



Strathprints Institutional Repository

Francos, Javier and Gros, Philippe C. and Kennedy, Alan R. and O'Hara, Charles T. (2015) Structural studies of (rac)-BIPHEN organomagnesiates and intermediates in the halogen-metal exchange of 2-Bromopyridine. *Organometallics*, 34 (11). pp. 2550-2557. ISSN 0276-7333 , <http://dx.doi.org/10.1021/om501225g>

This version is available at <http://strathprints.strath.ac.uk/54032/>

Strathprints is designed to allow users to access the research output of the University of Strathclyde. Unless otherwise explicitly stated on the manuscript, Copyright © and Moral Rights for the papers on this site are retained by the individual authors and/or other copyright owners. Please check the manuscript for details of any other licences that may have been applied. You may not engage in further distribution of the material for any profitmaking activities or any commercial gain. You may freely distribute both the url (<http://strathprints.strath.ac.uk/>) and the content of this paper for research or private study, educational, or not-for-profit purposes without prior permission or charge.

Any correspondence concerning this service should be sent to Strathprints administrator: strathprints@strath.ac.uk

Structural Studies of (*rac*)-BIPHEN Organomagnesiates and Intermediates in the Halogen-metal Exchange of 2-Bromopyridine

Javier Francos,[†] Philippe C. Gros,^{*,‡,¥} Alan R. Kennedy,[†] and Charles T. O'Hara^{*,†}

[†] WestCHEM, Department of Pure and Applied Chemistry University of Strathclyde, Glasgow, U.K. G1 1XL

[‡] HECRIN, Université de Lorraine, SRSMC, Boulevard des Aiguillettes, 54506 Vandoeuvre-Les-Nancy, France

[¥] HECRIN, CNRS, SRSMC, Boulevard des Aiguillettes, 54506 Vandoeuvre-Les-Nancy, France

Supporting Information

ABSTRACT: Four lithium magnesiate complexes (**2-5**) containing the dianionic (*rac*)-BIPHEN ligand have been prepared and characterized using X-ray crystallography and NMR spectroscopy. $(\text{THF})_3\text{Li}_2\text{Mg}\{(\textit{rac})\text{-BIPHEN}\}^n\text{Bu}_2$ **2**, $(\text{THF})_3\text{Li}_2\text{Mg}\{(\textit{rac})\text{-BIPHEN}\}(\text{CH}_2\text{SiMe}_3)_2$ **3** and $(\text{THF})_2\text{Li}_2\text{Mg}\{(\textit{rac})\text{-BIPHEN}\}^{\text{neo}}\text{Pe}_2$ **4** have been prepared by complexation of the appropriate dialkylmagnesium compound with *in-situ* prepared $\text{Li}(\textit{rac}\text{-BIPHEN})$ in a mixture of hydrocarbon/THF. For all structures, the Mg centers are four-coordinate (and retain the alkyl groups); however, in **2** and **3** the two Li centers have different coordination spheres (one binding to one THF molecule, the other to two). The solid-state structures of **2** and **3** are essentially isostructural with that of **4** except that both Li atoms in this molecule have equivalent coordination spheres. The solution behaviors of these three molecules have been studied by ¹H, ¹³C and DOSY NMR spectroscopy. During the synthesis of **2**, it was discovered that a (*rac*)-BIPHEN-rich (or *n*-butyl-free) lithium magnesiate $(\text{THF})_4\text{Li}_2\text{Mg}\{(\textit{rac})\text{-BIPHEN}\}\text{fo}_2$ **2b** could be isolated. The lithium precursor to **2-5**, $(\text{THF})_4\text{Li}_4\{(\textit{rac})\text{-BIPHEN}\}_2$ **1** has also been isolated. Within the molecular structure of this tetranuclear complex, there are three different Li coordination environments. Finally, **2** has already shown promise as a reagent in a halogen-metal exchange reaction with 2-bromopyridine. The structural chemistry at play in this reaction was probed by X-ray crystallography and NMR spectroscopy. The organometallic intermediate pyridyl-magnesiated **5** $(\text{THF})_2\text{Li}_2\text{Mg}\{(\textit{rac})\text{-BIPHEN}\}(2\text{-pyridyl})_2$ was isolated in high yield.

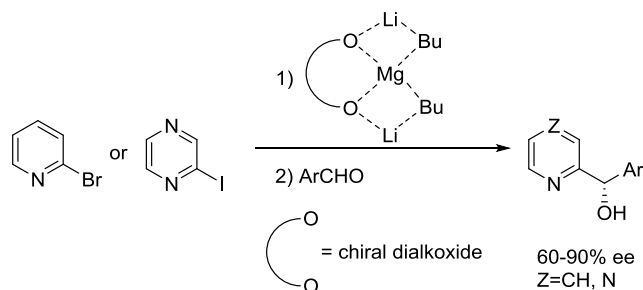
INTRODUCTION

The halogen-metal exchange of aromatic halides using bimetallic organometalates (ates) has attracted much attention, primarily because, in general, ates can be used under more user- and environmentally-friendly conditions than their organolithium counterparts (*i.e.*, temperatures closer to ambient temperature, in the presence of normally reactive functional groups and in greener solvents).¹⁻⁴ Alongside deprotonative metalation,^{2,5} the halogen-metal exchange methodology allows for more chemoselective reactions and the direct introduction of various lowly electropositive metals onto the aromatic rings. In this context, magnesium-based ate complexes have attracted a high degree of interest. Iida and Mase have reported the magnesiation of bromopyridines and aromatic halides using a substoichiometric amount of *n*-Bu₃MgLi⁶ while Oshima has shown that chemoselectivity can be easily tuned using *n*-BuMe₂MgLi.⁷ Here, the absence of an excess of reactive butyl ligands suppresses side reactions during the trapping step. The replacement of non-reactive alkyl ligands with alkoxides in organomagnesiates is an interesting alternative for concomitantly tuning the reactivity and allowing access to asymmetric synthesis by using appropriate chiral ligands.⁸⁻¹² Dilithium dialkylmagnesiates derived from lithium BINOLate have been reported by Noyori to promote a very good enantioselectivity in the alkylation of aldehydes.¹³ The key

point is to design a well-defined and robust bimetallic reagent ensuring the complete saturation of metal coordination sites thus limiting excess aggregation, which otherwise may subsequently lead to a loss of enantioselection.

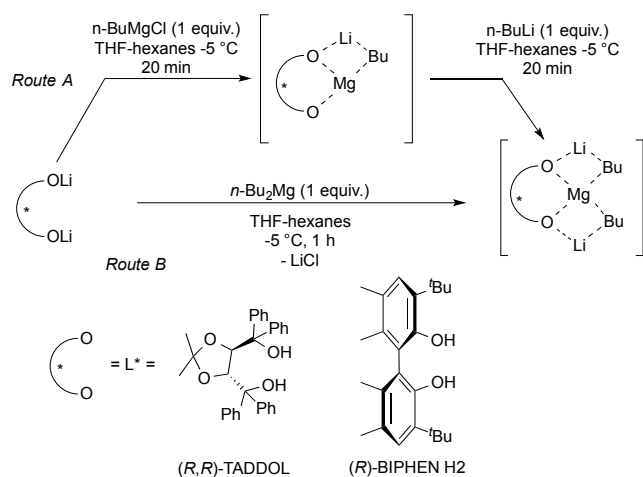
Recently we have reported that the incorporation of chiral ligands within organomagnesiates allows us to prepare reagents for the efficient ambient temperature bromine-magnesium exchange of sensitive halogenoazines and subsequent asymmetric transfer of the formed azinylorganometallics to carbonyl electrophiles.¹⁴⁻¹⁶ (Scheme 1). Despite their synthetic usefulness, to the best of our knowledge nothing is known about the solid (or solution) structures of these reagents, as well as those of the azinylorganometallic intermediates generated upon the halogen-metal exchange process. As structure is inextricably linked to reactivity, in this paper we have studied the solid- and solution-state structure of the magnesiate complexes and intermediates involved in the reaction of magnesiates with 2-bromopyridine. We also report the preparation and structural characterization of other related organomagnesiates, in an effort to provide structural information that may allow us to tailor the efficiency and stereoselectivity of the exchange/trapping reaction.

Scheme 1. The exchange-trapping sequence for synthesis of chiral azinyl carbinols from chiral ligand-containing magnesiate.



In our previous work, the chiral ligands employed were (*R,R*)-TADDOL and (*R*)-BIPHEN- H_2 (Scheme 2).^{14,16} The corresponding dibutylmagnesiate were prepared following two synthetic routes. In each case, the diol was di-deprotonated with BuLi (2 equivalents) then for Route A it was treated with an equivalent of $^n\text{BuMgCl}$ and then another equivalent of $^n\text{BuLi}$. For Route B the dilithiated diol was treated directly with an equivalent of $^n\text{Bu}_2\text{Mg}$ (as a 1 M heptane solution) (Scheme 2). In this study we attempt to elucidate the solution and structural of the di-*n*-butyl magnesiate reagents (and other alkyl congeners) as well as their respective products when they undergo magnesium-bromine exchange with 2-bromopyridine.

Scheme 2. Preparation of dibutylmagnesiate and proposed structure.



Solution studies of di-*n*-butylmagnesiate Both of the aforementioned preparative routes were studied by ^1H NMR spectroscopy. For these studies, reactions involving (*rac*)-BIPHEN- H_2 (L^*-H_2) were chosen as this ligand proves to be a useful probe to monitor metal environment changes in the formed magnesiate due to the simplicity of the resonances in the aromatic region of the respective ^1H NMR spectra. The relevant chemical shifts are presented in Table 1 (see spectra in supporting information, SI).

Table 1. ^1H NMR chemical shifts of magnesiate^[a]

Magnesiate	Route	H_{Ar} ligand	CH_2Mg
$L^*{}^n\text{BuMgLi}$	A	6.87 (1H) and 6.84 (1H)	-0.76 (1H) and -0.97 (1H)
$L^*{}^n\text{Bu}_2\text{MgLi}$	A	6.84 (2H)	-0.82 (2H) and -1.15 (2H)
$L^*{}^n\text{BuMgLi}$	B	6.80 (2H)	-0.83 (2H) and -1.15 (2H)

L^* is (*rac*)-BIPHEN. ^[a] Performed in THF- d^8 at 293K (400 MHz)

The chemical shifts appear to be in agreement with the structural formulae proposed in Scheme 2. The monobutyl magnesiate intermediate, $L^*{}^n\text{BuMgLi}$ formed in route A, showed two distinct singlets for aromatic protons of the ligand indicating two non-equivalent Ph rings, as expected for the monoalkyl intermediate (*i.e.*, one phenolic ring bridges between a Li and Mg center; whilst the other is terminally bound to only Mg). The hydrogen atoms of the methylene-C, α to the magnesium center (CH_2Mg) appear upfield as two multiplets at -0.76 and -0.97 ppm reflecting the diastereotopic nature of these protons. The introduction of an additional equivalent of $^n\text{BuLi}$ into $L^*{}^n\text{BuMgLi}$ resulted in the appearance of only one singlet in the aromatic region, which again is in agreement with the structure proposed in Scheme 2, for the higher order magnesiate $L^*{}^n\text{Bu}_2\text{MgLi}_2$. In addition, the CH_2Mg signals appear as two distinct multiplets at -0.82 (2H) and -1.15 ppm (2H), again in agreement with the diastereotopic environment for each hydrogen of the methylene groups. When the structural chemistry of route B was studied by solution NMR spectroscopy (*i.e.*, adding $^n\text{Bu}_2\text{Mg}$ directly to the dilithiated ligand) the ^1H NMR spectrum was found to be essentially identical to that obtained for the reaction performed in route A. Thus the preparation route appears to have no influence on the structure of the dibutylmagnesiate. Coincidentally, the reactivities and selectivities of the magnesiate [both (*R,R*)-TADDOL- H_2 and (*R*)-BIPHEN H_2 -containing species] prepared using the two synthetic strategies were also compared in a model metal-halogen exchange reaction using 2-bromopyridine as the organic substrate (Table 2). These data again suggest that the magnesiate preparation sequence has no significant effect on yields and enantioselectivity levels.

Table 2. Effect of preparation routes on yield and enantiomeric ratios

Ligand	Route A/B	Alcohol (%) ^[a,b]	<i>S</i> : <i>R</i> ^[c]
(<i>R,R</i>)-TADDOL	A	38	88:12 ¹⁴
	B	40	87:13
(<i>R</i>)-BIPHEN H_2	A	54	17:83 ¹⁴
	B	51	18:82

^[a] The bromine-metal exchange was complete. ^[b] Yields determined by GC. ^[c] Determined by chiral GC.

Synthesis and Solid State Study. As alluded to in the introduction, the main objective of this work was to elucidate the structure of chiral magnesiate both in solution and solid state. The NMR spectroscopic studies suggest structures in solution that correspond to those previously proposed.¹⁴⁻¹⁶ To gain further insight, we isolated, and analyzed by single crystal X-ray diffraction, crystals of the chiral lithium magnesiate. Although lithium magnesiate were our main focus, as a prelude we also investigated homometallic lithium complexes of (*rac*)-BIPHEN-H2 as to the best of our knowledge, these had not been studied prior to this work. Commercially-available (*rac*)-BIPHEN-H2 was chosen for the preparation and crystallographic studies of the reagents as it is considerably less expensive than the enantiopure reagent. (THF)₄Li₄{(*rac*)-BIPHEN}₂ **1**, can be synthesized by reacting (at 0°C) one equivalent of the corresponding diol in THF with two equivalents of ⁿBuLi. Removal of the solvent and recrystallization of the residue from hot hexane, lead to the formation of X-ray quality crystals of **1** in 47% yield. With respect to the metal-anion framework **1** is tetranuclear; however, the molecule contains three distinct Li environments (Figure 1). Two Li atoms (Li1 and Li1') are three coordinate bonding to two distinct (*rac*)-BIPHEN groups and a single THF molecule. Li2 is four coordinate, and has a distorted tetrahedral geometry (sum of angles around Li2, 663°) bonding exclusively to (*rac*)-BIPHEN O centers. Finally, Li3 is also four coordinate (sum of angles around Li3, 664°) binding to the symmetrically equivalent O2 and O2' atoms and two THF molecules. Most tetranuclear lithium complexes adopt either distorted cubane or ladders in compliance with 'laddering and stacking' principles.¹⁷⁻¹⁹ In **1**, two Li₂O₂ four-membered rings [Li1-O1-Li1'-O1'] and [Li2-O2-Li3-O2] are present, but rather than being stacked to give a cubane, or attach laterally to give a ladder, the rings are linked by Li2 forming inter-annular interactions with both O1 centers. The ring containing Li1 is severely puckered from planarity tautology (sum of endocyclic angles, 340.2°) whilst the ring containing Li2 and Li3 is planar (sum of endocyclic angles, 360.0°).

As **1** can be easily prepared, the more straightforward co-complexation approach (route B) was chosen for the next part of the study. After adding di-*n*-butylmagnesium (as a solution in heptane) to a hexane solution of **1**, colorless crystals of magnesiate (THF)₃Li₂Mg{(*rac*)-BIPHEN}₂ⁿBu₂ **2** were generated in good yield (65%) by adding THF (0.5 mL) and cooling the solution to -28°C. The molecular structure of the higher-order (*i.e.*, the ratio of lithium to magnesium in the structure is 2:1) magnesiate **2** is shown in Figure 2. The magnesium atom is four-coordinate, being bound to the two (*rac*)-BIPHEN oxygen centers and two butyl chains. Each butyl chain is also bound to a lithium atom. Interestingly, Li1 is three coordinate (bound to one THF molecule) and Li2 four-coordinate (bound to two THF molecules), with respect to oxygen atoms. The sterically less saturated Li1 coordination sphere is completed by an η¹-π interaction [Li1-C13, 2.681(6) Å] to a (*rac*)-BIPHEN Ph group.

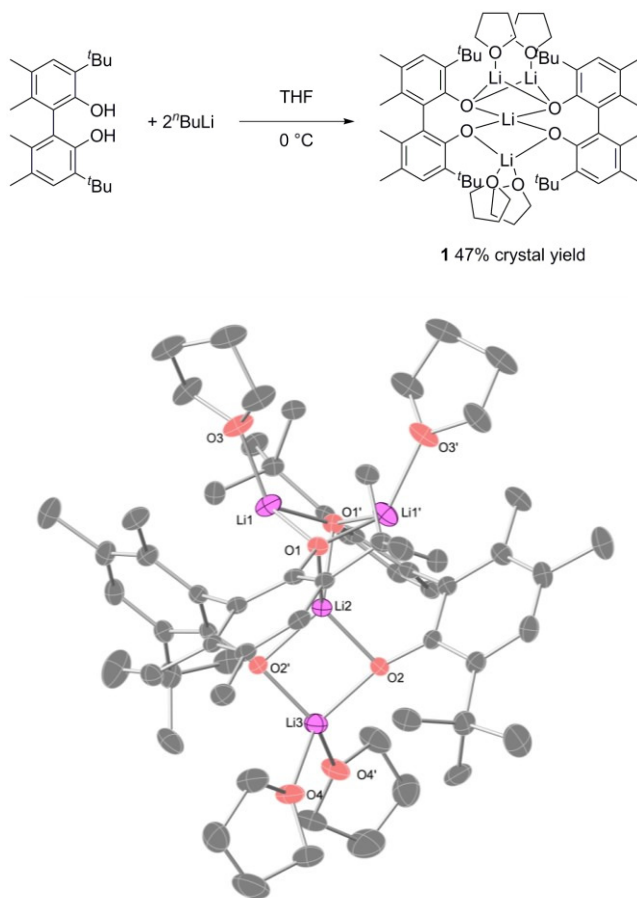
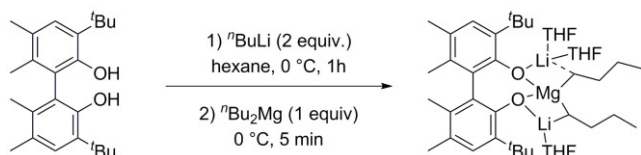


Figure 1. Molecular structure of complex **1**, Hydrogen atoms and disorder in THF molecules are omitted for clarity (30% ellipsoid probability). One ligand is *S* configuration, the other *R*. As it is a centrosymmetric crystal, no *S,S* or *R,R* diastereomers are present. Selected bond lengths [Å] and angles [°]: Li1-O1 1.901(3), Li1-O1' 1.907(3), Li1-O3 1.943(3), Li1-Li1' 2.587(6), Li1-C7 2.645(3), Li1-Li2 2.540(4), Li2-O1 2.070(3), Li2-O2 1.879(3), Li3-O2 1.875(3), Li3-O4 2.038(3), Li2-Li3 2.599(5), O1-Li1-O1' 84.53(12), O1-Li1-O3 115.81(15), O1'-Li1-O3 127.67(16), O1-Li1-C7 75.49(10), C7-Li1-O1' 120.03(14), C7-Li1-O3 111.84(13), O1-Li2-O1' 76.46(13), O1-Li2-O2 113.97(5), O1-Li2-O2' 133.04(5), O1'-Li2-O2 133.04(5), O1'-Li2-O2' 113.97(5), O2-Li2-O2' 92.27(17), O2-Li3-O2' 92.50(18), O2-Li3-O4 135.27(5), O2-Li3-O4' 99.82(4), O2'-Li3-O4 99.82(4), O2'-Li3-O4' 135.27(5), O4-Li3-O4' 100.86(18).



Scheme 3. Possible pathway for the formation of **2b**.

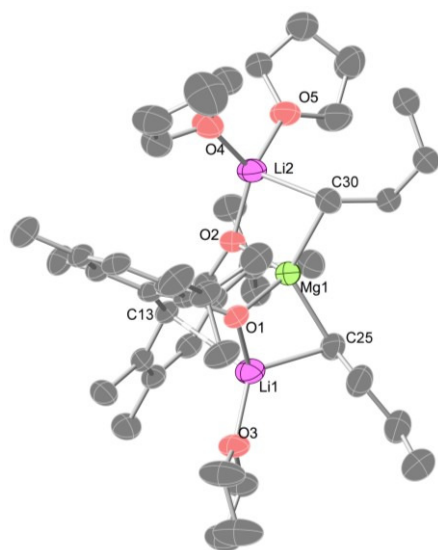
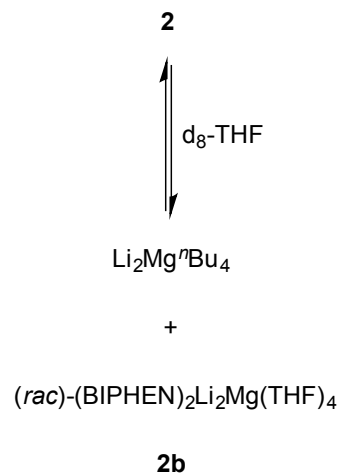
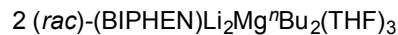


Figure 2. Molecular structure of dibutylmagnesiates **2** (30% ellipsoid probability). Hydrogen atoms and disorder in the THF molecules and butyl groups are omitted for clarity. Selected bond lengths [Å] and angles [°]: Li1-C25 2.193(6), Li1-O1 1.860(4), Li1-O3 1.875(4), Li1-C13 2.681(6), Mg1-C25 2.217(3), Mg1-O1 1.9978(17), Mg1-O2 2.0273(17), Mg1-C30 2.183(6), Li2-O2 1.849(4), Li2-C30 2.605(7), Mg1-Li2 2.813(4), Mg1-Li1 2.575(4), O2-Mg1-O1 97.36(7), O2-Mg1-C30 102.33(17), O1-Mg1-C30 121.56(15), O1-Mg1-C25 93.60(8), O2-Mg1-C25 116.62(9), C30-Mg1-C25 123.29(16), Li1-O1-Mg1 83.69(15), Li2-O2-Mg1 92.93(16), O2-Li2-C30 93.3(2), O1-Li1-C25 98.4(2).

During these studies we also isolated the (*rac*)-BIPHEN-rich (*i.e.*, butyl absent) species $(\text{THF})_4\text{Li}_2\text{Mg}\{(\text{rac})\text{-BIPHEN}\}_2$ **2b**. The formation of this butyl-free compound could be explained by a ligand reorganization reaction of **2** (Scheme 3) giving rise to **2b** and $\text{Li}_2\text{Mg}^n\text{Bu}_4$. Reorganizations such as this are common in magnesiates/zincates chemistry.^{20,21} It is plausible that **2** undergoes a (thermal) decomposition; however, we could not detect any expected by-products which would be generated if this were to occur. Unfortunately, the X-ray data of **2b** are not of sufficient quality to discuss the structural parameters; however, atom connectivity is unambiguous. The magnesiates **2b** contains two (*rac*)-BIPHEN ligands with their four O centers coordinating to the magnesium atom. In contrast to **1**, both Li atoms in **2** are four coordinate being bound to two THF molecules as well as to O atoms from different (*rac*)-BIPHEN ligands.



Given our success in obtaining the first structural determination of a (*rac*)-BIPHEN-magnesiates and to give us further structural insight, we studied whether it was possible to accommodate various other dialkylmagnesium complexes. The replacement of commercially-available $n\text{Bu}_2\text{Mg}$ by the β -hydrogen-free $(\text{Me}_3\text{SiCH}_2)_2\text{Mg}$ and $(\text{Me}_3\text{CCH}_2)_2\text{Mg}$ was examined by following an identical approach to that used for **2**. By slowly cooling THF solutions of the respective mixtures, the reactions produced colorless crystals of lithium magnesiates $(\text{THF})_3\text{Li}_2\text{Mg}\{(\text{rac})\text{-BIPHEN}\}(\text{CH}_2\text{SiMe}_3)_2$ **3** and $(\text{THF})_4\text{Li}_2\text{Mg}\{(\text{rac})\text{-BIPHEN}\}(\text{CH}_2\text{CMe}_3)_2$ **4** respectively in respective yields of 82 and 36%, the latter yield being adversely affected due to its high solubility in hydrocarbon solution. The main structural framework of **2** is preserved in **3** and **4** but in terms of THF incorporation **3** most resembles **2** as it contains three coordinated molecules of THF while **4** contains only two (*cf.*, **2b**). Table 3 compares the key structural parameters of **2-4**. These data show that the mean Mg-C_{alkyl} distance in **2-4** is essentially identical (2.202, 2.206 and 2.206 Å respectively) despite the asymmetry of the individual Mg-C_{alkyl} distances in **2** and **3**. A similar trend is found for the Li-C_{alkyl} distances in **2** and **3**; however, as both Li atoms in **4** are only monosolvated by THF, mean Li-C_{alkyl} bond distance in this complex is noticeably shorter (2.322 Å vs. 2.399 and 2.405 Å for **2** and **3** respectively).

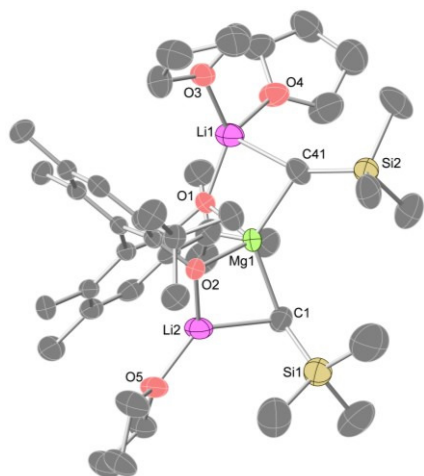
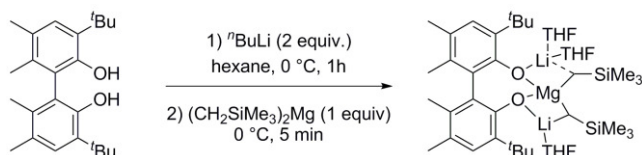


Figure 3. Molecular structure of dialkylmagnesiate **3**. Hydrogen atoms, disorder in THF, and disorder in TMS group have been omitted for clarity (30% ellipsoid probability). Selected bond lengths [Å] and angles [°]: Li1-C41 2.565(8), Li1-O1 1.832(7), Mg1-C41 2.164(4), Mg1-O1 2.033(2), Mg1-O2 1.995(2), Mg1-C1 2.248(4), Li2-O2 1.838(7), Li2-C1 2.244(8), Mg1-Li2 2.613(7), Mg1-Li1 2.941(7), O2-Mg1-O1 98.23(10), O2-Mg1-C41 122.62(15), O1-Mg1-C41 95.82(14), O2-Mg1-C1 95.07(14), O1-Mg1-C1 113.45(13), C41-Mg1-C1 128.51(17), O2-Mg1-Li2 44.55(16), O1-Mg1-Li2 97.3(2), C41-Mg1-Li2 163.0(2), C1-Mg1-Li2 54.36(19), O2-Mg1-Li1 114.65(15), O1-Mg1-Li1 37.97(15), C41-Mg1-Li1 57.96(18), C1-Mg1-Li1 138.70(17), Li2-Mg1-Li1 133.6(2).

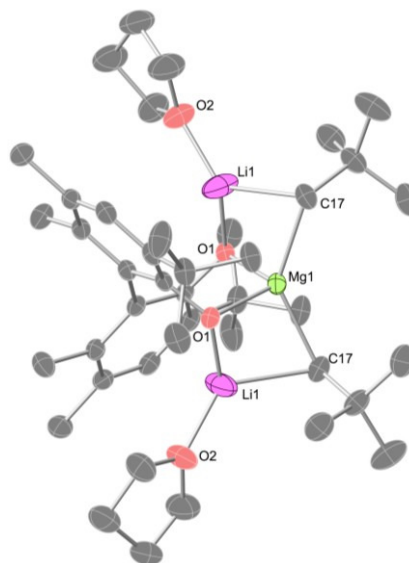
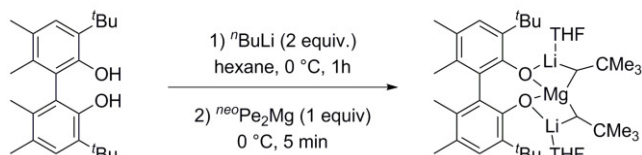


Figure 4. Molecular structure of dialkylmagnesiate **4** (30% ellipsoid probability). Hydrogen atoms are omitted for clarity. Selected bond lengths [Å] and angles [°]: Li1-C17 2.322(3), Li1-O1 1.813(3), Mg1-C17, 2.2064(16), Mg1-O1 2.0200(10), Li1-O2 1.868(3), Li1-Mg1 2.613(3), O1-Mg1-O1 96.12(6), O1-Mg1-C17' 96.13(5), O1'-Mg1-C17' 112.84(5), C17'-Mg1-C17 136.54(9), O1-Mg1-Li1 43.78(7), O1'-Mg1-Li1 93.68(9), C17'-Mg1-Li1 56.85(8), C17-Mg1-Li1 155.68(8), Li1-Mg1-Li1' 121.03(16).

Table 3. Mg-C and Li-C distance bonds and C-Mg-C angle for magnesiates 2, 3 and 4.			
Magnesiate	d Mg-C (Å)	d Li-C (Å)	Angle C-Mg-C (°)
2	2.186(6)	2.193(6)	123.29(16)
	2.217(3)	2.605(7)	
3	2.164(4)	2.244(8)	128.51(17)
	2.248(4)	2.565(8)	
4	2.2064(16)	2.322(3)	136.54(9)

Solution State Structures. Complexes **1-4** are soluble in *cyc*-C₆D₁₂ and d₈-THF solution, which allowed their solution behaviors to be probed by NMR spectroscopy. As alluded to earlier, the simplicity of the NMR spectra obtained with the (*rac*)-BIPHEN ligand is a particularly useful probe in understanding the solution structures of complexes incorporating the ligand. Focusing on **1**, in *cyc*-C₆D₁₂ and d₈-THF solutions only one broad signal is present in the respective ⁷Li NMR spectra (at 0.09 ppm in *cyc*-C₆D₁₂ and -0.27 ppm). This seems at odds with the solid state structure of **1**, which shows three distinct Li environments. A DOSY NMR experiment of a *cyc*-C₆D₁₂ solution shows the presence of two distinct species in the solvent medium. Interestingly, despite the non-polar nature

of the bulk solution, the molecules of THF in **1** do not appear to be within the same molecular unit as the (*rac*)-BIPHEN ligands. This study also suggests that the molecular weight for the species that contains the (*rac*)-BIPHEN ligands has a molecular weight of approximately 667 g mol⁻¹ (the molecular weight for a THF-free framework should be 732 g mol⁻¹ hence 9% error; for 20 mg of **1** in 0.5 mL of solvent). These data suggest that the double-BIPHEN skeleton remains intact (see Supporting Information) and that the tetranuclear molecule does not dissociate (or indeed aggregate) to give other oligomers. The diffusion coefficient for the THF component of the DOSY spectrum suggests a molecular weight of approximately 161 g mol⁻¹, which is obviously much greater than that for free-THF (72 g mol⁻¹). This phenomenon has been observed in related systems where dioxane has been used as a Lewis base donor²² and has been attributed to partial dynamic desolvation of the donor. As such the diffusion coefficient for the (*rac*)-BIPHEN-containing species (Figure 5) is likely to be the mean of the diffusion coefficients for all the potential solvated/unsolvated (*rac*)-BIPHEN species in solution. Another (albeit unlikely) possibility is that ate formation may be occurring in *cyc*-C₆D₁₂ solution, giving rise to [Li(THF)_x]⁺{(*rac*)-BIPHEN}₂Li₃⁻; however, the mass of the cation in this situation would match closely to the observed value only when *x* = 2 (to give 151 g mol⁻¹). A THF-solvated Li cation normally exists as [Li(THF)₄]⁺, although in some relatively rare cases a [Li(THF)₃]⁺ cation has been observed.²³⁻³⁰ It is also known that the ⁷Li NMR shift for a [Li(THF)₄]⁺ cation is concentration dependent, suggesting its propensity to exhibit intermolecular interactions.³¹ Therefore it appears that the former situation is more likely to represent the solution behavior of **1**.

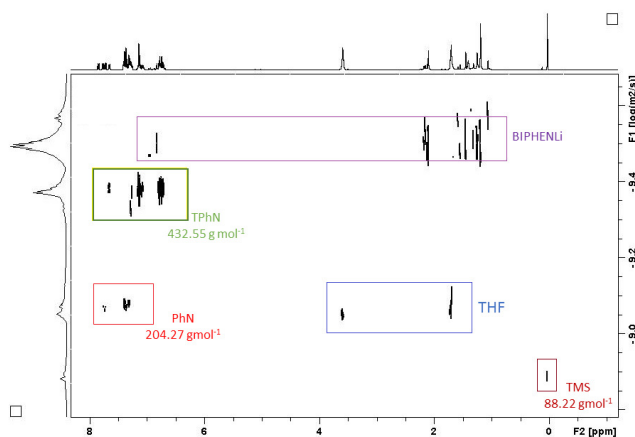


Figure 5. ¹H-DOSY NMR spectrum of **1** and the standards tetraphenylnaphthalene (TPhN), phenylnaphthalene (PhN) and tetramethylsilane (TMS) in *cyc*-C₆D₁₂ at 298 K.

Turning to the *cyc*-C₆D₁₂ solution structure of **2**, akin to **1**, DOSY NMR spectroscopy displays two distinct compounds in solution: they appear to be, firstly, the lithium magnesiate (metal-anion) framework and secondly, the molecules of THF which do not seem to bind to the lithium centers even in lowpolarity hydrocarbon solutions. ¹H NMR spectroscopic analysis of a d₈-THF solution of **2** showed that this compound

is stable at ambient temperature for more than 24 hours; however, after heating this solution to reflux for 2 hours, signals for *n*-butyl-free **2b** emerge in the spectra. This d₈-THF solution was analyzed after 24, 48 and 72 hours. After 72 hours, **2b** appears to be the sole (*rac*)-BIPHEN-containing present in solution. NMR spectroscopy of a *cyc*-C₆D₁₂ solution of **2b** (see Supporting Information) confirmed no butyl incorporation. Like **2**, magnesiates, **3** and **4** are soluble in polar and non-polar solvents so we studied their solution behavior using ¹H, ¹³C and ⁷Li NMR spectroscopy. NMR spectra (see supporting information) were measured in d₈-THF or *cyc*-C₆D₁₂ solutions at 298K, emphasizing the thermodynamic stability of the reagents. The relevant comparable chemical shifts for **2-4** are given in Table 4.

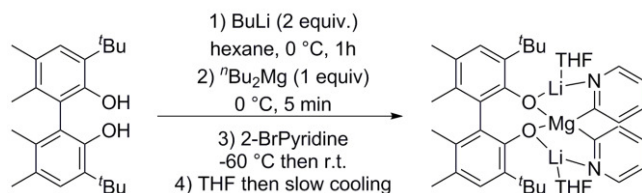
Table 4. Relevant NMR chemical shifts for magnesiates 2-4 . Performed in C ₆ D ₁₂ at 298K.					
	¹ H (400 MHz)		¹³ C (100 MHz)		⁷ Li (155 MHz)
	H _{Ar} (s)	CH ₂ Mg	C _{Ar} OMg	CH ₂ Mg	
2	6.80 (2H)	-0.83 (2H) -1.15 (2H)	162.0	9.0	1.41
3	6.92 (2H)	-1.65 (2H) -2.31 (2H)	159.0	-9.8	-0.18
4	6.91 (2H)	-0.13 (2H) -1.10 (2H)	159.3	25.5	0.07

The THF ligands undergo the same dynamic behavior as in **2** and are labile in hydrocarbon solution. With respect to the (*rac*)-BIPHEN ligands, ¹H NMR spectra for **2-4** showed only one aromatic hydrogen atom per complex indicating the symmetrical nature of the structure in each case. The CH₂Mg shifts were as expected strongly dependent on the electronic effects brought about by the remainder of the alkyl chains. This is most strikingly demonstrated for the Me₃SiCH₂ ligand in **3** with a marked shielding of the methylene hydrogen signals compared with the other reagents. For all three alkyl complexes, the CH₂Mg appeared as two distinct multiplets in agreement with different environments for diastereotopic CH protons. Complexes **3** and **4** containing Me₃SiCH₂ and its non-silylated analogue Me₃CCH₂ respectively displayed the largest difference between the two CH₂Mg chemical shifts (Δδ= 0.32, 0.66 and 0.97 for **2**, **3** and **4** respectively) indicating a probable higher rigidity of the coordination complex due to larger steric effects generated by the neopentyl-type substituents. The ¹³C NMR spectroscopic shifts were also consistent with these findings. Only one ⁷Li NMR spectroscopic resonance was observed in each case, providing further evidence that it is unlikely that multiple oligomeric forms of the magnesiates existed in solution under the conditions studied.

Reactivity Studies. As mentioned previously, the metal-halogen exchange reaction is of fundamental importance in modern organometallic chemistry.¹⁻³ In an effort to probe the structural chemistry of the reaction, we have reacted lithium

magnesiates **2** with 2-bromopyridine. Two reaction protocols were considered. Firstly, the classical synthetic route where the magnesiate **2** was first prepared and reacted in hexane with 2-bromopyridine (Scheme 4). Crystallization from the reaction medium was possible after addition of THF, and afforded crystals of complex **5** (Figure 6) in 47% yield, and hence with almost complete conversion of 2-bromopyridine to the 2-magnesiated pyridine (equivalent to 94% consumption of the pyridine).

Scheme 4. Preparation of **5**.



As shown in Scheme 4, the metal-halogen exchange process led to incorporation of two C-magnesiated pyridine molecules. The crystal structure unequivocally confirms the formation of the carbon-magnesium bond α to the pyridyl-N atom consistent with the 2-positioning of the halogen in the starting pyridine. The pyridyl-N atom coordinates to the lithium cation, whose coordination sphere is completed with a THF molecule, rendering the metal four-coordinate. As for **2-4**, the X-ray data for **5** reveal that the complexes are centrosymmetric and the BIPHEN ligands present are racemic mixtures of the *R* and *S* enantiomers. A second route was also examined to check the reactivity of the previously isolated magnesiate complexes. In this case, crystals of magnesiate **3** obtained above in high yield were reacted with two equivalents of 2-bromopyridine in hexane at -60°C . Warming to ambient temperature results in the precipitation of a yellow solid, which was subsequently filtered and dried under vacuum. ^1H NMR spectroscopic analysis in d_8 -THF of this solid (and filtrate) revealed the quantitative formation of **5** (isolated yield of crystalline material, 66%) (Scheme 5).

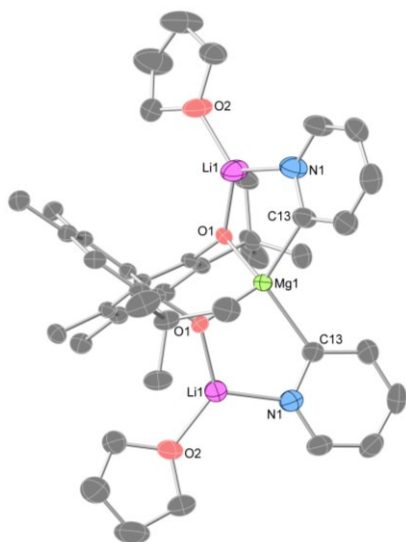
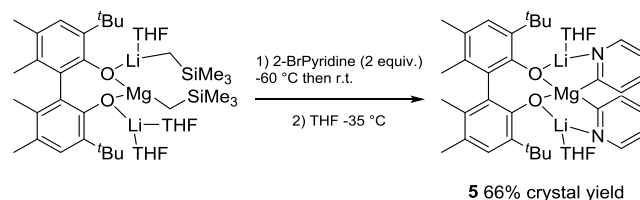


Figure 6. Molecular structure of complex **5** (30% ellipsoid probability). Hydrogen atoms are omitted for clarity. Selected bond lengths [Å] and angles [°]: Li1-O1 1.795(4), Li1-N1'

1.947(4), Mg1-O1 1.9915(14), Mg1-C13 2.197(2), O1-Li1-N1# 112.5(2), O1-Mg1-C13 129.09(7), Li1-O1-Mg1 103.65(14), C13-N1-Li1' 107.90(19), N1-C13-Mg1 117.46(16).

Scheme 5. Preparation of **5** from isolated crystals of **3**.



Complex **5** was also analyzed by NMR spectroscopy (see supporting information). The ^1H spectrum confirmed the complete replacement of the alkyl ligands in starting magnesiate **3** by pyridyl ones. Indeed signals in the upfield region of the spectrum are absent and the pyridine hydrogen atoms in the aromatic region appeared as four distinct multiplets in agreement with the presence of a metalated (2-substituted) pyridine molecule. The aromatic hydrogen atoms of the ligand appear as a singlet and its integration (2H) perfectly matched those of pyridine hydrogens each of them accounting for 2H. The formation of a pyridyl organometallic species was also clearly evidenced by a dramatically deshielded ^{13}C signal at 214.7 ppm. Interestingly **5** is stable at ambient temperature in a glove box for several weeks. As such, if an enantiopure BIPHEN ligand was used in the synthesis, instead of (*rac*)-BIPHEN, it should be possible to isolate an enantiopure magnesiated pyridine. This single species could subsequently be directly involved in reactions with prochiral electrophiles (*e.g.*, such as those shown in Scheme 1).

CONCLUSIONS

Five novel complexes incorporating the (*rac*)-BIPHEN ligand have been characterized in the solid state and in hydrocarbon solution. We have prepared lithium (**1**) and lithium magnesiate (**2-4**) reagents. Complex **3** has been utilized in a metal-halogen exchange reaction with 2-bromopyridine to yield the magnesiated pyridyl-containing **5**, which is isolable and stable for at least several weeks. In the future, we will use this knowledge to prepare new metal-halogen exchange intermediates, using enantiopure ligands, and utilizing them in asymmetric addition reactions.

EXPERIMENTAL SECTION

General Procedures

All reactions were performed under a protective argon atmosphere using standard Schlenk techniques. Hexane and THF were dried by heating to reflux over sodium benzophenone ketyl and distilling the solvent under nitrogen prior to use. *n,n*-Dibutylmagnesium (1 M solution in heptane), *n*-butyllithium (1.6 M solution in hexanes) and (*rac*)-BIPHEN- H_2 were purchased from Sigma-Aldrich and used as received. $\text{Mg}(\text{CH}_2\text{SiMe}_3)_2$ and $\text{Mg}(\text{}^{neo}\text{Pe})_2$ were prepared according to literature

methods.²⁷ NMR spectra were recorded on a Bruker DPX 400 MHz spectrometer, operating at 400.13 MHz for ¹H, 100.62 MHz for ¹³C and 155.50 MHz for ⁷Li. Elemental analyses were attempted using a Perkin-Elmer 2400 elemental analyzer; however, due to the extreme air sensitivity of the compounds satisfactory analyses could not be obtained. Crystallographic data were measured with Oxford Diffraction instruments at 123K. Selected crystallographic and refinement parameters are given in Table 5. All structures were refined against all unique reflections and against F^2 to convergence with SHELX-97.³² Structures **1** to **4** feature disorder in THF ligands and in butyl groups (**2**) and SiMe₃ groups (**3**). In all cases these disordered groups were refined over two sites and each required restraints to be applied on both thermal parameters and on bond lengths. For crystallographic data in CIF or other electronic format, see CCDC reference numbers CCDC 1036562 to 1036566.

Synthesis of [(rac)-BIPHEN]Li₂(THF)₄·(THF) (1**).** (rac)-BIPHEN (0.35 g, 1 mmol) was dissolved in THF (5 mL) and cooled to 0°C for 15 minutes. At this stage ⁿBuLi (1.4 mL, 2 mmol) were added. After stirring for 1 hour, the solvent was removed *in vacuo* to give a pale yellow solid. The resulting solid was recrystallized from 15 mL of hot hexane. To aid crystallization, the resulting colorless solution was placed in a freezer operating at -35 °C, depositing a crop of colorless crystals (0.24 g, yield 47%). ¹H NMR (400.13 MHz, 298 K, d₈-THF): 1.33 (36H, s, C(CH₃)₃), 1.61 (12H, s, CH₃), 1.81-1.85 (16H, m, OCH₂CH₂, THF), 2.15 (12H, s, CH₃), 3.65-3.68 (16H, m, OCH₂CH₂, THF), 6.76 (4H, s, Ph). ¹³C{¹H} NMR (100.62 MHz, 298 K, d₈-THF): 16.61 (CH₃), 19.75 (CH₃), 25.42 (OCH₂CH₂, THF), 30.40 (C(CH₃)₃), 34.04 (C(CH₃)₃), 67.27 (OCH₂CH₂, THF), 118.33, 125.59, 131.32, 132.31, 133.75, 161.95 (Ph). ⁷Li NMR (155.50 MHz, 298 K, d₈-THF): δ -0.27.

Synthesis of [(rac)-BIPHEN]Li₂MgBu₂(THF)₃ (2**).** (rac)-BIPHEN (0.35 g, 1 mmol) was dissolved in hexane (10 mL) and cooled to 0°C for 15 minutes. At this stage ⁿBuLi (1.4 mL, 2 mmol) were added and the mixture was stirred for 1 hour. (ⁿBu)₂Mg (1 mL of a 1M solution in heptane, 1 mmol) was added and the resulting suspension was heated gently, affording a clear solution. Addition of THF (0.24 mL, 3 mmol) and cooling to -28°C resulted in the formation of clear colorless crystals of **2** (0.46 g, yield 65%). ¹H NMR (400.13 MHz, 298 K, d₈-THF): -1.73-1.16 (2H, m, MgCH₂), -0.90-0.83 (2H, m, MgCH₂), 0.75-0.80 (6H, m, Bu), 1.11-1.39 (8H, s, Bu), 1.42 (18H, s, C(CH₃)₃), 1.51 (6H, s, CH₃), 1.77-1.79 (12H, m, OCH₂CH₂, THF), 2.08 (6H, s, CH₃), 3.60-3.63 (12H, m, OCH₂CH₂, THF), 6.80 (4H, s, Ph). ¹³C{¹H} NMR (100.62 MHz, 298 K, d₈-THF): 9.01 (MgCH₂), 15.10 (CH₃), 18.06 (CH₃), 21.43 (CH₃), 27.27 (2 x CH₂), 32.27(C(CH₃)₃), 34.09 (OCH₂CH₂, THF), 36.20 (C(CH₃)₃), 69.15 (OCH₂CH₂, THF), 122.26, 127.09, 134.34, 134.64, 136.26, 161.97 (Ph). ⁷Li NMR (155.50 MHz, 298 K, d₈-THF): δ 1.41.

Synthesis of [(rac)-BIPHEN]Li₂Mg(CH₂SiMe₃)₂(THF)₃ (3**).** (rac)-BIPHEN (0.35 g, 1 mmol) was dissolved in hexane (10 mL) and cooled to 0°C for 15 minutes. At this stage ⁿBuLi (1.4 mL, 2 mmol) were added and the mixture was stirred for 1 hour. (CH₂SiMe₃)₂Mg (0.2 g, 1 mmol) was then added, and the resulting suspension was heated gently, affording a clear colorless solution. Addition of THF (0.24 mL, 3 mmol) and slow cooling of a warm solution resulted in the formation of

clear colorless crystals of **3** (0.64 g, yield 82%). ¹H NMR (400.13 MHz, 298 K, C₆D₁₂): -2.31 (2H, m, MgCH₂Si(CH₃)₃), -1.65 (2H, m, MgCH₂Si(CH₃)₃), -0.02 (18H, s, Si(CH₃)₃), 1.45 (18H, s, C(CH₃)₃), 1.61 (6H, s, CH₃), 1.72-1.76 (12H, m, OCH₂CH₂, THF), 2.14 (6H, s, CH₃), 3.50-3.54 (12H, m, OCH₂CH₂, THF), 6.92 (2H, s, Ph). ¹³C{¹H} NMR (100.62 MHz, 298 K, C₆D₁₂): -9.74 (SiCH₂), 3.04 (Si(CH₃)₃), 16.04 (CH₃), 19.53 (CH₃), 25.16 (OCH₂CH₂, THF), 30.39 (C(CH₃)₃), 34.39(C(CH₃)₃), 67.63 (OCH₂CH₂, THF), 121.42, 126.07, 131.32, 132.29, 135.33, 158.97 (Ph). ⁷Li NMR (155.50 MHz, 298 K, d₈-THF): δ -0.18.

Synthesis of [(rac)-BIPHEN]Li₂Mg(^{neo}Pe)₂(THF)₂ (4**).** (rac)-BIPHEN (0.35 g, 1 mmol) was dissolved in hexane (10 mL) and cooled to 0°C for 15 minutes. At this stage ⁿBuLi (1.4 mL, 2 mmol) were added and the mixture was stirred for 1 hour. (^{neo}Pe)₂Mg (0.16 g, 1 mmol) was added and the resulting suspension was heated gently, affording a clear solution. Addition of THF (0.16 mL, 2 mmol) and slow cooling resulted in the formation of clear colorless crystals of **4** (0.25 g, yield 36%). ¹H NMR (400.13 MHz, 298 K, cyc-C₆D₁₂): -1.10 (2H, d, ³J_{HH} = 15Hz, MgCH₂), -0.13 (2H, d, ³J_{HH} = 15Hz, MgCH₂), 1.03 (18H, s, C(CH₃)₃), 1.44 (18H, s, C(CH₃)₃), 1.61 (6H, s, CH₃), 1.73-1.76 (12H, m, OCH₂CH₂, THF), 2.13 (6H, s, CH₃), 3.50-3.54 (12H, m, OCH₂CH₂, THF), 6.91 (4H, s, Ph). ¹³C{¹H} NMR (100.62 MHz, 298 K, cyc-C₆D₁₂): 16.12 (CH₃), 19.53 (CH₃), 25.17 (OCH₂CH₂, THF), 25.51 (2×MgCH₂), 30.14(C(CH₃)₃), 32.34 (C(CH₃)₃), 34.49 (C(CH₃)₃), 67.53 (OCH₂CH₂, THF), 121.01, 126.18, 130.97, 132.43, 135.55, 159.34 (Ph). ⁷Li NMR (155.50 MHz, 298 K, C₆D₁₂): δ 0.07.

Synthesis of [(rac)-BIPHEN]Li₂Mg(2-pyridyl)₂(THF)₂ (5**).** (rac)-BIPHEN (0.35 g, 1 mmol) was dissolved in hexane (10 mL) and cooled to 0°C for 15 minutes. At this stage ⁿBuLi (1.4 mL, 2 mmol) were added and the mixture was stirred for 1 hour. (ⁿBu)₂Mg (1 mL of a 1M solution in heptane, 1 mmol) was added at this point. The solution was then cooled to -60 °C with an external liquid nitrogen cooled isopropanol cold bath, before the addition of 2-bromopyridine (0.095 mL, 1 mmol). This resulted in the formation of a pale orange suspension. The mixture was allowed to reach ambient temperature slowly. Addition of THF (0.16 mL, 2 mmol), followed by gentle heating and then slow cooling of the solution, resulted in the formation of colorless crystals of **5** (0.32 g, yield 47%; 94% based on 2-bromopyridine consumption). An alternative stoichiometric synthesis could be achieved by reacting isolated crystals of [(rac)-BIPHEN]Li₂Mg(CH₂SiMe₃)₂(THF)₃ (**3**) (0.78 g, 1 mmol) with 2-bromopyridine (0.19 mL, 2 mmol) at -60°C. After slowly warming to ambient temperature, THF (0.16 mL, 2 mmol) was added, which resulted in the precipitation of a white suspension. The solution was heated strongly to produce a deep orange solution. To aid the crystallization the resulting solution was placed in the freezer operating at -35 °C, which deposited a crop of yellow crystals (0.46 g, yield 66%). ¹H NMR (400.13 MHz, 298 K, d₈-THF): 1.26 (18H, s, C(CH₃)₃), 1.76 (6H, s, CH₃), 1.79-1.82 (8H, m, OCH₂CH₂, THF), 2.16 (6H, s, CH₃), 3.63-3.67 (8H, m, OCH₂CH₂, THF), 6.69-6.73 (2H, m, Ar), 6.79 (2H, s, Ph), 7.06-7.10 (2H, m, Ar), 7.57 (2H, d, ³J_{HH} = 7.6 Hz, Ar), 8.24 (2H, d, ³J_{HH} = 5.2 Hz, Ar). ¹³C{¹H} NMR (100.62 MHz, 298 K, d₈-THF): 16.02 (CH₃), 19.24 (CH₃), 25.00 (OCH₂CH₂, THF), 30.33 (C(CH₃)₃), 33.88 (C(CH₃)₃), 66.86 (OCH₂CH₂, THF), 117.06 (Ar), 120.49, 125.52, 128.45 (Ph), 131.79 (Ar), 132.05, 134.50 (Ph),

135.23, 145.99 (Ar), 159.57 (Ph), 214.7 (Ar). ^7Li NMR (155.50 MHz, 298 K, d_8 -THF): δ 0.65.

ASSOCIATED CONTENT

Supporting Information

Tables, figures and CIF files giving crystallographic results, details of ^1H DOSY NMR studies, and NMR spectra. This material is available free or charge via the Internet at <http://pubs.acs.org>.

AUTHOR INFORMATION

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

We gratefully acknowledge the support of the EPSRC (J001872/1 and L001497/1) for the award of a Career Acceleration Fellowship to CTOH. The CNRS and French Ministry of Research are also thanked. We also thank Professor Robert Mulvey (Strathclyde) for thoughtful discussions.

DEDICATION

In memory of Professor Michael Lappert, a pioneer and inspirational figure in the field of organometallic chemistry.

REFERENCES

- (1) Mulvey, R. E.; Mongin, F.; Uchiyama, M.; Kondo, Y. *Angew. Chem., Int. Ed.* **2007**, *46*, 3802.
- (2) Haag, B.; Mosrin, M.; Ila, H.; Malakhov, V.; Knochel, P. *Angew. Chem., Int. Ed.* **2011**, *50*, 9794.
- (3) Mulvey, R. E. *Acc. Chem. Res.* **2009**, *42*, 743.
- (4) Tilly, D.; Chevallier, F.; Mongin, F.; Gros, P. *C. Chem. Rev.* **2014**, *114*, 1207.
- (5) Martínez-Martínez, A. J.; Kennedy, A. R.; Mulvey, R. E.; O'Hara, C. T. *Science* **2014**, *346*, 834.
- (6) Iida, T.; Wada, T.; Tomimoto, K.; Mase, T. *Tetrahedron Lett.* **2001**, *42*, 4841.
- (7) Inoue, A.; Kitagawa, K.; Shinokubo, H.; Oshima, K. *J. Org. Chem.* **2001**, *66*, 4333.
- (8) Richey, H. G.; Destephano, J. P. *J. Org. Chem.* **1990**, *55*, 3281.
- (9) Chubb, J. E.; Richey, H. G. *Organometallics* **2002**, *21*, 3661.
- (10) Farkas, J.; Stoudt, S. J.; Hanawalt, E. M.; Pajerski, A. D.; Richey, H. G. *Organometallics* **2004**, *23*, 423.
- (11) Fleming, F. F.; Gudipati, S.; Vu, V. A.; Mycka, R. J.; Knochel, P. *Org. Lett.* **2007**, *9*, 4507.
- (12) Fleming, F. F.; Gudipati, V.; Steward, O. W. *Org. Lett.* **2002**, *4*, 659.
- (13) Noyori, R.; Suga, S.; Kawai, K.; Okada, S.; Kitamura, M. *Pure Appl. Chem.* **1988**, *60*, 1597.
- (14) Catel, D.; Payen, O.; Chevallier, F.; Mongin, F.; Gros, P. C. *Tetrahedron* **2012**, *68*, 4018.
- (15) Dayaker, G.; Tilly, D.; Chevallier, F.; Hilmersson, G.; Gros, P. C.; Mongin, F. *Eur. J. Org. Chem.* **2012**, 6051.
- (16) Payen, O.; Chevallier, F.; Mongin, F.; Gros, P. C. *Tetrahedron-Asymmetry* **2012**, *23*, 1678.
- (17) Clegg, W.; Liddle, S. T.; Snaith, R.; Wheatley, A. E. H. *New J. Chem.* **1998**, 1323.
- (18) Gregory, K.; Schleyer, P. V.; Snaith, R. *Adv. Inorg. Chem.* **1991**, *37*, 47.
- (19) Mulvey, R. E. *Chem. Soc. Rev.* **1991**, *20*, 167.
- (20) Francos, J.; Fleming, B. J.; Garcia Alvarez, P.; Kennedy, A. R.; Reilly, K.; Robertson, G. M.; Robertson, S. D.; O'Hara, C. T. *Dalton Trans.* **2014**, *43*, 14424.
- (21) Garcia-Alvarez, P.; Kennedy, A. R.; O'Hara, C. T.; Reilly, K.; Robertson, G. M. *Dalton Trans.* **2011**, *40*, 5332.
- (22) Baillie, S. E.; Clegg, W.; Garcia-Alvarez, P.; Hevia, E.; Kennedy, A. R.; Klett, J.; Russo, L. *Organometallics* **2012**, *31*, 5131.
- (23) Kuppuswamy, S.; Bezpalko, M. W.; Powers, T. M.; Turnbull, M. M.; Foxman, B. M.; Thomas, C. M. *Inorg. Chem.* **2012**, *51*, 8225.
- (24) García, F.; Less, R. J.; McPartlin, M.; Michalski, A.; Mulvey, R. E.; Naseri, V.; Stead, M. L.; Morán de Vega, A.; Wright, D. S. *Chem. Commun.* **2011**, *47*, 1821.
- (25) Elschenbroich, C.; Lu, F.; Burghaus, O.; Pietzonka, C.; Harms, K. *Chem. Commun.* **2007**, 3201.
- (26) Duer, M. J.; García, F.; Goodman, J. M.; Hehn, J. P.; Kowenicki, R. A.; Naseri, V.; McPartlin, M.; Stead, M. L.; Stein, R.; Wright, D. S. *Chem. Eur. J.* **2007**, *13*, 1251.
- (27) Rosa, P.; Mezailles, N.; Ricard, L.; Mathey, F.; Le Floch, P.; Jean, Y. *Angew. Chem. Int. Ed.* **2001**, *40*, 1251.
- (28) Pauls, J.; Neumüller, B. *Inorg. Chem.* **2001**, *40*, 121.
- (29) Viehhaus, T.; Walz, A.; Niemeyer, M.; Schwarz, W.; Weidlein, J. Z. *Anorg. Allg. Chem.* **2000**, *626*, 2040.
- (30) Cheung, M.-S.; Chan, H.-S.; Xie, Z. *Organometallics* **2004**, *23*, 517.
- (31) Armstrong, D. R.; Crosbie, E.; Hevia, E.; Mulvey, R. E.; Ramsay, D. L.; Robertson, S. D. *Chem. Sci.* **2014**, *5*, 3031.
- (32) Sheldrick, G. M. *Acta Crystallogr.* **2008**, *64*, A112.