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The Rolling-Up of Oligophenylenes to Nanographenes by HF-Zipping Approach

A.-K. Steiner,[a] and K. Yu. Amsharov*[a]

Abstract: The intramolecular aryl-aryl coupling represents the key transformation in the rational synthesis of nanographenes and nanoribbons. In this respect the C-F bond activation was proved to be a versatile alternative enabling the synthesis of several unique carbon-based nanostructures. Here we describe an unprecedentedly challenging transformation showing that the C-F bond activation by aluminium oxide allows to perform highly effective domino-like C-C bond formation. Despite the flexible nature of oligophenylene-based precursors efficient regioselective zipping to the target nanostructures was achieved. We show that fluorine positions in the precursor structure unambiguously dictate the "running of the zipping-program" which results in rolling-up of linear oligophenylene chains around phenyl moiety yielding target nanographenes. The high efficiency of zipping makes this approach attractive for the synthesis of unsubstituted nanographenes which are difficult to obtain in pure form by alternative methods.

The fascinating properties of graphene,[1–3] one of the leading materials in today's science, have resulted in exploding interest in the rational synthesis of extra-large polycyclic aromatic hydrocarbons (PAHs) or nanographenes (NGs),[4] representing fragments of the graphene surface. Due to unique electronic and optoelectronic characteristics together with the possibility to tune properties in a wide range, this family of compounds is gradually becoming more attractive, than the parent zero-gap graphene.[5] The current progress in the synthesis of complex carbon-based architectures by bottom-up approach, allowing control on the atomic level, has generated enormous expectations about possible applications of these materials in the future generation of electronics.[6] In this respect, the Scholl reaction was proven to be a powerful method for the synthesis of well-defined nanographenes and carbon nanoribbons via multiple intramolecular cyclodehydrogenation of dendrimer-like oligophenylenes.[6,7] However, as a result of cationic (cation radical) nature,[7–9] the Scholl reaction is frequently accomplished by migration of alkyl/aryl groups or even by skeletal rearrangements yielding unexpected products.[10–16] Moreover, the Scholl oxidation commonly leads to an exhaustive cyclodehydrogenation which is not always desired. Among this, the cyclization usually fails in the case of small unsubstituted arenes due to oligomerization yielding complex mixtures of inseparable products.[17] It is worth to mention that unsubstituted nanographenes are virtually insoluble compounds whose purification represents a challenging task. Therefore, the development of new methods for the synthesis of nanographenes directly in pure form is highly desired. Recent progress in the C-F bond activation clearly demonstrates its high potential for intramolecular C-C bond formation.[18–22] Previously we have developed a facile approach for intramolecular aryl-aryl coupling via cyclodehydrofluorination (CDHF) on alumina that can address the above mentioned limitations.[23,24] Following this strategy, it was possible to construct various PAHs with near-quantitative yields including highly strained bowl-shaped systems which are not accessible via cyclodehydrogenation.[23-26] Surprisingly, it was found that activation of the aromatic C-F bond (the strongest bond to carbon) is tolerant to the more labile C-Cl and even C-Br bonds.[24] An even more exciting feature of the alumina mediated CDHF is an exceptionally high regioselectivity. Namely, it was discovered that the C-F bond can only be activated if the fluorine atom is placed in the cove or fjord region of the PAH molecule, whereas peripheral C-F bonds remain completely intact.[24,26] The unexpected high selectivity was explained by an aromatic transition state necessitating a close proximity of C-H and C-F bonds.[24] Taking this unusual behaviour into account it appears to be possible to perform tandem cyclization via CDHF in a truly domino-like manner where each subsequent step leads to the "activation" of one new C-F bond. Inspired by this fact, we decided to perform an unprecedentedly challenging transformation, converting virtually linear fluorinated oligophenylenes to nanographenes. Here we demonstrate that such transformation is indeed feasible and presents an efficient approach to nanographene systems which are not accessible via Scholl oxidation (Figure 1). We show that alumina mediated HF-zipping is characterized by exceptionally clean conversion to the target nanographenes, which makes the approach superior over existing aryl-aryl coupling methods.

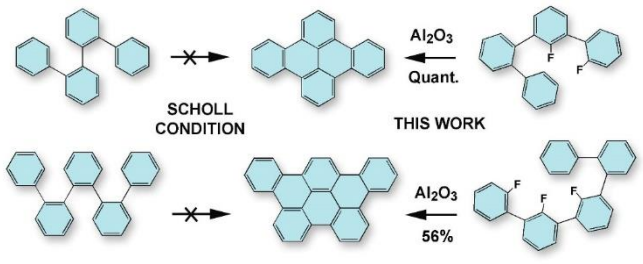

Figure 1. Example of the syntheses of small nanographenes by HF-zipping approach.

To investigate the domino-like CDHF process five specially "preprogrammed" fluorinated oligophenylenes (**P1-P5**) were synthesized by multi-step organic synthesis. The synthetic concept used is based on the synthesis of fluorinated *meta*-oligophenylene (*m*-OFP) chains (Scheme 1) which can be coupled to the central arene unit (Scheme 2). The *ortho*-position to the aromatic C-F bond can be lithiated selectively which allows facile *ortho*-functionalization of fluoroarenes. This includes halogenation,[27,28] borylation,[29,30] and arylation via Ullman-like

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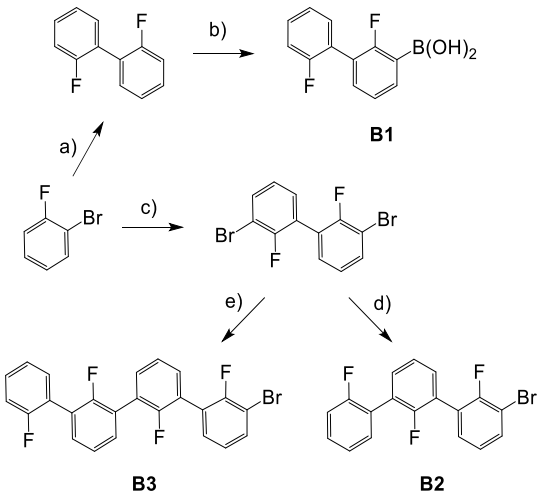
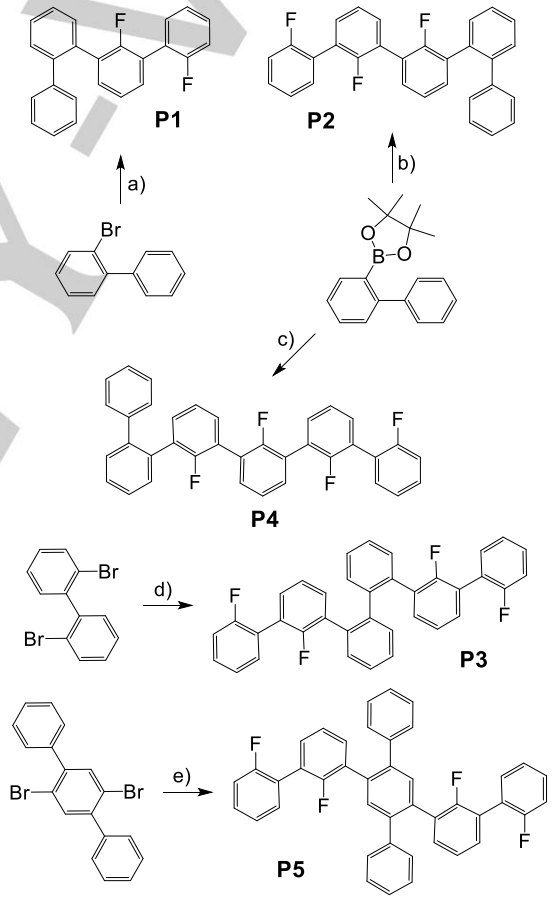
cross coupling.[31] The combination of a Suzuki reaction with the metal organic chemistry of fluoroarenes provides a simple access to the end-functionalized *meta*-fluorooligophenylenes. The required end-brominated and/or end-borylated *m*-OFP chains were obtained by this strategy with moderate to good yields as shown in Scheme 1 (see SI for more detail). The final precursor molecules **P1-P5** were obtained by Suzuki coupling of brominated/borylated *m*-OFP chains with the respective brominated central block (or respective boronic acid) as shown in Scheme 2.



Scheme 1. Synthesis of end-functionalized *meta*-oligofluorophenylene chains. Reaction conditions applied: a) 2-fluorophenylboronic acid, Cs_2CO_3, $Pd(PPh_3)_2Cl_2$, THF/H_2O 5:1, reflux, 18 h; 91 %. b) 1. *n*-BuLi, 2,2,6,6-tetramethylpiperidine (TMP), 2. $B(OMe)_3$, 3. HCl; 61 %. c) 1. *n*-BuLi, TMP, 2. $CuBr_2$, 3. nitrobenzene; 73 %. d) 2-fluorophenylboronic acid, K_2CO_3, $Pd(PPh_3)_4$, THF/H_2O 5:1, reflux, 20 h; 30 %. e) **B1**, K_2CO_3, $Pd(PPh_3)_4$, THF/H_2O 5:1, reflux, 18 h; 40 %.

The respective CDHF reactions were carried out in the presence of activated γ-aluminium oxide in the solid state as described previously.[23-25] The cyclization of difluorinated quaterphenyl **P1,** representing the smallest system where two-fold CDHF zipping can be performed, was chosen as a model reaction (Figure 2). Taking into account the high regioselectivity of the CDHF process discussed above the **P1** system can undergo single cyclization, since only one H···F pair is "activated" (Figure 2). However, after first ring closure the remaining fluorine atom appears in close proximity to hydrogen and becomes "activated" for the second CDHF step. Thus, the whole process can proceed via two subsequent HF elimination steps leading to the target **NG1**. The cyclizations of **P1** were performed at different temperatures (150-300 °C) and monitored by HPLC/UV after extraction with hot *o*-DCB (*ortho*-dichlorobenzene). In contrast to the single CDHF in *o*-terphenyl,[23] only poor conversion of **P1** to **NG1** was achieved at 150 °C which is connected with the relatively high strain induced in intermediate **P1a**. As shown in Figure 2a, after the first cyclization the phenyl group appears in the sterically hampered bay-region of the triphenylene moiety which is energetically unfavorable. However, an increase of the temperature to 200 °C shows that the steric strain can be effectively overcome. The reaction at 200 °C carried out for 15 h revealed clean but not complete conversion into the target compound **NG1** according to HPLC analysis**.** At 250 °C the reaction can be accomplished in 6 h yielding **NG1** with more than 80 % yield. Further increase of the reaction time leads to the exclusive transformation of the precursor to the target **NG1**. The optimal conditions were found to be 200 °C, 66 h. At these conditions the transformation of **P1** to **NG1** was achieved with close to quantitative yield according to HPLC and NMR analysis (see SI). The LDI-MS analysis of the reaction mixture shows a single peak corresponding to the target **NG1** and no other signals were detected. The respective HPLC profile and the MS spectrum of the product as obtained after reaction (reaction mixture) are shown in Figure 2. The only "impurity" found are trace amounts of the starting compound which however can be easily removed due to enhanced solubility. The precipitation from *o*-DCB solution with methanol yields **NG1** in pure form (90 % yield). Importantly, no intermolecular condensations (dimerization or oligomerization) were detected during CDHF process allowing to obtain **NG1** directly in pure form without additional purification steps.



Scheme 2. Synthesis of nanographene precursor molecules **P1**-**P5** via Suzuki coupling of *m*-OFP blocks. Suzuki conditions: a) 2-bromo-1,1'-biphenyl, **B1**, K_2CO_3, $Pd(PPh_3)_4$, THF/H_2O 5:1, reflux, 20 h; 66 %. b) **B2**, 2-([1,1'-biphenyl]-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, K_2CO_3, $Pd(PPh_3)_2Cl_2$, THF/H_2O 5:1, reflux, 18 h; 62 %. c) **B3**, 2-([1,1'-biphenyl]-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, K_2CO_3, $Pd(PPh_3)_4$, THF/H_2O 5:1, reflux, 18 h; 76 %. d) 2,2'-dibromo-1,1'-biphenyl, **B1**, Cs_2CO_3, $Pd(PPh_3)_2Cl_2$, THF/H_2O 5:1, reflux, 18 h; 30 %. e) 2',5'-dibromo-1,1':4',1''-terphenyl, **B1**, K_3PO_4, $Pd(PPh_3)_2Cl_2$, toluene/H_2O 10:1, reflux, 5 h; 46 %.

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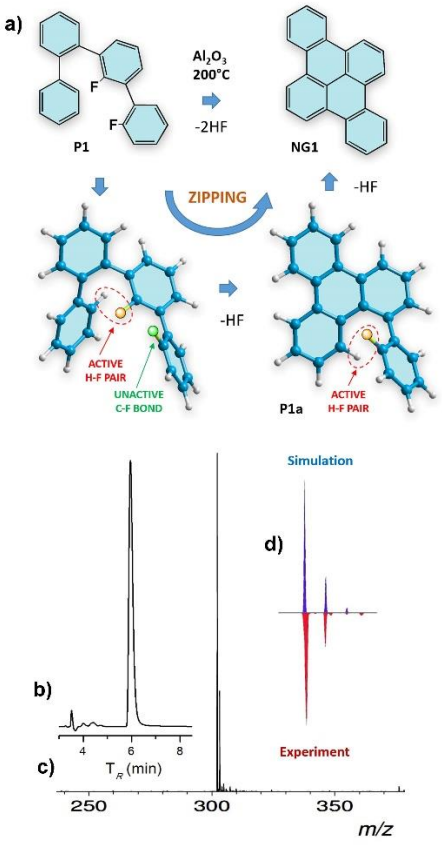

Figure 2. (a) The mechanism of CDHF zipping on the example of small **NG1** system. (b) HPLC profile and (c) LDI-MS spectrum of the reaction mixture as obtained after reaction (without purification) at 200 °C, 66 h, showing high selectivity of the cyclization. d) Calculated and experimentally observed isotopic distribution MS patterns of **NG1**.

As a consequence of the exceptionally high efficiency the multi-fold CDHF zipping appears to be possible. The extended precursors **P2, P3, P4,** and **P5** "preprogrammed" for the triple and quadrupole zipping were condensed to nanographenes under optimized conditions (200 °C, 66 h). In the first two cases very clean conversion to the target nanographenes **NG2** and **NG3** was observed as indicated by following MS analysis (Figure 3a and b). After Soxhlet extraction with *o*-DCB and precipitation with MeOH both nanographenes **NG2** (56 %) and **NG3** (61 %) were obtained in pure form according to HPLC/UV analysis (see SI). Despite the very low solubility we were able to perform high temperature ^{1}H NMR analysis of nanographenes **NG1**, **NG2,** and **NG3** providing direct structural confirmation of these fundamental PAHs, [32,33] for the first time (for details see supporting information). In the case of **NG4** only small conversion was observed after 66 h. Increasing the reaction time to 120 h has notably improved the conversion, although the reaction was still not fully completed (for details see SI). We attribute this with the low mobility of the intermediates on alumina in the solid state, which leads to a reduction of the total reaction rate. Furthermore, because of the solubility issue it was difficult to achieve effective extraction of **NG4** even by applying Soxhlet with *o*-DCB. Nevertheless, MS analysis of the *o*-DCB extract, reveals an effective fourfold zipping of **P4** to **NG4**, showing only single signal corresponding to the desired nanostructure (Figure 3c). Despite extremely poor solubility, it was possible to perform high temperature HPLC/UV analysis.

Finally, we have applied the zipping approach for the synthesis of the large nanostructure **NG5**. Rather unexpectedly, highly effective conversion to target nanographene **NG5** was observed already after 23 h despite the bigger size in comparison to **NG4**. Moreover, it was found that **NG5** shows notably better solubility than **NG4**. After Soxhlet extraction with *o*-DCB and precipitation with methanol pure **NG5** was isolated in 76 % yield (more than 92 % for a single cyclization). The high purity of the sample was confirmed by high temperature HPLC/UV and MS analysis. Notably, the UV-Vis spectrum of **NG5** was found to be different with the previously reported,[34] which shows many additional bands indicating low purity of the previously characterized sample (see SI).

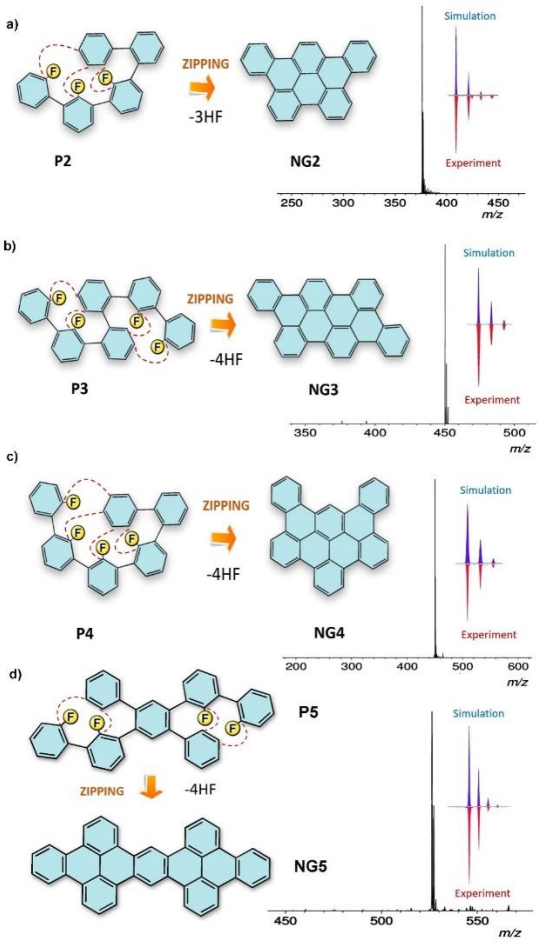

Figure 3. Synthesis of (a) **NG2**, (b) **NG3**, (c) **NG4** and (d) **NG5** by HF-zipping strategy. (right) The respective LDI-MS spectra of the reaction mixtures as obtained after reaction (200 °C, 66 h). The calculated and experimentally observed isotopic distribution MS-patterns are shown in inset.

The domino-like character of the **NG5** formation was additionally confirmed by analysis of the reaction extract before completion of the process. For this purpose, the reaction was carried out for only 6 h and the reaction extract was analyzed by means of MS spectrometry. The MS spectrum indicates the formation of all expected intermediates and no presence of any side components. Worth to mention, that the major signals in the MS spectrum correspond to the starting **P5** and final **NG5** whereas intensities

of signals of all CDHF intermediates are rather low. The similar behavior of CDHF process was also observed for other precursor molecules. Thus, in the course of zipping of the **P1** precursor the formation of only small amounts of monocyclized intermediate (**P1a**) were detected. The HPLC analysis of the reaction (before completion) shows that major components of the reaction mixture are starting compound and the final product. This indicates that the first cyclization step has a notably higher activation energy than the second one. As a consequence, the intermediate **P1a** undergoes quick transformation to the final product. The same tendency was observed for **P2**, **P3,** and **P4** precursors. This observation is in a good agreement with the previously made assumption stating that first cyclization is less favorable due to steric strain caused by the presence of the phenyl group in the bay-region. Since the mechanism of the CDHF is not fully understood it was not possible to calculate activation energies for individual CDHF steps. Therefore, we have performed DFT-based thermochemistry analysis of double, triple and quadrupole zipping on the example of **P1**, **P2,** and **P3**. For this purpose, we have evaluated the reaction enthalpy for each individual step and compared them with a model reference reaction. The transformation of fluorinated *o*-terphenyl to triphenylene was chosen as a model, for which smooth cyclization was experimentally observed already at 150 °C.[23] Taking the enthalpy of the model reaction (ΔH_{MODEL}) we adjust relative energy changes (ΔH-ΔH_{MODEL}) for all products and all intermediates (Figure 4). Since all CDHF belong to the same family of reactions (chemically related processes undergoing transformation through similar transition states) the correlation between ΔH and activation energies is expected. Our calculations show that for the whole series of precursors the first CDHFs are indeed thermodynamically less favorable in comparison to the cyclization of the reference compound (*o*-terphenyl). Consequently, higher activation barriers are expected for these steps which is in good agreement with experiment showing low degree of conversion at 150 °C. The enthalpy of following cyclization steps was found to be similar to the reference reaction, whereas the last CDHF is significantly more exothermic. This explains the low content of intermediates in the reaction mixture and presence of the starting compound.

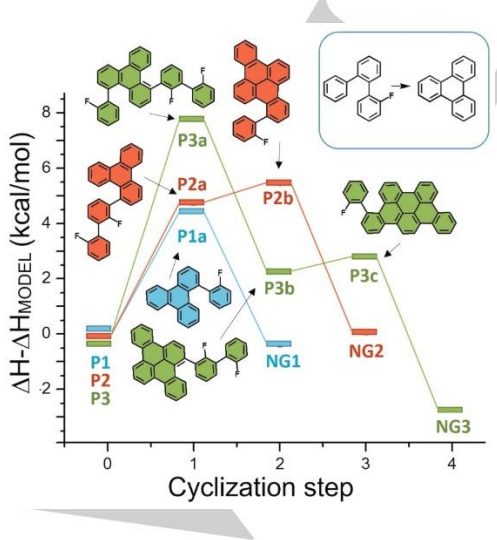

Figure 4. Graphical representation of the DFT-based thermochemistry analysis of the CDHF zipping process for precursors **P1**, **P2** and **P3**. The model reference reaction is shown in inset.

In summary, we have demonstrated the possibility of regioselective HF-zipping of *m*-oligophenylenes to the "preprogrammed" nanostructures via truly domino-like cyclodehydrofluorination. We show that the unique nature of the CDHF process allows to perform this challenging transformation in completely controlled manner. The high efficiency of the approach has been demonstrated by the effective transformation of five precursors to the target nanographenes by formal "rolling-up" of oligophenylene chains. Notably, all NGs were obtained in highly pure form without involving any additional purification procedures. Taking into account difficulties connected with purification of virtually insoluble unsubstituted NGs, which is highly crucial for electronic applications, the CDHF approach appears to be superior over existing aryl-aryl coupling techniques. Moreover, the CDHF-zipping approach could provide a facile way for bottom-up fabrication of nanographenes and nanoribbons directly on insulating metal-oxide surfaces,[35] which is crucial for generation of truly-working electronic nanodevices. Finally, since each cyclization step can be unambiguously predefined by the proper design of the precursor the presented technique opens access to highly interesting carbon-based nanostructures which are difficult to obtained by existing alternative methods.

Experimental Section

General Procedure: Al_2O_3-Mediated HF Elimination. Typically, a glass ampule was charged with γ-Al_2O_3 (500 mg) which was initially activated by annealing at 250 °C for 10 min in air. Afterwards, it was activated by annealing under vacuum (10^{-2} mbar) for 10–15 min while the temperature was increased from 250 °C to 550 °C in intervals of 100 °C. After cooling to room temperature the ampule was filled with argon and the respective fluoroarene (5 mg) was mixed with activated aluminium oxide. After repetitive evacuation of the ampule (10^{-2} mbar) it was sealed. The condensation was carried out at 200 °C for the indicated time in an oven while the ampule was rotated. Al_2O_3 was either extracted with hot *o*-dichlorobenzene or by Soxhlet extraction with *o*-DCB. The crude product mixture was analyzed by HPLC. Pure product was obtained by precipitation with MeOH.

Acknowledgements

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Keywords: Nanographene• C-F activation • Aryl-Aryl coupling • Domino reaction

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We describe an unprecedentedly challenging transformation consisting in the conversion of virtually linear fluorinated oligophenylenes to the "preprogrammed" nanographenes via effective domino-like aryl-aryl coupling. We show that fluorine positions in the precursor structure unambiguously dictate the running of the "HF-zipping-program" leading to the formation of target nanographene structure.

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