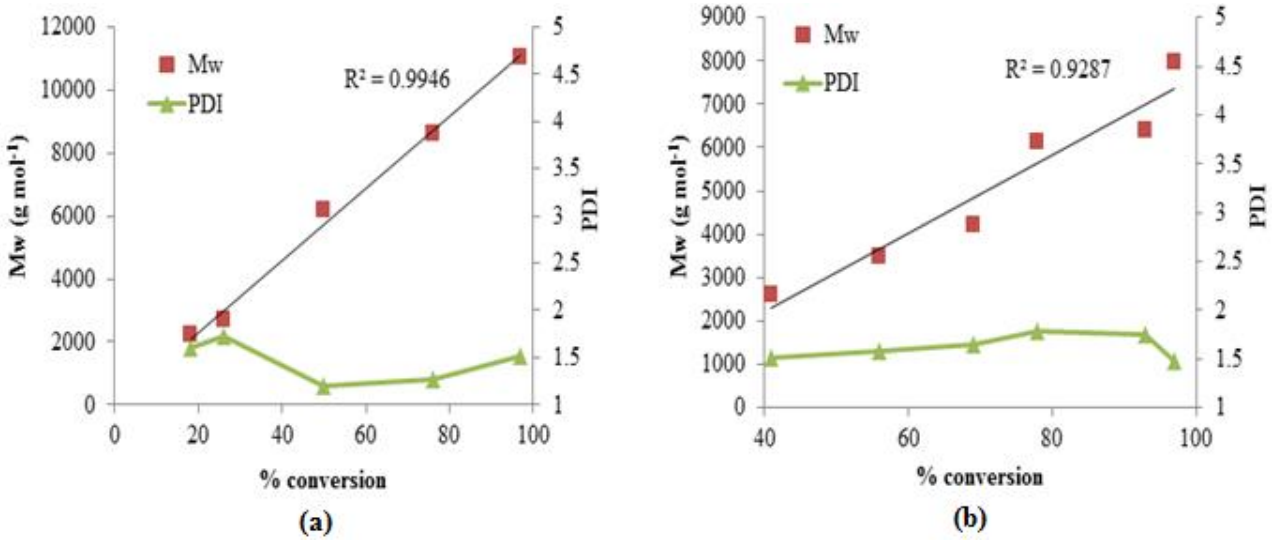


Fig. 4.7: Plot of PCL M_w (versus polystyrene standards) and molecular weight distribution (PDI) as a function of conversion at 100 ^oC in bulk. The rectangles represents experimental Mw determined by SEC, diamonds show theoretical Mw calculated from chain end group and triangles represents the PDIs. Using initiators (a) **1**, (b) **8**

Generally, the low Mw obtained for complexes **1-6** and **8-9** could be assigned to the presence of carboxylates as the initiating groups which are known to be poor initiators than alkoxide initiators.[36,37] Theoretical and experimental molecular weights were in good agreement even though the experimental Mw were much lower compared to molecular weights obtained using

(pyrazolylphenylimino)phenoxy Al and Zn catalysts 211 000 Da and 181 000 Da respectivey.[38] These deviations suggests rapid chain termination in our initiators and low initiator efficiencies of the carboxylate groups.

4.3.3.2 Dependency of polymer weight on identity of the monomer

The influence of monomer on polymer molecular weight and molecular weight distribution was probed by comparing molecular weights of PCL, PD,L-LA and Ps-LA using complex **5** (Table 4.1, entries 5, 10 and 11). Interestingly, polymerization of s-LA using **5** as an initiator resulted in high Mw and narrow PDI than the polymerization of D,L-LA. For instance, when using D,L-LA, very low molecular weight of 1 154g mol^{-1} at 97% conversion and molecular weight distribution of 2.02 were obtained (Table 4.1, entry 10) in comparison to molecular weight of 4 053 g mol^{-1} and PDI of 1.15 reported for S-LA monomer (Table 4.1, entry 11). The controlled character of s-LA polymerization over D,L-LA polymerization could be attributed to the effect of monomer stereochemistry. It is also interesting to note that even though the molecular weights of the resulted PLAs increase with increasing %conversion, the polymerization by complex **8** resulted in unexpectedly low Mw of the polymers compared to PCL. This agrees with the results obtained by Fritsch *et al*.[37,39]

Table 4.3 Summary of *ε*–CL polymerization data by complexes **1**, **5**, and **8**.[a]

Entry	Cat.	Time (h)	Conv. (%)[b]	M_n[c] (g mol^{-1})	M_w[c] (g mol^{-1})	PDI[d]	IE[e]
1	**1**	18	18	1372	2208	1.61	1.01
2		24	26	1572	2713	1.73	0.88
3		36	50	5138	6180	1.20	1.06
4		48	76	6751	8604	1.27	0.98
5		66	97	7291	11036	1.51	0.99
6	**5**	48	64	5776	7558	1.31	1.01
7		54	76	6806	8790	1.29	1.00
8		66	92	7315	10487	1.43	0.99
9		72	96	8168	11114	1.39	1.00
10	**8**	18	41	1728	2614	1.51	0.55
		24	56	2203	3487	1.58	0.54
12		30	69	2555	4205	1.65	0.53
13		36	78	3414	6135	1.79	0.68
14		48	93	3653	6408	1.75	0.60
15		54	97	5363	7954	1.48	0.71

[a] All polymerization reactions were carried at 110 ^{o}C for *ε*–CL monomer in bulk for different [M]:[I] ratio. [b] Maximum conversions achieved from ^{1}H NMR spectroscopy. [c] GPC M_n and M_w values. [e] Polydispersity indexes (PDI = M_w/M_n) from GPC. [e] Initiator efficiency (IE) = Mw_{exp}/Mw_{cal} = (M/I) × (% conversion) × $Mw_{(monomer)}$ + $Mw_{(chain\text{-}end\ groups)}$.

It is worth noting the molecular weights obtained for lactides were much lower compared to those obtained for CL. For instance, while complex **8** afforded PCL of Mw of 7 954 g/mol (Table 4.1, entry 1), D,L-LA and S-LA gave polylactides of Mw of 1 154 g/mol and 4 053 g/mol respectively (Table 4.1, entries 8, 10 and 11). Appavoo *et al.* have also reported a trend similar to this, and attributed it to the larger size of caprolactone monomer.[24]

4.3.3.3 Effect of catalyst concentration on polymer weight

We also investigated the effect of catalyst concentration on PCL molecular weight using complex **1** (Table 4.2, entries 1-5). Notably, we observed that there was an increase in molecular weight with increase in the ratio of monomer-to-catalyst (Fig. 4.8) indicating the "controlled" polymerization character of complex **1**. For example, an increase in monomer-to-catalyst (M/I) ratio from 50 to 150 led to increased molecular weights from 6 500 to 11 965 g mol^{-1} respectively (Table 4.2, entries 1-5). This is not surprising and is consistent with fundamental and literature findings. For instance, Vuorinen *et al*.,[40] Chen *et al*.[28] have reported similar trends using Bi(III) alkoxides, trinuclear Zn(II) alkoxide and homoleptic Zn(II) complex as catalysts for ring-opening polymerization of ε–CL .

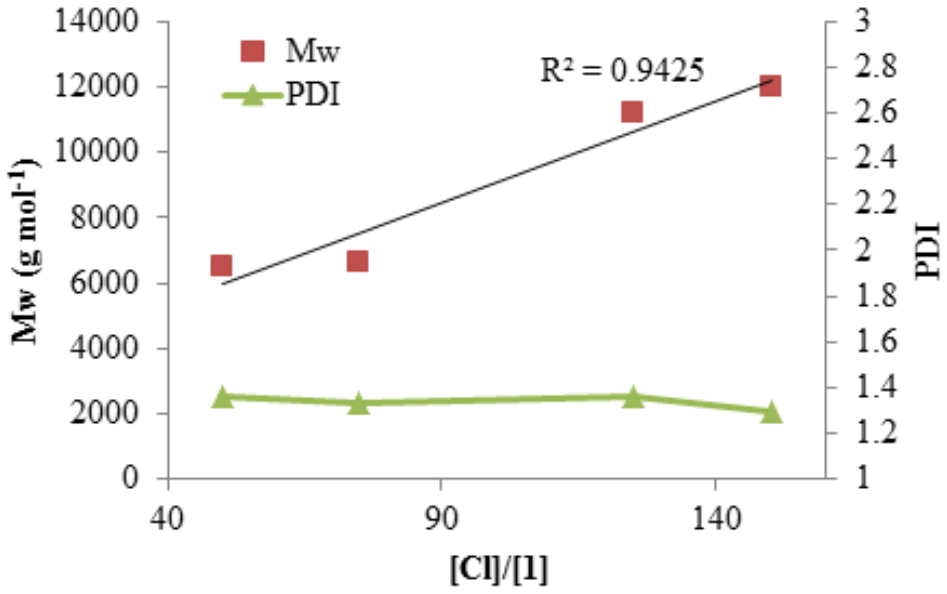


Fig. 4.8: Plot of the molecular weight (M_n from GPC) for different monomer-to-catalyst molar ratios in bulk *ε*–CL ROP by 1 at 110 ^{o}C.

4.3.3.4 The number of active sites in the catalyst

Degree of polymerization (i.e., number of repeat units, X_n) was plotted as a function of [*ε*–CL]/[**1**] ratio to establish the number of initiating active sites in catalyst **1**, (Fig. 4.9). Due to linear relationship between X_n and [*ε*–CL]/[**1**] the average number of initiating sites in **1** could be derived from the inverse of the slope of the line (0.5434).[41] Thus on average, initiator **1** has 1.84 active initiating sites per zinc center. This data suggests that **1** utilized only 2 Zn(II) active sites in the polymeric structure and this is consistent with the results obtained by chamberlain *et al*.[42] and has been attributed to catalyst aggregation. More recently, our research group reported that (pyrazolyl-methyl)pyridine Zn(II) acetates complexes do not utilize all the available active sites in polymerization of *ε*–CL.[19]

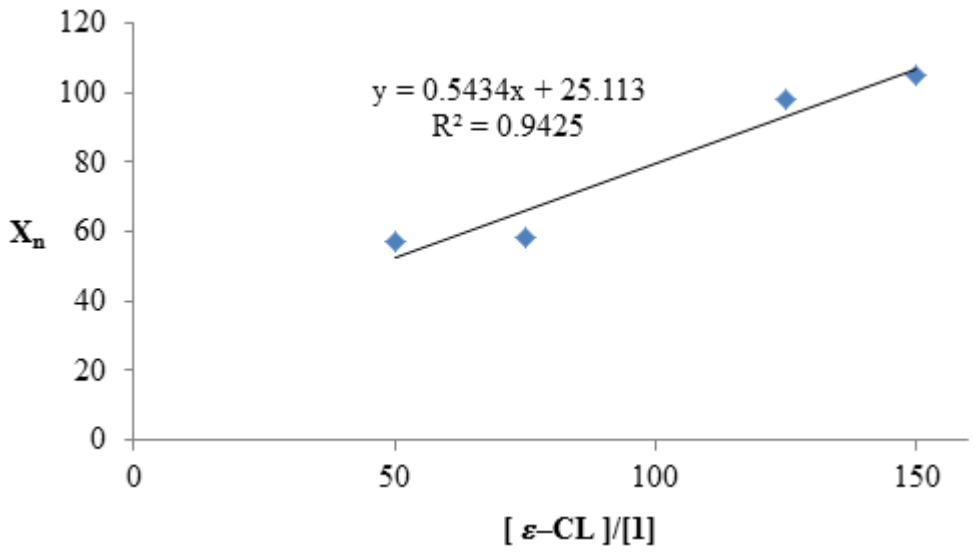


Fig. 4.9: Plot of degree of polymerization of *ε*–CL polymerization (X_n) vs [*ε*–CL]/[**1**] at 110 ^oC in bulk for the determination of the number of active sites in **1**. The inverse of the slope 0.5434 gives an average of 1.84 active sites in the polymeric structure.

4.3.4 Mechanism of *ε*–CL and LA Polymerization

Generally, Zn(II) and Cu(II) complexes initiate polymerization of cyclic esters *via* coordination-insertion mechanism (CIM) or activated-monomer mechanism (AMM).[43] ^1H NMR spectroscopy was thus employed to establish the mechanism of ROP of *ε*–CL and LA by complexes **1-6** and **8-9**. End-group analysis of the PCLs and PLAs derived from complex **1** by ^1H NMR spectroscopy confirmed the incorporation of benzoate group (benzoate, 2-Cl-C_6H_4COO, and 2-Br-C_6H_4COO) in the polymer structure (δ 7.4-8.1 ppm region, methine of benzene ring) (Fig. 4.10a). This suggests that ROP of *ε*–CL and LA occurred *via* coordination insertion mechanism in which the coordinated *ε*–CL or LA monomers are incorporated into the M-$O_{benzoate}$ (M = Zn or Cu) bonds during chain propagation.[20,44] In addition, first order dependency observed in Fig. 4.4 for rates

of kinetics confirmed that polymerization reactions of *ε*–CL follow coordination-insertion mechanism.

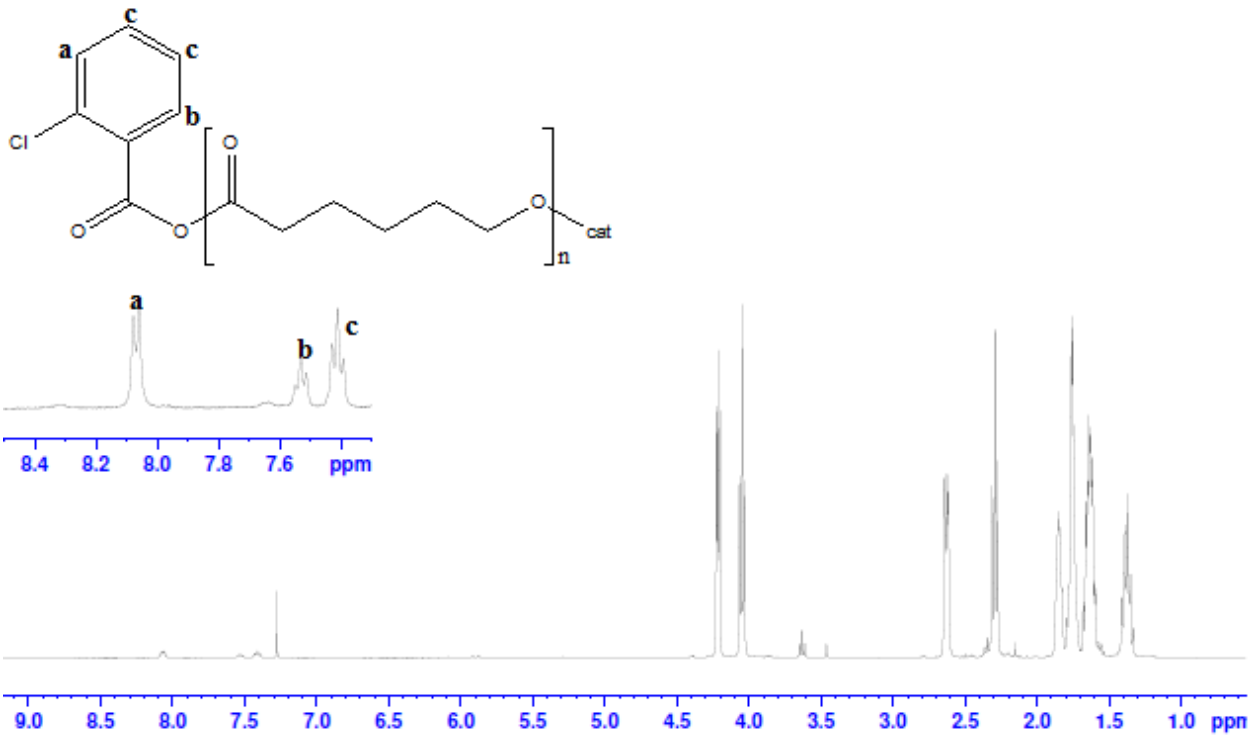


Fig. 4.10: ^{1}H NMR spectra of Polycaprolactone in $CDCl_3$ prepared from *ε*–CL initiated by **6** after 30 h.

Notably, the TOF MS ES spectrum of PCL when obtained from catalyst **6** (Fig. 4.11) showed fragmentation pattern corresponding to the presence 2-chlorobenzoate end group $[C_7H_4O_2Cl(C_6H_{10}O)_n]$. This is clear from the repeating units corresponding to the *ε*–caprolactone with m/z = 114 of n(114) + 54 which is consistent with the findings from ^{1}H NMR spectra. Thus,

it is plausible to conclude that there was incorporation of benzoates as end-groups in the polymer back-bone.

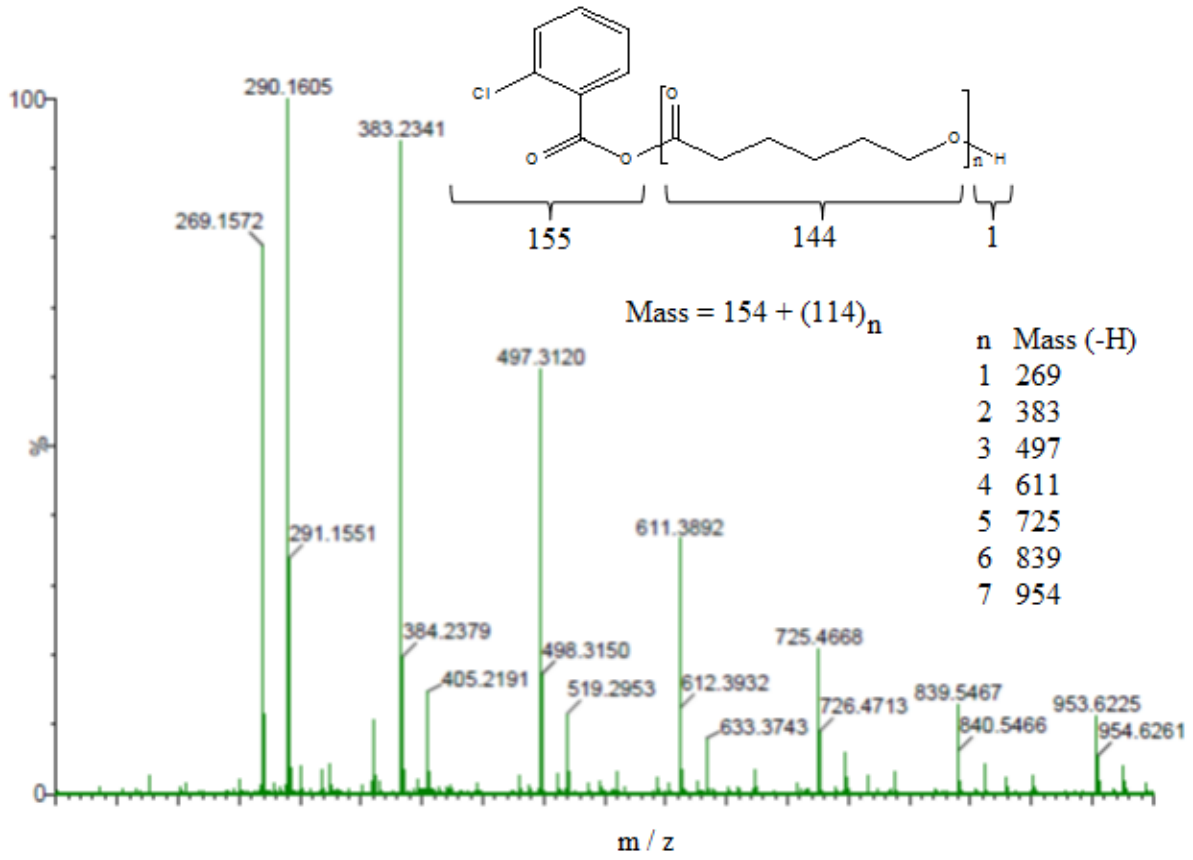


Fig. 4.11: TOF MS ES spectra of PCL prepared by polymerization of *ε*–CL using complex **6** with 21% monomer conversion after 18h.

4.4 Conclusions

Bis(pyrazolyl)pyridine complexes of Cu(II) and Zn(II), **1**-**6** and **8**-**9** form active catalysts in the ring-opening polymerization of *ε*–CL and lactides. The Zn(II) catalyst **8** bearing rigid bis(3,5-dimethyl-***N***-pyrazolyl)pyridine ligand was more active compared to Zn(II) complexes **5** and **6**

bearing flexible bis(pyrazol-1-ylmethyl)pyridine ligand. Varying the metal center of the complexes from Zn(II) to Cu(II) resulted in decreased activity and efficiency of the catalysts. Kinetic data revealed *pseudo*-first order kinetics with respect to *ε*–CL monomer. These complexes produced low to moderate molecular weight PLA and PCL with reasonably narrow polydispersities. The polymerization reactions were found to be "living" in nature. The polymeric Zn(II) complex utilized an average of 2 active sites. Ring-opening polymerization of *ε*–CL and LA proceeded *via* coordination-insertion mechanism.

References

1. Del Rosal, I.; Poteau, R.; Maron, L. *Dalton Trans*., **2011**, 40, 11228.
2. Platel, R. H.; Hodgson, L. M.; Wiliams, C. K. *Polym. Rev. Chem*., **2008**, 48, 11.
3. O'Keefe, B. J.; Hillmyer, M. A.; Tolman, W. B. *J. Chem. Soc., Dalton Trans*., **2001**, 2215.
4. Kamber, N. E.; Jeong, W.; Waymouth, R. M.; Pratt, R. C.; Lohmeijer, B. G. G.; Hendrik, J. L. *Chem. Rev*., **2007**, 107, 5813.
5. a) Cayuela, j.; Bounor-Legare, V.; Cassagnau, P.; Michel, A. *Macromolecules*, **2006**, 39, 1338; b) Wu, J.; Yu, T.-L.; Chen, C.-T.; Lin, C.-C. *Coord. Chem. Rev*., **2006**, 250, 602; c) Stridsberg, K. M.; Ryner, M.; Albertson, A.-C. *Polym. Sci*., **2002**, 157, 41.
6. a) Du, H.; Pang, X.; Yu, H.; Zhuang, X.; Chen, X.; Cui, D.; Wang, X.; Jing, X. *Macromolecules*, **2007**, 40, 1904; b) Jerome, C.; Lecomte, P. *Adv. Drug Delivery Rev*., 2008, 60, 1056.
7. Breyfogle, L. E.; Williams, C. K.; Young, V. G.; Hillmyer, M. A.; Tolman, W. B. *Dalton Trans*., **2006**, 928.
8. Albertson, A. C.; Varma, I. K. *Adv. Polym. Sci*., **2002**, 157, 1.
9. a) Oshimura, M.; Tang, T.; Takasu, A. *J. Polym. Sci. , Part A: Polym. Chem*., **2001**, 49, 1210; b) Liu, Y.-C.; Ko. B.-T.; Lin C.-C. *Macromolecules*, **2001**, 34, 6196.
10. Kiesewetter, M. K.; Shin, E. J.; Hedrick, J. L.; Waymouth, R. M. *Macromolecules*, **2010**, 43, 2093.
11. Wheaton, C. A.; Hayes, P. G.; Ireland, B. J. *Dalton Trans*., **2009**, 4832.
12. Dias, M. L.; Palermo, L. C.; Silvino, A. C. *Macromol. Symp*., **2011**, 156, 299.
13. Chisholm, M. H.; Eilerts, N.W. *Chem. Commun*., **1996**, 853.
14. Chisholm, M. H.; Eilerts, N. W.; Huffman, J. C.; Iyer, S. S.; Pacold, M.; Phomphrai, K. *J. Am. Chem. Soc*., **2000**, 122, 11845.
15. O'Keefe, B. J.; Breyfogle, M. A.; Hillmyer, M. A.; Tolman, W. B. *J. Am. Chem. Soc*., **2002**, 124, 4384.
16. Parrisnen, A.; Kohlmayr, M.; Leskela, M.; Lahcini, T.; Repo, T. *Polym. Chem*., **2010**, 1, 834.
17. Kricheldorf, H. R. *Chem. Rev*., **2009**, 109, 5579.
18. Darensbourg, J.; Karroonnirun, O. *Inorg. Chem*., **2010**, 49, 2360.
19. Ojwach, S. O.; Okemwa, T. T.; Attandoh, N. W.; Omondi, B. *Dalton Trans.*, **2013**, 42, 10735.

20. Attandoh, N. W.; Ojwach, S. O.; Munro, O. Q. *Euro. J. Inorg. Chem*., **2014**, 3053.
21. Gibson, V.C.; Spitzmesser, S.K. *Chem. Rev*., **2003**, 103, 283.
22. Park, S.; Han, Y.; Kim, S.K.; Lee, J.; Kim, H.K.; Do, Y. *J. Organomet. Chem*., **2004**, 689, 4263.
23. Piers, W.E.; Emslie, D.J.H. *Coord. Chem. Rev*., **2002**, 233, 131.
24. Appavoo, D.; Omondi, B.; Guzei, I. A.; van Wyk, J. L.; Zinyemba, O. Darkwa, J. *Polyhedron*, 69, **2014**, 55.
25. Labet, M.; Thielemans, W. *Chem. Soc. Rev*., **2009**, 38, 3484.
26. Alcazar-Roman, L. M.; O'Keefe, B. J.; Hillmyer, M. A.; Tolman, W. B. *Dalton Trans*., **2003**, 3082.
27. Williams, C. K.; Breyfogle, L. E.; Kyung choi, S.; Nam, W.; Young Jr., V. G.; Hillmyer, M. A.; Tolman, W. B. *J. Am. Chem. Soc*., **2003**, 125, 11350.
28. Chen, H.-Y,; Huang, B.-H.; Lin, C.-C. *Macromolecules*, **2005**, 38, 5400.
29. Chamberlain, B. M.; Jazdzewski, B. A.; Pink, R.; Hillmyer, M. A.; Tolman, W. B. *Macromolecules*, **2000**, 33, 3970.
30. Dubois, P.; Jacobs, C.; Jerome, R.; Teyssie, P. *Macromolecules*, **1991**, 24, 2266.
31. Duda, A.; Penczek, S.; *Macromol. Rapid Commun.*, **1994**, 15, 559.
32. Allen, F. A. *Acta Crytallogr*., **2002**, B58, 380.
33. Ouhadi, T.; Hamitou, A.; Jerome, R.; Teyssie, P. *Macromolecules*, **1977**, 9, 927.
34. Darensbourg, D. J.; Choi, W.; Karroonnirun, O.; Bhuvanesh, N. *Macromolecules*, **2008**, 41 (10), 3493.
35. a) Cheng, M.; Moore, D. R.; Reczek, J. J.; Chamberlain, B. M.; Lobkovsky, E. B.; Coates, G.W. *J. Am. Chem. Soc.*, **2001**, *123*, 8738; b) Azor, L.; Bailly, C.; Brelot, L.; Henry, M.; Mobian, P.; Dagorne, S. *Inorg. Chem.* **2012**, *51*, 10876; c) Jensen, T. R.; Schaller, C. P.; Hillmyer, M. A.; Tolman, W. B. *J. Organomet. Chem.* **2005**, *690*, 5881.
36. Chamberlain, B. M.; Jazdzewski, B. A.; Cheng, W.; Moore, D. R.; Ovitt, T. M.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc*., **2001**, 123, 3229.
37. Roberts, C. C.; Barnett, B. R.; Green, D. B.; Fristch, J. M. *Organometallics*, **2012**, 31, 4133.
38. Zhang, C.; Wang, Z.-X. *J. Organomet. Chem*., **2008**, 693, 3151.
39. Reyazee, N. M.; Gerling, K. A.; Rheingoldb, A. L.; Fristch, J. M. *Dalton Trans*., **2013**, 42, 50573.

40. Vuorerinen, S.; Lahcini, M.; Hatanpaa, T.; Sundberg, M.; Leskela, M.; Repo, T. *Macromol. Chem. Phys*., **2013**, 214, 707.
41. a) Steveles, W. M.; Ankone, M. J.; Dijksta, P. J.; Feijen, J. *Macromolecules*, **1996**, 29, 6132; b) MClain, J. S.; Ford, T. M.; Drysdale, N. E. Polym. Prepr. (*Am. Chem. Soc., Div. Polm. Chem*).**1992**, 33, 463.
42. Chamberlain, B. M.; Jazdzewski, B. A.; Pink, M.; Hillmyer, M. A.; Tolman, W. B. *Macromolecules*, **2000**, 33, 3970.
43. Labet, M.; Thielemans, W. *Chem. Soc. Rev*., **2009**, 38, 3484.
44. Liang, L.-C.; Lin, S.-T.; Chien, C.-C.; *Inorg. Chem.*, **2013**, 52, 1780.
45. Pilone, A.; Lambert, M.; Mazzeo, M.; Milione, S.; Pellecchia, C. *Dalton Trans*., **2013**, 42, 13036.
46. Bourissou, D.; Martin-Vaca, B.; Dumitrescu, A.; Grauller, M.; Lacombe, F. *Macromolecules,* **2005**, 38, 9993.

Chapter 5

Summary and Future Work

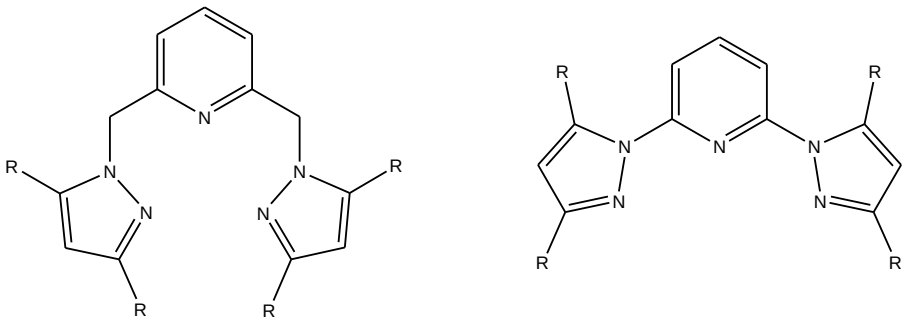
5.1 Summary of conclusions

A series of bis(pyrazolyl)pyridine Zn(II) and Cu(II) complexes have been successfully synthesized and were obtained in moderate to high yields. While the Zn(II) and Cu(II) benzoate complexes were obtained following the reactions of bis(3,5-dimethyl-pyrazol-1-ylmethyl)pyridine (**L1**) or bis(3,5-dimethyl-***N***-pyrazolyl)pyridine (**L2**) ligands with Zn(II) or Cu(II) carboxylates (benzoate, 2-chlorobenzoate, & 2-bromobenzoate), the Zn(II) and Cu(II) acetate complexes were obtained from the reaction of metal acetates with the bis(pyrazolyl)pyridine. The compounds were characterized using a combination of analytical techniques including ^{1}H NMR and IR spectroscopic techniques as well as mass spectrometry, magnetic susceptibility measurements, and single crystal X-ray analysis. Microanalysis was employed to confirm the empirical formulae and purity of the synthesised compounds. While the single crystal X-ray crystallography of complex **1** confirmed the polymeric binding mode of the ligands with distorted octahedral geometry, the single crystal X-ray crystallography of complex **2** confirmed the monomeric binding mode of the ligands with distorted square pyramidal geometry. On the other hand, the single crystal X-ray crystallography of complexes **5-9** confirmed that compounds are monomeric containing one tridentate **L2**, and monodentate carboxylate anions. EPR studies were also employed to confirm the geometry of complexes in both the solid and the solution state.

The synthesized bis(pyrazolyl)pyridine Zn(II) and Cu(II) complexes were employed as catalysts in the ring-opening polymerization of *ε*-caprolanone and lactides, and they form active catalysts. It was noted that, varying the metal center of the complexes from Zn(II) to Cu(II) decreases activity and efficiency of the catalysts. The kinetic data revealed *pseudo*-first order kinetics with respect to *ε*–CL monomer and second order overall rate. The complexes produced PLA and PCL with low to moderate molecular weight and narrow molecular weight distributions. Even though low to moderate Mw PLA and PCL were obtained, such low molecular weight polymers have useful applications where toughness is not a requirement. Polymerization reactions proceeded in a 'living' fashion. Initiator **1** utilized 2 of its active sites. Ring-opening polymerization of *ε*–CL and LA proceeded via coordination-insertion mechanism.

5.2 Future work

Having noted the significant role played by ligands framework or architecture and metal center in terms affording efficient catalysts for ring-opening polymerization of cyclic esters. The future prospects of this study are to further improve the activity and efficiency of the complexes reported in this study. This can be achieved by synthesizing and modifying the ligands structures (Fig. 5.1), i.e. substituting the R group in the ligands either with the electron donating substituents or electron withdrawing substituents can assist in achieving more stable and more electron positive metal centers. We believe this can enhance the activity and efficiency of the complexes towards initiating ring-opening polymerization of cyclic esters.



R = Ph, CF_3

Figure 5.1 New pyrazoly ligand systems aimed to improve our work.

However, we not only looking at modifying the ligand structures for future prospects but we would also be looking at changing the metal centers from Zn and Cu to other non-toxic metals such as magnesium, calcium and even lanthanides. Alternatively, to further modify our ligand systems in future we will investigate the catalytic behavior and efficiency of the alkoxides. We will also investigate chiral ligands for better control of polymer stereochemistry.