SYNTHESIS, CHARACTERIZATION, AND REACTIVITY OF NOVEL ZINC COORDINATION COMPLEXES

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by

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CHAPTER I

INTRODUCTION

The synthesis of well-defined low coordinate inorganic complexes has been a goal sought by inorganic chemist for at least half a century. Such compounds have been noted for their unique reactivities and, more recently, have made been sought after as precursors for nanoparticle synthesis,¹ catalysts for polymerization,² models for biological enzymes³,⁴ and starting materials for metal-metal bonded compounds.⁵ Because of their unique reactivity, the synthesis of stable metal compounds with coordination numbers of one, two, or three is rather difficult. These electron-deficient metal compounds tend to show heightened reactivity toward water and often may be oxidized readily in the presence of O₂. They are also prone to oligomerize into ill-defined aggregates. Therefore, the synthesis of these compounds is typically done in the rigorous absence of water and air and with the aid of bulky ligands. Many bulky ligands have been used over several decades but some of the most prevalent (non-cyclopentadienyl examples) would be bis(trialkylsilyl)amides,⁶ diketiminates,⁷ and aryloxides.⁸

Figure 1. Examples of Bis(trialkylsilyl)amides (I), Diketiminates (II), and Aryloxides (III)
A group of auxiliary ligands investigated recently are 1,1,3,3-tetraalkylguanidines (HTAG). Such ligands have been shown to produce stable well defined low coordinate compounds when used in conjunction with bis(trimethylsilyl)amide\textsuperscript{9} and aryloxides.\textsuperscript{10} A large family of compounds can be derived by the reaction of lithiated amine with the corresponding cyanamide\textsuperscript{9} or the similar amidine compound can be form by reaction with the corresponding nitrile.\textsuperscript{11}

**Figure 2. Several 1,1,3,3-tetraalkylguanidines**

![Several tetraalkylguanidines (HTAG) solvated aryloxide compounds](image)

Several tetraalkylguanidines (HTAG) solvated aryloxide compounds were found to be effective pre-catalysts and, in the presence of alcohol, catalyzed the ring opening polymerization (ROP) of lactide (LA) with modest stereochemical control.\textsuperscript{10} The role of the aryloxide and HTAG in the catalytic cycle is not fully understood.
This project will seek to expand this library of these HTAG derived complexes. Chapter II will discuss the synthesis and characterization of several HTAG solvated zinc thiolate complexes. These complexes’ Zn-S bonds compared to the previously synthesized Zn-O bonds can help shed light on the role of such bonds when examining the catalytic activity of such compounds. Zinc thiolate compounds are also of interest as models for various biological enzymes.\textsuperscript{12,13}

Chapter III will explore the preliminary steps in the synthesis and characterization of base-tethered polydentate ligands with the ultimate goal of synthesizing bidentate alkoxide-guanidine ligands. These ligands are ultimately to be polydentate analogues to the monodentate aryloxide/HTAG ligand system previously studied. Comparison between the reactivity of these compounds and their monodentate counterparts can help explain what effect the loss of the HTAG ligand has on ROP catalytic cycle. Preliminary synthetic routes following the previous reaction pathway for guanidine synthesis have shown an unexpected elimination product formation. Further investigation on the matter is still needed. Chapter IV will discuss the catalytic ring opening polymerization (ROP) of \textit{rac}-lactide (\textit{rac}-LA) by the complexes synthesized in Chapters II and III.
CHAPTER II
SYNTHESIS OF ZINC THIOLATE COMPLEXES

Introduction

Previous work has shown the utility of using 1,1,3,3-tetralkylguandinate ligands (TAG) to isolate crystalline low-coordinate zinc complexes.\textsuperscript{9,14}

Figure 3. $[\text{Zn}(\mu\text{-TAG})\{\text{N(SiMe}_3\text{)}_2\}]_2$

These complexes, upon further reaction with alcohols generate aryloxide (OAr) complexes “Zn(OAr)(HTAG)” that have been shown to be catalytically active for the ROP of LA to produce polylactide (PLA) with modest stereochemical control.\textsuperscript{10} A key step in the proposed ROP catalytic cycle is the nucelophilic insertion of a metal-alkoxide into a coordinated lactide. The auxiliary aryloxide ligands have been proposed to be nucleophilic enough to also insert into the coordinated lactide. The loss of aryoxide
ligands then lead to loss the stereochemical control of the polymerization. To synthesize alternatives to the Zn(OAr) system, several complexes utilizing thiolate ligands will be described herein. Zn-S bonds are noted for their strength due to the effective donation from the zinc’s filled d-orbitals to the empty d-orbitals of the sulfur. These stronger zinc-ligand bonds are notably less nucleophilic than aryloxides and there have been no reports of their insertion during the ROP catalytic cycle. The utility of these zinc thiolate compounds for the ROP of LA is discussed in Chapter IV.

**Experimental**

All compounds were handled with rigorous exclusion of air and water using standard glove box or Schlenk line techniques. All anhydrous solvents were stored under argon and used as received in sure-seal bottles. Diethyl zinc (1.0 M in hexanes), 1,1,3,3–tetramethylguanidine, and iso-propanol were used as received from commercial suppliers. FT-IR data were obtained on a Bruker Tensor 27 Instrument using KBr pellets under an atmosphere of flowing nitrogen. 4-Biphenylthiol was synthesized by a previously described method. Melting points were determined on samples sealed in a glass tube under an atmosphere of argon using an Electrothermal Mel-Temp apparatus and are uncorrected. Elemental analysis was performed on a Perkin-Elmer 2400 Series 2 CHN-S/O Elemental Analyzer.

**Synthesis of Complexes 1 and 2**

An appropriate amount of the thiol (1 = 4-biphenylthiol 2 = 2-napthalenethiol), dissolved in hexanes, was combined with 1,1,3,3–tetramethylguanidine, to yield a bright yellow
suspension. The solution was stirred at 60°C and THF was added drop-wise until the salt was completely suspended within the solution. Diethylzinc was added and the reaction was allowed to stir under heat until evolution of ethane had ceased. Additional THF was added until the solution became clear. X-ray suitable crystals were formed by allowing the solution to slowly evaporate in an argon atmosphere.

[Zn(µ-SC₁₂H₁₀)(Et)(H-TMG)]₂ (1) diethyl zinc (0.42 g, 0.54 mmol), tetramethylgaunidine (0.06 g, 0.5 mmol), and 4-biphenylthiol (0.10 g, 0.54 mmol) were used. Yield 49% (0.10 g, 0.13 mmol). Mp 94°C. ¹H NMR (benzene-d₆): δ = 8.07 (br. s, 4H, aromatic), 7.45 (d, J = 7.3Hz, 4H, aromatic), 7.36 (d, J = 8.0Hz, 4H, aromatic), 7.21 (t, J = 7.5Hz, 4H, aromatic), 7.10 (t, J = 7.3Hz, 2H, aromatic), 4.83 (br. s, 2H, HN=C(N(CH₃)₂)₂), 2.59 (s, 12H, HN=C(N(CH₃)₂)₂), 1.96 (br. s, 12H, HN=C(N(CH₃)₂)₂, overlap with nearby triplet), 1.94 (t, J = 8.1Hz, 3H, CH₂CH₃, overlap with nearby singlet), 0.96 (q, J = 7.7Hz, 2H, CH₂CH₃). ¹³C{¹H} NMR (benzene-d₆): δ = 167.8(HN=C(N(CH₃)₂)₂), 142.1, 134.7, 129.4, 129.0, 127.3, 127.2, (aromatic), 39.8, 38.6, (HN=C(N(CH₃)₂)₂), 14.8 (CH₂CH₃), 1.8 (CH₂CH₃). FT-IR (cm⁻¹): 3351 (s), 2928 (w), 2875 (w), 2837 (m), 1575 (m), 1533 (m), 1474 (m), 1426 (m), 1401 (m), 1298 (w), 1262 (w), 1227 (w), 1124 (m), 1089 (m), 1033 (m), 829 (w), 802 (w), 760 (m), 726 (w), 701 (m). Theoretical elemental analysis for C₃₈H₅₄Zn₂N₆S₂: C, 57.79; S, 8.19; H, 6.89; N, 10.64.
[Zn(µ-SC₁₀H₇)(Et)(H-TMG)]₂ (2) (Et)₂Zn (0.98 g, 1.2 mmol), H-TMG (0.14 g, 1.2 mmol), and 2-napthalenethiol (0.20 g, 1.2 mmol) were used. Yield 72% (0.33 g, 0.45 mmol). Mp 94°C. \(^1\)H NMR (benzene-\(d₆\)): \(\delta = 8.27\) (s, 2H, aromatic), 7.88 (apparent dd, \(J = 8.6\) Hz, 1.3 Hz, 2H, aromatic), 7.39 (apparent dd, \(J = 18\) Hz, 8.05 Hz, 4H, aromatic), 7.29 (d, \(J = 8.4\) Hz, 2H, aromatic), 6.99 (m, 4H, aromatic), 4.41 (br. s, 2H, \(HN=C(N(CH₃)₂)₂\)), 2.29 (s, 12H, asymmetric methylguanidine), 1.73 (t, \(J = 8.0\) Hz, 6H, \(CH₂CH₃\)), 1.50 (s, 12H, asymmetric methyl-guanidine), 0.79 (q, \(J = 7.9\) Hz, 2H, \(CH₂H₃\)). \(^{13}\)C\(^{1}\)H NMR (benzene-\(d₆\)): \(\delta = 167.6\) (\(HN=C(N(CH₃)₂)₂\)), 140.9, 135.3, 134.0, 131.6, 131.3, 128.2, 127.9, 127.2, 126.5, 124.6, (aromatic), 39.6, 38.2 (\(HN=C(N(CH₃)₂)₂\)), 14.8 (\(CH₂CH₃\)), 4.7 (\(CH₂CH₃\)). FT-IR (cm\(^{-1}\)): 3361 (s), 3345 (s), 3051 (m), 2937 (s), 2881 (s), 2846 (s) 2802 (s), 1622 (m), 1570 (s), 1539 (s), 1492 (m), 1427 (s), 1404 (s), 1377 (s), 1302 (m), 1268 (w), 1226 (m), 1194 (w), 1127 (s), 1070 (s), 1034 (m), 943 (m), 904 (w), 885 (w), 852 (m), 820 (m), 749 (m), 718 (m), 598 (m), 558 (w), 496 (w), 475 (m). Theoretical elemental analysis for \(C₃₄H₅₀Zn₂N₆S₂\): C, 55.3; S, 8.69; H, 6.86; N, 11.3.

**Synthesis of Compound 3**

Compound 2 was dissolved in 5 ml of toluene. A solution of isopropanol and toluene was added drop-wise and the solution was allowed to stir at room temperature for 15 minutes. X-ray suitable crystals were formed at -35°C after further concentration of the solution. [Zn(SC₁₀H₇)(µ-OCH(CH₃)₂)(H-TMG)]₂ (3) [Zn(µ-SC₁₀H₇)(Et)(H-TMG)]₂ (2) (0.201 g, 0.27 mmol), isopropanol (0.033 g, 0.54 mmol) were used. Yield 50% (0.109 g, 0.14 mmol). Mp 96°C. \(^1\)H NMR (benzene-\(d₆\)): \(\delta = 7.90\) (br. s, 2H, aromatic), 7.38 (m, 4H,
aromatic), 7.28 (d, J = 8.4Hz, 4H, aromatic), 7.02 (m, 2H, aromatic), 6.95 (m, 4H, aromatic), 4.43 (spt, J = 6.6Hz, 2H, μ-OCH(CH₃)₂), 4.29 (br. s, 2H, HN=C(N(CH₃)₂)₂), 2.41 (s, 12H, asymmetric HN=C(N(CH₃)₂)₂), 1.65 (s, 12H asymmetric HN=C(N(CH₃)₂)₂), 1.39 (t, 12H, J = 6.6Hz, 2H, μ-OCH(CH₃)₂).

^13^C{¹H} NMR (benzene-\textit{d}_6): δ = 167.71, 134.99, 130.89, 128.22, 127.29, 126.73, 126.15, 39.77, 38.51, 29.49. FT-IR (cm⁻¹): 3352(s), 2929(s), 2875(s), 2837(s), 2364(w), 1575 (s), 1533(s), 1475(s), 1426(m), 1401(m), 1298(m), 1262(m), 1227(m), 1125(s), 1089(s), 1033(s), 902(w), 829(m), 803(m), 760(m), 726(m), 701(m), 594(w), 546(w), 504(w), 477(w).

Anal. Calcd for C_{38}H_{54}Zn_2N_6S_2:  C, 57.79; S, 8.19; H, 6.89; N, 10.64. Found for C_{38}H_{54}Zn_2N_6S_2: C, 53.46; H, 7.14; N, 10.06.

**X-ray Crystal Structure Information.** X-ray crystallography was performed by mounting each crystal onto a thin glass fiber from a pool of Fluorolube™ and immediately placing it under a liquid N₂ cooled N₂ stream, on a Bruker AXS diffractometer. The radiation used was graphite monochromatized Mo Kα radiation (λ = 0.7107 Å). The lattice parameters were optimized from a least-squares calculation on carefully centered reflections. Lattice determination, data collection, structure refinement, scaling, and data reduction were carried out using APEX2 version 1.0-27 software package.

Each structure was solved using direct methods. This procedure yielded the Zn atoms, along with a number of the C, N, and S atoms. Subsequent Fourier synthesis yielded the remaining atom positions. The hydrogen atoms were fixed in positions of ideal geometry.
and refined within the XSHELL software. These idealized hydrogen atoms had their isotropic temperature factors fixed at 1.2 or 1.5 times the equivalent isotropic U of the C atoms to which they were bonded. The final refinement of each compound included anisotropic thermal parameters on all non-hydrogen atoms. Data collection parameters are listed in Table 1. Inter-atomic distances and angles are listed with the thermal ellipsoid plots (Figures 6–8).

**Results and Discussion.**

**General Considerations.** The syntheses of complexes 1–3 were performed under an argon atmosphere with the objective of outlining the reactivity of H-TMG, isopropanol and arylthiols with Et₂Zn. Each compound was isolated as a colorless crystalline solid in modest yield. 1–3 were moderately to slightly soluble in toluene and readily soluble in THF.

**Synthesis.** Compounds 1 and 2 were synthesized in a manner analogous to the previous syntheses of HTAG solvated zinc aryloxides.¹⁰ As shown in Figure 4, in a hexanes/THF solution, the “one-pot” reaction of two equivalents of 1,1,3,3-tetramethylguanidine (H-TMG), two equivalents of arylthiol (HSR) and two equivalents of diethyl zinc results in the immediate evolution of CH₃CH₃. Slow evaporation of the solvent in an argon atmosphere resulted in colorless crystals of [Zn(µ-SC₁₂H₁₀)(Et)(H-TMG)]₂ (1) and [Zn(µ-SC₁₀H₇)(Et)(H-TMG)]₂ (2), respectively. Retention of the zinc-bonded ethyl group for 1 and 2 is implied by the observation of a triplet (δ = 1.94 for 1 and 1.73 for 2) and a quartet (δ = 0.96 for 1 and 0.79 for 2) by ¹H NMR spectroscopy. FT-IR spectroscopy on
1 and 2 confirm absorption bands corresponding to \( \nu(N-H) \) and \( \nu(C=N) \) stretching modes around 3300 cm\(^{-1}\) and 1550 cm\(^{-1}\) respectively. 1 and 2 exhibited no SH peaks around 2600 cm\(^{-1}\) which is consistent with full exchange.

**Figure 4. Synthesis of Compounds 1 and 2**

The synthesis of 3 is depicted in Figure 5. For this reaction, compound 2 was dissolved in toluene and allowed to react with two equivalents of isopropanol. \( \text{CH}_3\text{CH}_3 \) evolved and a precipitate formed which would not dissolve upon heating. THF was added and the reaction was heated again until the reaction went clear. X-ray suitable crystals were formed at \(-35^\circ C\) after further concentration of the solution. \(^1\text{H}\) and \(^{13}\text{C}\) NMR spectroscopy were utilized to confirm the presence of O\(^3\text{Pr.}\) FT-IR spectroscopy on 3 confirm absorptions bands corresponding to \( \nu(N-H) \) and \( \nu(C=N) \) stretching modes around 3300 cm\(^{-1}\) and 1580 cm\(^{-1}\) respectively. Additional reactions of 2 with water, methanol, or trimethylacetic acid yielded amorphous intractable gels.
Figure 5. Synthesis of 3

![Synthesis of 3](image)

**Structural Descriptions**

All complexes were characterized by single crystal X-ray diffraction. Thermal ellipsoid plots and selected interatomic distances and angles of 1, 2, and 3 are presented in Figures 6, 7, and 8. Structural descriptions for each complex are provided in the following paragraphs. The Zn-S bond averaged 2.487Å for bridging thiolates and 2.276Å for terminal thiolates which is typical for such systems.\(^\text{17}\)

\[\text{[Zn}(\mu\text{-SC}_{12}\text{H}_{10})(\text{Et})(\text{H-TMG})]\text{]}_2 \text{ (1)}\]

The thermal ellipsoid for 1 is illustrated in Figure 6. This compound crystallizes in the triclinic space group \(\overline{P}\overline{1}\) with one molecule per unit cell. The molecular structures consist of a dinuclear unit with a distorted tetrahedral geometry for each zinc center. Each metal atom is coordinated to a terminal ethyl and H-TMG with two 4-biphenylthiolate bridging the metal centers. The compound showed symmetry along the zinc-sulfur plane, with one cluster of ligands above the plane and their symmetric equivalent below the plane. The
Zn-S bond averages 2.46 Å and the Zn-C bond averages 1.99 Å. The S-Zn-S angle is 93.88° whereas the C-Zn-N angle is 122°; indicating the considerable distortion due to the organometallic Zn-C bond.

\[
[Zn(\mu-SC_{10}H_{17})(Et)(H-TMG)]_2 \ (2)
\]

The thermal ellipsoid for 2 is illustrated in Figure 7. This compound crystallizes in the triclinic space group P\(\overline{1}\) with two molecules per unit cell. The molecular structures consist of a dinuclear unit with each Zn exhibiting distorted tetrahedral geometry. Each metal atom is coordinated to a terminal ethyl and a H-TMG group with the 2-napathanethiolate bridging the two metal centers. The compound, unlike 1, was not symmetric along the Zn-S plane due to distortions of the guanidine ligand. The Zn-S bond averages 2.47 Å and the Zn-C bond averages 1.99 Å. The S-Zn-S angle is 94.43° whereas the C-Zn-N angle is 123.38° also indicating distortion due to the organometallic Zn-C bond.

Overall, there are five dinuclear organozinc structures known in which a direct Zn-S bond is present, with the closest related compound being \([Zn(Me)\{SC_6H_4(R)-CH(Me)NMe_2\}]_2\).\(^{18-20}\) Compared to this organozinc compound, the Zn-C interatomic distances are slightly longer (2.035 Å (average) vs 1.99 Å (average) for 1 and 2). This can be attributed to the intramolecular coordination of the amino group in \([Zn(Me)\{SC_6H_4(R)-CH(Me)NMe_2\}]_2\).
[Zn(SC$_{10}$H$_7$)(µ-OCH(CH$_3$)$_2$)(H-TMG)]$_2$ (3)

The thermal ellipsoid for 3 is illustrated in Figure 8. This compound crystallizes in the monoclinic space group C2/c with four molecules per unit cell. The molecular structures consist of a dinuclear unit which forms a distorted tetrahedral geometry. Each metal atom is coordinated to a terminal 2-naphthenethiolate and H-TMG group with an isopropoxide group bridging the two metal centers. The terminal 2-naphthenethiolate groups are bent 102.36° toward the center of the ring. There seems to be no evidence of π stacking within the lattice structure with the naphthalene groups being orientated nearly 90° between two molecules and the shortest intermolecular C-C distance being 9.5 Å. There is no noticeable shielding of the enclosed isopropyl protons in the $^1$HNMR in d$_6$-benzene indicating that the orientation for the naphthalene groups observed in the crystal structure is not likely present in solution. The average Zn-S bond is 2.27 Å, the average Zn-O bond is 1.97 Å, and the average Zn-N bond is 2.01 Å.

Notably, 3 is dimeric complex with a central Zn$_2$O$_2$ unit in which the Zn atoms are bridged by two oxygen atoms and further coordinated by terminal nitrogen and sulfur atoms. This coordination geometry is without structural precedent. The closest resembling dinuclear Zn complexes have Zn atoms with coordination numbers of five and six.$^{21-35}$
Conclusion

Three dinuclear zinc thiolate compounds stabilized with H-TMG were synthesized and characterized by $^1$HNMR, $^{13}$CNMR, FT-IR, and X-ray crystallography. Compound 2 was further reacted with isopropanol to yield compound 3, a structure proposed as an intermediate in the ROP catalytic cycle (Chapter IV).
**Table 1:** Data Collections parameters for 1, 2, and 3

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<th>Compound</th>
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<td>C$<em>{34}$ H$</em>{50}$ N$_6$ S$_2$</td>
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<td>wR2$^b$ (%) (all data)</td>
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</table>

$^a$R1 = $\Sigma | |F_o|-|F_c|| / \Sigma |F_o| \times 100$

$^b$wR2 = $[\Sigma w (F_o^2-F_c^2)^2 / \Sigma (w |F_o|^2)^2]^{1/2} \times 100$
Figure 6. Thermal ellipsoid plot of 1. Ellipsoids are drawn at the 30% level. H atoms except those on the guanidine have been omitted for clarity. Selected inter-atomic distances (Å) and angles (°): Zn(1)-C(1) 1.999(2), Zn(1)-N(1) 2.0366(17), Zn(1)-S(1) 2.4157(7), Zn(1)-S(1A) 2.5078(7), C(1)-Zn(1)-N(1) 122.00(9), C(1)-Zn(1)-S(1) 126.86(8), N(1)-Zn(1)-S(1) 96.38(5), C(1)-Zn(1)-S(1A) 113.54(9), N(1)-Zn(1)-S(1A) 97.46(5), S(1)-Zn(1)-S(1A) 93.866(18), C(8)-S(1)-Zn(1) 110.49(7), C(8)-S(1)-Zn(1A) 106.71(7) and C(3)-N(1)-Zn(1) 132.32(14).
**Figure 7.** Thermal ellipsoid plot of 2. Ellipsoids are drawn at the 30 % level. H atoms except those on the guanidine have been omitted for clarity. Selected inter-atomic distances (Å) and angles (°): Zn(1)-C(6) 2.003(3), Zn(1)-N(1) 2.026(2), Zn(1)-S(1) 2.4421(7), Zn(1)-S(2) 2.4989(7), Zn(2)-C(13) 1.984(3), Zn(2)-N(4) 2.038(2), Zn(2)-S(2) 2.4244(8), Zn(2)-S(1) 2.5261(7), C(6)-Zn(1)-N(1) 125.38(11), C(6)-Zn(1)-S(1) 123.91(8), N(1)-Zn(1)-S(1) 99.75(7), C(6)-Zn(1)-S(2) 108.74(8), N(1)-Zn(1)-S(2) 97.54(6), S(1)-Zn(1)-S(2) 94.43(2), C(13)-Zn(2)-N(4) 123.38(12), C(13)-Zn(2)-S(2) 128.35(12), N(4)-Zn(2)-S(2) 94.34(6), C(13)-Zn(2)-S(1) 111.34(10), N(4)-Zn(2)-S(1) 98.32(6), S(2)-Zn(2)-S(1) 94.18(2), C(25)-S(1)-Zn(1) 107.47(9), C(25)-S(1)-Zn(2) 106.17(8), Zn(1)-S(1)-Zn(2) 84.78(2), C(15)-S(2)-Zn(2) 113.61(10), C(15)-S(2)-Zn(1) 107.07(9), Zn(2)-S(2)-Zn(1) 85.75(2), C(1)-N(1)-Zn(1) 135.67(18), C(7)-C(6)-Zn(1) 112.9(2) and C(14)-C(13)-Zn(2) 117.8(2).
Figure 8. Thermal ellipsoid plot of 3. Ellipsoids are drawn at the 30 % level. H atoms except those on the guanidine have been omitted for clarity. Selected inter-atomic distances (Å) and angles (°): Zn(1)-O(1) 1.9830(12), Zn(1)-N(1) 2.0106(15), Zn(1)-S(1) 2.2757(5), S(1)-C(1) 1.7736(19), O(1A)-Zn(1)-O(1) 81.59(5), O(1A)-Zn(1)-N(1) 109.75(6), O(1)-Zn(1)-N(1) 101.85(6), O(1A)-Zn(1)-S(1) 118.94(4), O(1)-Zn(1)-S(1) 122.05(4), N(1)-Zn(1)-S(1) 116.82(5), C(1)-S(1)-Zn(1) 102.36(6), and Zn(1A)-O(1)-Zn(1) 98.41(5).
CHAPTER III

SYNTHESIS OF BASE TETHERED POLYDENTATE COMPLEXES

Introduction

The use of polydentate multifunctional ligand complexes has been investigated in recent years.\textsuperscript{36} Out of this has emerged a novel classes of binucleating ligands\textsuperscript{37} which have been used to model cooperativity in catalysis and numerous metalloenzymes have binuclear reaction centers. A simple construction principle for these ligands consists in the use of a central bridging unit (phenolate, thiophenolate, bipyridine, pyrazole, etc.) to which polydentate side groups are attached. The functionalization of the binuclear reaction centers that can be achieved with such ligands has been impressively demonstrated by modeling iron and copper containing enzymes.\textsuperscript{38,39}

Additionally, such complexes show potential as bifunctional ligands. Bifunctional ligands exhibit the ability to interact with a bound substrate during the catalytic cycle. This interaction lowers the energy state of the transition state and such catalytic systems often show enhanced catalytic activity. Cooperative H-bonding between nearby residues has often been proposed to explain the reactivity of metalo-enzymes such as carbonic anhydrase.\textsuperscript{40} Industrial catalysts such as the Shvo\textsuperscript{41} type, Noyori\textsuperscript{42} type, and Grutzmacher\textsuperscript{43,44} type use similar bifunctional proton transfer ligands to catalyze hydrogenation and transfer hydrogenation of ketone and imine systems.\textsuperscript{41-44}
In this chapter, the use of two ligands will be evaluated in their capability to generate discrete Zn and Li complexes: 6-[[2-hydroxy-3,5-bis(tert-butyl)phenyl]carboximidoyl]-2,4-bis(tert-butyl)phenol (H$_2$L$_1$) and 2,4-di-tert-butyl-6-phenylaminophenol (H$_2$L$_2$) (Figure 10). L$_1$ and L$_2$ have the potential to act as either bifunctional ligands in a manner similar to the previously mentioned proton transfer ligands or binucleating ligands. Future work will evaluate this capability.
Experimental

All anhydrous solvents were stored under argon and used as received in sure-seal bottles. All compounds were used as received from commercial suppliers without further purification. FT-IR data were obtained on a Bruker Tensor 27 Instrument using KBr pellets under an atmosphere of flowing nitrogen. 2-Bromo-4,6-di-tert-butylphenol and 2,4-di-tert-butyl-6-phenylaminophenol were synthesized in a manner similar to literature reports. Melting points were determined using an Electrothermal Mel-Temp apparatus and are uncorrected.

Synthesis of 2-bromo-4,6-di-tert-butylphenol

10.0 g of 2,4-di-tert-butylphenol (97.4 mmol) was dissolved in acetonitrile. The solution was cooled to 0°C and 18.2 g of N-bromosuccinimide (102 mmol) was added to the solution in 2 g portions. The solution was allowed to warm to room temperature and stirred for 12 hours. The solution was concentrated partially then quenched with excess sodium bisulfite. The solution was extracted with hexane then passed through a plug of silica gel. Vacuuming down to dryness yielded 16.07g (58% yield) of product.

$^1$H NMR (benzene-$d_6$): $\delta = 7.33 (d, J = 2.4$Hz, 1H, aromatic), 7.25 (d, $J = 2.4$Hz, 1H, aromatic), 5.66 (s, 1H, phenol), 1.41 (s, 9H, para - tert-butyl), 1.29 (s, 9H, ortho - tert-butyl).
Synthesis of 2,4-di-tert-butyl-6-phenylaminophenol (H$_2$L$_2$)

5.00 g of 3,5-di-tert-butylcatechol (22.5 mmol) was suspended in a solution of n-heptane with 0.226 g of trimethylamine (4.65 mmol) and 2.10 g of aniline (22.5 mmol). The solution was refluxed for 5 hours then the solution cooled to 0°C overnight. The resulting crystals were filtered and washed with chilled n-heptane to yield 4.254g (63%) of tan crystals.

$^1$H NMR (chloroform-$d$): $\delta = 7.32$ (m, 2H, aromatic), 7.29 (s, 1H, aromatic), 7.13 (d, $J = 2.2$Hz, 1H, aromatic), 6.94 (t, $J = 7.3$Hz, 1H, aromatic), 6.76 (d, $J = 8.4$Hz, 2H, aromatic), 6.51 (br. s, 1H, phenol OH), 5.05 (s, 1H, aniline NH), 1.54 (s, 9H, para - tert-butyl), 1.36 (s, 9H, ortho - tert - butyl). $^{13}$C($^1$H) NMR (chloroform-$d$): $\delta = 149.38$, 146.78, 142.18, 135.29, 129.33, 127.71, 121.98, 121.51, 119.75, 115.11, 34.98, 34.35, 31.59, 29.51. FT-IR (cm$^{-1}$): 3366 (s), 3050 (m), 2962 (s), 2868 (s), 2537 (w), 1922 (w), 1701 (w), 1600 (s), 1497 (s), 1419 (s), 1364 (s), 1231 (s), 1175 (m), 1151 (m), 1117 (m), 1077 (w), 1026 (m), 882 (m), 825 (m), 808 (m), 749 (s), 692 (s), 618 (m) 544 (m), 474 (m).

Synthesis of [Li(µ-HL$_1$)(Et$_2$O)]$_2$ (4)

3.00 g of the previously synthesized 2-bromo-4,6-di-tert-butylphenol (10.5 mmol) was dissolved in ether. 6.12 g of a 2.5M solution of butyl lithium (22.1 mmol) was added drop wise at room temperature to the solution. The resulting solution was allowed to stir for 20 minutes. 0.740 g of dimethylcyanamide (10.5 mmol) was added drop wise to the solution and the mixture was allowed to stir overnight. The reaction was then quenched with excess isopropanol. Then was extracted using water and dried over magnesium sulfate.
X-ray quality crystals formed from the slow evaporation of ether from on top of the aqueous layer. Vacuuming the remaining ether layer yielded 2.545 g (55.2% yield) as a bright orange powder. $^1$H NMR (Chloroform-$d$): δ = 7.46 (d, $J = 2.4$Hz, 4H, aromatic), 7.28 (d, $J = 2.4$Hz, 4H aromatic), 3.38 (q, $J = 6.9$Hz, 8H, O(CH$_2$CH$_3$)$_2$), 2.61 (s, 2H, amine), 1.37 (s, 36H, meta – tert – butyl), 1.18 (s, 36H, ortho – tert – butyl), 1.11 (t, $J = 6.95$Hz, O(CH$_2$CH$_3$)$_2$), HO-Phenol not observed in this solvent. $^{13}$C{$^1$H} NMR (benzene-$d_6$): δ = 130.47, 127.57, 124.07, 123.50, 65.86, 35.28, 31.46, 29.66, 29.48, 15.27. (FT-IR (cm$^{-1}$): 3619(w), 3511(w), 3300(broad shoulder)2952(s), 1869(w), 1653(s), 1568(s), 1430(s), 1172(s), 1105(s), 1066(s), 1039(s), 913(m), 894(m), 820(s), 785(m), 750(m), 715(m), 636(w).

**Synthesis of [Zn(µ-HL$_2$)(Et)]$_2$ (5)**

0.20 g of 2,4-di-tert-butyl-6-phenylaminophenol (0.67 mmol) was dissolved in toluene. 0.486 g of a 1.0 M solution of diethylzinc in hexanes (0.67 mmol) was added drop wise. The solution was allowed to stir for 10 minutes. THF was added drop-wise until the solution became clear. X-ray quality crystals were formed by slow evaporation of the solution in an argon atmosphere. Yield 0.675g (100% yield). $^1$H NMR (benzene-$d_6$): δ = 7.44 (d, $J = 2.2$Hz, 2H, phenol aromatic), 7.08 (m, 4H, aniline aromatic), 6.94 (d, $J = 2.2$Hz, 2H, phenol aromatic), 6.85 (m, 6H, aniline aromatic), 5.30 (br. s, 2H, HN-Ph), 1.48 (s, 18H, meta – tert – butyl), 1.23 (t, $J = 8.1$Hz, 6H, -CH$_2$CH$_3$), 1.20 (s, 18H, ortho – tert – butyl), 0.41 (q, $J = 8.1$Hz, 4H, -CH$_2$CH$_3$). $^{13}$C{$^1$H} NMR (benzene-$d_6$): δ = 129.99, 124.64, 123.47, 120.98, 36.02, 30.90, 13.11. FT-IR (cm$^{-1}$): 3267(m), 2958(s), 2850(s), 2363(w), 1772(w), 1600(m), 1562(w), 1495(m), 1476(s), 1439(m), 1414(m), 1383(m).
1300(m), 1289(m), 1252(s), 1219(s), 1161(m), 1078(m), 886(m), 872(m), 828(s), 798(s), 693(s), 620(w), 517(m).

X-ray Crystal Structure Information. X-ray crystallography was performed by mounting each crystal onto a thin glass fiber from a pool of Fluorolube™ and immediately placing it under a 100 K N₂ stream, on a Bruker AXS diffractometer. The radiation used was graphite monochromatized Mo Kα radiation (λ = 0.7107 Å). The lattice parameters were optimized from a least-squares calculation on carefully centered reflections. Lattice determination, data collection, structure refinement, scaling, and data reduction were carried out using APEX2 version 1.0-27 software package.

Each structure was solved using direct methods. This procedure yielded the Zn atoms, along with a number of the Li, C, N, and O atoms. Subsequent Fourier synthesis yielded the remaining atom positions. The hydrogen atoms were fixed in positions of ideal geometry and refined within the XSHELL software. These idealized hydrogen atoms had their isotropic temperature factors fixed at 1.2 or 1.5 times the equivalent isotropic U of the C atoms to which they were bonded. The final refinement of each compound included anisotropic thermal parameters on all non-hydrogen atoms. Data collection parameters are listed in Table 2. Inter-atomic distances and angles are listed in beneath the thermal ellipsoid plots (Figures 14 and 15).

Results and Discussion.

Synthesis 2-bromo-4,6-di-tert-butylphenol was synthesized by previous reported methods. The ¹H NMR was consistent with the previously reported spectra as well as the
commercially available product. The doublets in the aromatic region with $J = 2.4$ are indicative of long range $\Omega$ coupling between each aromatic protons.

2,4-di-tert-butyl-6-phenylaminophenol ($H_2L_2$) was synthesized by previous reported methods.\textsuperscript{47} The $^1\text{H}$ NMR and $^{13}\text{C}$ NMR were consistent with its structure and previous reported spectra. FT-IR spectroscopy confirm an absorption band corresponding to $\nu$(N-H) stretching modes around 3300 cm$^{-1}$. This synthesized ligand is intended to be used as a starting material to synthesize further ligands.

The synthesis of compound 4, $[\text{Li(µ-L}_1\text{)(Et}_2\text{O)}]_2$, is shown in Figure 11. Compound 4 was synthesized by the addition of two equivalents of $n$BuLi to 2-bromo-4,6-di-tert-butylphenol followed by the addition of dimethylcyanamide at room temperature. The reaction was quenched with isopropanol and water and extracted with ether. X-ray quality crystals were formed by evaporation of the ether layer from above the aqueous layer and the bulk material was isolated in moderate yield by concentration of the ether solution. $^1\text{H}$ NMR of the bulk compound was consistent with the $^1\text{H}$ NMR of the crystalline sample. FT-IR spectroscopy on 4 confirm absorptions bands corresponding to $\nu$(N-H) and $\nu$(C=N) stretching modes around 3300 cm$^{-1}$ and 1580 cm$^{-1}$ respectively. Compound 4 was readily soluble in ether but only moderately so in toluene. Crystals were not air and moisture sensitive but were prone to de-solvation of the coordinated ether.
**Figure 11. Synthesis of \([\text{Li(µ-HL}_1](\text{Et}_2\text{O})]_2\) (4)**

The synthesis of compound 5, \([\text{Zn(µ-HL}_2](\text{Et})]_2\), is shown in Figure 12. Compound 5 was synthesized by addition of diethylzinc to a solution \(\text{H}_2\text{L}_2\) in toluene. Evolution of ethane was observed immediately. THF was added until the solution became clear and X-ray quality crystals were formed by evaporation in an argon atmosphere. \(^1\text{H} \text{NMR and } ^{13}\text{C NMR were consistent with previously reported values. FT-IR spectroscopy on 5 confirm an absorption band corresponding to } \nu(\text{N-H}) \text{ stretching modes around } 3300 \text{ cm}^{-1}. \) Compound 5 was soluble in THF but only moderately soluble in hexanes or toluene.

**Figure 12. Synthesis of \([\text{Zn(µ-HL}_2](\text{Et})]_2\) (5)**
Proposed Mechanism for Synthesis of $[\text{Li(µ-L}_2\text{)(Et}_2\text{O})]_2$ (4)

Previous work had shown the utility of using cyanamides and nitriles for the generation of a family of guanidine and aminidinate ligands.\textsuperscript{9} The ease and availability of such reactions showed promise as an alternative to the use of carbodiimides.\textsuperscript{48} The possibility of elimination pathways had been previously reported but had not been observed when synthesize similar TAGs.\textsuperscript{9,49} It is proposed the presence of strongly donating substituents on the phenyl ring help to stabilize the elimination product. Furthermore, under the current reaction conditions, lithium dimethylamide generated from the elimination is expected to react with dimethylcyanamide to generate a stable byproduct, lithium 1,1,3,3-tetramethylguandinate (LiTMG) driving the equilibrium further toward the elimination products. (Figure 13)
Figure 13. Proposed Mechanism for Synthesis of Compound 4
Structural Descriptions

Compounds 4 and 5 were characterized by X-ray crystallography. Thermal ellipsoid plots and selected interatomic distances and angles of 4 and 5 are presented in Figures 14 and 15. Structural descriptions for each complex are provided in the following paragraphs.

Compound 4

The thermal ellipsoid for 4 is illustrated in Figure 10. This compound crystallizes in the triclinic space group $\overline{P}1$ with one molecule per unit cell. The molecular structures consist of a dinuclear unit with each Li possessing a distorted tetrahedral geometry. Each Li has a diethyl ether coordinated to it along with the imine group of ligand. One of the phenoxide groups of the ligand bridges the two metal centers and the other phenol is protonated and directed inward in close proximity (1.04Å) to the nearby imine. This orientation is likely due to steric interactions between the phenol proton and the two nearby ortho - tert - butyl groups. The average Li-O bond length is 1.908Å. The average Li-N bond length is 1.937Å. The ether molecules are orientated 113° from the Li-O plane. The bridging phenols are orientated 115° from the Li-O plane. The angle between the aromatic rings is 121°.

Compound 5

The thermal ellipsoid plot for 5 is illustrated in Figure 11. This compound crystallizes in the monoclinic space group C 2/c with four molecules per unit cell. The molecular
structures consist of a dinuclear unit which forms a distorted tetrahedral structure around the zinc centers. Each zinc is coordinated to a terminal ethyl group and a protonated phenylamine with the phenoxide groups bridging the two centers. The average Zn-C bond length is 1.946 Å. The average Zn-O bond length is 2.047 Å. The average Zn-N bond is 2.167 Å. The Zn-O atoms compose a nearly square plane with adjacent angles equal to 84° and 95°. The phenylamines lie approximately 90° and 78° above and below the Zn-O plane. The ethyl groups both lie 127° from the Zn-O plane. The phenols lay 122° and 108° from the Zn-O plane.

**Conclusion**

Two complexes utilizing base tethered aryloxide ligands were synthesized, one involving lithium (4) and the other zinc (5). The synthesis of compound 4 involved an elimination step not previously noted. These compounds may be seen as the first tentative steps toward the development of a library of other base-tethered aryloxide ligands. Both compounds were characterized by $^1$HNMR, $^{13}$CNMR, FTIR, and X-ray crystallography.
Table 2. Data Collections parameters for 4, and 5

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ᵃR₁ = \Sigma | |F₀|-|Fᵣ| | / \Σ |F₀| x 100

ᵇwR² = \sqrt{\Sigma w(F₀²-Fᵣ²)^2 / \Sigma (w|F₀|^2)^2}^{1/2} x 100
**Figure 14.** Thermal ellipsoid plot of 4. Ellipsoids are drawn at the 50% level. H atoms except those on the guanidine and phenol have been omitted for clarity. The tert-butyl groups have been omitted for clarity on C(2), C(8), C(18), C(24), C(2A), C(8A), C(18A), and C(24A). Selected inter-atomic distances (Å) and angles (°): Li(1)-O(1A)1.858(7), Li(1)-O(1) 1.921(7), Li(1)-N(1) 1.943(7), Li(1)-O(3) 1.999(8), Li(1)-Li(1A) 2.486(14), O(1)-C(1) 1.300(4), O(1)-Li(1A) 1.858(7), O(2)-C(29) 1.355(4), O(3)-C(30) 1.406(6), O(1A)-Li(1)-O(1) 97.7(3), O(1A)-Li(1)-N(1) 114.9(4), O(1)-Li(1)-N(1) 89.9(3), O(1A)-Li(1)-O(3) 113.2(4), O(1)-Li(1)-O(3) 121.7(4), N(1)-Li(1)-O(3) 116.5(4), O(1A)-Li(1)-Li(1A) 50.0(2), O(1)-Li(1)-Li(1A) 47.8(2), N(1)-Li(1)-Li(1A) 108.2(4), O(3)-Li(1)-Li(1A) 134.4(5), C(1)-O(1)-Li(1A) 157.9(3), C(1)-O(1)-Li(1) 115.6(3), Li(1A)-O(1)-Li(1) 82.3(3).
Figure 15. Thermal ellipsoid plot of 5. Ellipsoids are drawn at the 50% level. H atoms except those on the aniline have been omitted for clarity. Selected inter-atomic distances (Å) and angles (°): Zn(1)-C(1) 1.946(2), Zn(1)-O(1) 2.0383(13), Zn(1)-O(1A) 2.0516(12), Zn(1)-N(1A) 2.1678(17), Zn(1)-Zn(1A) 3.0195(4), O(1)-C(3) 1.3585(19), O(1)-Zn(1A) 2.0517(12), N(1)-C(17) 1.439(2), N(1)-C(8) 1.466(2), N(1)-Zn(1A) 2.1677(17), C(1)-Zn(1)-O(1) 127.00(9), C(1)-Zn(1)-O(1A) 127.26(9), O(1)-Zn(1)-O(1A) 84.83(5), C(1)-Zn(1)-N(1A) 132.18(9), O(1)-Zn(1)-N(1A) 90.34(6), O(1A)-Zn(1)-N(1A) 78.50(5), C(1)-Zn(1)-Zn(1A) 144.85(8), O(1)-Zn(1)-Zn(1A) 42.59(3), O(1A)-Zn(1)-Zn(1A) 42.25(4), N(1A)-Zn(1)-Zn(1A) 82.45(5), C(3)-O(1)-Zn(1) 121.62(11), C(3)-O(1)-Zn(1A) 108.58(9), Zn(1)-O(1)-Zn(1A) 95.17(5), C(17)-N(1)-C(8) 118.08(15), C(17)-N(1)-Zn(1A) 114.58(12), C(8)-N(1)-Zn(1A) 103.53(11).
CHAPTER IV

CATALYTIC RING-OPENING POLYMERIZATION OF LACTIDE

Introduction

The interest in biodegradable plastics has increased considerably over the past decade.\textsuperscript{50} One such plastic that has been researched extensively is polylactide (PLA). Industrially, the formation of PLA is performed via the Ring Opening Polymerization (ROP) of lactide (LA) catalyzed by a Lewis acid. Lactide is derived by the cyclic dehydration of lactic acid. (Figure 16)

**Figure 16.** Dehydration of L-Lactic Acid.

![Dehydration of L-Lactic Acid](image)

L-Lactic acid is produced in biological systems via the Cori Cycle\textsuperscript{51} and may be produced industrially from various plantstock. Cyclization of this lactic acid produces a racemic mixture of D and L-lactide. Polymerization of this inexpensive racemic stock leads to polymers of varying stereochemical arrangements (Figure 17). The stereochemistry of chiral polymers is defined by the relative distribution of stereocenters within a polymer,
known as tactity. Broadly, there are three types of tactity: (1) *Isotactic* polymers show a preference for blocks of identical stereochemistry, (2) *Syndiotactic* polymers show a preference for blocks of alternating stereochemistry, and (3) *Atactic* polymers show no preference. The physical properties of the resulting polymer are highly dependent on its tactility.\(^{52}\)

**Figure 17.** Stereochemistry of PLA

The degree of tacticity is often quantified by the probability of two neighboring chiral centers having identical stereochemistry (known as a *meso* diad) or opposite stereochemistry (*racemic* diad). A perfectly atactic polymer would have a \(P_m = 0.5\). A \(P_m\) larger than 0.5 indicates isotactic preference and less than 0.5 indicates a syndiotactic preference.
Research into catalysis with low toxicity, high reactivity, and high stereochemical control of the resulting polymer is ongoing. The industry standard catalyst for atactic polymerization is derivatives of tin(II) oxalate.\textsuperscript{53} Such catalysts show the ability to very effectively form high weight polymers with a small polydispersion index. They do not, however, show any stereochemical preference in polymerization.

During polymerization a small amount of the catalyst gets incorporated into the polymer. Oxidized tin is toxic and therefore the use of such catalysts to generate plastics for biomedical applications is limited. Alternative metals such as Ti\textsuperscript{54}, In\textsuperscript{55}, Y\textsuperscript{56}, Al\textsuperscript{57}, and Zn\textsuperscript{58} have been investigated and shown to catalyze the ROP of LA efficiently and in some cases with stereochemical control of the polymerization.\textsuperscript{57, 59} Zinc compounds are of special note for their low toxicity and lack of coloration making them appealing for a variety of industrial and biomedical applications. Herein, the ability of the previously synthesized zinc thiolate complexes described in Chapter II (1 – 3) and the zinc aryloxide phenylamine compound (5) described in Chapter (IV) to catalyze the ROP of lactide will be described and compared to previously synthesized HTAG aryloxide compounds.

**Experimental**

An appropriate amount of compound was dissolved in toluene and combined with various equivalents of isopropanol and lactide. The full list of equivalents used in the trials is summarized in Table 3. For trials 7 and 8 the “immortal” ROP method\textsuperscript{60} was explored with five and two equivalents of isopropanol used, respectively. The solution was allowed to stir at ambient temperature for approximately 20 hours. A few drops of glacial
acetic acid or trimethylacetic acid were added to the solution and it was then quenched with excess methanol. The solvents were then removed via vacuum to yield the PLA as either a white powder or a clear gel.

The percent completion of each reaction was determined by $^1$H NMR by finding the ratio of PLA over the total LA. The average polymer molecular weight ($M_n$) was approximated by dividing the methyl region by six then multiplying by the mass of the repeating unit. Peaks for methyl PLA appeared as a doublet ($J = 6.95$ Hz) around 1.57 - 1.60 ppm and peaks for methyl lactide appeared as a doublet ($J = 6.59$ Hz) around 1.66 - 1.70 ppm.
Table 3. Amounts used in PLA trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>Catalyst</th>
<th>Amount of Catalyst</th>
<th>Lactide</th>
<th>% Recovered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>ZnCl$_2$</td>
<td>3.7 mg (27 μmol)</td>
<td>390 mg (2.7 mmol)$^b$</td>
<td>-</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>8.0 mg (10 μmol)</td>
<td>150 mg (1.0 mmol)$^b$</td>
<td>30</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>5.0 mg (6.3 μmol)</td>
<td>50 mg (0.3 mmol)</td>
<td>94</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>5.0 mg (6.3 μmol)</td>
<td>180 mg (1.3 mmol)</td>
<td>69</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>20 mg (27 μmol)</td>
<td>390 mg (2.7 mmol)$^b$</td>
<td>76</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
<td>20 mg (27 μmol)</td>
<td>780 mg (5.4 mmol)</td>
<td>53</td>
</tr>
<tr>
<td>6</td>
<td>2</td>
<td>10 mg (14 μmol)</td>
<td>780 mg (5.4 mmol)</td>
<td>34</td>
</tr>
<tr>
<td>7</td>
<td>2</td>
<td>10 mg (14 μmol)</td>
<td>980 mg (6.8 mmol)</td>
<td>38</td>
</tr>
<tr>
<td>8</td>
<td>2$^a$</td>
<td>20 mg (27 μmol)</td>
<td>390 mg (2.7 mmol)$^b$</td>
<td>78</td>
</tr>
<tr>
<td>9</td>
<td>3</td>
<td>10 mg (12 μmol)</td>
<td>180mg (1.2 mmol)</td>
<td>-</td>
</tr>
<tr>
<td>10</td>
<td>3</td>
<td>10 mg (12 μmol)</td>
<td>720 mg (5.0 mmol)$^b$</td>
<td>73</td>
</tr>
<tr>
<td>11</td>
<td>5</td>
<td>20 mg (26 μmol)</td>
<td>74 mg (0.5 mmol)</td>
<td>-</td>
</tr>
</tbody>
</table>

$^a$ THF used as solvent. $^b$ L-lactide used.

Determination of Tacticity

For catalytic trials involving rac-lactide, the tacticity of the resulting polymer was determined by measuring of the methane region of the homonuclear decoupled $^1$HNMR spectrum. The intensities of peaks corresponding stereochemical triads were identified (see Figure 18 for an example).$^{61}$
The distribution of relative intensities was fit to a simple probability model for 1\textsuperscript{st} and 2\textsuperscript{nd} order stereochemical control according to 1\textsuperscript{st} and 2\textsuperscript{nd} order Bernoulli models (see Table 4).\textsuperscript{62} Data generated from the first and second order model was fit to experimental data. The parameter $P_m$ was optimized for first order and the parameters $P_{mm}$ and $P_{rm}$ were optimized for second order. $P_m$ for second order was calculated by averaging $P_{mm}$ and $P_{rm}$. 

**Figure 18.** Methine region homonuclear decoupled spectrum of trial 5
<table>
<thead>
<tr>
<th>$1^{st}$ Order</th>
<th>$2^{nd}$ Order</th>
</tr>
</thead>
<tbody>
<tr>
<td>$mmm = (P_m)^3$</td>
<td>$mmm = \frac{1}{2}(P_{mm})^3 + (P_{rm})(P_{mn})^2$</td>
</tr>
<tr>
<td>$rrr = (1 - P_m)^3$</td>
<td>$rrr = \frac{1}{2}((1 - P_{rm})(1 - P_{mm})^2 + (1 - P_{rm})^3)$</td>
</tr>
<tr>
<td>$rmr = mrm = mnr = (1 - P_m)(P_m)^2$</td>
<td>$rmr = \frac{1}{2}((1 - P_{mm})^2(P_{rm}) + (P_{rm})(1 - P_{rm})(1 - P_{mm}))$</td>
</tr>
<tr>
<td>$rmr = rrr = mrr = (1 - P_m)^2(P_m)$</td>
<td>$rmr = \frac{1}{2}((P_{mm})(1 - P_{mm})(P_{rm}) + (P_{mm})(1 - P_{mm})(P_{rm}))$</td>
</tr>
<tr>
<td>$mmr = \frac{1}{2}((P_{mm})^2(1 - P_{mm}) + (P_{mm})(1 - P_{mm})(P_{rm}))$</td>
<td>$rrm = \frac{1}{2}((1 - P_{mm})(1 - P_{rm})(P_{rm}) + (P_{rm})(1 - P_{rm})^2)$</td>
</tr>
<tr>
<td>$mrm = \frac{1}{2}((P_{mm})(1 - P_{mm})(P_{rm}) + (P_{rm})^2(1 - P_{mm}))$</td>
<td></td>
</tr>
</tbody>
</table>
Results and Discussion

A complete list of calculated parameters can be found in Table 5. Most of the trials showed effective conversion within 20 hours. Reaction in a more coordinating solvent such as THF (see trial 8) showed a slowed rate but no change in stereochemical control. This is consistent with previous reported work. A small percentage of cyclic by-product were observed in many of the $^1$H NMR spectra as a disordered multiplet slightly upfield from the PLA. These byproducts contribute a very minor amount to the observed products and have not been reported herein. The $P_m$ values for most catalysts were generally around 0.50 indicating little stereochemical preference. There is little change overall in the reactivity or stereochemical control relative to previously synthesized aryloxides (see Figure 19 and Table 5).

The distributions of stereochemical triads were in most cases better fit to a second order Bernoulli distributions than first order. This fitting implies the coordination of lactide is dependent on the stereochemistry of the two previously coordinated lactides. It is typical with such fittings to verify with higher order tetrad or hexad distributions but given the general agreement between first order and second order fitting the reaction is proposed to proceed via a simple end chain mechanism in which the coordination of a lactide is dependent only on the stereochemistry of the lactide directly before it. A general proposed mechanism is provided in Figure 20.
Figure 19. Catalysts tested for ROP of LA
Table 5. Catalytic ROP of LA

<table>
<thead>
<tr>
<th>Trial Number</th>
<th>Catalysis</th>
<th>A</th>
<th>LA&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Percent Completion&lt;sup&gt;b&lt;/sup&gt;</th>
<th>$M_n$&lt;sup&gt;c&lt;/sup&gt;</th>
<th>$P_m$&lt;sup&gt;d&lt;/sup&gt;</th>
<th>$P_{mm}$&lt;sup&gt;e&lt;/sup&gt;</th>
<th>$P_{rm}$&lt;sup&gt;e&lt;/sup&gt;</th>
<th>$P_m$&lt;sup&gt;e&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 control</td>
<td>ZnCl&lt;sub&gt;2&lt;/sub&gt;</td>
<td>-</td>
<td>100&lt;sup&gt;f&lt;/sup&gt;</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>1</td>
<td>100&lt;sup&gt;f&lt;/sup&gt;</td>
<td>83.2</td>
<td>3663</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>1</td>
<td>50</td>
<td>94.2</td>
<td>3951</td>
<td>0.509</td>
<td>0.544</td>
<td>0.445</td>
<td>0.495</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>1</td>
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<td>86.0</td>
<td>10292</td>
<td>0.503</td>
<td>0.542</td>
<td>0.463</td>
<td>0.502</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>1</td>
<td>50&lt;sup&gt;f&lt;/sup&gt;</td>
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<td>-</td>
<td>-</td>
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<td>1</td>
<td>50</td>
<td>100</td>
<td>10869</td>
<td>0.486</td>
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<td>0.449</td>
<td>0.497</td>
</tr>
<tr>
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<td>200</td>
<td>100</td>
<td>37243</td>
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<td>0.545</td>
<td>0.460</td>
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<tr>
<td>7</td>
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<td>5</td>
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<td>100</td>
<td>10437</td>
<td>0.494</td>
<td>0.556</td>
<td>0.440</td>
<td>0.498</td>
</tr>
<tr>
<td>8&lt;sup&gt;g&lt;/sup&gt;</td>
<td>2</td>
<td>2</td>
<td>100</td>
<td>100</td>
<td>2221</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>11</td>
<td>3</td>
<td>-</td>
<td>50</td>
<td>93.1</td>
<td>4383</td>
<td>0.384</td>
<td>0.572</td>
<td>0.339</td>
<td>0.455</td>
</tr>
<tr>
<td>12</td>
<td>3</td>
<td>-</td>
<td>200&lt;sup&gt;f&lt;/sup&gt;</td>
<td>99.5</td>
<td>9716</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>13</td>
<td>5</td>
<td>1</td>
<td>100&lt;sup&gt;f&lt;/sup&gt;</td>
<td>100</td>
<td>925</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>14&lt;sup&gt;h&lt;/sup&gt;</td>
<td>VI</td>
<td>-</td>
<td>100</td>
<td>99</td>
<td>4394</td>
<td>0.39</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>15&lt;sup&gt;h&lt;/sup&gt;</td>
<td>VII</td>
<td>-</td>
<td>100</td>
<td>100</td>
<td>1180</td>
<td>0.40</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>16&lt;sup&gt;h&lt;/sup&gt;</td>
<td>VIII</td>
<td>-</td>
<td>100</td>
<td>99</td>
<td>4391</td>
<td>0.34</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

<sup>a</sup>Ratio of Zn : alchol : lactide is 1: A : LA.<sup>b</sup>Calculated by dividing methyl region of PLA by the sum of the entire methyl region.<sup>c</sup>Calculated by dividing methyl region by $6 \cdot 144.12 + 60.09$.<sup>d</sup>Calculated by first order Bernoulli distribution (see Table 4).<sup>e</sup>Calculated by second order Bernoulli distribution (see Table 4).<sup>f</sup>L-lactide used.<sup>g</sup>THF used as solvent.<sup>h</sup>from previous work
Figure 20. Proposed Mechanism for ROP of LA
Conclusions

The ability of several zinc thiolate complexes (1 – 3) as well as an amine tethered polydentate complex (5) in the ROP of LA was investigated. The average molecular weight and tacticity of the resulting PLA was determined by $^1$H-NMR. There appears to be no significant difference between the reactivity and stereocontrol of such catalysts compared to the previously tested Zn aryloxide compounds (VI, VII, VIII).
CHAPTER V

CONCLUSIONS

This thesis overall entails the synthesis and characterization of several novel zinc coordination complexes in attempt to develop alternative Zn catalysts for the ROP of LA. Chapter II described the synthesis and characterization of several zinc thiolate complexes supported by the 1,1,3,3-tetramethylguanidine (H-TMG) ligand. These compounds were synthesized in a very straightforward reaction with diethylzinc, the corresponding thiol, and H-TMG. Reaction of compound 2 yielded an isopropoxide bridged complex that is a proposed intermediate for the ROP of PLA.

Chapter III described the preliminary synthetic routes toward the synthesis of polydentate base tethered ligands. Reaction of a dilithiated 2-bromo-4,6-di-tert-butylphenol with dimethylcyanamide was shown to undergo elimination to yield compound 4. This elimination product had not been observed in previous methods for the synthesis of 1,1,3,3-tetraalkylguanidines (HTAG).

Finally, Chapter IV described the reactivity of these zinc thiolate compounds and base tethered polydentate complexes in the ROP of LA as well as a method for determining the tacticity of the PLA polymers. Results showed no change in neither reactivity of the zinc thiolate compounds nor stereochemical control of the reaction relative to the zinc aryloxide compounds. The polymerization using the Zn complex with the base tethered ligand requires additional work to completely evaluate its utility.
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