



Alkali-Metal-Mediated Magnesiations of an N-Heterocyclic Carbene: Normal, Abnormal, and “Paranormal” Reactivity in a Single Tritopic Molecule

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Abstract: Herein the sodium alkylmagnesium amide $[\text{Na}_4\text{Mg}_2(\text{TMP})_6(\text{nBu})_2]$ ($\text{TMP} = 2,2,6,6\text{-tetramethylpiperidide}$), a template base as its deprotonating action is dictated primarily by its 12 atom ring structure, is studied with the common N-heterocyclic carbene (NHC) IPr [1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene]. Remarkably, magnesiation of IPr occurs at the para-position of an aryl substituent, sodiation occurs at the abnormal C4 position, and a dative bond occurs between normal C2 and sodium, all within a 20 atom ring structure accommodating two IPr^{2-} . Studies with different K/Mg and Na/Mg bimetallic bases led to two other magnesiated NHC structures containing two or three IPr^- monoanions bound to Mg through abnormal C4 sites. Synergistic in that magnesiation can only work through alkali-metal mediation, these reactions add magnesium to the small cartel of metals capable of directly metalating a NHC.

Chemists often find fascination in synergistic systems, especially if the cooperativity can be usefully exploited in a practical application. Such effects are prominent in synthetic organometallic chemistry where two metals are involved.^[1] For example, elegant studies by Xi^[2] show that close proximity of two Li centers in 1,4-dilithio-1,3-butadienes can promote intra- and intermolecular reactions beyond the scope of monolithio systems. As a core tool in synthesis, metalation has advanced greatly in recent times through cooperative effects delivered, not by dimetallo dianions, but by combinations of different metal monoanion components.^[3] Knochel's salt boosted organometallic reagents,^[4] typified by $\text{TMPMgCl}\cdot\text{LiCl}$ ($\text{TMP} = 2,2,6,6\text{-tetramethylpiperidide}$), the use of which has recently been extended to continuous flow reactors,^[5] are exemplars of these multicomponent metalators. LiTMP lithiations can also be rendered synergistic by premixing the aromatic substrate with a salt (e.g., MgCl_2) so that sensitive lithiated substrates can be transmetalated rapidly (in situ trapping) to a more stable, more synthetically pliable form.^[6] Trans-metal-trapping with $[\text{iBu}_2\text{Al}(\text{TMP})]$ not only stabilizes LiTMP lithiated

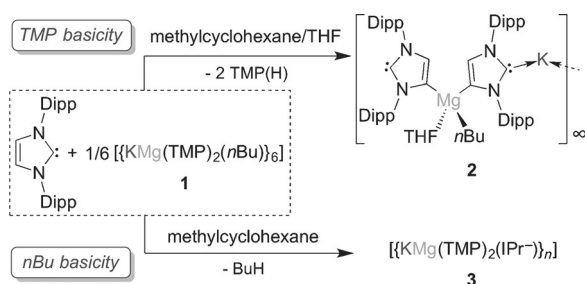
substrates but can shift equilibrium reactions towards the wanted product.^[7] Of special relevance in this work are pre-inverse-crowns,^[8] which are two-metal macrocyclic complexes whose deprotonating action is governed more by their template structures than by the substituents on the aromatic substrates. Thus the pre-inverse-crown $[\text{Na}_4\text{Mg}_2(\text{TMP})_6(\text{nBu})_2]$ can doubly deprotonate N,N-dialkylanilines and *tert*-butylbenzene selectively at the *meta,meta'* positions,^[9] and is in violation of directed *ortho*-metalation (DoM) principles.^[10] Here, in reporting the first metalation study between pre-inverse-crowns and N-heterocyclic carbenes (NHCs), we describe the first directly magnesiated NHCs at positions both expected and wholly unexpected.

NHC metalation (C–H to C–metal exchange) is a relatively recent development within the fast-growing NHC literature.^[11] Robinson and co-workers made a seminal breakthrough in 2010 by deprotonating IPr [1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene] at C4 (alkenic backbone) with nBuLi ^[12] to open up an abnormal construction point for functionalization. Waters and Goicoechea subsequently synthesized the potassium congener of this lithium carbanionic NHC by metathesis with *t*BuOK to use in ligand-transfer applications.^[13] Bertrand and co-workers achieved C4-functionalization by a different approach, that is, by making imidazolium IPr cations with the C2-position blocked by E substituents [$\text{E} = \text{e.g., PhC(O), PPh}_2$], which intramolecularly rearrange to a C4–E species upon deprotonation by KHMDs .^[14] Both indirect (by Robinson's lithiated NHC and Et_2Zn)^[15] and direct (by Hevia's sodium TMP-zincate reagent)^[16] methods of zincating IPr at C4 have also been reported. An unusual amido-directed lateral lithiation of a $\text{CH}(\text{Me})_2$ wingtip on a Dipp (diisopropylphenyl) group in a 4-amido NHC has recently been described by Braunstein and co-workers.^[17]

In this work, IPr was directly magnesiated by the pre-inverse-crown $[\{\text{KMg}(\text{TMP})_2(\text{nBu})_6\}]$ (**1**) in methylcyclohexane/THF to afford the bis(carbene) magnesiate $[\{\text{KMg}(\text{IPr})_2(\text{nBu})(\text{THF})\}_\infty]$ (**2**; Scheme 1, where IPr^- is $[\text{C}\{\text{N}(2,6\text{-iPr}_2\text{C}_6\text{H}_3)_2\}\text{CHC}^-]$). Interestingly this reaction is not a template metalation. When **1** acts as a template base, for example towards naphthalene, its six *n*Bu ligands are substituted by six 2-naphthalenide anions (*n*-butane is expelled) with retention of its 24-atom $(\text{KNMgN})_6$ ring architecture.^[8] In contrast, in making **2**, **1** acts formally as an amido dibase while retaining an *n*Bu group. The dibasicity of **1** can be inferred but the moderate yield of **2** (absolute 20%; with respect to IPr, 40%) and the failure to increase the yield on

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Scheme 1. Solvent-dependent reactions of IPr with **1**. Synthesis of $[\{KMg(IPr)_2(nBu)(THF)\}_\infty]$ (**2**) and $[\{KMg(TMP)_2(IPr)\}_n]$ (**3**). THF = tetrahydrofuran.

adding more IPr suggests a redistribution process is more likely starting from the putative $[KMg(IPr^-)(TMP)(nBu)]$, though the key point is, irrespective of **1** being a mono- or diamido base, *n*Bu is retained. The groups of Robinson and Goicoechea have reported related redistribution processes with anionic NHCs of Zn^[15] and Mn,^[18] respectively. The crystalline **2** was also fully characterized by NMR spectroscopy in $[D_8]THF$ solution.^[19] A 2:1 ratio for IPr^- and *n*Bu ligands is observed in the ¹H NMR spectrum and is in agreement with the formulation of **2**. The $CH(CH_3)_2$ fragments of the Dipp groups resonate as two distinct sets of signals in the ¹H and ¹³C NMR spectra as a result of the symmetry loss in IPr^- . The symmetry loss, as a result of the metalation in the backbone of the imidazole ring, is also mirrored by a large downfield resonance at $\delta = 156.4$ ppm in the ¹³C NMR spectrum for the Mg–C4 fragment ($\delta = 122.5$ ppm in the free IPr). In addition, the resonance assigned to the carbonic C2 is shifted upfield ($\delta = 214.1$ ppm) compared to that observed in free IPr ($\delta = 221.1$ ppm), thus reflecting the formation of an NHC complex with potassium. A fluxional process at room temperature makes equivalent the dative $C2 \rightarrow K$ interaction on both IPr^- fragments, hence explaining the single resonance for C2. More significantly, a unique broad singlet is observed for the two imidazole CH moieties at $\delta = 4.96$ ppm, and is dramatically upfield to that in free IPr ($\delta = 7.20$ ppm) and previous C4-metalated examples (range: $\delta = 6.07$ – 6.66 ppm).^[12–13,16] This unexpected shielding of the imidazole CH in **2** correlates with the upfield resonances for the *para* and *meta* CH groups (at $\delta = 6.43$ and 6.86 ppm, respectively) of one of two inequivalent Dipp groups. This effect can be explained by a close intramolecular spatial proximity between the imidazole CH of one IPr^- and a Dipp ring from the second IPr^- moiety (and vice versa), and results in an overall mutual shielding by anisotropic effects. THF could be a factor in the lack of a template effect in the metalation as this lone-pair donor can compete for metal coordination sites and deaggregate the $(KNMgN)_6$ 24 atom ring structure. Significantly donor-solvated potassium magnesiate $[(PMDTA)KMg(TMP)_2(CH_2SiMe_3)]$ is known to deprotonate aromatic substrates kinetically through TMP.^[20] The crystalline **2** exhibits an infinite, zig-zag chain structure (Figure 1). Mg occupies a distorted tetrahedral (C_3O) anionic site comprising two distinct C4-deprotonated IPr^- groups, one *n*Bu, and one THF ligand. Alternating with anionic moieties along the chain, K^+ bridges two normal IPr^- sites (C1 and

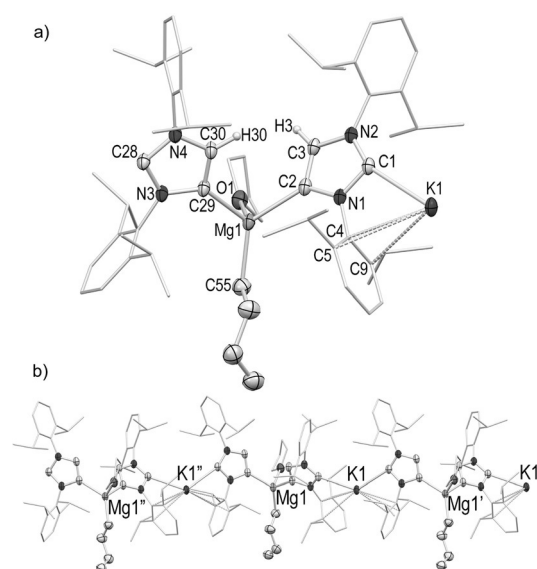


Figure 1. a) Molecular structure of $[\{KMg(IPr)_2(nBu)(THF)\}_\infty]$ (**2**),^[23] showing the contents of the asymmetric unit, which corresponds to a single turn of the zig-zag chain. Displacement ellipsoids are displayed at 35% probability. Hydrogen atoms (except H3 and H30) and disordered components for *n*Bu and *i*Pr groups are omitted for clarity. Dipp and THF groups are pictured as capped sticks for clarity. The dashed lines illustrate $K \cdots C(aryl)$ contacts. b) Section of the extended framework structure showing atom connectivity between normal C2 (C1 and C28) sites and K, and both abnormal C4 (C2 and C29) and *n*Bu ligand to Mg.

C28': mean bond length, 2.87 Å) and engages in longer $K-\eta^3C_6$ π -arene interactions with one Dipp substituent on each IPr^- at *ipso*, *ortho*, and *meta* sites [length range: 3.029(2)–3.406(3) Å]. Repeating the reaction without THF (Scheme 1) gave only an oily mixture from which a brown solid was extracted. Though this product could not be obtained as single crystals, NMR characterization in $[D_8]THF$ solution^[19] is consistent with a single compound of empirical formula $[\{KMg(TMP)_2(IPr)\}_n]$ (**3**), where IPr is deprotonated at C4.^[21] Most compelling is that the ¹H DOSY NMR^[22] data of **3** in $[D_8]THF$ confirm a single monomeric version of **3** $[(D_8]THF)_3KMg(IPr^-)(TMP)_2]$.^[19] Significantly, this formulation is consistent with a template metalation through *n*Bu basicity (butane loss), thus matching other reactions of **1** in non-donor media. This implies that here IPr acts as a C–H substrate as opposed to a donor, since donor IPr synergic metalations usually show TMP basicity [TMP(H) loss] as evidenced by the TMP zincate study by Hevia and co-workers.^[16]

The sodium magnesiate $[(TMEDA)NaMg(TMP)_2(nBu)]$ ^[24] (**4**) reacted with IPr in a 1:1 stoichiometry in *n*-hexane and after a crystallization process in *n*-hexane/THF, the tris(mononionic) carbene $[(THF)_3Na(\mu-IPr^-)Mg(THF)(IPr^-)_2]$ was isolated (**5**; Figure 2). Our NMR studies point to a complicated ligand redistribution process in forming **5** (Scheme 2) when THF is present in the reaction media.^[19] When **4** was subjected to IPr in a 1:3 molar ratio in *n*-hexane a similar compound to **2**, of empirical formula $[(THF)NaMg(IPr^-)_2(nBu)]$ (**6**; Scheme 2), was isolated and characterized

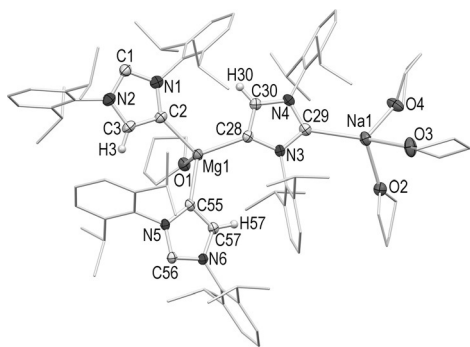
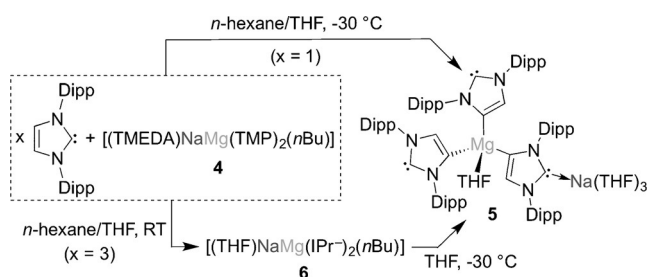


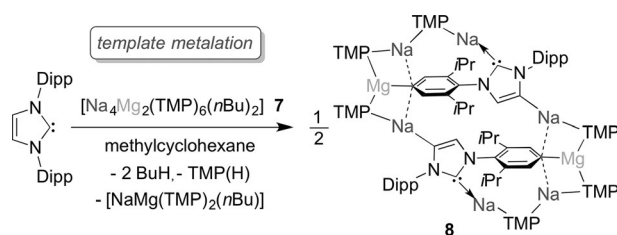
Figure 2. Molecular structure of $[(\text{THF})_3\text{Na}(\mu\text{-IPr}^-)\text{Mg}(\text{THF})(\text{IPr}^-)_2]$ (**5**).^[23] Displacement ellipsoids are displayed at 35% probability. Hydrogen atoms (except H3, H30, and H57) and disordered components for one THF molecule and one IPr group are omitted for clarity. Dipp and THF groups are pictured as capped sticks for clarity.



Scheme 2. Synthesis of $[(\text{THF})_3\text{Na}(\mu\text{-IPr}^-)\text{Mg}(\text{THF})(\text{IPr}^-)_2]$ (**5**) and $[(\text{THF})\text{NaMg}(\text{IPr}^-)_2(n\text{Bu})]$ (**6**).

by NMR spectroscopy. ^1H NMR data of **6** in $[\text{D}_8]\text{THF}$ solution show a singlet for the imidazole CH at $\delta = 6.30$ ppm, two discrete resonance sets for the Dipp groups, and a characteristic MgCH_2 signal at $\delta = -1.25$ ppm for the *n*Bu group. Abnormal C4 exhibits a resonance at $\delta = 161.0$ ppm in the ^{13}C NMR spectrum, and is in agreement with that seen in **2**. Similarly, the formation of the crystalline **5** was observed when **6** was dissolved in *n*-hexane/THF, thus reinforcing the idea of a ligand-induced redistribution phenomena in forming **5**. The discrete contacted ion pair structure of **5** has a distorted tetrahedral tris(THF)-solvated Na^+ bound to a carbenic C2 [Na1-C29 , 2.492(4) Å], as previously seen in the zincate $(\text{THF})_3\text{Na}[\text{C}\{\text{N}(2,6\text{-}i\text{Pr}_2\text{C}_6\text{H}_3)_2\}\text{CHCZn}(t\text{Bu})_2]$.^[16] However, the counter anion is unique, thus exhibiting a distorted tetrahedral Mg, bound to one THF molecule and the C4-positions of three IPr^- ligands and, two terminal and one bridging to Na. Homoleptic metal complexes containing three anionic NHC ligands are extremely rare.^[25]

The most extraordinary result came upon subjecting IPr to the pre-inverse-crown $[\text{Na}_4\text{Mg}_2(\text{TMP})_6(n\text{Bu})_2]$ (**7**) in hydrocarbon media. An equimolar reaction (Scheme 3) produced the remarkable inverse crown $[\{\text{Na}_3\text{Mg}(\text{TMP})_3(\text{IPr}^{2-})\}_2]$ (**8**; IPr^{2-} : $[\text{C}\{\text{N}(2,6\text{-}i\text{Pr}_2\text{C}_6\text{H}_2\text{-}4)\text{N}(2,6\text{-}i\text{Pr}_2\text{C}_6\text{H}_3)\text{CHC}^-]\}$), which was isolated in a high (crystalline) yield of 72% (with respect to IPr, quantitative conversion determined by NMR spectroscopy). The formation of an inverse crown, the



Scheme 3. Template metalation of IPr with $[\text{Na}_4\text{Mg}_2(\text{TMP})_6(n\text{Bu})_2]$ (**7**), and formation of the inverse crown $[\{\text{Na}_3\text{Mg}(\text{TMP})_3(\text{IPr}^{2-})\}_2]$ (**8**).

absence of *n*Bu in its formula, and the fact that the bulk solvent was donor-free, collectively signal a template, or at least partial template metalation. Byproducts of butane, $\text{TMP}(\text{H})$, and $[\text{NaMg}(\text{TMP})_2(n\text{Bu})]$ would balance the reaction equation.

Figure 3 shows the discrete structure of one of two crystallographically unique molecules of **8**. Inverse crowns

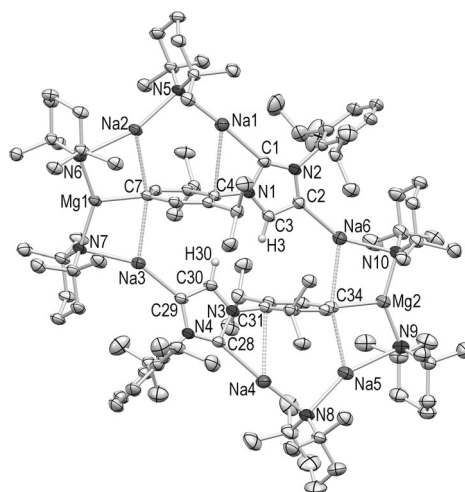
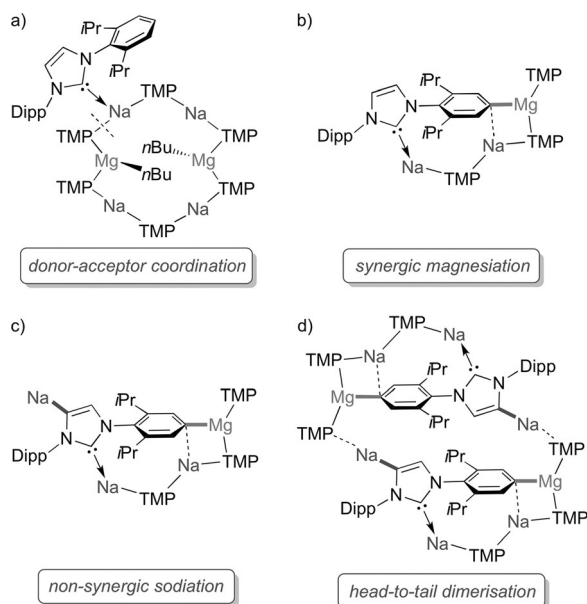


Figure 3. Molecular structure of the inverse crown $[\{\text{Na}_3\text{Mg}(\text{TMP})_3(\text{IPr}^{2-})\}_2]$ (**8**).^[23] showing one of the two crystallographically independent molecules. Displacement ellipsoids are displayed at 35% probability. Hydrogen atoms (except H3 and H30) and methylcyclohexane molecules of crystallization are omitted for clarity. The dashed lines illustrate $\text{Na}\cdots\text{C}(\text{aryl})$ contacts.

are defined by an outer polymetallic cationic ring charge balanced by an inner anionic moiety.^[26] Each dimer of **8** displays a 20 atom $[(\text{NaMgNNaCNCN})_2]^{2+}$ ring, which encapsulates two IPr^{2-} dianions, but since one each of their negatively charged atoms (C2 and C29) lies within the ring wall the inner cavity carries only a 2– charge through C7 and C34 of the Dipp substituents. Thus the number of inner carbanion sites matches the number of outer-ring Mg atoms (through C7–Mg1; C34–Mg2), and is a signature feature of inverse crowns.^[26] From an NHC perspective, IPr datively binds to Na through its normal C2 position (C1–Na1, C28–Na4), and is metalated by a second Na at its abnormal C4 (C2–Na6, C29–Na3), the ones nearest the intact Dipp groups, and by Mg at the *para* (paranormal) position of the other Dipp groups (C7–Mg1, C34–Mg2). Among many

unique features, **8** represents the first crystallographically characterized sodium anionic carbene, whereas the simple C4-sodiated Na^+IPr^- exists as an insoluble, presumably polymeric solid.^[19] Based on well-established metalation patterns a pathway of intermediates leading to **8** can be proposed (Scheme 4). Being an excellent σ -donor, IPr would



Scheme 4. Proposed four key stages (a–d) in the formation of the new inverse crown **8**, starting from IPr and **7**.

initially coordinate to the more exposed acceptor Na in the pre-inverse-crown leading to template cleavage. Complexes of type $[(\text{donor})\text{NaMg}(\text{TMP})_2(n\text{Bu})]$ are common.^[24] Pre-inverse-crowns invariably magnesiate through $n\text{Bu}$ basicity so part of the template attached to C2, through Na, could execute the *para*-aryl magnesiation.^[27] However, given the extended length of emergent IPr^- with respect to substituted benzene substrates, this magnesiation is likely to be accompanied by template fragmentation as its 12 atom ring would be too small to circumnavigate IPr^- . The hemi-inverse-crown $[\text{Na}_2\text{Mg}(\text{TMP})_3(\text{IPr}^-)]$ could result, hence stabilizing the anionic carbene by both a *para*-aryl C–Mg and normal C2→Na bond. A test reaction between **7** and IPr in a 1:2 stoichiometry showed that the metalation could not be stopped at the $[\text{Na}_2\text{Mg}(\text{TMP})_3(\text{IPr}^-)]$ but proceeded to form **8**, as observed by NMR spectroscopy, thus implying that a cascade reaction is operative.^[19] Related motifs are known when sodium TMP magnesiates deprotonate heterocyclic substrates such as tetrahydrothiophene, thus leading to C–Mg and heteroatom–metal dative bonds (e.g., $\text{S} \rightarrow \text{Na}$).^[28] In theory, the byproducts could be $[\text{NaMg}(\text{TMP})_2(n\text{Bu})]$ and NaTMP, or alternatively, $[\text{NaMg}(\text{TMP})_3]$ and $n\text{BuNa}$, or a mixture of both pairs. Conventional Group 1 bases target abnormal C4 sites (recall Robinson's $n\text{BuLi}$ reaction) so either NaTMP or $n\text{BuNa}$ could effect a second deprotonation at C4 (i.e., C2 and C29 in **7**) to generate dianionic IPr^{2-} . Since $n\text{Bu}$ is attached to Mg in the template, NaTMP seems the

more logical candidate for this sodiation, a choice reinforced by a control reaction between NaTMP and IPr, which upon Me_3SiCl quenching gave near-quantitative Me_3Si incorporation at C4.^[19] Head-to-tail dimerization through N10–Na6 and N7–Na3 bonds involving TMP would complete the structure of **8**. A notable metric feature of **8** is that the N5–Na1–C1 and N8–Na4–C28 bond angles involving normal C2 atoms (mean, 174.4°) approach linearity, whereas N10–Na6–C2 and N7–Na3–C29 involving abnormal C4 are distinctly bent (mean, 154.3°). Aside from bridging two TMP N atoms, Na2, Na3, Na5, and Na6 interact with paranoormal magnesiated C7 and C34 (mean length $2.74 \text{ \AA}$), while bridging TMP N and carbene C2 atoms, Na1, and Na4 engage in longer contacts with Dipp *ipso* C4/C31 atoms (mean length, $2.92 \text{ \AA}$). Mg atoms have distorted trigonal-planar (N_2C) coordination. NMR characterization of **8** in $[\text{D}_{12}]\text{cyclohexane}$ solution^[19] revealed a singlet at $\delta = 6.41 \text{ ppm}$ in the ^1H spectrum for the remaining imidazole CH, which is slightly upfield to that of free IPr ($\delta = 6.87 \text{ ppm}$), and an extraordinary downfield resonance for sodiated C4 in the ^{13}C spectrum ($\delta = 170.4 \text{ ppm}$ in **8**; reference $\delta = 121.6 \text{ ppm}$ in free IPr). A resonance for the carbenic C2 at $\delta = 200.2 \text{ ppm}$ in the ^{13}C spectrum confirms the dative $\text{C2} \rightarrow \text{Na}$ bond in **8**. Reflecting not only the loss of symmetry in the IPr^{2-} moiety but also the metalation in the *para* position of one Dipp group, two distinct sets of resonances are present for the Dipp groups in the ^1H and ^{13}C spectra. Two different signals are seen at $\delta = 2.79$ and 2.91 ppm for the CH of the *iPr* groups in the ^1H NMR spectrum, and more informative, is that a unique downfield singlet at $\delta = 7.67 \text{ ppm}$ appears for the two equivalent *meta*-CH moieties of the metalated Dipp aromatic ring (nonmetalated aromatic CH of the Dipp group, $\delta = 7.00$ – 7.12 ppm). Also, the paranoormal magnesiated Dipp C exhibits an extreme downfield resonance in the ^{13}C NMR spectrum ($\delta = 167.3 \text{ ppm}$ in **8** relative to the typical Dipp resonances of 122.8 – 146.7 ppm).

In summary, while this study set out to introduce Mg to the cartel of metals which can directly metalate a NHC, an aim duly realized in both predictable and unpredictable ways, it has taken on greater significance with recognition that pre-inverse-crown template bases can undergo remarkable reactions with mismatched substrates, which are sterically incompatible with the ring template.

Experimental Section

Full experimental details and copies of ^1H and ^{13}C NMR spectra are included in the Supporting Information. CCDC 1417920 (**2**), 1417921 (**5**), and 1417922 (**8**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

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