Aluminium-mediated aromatic C F bond activation: regioswitchable construction of benzene-fused triphenylene frameworks

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Aluminium-mediated Aromatic C–F Bond Activation: Regioswitchable Construction of Benzene-fused Triphenylene Frameworks

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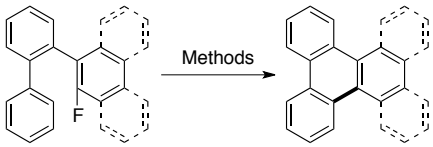
The selective synthesis of benzo[*f*]tetraphenes or benzo[*g*]chrysenes was achieved via aromatic C–F bond cleavage and unprecedentedly regioselective C–C bond formation depending upon the choice of aluminium reagents. On treatment with $AlCl_3$, 2-(biphenyl-2-yl)-1-fluoronaphthalenes afforded exclusively benzo[*f*]tetraphenes via C–C bond formation on the carbon atom γ to the original position of the fluorine substituent. In contrast, α-selective C–C bond formation was promoted by treatment with γ-Al_2O_3 to give benzo[*g*]chrysenes.

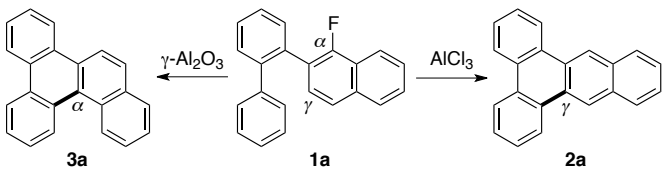
Chemical transformations of aromatic carbon–halogen bonds are widely utilised in materials science as well as life science. Among them, reactions involving aromatic carbon–fluorine (C–F) bond cleavage but still remain difficult owing to its high bond energy.[1] Activation of aromatic C–F bonds has been conventionally achieved via nucleophilic substitution (S_NAr)[2] or recently via transition-metal-catalysed oxidative addition.[3] However, the former method is typically limited to electron deficient fluoroarene substrates, while the latter often requires special ligands, directing groups and/or harsh conditions. As new approaches, Siegel and Amsharov independently reported the synthesis of polycyclic aromatic hydrocarbons (PAHs) by cationic cyclisations via aromatic C–F bond activation using silylium equivalents (Scheme 1a)[4] and γ-Al_2O_3 (Scheme 1b),[5] respectively.[6] In contrast, Ichikawa accomplished dibenzo[*g*,*p*]chrysene synthesis via the $FSO_3H{\cdot}SbF_5$- or TiF_4-promoted double C–F bond activation of 1,1-difluro-1-alkenes bearing two biaryl groups, where aromatic C–F bond activation was involved in the second cyclisation of intermediary 9-(biaryl-2-yl)-10-fluorophenanthrenes (Scheme 1c).[7]



Methods
(a) Siegel: $ArMe_2Si^+X^-$
(b) Amsharov: γ-Al_2O_3
(c) Ichikawa: $FSO_3H{\cdot}SbF_5$ or TiF_4 / $(CF_3)_2CHOH$

Scheme 1 PAH synthesis by cationic cyclisation via aromatic C–F bond activation.

In the course of our studies on acid-promoted aromatic C–F bond activation,[7,8] we found that treating 2-(biphenyl-2-yl)-1-fluoronaphthalene (**1a**) with $FSO_3H{\cdot}SbF_5$ or TiF_4 selectively afforded benzo[*f*]tetraphene (**2a**). In this reaction, fluoronaphthalene **1a** underwent intramolecular cyclisation via C–F bond cleavage and unprecedentedly regioselective C–C bond formation at the carbon atom γ to the original position of the fluorine substituent.[9] As a result of acid screening, $AlCl_3$ was found to be the best acid for this reaction (Scheme 2). Conversely, when **1a** was treated with γ-Al_2O_3, benzo[*g*]chrysene (**3a**) was selectively obtained via C–F bond cleavage and C–C bond formation at the α-carbon atom (Scheme 2). Thus, we achieved the complete switching of the regioselectivity in defluorinative intramolecular cyclisation of the single substrate **1a** using different aluminium reagents, which led to the synthesis of differently benzene-fused triphenylene compounds.[10,11]



3a **1a** **2a**

Scheme 2 Regioswichable synthesis of benzene-fused triphenylenes depending on the aluminium reagent employed.

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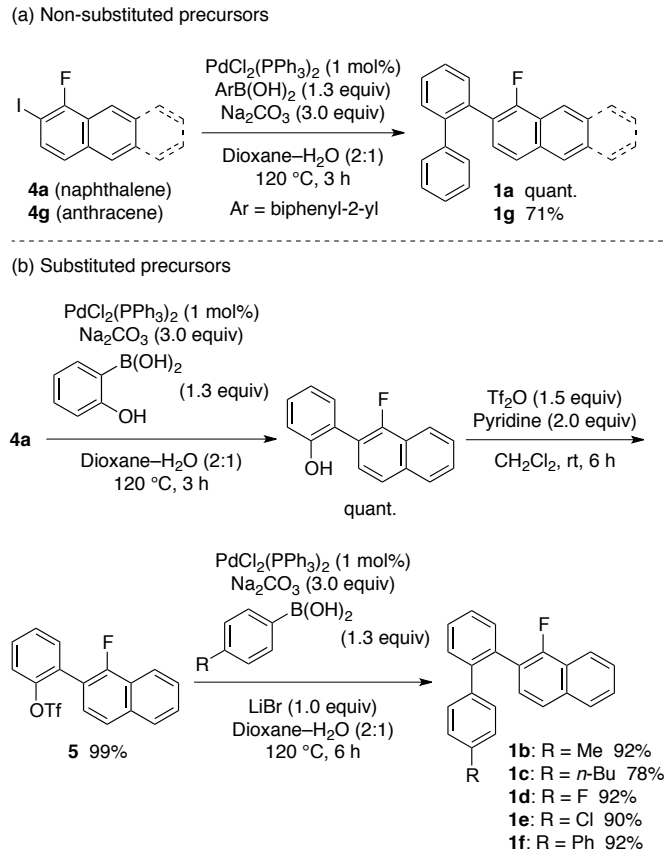
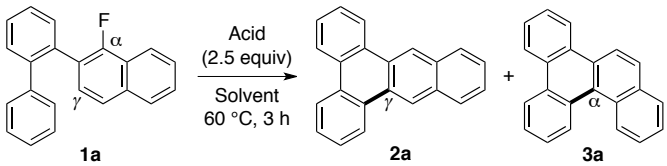
The 2-(biaryl-2-yl)-1-fluoronaphthalene cyclisation precursors **1** were prepared from 1-fluoro-2-iodonaphthalene (**4a**, Scheme 3). 2-(Biphenyl-2-yl)-1-fluoronaphthalene (**1a**) was prepared directly from **4a** via the Suzuki–Miyaura coupling with (biphenyl-2-yl)boronic acid in a quantitative yield (Scheme 3a). The preparation of ring-substituted precursors involved double Suzuki–Miyaura coupling reactions of **4a** with (2-hydroxyphenyl)boronic acid and of the resulting 2-(1-fluoronaphthalen-2-yl)phenyl trifluoromethanesulfonate (**5**) with 4-substituted phenylboronic acids (Scheme 3b). Thus, methyl-, butyl-, fluoro-, chloro- and phenyl-bearing 2-(biphenyl-2-yl)-1-fluoronaphthalenes **1b–1f** were obtained in high yields. Furthermore, 2-(biphenyl-2-yl)-1-fluoroanthracene (**1g**) was prepared via the Suzuki–Miyaura coupling of 1-fluoro-2-iodoanthracene (**4g**) with (biphenyl-2-yl)boronic acid according to the procedure for the preparation of **1a** from **4a** (Scheme 3a).



Scheme 3 Preparation of cyclisation precursors **1**.

On treatment with $FSO_3H{\cdot}SbF_5$ or TiF_4, which were suitable acids for the synthesis of dibenzo[*g*,*p*]chrysenes from 1,1-difluoro-1-alkenes, in 1,1,1,3,3,3-hexafluoropropan-2-ol (HFIP),[7,8] 2-(biphenyl-2-yl)-1-fluoronaphthalene (**1a**) selectively afforded benzo[*f*]tetraphene (**2a**) in 12% or 47% yield (Table 1, entries 3 and 4). In these cases along with C–F bond cleavage, C–C bond formation proceeded at the carbon γ to the fluorine substituent instead of at the α carbon. We thus sought suitable conditions for the synthesis of **2a** via defluorinative cyclisation of **1a** with a series of Brønsted and Lewis acids (Table 1). While *p*-toluenesulfonic acid (TsOH) gave no cyclised products (entry 1), treating **1a** with 2.5 equiv of trifluoromethanesulfonic acid (TfOH) selectively afforded **2a** in 97% yield (entry 2). Among the Lewis acids examined (entries 4–10), $AlCl_3$ and $ZrCl_4$ effectively promoted the cyclisation of **1a** in HFIP to give **2a** in almost quantitative yields (entries 7 and 10). Screening of solvents used with $AlCl_3$ revealed that chlorobenzene also exhibited a high efficiency comparable to that of HFIP (entry 11). We thus decided to use $AlCl_3$ as the reagent and chlorobenzene as the solvent for cyclisation of **1a** owing to their low cost. Finally, the reaction still proceeded with quantitative yield when the amount of $AlCl_3$ was decreased from 2.5 equiv to 1.5 equiv (entry 12).

Table 1 Screening of conditions for selective synthesis of benzo[*f*]tetraphene (**2a**)

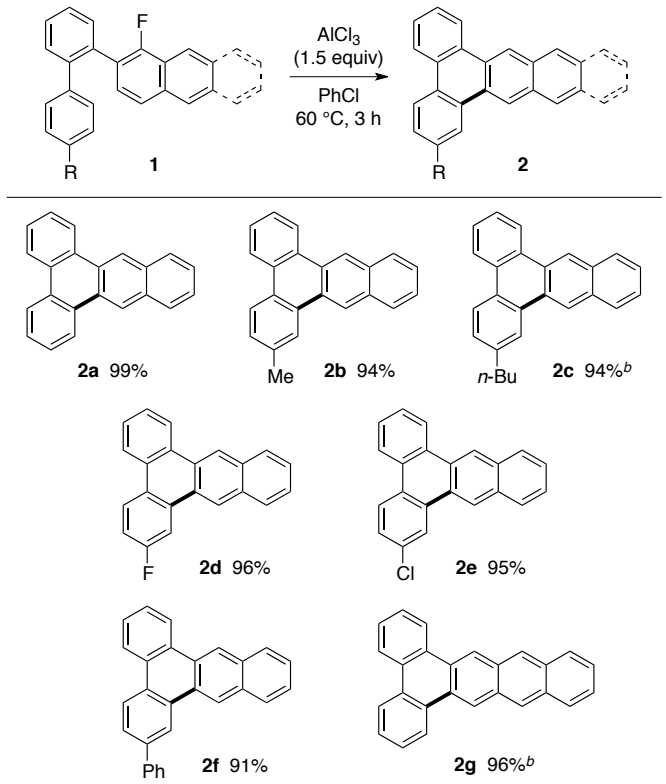


Entry	Acid	Solvent	**2a** (%)[a]	**3a** (%)[a]
1	TsOH	$(CF_3)_2CHOH$	N.D.[b]	N.D.[b]
2	TfOH	$(CF_3)_2CHOH$	97	< 1
3[c]	$FSO_3H{\cdot}SbF_5$	$(CF_3)_2CHOH$	12	N.D.[b]
4	TiF_4	$(CF_3)_2CHOH$	47	N.D.[b]
5	$TiCl_4$	$(CF_3)_2CHOH$	N.D.[b]	N.D.[b]
6	ZrF_4	$(CF_3)_2CHOH$	N.D.[b]	N.D.[b]
7	$ZrCl_4$	$(CF_3)_2CHOH$	99	< 1
8	Me_3SiOTf	$(CF_3)_2CHOH$	52	N.D.[b]
9	$BF_3{\cdot}OEt_2$	$(CF_3)_2CHOH$	N.D.[b]	N.D.[b]
10	$AlCl_3$	$(CF_3)_2CHOH$	99 (98)	< 1
11	$AlCl_3$	PhCl	99	< 1
12	$AlCl_3$[d]	PhCl	99 (99)	< 1

[a] Yield was determined by ^1H NMR measurement using CH_2Br_2 as an internal standard. Isolated yield is given in parentheses. [b] N.D. = Not detected. [c] 0 °C, 1 h. [d] $AlCl_3$ (1.5 equiv).

The defluorinative cyclisation of 2-(biaryl-2-yl)-1-fluoronaphthalenes **1** with different substituents was examined using the optimised conditions obtained above for synthesis of **2a** from **1a** (Table 2). Alkyl-substituted 2-(biphenyl-2-yl)-1-fluoronaphthalenes **1b** and **1c** successfully underwent defluorinative cyclisation to afford the corresponding benzo[*f*]tetraphenes **2b** and **2c** in high yields; however, the effective cyclisation of butyl-bearing substrate required HFIP as the solvent instead of chlorobenzene. The cyclisation of the fluorinated and chlorinated 2-(biphenyl-2-yl)-1-fluoronaphthalenes **1d** and **1e** proceeded without the loss of the halogen atoms at the 4'-positions. Phenyl-substituted benzo[*f*]tetraphene **2f** was also obtained in 91% yield from 1-fluoronaphthalene **1f** bearing a *p*-terphenyl moiety. The reaction of fluoroanthracene derivative **1g** proceeded in HFIP to afford dibenzo[*a*,*c*]tetracene (**2g**) in 96% yield.

Table 2 Selective synthesis of benzo[*f*]tetraphenes **2**[a]

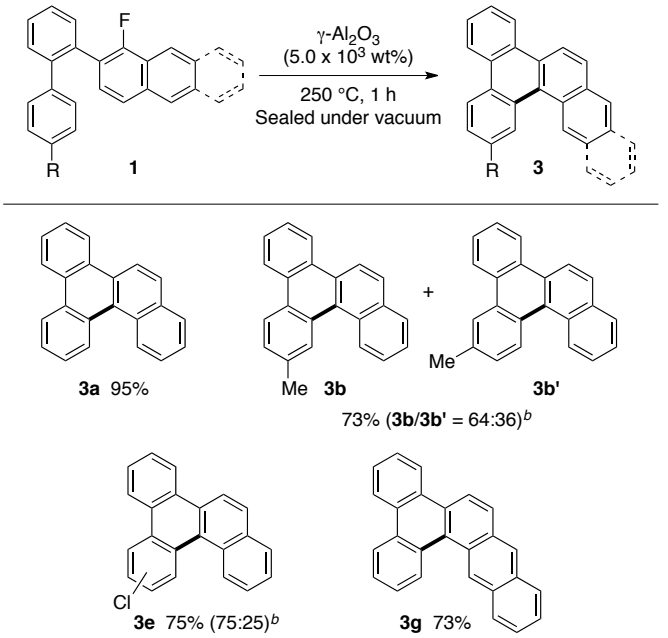


[a] Isolated yield. [b] HFIP was used as the solvent instead of PhCl.

In contrast to the reactions with $AlCl_3$, γ-Al_2O_3 promoted defluorinative cyclisation of fluoronaphthalenes **1** at the carbon α to the fluorine substituent (Table 3). Treatment of **1a** with 5.0 x 10^3 wt% of γ-Al_2O_3 at 250 °C in a pre-evacuated sealed tube afforded benzo[*g*]chrysene (**3a**) in 95% yield as the sole product. α-Selective cyclisation of methyl- and chlorine-substituted fluoronaphthalenes **1b** and **1e** also proceeded successfully to afford the corresponding benzo[*g*]chrysenes in 73% and 75% yields, respectively. In these reactions, partial migration of the substituents occurred during cyclisations probably by *ipso* attack of the biaryl moiety, indicating that the reaction would proceed via C–F bond polarization leading to aryl cation-like intermediate (vide infra).[12] Because of the high tolerance of C–F bond activation conditions to aryl C–Cl bonds as shown in Tables 2 and 3, both approaches open a facile way to various chlorinated PAHs, which are less accessible by other methods. Furthermore, dibenzo[*a*,*c*]tetraphene (**3g**) was produced by the reaction of 2-(biphenyl-2-yl)-1-fluoroanthracene (**1g**) in 73% yield under the same conditions.

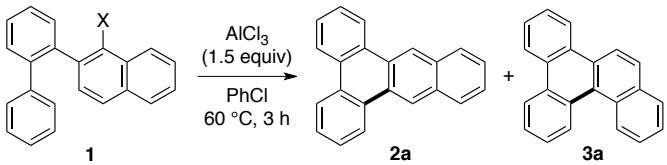
In order to gain mechanistic insight into the γ-selective cyclisation of 2-(biaryl-2-yl)-1-fluoronaphthalenes **1**, the effect of the fluorine substituent was investigated by comparing the efficiency of the cyclisation with the corresponding halonaphthalenes (Table 4). When 1-chlorinated, -brominated and -iodinated 2-(biphenyl-2-yl)naphthalenes **1h–j** were subjected to the optimal conditions used for γ-selective cyclisation of fluoro substrate **1a**, all the halides exhibited diminished yields of cyclised product **2a** compared to that of **1a** (entries 2–4 vs. entry 1). These results indicate that the high efficiency in γ-selective cyclisation of **1a** can be attributed to the relatively ready generation of the fluorine-stabilised intermediary arenium ions.[7,13]

Table 3 Selective Synthesis of Benzo[*g*]chrysenes **3**[a]



[a] Isolated yield. [b] Regioisomer ratio was determined by ^{1}H NMR measurement.

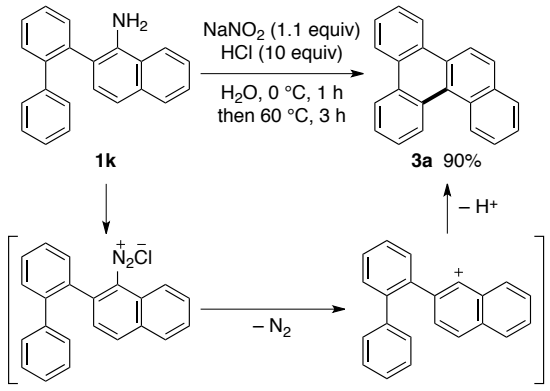
Table 4 Effect of halogen substituents



Entry	**1**	**2a** (%)[a]	**3a** (%)[a]
1	**1a**: X = F	99	< 1
2	**1h**: X = Cl	73	2
3	**1i**: X = Br	39	4
4	**1j**: X = I	22	3

[a] Yield was determined by ^{1}H NMR measurement using CH_2Br_2 as an internal standard.

In contrast, cyclisation of an aryl cation intermediate generated from a fluorine-free precursor exhibited opposite regioselectivity (Scheme 4). When 2-(biphenyl-2-yl)naphthalene-1-diazonium chloride, prepared from 2-(biphenyl-2-yl)naphthalen-1-amine (**1k**), was heated at 60 °C, benzo[*g*]chrysene (**3a**) was obtained in 90% yield as the sole product.[14] This result suggests that the reaction of 2-(biphenyl-2-yl)-1-fluoronaphthalene (**1a**) with γ-Al_2O_3 might proceed via an aryl cation-like intermediate.



Scheme 4 Cyclisation of an aryl cation intermediate.

In summary, we have achieved highly effective cyclisations of 1-fluoronaphthalenes bearing biaryl groups via aromatic C–F bond activation mediated by aluminium reagents. It is noteworthy that the choice of aluminium reagents altered the regioselectivities in the cyclisation of common 2-(biaryl-2-yl)-1-fluoronaphthalene precursors, enabling the selective synthesis of two different benzotriphenylenes, i.e., benzo[*f*]tetraphenes and benzo[*g*]chrysenes. Since higher order PAHs are particularly promising constituents in organic electronic devices,[15] the formation of extended π-systems by the current methodology appears to be a powerful route to functional materials.

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