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Dimerization

Cross-Coupling Reactions between Stable Carbenes**

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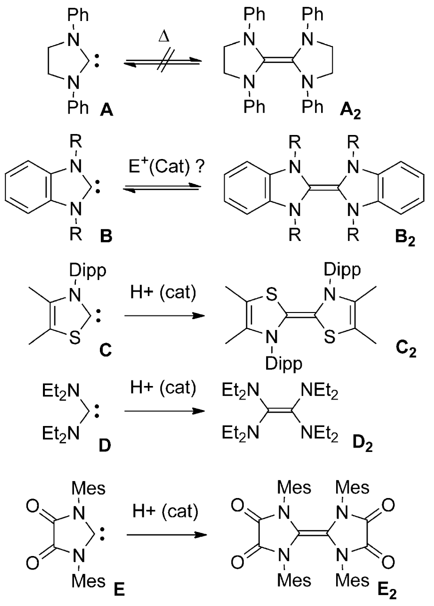
***Abstract:** By utilizing stable carbenes with low-lying LUMOs, coupling with the stable nucleophilic diaminocyclopropenylidene was achieved. This reaction resulted in the formation of two new and rare examples of a bent allene as well as the isolation of the first carbene–carbene heterodimer.*

Since the seminal work by Wanzlick et al.,[1] who proposed the existence of an equilibrium between the imidazolidin-2-ylidene **A** and its dimer $\mathbf{A}_2$, namely a tetraazafulvalene, the dimerization of singlet carbenes and the reverse reaction have been a subject of controversy[2,3] (Scheme 1). Two of the most convincing pieces of evidence for a spontaneous dissociation reaction were reported independently by Hahn et al.[4] and Lemal et al.[5] Both groups were able to observe, by NMR spectroscopy, the formation of the benzimidazolin-2-ylidenes **B** from solutions of the dibenzotetraazafulvalenes $\mathbf{B}_2$. However, Lemal et al. were cautious, thus suggesting that adventitious electrophilic catalysis of equilibration might be occurring. Arduengo et al.[6] isolated both the thiazol-2-ylidene **C** and its dimer $\mathbf{C}_2$, and Alder et al.[7] reported the spectroscopic characterization of the acyclic bis(amino)carbene **D** and isolated the corresponding tetra(amino)alkene $\mathbf{D}_2$.[8] However, in both cases, it has been demonstrated that the dimerization occurs only in the presence of an acid catalyst. The most recent striking example was the isolation by Bielawski et al.[9a] of the diamidocarbene **E** prepared by reduction of the corresponding dichloro derivative, while Ganter et al.[9b] reported that **E** spontaneously dimerizes to $\mathbf{E}_2$ when generated by deprotonation. Crossover experiments have also been successfully carried out,[2,3a,c] but here again, Lemal et al.[3d] showed that the reaction occurs only with an electrophilic catalyst. The noncatalyzed dimerization of singlet carbenes follows a non-least motion pathway which involves the attack of the occupied in-plane σ orbital of one carbene on the out-of-plane vacant p_π orbital of a second carbene.[10] Although thermodynamically favorable, this process is hampered by a significant energy barrier, which results from the stabilization of the vacant orbital by the donation of the lone pairs from the substituents.[11] It is therefore readily understandable that protonation of the carbene, which considerably decreases the energy of the LUMO, facilitates the dimerization reaction.



Scheme 1. The Wanzlick equilibrium most likely involving electrophilic catalysis. Dipp = 2,6-$i\mathrm{Pr}_2\mathrm{C}_6\mathrm{H}_3$, Mes = 2,4,6-$\mathrm{Me}_3\mathrm{C}_6\mathrm{H}_2$.

This short analysis indicates that the coupling reaction involving stable carbenes featuring a rather low-energy LUMO should be possible,[12,13] especially if the other carbene partner has a high-energy HOMO. Herein we report the first unambiguous examples of noncatalyzed cross-coupling reactions between two stable carbenes.

Because the activation energy barrier is sensitive to steric hindrance, we chose the cyclopropenylidene **1**[14] as the nucleophilic partner (Scheme 2). Indeed, the two amino substituents are directed towards the back of the ring, thus leaving the carbene center readily accessible. For the electrophilic partner, we first considered the cyclic (alkyl)(amino)carbene (CAAC) **2a**.[15] Stirring a solution of a stoichiometric mixture of **1** and **2a** in hexanes overnight led to compound **5a**, which was isolated as single crystals in 33% yield. Although mass spectrometry was consistent with the formation of a cross-coupled product, a singlet at δ = 3.85 ppm in the ^{1}H NMR spectrum, integrating for one proton, suggested that **5a** was not the expected alkene **3a**. Indeed, a single-crystal X-ray diffraction study[16] (Figure 1) showed that **5a** was a rearrangement product, in which the cyclopropenylidene moiety underwent a ring-expansion reaction to form a rare example of a stable bent allene.[17] It features a C-C-C bond angle of 164.4(1)° and can be viewed as

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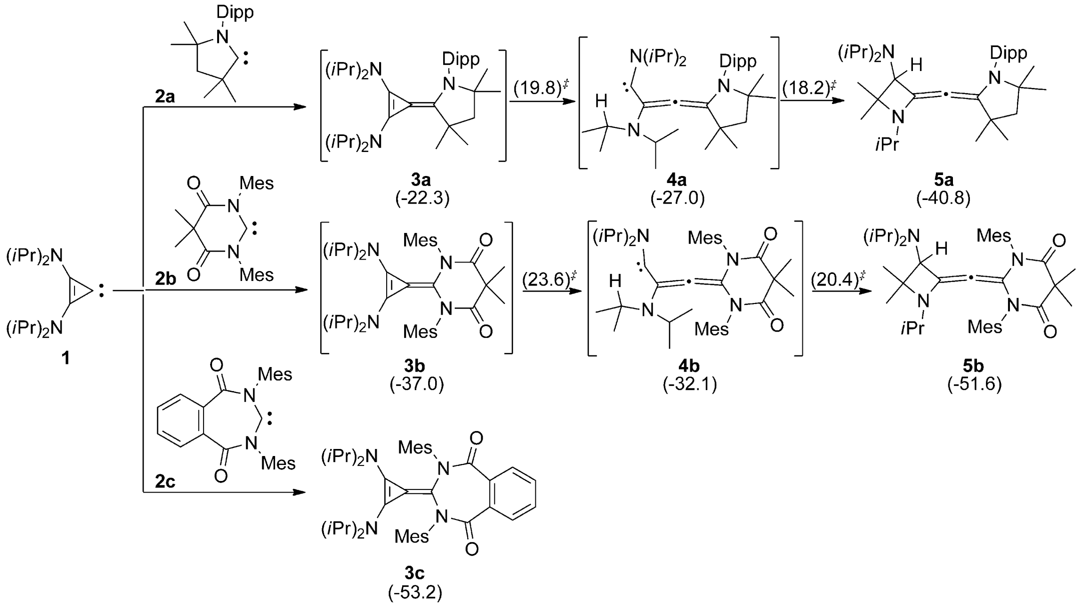

Scheme 2. Reactions of the cyclopropenylidene **1** with the CAAC **2a**, 6-DAC **2b**, and 7-DAC **2c**. Energies (ΔG and $\Delta G^{\ddagger}$) are within parentheses and given in kcal mol^{-1}.

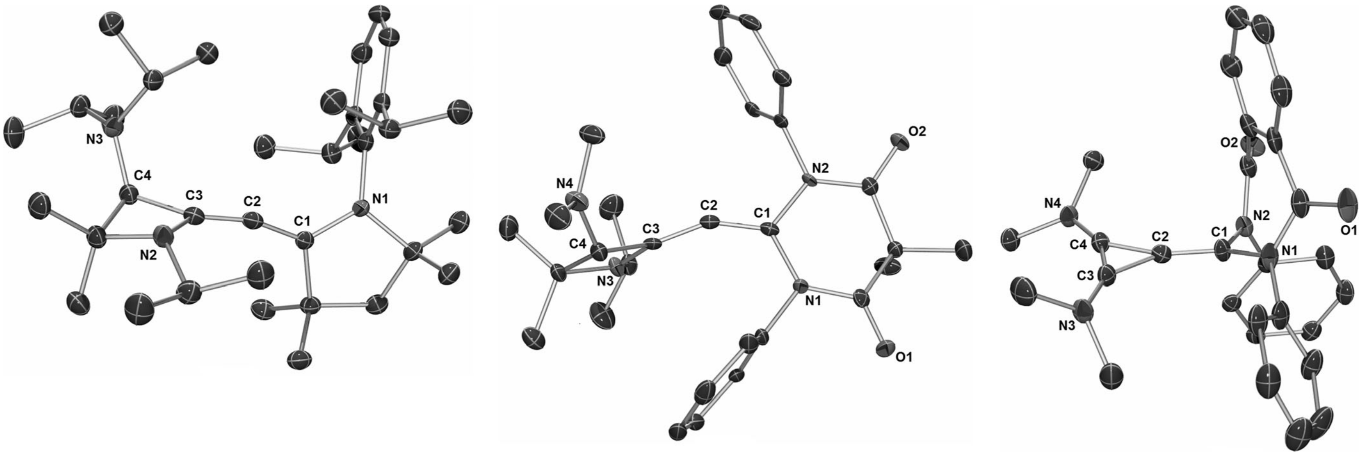

Figure 1. Structures of **5a** (left), **5b** (middle), and **3c** (right) in the solid state. Thermal ellipsoids resolved at 50% probability levels. CH_3 groups of Mes and *i*Pr for **5b** and **3c**, as well as hydrogen atoms have been removed for clarity. Selected bond lengths [Å] and angles [°] are given: **5a** C1–C2 1.317(2), C2–C3 1.311(2), C3–C4 1.541(1); C1-C2-C3 164.4(1). **5b** C1–C2 1.313(3), C2–C3 1.332(2), C3–C4 1.540(2); C1-C2-C3 152.1(2). **3c** C1–C2 1.351(3).

a carbo(dicarbene)[18] with the CAAC **2a** on one end, and the newly formed four-membered CAAC on the other.

To better understand the process leading to **5a**, we performed ab-initio calculations at the B3LYP/6-311++G-(2d,p)//B3LYP/6-31G(d) level of theory. The cross-coupling process leading to **3a** was found to be exothermic by 22.3 kcal mol^{-1}, and the observed product **5a** was calculated to be 18.5 kcal mol^{-1} lower in energy than **3a**. We postulate that the ring expansion of the three-membered-ring involves the transient formation of the aminocarbene **4a**, located 4.7 kcal mol^{-1} below **3a**, which then inserts into a CH bond of an isopropyl substituent. The transformations of **3a** into **4a** and **4a** into **5a** occur with small energy barriers of 19.8 and 18.2 kcal mol^{-1}, respectively (see the Supporting Information for details).

We then considered the more electrophilic six-membered-ring diamidocarbene (6-DAC) **2b**, which was discovered by Bielawski et al (Scheme 2).[19] By stirring a toluene solution of **1** and the carbene **2b** overnight, we isolated, after work up, the compound **5b** in 72% yield. However, once again, the ^{1}H NMR spectrum showed a singlet representing one hydrogen atom at $\delta = 2.86$ ppm, thus suggesting that **5b** was similar to the bent allene **5a**, and was confirmed by a single-crystal X-ray diffraction study (Figure 1).

The reaction of **1** with **2b** to give **3b** is 14.7 kcal mol^{-1} more exothermic than in the case of **3a**. Additionally, the activation energy for opening the three-membered ring of **3b** to give **4b** is 3.8 kcal mol^{-1} higher than the analogous process for **3a**. This difference led us to hypothesize that if an even more electrophilic carbene were used, the carbene–carbene heterodimer should even be more stable. To support our hypothesis, we first performed ab-initio calculations on the reaction between **1** and the most electrophilic stable carbene known to date, namely the seven-membered diamidocarbene (7-DAC) **2c** (Scheme 2), reported recently by Bielawski et al.[20] Gratifyingly, not only was the formation of the cross-coupling product exothermically favored by 53.2 kcal mol^{-1}, but also the activation energy for the three-membered ring opening was determined to be 30.6 kcal mol^{-1}, thus indicating that the desired alkene product should be stable enough to be isolated.[21]

Following the experimental procedure used for **2b**, but using the carbene **2c** instead, we were able to isolate the product **3c** in 57 % yield. To our delight, two ^{13}C NMR signals corresponding to the formation of a polarized alkene were observed at $\delta = 118.3$ and 91.4 ppm. A single-crystal X-ray diffraction study (Figure 1) confirmed that **3c** was the desired carbene–carbene heterodimer. As expected for a polarized alkene,[22] it is slightly twisted [N1-C1-C2-C4 = 17.71(3)°], but the C1–C2 bond length is in the typical range for regular alkenes [1.351(3) Å].

To further study the electronics of **3c**, we ran a molecular orbital analysis at the B3LYP/6-311g(d,p) level of theory. As apparent from the HOMO, the majority of the electron density from the π orbital of the newly formed alkene is localized on the 7-DAC carbene carbon atom (Figure 2). Moreover, the computed nucleus independent chemical shift[23] NICS(0) (at the center of the three-membered ring) and NICS(1) (at 1 Å above the ring plane) values are −29.1 and −8.5 ppm, respectively. This data is a clear indication that the three-membered ring of **2c** is a 2π-electron aromatic, thus further demonstrating the polarization of the double bond.

These results highlight the diversity of the electronic properties of the different known stable carbenes. It is the first demonstration that noncatalyzed cross-coupling reactions between stable carbenes are possible. It is quite likely that this process, which gives access to highly polarized alkenes, and even bent allenes, has a broad scope of applications.

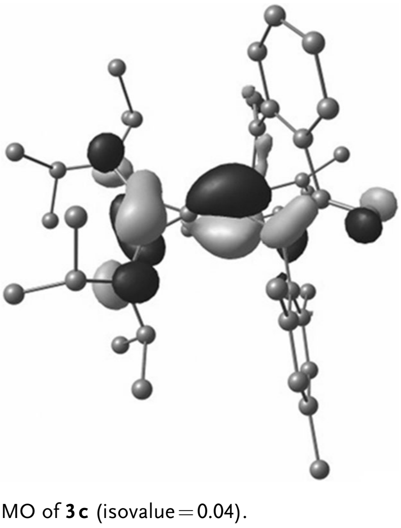

Figure 2. HOMO of **3c** (isovalue = 0.04).

Experimental Section

General procedure. The cyclopropenylidene **1** and the desired carbene **2** (1 equiv) were loaded in a Schlenk tube. Anhydrous hexanes (**2a**) or toluene (**2b,c**) was added at room temperature, and the reaction was stirred for 16 h (**2a**), 1.5 h (**2b**), and 3 h (**2c**), respectively. The solvent was removed in vacuo and single crystals were obtained from a concentrated solution (**2a, 2b**, hexanes; **2c**, toluene) at −30 °C. See the Supporting Information for the full characterization of all compounds.

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