SYNTHESIS AND CHARACTERIZATION OF MONOMERIC MAGNESIUM AND ZINC COMPLEXES SUPPORTED BY 1,5,9–TRIMESITYLDI PYRROMETHENE FOR USE IN POLYMERIZATION STUDIES

THESIS

Presented in Partial Fulfillment of the Requirements for the Degree Master of Science in the Graduate School of The Ohio State University

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2011

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Abstract

Magnesium and zinc complexes supported by a bulky bidentate ancillary ligand have been synthesized and characterized. The compounds (pyac)MgBu(THF),\textit{1}; (pyac)ZnBu,\textit{2}; (pyac)Mg(CH$_2$CH$_2$Ph)(THF), \textit{3}; (pyac)ZnEt, \textit{4}; and (pyac)MgOBu(THF),\textit{5}; where pyac = 1,5,9 – trimesityl dipyrromethene ligand, are all moisture and air sensitive. The n–butyl group in compounds \textit{1}, \textit{2} and \textit{3} showed unexpected $\alpha$ – $^1$H NMR pattern in solution that may be simulated as an AA’XX’ pattern. Single crystal X-ray diffraction studies carried out on \textit{1} and \textit{5} revealed a distorted tetrahedral structure about the metal centre. Compounds \textit{1}, \textit{2} and \textit{5} react with $^{13}$CO$_2$ forming carboxylates.

Preliminary polymerization studies showed that all compounds initiate and sustain ring opening polymerization of lactides and $\varepsilon$-caprolactone. However, the zinc alkyls were comparatively very slow when compared to the magnesium alkyls. Compound \textit{1} exhibited good stereocontrol in the polymerization of rac and L – Lactide resulting in heterotactic and isotactic polylactide respectively.

Reaction of compound \textit{1} with benzophenone results in the formation of an alkoxide with the elimination of 1 - butene. In the case of Grignard reagents (depending on the R group), the same reaction gives tertiary alcohol, or a mixture of secondary and tertiary alcohol. The reactivity mechanism of compound \textit{1} proceeds exclusively via $\beta$ – hydrogen transfer. However, presence of a $\beta$ – hydrogen in the R group of the Grignard
reagents results in secondary alcohol as the majority product. If the R group is a methyl
the tertiary alcohol is exclusively obtained.
Dedication

This document is dedicated to my Mum, Beata Mwikali Wambua.
Acknowledgments

The success of this work would not have been possible without the support of my Advisor, colleagues, friends and family.

First and foremost, I want to thank my advisor, Professor Malcolm Chisholm. His timely guidance, advice, superb ideas and constant effort to teach me on every occasion is immeasurable. He is a very understanding boss and has always created time for me whenever I needed him. I would have been toast without him.

I wish to thank my group members for all their support on and off campus. My sincere thanks go to Dr. Ruaraidh McIntosh for walking me through the baby steps of my first year in the lab. I cannot forget Dr. Yang li who always challenged me to see chemistry in a different perspective. I also wish to thank Dr. Judith Gallucci (OSU X-ray laboratory) and Dr. Tanya Young (Chemistry NMR facility)

My appreciation also goes to Kittisak Choojun for being a true friend and colleague. I also wish to thank Dr. Edwin Montari, Teodora Zujovic and Tushar Kabre for all their time and for being amazing reliable friends.

I wish to thank the Chemistry department for granting me the opportunity to pursue my graduate studies and also the department of energy for funding my research. I sincerely thank all the professors who taught me. I also thank Judy Brown and Lacey Stevens for all their kind support.

Last and not the least, I am very grateful to my family. To my dearest mum I say thank you for believing in me and seeing me through all the rough roads. It would have
been difficult to achieve this without my son; he gives me the extra motivation to work hard.
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Table of Contents

Abstract ............................................................................................................................... ii
Dedication .......................................................................................................................... iv
Acknowledgments ........................................................................................................... v
Vita ....................................................................................................................................... vii
List of Tables ...................................................................................................................... x
List of Figures .................................................................................................................... xi
List of Schemes ................................................................................................................ xiii

1. Chapter 1: Introduction ............................................................................................ 1
   1.1. History of Grignard Reagents ............................................................................. 1
   1.2. Preparation of Grignard Reagent ................................................................. 3
   1.3. The Mechanism of Grignard Reagent formation ........................................... 6
   1.4. Composition of Grignard Reagents in Solution .............................................. 8
   1.5. Reaction Mechanisms of Grignard Reagents ................................................. 11
   1.6. Highly Functionalized Organomagnesium Reagents .................................. 17
   1.7. Statement of Purpose ..................................................................................... 21

2. Chapter 2: Results and Discussion ......................................................................... 22
   2.1 Synthesis ........................................................................................................... 22
   2.2 Single Crystal and Molecular Structure .......................................................... 24
2.3 Solution NMR characterization of compound 1, 2 and 3 ........................................ 30

2.4 Reactivity studies ........................................................................................................ 39

2.4.1 Reaction with carbon dioxide .............................................................................. 39

2.4.2 Preliminary Polymerization studies ..................................................................... 41

2.4.3 Reaction of (pyac)MgBu(THF) with benzophenone and diphenyl methanol .............. 42

2.5 Experimental Section ............................................................................................. 45

2.6 Conclusion and future work ..................................................................................... 53
List of Tables

Table 1: Selected Bond distances (Å) and Angles (deg) for (pyac)MgBu(THF) ............ 26
Table 2: Selected Bond distances (Å) and Angles (deg) for (pyac)MgOBu(THF) ....... 29
List of Figures

Figure 1: Association of several Grignard compounds in tetrahydrofuran\textsuperscript{31} ......................... 9

Figure 2: Association of several alkyl- and aryl magnesium bromides and iodides and related magnesium compounds in diethyl ether ................................................................. 9

Figure 3: Association of alkyl magnesium chlorides in diethyl ether ...................................................... 10

Figure 4: (A) (pyacH) ligand (B) Resonance structure of $\beta$-diiminato ligand .......................... 21

Figure 5: ORTEP drawing of (pyac)MgBu(THF) with thermal ellipsoids drawn at the 50\% probability level. The structure shows a distorted tetrahedral geometry around the Mg metal centre. All hydrogen atoms are omitted for clarity .................................................. 25

Figure 6: ORTEP drawing of (pyac)MgOBu(THF) with thermal ellipsoids drawn at the 50\% probability level. All hydrogen atoms are omitted for clarity ........................................ 28

Figure 7: Expanded $\alpha$–proton region of the magnesium and zinc alkyl compounds 1, 2 and 3. The $\alpha$–proton signal resembles an AA’XX’ pattern ............................................... 31

Figure 8: Homonuclear decoupled $^1$H NMR spectra of (pyac)MgBu(THF) showing the butyl region .......................... ......................................................................................... 31

Figure 9: Homonuclear decoupled $^1$H NMR spectra of (pyac)Zn(nBu) showing the butyl region ......................................................................................................................... 32

Figure 10: Simulation of (pyac)Mg\textsuperscript{9}Bu(THF) $\alpha$ - protons using the topspin program. Long range coupling of the $\alpha$ to $\gamma$ protons was evident although with a small J - coupling ................................................. 33
Figure 11: (pyac)MgnBu(THF) $^1$H NMR ................................................................. 34
Figure 12: (pyac)MgnBu(THF) $^{13}$C NMR ................................................................. 35
Figure 13: (pyac)Mg(CH2CH2Ph)THF $^1$H NMR ...................................................... 36
Figure 14: (pyac)Zn(nBu) $^1$H NMR ........................................................................ 37
Figure 15: (pyac)Zn(nBu) $^{13}$C NMR ....................................................................... 38
Figure 16: $^1$H NMR for (pyac)MgnBu(THF) showing the butyl region before and after
$^{13}$CO2 insertion. Notice the $\alpha$ - proton signal after $^{13}$CO2 insertion attains a normal triplet.
........................................................................................................................................... 39
Figure 17: Cosy NMR for (pyac)MgOCO(nBu) ............................................................ 40
Figure 18: $^1$H NMR spectra (CDCl3, 400MHz) of the homonuclear decoupled methine
resonance of poly(rac-lactide) shows heterotactic poly lactide. Polymerization was done
in THF at room temperature using compound $\mathbf{1}$. Ratio of Initiator to monomer was 100:1.
........................................................................................................................................... 41
Figure 19: $^1$H NMR showing products of the reaction between (pyac)MgnBu(THF) and
benzophenone. .................................................................................................................. 43
Figure 20: $^1$H NMR showing products of the reaction between (pyac)Mg$^n$Bu(THF) and
diphenyl methanol............................................................................................................ 44
Figure 21: (pyac)ZnEt $^1$H NMR ............................................................................... 50
Figure 22: (pyac)MgOBut(THF) $^1$H NMR ................................................................. 51
Figure 23: (pyac)MgOBut(THF) $^{13}$C NMR .................................................................. 52
List of Schemes

Scheme 1: Summary of Grignard reaction ................................................................. 2
Scheme 2: Proposed mechanisms of Grignard reagent formation ................................. 7
Scheme 3: Blicke and Powers proposed mechanism ..................................................... 11
Scheme 4: (A) 1,1-diphenyl-3,3-dimethyl butanol, (B) Benzopinacol, (C) Neopentane . 12
Scheme 5: Blomberg and Mosher Proposed mechanism ............................................. 13
Scheme 6: Proposed Mechanism via Single electron transfer intermediate (I) ............... 15
Scheme 7: Ashby et. al “solvent cage” proposed mechanism ........................................ 15
Scheme 8: Bromine-magnesium exchange .................................................................. 17
Scheme 9: Halogen - magnesium exchange between 1-(chloro/bromo/Iodo)- 2,3,4,5,6 -
pentafluorobenzene with ethylmagnesium bromide .................................................. 18
Scheme 10: Mechanism for (pyac)MgnBu(THF) with benzophenone. L represents the
ligand (pyac). ............................................................................................................... 42
Scheme 11: Mechanism for (pyac)MgnBu(THF) with diphenyl methanol. L represents
the ligand (pyac). ........................................................................................................ 43
1. Chapter 1: Introduction

1.1. History of Grignard Reagents

Grignard reagents are arguably the most used organometallic reagents in synthetic chemistry, as well as in the industrial production of building blocks for applications in the pharmaceutical and food industry, as well as in the production of many other useful chemicals. The earliest form of Grignard reaction was reported by Professor P. Barbier in what has come to be known as the Barbier reaction.\(^1\) This reaction involved a mixture of methyl iodide, magnesium metal and a methyl ketone in diethyl ether giving a tertiary alcohol. Victor Grignard, a French Chemist, working as a graduate student under Professor P. Barbier at the University of Lyon in France, discovered the Grignard reagent which he outlined in a paper published in 1900.\(^2\) Extensive study on this work was well detailed in his dissertation\(^3\) the following year. A summary of his observations is presented in Scheme 1 below.\(^3,4\)
Scheme 1: Summary of Grignard reaction

The significance of this mechanism to synthetic chemistry was tremendous due to the general simplicity of this sequence. It made it easier to synthesize a wide variety of new compounds. In 1912, at the young age of 39, Victor Grignard was awarded the Nobel Price in chemistry in recognition for his excellent work.

However, commercialization of the Grignard reagents posed a challenge due to the costly magnesium, organic bromides and iodides. Hazards posed by diethyl ether as a solvent were another obstacle as well. The use of tetrahydrofuran (THF) to substitute diethyl ether and the replacement of organic bromides and iodides with the less reactive but cheaper organic chlorides in the 1950’s, led to improved industrial procedures.\textsuperscript{5-9} Fast forward to 1994, industrial production and sale of Grignard reagents was projected to surpass the 50,000 tons mark.\textsuperscript{4,10}
1.2. Preparation of Grignard Reagent

The common preparative route of Grignard reagents involves the refluxing of magnesium metal with an alkyl or aryl halide (RX) in an ethereal solvent. Manipulations of the reactants and solvents must be carried out under standard Schlenk or glovebox technique in order to keep oxygen and water from interfering with the reaction. Activation of the magnesium generally occurs upon addition of 10 - 20 wt % of the RX. This is evidenced by a large exotherm with the magnesium turnings, changing from their usual silver color to gray-black. However, this color change might at times be a misleading indicator that the reaction initiation has taken place, especially if the agitation is strong enough to cause shearing of the magnesium (Mg). One should only add more than 20% of the RX after initiation is certainly confirmed to avoid the risk of starting a rapid exothermic reaction when all the alkyl/aryl halide has been added. If this happens, one risks release of reactor contents into the atmosphere posing an environmental hazard. To avoid this, especially for a novice chemist, a proper hazard review and caution should be undertaken before this reaction is done.

Presence of water in both the reactants and apparatus should be limited to less than 0.02 wt % to ensure proper initiation. Water percentage above this will result in abrupt initiation of the reaction once all the alkyl/aryl halide has been added, hence leading to a large exotherm that spews the reactor contents into the atmosphere. This hazard can easily be avoided by using dry reactants and solvents while, at the same time, carrying out all manipulation under standard glovebox/schlenk techniques. Usually water leads to formation of the protonated product (Eq. 1) upon reacting with the
Grignard reagents. On the other hand, water is eliminated from the system by simply introducing the same Grignard reagent previously synthesized. On industrial scale this is the most cost effective way of eliminating water in Grignard reagent synthesis.\textsuperscript{10}

\[
RMgX + H_2O \rightarrow R\text{-}H + MgX(OH) \quad (\text{Eq. 1})
\]

The choice of solvent in Grignard reactions is crucial and mostly dictated by the desired chemistry, cost, safety and reactivity.\textsuperscript{4} Herbert Brown and Uday Racheria of Purdue University carried out synthesis of tetraorganylborate complexes in diethyl ether and THF and observed that the yield was significantly affected depending on the solvent used.\textsuperscript{13} Upon reacting ethylmagnesium bromide and triethylboron in ethyl ether (EE) little or no reaction was noticed. However, the same reaction proceeds to completion in THF to give tetraethyl boron magnesium bromide, Et\textsubscript{4}BMgBr (Eq. 2 & 3).\textsuperscript{13}

\[
\begin{array}{cccc}
\text{Et}_3B & + & \text{EtMgBr} & \rightarrow \text{Et}_4\text{BMgBr} \quad \text{EE, 6h} \\
96\% & 96\% & 4\% & \text{THF} \\
25^\circ C & & & \\
\end{array}
\quad (\text{Eq 2})
\]

\[
\begin{array}{cccc}
\text{Et}_3B & + & \text{EtMgBr} & \rightarrow \text{Et}_4\text{BMgBr} \quad \text{THF, 6h} \\
4\% & 4\% & 96\% & \text{THF} \\
25^\circ C & & & \\
\end{array}
\quad (\text{Eq 3})
\]

Novis Smith Jr\textsuperscript{14} et al. showed that use of hydrocarbon solvents (e.g. hexane, toluene, benzene) leads to formation of diorganomagnesium derivatives.\textsuperscript{15} This is due to the fact that magnesium dihalides have poor solubility in these solvents, which apparently facilitates a cost effective method of preparing diorganomagnesium derivatives.\textsuperscript{4,14-17} The
use of 1,4-dioxane in some Grignard reagents precipitates out the magnesium dihalide (MgX₂) due to their low solubility, providing an effective procedure of synthesizing diorganomagnesium compounds.¹⁷-¹⁹ (Eq.4)

\[
[\text{Me}_3\text{Si}CH_2]\text{MgCl} \xrightarrow{\text{Et}_2\text{O}} 1/2[(\text{Me}_3\text{Si})\text{CH}_2\text{Mg} + 1/2\text{MgCl}_2 \cdot 2(\text{1,4-dioxane}) \quad \text{(Eq.4)}
\]

Nagano et al.²⁰ showed how solvent choice can influence diastereoselectivity (see Eq. 5).

Ethereal solvents have traditionally been the solvent of choice in synthesis of Grignard reagents due to their high solubility.¹⁰ On the other hand, they possess very low flash points (e.g. Et₂O, -45°C) in comparison to THF (-15°C), which is a safety hazard. They are also relatively expensive compared to THF and hydrocarbon solvents.⁴,¹⁰,²¹ Therefore it is no surprise that THF is an all-around preferred solvent for Grignard reagents synthesis.
1.3. The Mechanism of Grignard Reagent formation

Since the discovery of the Grignard reagent a century ago, no topic has drawn more debate than its formation mechanism. In 1901, Grignard observed that iodine acted as an activator to Grignard reagent formation, thus spurring a quest by many researchers in elucidating its mechanism.\textsuperscript{22} In 1954, Kharasch and Reinmuth first suggested that formation of Grignard reagents proceed via radical reactions and this involves “surface adherent radicals, at least in part”.\textsuperscript{4,12} Walborsky and co-workers carried out reactions of magnesium with optically active organic halides and proposed a competitive two path mechanism of Grignard reagent formation, presumably taking place on the magnesium surface (Scheme 2).\textsuperscript{23-26} They suggested that the rate determining step was the single electron transfer from magnesium surface to the alkyl halide (path 1) to generate an intermediate/transition state where \( RX^- \) closely associates with \( Mg^+ \) (see Scheme 2). Collapse of the intermediate can lead to formation of the Grignard reagent with full retention of stereochemistry (path 4). Dissociation of intermediate (path 3) leads to the formation of alkyl radicals (and halide anion) that eventually undergoes a 180° rotation relative to the magnesium surface loosing its stereochemistry and subsequently associates with the magnesious halide radical (path 5) to form racemic Grignard reagent.\textsuperscript{4,26,27} The organic radicals (bound to the magnesium surface) can alternatively disproportionate, dimerize, isomerizes or abstract proton or halide from products or solvent (path 6).
Scheme 2: Proposed mechanisms of Grignard reagent formation

(J. Am. Chem. Soc. 1993, 115, 6406-6408)

To date there is a wide consensus in the scientific world that radicals take part in the mechanism of formation of Grignard reagents and this finds significant experimental support. \(^{4,12,26-28}\)
1.4. Composition of Grignard Reagents in Solution

Research papers and textbooks usually represent Grignard reagent simply as “RMgX”, (R = alkyl/aryl and X = halide), although their composition in ethereal solutions is somewhat complex. Schlenk & Schlenk Jr. discovered the existence of several magnesium species in diethyl ether at equilibrium and this is now commonly known as the Schlenk equilibrium (Eq. 6).29

\[
2\text{RMgX} \rightleftharpoons \text{R}_2\text{Mg} + \text{MgX}_2 \quad \text{(Eq. 6)}
\]

Since MgX\(_2\) readily precipitates out of 1,4-dioxane in diethyl ether (refer to Eq. 4), the authors reasoned that they could use this observation to determine the molecular composition of Grignard reagent present at equilibrium.\(^{29}\) Ashby et al. observed the first evidence, using 100 MHz nuclear magnetic resonance at -105°C, of Me\(_2\)Mg and MeMgBr existence in dynamic exchange.\(^{30}\) Ashby and Walker further monitored the association factors of different Grignard reagents versus concentration in THF and diethyl ether using ebullioscopic measurements of molecular weights.\(^{31}\) They observed that all reagents studied exist as monomers in THF (Figure 1). However, in diethyl ether alkyl/aryl magnesium bromide or iodide increased in association (mostly into oligomers) as concentration increased, and remained as monomers at low concentration (<0.1M) (see Figure 2).\(^{31}\) On the other hand, alkyl magnesium chlorides appeared to completely form stable dimers in diethyl ether (see Figure 3).
Figure 1: Association of several Grignard compounds in tetrahydrofuran$^{31}$

Figure 2: Association of several alkyl- and aryl magnesium bromides and iodides and related magnesium compounds in diethyl ether. (J. Am. Chem. Soc. 1969, 91, 3848)
Figure 3: Association of alkyl magnesium chlorides in diethyl ether (J. Am. Chem. Soc. 1969, 91, 3848).
1.5. Reaction Mechanisms of Grignard Reagents

Although Grignard reagents were discovered in the beginning of 1900, it was not until the 1960’s when earnest research into their reaction mechanism got accelerated. This was attributed to the fact that little was previously known about the composition of the organometallic reagents in solution and the identity of products formed in the reaction.\(^4\) To date, there is no exclusive consensus as to whether these reactions proceed via single electron transfer or by a concerted mechanism (polar). Furthermore, evidence does exist in support of both schools of thought. To elucidate these reaction mechanisms extensive research has been carried out using carbonyl compounds, especially benzophenone. The use of ketones in mechanistic studies is driven by their various attributes e.g. lack of \(\alpha\)-hydrogens ensures enolization does not take place, products are easily detected because of their higher molecular weights and reactions rates are slower.\(^4\)

In 1929 Blicke and Powers hypothesized that radicals accounted for the formation of reduced ketone products when they reacted alkylmagnesium halides with various ketones.\(^32\) Good yields of methyl and ethyldiphenyl carbinol were realized from reactions involving methyl/ethyl magnesium iodide/bromide and benzophenone, respectively.\(^32\) They proposed a mechanism (Scheme 3) to support their hypothesis but lacked the experimental evidence to support a radical mechanism.

![Scheme 3: Blicke and Powers proposed mechanism](J. Am. Chem. Soc. 1929, 51, 3378)
In 1964 availability of electron-spin resonance (ESR) and visible spectroscopy technique were used by Maruyama to provide evidence of stable radical species being present when Grignard reagents were reacted with ketones in tetrahydrofuran (THF).\textsuperscript{33,34} From these observations the author suggested that contribution of radical species was significant.

In 1968 Blomberg and Mosher, using the same ESR techniques, reported the formation of benzopinacol and neopentane each at 20% yield as products (besides the expected main ("normal") product 1,1-diphenyl-3,3-dimethyl butanol) when they reacted benzophenone with neopentyl magnesium chloride in THF (Scheme 4).\textsuperscript{35}

Scheme 4: (A) 1,1-diphenyl-3,3-dimethyl butanol, (B) Benzopinacol, (C) Neopentane

The authors proposed a mechanism (Scheme 5) in which they postulated that the “steric bulk of the neopentyl group (\(R\)) so retards the normal addition reaction as represented by \(k_1\).\textsuperscript{35} Benzophenone ketyl and neopentyl radicals are formed via a single electron transfer in a “solvent cage”.\textsuperscript{35} Collapse of this cage releases the radicals in which case neopentane is realized through proton abstraction from the solvent by neopentyl radical while dimerization of the ketyl gives “magnesium halide salt of benzopinacol” (\(k_4\)).
Subsequently the addition reaction can lead to formation of the normal/expected product ($k_3$).\textsuperscript{35}

![Chemical reaction diagram](image)


Ashby and Bowers questioned and proved that free radicals, initially proposed by Blomberg-Mosher\textsuperscript{35} and supported by Holm and Crossland\textsuperscript{36}, are not involved in the single electron transfer mechanism.\textsuperscript{37} Their approach was to “trap” or “observe”, by use of radical probes, any “intermediate radical or radical anion” and this would address whether the intermediate radicals are indeed free.\textsuperscript{37} Reaction of the vinylic Grignard reagent, cis-propenyl magnesium bromide, with a ketone (benzophenone) gave the normal 1,2-addition tertiary alcohol as the exclusive product (Eq. 7). Since no cyclization or isomerization was observed they argued that the mechanism was either polar, or if it proceeded via single electron transfer, no “free” radical behavior was evident.\textsuperscript{37}

$$\text{MgBr} + \text{Ph} = \text{O} \quad \xrightarrow{\text{H}^+} \quad \text{Ph} \text{Ph} \text{OH} \quad \text{(Eq. 7)}$$
The group further demonstrated the reaction between a tertiary Grignard reagent, 1,1-dimethyl-5-hexenylmagnesium chloride, with benzophenone and obtained both 1,2-addition (38%) and 1,6-addition (62%) products (Eq. 8).

\[
\begin{align*}
\text{MgBr} & \quad \text{O} \\
\text{OH} & \quad \text{O} \\
38\% & \quad 46\% & \quad 16\%
\end{align*}
\]

(Eq. 8)

No cyclization was observed in the latter 1,6-addition product drawing the conclusion that the 1,2-addition product results from collapse of the “radical anion-radical cation pair” with the “R” of the Grignard still tightly bound to the magnesium as a radical cation (RMgX⁺).\(^{37}\) Ashby et al. using p-nitrobenzene (a radical anion scavenger)\(^{38}\) observed a complete suppression of pinacol formation upon reacting 2-methylbenzophenone with MeMgBr and t-BuMgCl.\(^{39}\) On the other hand, the ratio or rate of formation of the 1,2- and 1,6-addition products was not affected by the same scavenger, thus a “free ketyl” is not involved in the process as earlier proposed by Blomberg et.al.\(^{35}\) Thus, the possibility that all ketonic reactions with Grignard reagents proceed via a single electron transfer intermediate (SET) (I) was proposed (Scheme 6).
Scheme 6: Proposed Mechanism via Single electron transfer intermediate (I). (Taken from reference $^{4,39}$)

The 1,2-addition product may arise directly from the intermediate I, (Scheme 7, path a).

Scheme 7: Ashby et. al “solvent cage” proposed mechanism (J. Am. Chem. Soc. 1977, 99, 850)

Likewise, the SET intermediate can dissociate resulting in a radical anion and a free radical within the solvent cage (path b). Collapse of the cage may directly form the 1,6-addition product, whereas when radicals escape from the cage they may react to give benzopinacol and R’ that can abstract a proton from the solvent to form R-H.$^{37}$ Another
noteworthy mechanism, in the same line as Ashby’s, was proposed by Maruyama and Katagiri.\textsuperscript{40,41,42}

In the last four decades tremendous progress has been made in understanding the reaction mechanisms of Grignard reagents with ketones as the main substrates. To date there is an overwhelming consensus across the scientific world that these reactions proceed via a single electron transfer (radical) or by polar/concerted mechanism. The reaction mechanism pathway seems to be dictated by both substrate reduction potential and organomagnesium species oxidation potentials.\textsuperscript{4} May be the specific reaction pathway depends on the specific reaction, the solvent and other conditions.
1.6. **Highly Functionalized Organomagnesium Reagents**

For the past decade Paul Knochel et al., from the University of Munich, have brought a new dimension into the preparation of stable and highly reactive functionalized Grignard reagents (turbo Grignard reagents).\(^{43,44}\) The traditional direct reaction of magnesium metal with organic halides has for a long time been the first choice for Grignard reagent synthesis. On the other hand, the halogen-magnesium exchange reaction is another route by which functionalized Grignard reagents can be realized. The earliest example of this kind was reported by Prévost in 1931.\(^{45}\) Cinnamylmagnesium bromide was synthesized in a moderate yield by reacting cinnamyl bromide with ethyl magnesium bromide (see equation 9).

\[
\text{Ph}-\text{C}=\text{C}-\text{Ph} + \text{EtMgBr} \underset{20^\circ \text{C}, 12 \text{h}}{\xrightarrow{\text{Et}_2\text{O}}} \text{Ph}-\text{C}=\text{C}-\text{MgBr} + \text{EtBr} + \text{other products} \quad (\text{Eq. 9})
\]

Villiéras Jean et al. initiated the magnesium carbenoids study by use of the halogen-magnesium exchange (see Scheme 8).\(^{46,47}\) It was later shown that the rate of halogen-magnesium exchange is improved when electronegative substituents are present.\(^{48,49}\)

\[
\text{HBr}_3 + \text{i-PrMgCl} \underset{-78^\circ \text{C}}{\xrightarrow{\text{i-PrMgCl}}} \text{HBr}_2\text{CMgCl} \underset{\text{E}^+}{\xrightarrow{}} \text{HBr}_2\text{CSiMe}_3 \\
\text{90\%} \\
\text{E}^+ = \text{Me}_3\text{SiCl}
\]

Scheme 8: Bromine-magnesium exchange\(^{46,47}\)
Tamborski and Moore readily synthesized polyfluoroaromatic compounds in high yields by employing the halogen-magnesium exchange reaction. The halogen atom influences the reactivity order, namely I > Br > Cl >> F, which is dictated by the carbon-halogen bond strength as well as the polarizability and electronegativity of the halogen (see Scheme 9). Notice reaction takes longer time (1 hour) at 25 °C to reach completion when X = Cl.

![Scheme 9: Halogen - magnesium exchange between 1-(chloro/bromo/Iodo)- 2,3,4,5,6 - pentafluorobenzene with ethylmagnesium bromide](image)

Temperature plays a major role when deciding what procedure to use in the synthesis of functionalized Grignard reagents. The fact that carbon-magnesium bond reactivity is temperature dependent and electrophiles (e.g. ketones, aldehydes) readily react at temperatures lower than 0 °C, has made halogen-magnesium exchange reaction a more favorable choice when preparing Grignard reagents bearing reactive functional groups.

P. Knochel et al. showed the synthesis of various functionalized aryl magnesium compounds from functionalized iodoarenes using i-PrMgCl/Br in THF. These reactions were done under mild conditions (below 0 °C) hence facilitating tolerance of sensitive carbonyl group derivatives, e.g. nitriles, esters, amides, (see Eq. 9).
Extra fine tuning to the reactivity of these functionalized Grignard reagents was achieved by transmetallation to zinc, copper\textsuperscript{61} or titanium. The resulting transmetallation species are usually “less reactive but more chemoselective” (see Eq. 10).\textsuperscript{44}

While bromopyridines undergo halogen-magnesium exchange at room temperature with i-PrMgBr, much improved yields are obtained in the presence of lithium chloride salt (see Eq. 11).\textsuperscript{62,63} The magnesium product readily reacts with an electrophile (benzaldehyde) yielding an alcohol.

Knochel et al. showed that the presence of a strong electron withdrawing group, tosyloxy (OTs), at position 2 facilitates regioselectivity in the bromine-magnesium exchange reaction at position 3 of 3,5-dibromopyridine.\textsuperscript{64}
The halogen-magnesium exchange has provided a wide array of polyfunctionalized magnesium species.\textsuperscript{65-67} They have been applied in stereoselective cyclization reactions,\textsuperscript{68,69} complex natural products syntheses (e.g. antibiotic vancomycin)\textsuperscript{70,71} and cross-coupling reactions\textsuperscript{72}, just to mention a few. This has vastly increased the number of available functionalized organomagnesium species in organic synthesis. The fact that synthesis of these reagents takes place under mild conditions (below 0 °C), plays a key role in preventing hazards associated with high temperature reactions. Mild conditions also ensure very high tolerance to the functional groups as far as the halogen-magnesium exchange reaction is concerned.
1.7. **Statement of Purpose**

We set out to synthesize and characterize single site magnesium and zinc alkyl reagents supported by a bulky bidentate ancilliary ligand. This would render the reagents less susceptible to the Schlenk equilibrium as is the case with Grignard reagents, hence enabling long storage of these compounds in an inert atmosphere or solvent. Use of the ligand, 1,5,9-trimesityldipyrrromethene (pyacH) would induce stereocontrol and selectivity in ring opening polymerization reactions of biodegradable monomers such as lactides, butyrolactones and ε-caprolactones. Preference for pyacH ligand (see Scheme 11) was driven by the fact that its negative charge is evenly delocalized over its aromatic framework, hence effectively subjecting it to just being a spectator ligand. In comparison, β-diiminato ligand has some resemblance to pyacH ligand framework. However, its negative charge can be localized over one nitrogen or the unprotected β-CH (see Scheme 12) accounting for its known participation in certain reactions.

Figure 4: (A) (pyacH) ligand    (B) Resonance structure of β-diiminato ligand
2. Chapter 2: Results and Discussion

2.1 Synthesis

**(pyac)Mg\textsuperscript{\textit{n}}Bu(THF), 1:** Reaction of 1.2 equivalent of (\textsuperscript{\textit{n}}Bu)\textsubscript{2}Mg with 1 equivalent pyacH ligand in THF at room temperature for several hours gave compound 1 as an orange solid upon removal of solvent. Proton transfer occurs with elimination of butane as a gas. X-ray-suitable single crystals were successfully grown from a concentrated hexane solution of compound 1. Growing crystals in THF and toluene only gave fine crystals unsuitable for X-ray crystal analysis. The compound is very air and moisture sensitive.

**(pyac)Mg(CH\textsubscript{2}CH\textsubscript{2}Ph)THF, 2:** The best yield was obtained upon reacting 1 equivalent of (pyac)Li.THF\textsuperscript{74} with 1.20 equivalent of (PhCH\textsubscript{2}CH\textsubscript{2})MgCl in toluene. Both reactants were frozen cold using liquid nitrogen and thawed prior to dropwise addition of the Grignard reagent solution into that of (pyac)Li.THF. Interestingly, use of THF as the reaction solvent afforded a product mixture. X-ray suitable crystals were grown from a concentrated toluene solution placed in the freezer overnight. This compound is also very air and moisture sensitive.

**(pyac)Zn(\textit{n}Bu), 3:** Product was obtained in good yield by reaction of a thawing THF solution of (pyac)ZnCl (1 equivalent) and \textit{n}BuLi (1.08 equivalent) at room temperature with subsequent removal of solvent under dynamic vacuum affording a dark orange solid. Extraction of product in hexane or benzene effectively precipitates out all
the LiCl. Centrifugation makes it easier to remove the fine LiCl powder. The product is air and moisture sensitive.

**(pyac)ZnEt, 4:** The reaction of 1 equivalent of pyacH with 1.15 equivalent of diethyl zinc in THF at room temperature afforded the product in quantitative yield. Proton transfer leads to elimination of ethane gas. Fine crystals were obtained by placing a concentrated THF solution in the freezer. Compound 4 is both air and moisture sensitive.

**(pyac)MgOBu†(THF), 5:** The best preparative route for this compound involved the mixing of 1 equivalent †BuOH with THF to facilitate easy handling. This mixture was added dropwise to a solution of compound 1. Proton transfer occurs with elimination of butane gas. Removal of solvent under a dynamic vacuum pump affords compound 5 as an orange solid. Single Crystals for X-ray analysis were grown from a concentrated THF solution. This compound is very air and moisture sensitive.
2.2 Single Crystal and Molecular Structure

All data collection and examination of the diffraction pattern was done on a Nonius kappa CCD diffractometer at 180 K using an Oxford Cryosystems Cryostream cooler. This showed a triclinic and monoclinic crystal system for compound 1 and 5 respectively (see Table 1 for more details). Both crystals were coated in oil under a nitrogen gas stream.

(pyac)Mg\textsuperscript{Bu}(THF), 1. An ORTEP drawing showing the molecular structure of compound 1 is given in Figure 5. Selected bond distances and angles are given in Table 1. The structure has a distorted tetrahedral geometry around the magnesium. The ligand’s NC\textsubscript{5} plane is perpendicular to the Mg-O\textsubscript{THF} axis. The mesitylenes on C1 and C9 appear to be perpendicular to the plane of NC\textsubscript{5} forming a pocket around the magnesium metal. Part of the THF ligand is disordered along C41, C42 and C15 with angles C41-C42a-C43a and C44a-C43a-C42a at 100.7(7)^o and 101.9(7)^o respectively. The bond distances of Mg-N1, Mg-N2, Mg-O\textsubscript{THF} and Mg-C37 are comparable from 2.0557(15)\AA to 2.122(2)\AA. The N1-Mg-N2 angle associated with the ligand is 89.97(6)^o, while angles of N1-Mg-C37 and N2-Mg-C37 are 130.49(8)^o and 130.87(8)^o respectively. Summation of the angles gives a total of 351^o indicating a significant distortion from the tetrahedral geometry of 328.5^o.
Figure 5: ORTEP drawing of (pyac)MgnBu(THF) with thermal ellipsoids drawn at the 50% probability level. The structure shows a distorted tetrahedral geometry around the Mg metal centre. All hydrogen atoms are omitted for clarity.
Table 1: Selected Bond distances (Å) and Angles (deg) for (pyac)MgnBu(THF)

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(pyac)MgOBu\textsubscript{t}(THF), 5: An ORTEP drawing showing the molecular structure of compound 5 is given in Figure 6. Selected bond distances and angles are given in Table 2. It’s interesting to note that besides the main magnesium complex, two solvent molecules of THF were contained in the asymmetric unit. Several similarities and slight differences can be seen with the compound 1 structure. The Mg-\textsubscript{THF} bond distance is 2.044(17)Å which is slightly shorter to that of compound 1. The pyacH ligand N\textsubscript{1} – Mg and N\textsubscript{2} – Mg bond distances are 2.067(18)Å and 2.066(18) respectively, which again is slightly shorter to the corresponding compound 1 bond distances. The structure adopts a distorted tetrahedral geometry around the magnesium metal. The NC1 – C5 – C9 plane appears to be planar while the mesitylenes on C1, C5 and C9 are perpendicular to the NC1 – C5 – C9 plane The THF ligand and OBu\textsubscript{t} seem to be contained within the ligand’s pocket. Angles associated with N1 - Mg - N2, N1 - Mg - O1 and N2 – Mg – O1 are 92.41(7)°, 124.03(8)° and 124.36(8)° respectively. The summation of this three angles is 340° indicating somewhat a significant distortion from the normal tetrahedral geometry.

A close resemblance exist between compound 5 and BDIMgO\textsubscript{Bu}(THF) \textsuperscript{75} synthesized by our group. The two compounds bond distances of Mg – N, Mg – \textsubscript{THF} and Mg – O\textsubscript{Bu} are almost perfectly equal. The N – Mg – N angles of compound 5 and BDIMgO\textsubscript{Bu}(THF) are 92.41(7)° and 92.20(9)° respectively.
Figure 6: ORTEP drawing of (pyac)MgOBu(THF) with thermal ellipsoids drawn at the 50% probability level. All hydrogen atoms are omitted for clarity.
Table 2: Selected Bond distances (Å) and Angles (deg) for (pyac)MgOBu(THF)

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2.3 Solution NMR characterization of compound 1, 2 and 3

The Mg and Zn alkyl compounds (1, 2 and 3) synthesized showed an unexpected α – proton pattern that deviated from the anticipated usual triplet (see Figure 7). Homonuclear decoupling of the butyl γ and δ protons of compounds 1 and 3 indicated that there was long range coupling to the α – protons which also contributed to the unusual pattern (See Figure 8 and Figure 9). Topsin program was used for the simulation of (pyac)Mg\textsuperscript{n}Bu(THF) α – protons as an AA’XX’ spectrum. Long range coupling was evident with the γ - protons, although with a small J – coupling (see Figure 10). Refer to Figure 11 – 15 for \textsuperscript{1}H and \textsuperscript{13}C NMR of compounds 1, 2 and 3.

Whitesides et. al first observed the AA’XX’ pattern in 3,3–dimethylbutyl chloride and bis (3,3–dimethyl butyl) magnesium\textsuperscript{76} In the former, steric hindrance orients the \textit{t}-butyl group anti to the chloride atom, hence the –CH\textsubscript{2}Cl protons become chemically equivalent but magnetically unequivalent. This makes them to couple differently to the –CH\textsubscript{2}C(CH\textsubscript{3})\textsubscript{3} protons hence accounting for the AA’XX’ pattern.\textsuperscript{76}
Figure 7: Expanded α – proton region of the magnesium and zinc alkyl compounds 1, 2 and 3. The α – proton signal resembles an AA’XX’ pattern.

Figure 8: Homonuclear decoupled $^1$H NMR spectra of (pyac)Mg$^n$Bu(THF) showing the butyl region.
Figure 9: Homonuclear decoupled $^1$H NMR spectra of (pyac)Zn(nBu) showing the butyl region.
Figure 10: Simulation of (pyac)Mg^nBu(THF) α - protons using the topspin program.

Long range coupling of the α to γ protons was evident although with a small J - coupling.
Figure 11: (pyac)MgnBu(THF) $^1$H NMR
Figure 12: (pyac)MgnBu(THF) $^{13}$C NMR
Figure 13: (pyac)Mg(CH2CH2Ph)THF $^1$H NMR
Figure 14: (pyac)Zn(nBu) $^1$H NMR
Figure 15: (pyac)Zn(nBu) $^{13}$C NMR
2.4 Reactivity studies

2.4.1 Reaction with carbon dioxide

Carbon dioxide reacts readily with Compound 1 in C₆D₆ forming a carboxylate, (pyac)Mg(OCO)⁹Bu(THF) as the single detectable product by ¹H and COSY NMR. Upon ¹³CO₂ insertion, the α-protons assume a normal triplet pattern deviating from the AA'XX' like pattern observed before the ¹³CO₂ insertion (see Figure 16 and Figure 17). The α-proton signal moves downfield from -0.77 to 0.88 ppm. This might be due to the fact that the n-butyl group is now pushed outside the ligand pocket.

Compounds 2 and 5 also readily react with ¹³CO₂ in C₆D₆ to presumably give magnesium carbonates. Their ¹H NMR spectra were complex.

Figure 16: ¹H NMR for (pyac)MgnBu(THF) showing the butyl region before and after ¹³CO₂ insertion. Notice the α - proton signal after ¹³CO₂ insertion attains a normal triplet.
Figure 17: Cosy NMR for (pyac)MgO\(^{13}\)CO\(^{n}\)Bu

• \(\alpha\) couples to \(\beta\) and \(\gamma\)
• \(\beta\) and \(\gamma\) couples to \(\delta\)
2.4.2 Preliminary Polymerization studies

Compound 1 showed good stereocontrol in the polymerization of rac and L-lactide resulting in heterotactic and isoctactic polymers, respectively (see Figure 18). The zinc alkyl compounds 3 and 4 showed very low reactivity towards lactide polymerization. More studies on polymerization of biodegradable monomers, such as β-butyrolactone, ε-caprolactone and lactide are ongoing.

Figure 18: $^1$H NMR spectra (CDCl$_3$, 400MHz) of the homonuclear decoupled methine resonance of poly(rac-lactide) shows heterotactic poly lactide. Polymerization was done in THF at room temperature using compound 1. Ratio of Initiator to monomer was 1:100.
2.4.3 Reaction of (pyac)Mg^aBu(THF) with benzophenone and diphenyl methanol

Compound 1 was reacted with benzophenone and diphenyl methanol with the aim of probing its reactivity mechanism. Both reactions were done in a J-young tube. The reaction with benzophenone proceeds with the $\beta$-elimination of a hydrogen on the butyl group that in turn attacks the carbonyl carbon on the substrate. This also results in the formation of an alkene (butane) and an alkoxide (see Scheme 10 and 11).

On the other hand, reaction of compound 1 with diphenyl methanol initiates with the C-Mg bond attacking the hydroxyl group of the alcohol. The hydrogen abstraction leads to the formation of butane and an alkoxide (see Figure 19 and Figure 20).

Scheme 10: Mechanism for (pyac)Mg^aBu(THF) with benzophenone. L represents the ligand (pyac).
Scheme 11: Reaction mechanism of (pyac)Mg^nBu(THF) with diphenyl methanol. L represents the ligand (pyac).

Figure 19: ^1H NMR showing products of the reaction between (pyac)Mg^nBu(THF) and benzophenone.
Figure 20: $^1$H NMR showing products of the reaction between (pyac)MgBu(THF) and diphenyl methanol.
2.5 Experimental Section

General Synthetic Considerations:

Manipulation of all air sensitive compounds was carried out in the absence of oxygen and moisture using standard Schlenk line and drybox technique. All glassware was dried overnight in the oven before use in the glovebox. Hexane, tetrahydrofuran, toluene and benzene were distilled (under oxygen free nitrogen) from potassium metal, sodium/benzophenone, sodium metal and calcium hydride respectively. The solvents were stored over 4 Å molecular sieves (previously dried under vacuum for a minimum of 8 hours). CD$_2$Cl$_2$, CDCl$_3$ and C$_6$D$_6$ were purchased from Cambridge Isotope labs, degassed and stored over 4 Å activated molecular sieves before use. 1,5,9-trimesityldipyromethene ligand, (pyac)(Li.THF) and (pyac)ZnCl were synthesized according to literature.$^{74}$ Anhydrous zinc dichloride, 2.5 M $n$-butyl lithium in hexane, tert-butanol, 1.0 M di-$n$-butyl magnesium in heptane, 1.0 M phenethylmagnesium chloride in THF, 1.0 M of diethyl zinc in hexane and diisopropylamide were bought from sigma Aldrich and used as received. Carbon dioxide was purchased from The BOC Group, Inc and used as received. rac-Lactide and L-Lactide were purchased from sigma Aldrich and sublimed four times before use.

Physical Measurements:

$^1$H and $^{13}$C NMR spectra were recorded in CD$_2$Cl$_2$, CDCl$_3$ and C$_6$D$_6$ on Bruker DPX-400 NMR spectrometer. These were referenced to the residual protic impurity peak
(CD$_2$Cl$_2$, $\delta$ 5.32; CDCl$_3$, $\delta$ 7.26 and C$_6$D$_6$, $\delta$ 7.16 for $^1$H NMR; and C$_6$D$_6$, $\delta$ 128.39; CD$_2$Cl$_2$, $\delta$ 53.8, for $^{13}$C NMR).

(ppyac)Mg$^n$Bu(THF), 1: In a 25ml Schlenk flask ppyacH (0.93 g, 1.87 mmol) was dissolved with THF (15 mL). From another Schlenk flask di-n-butylmagnesium (2.25 ml, 2.15 mmol) was added dropwise via cannula immediately changing reaction color from light to dark orange. The reaction was stirred for 5 h at room temperature then THF was removed under dynamic vacuum to give an orange solid. Washing with hexane precipitated out the product as an orange powder. Cannula filtration and drying under vacuum afforded the product in quantitative yield. Fine crystals were obtained from a concentrated hexane solution left overnight in the freezer. $^1$H NMR (400 MHz, C$_6$D$_6$): 6.88 (s, 6H, meta-C$_6$H$_2$(CH$_3$)$_2$), 6.78 (d, $J_{HH} = 4$ Hz, 2H, pyrrole C-H), 6.21 (d, $J_{HH} = 4$ Hz, 2H, pyrrole C-H), 3.38 (m, 4H, THF), 2.30 (s, 6H, para-C$_6$H$_2$(CH$_3$)$_3$), 2.27 (s, 3H, para-C$_6$H$_2$(CH$_3$)$_3$), 2.24 (s, 12H, ortho-C$_6$H$_2$(CH$_3$)$_3$), 2.20 (s, 6H, ortho-C$_6$H$_2$(CH$_3$)$_3$), 1.36 (m, 2H, $\gamma$-CH), 1.17 (m, 4H, THF), 1.07 (m, 3H, $\delta$-CH), 1.02 (m, 2H, $\beta$-CH), -0.82 to -0.77 (m, 2H, $\alpha$-CH). (see Figure 11) $^{13}$C NMR (400 MHz, C$_6$D$_6$): 162.25, 146.86, 141.35, 137.87, 137.37, 137.20, 134.52, 132.47, 119.48, 69.16, 33.17, 32.79, 25.71, 21.78, 21.07, 20.49, 14.77, 7.33. (see Figure 12)

(ppyac)Mg(CH$_2$CH$_2$Ph)THF, 2: (ppyac)Li.THF (0.220 g, 0.384 mmol) was dissolved with 10 ml toluene in a 25 ml Schlenk flask. In another flask (PhCH$_2$CH$_2$)MgCl (0.46 ml, 0.461 mmol) was mixed with toluene (10 ml). Both flasks were partially frozen in liquid nitrogen. (PhCH$_2$CH$_2$)MgCl thawing solution was
dropwise added to the thawing solution of (pyac)LiTHF. Mixture was stirred for 4 h at room temperature. The solvent was removed in vacuo to give a deep orange solid. Washing with benzene extracts the product and precipitates out LiCl. Solvent was removed in vacuo to give a bright orange solid (0.231g, 86.5%). X-ray single crystals were grown by placing a concentrated toluene solution in a freezer. $^1$H NMR (400 MHz, C$_6$D$_6$): 7.26-7.28 (m, 2H, ortho-ArH), 7.32-7.35 (m, 3H, meta and para- ArH), 6.89 (s, 6H, meta-C$_6$H$_2$(CH$_3$)$_2$), 6.78 (d, J$_{HH}$ = 4 Hz, 2H, pyrrole C-H), 6.22(d, J$_{HH}$ = 4 Hz, 2H, pyrrole C-H), 3.30 (m, 4H, THF), 2.33-2.38 (m, 2H, $\beta$-CH), 2.29 (s, 6H, para-C$_6$H$_2$(CH$_3$)$_3$), 2.28 (s, 3H, para-C$_6$H$_2$(CH$_3$)$_3$), 2.24 (s, 6H, ortho-C$_6$H$_2$(CH$_3$)$_3$), 2.22 (s, 12H, ortho-C$_6$H$_2$(CH$_3$)$_3$), 1.16 (m, 4H, THF), -0.636 to -0.592 (m, 2H, $\alpha$-CH). (see Figure 13)

(Pyac)Zn(nBu), 3: In a 25 ml Schlenk flask (pyac)ZnCl (1.26 g, 1.87 mmol) was dissolved with 15 ml THF. In another flask, 5 ml THF was added to nBuLi (0.814 ml, 2.04 mmol). Both flasks were partially frozen before adding the thawing solution of nBuLi dropwise to the thawing solution of (pyac)ZnCl. Reaction mixture was stirred at room temperature for 4 h with subsequent solvent removal in vacuo affording a dark orange solid. Product was extracted in benzene while precipitating out LiCl. Solvent removal under a dynamic vacuum affords a bright orange solid (1.06 g, 91%). X-ray suitable single crystals were obtained by recrystallization in THF. $^1$H NMR (400 MHz, CD$_2$Cl$_2$): 6.97 (s, 2H, meta-C$_6$H$_2$(CH$_3$)$_2$), 6.87 (s, 4H, meta-C$_6$H$_2$(CH$_3$)$_2$), 6.54 (d, J$_{HH}$ = 4 Hz, 2H, pyrrole C-H), 6.22 (d, J$_{HH}$ = 4 Hz, 2H, pyrrole C-H), 2.38 (s, 3H, para-C$_6$H$_2$(CH$_3$)$_3$), 2.27 (s, 6H, para-C$_6$H$_2$(CH$_3$)$_3$), 2.19 (s, 6H, ortho-C$_6$H$_2$(CH$_3$)$_3$), 2.09
(s,12H,ortho-C₆H₂(CH₃)₃), 0.54 to 0.64 (m, 2H, γ-CH), 0.51 (t, 3H, δ-CH), 0.29 to 0.37 (m,2H, β-CH), -0.78 to -0.75 (m, 2H, α-CH). (see Figure 14). ¹³C NMR (400 MHz, CD₂Cl₂): 162.18, 146.15, 139.99, 138.31, 137.85, 137.33, 137.21, 135.91, 133.56, 131.95, 128.52, 128.12, 119.26, 30.19, 29.57, 21.46, 21.38, 20.81, 20.17, 13.95, 8.06, 1.36. (see Figure 15)

**(pyac)ZnEt, 4:** A 25 ml Schlenk flask was charged with pyacH (0.498 g, 2.01 mmol) and dissolved with 15 ml THF. Diethyl zinc (2.3 ml, 2.3 mmol) was added dropwise to the ligand mixture then stirred for 4 h at room temperature. Solvent was removed under a dynamic vacuum to give a brown solid in quantitative yield. Fine crystals were grown from a concentrated THF solution placed in the freezer overnight. ¹H NMR (400 MHz, C₆D₆): 6.86 (s, 2H, meta-C₆H₂(CH₃)₂), 6.79 (s, 4H, meta-C₆H₂(CH₃)₂), 6.76 (d, J_HH = 4 Hz, 2H, pyrrole C-H), 6.21 (d, J_HH = 4 Hz, 2H, pyrrole C-H), 2.29 (s, 6H, para-C₆H₂(CH₃)₃), 2.25 (s, 3H, para-C₆H₂(CH₃)₃), 2.19 (s, 12H, ortho-C₆H₂(CH₃)₃), 2.10 (s, 6H, ortho-C₆H₂(CH₃)₃), 0.64 (t, 3H, β-Me), -0.23 to -0.17 (q, 2H, α-CH). (see Figure 21)

**(pyac)MgOBu' (THF), 5:** Compound 1 (0.30 g, 0.461 mmol) was dissolved in 10 ml THF. ¹BuOH (44 μl, 0.461 mmol) was mixed with THF (5 ml) in a separate flask before adding it dropwise into the solution of compound 1. The overall mixture was stirred for 1 h at room temperature. Solvent removal under dynamic vacuum pump affords an orange solid in quantitative yield. X-ray-suitable single crystals were grown from a concentrated solution of THF placed in the freezer overnight. ¹H NMR (400 MHz, C₆D₆): 6.88 (s, 6H, meta-C₆H₂(CH₃)₂), 6.76 (d, J_HH = 4 Hz, 2H, pyrrole C-H), 6.18 (d,
$J_{HH} = 4 \text{ Hz, 2H, pyrrole C-H}$, 3.46 (m, 4H, THF), 2.29 (s, 18H, ortho-$C_6H_2(CH_3)_3$), 2.27 (s, 3H, para-$C_6H_2(CH_3)_3$), 2.23 (s, 6H, para-$C_6H_2(CH_3)_3$), 1.18 (m, 4H, THF), 0.99 (s, 9H, OBu$^t$). (see Figure 22) $^{13}$C NMR (400 MHz, C$_6$D$_6$): 162.47, 146.75, 141.67, 137.98, 137.81, 137.54, 137.37, 137.22, 134.68, 132.80, 119.89, 69.41, 35.51, 25.60, 21.54, 21.28, 20.49, 1.75 (see Figure 23).
Figure 21: (pyac)ZnEt $^1$H NMR
Figure 22: (pyac)MgOBu(t)(THF) $^1$H NMR
Figure 23: (pyac)MgOBu(THF) $^{13}$C NMR
2.6 Conclusion and future work

We have synthesised and characterized monomeric magnesium and zinc compounds using single crystal X-ray diffraction, $^1$H and $^{13}$C NMR. Magnesium compounds 1 and 5 have been shown to be monomeric with a distorted tetrahedral structure around the metal. Preliminary polymerization reactivity using the magnesium compounds looks promising in regard to their stereocontrol and Kinetics. It was interesting to note the unexpected α–protons pattern in the magnesium and zinc alkyl compounds (1, 2, and 3) which shows that the compounds are sterically constrained. We plan to use these compounds as initiators for the ring opening polymerization studies of lactides, β-butyrolactone, ε-caprolactone.
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