

Rearrangement of Biaryl Monoaminocarbenes via Concerted Asynchronous Insertion into Aromatic C–H Bonds

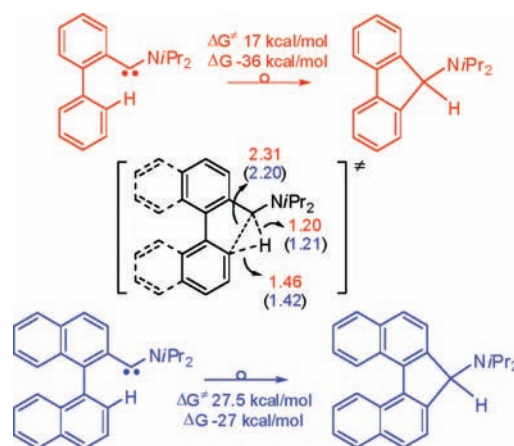
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ABSTRACT



The biphenyl and binaphthyl diisopropylaminocarbenes were found to be only transient species that spontaneously and quantitatively rearrange into the corresponding aminofluorenes. DFT calculations confirm that these insertion reactions of aminocarbenes into proximal aromatic C–H bonds require only a moderate energy barrier and support a concerted, strongly asynchronous, mechanism dominated by $C_{\text{arom}} \rightarrow C_{\text{carbene}}$ proton transfer.

Over the past 20 years, spectacular progress has been achieved in carbene chemistry. These divalent six-valence-electron fleeting intermediates have shifted into the realm

of isolable compounds,¹ and the availability of a variety of stable singlet carbenes has allowed for considerable synthetic

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developments in metal-mediated² as well as organo-catalyzed transformations.³ More insight has also been gained into typical carbene reactivity including cyclopropanation,⁴ dimerization,⁵ 1,2- and 1,3-migration,⁶ as well as O–H, N–H,⁷ and C_{sp}- and C_{sp}³-H^{8,9} insertion reactions. In addition, unusual transformations such as radical fragmentation¹⁰ and nucleophilic substitution at the carbene center¹¹ have been evidenced.

In this context, our interest for increasing further the structural variety of singlet carbenes prompted us to investigate biaryl monoaminocarbenes, and we recently reported the synthesis and original coordination behavior of the stable biphenyl and binaphthyl representatives **I** and **II** (Figure 1).¹²

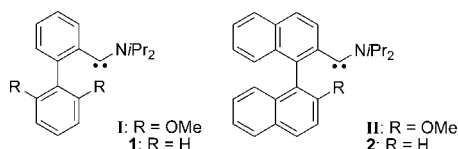
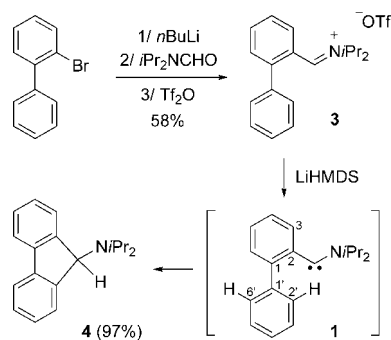


Figure 1. Biaryl monoaminocarbenes **I**, **II**, **1**, and **2**.

In continuation of this work, we became interested into the corresponding carbenes **1** and **2** free of methoxy groups on the biaryl moieties and report here on the spontaneous rearrangement of these transient carbenes via an unprecedented insertion into C_{sp}³-H bonds.

A *one-pot* procedure¹³ starting from commercially available 2-bromobiphenyl afforded the biphenyl iminium salt **3** in 58% overall yield (Scheme 1). The characteristic CH iminium signals were observed at 8.75 and 173.5 ppm in

Scheme 1. Generation and Rearrangement of the Biphenyl Aminocarbene **1**



the respective ¹H and ¹³C NMR spectra. In addition, the presence of only seven CH_{arom} signals in the ¹³C NMR spectrum indicated free rotation around the biphenyl axis on the NMR time scale. Monitoring the reaction of **3** with LiHMDS in THF by ¹H and ¹³C NMR at low temperature indicated that deprotonation immediately and cleanly occurred at –80 °C. However, the characteristic low-field ¹³C NMR signal expected for carbene **1** was not observed, and the resulting product was unambiguously identified as the diisopropylaminofluorene isomer **4**. The ¹H NMR chemical shift for the central CH (4.96 ppm) is identical to that reported previously,¹⁴ and the presence of only 4 CH_{arom} and 2 C_q in the ¹³C NMR spectrum indicates the symmetrization of the biphenyl backbone. From a mechanistic viewpoint, the formation of **4** most likely results from the insertion of the transient carbene **1** into a proximal aromatic C–H bond. The other conceivable mechanism consisting in regioselective deprotonation of the biphenyl group followed by ring closure has been ruled out by labeling experiments.¹⁵ Although, as mentioned above, examples of insertion reactions of aminocarbenes have been documented for C_{sp}-H and C_{sp}³-H

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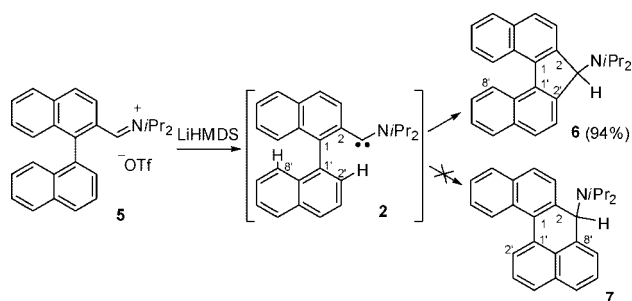
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(15) See the Supporting Information for details.

bonds,^{8,9} in the case of C_{sp^2} -H bonds, only the reverse process, namely α -elimination, has been evidenced.¹⁶ In this regard, the spontaneous rearrangement of **1** is rather surprising and markedly contrasts with the indefinite stability of the related bis(methoxylated) carbene **I** at room temperature.

In order to assess the generality of such a process, the related binaphthyl carbene **2** was then investigated, the higher rigidity around the biaryl axis being anticipated to induce geometric constraints. In addition, insertion reactions in both the C_2 -H and C_8 -H bonds were envisageable, raising a selectivity issue (Scheme 2). The binaphthyl iminium salt **5**

Scheme 2. Generation and Rearrangement of the Binaphthyl Aminocarbene **2**



was prepared following the same procedure as for **3**, starting from the readily available 2-bromobinaphthyl.¹⁷ Then, **5** was rapidly and quantitatively deprotonated by LiHMDS in THF at -80 °C, and the aminodibenzofluorene **6** was obtained in 94% yield. The signal observed at 62.9 ppm in the ^{13}C NMR spectrum of **6** is very similar to that found for **4** (61.7 ppm). In addition, the symmetrization of the binaphthyl backbone, as deduced from the presence of only six CH_{arom} signals for **6** (compared to 13 CH_{arom} signals for **5**), indicated the selective insertion of the carbene center into the C_2 -H bond. No trace of the isomeric product **7** that would have resulted from a carbene insertion into the C_8 -H bond could be detected.

To gain more insight into the spontaneous rearrangement of biaryl carbenes **1** and **2**, DFT calculations were performed at the BP3LYP/6-31G** level.¹⁵ The potential energy surface of the biphenyl carbene **1** was scrutinized first (Figure 2). As anticipated, carbene **1** was found to have a singlet ground state (the corresponding triplet state lies 17.9 kcal/mol higher in energy). The $C_{carbene}$ -N bond is short (1.32 Å) and the nitrogen atom is in a planar environment, indicating strong interaction between the nitrogen lone pair and the carbene empty orbital. In addition, the acute N- $C_{carbene}$ - C_2 angle (121.7°) and the long $C_{carbene}$ - C_2 distance (1.46 Å) indicate that the biphenyl group merely behaves as a spectator group toward the carbene center.^{8b} The intramolecular rearrange-

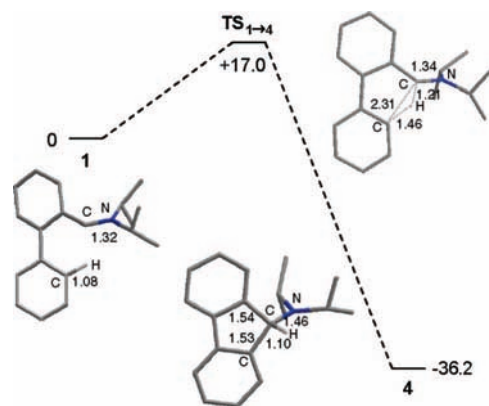


Figure 2. Energy profile computed at the BP3LYP/6-31G** level (free energies G at 25 °C including ZPE correction in kcal/mol, distances in Å) for the rearrangement **1** \rightarrow **4**.

ment of **1** leading to the aminofluorene **4** was predicted to be highly exothermic (ΔG -36.2 kcal/mol), and a transition state TS_{1-4} connecting both compounds was located 17.0 kcal/mol higher in energy than **1**. This profile is in good agreement with the spontaneous rearrangement observed at low temperature, and the structure of TS_{1-4} provides interesting information regarding the mechanism of the carbene insertion. The planarization of the biphenyl backbone (as quantified by the decrease of the C_2 - C_1 - C_1 - C_2 dihedral angle from 36° in **1** to 1° in TS_{1-4}) allows the carbene center to approach the C_2 -H bond enough for the insertion to occur. The disrupting C_2 -H bond is elongated in TS_{1-4} by 35% compared to that of carbene **1** (1.46 vs 1.08 Å), while the forming $C_{carbene}$ -H bond is elongated in TS_{1-4} by only 10% compared to that of the insertion product **4** (1.21 vs 1.10 Å), indicating a very advanced proton transfer from C_2 to the carbene center.¹⁸ In parallel, the distance between the two carbon centers $C_{carbene}$ and C_2 remains long (2.31 Å) and the N- $C_{carbene}$ π -interaction remains strong. These calculations thus support a concerted but strongly asynchronous pathway for the insertion of the carbene center into the proximal aromatic C-H bond.

In order to assess the influence of the amino group on the ease and asynchronicity of the insertion reaction, similar calculations were then performed on the biphenyl hydrogencarbene **1***.^{15,19} As expected from the removal of the strongly donating amino group, carbene **1*** adopts a triplet ground state, with a singlet-triplet separation of 8.7 kcal/mol.²⁰ In order to compare **1** to **4**, the rearrangement of **1*** into fluorene **4*** was studied on the closed-shell surface. The intramolecular CH insertion reaction was found to be highly favorable energetically (ΔG -85.1 kcal/mol) and to proceed

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with almost no energy barrier (ΔG^\ddagger 3.9 kcal/mol). The corresponding transition state $\text{TS}_{1^* \rightarrow 4^*}$ is very early, with a disrupting $\text{C}_2\text{-H}$ bond elongated by only 5% in $\text{TS}_{1^* \rightarrow 4^*}$ compared to that of $\mathbf{1}^*$, and forming $\text{C}_{\text{carbene}}\text{-H}$ and $\text{C}_{\text{carbene}}\text{-C}_2$ bonds still 40 and 64% longer in $\text{TS}_{1^* \rightarrow 4^*}$ than in fluorene $\mathbf{4}^*$. Comparing the profiles computed for $\mathbf{1}$ and $\mathbf{1}^*$, the diisopropylamino group can be estimated to stabilize the biphenyl carbene over the corresponding fluorene derivative by about 50 kcal/mol. At the same time, the R_2N group increases the energy barrier for the insertion reaction by 13 kcal/mol, but this is not sufficient to prevent the spontaneous insertion process.

Finally, the potential surface of the binaphthyl aminocarbene $\mathbf{2}$ was investigated (Figure 3). Accordingly, $\mathbf{2}$ was

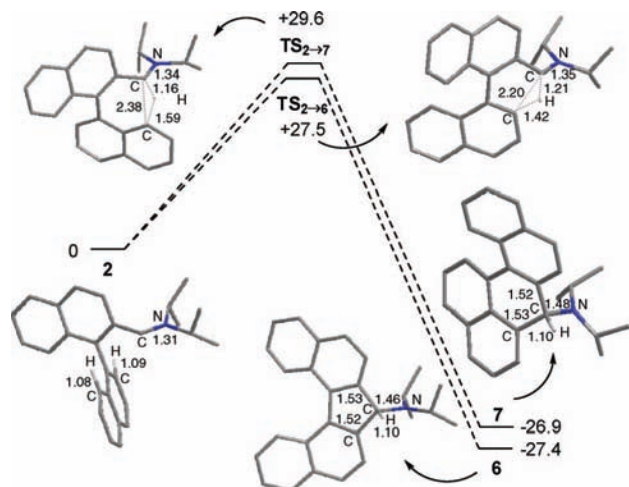


Figure 3. Energy profiles computed at the BP3LYP/6-31G** level (free energies G at 25 °C including ZPE correction in kcal/mol, distances in Å) for the rearrangements $\mathbf{2} \rightarrow \mathbf{6}$ and $\mathbf{7}$.

predicted to have a singlet ground state (lying 16.0 kcal/mol below the triplet state) and to rearrange exothermically into the aminodibenzofluorene $\mathbf{6}$ (ΔG -27.4 kcal/mol). Here also, a transition state $\text{TS}_{2 \rightarrow 6}$ directly connecting the carbene and insertion product could be located. The energy barrier predicted for this concerted process (ΔG^\ddagger 27.5 kcal/mol) is about 10 kcal/mol larger than that calculated for the related biphenyl carbene $\mathbf{1}$ but remains low enough for the rearrangement to occur spontaneously. As anticipated, the torsion angle around the biaryl axis is more pronounced with the binaphthyl than the biphenyl backbone (the dihedral angle $\text{C}_2\text{-C}_1\text{-C}_1'\text{-C}_2'$ reaches 105° in carbene $\mathbf{2}$ vs 36° in $\mathbf{1}$). The greater rigidity of the binaphthyl backbone prevents complete

planarization in $\text{TS}_{2 \rightarrow 6}$ (the dihedral angle $\text{C}_2\text{-C}_1\text{-C}_1'\text{-C}_2'$ still amounts to 20°), but rotation around the $\text{C}_{\text{carbene}}\text{-C}_2$ bond (the $\text{N-C}_{\text{carbene}}\text{-C}_2\text{-C}_3$ dihedral angle decreases by about 25° from $\mathbf{2b}$ to $\text{TS}_{2 \rightarrow 6}$) allows the carbene to approach the hydrogen atom at C_2' . The geometry of $\text{TS}_{2 \rightarrow 6}$ does not differ fundamentally from that of $\text{TS}_{1 \rightarrow 4}$ and supports a strongly asynchronous pathway for the C-H insertion reaction. In particular, the proton is substantially transferred from C_2' to $\text{C}_{\text{carbene}}$ (the respective CH distances in $\text{TS}_{2 \rightarrow 6}$ are 1.21 and 1.42 Å), and the $\text{C}_2\text{-C}_{\text{carbene}}$ remains long (2.20 Å).

The competitive rearrangement of carbene $\mathbf{2}$ leading to $\mathbf{7}$ (ΔG -26.9 kcal/mol) by insertion into the $\text{C}_8\text{-H}$ bond was also studied. The geometric features of the corresponding transition state $\text{TS}_{2 \rightarrow 7}$ are very similar to those of $\text{TS}_{2 \rightarrow 6}$ and also correspond to a strongly asynchronous process with extensive proton transfer from C_8' to the carbene center. An energy barrier of 29.6 kcal/mol is predicted for this pathway. Although fairly small, the difference in energy between $\text{TS}_{2 \rightarrow 6}$ and $\text{TS}_{2 \rightarrow 7}$ is in good agreement with the selectivity observed experimentally.

In conclusion, the biaryl monoaminocarbenes $\mathbf{1}$ and $\mathbf{2}$ were found to be only transient species that spontaneously rearrange into the corresponding aminofluorene derivatives $\mathbf{4}$ and $\mathbf{6}$. According to DFT calculations, the insertion of the carbene center into the proximal aromatic C-H bonds results from a low energy concerted asynchronous process with advanced $\text{C}_{\text{arom}}\text{-C}_{\text{carbene}}$ proton transfer in the transition state. Besides its fundamental interest, this work also opens interesting synthetic perspectives. Indeed, (i) biaryl iminium salts are readily available, and (ii) the deprotonation/insertion sequence proceeds quantitatively under mild conditions and with complete selectivity in the case of the binaphthyl backbone. This offers an efficient access to amino(dibenzo)fluorenes and may thereby facilitate the investigation of their coordination behavior.^{14b,21}

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Supporting Information Available: Experimental procedures, spectroscopic characterizations for all new compounds, computational details, and Z-matrices for all optimized structures. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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