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Ambiphilicity of ring-expanded N-heterocyclic carbenes†

François Vermersch, ‡ Victor T. Wang, ‡ Mehdi Abdellaoui, Rodolphe Jazzar * and Guy Bertrand *

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 σ-withdrawing, π-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.[1] More than a decade ago, our group discovered that cyclic (alkyl)(amino)carbenes (**CAAC-5**),[2,3] a class of highly ambiphilic carbenes, could react with carbon monoxide,[4] H_2,[5] NH_3 (ref. 5) and P_4.[6] More recently, it has been shown that **CAAC-5**s not only activate a variety of bonds (C–H, Si–H, B–H…)[7] but also promote catalytic reactions.[8] In comparison, imidazole-2-ylidenes[9] and imidazolin-2-ylidenes,10 the classical N-heterocyclic carbenes (**NHC-5**s), are much less ambiphilic due to their two π-donating amino substituents. Consequently, they are reluctant to activate small molecules, as illustrated by their lack of reactivity with CO.[11,12] Much less studied than **NHC-5**s are the so-called ring-expanded N-heterocyclic carbenes (RE-NHCs).[13] Herein we compare the ambiphilic nature of **NHC-5** with RE-NHCs (−6,[13a] −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-5**s, RE-NHCs display a larger N–C–N bond angle ($\angle_{carb}$) which imposes greater steric constraint when used as a ligand for transition metals, a feature used to enhance catalytic activity.[15] 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.[16] Comparatively, the LUMO is less affected since ring expansion does not significantly disrupt the planarization of the α-amino fragments, which leaves the mesomeric stabilization of the p_π orbital by the nitrogen lone pairs nearly identical.

The ambiphilicity of a carbene can be estimated computationally by considering the singlet–triplet gap (ΔE_{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,[17] but seldomly described with NHCs (one example has been reported using acetylene gas).[18] We first investigated the reaction of *p*-tolylacetylene [pK_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**[13a] **NHC-7**[15] and **NHC-8**[13c] giving adducts **1b–d** as shown by characteristic ^{1}H NMR signals at 6.04, 5.87 and 5.64 ppm, and ^{13}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.

UCSD-CNRS Joint Research Chemistry Laboratory (IRL 3555), Department of Chemistry and Biochemistry, University of California, La Jolla, San Diego, California 92093-0358, USA. E-mail: rjazzar@ucsd.edu; gbertrand@ucsd.edu

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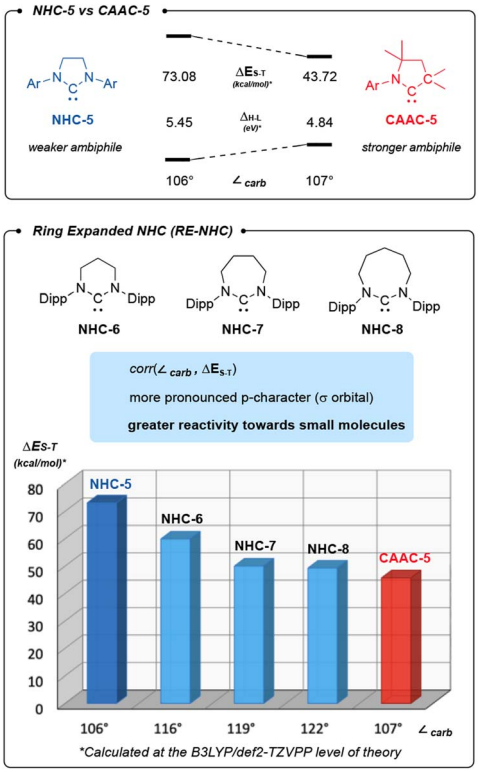
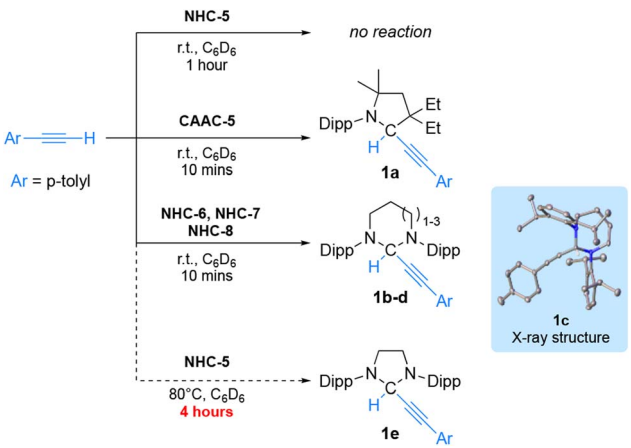
‡ These authors contributed equally to this work.

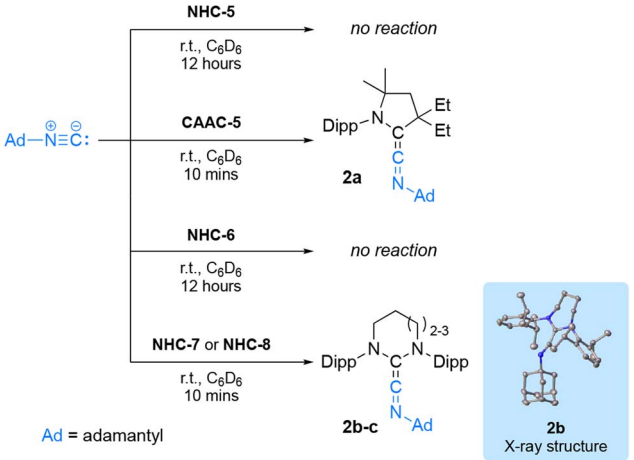


Scheme 1 CAAC-5 is more ambiphilic than NHC-5. NHC ambiphilicity is improved in ring-expanded NHC (ReNHCs) as shown by their decreasing singlet–triplet gap (ΔE_{S-T}).



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

They only include the anti-Bredt NHC[19] 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.[21] This result contrasts with **CAAC-5** which cleanly afforded the ketenimine **2a**

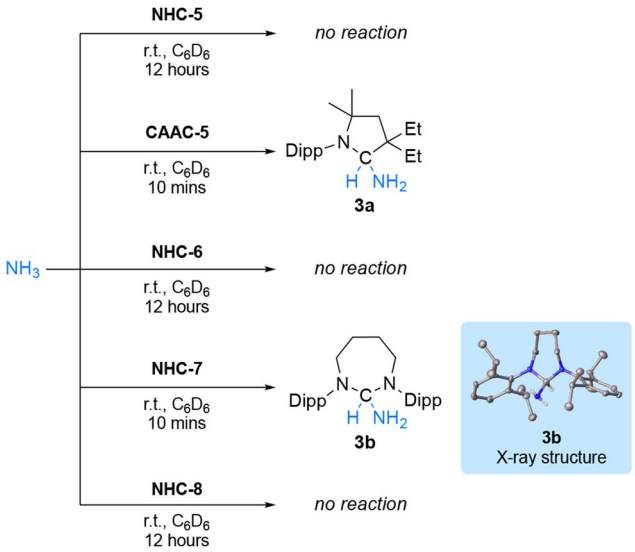


Scheme 3 Reactivity of NHC-5–8 and CAAC-5 with adamantyl isocyanide.

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 ^{13}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°)[20b] 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.[5] Under 2 atmospheres of NH_3, no reaction occurred with **NHC-5**, which was expected since several diaminocarbenes have even been generated in liquid ammonia.[22] (Scheme 4). In agreement with literature precedent,[5] 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 ^1H and ^{13}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**.

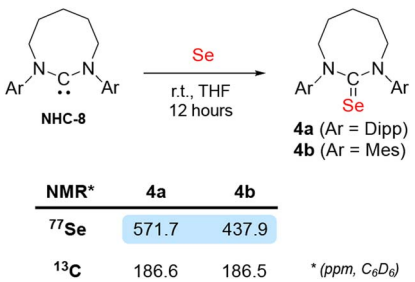
We previously reported that the steric environment of **CAAC-5** is a determining factor in controlling the reversibility of E–H bond activation (E = N–H, P–H).[8] Compared to **CAAC-5** ($\angle_{carb} = 106°$), **NHC-8** is more sterically constrained around the carbene carbon due to its large N–C_{NHC}–N bond angle ($\angle_{carb} = 122°$).[13c] 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** (^{Mes}**NHC-8**) since its steric profile is significantly smaller



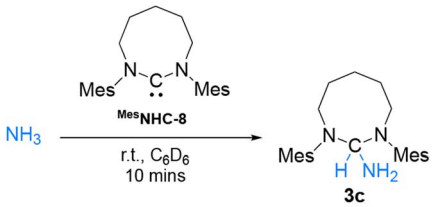
Scheme 4 Reactivity of NHC-5–8 and CAAC-5 with ammonia.

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†) and percent buried volumes (%V_{bur}[23]) around the carbene carbon. **NHC-8** (80.1%) compared to ^{Mes}**NHC-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}Se NMR downfield shift of the **NHC-8**-Se adduct **4a** (571.1 ppm) compared to ^{Mes}**NHC-8**-Se adduct **4b** (437.9 ppm) (Scheme 5). Indeed, ^{77}Se NMR is a spectroscopic marker for highlighting non-classical bonding (NCB) interactions between pendant *N*-Dipp substituents and the selenium atom.[24] 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.[13c]

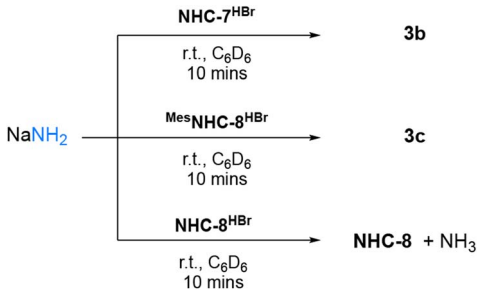
Having confirmed that ^{Mes}**NHC-8** is less sterically hindered than **NHC-8** and even **NHC-7**, we evaluated its reactivity towards ammonia. Gratifyingly, rapid formation of the corresponding ammonia adduct was observed when performing the reaction in C_6D_6 under 2 atmospheres of NH_3 (Scheme 6). 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 NH_2^- (Scheme 7).



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



Scheme 6 Reactivity of ^{Mes}NHC-8 with ammonia.



Scheme 7 Reactivity of NHC-7, ^{Mes}NHC-8 and NHC-8 conjugate acid salts with $NaNH_2$.

Note that under these conditions, reaction of **NHC-8**^{HBr} with $NaNH_2$ 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[9] and imidazolin-2-ylidenes,[10] the popular class of singlet carbenes introduced by Arduengo, have not proven to be ambiphilic owing to the two σ-withdrawing, π-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.†

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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