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## Ambiphilicity of ring-expanded N-heterocyclic carbenes†

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N-heterocyclic carbenes, such as imidazole-2-ylidenes and imidazolin-2-ylidenes, the popular class of singlet carbenes introduced by Arduengo in 1991 have not been shown to be ambiphilic owing to the two  $\sigma$ -withdrawing,  $\pi$ -donating amino groups flanking the carbene centre. However, our experimental data suggest that ring-expanded N-heterocyclic carbenes (RE-NHCs), especially the seven and eight membered rings, are significantly ambiphilic. Our results also show that the steric environment in RE-NHCs can become a determining factor for controlling the E–H bond activation.

## Introduction

Thanks to growing efforts in main group chemistry, the activation of enthalpically strong bonds and industrially relevant small molecules is no longer restricted to transition-metals.<sup>1</sup> More than a decade ago, our group discovered that cyclic (alkyl)(amino)carbenes (CAAC-5),<sup>2,3</sup> a class of highly ambiphilic carbenes, could react with carbon monoxide,<sup>4</sup> H<sub>2</sub>,<sup>5</sup> NH<sub>3</sub> (ref. 5) and P<sub>4</sub>.<sup>6</sup> More recently, it has been shown that CAAC-5s not only activate a variety of bonds (C–H, Si–H, B–H...) but also promote catalytic reactions.<sup>8</sup> In comparison, imidazole-2-ylidenes<sup>9</sup> and imidazolin-2-ylidenes,<sup>10</sup> the classical N-heterocyclic carbenes (NHC-5s), are much less ambiphilic due to their two  $\pi$ -donating amino substituents. Consequently, they are reluctant to activate small molecules, as illustrated by their lack of reactivity with CO.<sup>11,12</sup> Much less studied than NHC-5s are the so-called ring-expanded N-heterocyclic carbenes (RE-NHCs).<sup>13</sup> Herein we compare the ambiphilic nature of NHC-5 with RE-NHCs (–6,<sup>13a</sup> –7 (ref. 14) and –8 (ref. 13c)) and CAAC-5 through DFT calculations and their reactivity with small molecules.

## Results and discussion

Compared to NHC-5s, RE-NHCs display a larger N–C–N bond angle ( $\angle_{\text{carb}}$ ) which imposes greater steric constraint when used as a ligand for transition metals, a feature used to enhance catalytic activity.<sup>15</sup> Arguably less emphasized, is the larger carbene bond angle, which increases the p-character of the lone

pair, and thus the energy level of the HOMO.<sup>16</sup> Comparatively, the LUMO is less affected since ring expansion does not significantly disrupt the planarization of the  $\alpha$ -amino fragments, which leaves the mesomeric stabilization of the  $p_{\pi}$  orbital by the nitrogen lone pairs nearly identical.

The ambiphilicity of a carbene can be estimated computationally by considering the singlet-triplet gap ( $\Delta E_{\text{S-T}}$ ) (Scheme 1). As expected, our calculations indicate a correlation between the ring size and ambiphilicity of a carbene. Interestingly, the data also suggests that the ambiphilicity of NHC-7 and NHC-8 approaches that of CAAC-5.

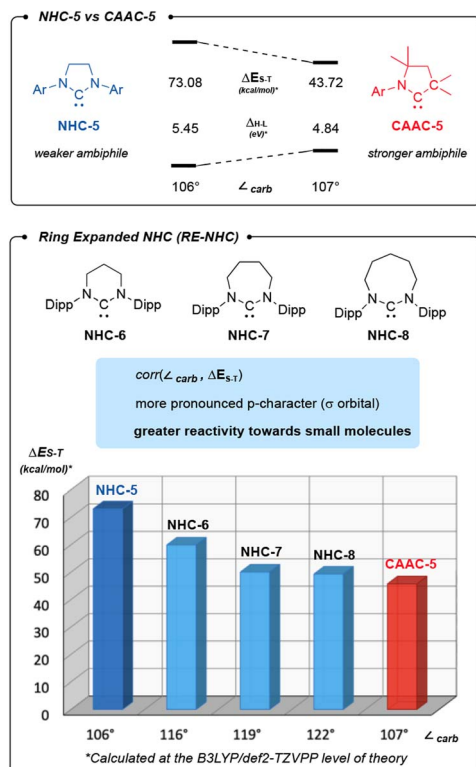
To compare experimentally the ambiphilicity of NHCs with that of CAAC-5, we first considered the activation of sp-hybridized CH bonds which has been reported with CAACs,<sup>17</sup> but seldomly described with NHCs (one example has been reported using acetylene gas).<sup>18</sup> We first investigated the reaction of *p*-tolylacetylene [ $pK_{\text{a}}$  (DMSO) = 28.8 vs. 25 for acetylene] with NHC-5 at room temperature in benzene solution (Scheme 2). In this case, no reaction was observed within 1 hour. In marked contrast, using CAAC-5 the oxidative addition product **1a** was quantitatively obtained within minutes. Under the same conditions a rapid and clean reaction was also observed with NHC-6<sup>13a</sup>, NHC-7<sup>15</sup> and NHC-8<sup>13c</sup> giving adducts **1b–d** as shown by characteristic <sup>1</sup>H NMR signals at 6.04, 5.87 and 5.64 ppm, and <sup>13</sup>C NMR signals at 72.3, 73.9 and 77.1 ppm, respectively. The structure of adduct **1c** (from NHC-7) was confirmed by X-ray crystallography. Because of the significant difference in reactivity observed between NHC-5 and the RE-NHCs, we re-evaluated the reaction of NHC-5 with *p*-tolylacetylene and observed very slow conversion to adduct **1e** upon performing the reaction at 80 °C for 4 hours.

These initial results prompted us to search for more challenging molecules to activate. Examples of stable carbenes reacting with isonitriles to afford ketenimines are scarce.

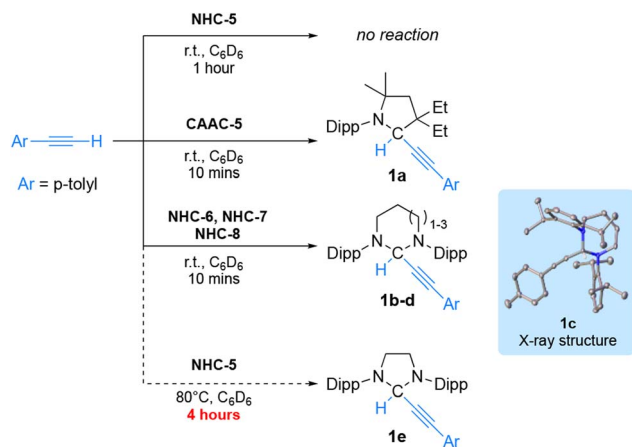
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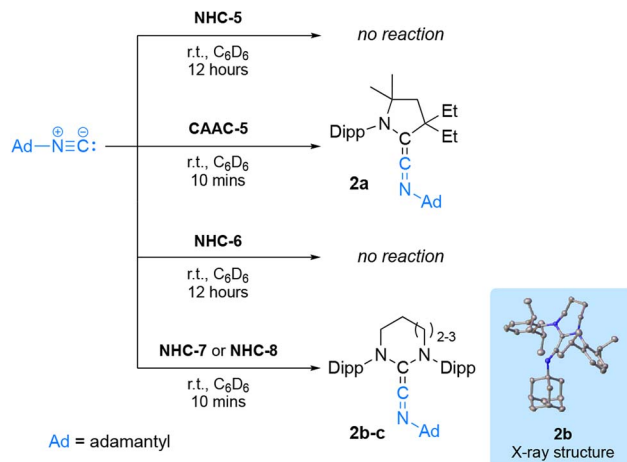


Scheme 1 CAAC-5 is more ambiphilic than NHC-5. NHC ambiphilicity is improved in ring-expanded NHC (RE-NHCs) as shown by their decreasing singlet–triplet gap ( $\Delta E_{S-T}$ ).



Scheme 2 Reactivity of NHC-5–8 and CAAC-5 with *p*-tolylacetylene.

They only include the anti-Bredt NHC<sup>19</sup> and diamidocarbenes (DAC) 20 thanks to their enhanced electrophilicity resulting from reduced donation of the nitrogen lone-pair into the empty p-type orbital of the carbene carbon. Curious to probe the reactivity of RE-NHCs, we considered their reactivity and that of NHC-5 or CAAC-5 with adamantyl isocyanide (Scheme 3). CAAC-5 cleanly afforded the ketenimine 2a within minutes, while no reaction occurred with NHC-5 after 12 hours at room temperature in benzene solution.<sup>21</sup> This result contrasts with CAAC-5 which cleanly afforded the ketenimine 2a



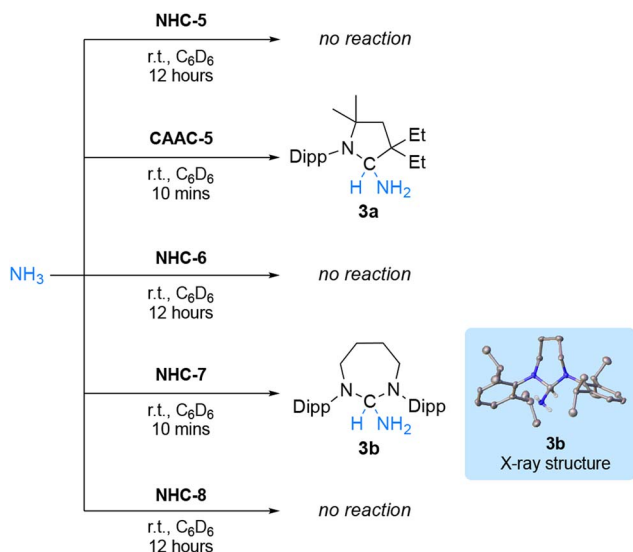
Scheme 3 Reactivity of NHC-5–8 and CAAC-5 with adamantyl isocyanide.

within minutes. With NHC-6, no reaction was observed even after 12 hours. However, with NHC-7 and NHC-8, the quantitative formation of compound 2b and 2c, was observed after 10 minutes, as evidenced by the diagnostic <sup>13</sup>C NMR signal for the central carbon of ketenimines at 216.9 ppm and 211.5 ppm, respectively. We confirmed the structure of compound 2b by X-ray crystallography. Interestingly, the solid-state structure of 2b revealed a pronounced bent geometry ( $C_{NHC}-C-N$  angle: 158.5°) compared to that of diamido cyclohexylketenimine ( $C_{DAC}-C-N$  angle: 173.8°)<sup>20b</sup> with a longer  $C_{NHC}-C_{ket}$  bond (133.8 pm vs. 129.7 pm for DAC). This observation indicates that NHC-7 is less electrophilic than DAC.

Collectively, the reactions with terminal alkynes and isocyanides suggest that the ambiphilicity of the carbenes is in the order NHC-5 < NHC-6 < NHC-7 < NHC-8 < CAAC-5, which is in agreement with their singlet–triplet gap. To deconvolute these results further, we wondered if RE-NHCs, notwithstanding their lower electrophilicity could compare with CAAC-5 in the activation of ammonia.<sup>5</sup> Under 2 atmospheres of NH<sub>3</sub>, no reaction occurred with NHC-5, which was expected since several diaminocarbenes have even been generated in liquid ammonia.<sup>22</sup> (Scheme 4). In agreement with literature precedent,<sup>5</sup> under the same conditions, CAAC-5 rapidly led to the ammonia adduct 3a. Switching to RE-NHCs, no reaction was observed with NHC-6 despite prolonged reaction time, while NHC-7 led to the clean formation of product 3b with distinctive <sup>1</sup>H and <sup>13</sup>C NMR signals at  $\delta$  = 5.25 ppm and 85.8 ppm, respectively. This result was confirmed by single crystal X-ray diffraction. However, to our surprise, no reaction was observed with NHC-8.

We previously reported that the steric environment of CAAC-5 is a determining factor in controlling the reversibility of E–H bond activation (E = N–H, P–H).<sup>8</sup> Compared to CAAC-5 ( $\angle_{carb}$  = 106°), NHC-8 is more sterically constrained around the carbene carbon due to its large  $N-C_{NHC}-N$  bond angle ( $\angle_{carb}$  = 122°).<sup>13c</sup> We hypothesized this could explain its lack of reactivity with ammonia despite favourable electronics. To probe this hypothesis, we prepared the *N*-Mesityl (-Mes) substituted NHC-8 (<sup>Mes</sup>NHC-8) since its steric profile is significantly smaller

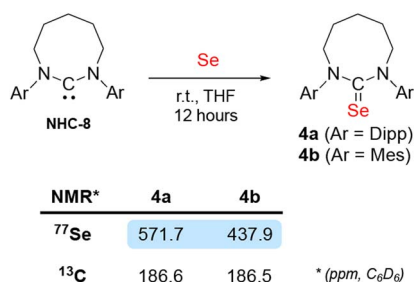




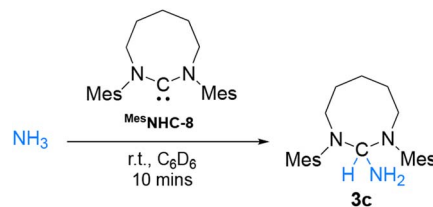
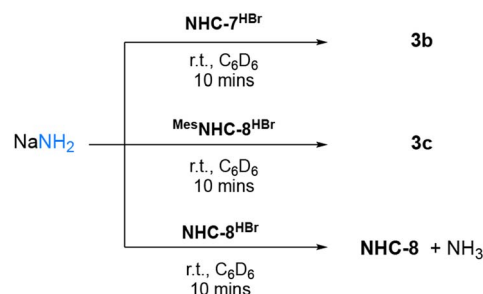
Scheme 4 Reactivity of NHC-5–8 and CAAC-5 with ammonia.

than that of the Dipp-substituted **NHC-8**. This is apparent from the solid state structures, when considering the steric maps (see ESI for details<sup>†</sup>) and percent buried volumes (% $V_{\text{bur}}^{23}$ ) around the carbene carbon. **NHC-8** (80.1%) compared to **MesNHC-8** (77.2%) which is closer to that of **NHC-7** (78.4%). The larger steric hindrance is also apparent in solution when considering the unusual  $^{77}\text{Se}$  NMR downfield shift of the **NHC-8-Se** adduct **4a** (571.1 ppm) compared to **MesNHC-8-Se** adduct **4b** (437.9 ppm) (Scheme 5). Indeed,  $^{77}\text{Se}$  NMR is a spectroscopic marker for highlighting non-classical bonding (NCB) interactions between pendant *N*-Dipp substituents and the selenium atom.<sup>24</sup> Note that when comparing the reactivity of *N*-tolyl and *N*-Dipp 8-membered NHCs with silver chloride, Cavell and co-workers discovered that in very large ring NHCs the steric environment provided by *N*-Dipp substituents can become so overwhelming that it prevents coordination.<sup>13c</sup>

Having confirmed that **MesNHC-8** is less sterically hindered than **NHC-8** and even **NHC-7**, we evaluated its reactivity towards ammonia. Gratifyingly, rapid formation of the corresponding ammonia adduct was observed when performing the reaction in  $\text{C}_6\text{D}_6$  under 2 atmospheres of  $\text{NH}_3$  (Scheme 6). To confirm these results, we also investigated the reactivity of the corresponding imidazolium salts with sodium amide which provided the expected adducts *via* nucleophilic addition of  $\text{NH}_2^-$  (Scheme 7).



Scheme 5 Selenium adducts of Dipp- and Mes-substituted NHC-8.

Scheme 6 Reactivity of **MesNHC-8** with ammonia.Scheme 7 Reactivity of **NHC-7**, **MesNHC-8** and **NHC-8** conjugate acid salts with  $\text{NaNH}_2$ .

Note that under these conditions, reaction of **NHC-8<sup>HBr</sup>** with  $\text{NaNH}_2$  afforded the free **NHC-8** and ammonia. Overall, these results suggest that for 8-membered ring NHCs, the activation of ammonia is controlled by steric parameters and possibly reversible.

## Conclusions

Imidazole-2-ylidenes<sup>9</sup> and imidazolin-2-ylidenes,<sup>10</sup> the popular class of singlet carbenes introduced by Arduengo, have not proven to be ambiphilic owing to the two  $\sigma$ -withdrawing,  $\pi$ -donating amino groups stabilizing the carbene centre. However, our experimental data demonstrate that ring-expanded *N*-heterocyclic carbenes, **NHC-7s** and **NHC-8s**, belong to the class of ambiphilic carbenes. Our results also show that the steric environment in RE-NHCs can become a determining factor for controlling the E–H bond activation. We anticipate these results will have far reaching implications in the design and applications of large ring singlet carbene skeletons.

## Data availability

All the data available has been provided in the ESI.<sup>†</sup>

## Author contributions

F. V. and R. J. conceptualized this work. F. V., V. T. W. and M. A. performed the synthetic work. R. J. performed X-ray diffraction analysis. The manuscript was written by R. J. and G. B. and reviewed by all the authors. R. J. and G. B. guided the project.

## Conflicts of interest

There are no conflicts to declare.



## Acknowledgements

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