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C-N Bond Activation and Ring Opening of a Saturated
N-Heterocyclic Carbene via Lateral Alkali-Metal-Mediated
Metallation (AMMM)

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Abstract: Combining alkali-metal mediated metallation (AMMM) and
N-heterocyclic carbene (NHC) chemistry, a novel C-N bond
activation and ring-opening process is described for these
increasingly important NHC molecules, which are generally
considered robust ancillary ligands. Here, mechanistic investigations
on reactions of saturated NHC SiMes ([SiMes = \{C(N(2,4,6-
Me_2C_6H_3)CH_3)\}] with group 1 alkyl bases suggest this destructive
process is triggered by lateral metallation of the carbene. Exploiting
co-complexation and trans-metal-trapping strategies with lower
polarity organometallic reagents (Mg(CH_3SiMe_3) and Al(TMPTBu)),
key intermediates in this process have been isolated and structurally
defined.

Since Arduengo’s landmark isolation of the first N-heterocyclic
carbene (NHC),[1] an enormous amount of research activity has
been devoted to advancing the applications of these special
ligands, leading to important breakthroughs in transition-metal
catalysis and organic synthesis,[2] as well as in main group
chemistry.[3] Many of these discoveries have been driven by the
fine tunability, relative stability and robustness of these
molecules as strong two electron sigma donors. Contrasting with
the myriad of studies involving NHC-transition metal
complexes,[2] the use of these ligands in s-block metal chemistry
has been limited to a few select investigations.[4] Of these, key
contributions from the groups of Arnold and Hill have
demonstrated the excellent potential of NHCs for advancing s-
block homogeneous catalysis,[5] as well as for stabilizing novel
Mg hydride clusters.[6] Furthermore, the seminal work of
Robinson[7] on the deprotonation of IPr (1,3-bis(2,6-
diisopropylphenyl)imidazol-2-ylidine) at its C4 position (alkenic
backbone) with nBuLi has pushed forward the applications of
anionic NHCs,[8] opening up a new construction point for the
functionalization of these ligands. Other examples of direct C4-
metallation of unsaturated NHCs have been reported using Na[9]
and K[10] bases as well as mixed-metal systems such as sodium
zincates[11] or magnesiates.[12] A novel example of this alkali-
metal-mediated metallation (AMMM) involves the template base
[Na_2Mg_2(TMPTBu)](nBuLi) (TMPTBu = 2,2,6,6,-tetramethylpiperidine),
which simultaneously deprotonates the backbone of IPr along
with one Dipp (Dipp = diisopropylphenyl) substituent at its para-
position.[12] Related to that finding, Braunstein has also
described the unexpected lateral lithiation of a CH(Me)_2 wingtip
of a Dipp in a 4-amido-substituted NHC.[13] Surprisingly, despite
all this recent activity, the metallation of dihydro saturated NHCs,
containing non-aromatic C3N2 rings has hardly been touched
upon, probably as a dual consequence of being less robust than
their unsaturated congeners and having reduced acidity of their
backbone hydrogen atoms. This has been nicely illustrated for
the contrasting reactivities of IPr and its saturated analog SiPr
when treated with lithium metal, with the former undergoing C4
metallation whereas the latter affords a ring-cleaved amidinate
complex, although the mechanism of this reaction is unknown.[14]

Breaking new ground, here, in reporting the first metallation
study between a saturated carbene and alkali-metal bases
[MCH_3SiMes] (M= Li, K), we disclose a novel s-block metal-
mediated activation process. Moreover, structurally mapping
these reactions using SiMes ([SiMes = \{C(N(2,4,6-
Me_2C_6H_3)CH_3)\}] as a case study, gives unique mechanistic
insights into these transformations.

We started by reacting equimolar amounts of the silylalkyl
reagents MR (M = Li, K R = CH_3SiMe_3) with SiMes at room
temperature, which gave oily solids. Adding donor ligands (one
extra equivalent of SiMes and THF for M = Li and tridentate N-
donor PMDETA for M= K, Scheme 1) allowed isolation of
complexes 1 and 2 as crystalline products in 61% and 66%
yields respectively.

X-ray diffraction analysis of crystals of 1 and 2 revealed the
presence of the same non-symmetrical amide ligand, containing
mesityl and C_6H_4R arms, where R is a 1-indolyl substituent (Fig.
1), presumably resulting from activation of neutral NHC SiMes.
Reflecting the different coordination preferences of lithium and
potassium, in 1 this amide ligand binds terminally to the metal
via its amido N (N3 in Fig. 1). Contrasting, in 2, a chelating

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bonding mode is observed, where the K-N_{\text{mes}} bond is supported by a series of stabilizing π-electrostatic interactions with the indolyl C=C bonds, as well as with the C_{\text{mes}} of the mesityl group. To engage in these π-contacts, K adopts a near perpendicular disposition to the planes defined by both aromatic rings. The coordination sphere of the alkali-metals is completed by a THF molecule and one neutral SIMes ligand for 1, whereas in 2 K is chelated by tridentate PMDETA.

![Scheme 2](image)

**Scheme 2.** Proposed mechanism for the formation of 1

Although NHCs are generally accepted as robust spectator ligands, a number of studies have reported that when coordinated to transition metals they can undergo both C-H and C-N activation.[15] To date, this reactivity has been missing in s-block chemistry, with the exception of Hill's[16] work in the formal insertion of BeH$_2$ into a C=N bond of the unsaturated NHC IPr and the aforementioned reduction of SIPr with Li metal.[14] The formation of 1 and 2 shows that under the conditions studied both alkali-metal MCH$_2$SIMes reagents are able to promote the cleavage of the SIMes C-N bond, that is significantly different from the reactivity observed when potassium bis(trimethyl)silyl amide is treated with unsaturated NHCs, where only donor-acceptor coordination of the NHC to the K centre is observed.[17]

While as far as we can ascertain the activation of SIMes to give the anionic group present in 1 and 2 is unprecedented, it should be noted that investigations on other ring expanded carbenes containing N-mesityl substituents lead to the insertion of the carbene into one of their own ortho-methyl C-H bonds upon heating, furnishing N-alkyl indole products.[18] Interestingly, the same studies have also reported the thermal resistance of SIMes to undergo insertion, even after prolonged periods of time (72h at 70°C).

In 1 and 2, the transformation of SIMes into the anionic amide N(Mes)(C$_2$H$_4$R) can be rationalised assuming that lateral metallation of one ortho- Me of its mesityl group occurs (II in Scheme 2). This transformation is probably favoured by initial NHC pre-coordination to the alkali-metal alkyl complex (I in Scheme 2). This will not only activate the organometallic reagent by reducing its aggregation,[19] but will also bring the ortho-$\text{Me}$ into close proximity to the reactive alkyl group, akin to the complex-induced proximity effect (CIPE) in directed-ortho metallation.[20] As mentioned above, lateral deprotonations in NHC chemistry are extremely rare with only two examples described for unsaturated NHCs.[12,14] Notably, while these species are stable and can be structurally characterised, putative intermediate II must rapidly change to the ring open product III (Scheme 2), through the coupling of the benzyl CH$_2$

Attempts to isolate or even detect the postulated intermediates in Scheme 2 by reducing the temperature of the reaction were unsuccessful. Recently in collaboration with Mulvey we introduced the concept of trans-metal-trapping (TMT),[24] where addition of low polarity organometallics such as Al or Ga species to lithiated substrates containing fragile anions allows stabilization and entrapment of these sensitive intermediates. Applying this approach to the lithiation of SIMes, we found that by using Mg(CH$_2$SIMes)$_2$ (0.5 equivalents) as an organometallic trap it is possible to intercept the postulated coordination adduct I (Scheme 2), which is isolated as the tetraorganomagnesiate 3 in a 56% yield (Scheme 3).

X-ray crystallographic studies confirmed the bimetalllic Weiss-motif[23] constitution of 3 which can be envisaged as a co-complexation product of two equivalents of [SIMesLi(CH$_2$SIMes)$_2$] with one Mg(CH$_2$SIMes)$_2$ (Fig. 2a). Isolation of 3 implies that by forming a tetraalkylmagnesiate anion, containing significantly less polar and therefore less reactive metal-C bonds, the lateral metallation of IMes is inhibited.

In an attempt to trap the proposed metallated species prior to the ring-opening step we moved to the bimetallic combination LiTMP/Al(TMP)/Bu$_2$, where the steric mismatch between the two single-metal components precludes their co-complexation to form a lithium aluminate though they can still cooperate in a...
sequential manner to promote aluminisation of aromatic molecules,[24] 1H NMR monitoring of the reaction of SiMes with LiTMP in deuterated THF,[25] demonstrated the formation of N(Mes)(C₂H₅R) amide fragment resulting from activation of the C-N bond in the carbene. On the other hand performing the same reaction in the presence of the aluminium trap [Al(TMP)₂Bu₃] furnished lithium aluminate 4 in a 59% yield (Scheme 3), whose molecular structure was determined by X-ray crystallographic studies (Fig. 2b).

Exhibiting a contacted ion pair structure, Li and Al are connected by an anionic SiMes ligand, which has been deprotonated at one ortho-Me of a mesityl ring, coordinating to Al via this benzylic C (C20 in Fig 2); whereas Li is attached to its normal carbencic position (C1 in Fig 2). The formation of 4 can be rationalised considering the fast transmetallation of the lateral lithiated intermediate II (Scheme 2) to the more carbophilic [Al(TMP)₂Bu₃] fragment. Consistent with this interpretation, and illustrating the synergistic reactivity of this Li/Al bimetallic partnership, even when they operate in a non-synchronised manner, we found that on its own weak base [Al(TMP)₂] furnishes lithium aluminate 4 in a 59% yield (Scheme 3), whose molecular structure was determined by X-ray crystallographic studies (Fig. 2b).

Since 1 still contains a neutral SiMes ligand coordinated to the Li centre, we pondered whether it could be also activated. While an excess of LiCH₂SiMes₂ does not seem to be effective, the reaction with the heavier alkali metal alkyl KCH₂SiMes₂ led to the isolation of the novel mixed lithium/potassium complex 5 in 58% yield (Scheme 4).

The molecular structure of 5 displays two N(Mes)(C₂H₅R) anions coordinated to the lithium centre via their N atoms, forming a novel potassium diamidolithiate complex. Contrastingly, K forms a series of π-K…C interactions, engaging in a π-fashion with the mesityl fragments of the two amido ligands. These well-defined distinct bonding modes of Li and K contrast with those found in other mixed lithium/potassium amides such as [LiK(TMP)₂PMDETA] where both metals are bridged by amide N atoms.[27] Potassium is further solvated by two molecules of THF while another THF completes the distorted trigonal planar geometry around Li (sum of the angles around Li, 359.8°), with a noticeably obtuse NLiN angle [133.3(4)°]. This distortion is
probably imposed by the formation of a coordination pocket for the [K(THF)]^+ cation with the mesityl rings. Structurally defined potassium lithiates are extremely rare, with a recent example of a potassium diboryllithiate reported by Nozaki[28] in 2016, where similar Li-B/K-aryl interactions are observed.

Figure 4. Molecular structure of 3 with thermal ellipsoids at 30% probability. Hydrogen atoms except for those attached to C12, C19, C39 and C40 are omitted for clarity.

In summary by describing the unprecedented metallation of the saturated NHC SIMes using Li and K alkyl bases, we have disclosed a novel alkali-metal-mediated C-N bond activation and ring opening process in NHC chemistry, which seems to be initiated by lateral metallation of the carbene. Exploiting co-complexation and trans-metal-trapping strategies with lower polarity organometallics reagents, potential key intermediates in this process, which otherwise would be too reactive to detect, have been isolated and structurally defined.

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Keywords: alkali-metal, C-N activation, metalation, mixed-metal chemistry; N-heterocyclic carbene

Co-lateral damage! Lateral metallation of saturated NHC SiMes triggers a destructive process, inducing C-N bond activation and ring opening of the five-membered heterocyclic ring.