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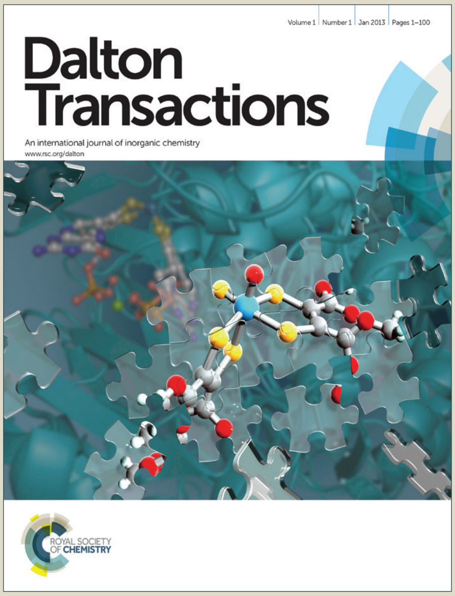

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ARTICLE

Activation of the C-N bond of N-heterocyclic carbenes by inorganic elements

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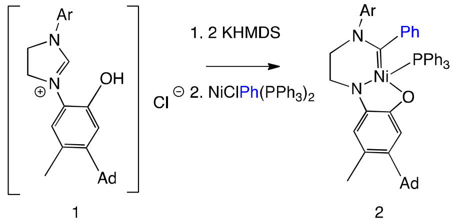
N-heterocyclic carbenes (NHCs) are generally considered to be extremely robust, ideal spectator ligands. However, in the past two years there have been several reports of the activation of the endocyclic C-N bond with subsequent insertion into element-hydrogen and element-carbon bonds. The new reaction pathway casts the reactivity of the NHC heterocyclic ring into a new light, especially in the context of potential catalyst decomposition. The synthetic reports and theoretical studies in this rapidly developing area are summarized here.

Introduction

The activation of small molecules such as NH_3, P_4 and H_2 using N-heterocyclic carbenes (NHCs) and related stable carbenes has been a topic of recent major interest.[1] Much less explored is the activation of the carbenes themselves, in part since NHCs have generally been considered as highly robust spectator ligands.[2] For example the second generation Grubbs' catalyst includes an appended NHC and displays superior stability and turnovers as compared to the first generation catalyst with a phosphine ligand.[3] NHCs have also found great use in main group chemistry, most conspicuously in stabilizing low-oxidation state mono- and di-atomic compounds.[4-6] Pertinent to this review, NHCs have also recently been used to stabilize main group hydrides.[7-12] However, in the past two years there have been a series of reports describing a new type of reactivity for NHCs: heterocyclic C-N bond cleavage and ring expansion, predominantly by hydrides (E-H). Such reactivity is quite unique, as it modifies the heterocycle itself. There have been several complementary theoretical studies examining the possible scope and mechanism of this reaction. In this Frontier article, we summarize the developments to date in this rapidly growing area.

Synthetic Reports

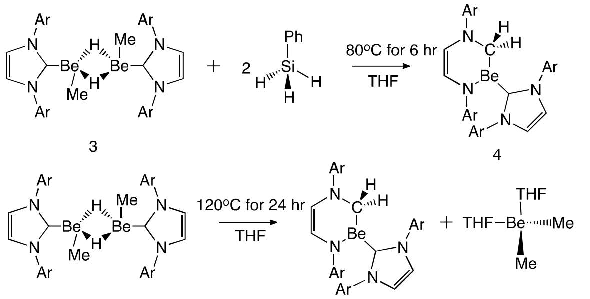
In 2006 Grubbs described a reaction where a phenol substituted imidazolium cation (**1**) was treated with two equivalents of base and $NiClPh(PPh_3)_2$ at room temperature (Scheme 1).[13] Compound **2** was the unexpected product of the reaction, with an insertion of Ni into the C-N bond and migration of the Ph group to the "carbenic" carbon, which at the time was an unknown reaction for an NHC.



Scheme 1. Insertion of Ni into an NHC C-N bond reported by Grubbs in 2006.

Recently, observations by a number of groups have resulted in a surge of interest in similar reactions in main group chemistry.

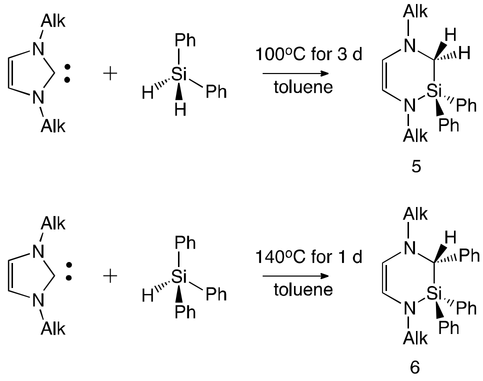
The first report of main group induced ring expansion of NHCs was by Hill and co-workers involving Be (Scheme 2). Upon heating the hydrido-methyl bridged NHC-Be dimer **3** to 80 ºC in the presence of $PhSiH_3$ as a hydride source, insertion of the Be into an NHC C-N bond occurred giving **4**.[14] An unobserved NHC-BeH_2 intermediate was proposed as the reactive species for the ring expansion. The carbenic carbon of the NHC received the two hydrogen atoms from the beryllium.



Scheme 2. Insertion of "BeH_2" into $Dipp_2NHC$ giving **4**. (Ar = 2,6-diisopropylphenyl)

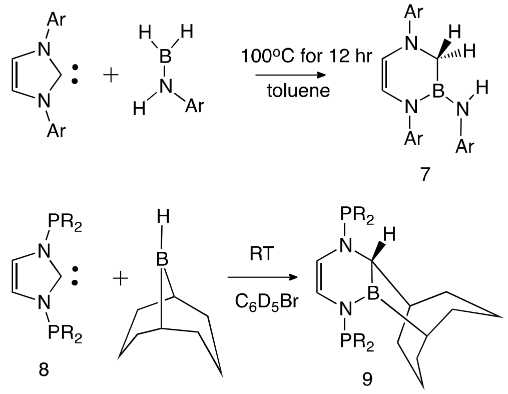
Importantly, is was also found that the external hydride source could be omitted if the reaction temperature was increased, indicating the reaction was independent of the silane, which was indeed simply supplying a source of H for the reaction at lower temperatures. Low-oxidation state beryllium compounds have been shown computationally to potentially activate the NHC C-N bond as well.[15]

A report from Radius and co-workers followed soon after on the analogous reaction involving NHCs and silanes (Scheme 3).[16] With $PhSiH_3$ and Ph_2SiH_2 the silicon inserted into the N-C bond on heating to moderately high temperatures, with two hydrogen atoms migrating to the carbenic carbon (**5**). Furthermore, for Ph_3SiH, the same insertion was observed on heating to 140 ºC, with migration of the hydrogen atom as well as a phenyl group (**6**).



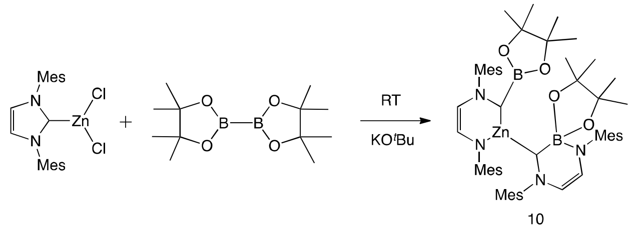
Scheme 3. Insertion of silanes into the C-N bond of NHCs.

The next report came from the group of Rivard (Scheme 4), which described a similar transformation with a dihydridoborane inserting into an NHC C-N bond at 100 ºC giving **7**.[17] More recently Stephan reported activation of the C-N bond of a phosphine substituted NHC **8** with 9-BBN at room temperature, in this case involving hydride and alkyl migration onto the carbenic carbon (**9**).[18] Bertrand has also reported activation of saturated NHCs in the presence of 9-BBN with substantially more destruction of the NHC involving complete opening of the NHC ring and coupling of two NHC units.[19]



Scheme 4. Insertion of boranes into NHC C-N bonds.

In their respective reports Hill, Radius and Rivard all explicitly state that this previously unrecognized and apparently fairly general transformation is potentially important in the context of NHC degradation in catalytic systems. Very recently Marder and co-workers brought this supposition into context, reporting on a transformation involving simultaneous Zn and B insertion into the NHC of a $ZnCl_2$ complex by B_2Pin_2 in the course of investigating borylation of alkyl halides catalysed by Zn (**10**, Scheme 5).[20]



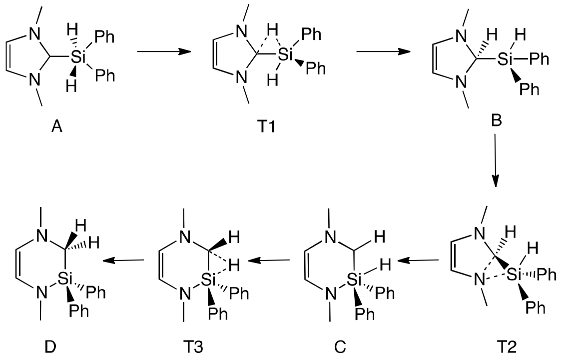
Scheme 5. Simultaneous insertion of Zn and B into NHC C-N bonds.

Theoretical Studies

In their synthetic report Radius and co-workers proposed a reaction pathway/mechanism for the reaction between the NHC and Ph_2SiH_2, involving three key steps (Scheme 6):

1. Migration of a hydrogen atom from the silicon to the carbenic carbon (**T1**).
2. Insertion of the silicon atom into the C-N bond (**T2**)
3. Migration of the second hydrogen atom giving the final product (**T3**).

The proposed reaction pathway has been investigated and validated by several groups computationally, including our own.[21-24] The initial step at the beginning of the reaction is the formation of the NHC-EH_xR_x adduct **A**, from which all relative energies are defined, and which allows for a better comparison of the energetics of various systems. The calculated reaction free energy coordinates for selected representative examples are depicted in Figure 1.



Scheme 6. Pathway for insertion/ring expansion reaction as proposed by Radius.[16]

The reaction pathway is common across Be, Si and B as reported synthetically by Hill, Rivard and Radius, with the only major difference being for Be, where a second equivalent of NHC is required. Our group demonstrated theoretically, that the second NHC is likely incorporated from the beginning, with 2 NHC ligands bound to BeH_2 in **A**.[22]

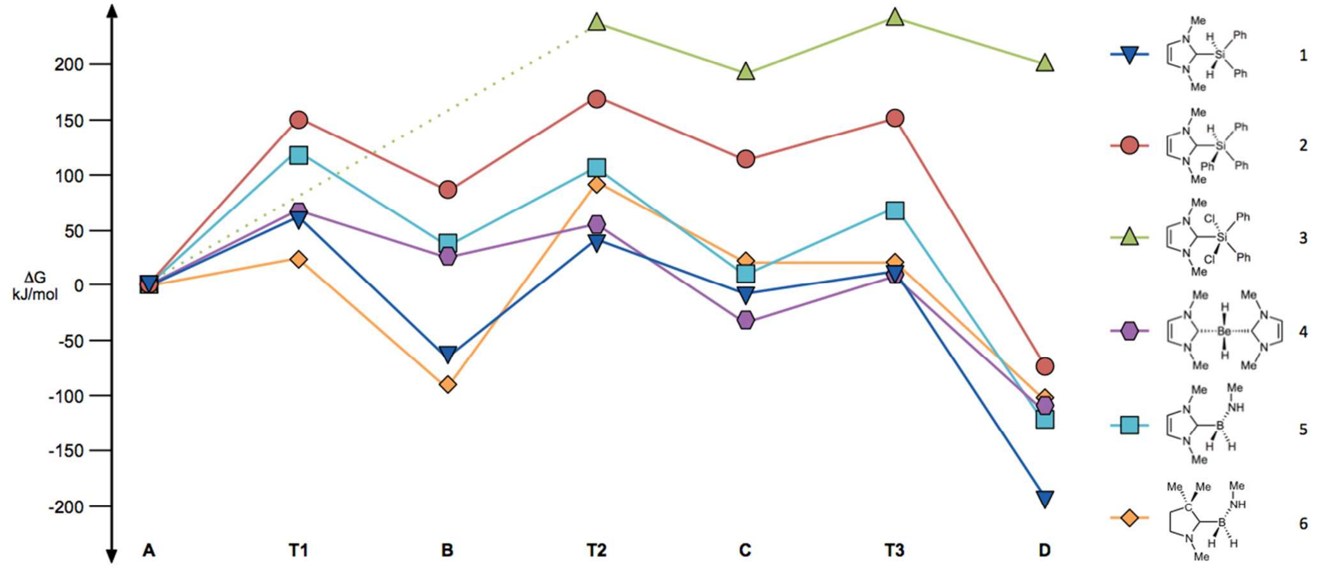


Figure 1. Calculated reaction coordinates for selected examples of the insertion/ ring expansion reactions. For Ph_2SiCl_2 no minima/transition state could be located for B and T1. Methods (numbered top to bottom): SCS-MP2/def2-TZVP//M06-2X/def2-TZVP (1,4,5); M06-2X/6-31++G(d,p) with toluene SCRF (2); MP2/def2-TZVP//M06-2X/6-31G(d) (3); M06-2X/cc-pVDZ (6).

The rate-limiting step is in most cases **T1**; migration of the first H atom from the main group element to the carbenic carbon giving **B**. The calculated barriers for the observed reactions involving migration of two hydrogen atoms range from 55–120 kJ/mol from the adducts, consistent with the elevated temperatures and extended reaction times reported. The barrier for **T1** where one H atom is replaced by a phenyl group (Ph_3SiH) is increased to nearly 150 kJ/mol, consistent with the increased reported temperature and reaction time.[24] On the basis of theoretical calculations, Rivard and Brown have predicted that if the cyclic alkylaminocarbene (cAAC) ligand is used in place of the NHC, then the steps subsequent to **B** are energetically unfeasible, making the ring expansion unlikely for cAAC.[23] Many NHC-main group halide compounds are known to be highly stable,[25] in the context of this work we have demonstrated that if E-Cl was considered rather than E-H all reaction steps are considerably higher in energy as for the example of Ph_2SiCl_2. This led us to the conclusion that the driving force for the insertion/ring expansion is the formation of strong C-H or C-C bonds in place of weaker E-H/E-C bonds.[2126]

Conclusions

There are a growing number of experimental reports of heterocyclic NHC C-N bond cleavage and ring expansion reactivity, which may be expected to expand to additional element-hydrides and ligand types in coming years. In general, the results of the studies summarized here and the earlier work of Grubbs make it clear that scientists studying NHC complexes also containing M-H or M-C (and perhaps M-B) bonds should carefully observe for insertion into the NHC C-N bond as a possible side reaction or alternate pathway.

Acknowledgements

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Notes and references

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26. A referee suggested that the driving force for the initial hydride migration could be the increased electrophilicity of the carbenic carbon on formation of the adduct. This is a reasonable hypothesis, but none of the studies to date address this specific point. In reference 23 Rivard and Brown found that the partial negative charge on the hydrogen atoms in the Si-H bond was increased on formation of the NHC-silane adduct, lending support to this mode of activation. Conversely, by examination of the frontier orbitals, Fang in reference 24 suggests a protic activation of the migrating hydrogen by the partially filled p-orbtial on the carbenic carbon.

Kalon J. Iversen completed his Bachelor of Science with honours (H1) in 2012 at La Trobe University. He is currently undertaking a PhD at La Trobe under David J. D. Wilson and Jason L. Dutton studying mechanistic inorganic chemistry through computational methods.

David Wilson obtained his PhD in 2003 from the University of Newcastle, Australia. In 2005 he gained an appointment at La Trobe University, Australia where he is now Senior Lecturer. His current research is centred around applying quantum chemistry to systems with novel bonding environments.

Jason Dutton obtained his PhD from The University of Western Ontario (Canada) in 2010. He is currently a Lecturer at La Trobe University with a research program focused on synthetic and theoretical inorganic chemistry.

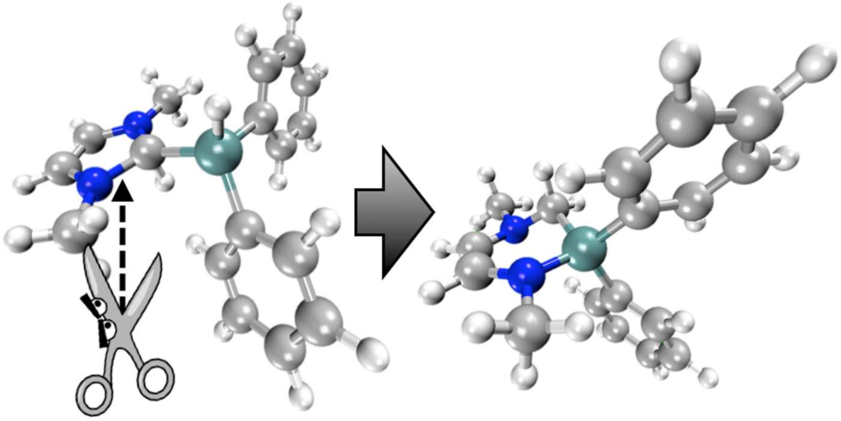

Table of contents entry:

This frontier article summarizes the recent activity around a new mode of reactivity for N-heterocyclic carbenes: Insertion of inorganic elements into the C-N bond of the carbene ring.