# Intramolecular Aryl–Aryl Coupling of Fluoroarenes through Al$_2$O$_3$-Mediated HF Elimination

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S *Supporting Information*

ABSTRACT: A strategy for effective intramolecular aryl–aryl coupling of fluoroarenes through Al$_2$O$_3$-mediated HF elimination is reported. It is demonstrated that the C−F bond, which is widely believed to be the most passive functionality in organic chemistry, can be reconsidered as a useful functional group allowing very effective C−C bond formation. The solid-state strategy presented in this study opens the possibility for facile syntheses of insoluble extended polycyclic aromatic hydrocarbons.
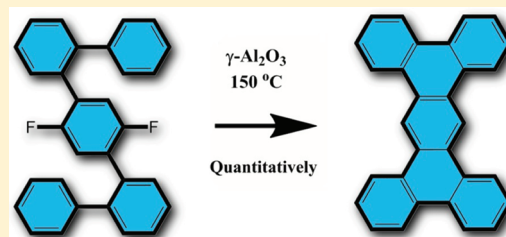
The carbon–fluorine bond is one of the least reactive functionalities encountered in chemistry, and its selective transformation leading to C−C bond formation is a major challenge in modern organic chemistry.[1] C−F activation in the coordination sphere of a transition metal is the most commonly used approach.[2] Despite significant progress in this field, only a few examples of effective aryl–aryl coupling using aryl fluorides have been reported so far.[1−3] Moreover, in the case of transition-metal-catalyzed C−F activation, moderate yields have been achieved only for electronically activated aryl fluorides and/or in the presence of directing groups. Rather selective intramolecular fluorine-promoted aryl–aryl coupling has been observed under flash vacuum pyrolysis condition.[4,5] The main drawbacks in this case are minimum functional group tolerance as a consequence of the harsh reaction conditions required and difficulties in scale up. Alternatively, the C−F bond can be effectively activated under transition-metal-free conditions utilizing silylium−carborane catalysis.[6] Recently, this methodology has been successfully applied for intramolecular aryl–aryl coupling.[7] Unfortunately, the use of an exotic and expensive carborane cluster limits the application of the approach at the preparative scale. Recently, we have demonstrated that intramolecular aryl–aryl coupling in the cove region of 1-fluorobenzo[*c*]phenanthrene (compound **1**) and several structurally related compounds can be realized very effectively through HF elimination on thermally activated γ-Al$_2$O$_3$.[8] Under these conditions, the conversion to the target molecules has been achieved quantitatively, even in the case of multifold condensations. The process discovered is characterized by an unprecedentedly high chemoselectivity and regiospecificity. Simplicity, high efficiency, and easy availability of aluminum oxide make the reaction very attractive as a general synthetic strategy. In this paper, we report that the scope of condensation via Al$_2$O$_3$-mediated HF elimination can be extended to the synthesis of various polycyclic aromatic hydrocarbons (PAHs), thus providing a new general approach for effective intramolecular aryl–aryl coupling.

2-Fluorobiphenyl (**3**), 1-(2-fluorophenyl)naphthalene (**5**), and 1-(2-fluorophenyl)-2-phenylbenzene (**7**) representing

small arenes where four-, five-, and six-membered rings can be formed by intramolecular aryl–aryl coupling were chosen as model compounds (Figure 1). The condensations of the respective fluoroarenes were carried out at 100−250 °C using thermally activated γ-Al$_2$O$_3$. The reaction products were extracted with toluene and subsequently analyzed.

As expected, fluorobiphenyl **3** has remained completely intact under condensation conditions. Neither condensation nor C−F bond cleavage was observed, demonstrating that the C−F bond remains completely inert if no appropriate position for coupling is offered by the structure. In contrast, the phenylnaphthalene **5** readily undergoes transformation to fluoranthene (**6**) already at 100 °C. In comparison to benzophenanthrene **1**, the condensation of **5** requires a longer time. While **1** can be condensed quantitatively to **2** at 200 °C after several minutes, **5** gave low conversion to **6** under the same conditions. Moreover, it was found that the condensation process is extremely sensitive to the pretreatment activation of Al$_2$O$_3$. Thus, only trace amounts of fluoranthene formed if nonactivated Al$_2$O$_3$ was used, and only low conversion to the target compound was observed with aluminum oxide activated at 300 °C. The effective condensation of **5** to **6** can be achieved only after proper activation of Al$_2$O$_3$ at 600 °C (for details, see the Supporting Information). When such an activated Al$_2$O$_3$ was used, the full conversion was achieved after 10 h at 200 °C. In this case, the target fluoranthene was obtained in pure form after simple extraction with toluene as indicated by HPLC and NMR analysis. Although almost no side products were detected in the toluene extract, the isolated yield of fluoranthene was found to be only 60%. This indicates that about 40% of **5** react with aluminum oxide forming nonextractable products.[9] Fortunately, the side processes can be effectively suppressed at lower temperatures. Thus, the condensation of **5** at 150 °C for 60 h gave fluoranthene with more than 80% yield.

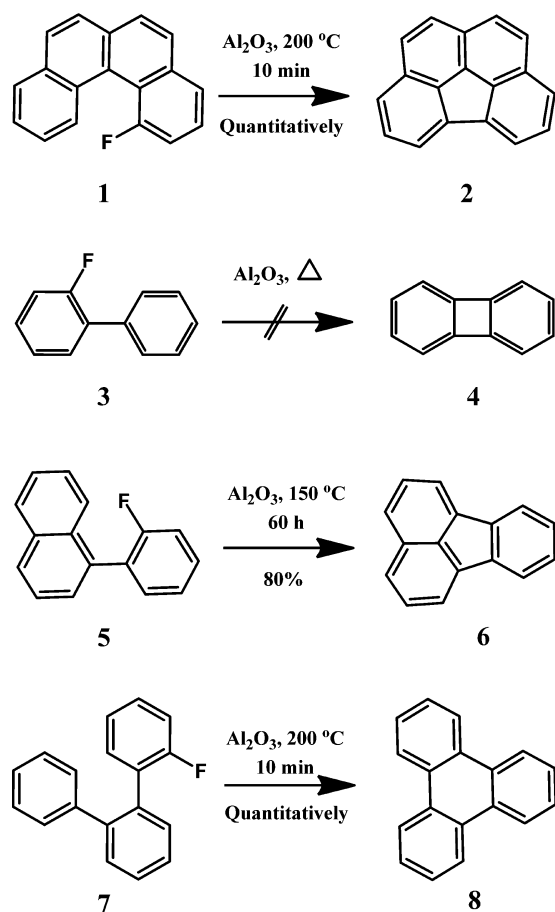**Figure 1.** Aryl−aryl coupling via Al$_2$O$_3$-mediated HF elimination.

Figure 2. Double aryl−aryl coupling via Al$_2$O$_3$-mediated HF elimination.

In contrast to pentagon formation, the closure of the six-membered ring in diphenylbenzene **7** proceeds very smoothly. Rather effective condensation of **7** to triphenylene (**8**) can be achieved already at 100 °C after 10 h. At 200 °C, the same process can be completed in several minutes with quantitative formation of triphenylene (isolated yield 99.5%).

Despite the moderate yield in the case of pentagon closure, the approach is rather efficient since the product obtained requires no further purification. The efficiency has been demonstrated on the example of double HF elimination in diphenylnaphthalene **9** (Figure 2). Annealing at 200 °C for 60 h gave compound **10** in pure form with 34% yield (see the Supporting Information). The efficiency of hexagon closure has been demonstrated on the example of double HF elimination in compound **11**. Quinquephenyl **11** was quantitatively transformed to phenanthrotriphenylene **12** at 150 °C after 120 h. The product was obtained in pure form after Soxhlet extraction with toluene.

The most probable mechanism of condensation includes aromatic transition states which explains the high selectivity and low activation barrier allowing the reaction to take place under rather mild conditions.[8] As previously observed, Al$_2$O$_3$ mediated 1,2-dehydrofluorination in difluorocycloalkanes has probably a similar mechanism of elimination as evidenced by highly selective fluorocycloalkenes formation.[10] The driving force of the elimination is the formation of an Al−F bond which is characterized by substantial bond strength. Indeed, it has been found that Al$_2$O$_3$ plays a crucial role in the reaction. Thus, among several oxides tested (BeO, B$_2$O$_3$, MgO, Al$_2$O$_3$,

SiO$_2$, Sc$_2$O$_3$, TiO$_2$, ZnO, Ga$_2$O$_3$, GeO$_2$, ZrO$_2$, SnO, Nb$_2$O$_5$, In$_2$O$_3$, and HfO$_2$) only Al$_2$O$_3$ has shown high activity in condensation.[11]

Considering the proposed mechanism of condensation the molecule should be in close contact to an active site of aluminum oxide in order to undergo elimination. In the cases of small fluoroarenes which melt below the temperatures used for condensation, there are obviously no obstacles for free diffusion. Interestingly, when both starting materials and products have remarkably higher melting points than the temperature of the reaction the elimination can also be realized very effectively, demonstrating sufficient mobility of the reacting molecules.[8] Such a behavior is understandable since diffusion and therefore the reaction between two solids frequently begins far below the melting point (Tammann temperature). Nevertheless, in the case of extra-large PAHs, a decrease in activity cannot be excluded. On the other hand, the problem of mobility can be solved by using an appropriate solvent. It has been found that the reaction proceeds with the same efficiency in refluxing dodecane, 1,2,4-trichlorobenzene, and naphthalene.[12] The use of polar solvents such as dimethylacetamide completely inhibits the process, probably due to blocking of active sites on the Al$_2$O$_3$ surface. The possibility of carrying out the process in trichlorobenzene additionally demonstrates a high tolerance to the C$_{Aryl}$-Cl functionality,[13] whereas an effective condensation in naphthalene, which represents an excellent scavenger of carbocations, rules out the possibility of condensation via carbocation intermediates.

In summary, a facile solid-state strategy for effective aryl−aryl coupling by Al$_2$O$_3$-mediated HF elimination is presented. Our finding shows that the C−F bond is a useful functional group allowing effective C−C bond formation. The efficiency of the approach has been shown by the syntheses of several PAH structures. Importantly, the desired products can be obtained in pure form after simple extraction, and no additional purification procedures are required (see the Supporting Information). It

was also demonstrated that the C−F bond remains intact if no possibility for cyclization is offered. Such a regiospecifity, which is without precedent in fluoroorganic chemistry, offers the possibility for condensations in a domino-like fashion. Moreover, the high tolerance to chlorine and bromine functionalities[13] makes the approach a very powerful synthetic tool for the synthesis of halogenated PAHs, which are useful building blocks for the construction of more complex structures. The exceptionally high conversion level for hexagon closure and the applicability to insoluble materials open new horizons for construction of extra-large PAHs via multifold intramolecular cyclization. In particular, the approach is of great interest for the rational synthesis of carbon-based nanostructures, including fullerenes,[14,15] nanotubes,[16] nanographenes, and nanoribbons.[17]

EXPERIMENTAL SECTION

NMR spectra were measured at 20 °C. R_f were determined on TLC-PET sheets coated with silica gel with fluorescent indicator 254 nm (layer thickness 0.25 mm, medium pore diameter 60 Å). HPLC analyses were carried out using a Cosmosil 5-PYE (4.6 mm × 250 mm) column and toluene/methanol mixture as eluent (UV−vis detection). Chromatographic purifications were carried out with flash grade silica gel Kieselgel 60 (0.06−0.2 mm). HF elimination experiments were carried out using commercially available aluminum oxide (activated, neutral, 50−200 μm). The aluminum oxides obtained from different suppliers have shown similar activity in the condensation (see the Supporting Information). 1-(2-Fluorophenyl)naphthalene (**5**) and 1-(2-fluorophenyl)-2-phenylbenzene (**7**) were synthesized according to the previously reported procedure.[7]

General Procedure for Al$_2$O$_3$-Mediated HF Elimination. Typically, 5 g of γ-Al$_2$O$_3$ was placed in a glass ampule and activated by annealing under vacuum (10^{-3} mbar). The temperature was increased gradually and kept for 15 min at 600 °C. After the mixture was cooled to room temperature, the ampule was filled with argon. The respective fluoroarene (50−100 mg) was carefully mixed with activated aluminum oxide. The ampule was evacuated again and sealed. The condensation was carried out without stirring at 100−250 °C. The respective condensation products were obtained after extraction with toluene and subsequent solvent evaporation.

1,4-Bis(2-fluorophenyl)naphthalene(9). A 1.0 g portion of 1,4-dibromonaphthalene (3.5 mmol), 1.0 g of 2-fluorobenzeneboronic acid (7.15 mmol), 4.7 g of Cs$_2$CO$_3$ (14.3 mmol), and 416 mg of Pd(PPh$_3$)$_4$ (0.36 mmol) were added to the mixture of 30 mL of toluene and 15 mL of methanol. The reaction mixture was degassed under dynamic vacuum and stirred for 12 h at 110 °C under argon atmosphere. After the mixture was cooled to room temperature, 250 mL of diethyl ether was added, and the resulting mixture was washed three times with 100 mL of water. The organic layer was dried over sodium sulfate, and the solvent was removed under reduced pressure. Compound **9** was purified by filtration through silica gel using petroleum ether/dichloromethane mixture (1:1). After evaporation, the product was obtained as a white solid (0.79 g, 71% yield): R_f (CCl$_4$) = 0.57; mp 158.1 °C; ^{1}H NMR (300 MHz, CD$_2$Cl$_2$) δ 7.72−7.65 (m, 2H), 7.48 (s, 2H), 7.47−7.37 (m, 6H), 7.25 (m, 4H); ^{13}C NMR (75 MHz, CD$_2$Cl$_2$) δ 160.3 (d, J = 245.8 Hz), 134.4 (s), 132.5 (s), 132.0 (s), 129.8 (d, J = 8.1 Hz), 128.0 (d, J = 16.4 Hz), 127.2 (d, J = 0.9 Hz), 126.3 (s), 126.2 (d, J = 1.4 Hz), 124.4 (d, J = 3.5 Hz), 115.7 (d, J = 22.4 Hz); HRMS (ESI-TOF) m/z = [M]$^+$ calcd for C$_{22}$H$_{14}$F$_2$ 316.1064, found 316.1057.

1,4-Bis(biphenyl-2-yl)-2,5-difluorobenzene (11). A 0.65 mg portion of 1,4-dibromo-2,5-difluorobenzene (2.4 mmol), 1.0 g of 2-biphenylboronic acid (5.05 mmol), 1.56 g of Cs$_2$CO$_3$ (4.8 mmol), and 277 mg of Pd(PPh$_3$)$_4$ (0.24 mmol) were added to a mixture of 30 mL toluene and 15 mL of methanol. The reaction mixture was degassed under dynamic vacuum and stirred for 15 h at 110 °C under argon atmosphere. After the mixture was cooled to room temperature, 200 mL of diethyl ether was added, and the resulting mixture was washed three

times with 100 mL of water. The organic layer was dried over sodium sulfate, and the solvent was removed under reduced pressure. The **11** was purified by flash chromatography on silica gel using CCl$_4$ as eluent. After evaporation, the product was obtained as a white solid (0.81 g, 81% yield): R_f (CCl$_4$) = 0.45; mp 182.0 °C; ^{1}H NMR (300 MHz, CD$_2$Cl$_2$) δ 7.46−7.27 (m, 8H), 7.25−7.15 (m, 6H), 7.13−7.04 (m, 4H), 6.68 (t, J = 7.9 Hz, 2H); ^{13}C NMR (75 MHz, CD$_2$Cl$_2$) δ 155.3 (dd, J = 243.8, 3.7 Hz), 141.9 (s), 141.2 (s), 133.4 (s), 131.0 (s), 130.4 (s), 129.8 (dd, J = 14.6, 12.2 Hz), 129.3 (s), 128.8 (s), 128.2 (s), 127.5 (s), 127.1 (s), 118.8−118.1 (m); HRMS (ESI-TOF) m/z = [M]$^+$ calcd for C$_{30}$H$_{20}$F$_2$ 418.1533, found 418.1538.

Fluoranthene (6). Fluoranthene was synthesized from **5** (202 mg) according to the general procedure using 5 g of activated Al$_2$O$_3$. The condensation was carried out at 150 °C for 60 h. Extraction with toluene and subsequent evaporation gave pure **6** as white crystals (146 mg, 79% yield). Spectroscopic data were found to be in agreement with those previously reported.[18]

Triphenylene (8). Triphenylene was synthesized from **7** (111 mg) according to the general procedure using 5 g of activated Al$_2$O$_3$. The condensation was carried out at 250 °C for 10 min. Extraction with Soxhlet (toluene) and subsequent evaporation gave pure **8** as white crystals (104 mg, quantitatively). Spectroscopic data were found to be in agreement with those previously reported.[18]

Indeno[1,2,3-cd]fluoranthene (10). Compound **10** was synthesized from **9** (172 mg) according to the general procedure using 5 g of activated Al$_2$O$_3$. The condensation was carried out at 200 °C for 60 h. Extraction with toluene and subsequent evaporation gave pure **10** as orange crystals (51 mg, 34% yield). Spectroscopic data were found to be in agreement with those previously reported.[18]

Phenanthro[9,10-b]triphenylene (12). Compound **12** was synthesized from **11** (130 mg) according to the general procedure using 5 g of activated Al$_2$O$_3$. The condensation was carried out at 150 °C for 120 h. Extraction with Soxhlet (toluene, 3 days) and subsequent evaporation gave pure **10** as white crystals (114 mg, 97%; additional extraction with boiling xylene and subsequent HPLC analysis showed that the product was extracted not completely). Spectroscopic data were found to be in agreement with those previously reported.[19]

ASSOCIATED CONTENT

ⓢ Supporting Information

HPLC chromatograms and UV−vis spectra of the condensation products and ^{1}H and ^{13}C NMR spectra for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes
The authors declare no competing financial interest.

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(9) The "non-extractable" side products can be extracted with toluene only after hydrolysis with water or alcohol.

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(11) 1-Fluorobenzo[*c*]phenanthrene (**1**) has been used as a model compound. All experiments were carried out at 300 °C for 10 min, and the products were analyzed by means of HPLC. Interestingly, in the case of SiO_2, Ga_2O_3, In_2O_3, Nb_2O_5, and HfO_2, trace amounts of the condensation product have been detected.

(12) Compounds **1**, **9**, and **11** were used as model compounds. The condensation experiments were carried out under refluxing conditions (10 min), and the products were analyzed by means of HPLC.

(13) Recently, we have demonstrated that chlorinated and brominated PAHs remain completely intact under Al_2O_3-mediated condensation conditions up to 250 °C. See ref 8.

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