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Polar Organometallic Strategies for Regioselective C-H Metallation of N-Heterocyclic Carbenes

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N-heterocyclic carbenes (NHCs) have become indispensable ligands across a broad swathe of the synthetic and catalytic landscape, not in small part due to their ease of electronic and steric tuneability. One of the latest additions to this important family of ligands are anionic NHCs, which have become valuable precursors to access abnormal NHC complexes as well as shown great potential for further NHC functionalisation. Deprotonative metallation has emerged as one of the most versatile methodologies to access anionic NHCs, where judicious choice of reaction conditions and metallating agent can finely tune the regioselectivity of the reaction. This Feature Article focuses on the recent emergence of s-block metal-mediated NHC metallations and the new opportunities this methodology offers.

Introduction

Deprotonative metallation, where a non-polar C-H bond is transformed into a more reactive C-Metal bond by a metallating reagent, is one of the most fundamental and widely applied chemical transformations in synthesis.¹ This is best illustrated by the ubiquitous utility of directed-*ortho*-metallation (DoM),² the seminal concept in polar organometallic chemistry pioneered independently by Gilman³ and Wittig,⁴ which matches or arguably surpasses classic aromatic electrophilic substitution as the most powerful strategy for the regioselective functionalization of aromatic rings. Organolithium compounds and lithium amides have been unrivalled for many decades in performing these metallation transformations, although sometimes their reactivity is too high and can compromise their regioselectivity and functional group tolerance. Overcoming some of these limitations, a new generation of metallating agents has emerged, made up by multimetallic mixtures, which combine metals of markedly different electronegativities (that in

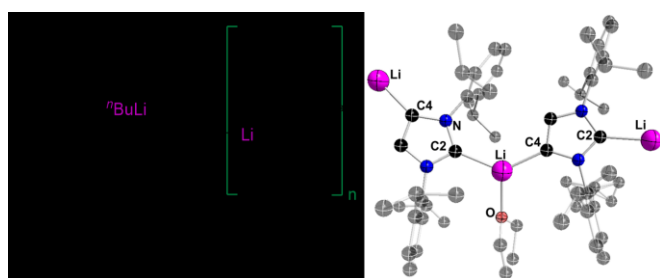
turn produce markedly different bond polarities) such as a group 1 metal paired with Mg, Al or Zn, to name just a few.^{1b,5} While research activity on the metallation of aromatic and heteroaromatic scaffolds has been very intense, the untapped potential that this synthetic tool offers for the functionalization of N-heterocyclic carbenes (NHCs) has only begun to be tapped into recently. Despite the important applications of these increasingly popular ligands, and the fact that modifications on their substituents (either in their imidazole backbone or those substituents attached to the N atoms) can finely tune their steric and electronic properties,⁶ it was only in 2010 that the first lithiation of a free N-heterocyclic carbene was reported by Robinson in a seminal paper on the reactivity of unsaturated **IPr** (**IPr** = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene) with ^tBuLi.⁷ Prior to this work, studies by Arnold on treating amido-tethered NHC lanthanide complexes with potassium naphthalenide had already established that regiospecific deprotonation of an NHC backbone can be accomplished, furnishing heterobimetallic systems where the generated anionic carbene acts as bridge between the two metals.⁸ Building on these landmarks, the chemistry of anionic NHCs has thrived over the past few years, finding numerous applications in transition metal catalysis and main group metal chemistry. Thus, along with deprotonative metallation, other methods have emerged to access these ligand types, including chemical reduction and transition-metal mediated C-H bond activation.⁹ Reflecting the widespread interest that the growing family of anionic NHCs keeps attracting from the scientific community, the chemistry of these systems has already been summarized in two recent authoritative reviews.^{9,10} Approaching this area from a different perspective, considering our long-standing interest in polar organometallic reagents and their applications in metallation chemistry, here we survey the different metallating strategies that have recently been reported for accessing anionic NHCs.¹¹ Showcasing recent studies in the field, including some of our own work, this Feature article highlights the crucial role of the metallating agents employed for these metal-hydrogen exchange processes, which not only control the

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regioselectivity and efficiency of the reaction but also the stability and structure of the newly formed organometallic intermediates containing the anionic NHC fragments.

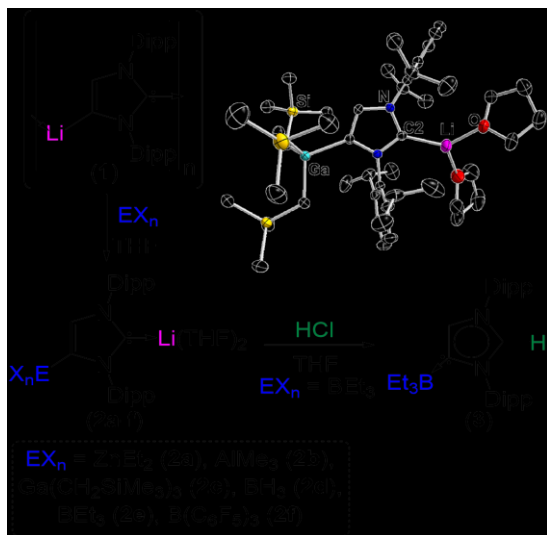
Single-metal s-block metallating agents

Stimulated by their relative stability, ease of preparation and high tunability, imidazol-2-ylidenes have been quickly established as one of the most widely used class of NHCs in synthesis.^{6a,6e} Deprotonation at the olefinic backbone of these carbenes can be accomplished in almost quantitative yields by using commercially available ⁿBuLi,⁷ as learned from Robinson for the C4-lithiation of **IPr** which affords $[\text{:C}\{\text{N}(2,6\text{-}^i\text{Pr}_2\text{C}_6\text{H}_3)\}_2\text{CHLi}\cdot\text{THF}]_n$ (**1**·THF) (Scheme 1).



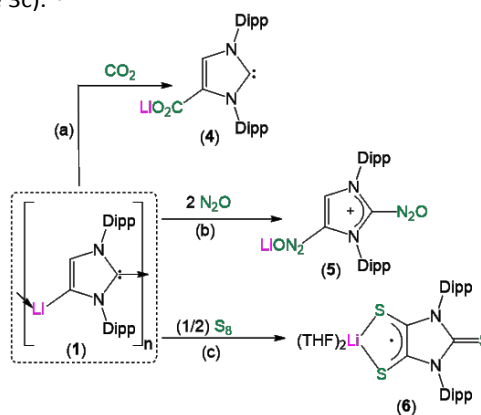
Scheme 1 Lithiation of **IPr** by ⁿBuLi to form $[\text{:C}\{\text{N}(2,6\text{-}^i\text{Pr}_2\text{C}_6\text{H}_3)\}_2\text{CHLi}\cdot\text{THF}]_n$ (**1**·THF) (left) and section of the polymeric structure of **1**·THF established by X-ray crystallography (right).⁷

Exhibiting a unique polymeric structure, where the $\{\text{Li}(\text{THF})\}$ cations are connected by anionic NHC bridges through their normal C2 and C4 (so-called abnormal) positions, **1** has become a versatile precursor for accessing anionic carbene complexes of main group elements such as B,^{7,12} Al,⁷ Ga,¹³ Zn¹⁴ or Sn¹⁵ amongst others (**2a-f**, Scheme 2). These reactions are driven by the stronger electronegative (carbophilic) character of the main group element, which undergoes fast transmetallation with **1** at its C4 position, with Li being trapped by coordination to its normal carbenic site (Scheme 2).



Scheme 2 Transmetalation reactions of **1** to main group element compounds, followed by selective quenching and formation of abnormal NHC main group element complexes. Inset: molecular structure of heteroleptic lithium gallate **2c** established by X-ray crystallography.¹³

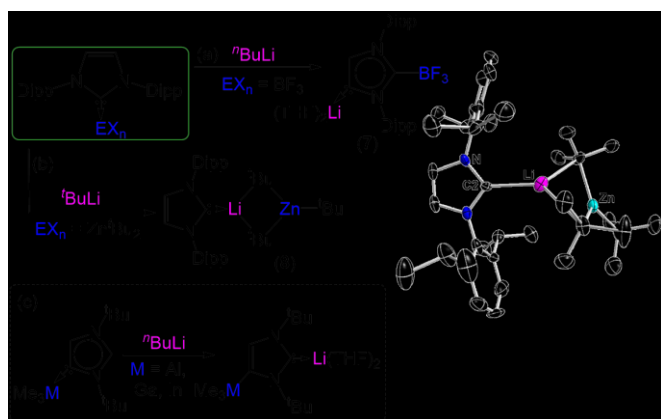
Interestingly some of these heteroleptic complexes react with electrophiles such as HCl, MeOH or MeOTf, by selective quenching at their C2 position, enabling isolation of several novel abnormal NHCs main group element complexes that until recently had remained elusive (as shown in Scheme 2 for **3** using BEt_3).^{7,13,14} Access to this new class of NHC complexes could be particularly relevant considering recent reports on the excellent catalytic activity of abnormal NHC complexes of organozinc and organoaluminium for ring opening polymerisation of rac-lactide, ϵ -caprolactone, δ -valerolactone.¹⁶ Alternatively, **1** can also promote small molecule activation processes by reacting with unsaturated substrates such as CO_2 or N_2O (Scheme 3). Thus **1** undergoes selective carboxylation at its C4 position, leaving the C2 position untouched (**4** in Scheme 3a),¹⁷ contrasting with reactivity previously described for free NHCs which insert CO_2 rapidly via their carbenic site.¹⁸ Fixation of the inert gas nitrous oxide has also been reported by Severin, with **1** forming a stable adduct with two equivalents of N_2O using both C2 and C4 sites (**5** in Scheme 3b).¹⁹ Sulfurization of **1** with elemental sulfur (in a 1:4 stoichiometry) gives a unique lithium salt of an anionic dithiolene radical (**6** in Scheme 3c) resulting from insertion of two S atoms into both Li-C bonds (i.e., at C2 and C4), and an unexpected C-H bond activation (**6** in Scheme 3c).²⁰



Scheme 3 Small molecule activation by **1** with a) CO_2 ,¹⁷ b) N_2O ¹⁹ and c) elemental sulfur.²⁰

Lithiation of NHC complexes has also been documented, although in those cases it seems that the reaction outcome is dictated by the strength of the element-C bond in these complexes. Thus, NHC-borane BX_3 ($\text{X} = \text{H}$,²¹ F ,²² Et ²³) complexes, where the carbene binds strongly to the BX_3 fragment, upon reaction with ⁿBuLi, undergo C4 lithiation at their NHC backbone, affording **7** with Li and B coordinated to the C4 and C2 positions of the anionic NHC, respectively (Scheme 4a).²¹⁻²³ Borate **7** can be envisaged as a reversed constitutional isomer of **2e** (Scheme 2), resulting from lithiation of free **IPr** and tandem addition of BX_3 ($\text{X} = \text{Et}$).⁷ Contrastingly, we have shown that for **IPr**· MR_n complexes [$\text{MR}_n = \text{Zn}^i\text{Bu}_2$,²⁴ $\text{Ga}(\text{CH}_2\text{SiMe}_3)_3$ ¹³] where the metal-C bonds are significantly elongated due primarily to the large steric bulk around the metal centre, reaction with RLi bases ($\text{R} = ^i\text{Bu}$, CH_2SiMe_3) favours co-complexation of the organometallic species. This forms the relevant lithium zincate and lithium gallate (**8** in Scheme 4b),

which is further stabilised by coordination of the carbene (the backbone of which has been left untouched) to the Li centre.

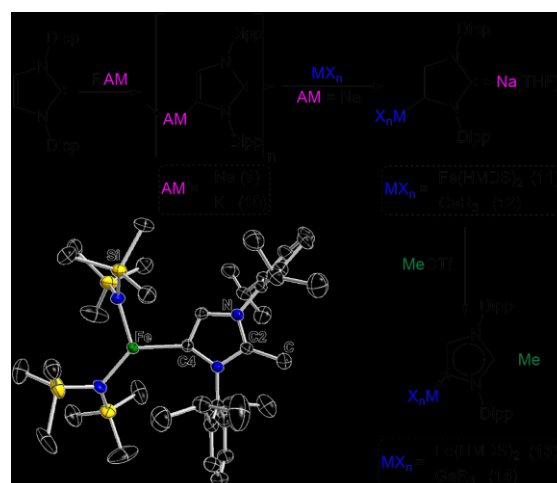


Scheme 4 Lithiation of NHC complexes: a) deprotonation of the backbone of NHC-borane complex; b) co-complexation of NHC-zinc complex with alkyl lithium affording lithium zincate; c) deprotonation of the abnormal *alPr*-EX₃ complex. Inset: structure of IPr-LiZnⁿBu₃ complex determined by X-ray crystallography.

Consistent with this trend, abnormal NHC complexes **aNHC**.EX₃ [*aNHC* = *alPr*, *alBu*; EX₃ = BH₃, AlMe₃, Ga(CH₂SiMe₃)₃ which are known to form very stable coordination adducts with short E-C bond distances, can also be lithiated with ⁿBuLi at their C2 position, with no competing ate formation or exchange of C2/C4 positions between the metals (Scheme 4c).²⁵

Interestingly **1** can also be accessed by other commercial lithium reagents such as amide Li(TMP)²⁶ (TMP = 2,2,6,6-tetramethylpiperdide), LiCH₂SiMe₃¹³ or even lithium metal.^{6c,7} These metallating studies contrast from the reactivity previously observed when 1,2,4-tris(trimethylsilyl)-cyclopentadienide lithium is treated with unsaturated carbene **I^tBu** (**I^tBu** = 1,3-di-*tert*-butylimidazol-2-ylidene) where only donor-acceptor NHC-Li coordination is observed.²⁷

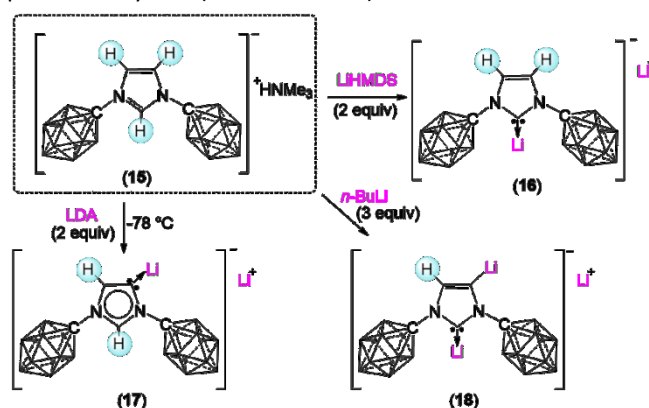
Heavier alkali-metal alkyls MCH₂SiMe₃ (M = Na, K)^{28,29} have also proved to be powerful bases for the metallation of **IPr**, mimicking the same C4-regioselectivity seen for the lithium reagents. While the Na analogue of **1** (**9** in Scheme 5) cannot be structurally or spectroscopically characterized, due to its lack of solubility even using large amounts of the polar solvent THF, indirect proof of its formation was found on its reaction with low polarity metal complexes such as Fe(HMDS)₂²⁸ (HMDS = 1,1,1,3,3,3-hexamethyldisilazide) and Ga(CH₂SiMe₃)₃,²⁹ in forming the relevant soluble sodium ferrate (**11**) and gallate (**12**) complexes. Mirroring the reactivity shown by **1**, in these ate complexes Na attaches to the C2 site of the anionic NHC whereas Fe and Ga prefer the C4 position that initially underwent sodiation (Scheme 5). Interestingly, electrophilic interception of **11** with MeOTf affords novel abnormal NHC complex [*alPr*^{Me}Fe(HMDS)₂] (*alPr*^{Me} = 1,3-bis(2,6-diisopropylphenyl)-2-methyl-imidazol-4-ylidene) (**13**), expanding the scope of these NHC metallation/electrophilic interception protocols to prepare abnormal NHC complexes to transition metals.



Scheme 5 Stepwise metallation/electrophilic interception protocol for accessing abnormal functionalised NHC-metal complexes. Inset: structure of [*alPr*^{Me}Fe(HMDS)₂] complex determined by X-ray crystallography.^{28,29}

Potassium complex [*C*{N(2,6-*i*Pr₂C₆H₃)₂CHCK(THF)₂}]_n (**10**-THF₂) exhibits a structure reminiscent to that reported for **1** although consistent with the larger size of the alkali-metal, the potassium centres are solvated by two molecules of THF instead of just one.³⁰ While **10** can be accessed by direct metallation of **IPr** by KCH₂SiMe₃,²⁹ Goicoechea has described its alternative synthesis by reacting **1** with KO^tBu.³⁰

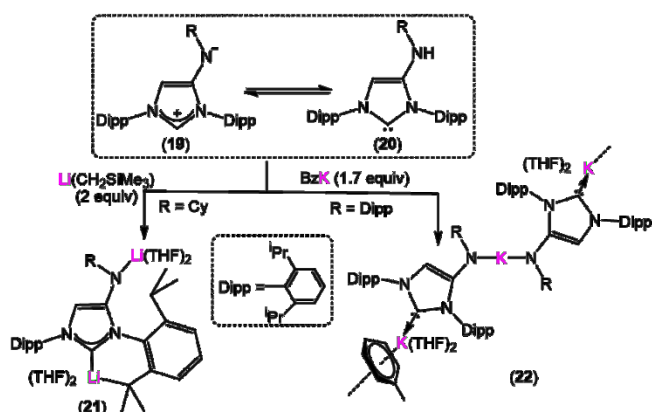
Related to these studies, highlighting the crucial role of the metallating reagent, Lavallo has shown that using imidazolium precursor **15**, which has been N-functionalized with anionic carba-*clos*-dodecaboranes, it is possible to selectively form the C2 normal and C4 abnormal NHC constitutional isomers (via deprotonation of **15** with two equivalents of LiHMDS or LDA respectively) (**16** and **17** respectively in Scheme 6). Furthermore, treating **15** with 3 equivalents of ⁿBuLi, gives trianionic doubly deprotonated C2-C4 species in almost quantitative yields (**18** in Scheme 6).³¹



Scheme 6 Syntheses of polyanionic normal (C2, **16**), abnormal (C4, **17**) and C2/C4 deprotonated species (**18**) by reaction of **15** with different lithium bases.³¹

Along with metallation of the imidazole ring, Braunstein has reported the unprecedented lateral lithiation at one *o*-CH(CH₃)₂ of a Dipp (Dipp = 2,6-diisopropylphenyl) wingtip in a remote

substituted amido NHC (Scheme 7), by reacting tautomeric mixtures of 4-amido-imidazolium (**19**) and 4-amino-carbene (**20**) with an excess of $\text{LiCH}_2\text{SiMe}_3$, affording **21** where a dianionic NHC coordinates to two Li atoms: one bound to an amido group and the other bound to the CMe_2 of a tertiary carbanion and the normal $\text{C}2$ -carbenic position.³² DFT calculations suggest that this unusual regioselectivity is thermodynamically driven. Contrastingly, when reacting these tautomeric mixtures with excess benzylpotassium (BzK), remote lateral metallation is not observed, but instead a mixed aggregate resulting from the co-complexation of the potassium amido-NHC with BzK is obtained (**22** in scheme 7).³³



Scheme 7 Contrasting reactivities of excess alkyllithium and benzyl potassium bases towards a mixture of 4-amido-imidazolium and 4-amino-carbene tautomers affording lateral metallation **21** and a mixed aggregate **22**.⁷

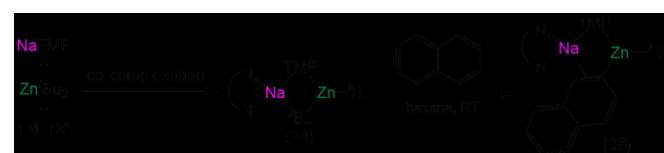
So far all these deprotonation studies using single-metal reagents involve the use of highly polar group 1 organometallic systems. It is noteworthy that when moving to group 2 metal bases, including Grignard reagents,³⁴ dialkylmagnesium^{34–36} or magnesium amides,^{34,37} no NHC deprotonation has been documented. Instead, several coordination adducts including those of **IPr** with $\text{Mg}(\text{HMDS})_2$ or MgBu_2 have been structurally characterised. The same failure of metallation has been noted for zinc amide and alkyl complexes.^{24,36}

Introducing Alkali-metal Mediated Metallation to NHC chemistry

As already mentioned, cooperative bimetallic bases have gained prominence over the past decade as more efficient and chemoselective alternatives to common alkyllithiums or lithium amides.^{1b,5} Other key advantages of these systems are their superior functional group tolerance and their applications at room temperature and in ethereal solvents. Examples of the remarkable reactivity of these systems, which usually combine an alkali-metal with a *s*- or *p*-block lower polarity metal such as Mg, Zn, or Al, include the regioselective α -zincation of THF^{38,39} and the *ortho-meta'* and *meta-meta'* directed dimagnesiations of a series of arenes using sodium magnesiate $[\text{Na}_4\text{Mg}_2(\text{TMP})_6(n\text{Bu})_2]$ (**23**).⁴⁰

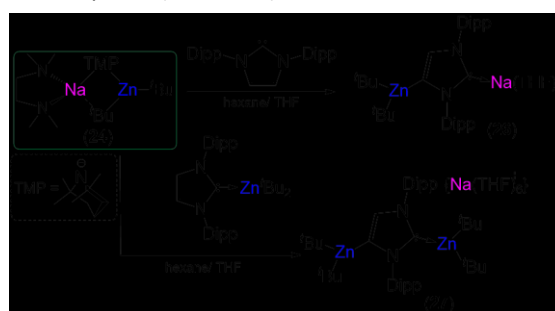
Many of these bimetallic mixtures are ate formulations which can be constructed by co-complexation of two single-metal components as shown in Scheme 8 for sodium zincate

$[(\text{TMEDA})\text{NaZn}(\text{TMP})^t\text{Bu}_2]$ (**24**). Reported by Mulvey in 2005, **24** has been established as a powerful and versatile zincating reagent.⁴¹ Contrastingly with the lack of kinetic basicity observed in simple organozinc reagents (alkyl, amides), the cooperative partnership of Na and Zn in **24** enables the selective zincation of non-activated arenes such as naphthalene (see **25** in Scheme 8)⁴² as well as promoting *ortho*- and *meta*-zincation of substituted arenes.^{43,44} Structural and mechanistic investigations⁴⁵ have established that these reactions are genuine examples of direct (C-H to C-Zn) zincations, with the alighting hydrogen being replaced by Zn, but since the co-presence of the alkali-metal is needed to facilitate this process, they are best described as alkali-metal-mediated zincations (AMMZn).



Scheme 8 Formation of sodium zincate **24** employed for selective C-metallation of unactivated arene naphthalene via AMMZn affording **25**.⁴²

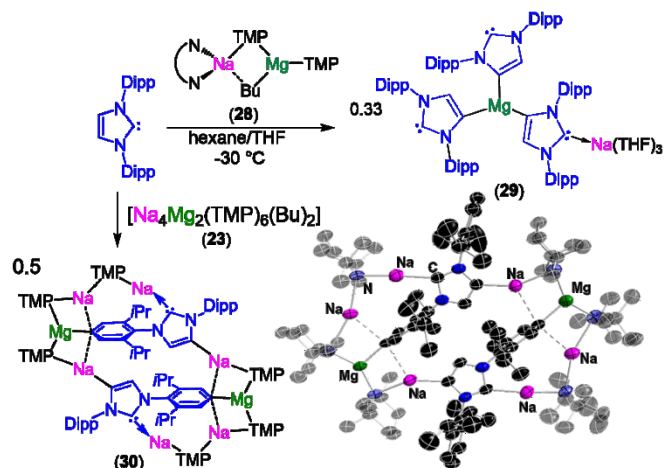
Exporting this bimetallic approach into NHC chemistry, we have reported the first studies in which AMMZn through **24** is applied to the metallation of several free unsaturated carbenes including **IPr** and **IMes** as well as the NHC-zinc complex **IPr-Zn^tBu₂** (Scheme 9).²⁴ In all cases, regioselective zincation at the $\text{C}4$ position of the imidazole backbone is observed, with the bimetallic agent acting as an amide base with concomitant generation of $\text{TMP}(\text{H})$. For the reactions with the free carbenes, Na coordinates to the vacant $\text{C}2$ site of the anionic NHC (**26** in Scheme 9). Interestingly the $\text{C}4$ -zincation of **IPr-Zn^tBu₂** rendered an unusual solvent separated ion pair zincate, which retains the original $\text{Zn-C}_{\text{carbene}}$ bond, while sodium is solvated by six THF molecules (**27** in Scheme 9). This reactivity contrasts with that alluded to above for reaction of **IPr-Zn^tBu₂** with ^tBuLi where no deprotonation of the carbene is observed forming instead zincate complex **8** (Scheme 4).²⁴



Scheme 9 AMMZn of the imidazole backbone of free **IPr** and **IPr-Zn^tBu₂** adduct by sodium zincate **24** producing novel sodium zincates **26** and **27**.²⁴

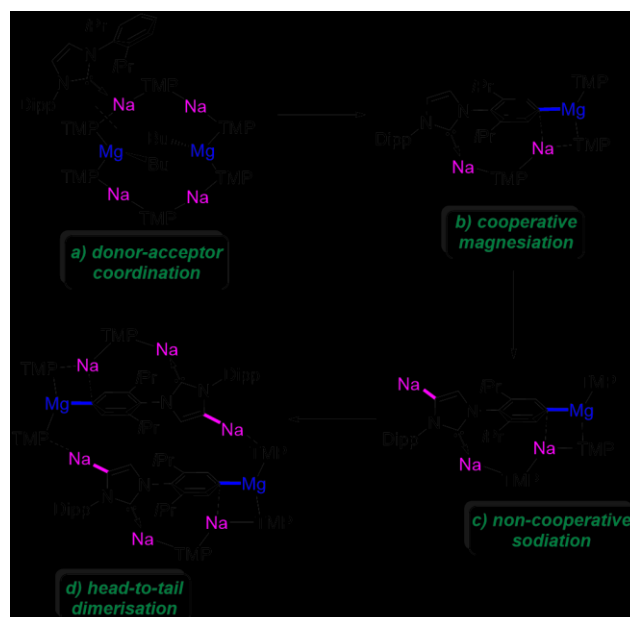
Building on the successful direct zincations of imidazole-derived NHCs, we next pondered if this bimetallic approach could also extend to other metals, in particular magnesium. Thus, in collaboration with Mulvey and O'Hara, we systematically investigated the reactivity of a series of alkali-metal magnesiates with **IPr**.⁴⁶ Surprisingly while synergic magnesiation was observed for several bimetallic systems,

these studies revealed that the regioselectivity of their reactions is finely tuned by the structure of the alkali-metal magnesiate base employed. Thus, monomeric [(TMEDA)NaMg(TMP)₂Bu] (**28**) when reacted with **IPr** in a 1:1 stoichiometry afforded tris(mononionic) carbene magnesiate **29**, where Mg binds to a THF molecule and three anionic NHCs via their C4 atom, with one ligand also bonded to Na via its normal C2 site (Scheme 10). While initially it can be thought that **29** forms by activation of the three basic (two amido and one alkyl) sites of **28** which potentially could metallate three molecules of **IPr**, NMR studies showed that **29** was actually produced as a result of a complicated ligand redistribution



Scheme 10 Alkali-metal-mediated magnesiation (AMMMg) of **IPr** by monomeric dinuclear **28** and dimeric hexanuclear **23**. Inset: X-ray structure of newly formed inverse crown complex **30**.⁴⁶

The most exciting result came upon treating **IPr** with donor free [Na₄Mg₂(TMP)₆(nBu)₂] (**23**) using non-donor methylcyclohexane as a solvent. This bimetallic base has been described as a pre-inverse crown, which is a family of macrocyclic complexes whose metallating reactivities are controlled predominately by their template structures rather than the directing effects of the substituents on aromatic substrates as in DoM chemistry.⁴⁷ Thus, for example O'Hara and Mulvey have recently used **23** to doubly-deprotonate *N,N*-dialkylanilines at their *meta-meta'* positions, overriding the *ortho*-directing effect of the NR₂ substituents witnessed in organolithium chemistry.⁴⁰ As shown in Scheme 10, the reaction of macrocyclic **23** with equimolar amounts of **IPr** furnished the spectacular inverse crown complex **30** (Scheme 10) comprising a unique 20 atom {(NaNMgNnNaCNnNa)₂} dicationic ring which hosts two anionic NHC fragments, each of them doubly deprotonated.⁴⁶ Thus, each carbene has been sodiated at its abnormal C4 position but also magnesiated at the *para* position of one Dipp substituent. This unprecedented regioselectivity is believed to originate from the steric incompatibility of the "guest" substrate (dideprotonated NHC molecule) and the "host" template ring (formed on release of its alkyl base ligands), which sets in motion a remarkable chain of reactions. As portrayed in Scheme 11, **IPr** would probably first coordinate to the more exposed Na atom at the pre-inverse crown inducing cleavage of the template into smaller fragments (a in scheme 11).

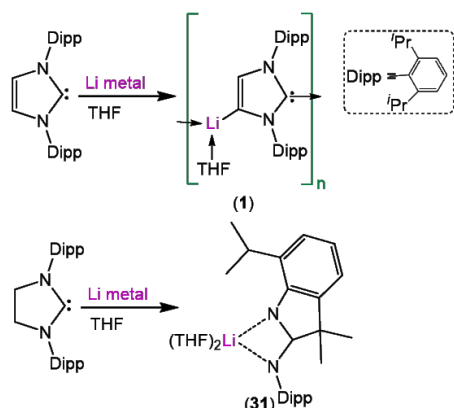


Scheme 11 Chain of reactions set in motion upon treatment of **IPr** with macrocyclic sodium magnesiate **23** affording inverse crown complex **30**.⁴⁶

These heterobimetallic bases are known to induce regioselective magnesiations using their Bu groups, so the fragment of the template attached to C2 through Na can execute the synergic Mg-H exchange at the *para* position of one of the aryl groups (b in Scheme 11). This proposed intermediate can then react with other organometallic fragments of the template cleavage, most likely NaTMP, which as seen before for single metal bases, could execute the C4 metallation of the imidazole ring (c in Scheme 11). A final head to tail dimerization step (d in Scheme 11) would result in **30** which can be isolated and structurally defined.

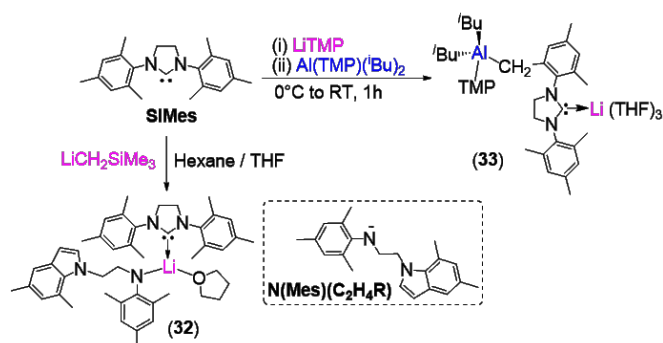
Interestingly, the rich metallating chemistry exhibited by these TMP-based sodium magnesiates contrasts with that reported by Hill for related alkali-metal tris(amido) magnesiates MMg(HMDS)₃ (M=Li, Na, K) which form coordination adducts {[M(IPr)₂]⁺[Mg(HMDS)₃]⁻}, exhibiting solvent-separated ion pair structures with the alkali metal coordinated by two neutral NHC ligands in a pseudo-linear disposition [C-M-C angles ranging from 168.94(18) to 180.00(6)°].⁴⁸

While most research activity in the field of anionic NHCs has focused on unsaturated carbenes, recently we added saturated NHCs to the reckoning focusing on **SIMes** [= 1,3-bis(2,4,6-trimethylphenyl)imidazolidin-2-ylidene] as a case study.⁴⁹ Containing non-aromatic C₃N₂ rings, saturated carbenes are usually less robust than their unsaturated congeners and their backbone hydrogens are significantly less acidic. This can be exemplified by comparing the reactivities reported by Robinson for **IPr** and its saturated analog **SIPr** towards lithium metal. This comparison showed that while **IPr** undergoes C4-lithiation (via metal reduction) to form **1**, **SIPr** affords ring-cleaved amidinate complex **31** (Scheme 12), although the mechanism of this reaction remains to be solved.^{6c}



Scheme 12 Contrasting reactivities of IPr and SIPr with Li metal.^{6c}

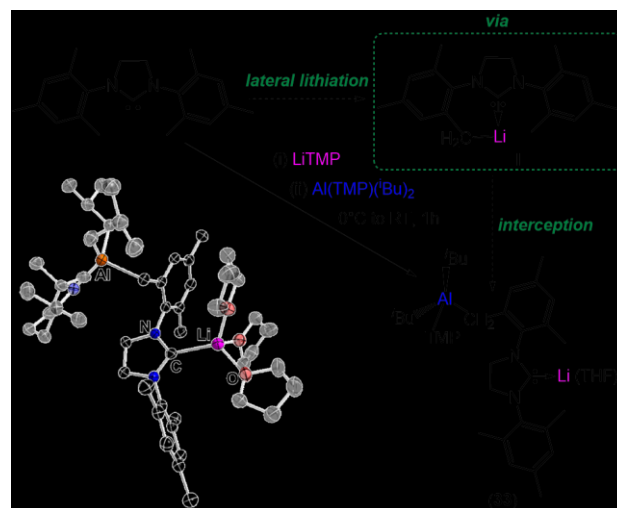
We first looked at the reaction of **SIMes** with equimolar amounts of the single metal base $\text{LiCH}_2\text{SiMe}_3$, which surprisingly furnished amido complex **32**. In monomeric **32** (Scheme 13), the three-coordinate Li binds to a non-symmetrical $\text{N}(\text{Mes})\text{CH}_2\text{R}$ ($\text{R} = 1$ -indolyl substituent) amide ligand, presumably obtained by activation of neutral **SIMes**, one unreacted **SIMes**, which merely acts as a neutral donor, and a more common THF donor molecule.⁴⁹



Scheme 13 Reaction of **SIMes** with single metal Li-base affording amido complex **32** and with bimetallic Li/Al TMT mixture affording lithium aluminate **33**.⁴⁹

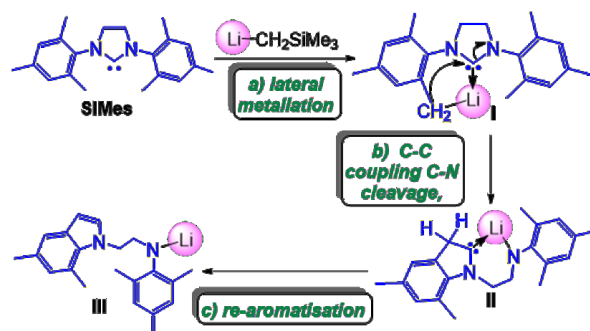
Formation of **32** suggests that while $\text{LiCH}_2\text{SiMe}_3$ may be able to deprotonate **SIMes**, the ensuing intermediate seems to be unstable and decomposes via a C-N bond activation/ring-opening process. Some of our recent work on molecules that are highly sensitive when metallated such as diazines⁵⁰ or fluoroarenes,⁵¹ has shown that it is possible to stabilise and trap metallated intermediates of these key organic scaffolds by using bimetallic mixtures of LiTMP/MR_3 ($\text{M} = \text{Al}(\text{TMP})\text{tBu}_2$, $\text{Ga}(\text{CH}_2\text{SiMe}_3)_3$). Unlike the magnesiate and zincate systems described above, where both metals are integrated within the same molecular scaffold and cooperate in a synchronised way, in these Li/Al and Li/Ga mixtures, the steric incompatibility between the single-metal components precludes co-complexation (ate formation), though they can cooperate in a sequential manner. Thus, for example, the LiTMP-induced *ortho* metallation of anisole can be dramatically increased from 5% of lithiated anisole to 99% of aluminated product by adding $\text{Al}(\text{TMP})\text{tBu}_2$ as a metal trap, in a process driven by the strong carbophilicity and bulk of the aluminium reagent via a trans-metal-trapping (TMT) procedure.^{26,52} Reacting **SIMes** with an

equimolar amount of the bimetallic mixture $\text{LiTMP}/\text{Al}(\text{TMP})\text{tBu}_2$ enabled the isolation of lithium aluminate **33**, where both metals are connected by an anionic **SIMes** ligand, which remarkably has been deprotonated at the *ortho*-Me arm of a mesityl substituent (Scheme 13).⁴⁹ While the carbon that has experienced the metallation is attached to Al, whereas Li coordinates to the C2-carbenic site of the anionic NHC, it should be noted that **33** results from the stepwise lateral alumination of **SIMes**. Its formation can be rationalised via intermediate **I** resulting from the lateral lithiation of **SIMes** by LiTMP, which as soon as it is formed is intercepted by the bulky trapping agent, $\text{Al}(\text{TMP})\text{tBu}_2$, furnishing **33** (Scheme 14).



Scheme 14 Proposed rationale for formation of **33**. Inset: X-ray structure of lithium aluminate **33**.⁴⁹

Contrastingly, when using lithium-only metallating reagents, lithiation of **SIMes** triggers a catastrophic cleavage of the saturated NHC. Thus, putative intermediate **I**, in the absence of a stabilizer, evolves to ring-opened **II** via coupling of its CH_2 group and its carbenic C, inducing the cleavage of the C-N bond of the C_3N_2 heterocyclic ring. Rearomatization of the five membered ring of **II** via a 1,2-hydrogen shift process renders the amido ligand present in **32** (Scheme 15).



Scheme 15 Proposed steps in the cleavage of saturated NHC upon lithiation of **SIMes**.⁴⁹

Interestingly, while the remaining neutral **SIMes** ligand present in **32** cannot be deprotonated by excess lithium base, when **32** is treated with the heavier alkali-metal alkyl $\text{KCH}_2\text{SiMe}_3$ novel potassium lithiate **34** is produced. Its molecular structure contains two amido fragments, which coordinate to Li via their

- Organocatalysis; Springer: Netherlands, 2011; e) S. Diez-Gonzalez, N-Heterocyclic Carbenes: From Laboratory Curiosities to Effective Synthetic Tools; RSC Publishing: Cambridge, 2010.
- 7 Y. Wang, Y. Xie, M. Y. Abraham, P. Wei, H. F. Schaefer III, P. v. R. Schleyer, G. H. Robinson, *J. Am. Chem. Soc.*, 2010, **132**, 14370.
 - 8 a) P. L. Arnold, S. T. Liddle, *Organometallics*, 2006, **25**, 1485; b) P. L. Arnold, S. T. Liddle, *Chem. Commun.*, 2006, 3959.
 - 9 J. B. Waters, J. M. Goicoechea, *Coord. Chem. Rev.*, 2015, **293-294**, 80.
 - 10 A. Nasr, A. Winkler, M. Tamm, *Coord. Chem. Rev.*, 2016, **316**, 68.
 - 11 It should be noted that while this Feature article focuses on C-H metallation studies as a vehicle to access anionic NHCs, there are also several examples of anionic NHCs resulting from the deprotonation of acidic NHR or OH substituents. See reference 10 and 8b.
 - 12 a) S. Kronig, E. Theuergarten, C. G. Daniliuc, P. G. Jones, M. Tamm, *Angew. Chem. Int. Ed.*, 2012, **51**, 3240; b) E. L. Kolychev, S. Kronig, K. Brandhorst, M. Freytag, P. G. Jones, M. Tamm, *J. Am. Chem. Soc.*, 2013, **135**, 12448.
 - 13 M. Uzelac, A. Hernán-Gómez, D. R. Armstrong, A. R. Kennedy, E. Hevia, *Chem. Sci.*, 2015, **6**, 5719.
 - 14 Y. Wang, Y. Xie, M. Y. Abraham, R. J. Gilliard Jr., P. Wei, C. F. Campana, H. F. Schaefer III, P. v. R. Schleyer, G. H. Robinson, *Angew. Chem. Int. Ed.*, 2012, **51**, 10173.
 - 15 J. B. Waters, L. S. Tucker, J. M. Goicoechea, DOI: 10.1021/acs.organomet.7b00352.
 - 16 T. K. Sen, S. C. Sau, A. Mukherjee, P. K. Hota, S. K. Mandal, B. Maity D. Koley, *Dalton Trans.*, 2013, **42**, 14253.
 - 17 M. Vogt, C. Wu, A. G. Oliver, C. J. Meyer, W. F. Schneider, B. L. Ashfeld, *Chem. Commun.*, 2013, **49**, 11527.
 - 18 H. Song, Y. Kim, J. Park, K. Kim, E. Lee, *Synlett*, 2016, **27**, 477.
 - 19 L. Y. M. Eymann, R. Scopelliti, F. T. Fadaei, G. Cecot, E. Solari, K. Severin, *Chem. Commun.*, 2017, **53**, 4331.
 - 20 Y. Wang, H. P. Hickox, Y. Xie, P. Wei, S. A. Blair, M. K. Johnson, H. F. Schaefer III, G. H. Robinson, *J. Am. Chem. Soc.*, 2017, **139**, 6859.
 - 21 A. Jana, R. Azhakar, G. Tavčar, H. W. Roesky, I. Objartel, D. Stalke, *Eur. J. Inorg. Chem.*, 2011, 3686.
 - 22 C. Pranckevicius, D. W. Stephan, *Chem. Eur. J.*, 2014, **20**, 6597.
 - 23 M. Chen, Y. Wang, R. J. Gilliard, P. Wei, N. A. Schwartz, G. H. Robinson, *Dalton Trans.*, 2014, **43**, 14211.
 - 24 D. R. Armstrong, S. E. Baillie, V. L. Blair, N. G. Chabloy, J. Diez, J. Garcia-Alvarez, A. R. Kennedy, S. D. Robertson, E. Hevia, *Chem. Sci.*, 2013, **4**, 4259.
 - 25 G. Schnee, O. Nieto Faza, D. Specklin, B. Jacques, L. Karmazin, R. Welter, C. Silva Lopez, S. Dagorne, *Chem. Eur. J.*, 2015, **21**, 17959.
 - 26 M. Uzelac, A. R. Kennedy, E. Hevia, *Inorg. Chem.*, 2017, **56**, 8615.
 - 27 A. J. Arduengo III, M. Tamm, J. C. Calabrese, F. Davidson, W. J. Marshall, *Chem. Lett.*, 1999, 1021.
 - 28 L. C. H. Maddock, T. Cadenbach, A. R. Kennedy, I. Borilovic, G. Aromí, E. Hevia, *Inorg. Chem.*, 2015, **54**, 9201.
 - 29 M. Uzelac, A. R. Kennedy, A. Hernán-Gómez, M. Á. Fuentes, Z. *Anorg. Allg. Chem.*, 2016, **642**, 1241.
 - 30 J. B. Waters, J. M. Goicoechea, *Dalton Trans.*, 2014, **43**, 14239.
 - 31 A. El-Hellani, V. Lavallo, *Angew. Chem. Int. Ed.*, 2014, **53**, 4489.
 - 32 A. A. Danopoulos, P. Braunstein, E. Rezabal, G. Frison, *Chem. Commun.*, 2015, **51**, 3049.
 - 33 A. A. Danopoulos, P. Braunstein, *Chem. Commun.*, 2014, **50**, 3055.
 - 34 A. R. Kennedy, R. E. Mulvey, S. D. Robertson, *Dalton Trans.*, 2010, **39**, 9091.
 - 35 A. R. Kennedy, J. Klett, R. E. Mulvey, S. D. Robertson, *Eur. J. Inorg. Chem.*, 2011, 4675.
 - 36 A. J. Arduengo III, H. V. Rasika-Dias, R. Davidson and R. L. Harlow, *J. Organomet. Chem.*, 1993, **462**, 13.
 - 37 M. Arrowsmith, M. S. Hill, D. J. MacDougall, M. F. Mahon, *Angew. Chem. Int. Ed.*, 2009, **48**, 4013.
 - 38 A. R. Kennedy, J. Klett, R. E. Mulvey, D. S. Wright, *Science*, 2009, **326**, 706.
 - 39 E. Crosbie, P. Garcia-Alvarez, A. R. Kennedy, J. Klett, R. E. Mulvey, S. D. Robertson, *Angew. Chem. Int. Ed.*, 2010, **49**, 9388.
 - 40 A. J. Martínez-Martínez, A. R. Kennedy, R. E. Mulvey, C. T. O'Hara, *Science*, 2014, **346**, 834.
 - 41 P. C. Andrikopoulos, D. R. Armstrong, H. R. L. Barley, W. Clegg, S. H. Dale, E. Hevia, G. W. Honeyman, A. R. Kennedy, R. E. Mulvey, *J. Am. Chem. Soc.*, 2005, **127**, 6184.
 - 42 W. Clegg, S. H. Dale, E. Hevia, L. M. Hogg, G. W. Honeyman, R. E. Mulvey, C. T. O'Hara, *Angew. Chem. Int. Ed.*, 2006, **45**, 6548.
 - 43 D. R. Armstrong, W. Clegg, S. H. Dale, E. Hevia, L. M. Hogg, G. W. Honeyman, R. E. Mulvey, *Angew. Chem. Int. Ed.*, 2006, **45**, 3775.
 - 44 D. R. Armstrong, J. Garcia-Alvarez, D. V. Graham, G. W. Honeyman, E. Hevia, R. E. Mulvey, *Chem. Eur. J.* 2009, **15**, 3800.
 - 45 a) D. R. Armstrong, V. L. Blair, W. Clegg, S. H. Dale, J. Garcia-Alvarez, G. W. Honeyman, E. Hevia, R. E. Mulvey and L. Russo, *J. Am. Chem. Soc.*, 2010, **132**, 9480; b) W. Clegg, B. Conway, E. Hevia, M. D. McCall, L. Russo and R. E. Mulvey, *J. Am. Chem. Soc.*, 2009, **131**, 2375; c) D. Nobuto and M. Uchiyama, *J. Org. Chem.*, 2008, **73**, 1117.
 - 46 A. J. Martínez-Martínez, M. Á. Fuentes, A. Hernán-Gómez, E. Hevia, A. R. Kennedy, R. E. Mulvey, C. T. O'Hara, *Angew. Chem. Int. Ed.*, 2015, **54**, 14075.
 - 47 A. J. Martínez-Martínez, D. R. Armstrong, B. Conway, B. J. Fleming, J. Klett, A. R. Kennedy, R. E. Mulvey, S. D. Robertson, C. T. O'Hara, *Chem. Sci.*, 2014, **5**, 771.
 - 48 M. S. Hill, G. Kociok-Köhn, D. J. MacDougall, *Inorg. Chem.*, 2011, **50**, 5234.
 - 49 A. Hernán-Gómez, A. R. Kennedy, E. Hevia, *Angew. Chem. Int. Ed.*, 2017, **56**, 6632.
 - 50 M. Uzelac, A. R. Kennedy, E. Hevia, R. E. Mulvey, *Angew. Chem. Int. Ed.*, 2016, **55**, 13147.
 - 51 R. McLellan, M. Uzelac, A. R. Kennedy, E. Hevia, R. E. Mulvey, *Angew. Chem. Int. Ed.*, 2017, **56**, 9566.
 - 52 D. R. Armstrong, E. Crosbie, E. Hevia, R. E. Mulvey, D. L. Ramsay, S. D. Robertson, *Chem. Sci.*, 2014, **5**, 3031.