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Conformational effects in β-diiminate ligated magnesium and zinc amides. Solution dynamics and lactide polymerization

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Dedicated to Professor Pierre Braunstein

Abstract

The preparation of the compounds $LMg(N^iPr_2)(THF)$ (**1**); and $LZnN^iPr_2$ (**2**), are reported for L = the bulky β-diiminate ligand, $CH(CMeN\text{-}2\text{-}^tBuC_6H_4)_2$. In solution compound **2** is shown to exist as a mixture of *syn*- and *anti*-rotamers that do not interconvert significantly. Compound **1** readily and reversibly dissociates THF in benzene-d_6 or toluene-d_8 from a site where THF is *syn* to the ^{t}Bu group of L. Both **1** and **2** are catalyst precursors for the ring-opening polymerization of lactides and it is shown that the *syn*-conformer of **2** reacts much faster than the *anti*. Polymerization of *rac*-lactide employing **2** in benzene or CH_2Cl_2 or **1** in THF yield approximately 90% heterotactic PLA (*isi*+*sis*). These results are compared with related work by Coates [J. Am. Chem. Soc. 123 (2001) 3229]; and us [J. Chem. Soc., Dalton Trans. (2001) 222] and us employing the symmetric β-diiminate ligand $CH(CMeN\text{-}2,6\text{-}^iPr_2C_6H_3)_2$.

Keywords: Conformational effects; β-Diiminate ligated magnesium; Zinc amides

1. Introduction

Polylactide (PLA) has been gaining attention in both academic and industrial circles due to its biocompatibility and biodegradability [1–3]. It can be used in applications such as biodegradable packaging materials, artificial tissue matrices, surgical sutures, and drug delivery systems [4]. In order to obtain desired mechanical properties, PLA is often copolymerized with other monomers such as glycolide and caprolactone [5–9]. Recently, single-site catalysts have been employed in lactide polymerization providing an entry point to new PLA microstructures [10,11]. For example, syndiotactic PLA was synthesized from *meso*-lactide using a chiral aluminum isopropoxide catalyst by Coates et al. [12] and, in their subsequent work, they were able to make heterotactic PLA from *rac*-lactide using a β-diiminato zinc complex [13,14]. Another challenge in PLA microstructure is to make a 1:1 mixture of L-PLA and D-PLA, called a stereocomplex, that has a high melting temperature (T_m) ~230 °C compared with T_m 180 °C of pure L-PLA [15–17]. This higher melting temperature gives rise to a broader range of applications. However, the normal synthesis of the stereocomplex requires a chiral separation of the enantiomers L- and D-lactide which adds significantly to the cost of production. Baker et al. tried to circumvent this problem by using a racemic aluminum isopropoxide catalyst to polymerize *rac*-lactide [11]. The idea was that one catalyst enantiomer would polymerize D-lactide and the other catalyst enantiomer would polymerize L-lactide in parallel thereby giving a mixture of pure D-PLA and L-PLA chains. However, this result was later challenged by Coates et al. who, upon detailed examination of the polymer microstructure, showed that the resulting polymer was not the stereocomplex but rather a stereo block $[(D\text{-}PLA)_m(L\text{-}PLA)_m]_n$ where $m \sim 11$ [18]. Therefore, the synthesis of the stereocomplex from commercially available *rac*-lactide remains to be achieved [19].

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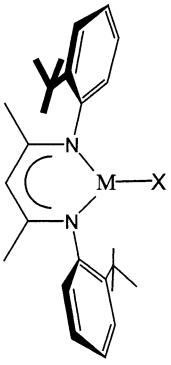
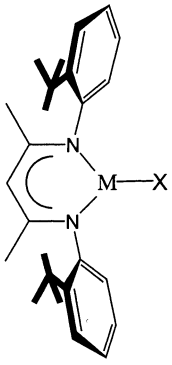
Prompted by these considerations and the success of single-site catalyst systems employing zinc and magnesium with β-diiminato ligands [13,14,20,21], we undertook the following study employing the 2-((2-*tert*-butylphenyl)amino)-4-((2-*tert*-butylphenyl)imino)-2-pentene ligand (LH). The premise was a simple one, namely that the bulky ^{t}Bu groups would prefer to adopt the *anti* conformation, in preference to the *syn* as represented by the drawings shown in **A** and **B**, respectively. The *anti*-confirmation has virtual C_2 symmetry and thus the metal center is chiral and exists as a 50:50 enantiomeric mixture.



A(anti)



B(syn)

2. Results and discussion

2.1. Syntheses and characterization

2.1.1. $LMg(N^iPr_2)(THF)$ (**1**)

The reaction of $Mg(N^iPr_2)_2$ with 1 equiv. of the free β-diiminato ligand LH in refluxing THF gives compound **1** as a green–yellow solid.

2.1.2. $LZn(N^iPr_2)$ (**2**)

Our best preparation of compound **2** is from the reaction between LiN^iPr_2 (2 equiv.), LH (1 equiv.) and a solution of $ZnCl_2$ (1 equiv.) in THF. Subsequent extraction of the dried reaction residue with hexanes gave compound **2** as a yellow solid. Elemental analyses and full details of the preparation are given in the Section 3 together with spectroscopic data.

2.2. Solution characterization of compounds **1** and **2**

With our recent characterization of related β-diiminato complexes of magnesium and zinc [20], there can be no doubt that compound **1** has a four-coordinate Mg^{2+} ion in a distorted tetrahedral environment and that compound **2** contains a trigonal-planar three coordinate Zn^{2+} ion. A similar trigonal-planar zinc complex $LZnNSi_2Me_6$ was characterized by Coates et al. where $L = CH(CMeN\text{-}2,6\text{-}^iPr_2C_6H_3)_2$ [22]. What is particularly pertinent is the disposition of the two ^{t}Bu groups in **1** and **2**.

The ^{1}H NMR spectrum of the zinc compound **2** in toluene-d_8 reveals the presence of two species in the temperature range of −70 to 80 °C. The relative concentration of each species is little influenced by variations in temperature and the NMR spectra can be assigned as arising from a mixture of *anti*:*syn* conformers in an approximately 60:40 ratio. These do not interconvert rapidly on the NMR time-scale nor as we show later even on the chemical reaction time-scale. For the *anti*-conformer the N^iPr groups are equivalent but contain diastereotopic methyl groups. For the *syn*-conformer there is a virtual mirror plane of symmetry and the ^{1}H NMR spectrum shows only one ^{i}Pr methyl doublet within the −70 to 80 °C temperature range indicating that rotation about the $Zn–N^iPr_2$ bond is rapid on the NMR time-scale. These key features are shown in Fig. 1.

The solution behavior of the magnesium compound **1** is slightly more complicated because of the reversible equilibrium shown in Eq. (1) which is temperature dependent in toluene-d_8. As shown in Fig. 2, the spectra are temperature dependent, although only one set of signals for the various groups present is ever seen at any given temperature. For example, we observe only one N^iPr_2 methyl doublet which is sharp at high temperature and again at low temperature. The line broadening that occurs in between is clearly due to the relative rates of exchange involving THF-ligated and THF-free metal complex.

$$LMg(N^iPr_2)(THF) \rightleftharpoons LMg(N^iPr_2) + THF \quad (L = CH(CMeN-2-{}^tBuC_6H_4)_2) \tag{1}$$

In the presence of added THF, the low temperature spectra indicate that the equilibrium **1** lies to the extreme

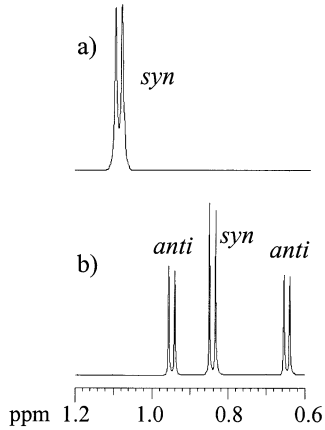


Fig. 1. ^{1}H NMR spectra (400 MHz, C_6D_6) of the methyl groups of the diisopropyl amide in (a) $LMg(N^iPr_2)(THF)$ and (b) $LZn(N^iPr_2)$.

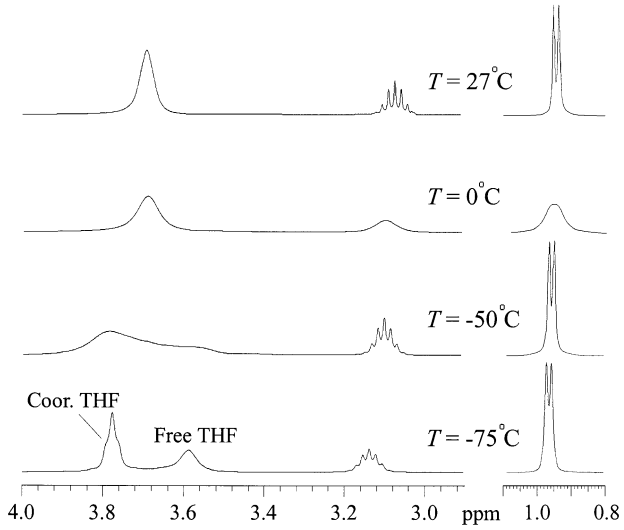
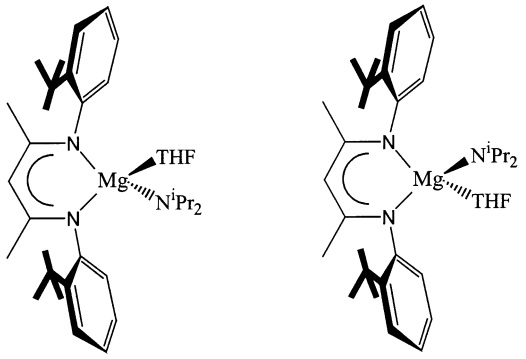


Fig. 2. VT ^{1}H NMR spectra (400 MHz, toluene-d_8) of LMg(N^iPr_2)(THF) when 0.5 equiv. of THF was added.

left, and furthermore, that exchange between free and coordinated THF is frozen out on the NMR time-scale. This parallels our earlier observation of the related magnesium complex [CH(CMeN-2,6-^{i}Pr$_2$C$_6$H$_3$)$_2$]Mg(O^t-Bu)(THF) [20,21]. The ^{1}H NMR spectra indicate that irrespective of temperature, only the *syn*-conformer of the β-diiminate ligand is present at the metal center. This caused us to question whether or not the THF was adjacent or removed from the ^{t}Bu group of the β-diiminate. These possibilities are pictorially represented by **C** and **D** below.



C (adjacent) **D** (removed)

In an attempt to address this matter, we employed NOE difference spectroscopy at low temperature (−70 °C). Irradiation of the ^{t}Bu protio-resonance caused an enhancement of the α-proton of the coordinated THF ligand. From this, we can reasonably conclude that the THF molecule is bound in close proximity to the *syn*-^{t}Bu groups. The bulky N^iPr_2 group is thus further removed from these groups.

From the ^{1}H NMR spectra of **1** at high temperature, we can infer that only the *syn*-conformer is present, yet under comparable conditions for the zinc compound **2**, both *syn*- and *anti*-conformers are present and are not interconverting rapidly on the NMR time-scale. We shall return to the significance of this later.

2.3. Polymerization of lactide employing *1* and *2*

Both the magnesium and zinc compounds are active in the polymerization of lactide. The magnesium compound is notably more reactive polymerizing 100 equiv. of lactide in THF within 2 min at room temperature. With *rac*-lactide, the polymer formed is significantly enhanced in heterotactic tetrads, *sis* and *isi*, when the polymerization is carried out in THF, but in benzene, the polymer is atactic. In contrast, the zinc compound polymerizes *rac*-lactide (100 equiv.) to give approximately 90% heterotactic PLA in THF, CH_2Cl_2 and benzene. The latter result parallels that of Coates et al. employing the related β-diiminate complex [HC(CMeN-2,6-^{i}Pr$_2$C$_6$H$_3$)$_2$Zn(μ-O^{i}Pr)]$_2$ [13]. However, an examination of the molecular weight profile for the polymerization of 100 equiv. of lactide by **1** and **2** (and with that of Coates catalyst noted above), revealed some interesting differences. For **1** in THF, $M_n = 14.7$ kDa and PDI = 1.6 but for **2**, $M_n = 29.3$ kDa and PDI = 1.5. For a living polymerization catalyst wherein $k_{initiation} \sim k_{propagation}$ we would expect $M_n \sim 14.4$ kDa and a PDI of 1.0. The latter is close to what is found for the zinc catalyst of Coates. The observed M_n value of approximately 30 kDa found employing the zinc compound **2** thus requires comment. We propose that this high molecular weight arises from the fact that the *syn*-conformer is much more active in the polymerization of lactide relative to the *anti*, and that rotation about the N–C(aryl) bond does not occur in solution to a significant extent. The *syn*–*anti* ratio observed reflects the formation of the compound. This is supported by two observations. (1) The *syn*–*anti* ratio of **2** is found to be independent of solvent (THF, toluene-d_8, C_6D_6) and added donor ligands such as pyridine. (2) When compound **2** was allowed to react with approximately 0.5 equiv. of *rac*-lactide, we observed the preferential depletion of the *syn*-conformer. Upon lactide ring-opening, all of the *syn*-conformer signals associated with LZnN^{i}Pr$_2$ disappeared and only those of *anti*-LZn^{i}Pr$_2$ remained and did not react to regenerate *syn*-LZnN^{i}Pr$_2$. A slower $k_{initiation}$ relative to $k_{propagation}$ could be responsible for a broad PDI as well as transesterification that occurs at high conversion.

2.4. Concluding remarks

Steric factors evidently suppress the interconversion of *syn*- and *anti*-conformers of these sterically demanding β-diiminate complexes and the *syn*-conformer is significantly more active in lactide polymerization.

Polymerization of *rac*-lactide yields heterotactic PLA via the *syn*-conformer which is achiral prior to the formation of the optically-active growing polymer chain LMOC*HMeR.

3. Experimental

3.1. General considerations

The manipulation of air-sensitive compounds involved the use of anhydrous solvents and dry and oxygen-free nitrogen employing standard Schlenk line and drybox techniques. *rac*-Lactide was purchased from Aldrich and was sublimed three times prior to use. Tetrahydrofuran, dichloromethane, and hexanes were distilled under nitrogen from sodium/benzophenone, calcium hydride, and potassium metal, respectively. The β-diiminato ligand $CH(CMeN\text{-}2\text{-}^tBuC_6H_4)_2$ [23] and $Mg(N^iPr_2)_2$ [24] were prepared according to literature procedures. Hydrous $ZnCl_2$ was dried using chlorotrimethylsilane [25]. LiN^iPr_2 was prepared from the reaction of BuLi and HN^iPr_2.

3.2. Measurements

^1H and $^{13}C\{^1H\}$ spectra were recorded in C_6D_6 and toluene-d_8 on Bruker DPX-400 NMR spectrometers and were referenced to the residual protio impurity peak (C_6D_6, δ 7.15; toluene-d_8, δ 2.09 for ^1H and, C_6D_6, δ 128.0; toluene-d_8, δ 20.4 for $^{13}C\{^1H\}$). Elemental analyses were done by Atlantic Microlab, Inc. Gel permeation chromatography measurements were carried out using a Waters 1525 binary HPLC pump and Waters 410 differential refractometer equipped with styragel HR 2&4 columns (100 and 10 000 Å). The GPC was eluted with THF at 35 °C running at 1 ml min^{-1} and was calibrated using polystyrene standard. Mass spectrometry was done by electron impact ionization at 60 eV using a Kratos MS890 double-focusing magnetic-sector instrument at 6000 V ion-acceleration energy in the extended mass-range mode of the magnet.

3.3. $LMg(N^iPr_2)(THF)$ (**1**)

THF (15 ml) was added to a mixture of LH (0.500 g, 1.38 mmol) and $Mg(N^iPr_2)_2$ (0.310 g, 1.38 mmol). The clear solution was then refluxed for 2.5 h. After cooled down to room temperature (r.t.), the volatile components were removed under dynamic vacuum giving a green–yellow solid (0.71 g, 92%). By NMR analysis, the product is 100% in a *syn* conformation. *Anal.* Calc. for $C_{35}H_{55}N_3OMg$: C, 75.38; H, 9.86; N, 7.53. Found: C, 75.01; H, 9.76; N, 7.44%. ^1H NMR (C_6D_6): 7.42, 6.88–7.13 (m, 8H, Ar–H), 4.71 (s, 1H, β-CH), 3.64 (br, 4H, $O(CH_2CH_2)_2$), 3.13 (sept, 2H, $J = 6.3$ Hz, $CHMe_2$), 1.68 (s, 6H, α-Me), 1.51 (s, 18H, ^{t}Bu), 1.31 (br, 4H, $O(CH_2CH_2)_2$), 1.11 (d, 12H, $J = 6.3$ Hz, $CHMe_2$). $^{13}C\{^1H\}$ NMR (C_6D_6): 168.28 (C=N), 150.58, 143.07, 129.02, 127.57, 126.44, 124.71 (Ar–C), 94.18 (β-C), 69.52 ($O(CH_2CH_2)_2$), 48.22 ($CHMe_2$), 36.30 (CMe_3), 32.60 (CMe_3), 28.13 ($CHMe_2$), 25.18 ($O(CH_2CH_2)_2$), 24.96 (α-Me).

3.4. $LZn(N^iPr_2)$ (**2**)

THF (20 ml) was added to a mixture of LH (1.00 g, 2.76 mmol) and LiN^iPr_2 (0.592 g, 5.53 mmol) at r.t. The resulting solution was then stirred for 30 min and then added a solution of $ZnCl_2$ (0.380 g, 2.79 mmol) in 10 ml THF slowly. The mixture was then stirred for 1 h and any volatile components were removed under dynamic vacuum. The product was extracted with 20 ml hexanes giving a light yellow sticky solid (0.98 g, 68%). MS (EI): $m/z = 525.3$ (M^+). *Anal.* Calc. for $C_{31}H_{47}N_3Zn$: C, 70.69; H, 8.92; N, 7.97. Found: C, 70.01; H, 8.94; N, 7.47%. ^1H NMR (C_6D_6) *anti*: 6.70–7.40 (m, 8H, ArH), 4.86 (s, 1H, β-CH), 3.03 (sept, 2H, $J = 6.3$ Hz, $CHMe_2$), 1.67 (s, 6H, α-Me), 1.49 (s, 18H, ^{t}Bu), 0.95 (d, 6H, $J = 6.4$ Hz, $CHMe_2$), 0.65 (d, 6H, $J = 6.3$ Hz, $CHMe_2$). *syn*: 6.70–7.40 (m, 8H, ArH), 4.78 (s, 1H, β-CH), 2.87 (sept, 2H, $J = 6.4$ Hz, $CHMe_2$), 1.64 (s, 6H, α-Me), 1.45 (s, 18H, ^{t}Bu), 0.84 (d, 6H, $J = 6.4$ Hz, $CHMe_2$). $^{13}C\{^1H\}$ NMR (C_6D_6) *anti*: 168.04 (C=N), 148.47, 142.58, 129.22, 128.43, 126.48, 125.56 (Ar–C), 95.42 (β-C), 49.99 ($CHMe_2$), 36.40 (CMe_3), 33.13 (CMe_3), 28.16 ($CHMe_2$), 25.57 ($CHMe_2$), 25.12 (α-Me). *syn*: 168.67 (C=N), 149.06, 142.60, 129.29, 129.03, 126.93, 125.65 (Ar–C), 95.60 (β-C), 48.89 ($CHMe_2$), 36.13 (CMe_3), 32.44 (CMe_3), 27.55 ($CHMe_2$), 25.03 (α-Me).

3.5. General polymerization procedure

rac-Lactide (0.500 g, 3.47 mmol) was dissolved in 6.0 ml CH_2Cl_2 or THF. A solution of the corresponding catalyst (0.0347 mmol) in 1.5 ml CH_2Cl_2 or THF was then added to the lactide solution (100:1 [lactide]:[catalyst]). The reaction was stirred at r.t., and at the desired time, small aliquots were taken to monitor the conversion. When the conversion was greater than 90%, the polymerization was quenched with excess methanol. The polymer precipitate was then filtered and dried under vacuum to constant weight.

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References

[1] B.J. O'Keefe, M.A. Hillmyer, W.B. Tolman, J. Chem. Soc., Dalton Trans. (2001) 2215.
[2] G.W. Coates, J. Chem. Soc., Dalton Trans. (2002) 467.
[3] M.H. Chisholm, N.W. Eilerts, J.C. Huffman, S.S. Iyer, M. Pacold, K. Phomphrai, J. Am. Chem. Soc. 122 (2000) 11845.
[4] Examples of polyesters in pharmaceutical products are Dexon®, Vicryl®, Leupron Depot® and Zoldex® from Davis & Geek Inc., Ethicon Inc., Takeda Chemical Industries Ltd., and ICI pharmaceuticals, respectively.
[5] N. Spassky, V. Simic, in: C. Scholz, R.A. Gross (Eds.) Polymers from renewable resources; Biopolyesters and Biocatalysis, ACS Symp. Ser. 764 ACS, Washington D.C., 2000, p. 146.
[6] P.J.A. In't Veld, E.M. Velner, P. Van De Witte, J. Hamhuis, P.J. Dijkstra, J. Feijen, J. Polym. Sci., Part A: Polym. Chem. 35 (1997) 219.
[7] D.D. Hile, M.V. Pishko, J. Polym. Sci., A: Polym. Chem. 39 (2001) 562.
[8] P. Dobrzynski, J. Kasperczyk, H. Janeczek, M. Bero, Macromolecules 34 (2001) 5090.
[9] P. Dobrzynski, J. Kasperczyk, M. Bero, Macromolecules 32 (1999) 4735.
[10] N. Spassky, M. Wisniewski, C. Pluta, A. Le Borgne, Macromol. Chem. Phys. 197 (1996) 2627.
[11] C.P. Radano, G.L. Baker, M.R. Smith, III, J. Am. Chem. Soc. 122 (2000) 1552.
[12] T.M. Ovitt, G.W. Coates, J. Am. Chem. Soc. 121 (1999) 4072.
[13] M. Cheng, A.B. Attygalle, E.B. Lobkovsky, G.W. Coates, J. Am. Chem. Soc. 121 (1999) 11583.
[14] B.M. Chamberlain, M. Cheng, D.R. Moore, T.M. Ovitt, E.B. Lobkovsky, G.W. Coates, J. Am. Chem. Soc. 123 (2001) 3229.
[15] N. Yui, P.J. Dijkstra, J. Feijen, Makromol. Chem. 191 (1990) 481.
[16] H. Tsuji, Y. Ikada, Polymer 40 (1999) 6699.
[17] Y. Ikada, K. Jamshidi, H. Tsuji, S.H. Hyon, Macromolecules 20 (1987) 904.
[18] T.M. Ovitt, G.W. Coates, J. Polym. Sci., Part A: Polym. Chem. 38 (2000) 4686.
[19] N. Nomura, R. Ishii, M. Akakura, K. Aoi, J. Am. Chem. Soc. 124 (2002) 5938.
[20] M.H. Chisholm, J. Gallucci, K. Phomphrai, Inorg. Chem. 41 (2002) 2785.
[21] M.H. Chisholm, J.C. Huffman, K. Phomphrai, J. Chem. Soc., Dalton Trans. (2001) 222.
[22] M. Cheng, D.R. Moore, J.J. Reczek, B.M. Chamberlain, E.B. Lobkovsky, G.W. Coates, J. Am. Chem. Soc. 123 (2001) 8738.
[23] R.F. Jordan, M.P. Coles, US Patent 6,228,794, 1998.
[24] E.C. Ashby, J.J. Lin, A.B. Goel, J. Org. Chem. 43 (1978) 1564.
[25] P. Boudjouk, J.H. So, M.N. Ackermann, S.E. Hawley, B.E. Turk, Inorg. Synth. 29 (1992) 108.