Annulation Cascade of Aryl Alkynes Induced by Alumina-Mediated C—F Bond Activation

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Alumina-mediated C—F activation (AmCFA) is an established method to generate incipient phenyl cation (IPC) through polarization of C(aryl)—F bonds. Herein, it is reported that AmCFA can be used to induce intramolecular arylation of aryl alkynes containing one, two, and three triple bonds. During the reaction, a single formally eliminated hydrogen fluoride (HF) leads to the formation of two, three, and four C—C bonds, respectively. Thus, the transformation gives rapid access to π-extension and serves as an interesting example of solid-state rational domino annulation enabling the bottom-up construction of nanographenes.

1. Introduction

The C—F bond stands out from the other single bonds with carbon due to its high energies[1] rendering fluorine as a not particularly attractive functional group. Thus, C(aryl)—F has been for a long time considered as a functionality that can be used only within activated (i.e., electron-poor) substrates.[2,3] Although some progress has been achieved using transition metal complexes,[4] only a few techniques based on main-group catalysis enable C(aryl)—F activation in nonactivated fluoroarenes. Thus, Siegel et al. showed that silyl cations induce intramolecular hydrogen fluoride (HF) elimination enabling Friedel–Craft-like aryl coupling of fluorinated polycyclic aromatic hydrocarbons

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(PAHs).[5,6] Another methodology is based on the usage of aluminum-containing Lewis acids,[7] among which activated γ-alumina has been intensively investigated.[8–10] The mentioned reactions are assumed to occur via cationic intermediates generated through the formation of incipient phenyl cation (IPC). It has been shown that such species may interact not only with aromatic π-systems leading to aryl–aryl coupling but also with other nucleophiles. Thus, it has been shown that IPCs are capable of chemical interactions with CH3-group,[11] O-, and N-nucleophiles.[12,13] Among alternative nucleophiles, we envisioned triple bonds to be an appealing functionality promising fruitful chemistry upon C—F activation.

Due to the large thermodynamic driving force associated with alkyne hydroannulation,[14] C≡C represents a useful functionality for the synthesis of nanographenes (NGs). Thus, it has been used in benzannulation induced by transition metals,[15] Brønsted acids,[16] flash-vacuum pyrolysis,[17] photochemical excitation, etc. However, all these methods enable only single C—C bond formation per triple bond. Alabugin and Gonzalez-Rodriguez successfully overcame this 1:1 ratio using a traceless directing group initiating a radical domino process.[18] However, sufficiently large NGs suffer from low solubility and therefore poor processability, which does not allow the implementation of the obtained NGs in devices. A typical solution of the problem would be to use a processable precursor that after dislocation on the device's surface transforms into the target structure. It is therefore vital to develop the chemical transformations that can be implemented directly on nonconducting surfaces. Recently, we have successfully transferred the developed alumina-mediated C—F activation (AmCFA domino reaction[19]) to the rutile titania surface.[20] In this context, the development of the preparative solid-state reactions serves as an important prerequisite to the atomically precise bottom-up fabrication of the carbon materials. Herein, we report an unprecedented solid-state cascade annulation of aryl alkynes leading to π-extension of PAHs bearing *bay*- (Figure 1) or *L*-region (Figure 2). Moreover, we show two substrates, where a single HF elimination induces the formation of three and four C—C bonds. The key steps of the domino reaction are a) AmCFA and generation of ICP as the initiating step; b) electrophilic attack of the neighboring triple bond and formation of either a 5-*exo* or 6-*endo* cationic intermediate; c) which in its turn attacks the next nucleophilic neighbor. The reaction is terminated once the cationic intermediate attacks the aromatic π-system, enabling the elimination of the proton and formation of the final aromatic compound.

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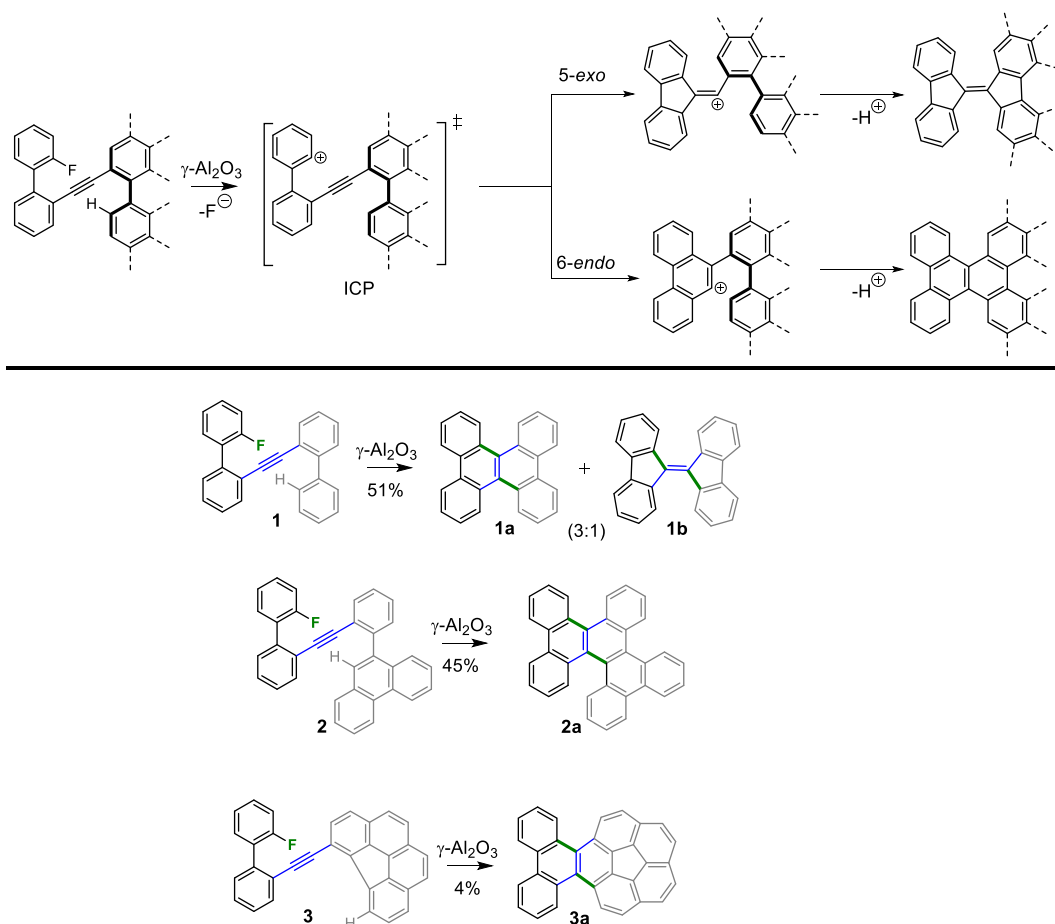
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Figure 1. Domino annulation of aryl alkynes bearing a bay-region (marked bold). The newly formed C—C bonds are marked green.

2. Results and Discussion

To demonstrate the scope of the developed reaction, we have synthesized precursor alkynes **1**–**8** (the synthesis procedures can be found in the Supporting Information).

We have initiated our study with precursor **1**, annulation of which under our initial assumption could proceed via 5-*exo* or 6-*endo* routes. The exposure of **1** to γ-Al$_2$O$_3$ at 190 °C has, indeed, resulted in the formation of the **1a**–**1b** (3:1) mixture. What is noteworthy is that unlike previously reported AmCFA syntheses, in this setup HF elimination induces the formation of two C—C bonds. Interestingly, in the case of **2** the ratio of the two chemical routes was drastically shifted toward 6-*endo* because **2a** was obtained as the only major product. Synthesizing the precursor **3**, we have attempted to push the substrate to extreme energy barriers associated with the construction of the corannulene core. Despite this severe obstacle, we have been able to isolate **3a**. Although the yield of the transformation is fairly poor, such synthesis serves as a rare example of the nonpyrolytic approach to corannulene's derivatives.[21]

From a structural standpoint, these three transformations resemble an annulative π-extension (APEX) reaction recently developed by Itami and coworkers[22] The transformation enables π-extension of PAHs bearing bay-regions. In contrast, our approach is also suitable for the extension of PAHs with zig-zag (i.e., *L*-region) periphery. Thus, the transformations of **4** and **5** lead to the formation of the anticipated products **4a** and **5a**, respectively. In the first case, we have also isolated the product of 5-*exo* cyclization **4b**. As the formation of the four-membered ring is energetically unfavorable, the cationic intermediate undergoes a 1,3-hydrogen shift, leading to the redislocation of the cation and subsequent formation of the hexagon. The mechanism of this cascade is confirmed by the transformation of **6** into **6a**. While the former does not have alternative possibilities for intramolecular chemistry, a corresponding product is not observed in the case of perylene's derivative apparently due to a higher reactivity in S$_E$Ar of the carbon attached to H$_a$.

We assumed that the incorporation of additional triple bonds could enable a stepwise transfer of the cationic intermediates that could extend the domino cascade to more than two C—C bonds. To check this assumption, we designed the precursors **7** and **8** containing two and three C≡C bonds, respectively. The transformation of these molecules into **2a** and **8a**, respectively, represents an extrapolation of the previous examples. Thus, instead of terminating the cascade, the first cationic intermediates yields the second cationic species. The whole process reminds us of the chain transfer occurring in a polymerization reaction. Considering the number of formed C—C
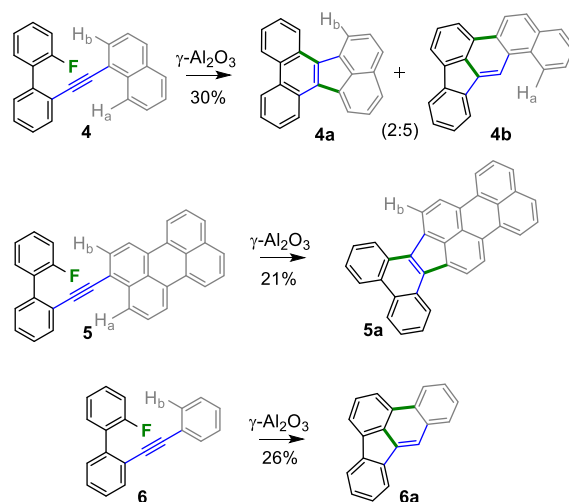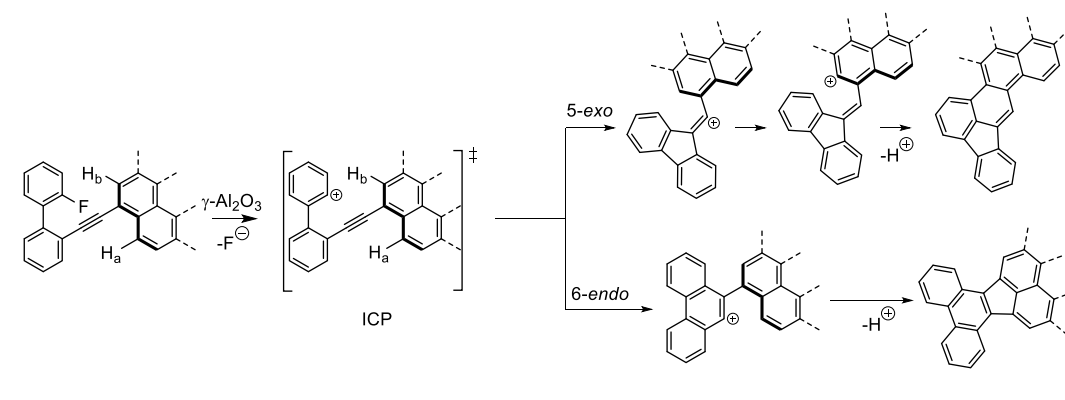
Figure 2. Domino annulation of aryl alkynes bearing an *L*-region (marked bold). The newly formed C—C bonds are marked green.
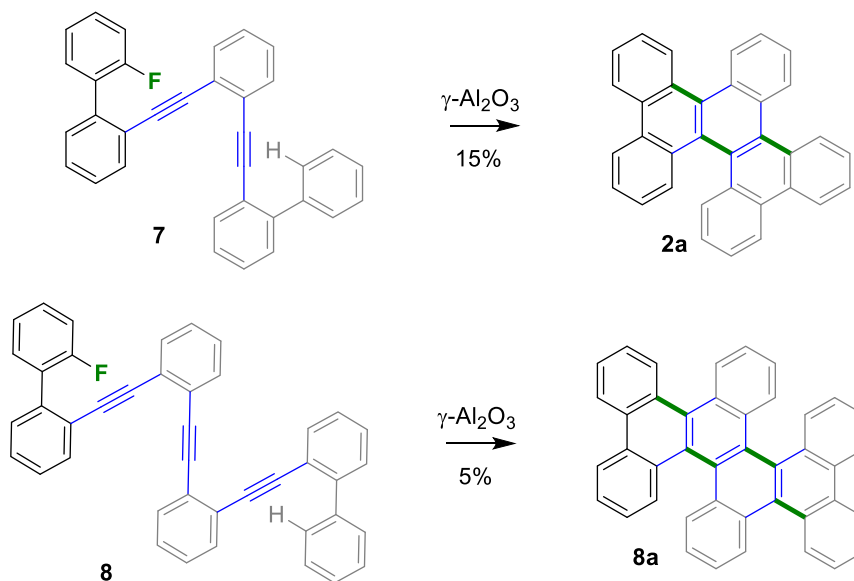

Figure 3. Domino benzannulations of oligoalkynes.

bonds, the yields of these folding processes can be estimated as 53% and 47% per C—C bond for **7** and **8**, respectively (**Figure 3**).

3. Conclusion

In summary, we have designed and implemented the cascade annulation of aryl alkynes initiated via AmCFA. The reaction can be formally considered as a single HF elimination that depending on the substrate induces two, three, or four C—C bonds. The reaction occurs on the surface of the activated γ-alumina and represents an important transformation that can be potentially transferred to the nonconducting surfaces for the bottom-up construction of sp²-carbon-based materials directly within a device.

Supporting Information

Supporting Information is available from the Wiley Online Library or from the author.

Conflict of Interest

The authors declare no conflict of interest.

Keywords

alkyne annulations, C—F bond activation, nanographenes

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