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Cyclic (amino)(barrelene)carbenes: an original family of CAACs through a novel synthetic pathway†

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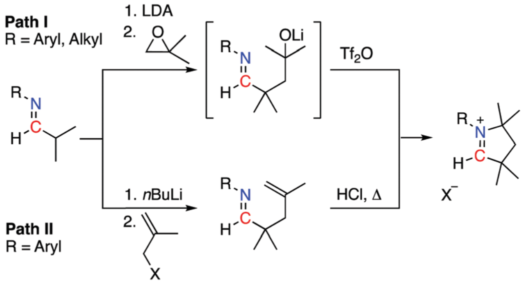
A novel family of cyclic (alkyl)(amino)carbenes, which we name cyclic (amino)(barrelene)carbenes (CABCs) is reported. The key synthetic step involves an intramolecular [4+2] cyclization of an anthracene derivative with an alkyne. This synthetic approach allows for the attachment of both aryl and alkyl groups on the nitrogen atom. When used as ligand, two of the barrelene hydrogens are in close contact with the metal, which could stabilize low valent catalytic intermediates.

Since their discovery in 2005,[1] cyclic (alkyl)(amino)carbenes (CAACs) have led to numerous breakthroughs in various fields of chemistry from catalysis to materials science.[2] CAACs have proved to be more efficient than the classical NHCs (cyclic diaminocarbenes) for the activation of enthalpically strong bonds;[3] they even catalyze carbonylation reactions, a task typically reserved for transition metals.[4] Most of the advantages of CAACs over NHCs can be traced back to their stereoelectronic properties.[5] The replacement of a π-donating and σ-withdrawing amino group with a σ-donating quaternary carbon, makes CAACs both more π-accepting and σ-donating. Recently, novel families of CAACs featuring different ring sizes,[6] pendant functionalities,[7] and even enantiopure versions have been prepared.[8] All these carbenes have been synthesized starting from an aldimine of choice following two different synthetic routes, both of which have limitations (Scheme 1).[1,9] For example, Path **II** is a higher yielding route than Path **I**, but is incompatible with *N*-alkyl substituents, as the intermediate is too basic to facilitate the hydroiminiumation reaction. Herein, we report a novel, straightforward synthetic route to an original family of CAACs which we name cyclic (amino)(barrelene) carbenes (CABCs). The key step is an intramolecular [4+2] cyclization of an anthracene derivative with an alkyne.[10] Our synthetic strategy complements existing methodologies and allows for the modulation of electronic and steric demands through access to both alkyl and aryl groups on the nitrogen.

The cyclic imine precursor **1**, featuring the barrelene scaffold, was prepared in 71% yield in one step by condensation of 9-anthraldehyde with 1,1-dimethyl-propargyl amine and subsequent [4+2]cycloaddition (Scheme 2). Then, a slight excess of alkylating agent[11] was added to **1** in boiling acetonitrile or in hexanes, giving rise to the CABC conjugate acids **2**. The solutions of **2** were concentrated and their residues were washed with diethyl ether. Salts **2** were isolated as moisture stable solids in good to excellent yields by crystallization from slow diffusion of diethyl ether into acetonitrile.

The arylation of cyclic imine **1** was accomplished using diaryliodonium salts with a catalytic amount of $Cu(OAc)_2$ in DMF (Scheme 2).[12] Salts **3** were obtained as air stable solids in good yields after crystallization through slow diffusion of diethyl ether into acetonitrile or dichloromethane. In pursuit of a more sterically encumbered *N*-aryl CABC, all attempts to arylate **1** with a mesityl group were not successful despite forcing conditions. Conversely, the desired bulky CABC conjugate acid **3d** could be obtained through an alternative synthetic route. The reaction of *N*-mesityl dimethyl propargyl amine **4** with 9-bromomethyl anthracene, in the presence of K_2CO_3 in acetonitrile, gives the substituted anthracene **5** in 45% yield after 48 hours (Scheme 3). Hydride abstraction from



Scheme 1 Classical syntheses of cyclic (alkyl)(amino)carbene precursors.

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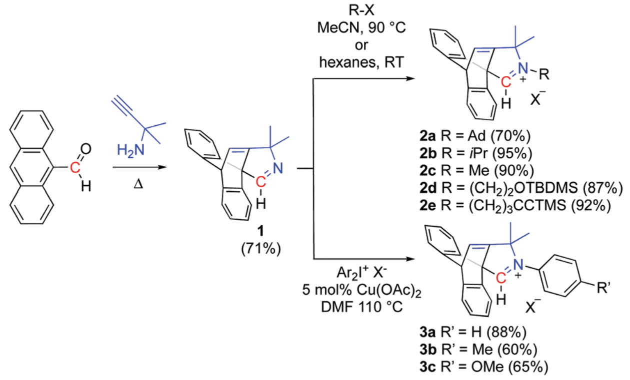
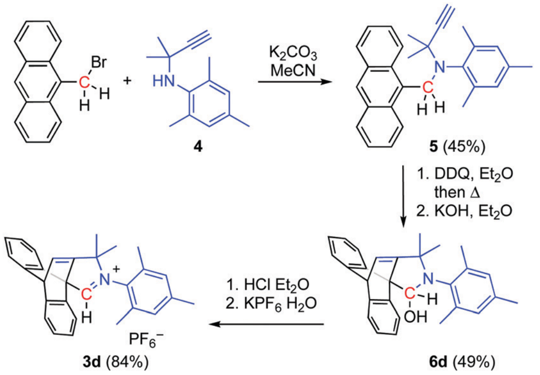


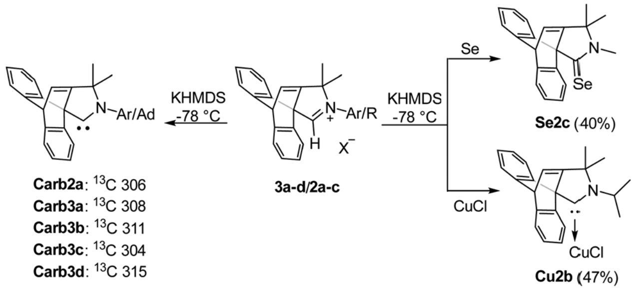
Scheme 2 Synthesis of cyclic (amino)(barrelene) conjugate acids **2** and **3**.



Scheme 3 Synthesis of CABC conjugate acid **3d**.

the CH_2 motif in **5** was accomplished with DDQ which induces the desired [4+2] cyclization under heating conditions. To facilitate purification, a basic workup of the precipitate yields the hydroxy pyrrolidine **6d**. The latter readily reacted with HCl generating the corresponding iminium chloride salt. Subsequent salt metathesis using KPF_6 afforded **3d**, which can be further purified by crystallization through slow diffusion of diethyl ether into dichloromethane.

Iminium salts **2a** and **3a–d** can be deprotonated with KHMDS at −78 °C to afford the corresponding carbenes **Carb2a** and **Carb3a–d** (Scheme 4). ^{13}C NMR spectra exhibit singlets at 306 ppm (**Carb2a**), 304–315 ppm (**Carb3a–d**), in the range observed for classical five-membered CAACs (304–319 ppm).[2] **Carb2a** and **Carb3d** demonstrate a good thermal stability with the latter being stable up to 70 °C in benzene for at least 1 h. Deprotonation of iminiums **2c** and **2b** also occurred with KHMDS at −78 °C, but the corresponding free carbenes **Carb2c** and **Carb2b** could not be observed. However, they can be trapped *in situ* as shown by the formation of the selenium adduct **Se2c** and copper complex **Cu2b**.

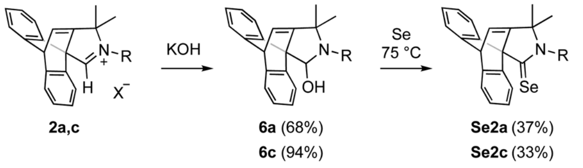


Scheme 4 Deprotonation of cyclic iminiums leading either to isolable carbenes, or to the trapped products of non-isolable carbenes.

Note also that in the presence of selenium, the hydroxy pyrrolidines **6a** and **6c** (readily obtained by addition of KOH to cyclic iminiums **2a** and **2c**), led in refluxing THF to **Se2a** and **Se2c**. These results demonstrate the existence of a thermal equilibrium between CABC-derived hydroxy pyrrolidines and the corresponding carbenes (Scheme 5).[13]

Unsurprisingly, the overall donating properties of CABCs are similar to those of CAACs, as indicated by the infrared ν^{av}_{CO} frequency of (**Carb2c**)$Rh(CO)_2Cl$ complex (ν^{av}_{CO} = 2038 cm^{-1}) compared to CAAC analogous complexes (2036 cm^{-1}).[14] Interestingly, the ^{77}Se NMR signal[15] of CABC selenium adducts appeared at much lower field than for CAACs as shown in Fig. 1. We have already demonstrated[16] that the higher chemical shift observed for the adamantyl-CAAC compared to the diethyl analogue was due to non-classical $C(sp^3)H$–selenium bonding interactions between the Se and two adamantyl hydrogens. Such interactions also exist in CABCs but, in addition, two barrelene hydrogen atoms are also involved, as first evidenced by the single crystal X-ray diffraction study of **Se2a** and **Se3d**. Note that compared to $C(sp^3)H$–X, $C(sp^2)H$–X non-classical hydrogen bonding interactions are known to be weaker,[17] which explains the longer barrelene-H–Se distances compared to that of the adamantyl-H–Se. Importantly, the barrelene-H–Se interactions are also seen when the proton spectra of the iminium salts **2a** and **3d** are compared to their corresponding Se adducts. While the iminium barrelene protons are upfield of 7.5 ppm, their selenium adducts consistently shift two barrelene protons downfield to 8.40 ppm (**Se2a**) and 8.36 ppm (**Se3d**).

This observation prompted us to prepare CABC copper and gold complexes, in order to investigate if agostic interactions also existed between barrelene hydrogens and a metal. As already mentioned, **Cu2b** was prepared by deprotonation of the corresponding iminium salt **2b** in the presence of CuCl. **Au2b** was synthesized in 54% yield by trapping of **Carb2b** with $AuPh(PPh_3)$, followed by cleavage of the phenyl group with HCl, whereas **Au3d** was readily accessible (63% yield) by addition of (tht)AuCl to **Carb3d**. As can be seen in Fig. 2, X-ray crystal structures revealed that, in all cases, short H_1- and H_2-M distances were observed. Again, when the proton NMR spectra of the iminium compounds are compared to those of their



Scheme 5 Generation and trapping of carbenes **Carb2a** and **Carb2c** from hydroxy pyrrolidines **6a,c**.

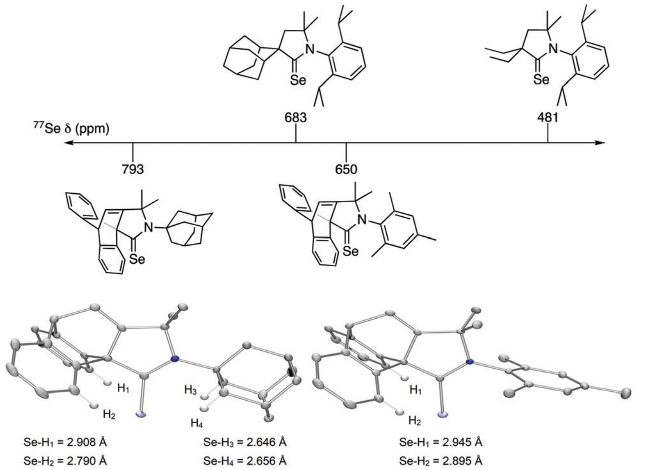


Fig. 1 The ^{77}Se NMR chemical shift of comparable CABC and CAAC selenium adducts (top), with the solid-state structure of **Se2a** (bottom left) and **Se3d** (bottom right) showing non-classical bonding between the Se, two adamantyl hydrogens, and two barrelene hydrogens.

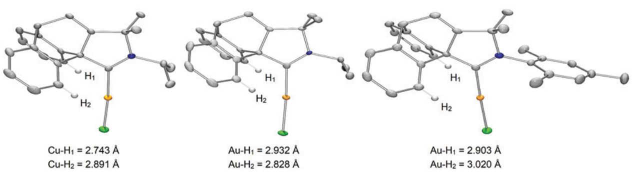


Fig. 2 Solid-state structure of **Cu2b** (right), **Au2b** (center) and **Au3d** (left) showing two barrelene hydrogens in proximity of the metal.

corresponding metal complexes, we observe a downfield shift of two barrelene hydrogens from 7.5 ppm, to 7.73 (**Cu2b**), 8.08 (**Au2b**) and 8.20 ppm (**Au3d**), confirming the interaction.

In summary, a new family of cyclic (alkyl)(amino)carbenes has been prepared through intramolecular [4+2] cyclization of anthracene derivatives with an alkyne. This new framework preserves the electronic properties of CAACs and allows the attachment of either aryl or alkyl groups on the nitrogen atom. Additionally, when used as ligands, two of the barrelene hydrogen atoms are positioned to interact with the metal, which could stabilize low valent catalytic intermediates.

M. R. S. performed the synthetic experiments and analyzed the experimental data. M. M. and G. B. conceived the concept and directed the project. All authors wrote the paper.

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Conflicts of interest

There are no conflicts to declare.

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