Pyridine-promoted dediazoniation of aryldiazonium tetrafluoroborates: Application to the synthesis of SF$_5$-substituted phenylboronic esters and iodobenzenes

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**Abstract**

Pyridine promotes dediazoniation of aryldiazonium tetrafluoroborates. The formed aryl radicals were trapped with B$_2$pin$_2$, iodine, or tetrahydrofuran to afford boronic esters, iodobenzenes and benzenes, respectively. The application to the synthesis of (pentafluorosulfanyl)phenylboronic esters, iodo(pentafluorosulfanyl)benzenes and (pentafluorosulfanyl)benzene is shown.

**Introduction**

Pentafluorosulfanyl-containing compounds have been known for more than half a century [1-4]; however, for a long time they remained a relatively underdeveloped class of compounds [5,6]. The main reason for the slow development of the chemistry of SF$_5$-containing compounds was the lack of availability of key building blocks. However, in recent years, the scientific community has been witnessing a renewed interest in this functional group. Synthetic methods towards aliphatic SF$_5$-containing compounds are based on free radical addition of SF$_5$Cl or SF$_5$Br to unsaturated compounds [7-9], whereas aromatic derivatives are available either by the Umemoto’s two-step synthesis from diaryl disulfides or benzenethiols [10-12], or by the reaction of nitrophenyl disulfides with elemental fluorine [13-16]. Aromatic and heteroaromatic SF$_5$ compounds are mostly prepared by the derivatization of commercial nitro(pentafluorosulfanyl)benzenes [14,17-27] and approaches from SF$_5$-aliphatics have also been studied [28-30]. The unique combination of properties the SF$_5$ group imparts includes high chemical, thermal, and metabolic stability, strong electron-acceptor property, and high lipophilicity. Furthermore, applications of SF$_5$ compounds in catalysis [31,32], life-science [6,18,33-38], and material sciences [5,19,38,39] are emerging.

Arylboronic acids and arylboronates represent versatile building blocks in organic synthesis [40]. They have found wide applications in transition metal-catalyzed cross-coupling reactions [41,42]. These boron compounds are accessed mainly by the reactions of arylmagnesium or aryllithium species withtrialky-
boronates [43,44], Pd- or Cu-catalyzed borylations of aryl halides using B$_2$Pin$_2$, H-Bpin [45-50] or R$_2$N-BH$_2$ [51], direct borylations via aromatic C–H bond activations [52-58], Lewis acid catalyzed electrophilic borylations of electron-rich arenes [59-62], and Sandmeyer-type borylation of arylamines or diazo- nium salts with B$_2$Pin$_2$ [63-67], B$_2$(OH)$_4$ [68] or R$_2$N-BH$_2$ [69]. Several attempts were made to synthesize the SF$_5$-phenylboronates. Patent literature describes the synthesis of 3- or 4-(pentafluorosulfanyl)phenylboronates or boronic acids from SF$_5$-bromobenzenes via lithiation or magnesi nation. These approaches suffer from low yields and other drawbacks [70,71]. For lithiation of the aryl bromide, t-BuLi had to be used and the formation of Grignard reagents is inefficient. On the other hand, Shibata and co-workers have recently reported the synthesis of 3,5-bis(pentafluorosulfanyl)phenylboronic acid from the corresponding aryliodine, trimethyl borate and iPrMgBr [32]. Finally, Joliton and Carreira have recently shown efficient Ir-catalyzed C–H borylation of several 1-substituted-3-(pentafluorosulfanyl)benzenes and applied the products of borylation to the Pd-catalyzed Suzuki–Miyaura reaction with aryl bromides or iodides. However, the reaction is limited to borylations in position five of 1-substituted-3-(pentafluorosulfanyl)-benzenes [72].

Straightforward access to SF$_5$-phenylboronic acids or boronates would be highly desirable since it would allow easy installation of the SF$_5$-phenyl group by the subsequent Suzuki–Miyaura reaction. Nitro-(pentafluorosulfanyl)benzenes are the primary industrial SF$_5$-aromatics, therefore the easiest access to SF$_5$-phenylboronates appears to be starting from readily available SF$_5$-substituted anilines or diazonium salts rather than SF$_5$-containing halobenzenes. Herein, we report a new protocol for efficient borylation, iodoniation and hydrodeiodination of SF$_5$-phenyl/diazonium tetrafluoroborates in the presence of pyridine. The generality of the borylation and iodoniation reactions was demonstrated on several examples.

**Results and Discussion**

At the onset of our investigation, Sandmeyer-type borylation of 3- and 4-(pentafluorosulfanyl)anilines (1a and 1b, respectively) to pinacolboronates 2a and 2b according to Wang and co-workers was studied [64,65] (Table 1). The borylation of 1a took place in a reasonable yield in the presence of catalytic amounts of benzoyl peroxide (BPO, Table 1, entry 1), while for 1b, heating without any additives was preferable; however, the yield of 2b was only moderate (Table 1, entry 3).

For a detailed investigation of the borylation reaction, the diazonium tetrafluoroborates 3a and 3b were prepared and isolated according to Doyle conditions [73]. High yields (above 90%) of both isomers of the diazonium tetrafluoroborates 3a and 3b were obtained on 0.3–6 g scale (Table 2). Crystal structures of 3a (CCDC 1009848) and 3b (CCDC 1009849) were determined confirming the nature of the products. During the course of our studies, Okazaki and co-workers reported the synthesis of 3b in 84% yield under similar conditions and have shown its reactivity in various cross-coupling reactions with varied degree of success. The most efficient cross-coupling reactions were the Heck reactions with alkynes, a biaryl homocoupling reaction, an azo coupling to electron-rich arenes, and a diazoniataion with TMSN$_3$ in an ionic liquid medium [74,75].

An efficient borylation of aryldiazonium tetrafluoroborates with NH$_2$-Pd catalysts was reported recently [63]. When applied to 3a and 3b using Pd(OAc)$_2$ and NH$_2$ ligand precursors L, the borylated products 2a and 2b were isolated in only moderate yields (Table 2, entries 1 and 2). However, it was found that the Pd catalyst was not required for an efficient reaction. Alkali metal acetates are known to facilitate decomposition of aryldiazonium salts by the formation of diazoacettes and diazo anhydrides, which decompose to aryl radicals [76]. These additives were used in Meerwein arylation of isopropenyl acetate [77]. In our case, two-fold excess of sodium acetate in acetonitrile afforded 2a and 2b in good and moderate yields, respectively (Table 2, entries 3 and 4). The conditions reported by Yu and co-workers [66] (Table 2, entry 5) provided a mixture with starting 3b as the major component. While the diazonium salts 3a and 3b were found to be stable in acetonitrile, we observed slow decomposition in methanol and in the presence of B$_2$Pin$_2$ under strictly Pd-free conditions (new Teflon stirring bar and glassware), the borylation took place with low conversion (Table 2, entry 6) [78]. In pyridine, however, the decomposition of 3b was very fast and a vigorous evolution of nitrogen was observed affording the borylated product in a moderate yield together with a mixture of SF$_5$-pyridines in ca. 10% GC–MS yield (Table 2, entry 7). Finally, the use of a

<table>
<thead>
<tr>
<th>Entry</th>
<th>Additive</th>
<th>Temp. (°C)</th>
<th>Yield (%$^c$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1a, 3-SF$_5$ BPO</td>
<td>rt</td>
<td>2a, 70</td>
</tr>
<tr>
<td>2</td>
<td>1b, 4-SF$_5$ BPO</td>
<td>rt</td>
<td>2b, traces</td>
</tr>
<tr>
<td>3</td>
<td>1b, 4-SF$_5$ —</td>
<td>80</td>
<td>2b, 55$^c$</td>
</tr>
</tbody>
</table>

$^c$Reaction conditions: 1 (1 mmol), t-BuONO (1.5 mmol), B$_2$Pin$_2$ (1.1 mmol), additive (2 mol %), MeCN (4 mL). $^d$Isolated yield. $^e$82% purity.
tuted phenyldiazonium tetrafluoroborates undergo efficient borylation with an equimolar amount of B$_2$pin$_2$ (Scheme 1); however, ortho-substituted phenyldiazonium salts were found to be either not efficient substrates (3f) or completely unreactive (3g), presumably due to a large steric demand of B$_2$pin$_2$.

Pyridine is known to induce decomposition of aryl diazonium salts. Zollinger and Abramovich studied the interaction of pyridine with aryl diazonium tetrafluoroborates and suggested the formation of diazopyridinium salts which homolytically decompose to aryl radicals, nitrogen and a pyridinium tetrafluoroborate radical [79,80]. Tanaka and co-workers have used the combination of PhN$_2^+$BF$_4^-$ and pyridine for arylations of silylenol ethers [81]. They have observed the formation of large amounts of phenylpyridines. In our case, we detected SF$_3$-phenylpyridines in trace amounts only during borylation using pyridine as a solvent. The major products in the borylation reaction apart from 2a and 2b were found to be F-Bpin and pyridine BF$_3$ complexes. Both compounds are easily hydrolyzable but they were observed by NMR of the crude reaction mixture and compared to the synthesized authentic samples. On the other hand, we were not able to observe a pyridine-B$_2$pin$_2$ complex by $^{13}$B NMR in CD$_2$CN or CDC$_3$. The borylation was extended to several other aryl diazonium tetrafluoroborates showing that both electron-donor and electron-acceptor substituted phenyldiazonium tetrafluoroborates undergo efficient borylation with an 4-fold excess of pyridine in acetonitrile was found to be optimal. Conducting the reaction on a gram scale proceeded without a notable loss of efficiency and the reaction can be performed in air (Table 2, entries 8–10).

The mechanism of this borylation reaction remains to be elucidated. Based on experimental results and literature precedent, we propose the following free-radical mechanism (Scheme 2). Aryldiazonium salt 3 reacts with pyridine to form aryl diazopyridinium 4 which decomposes to an aryl radical, a pyridinium tetrafluoroborate radical and the Bpin radical. The byproducts pyridine BF$_3$ and F-Bpin are formed by the reaction of the Bpin radical (likely to be stabilized by pyridine) [82]. The byproducts pyridine BF$_3$ and F-Bpin are formed by the reaction of the pyridinium tetrafluoroborate radical and the Bpin radical.

Subjecting the diazonium salt 3i to the borylation conditions gave further indirect evidence for the formation of aryl radicals (Scheme 3). Full conversion of 3i was observed affording a mixture of products 2i, 2i', 5i (two isomers of unknown configuration) and 6i in 16:31:28:25 GC–MS ratio. The presence of these products can be explained only by the formation of the substituted SF$_3$-phenyl radical which undergoes borylation to 2i, hydrogen atom transfer followed by borylation to 2i', intramolecular cyclization to 5i or hydrogen abstraction to 6i.

### Table 2: Synthesis of diazonium tetrafluoroborates 3 and boronates 2.

<table>
<thead>
<tr>
<th>Entry</th>
<th>3 (mmol)</th>
<th>Reagents (equiv), solvent</th>
<th>Temp. (°C)</th>
<th>Time (h)</th>
<th>2, Yield (%)$^c$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3a (1)</td>
<td>Pd(OAc)$_2$ (0.01), L (0.02), THF</td>
<td>rt</td>
<td>18</td>
<td>2a, 43</td>
</tr>
<tr>
<td>2</td>
<td>3b (1)</td>
<td>Pd(OAc)$_2$ (0.01), L (0.02), THF</td>
<td>rt</td>
<td>18</td>
<td>2b, 57</td>
</tr>
<tr>
<td>3</td>
<td>3a (1)</td>
<td>NaOAc (2), MeCN</td>
<td>−50 to rt</td>
<td>3</td>
<td>2a, 73</td>
</tr>
<tr>
<td>4</td>
<td>3b (1)</td>
<td>NaOAc (2), MeCN</td>
<td>−50 to rt</td>
<td>3</td>
<td>2b, 49</td>
</tr>
<tr>
<td>5</td>
<td>3b (1)</td>
<td>CuBr (0.05), MeCN/H$_2$O (3:1)</td>
<td>rt</td>
<td>330</td>
<td>2b, 23</td>
</tr>
<tr>
<td>6</td>
<td>3a (1)</td>
<td>—, MeOH</td>
<td>rt</td>
<td>24</td>
<td>2a, 32</td>
</tr>
<tr>
<td>7</td>
<td>3b (1)</td>
<td>—, pyridine$^d$</td>
<td>−30 to rt</td>
<td>2</td>
<td>2b, 55</td>
</tr>
<tr>
<td>8</td>
<td>3b (1)</td>
<td>pyridine (4), MeCN$^d$</td>
<td>−30 to rt</td>
<td>2</td>
<td>2b, 77</td>
</tr>
<tr>
<td>9</td>
<td>3b (3)</td>
<td>pyridine (4), MeCN$^d$</td>
<td>−30 to rt</td>
<td>2</td>
<td>2b, 77</td>
</tr>
<tr>
<td>10</td>
<td>3a (2)</td>
<td>pyridine (4), MeCN$^d$</td>
<td>−30 to rt</td>
<td>2</td>
<td>2a, 80</td>
</tr>
</tbody>
</table>

$^a$Reaction conditions: 1 (1–28 mmol), BF$_3$OEt$_2$ (2.1 equiv), t-BuONO (1 equiv), CH$_2$Cl$_2$ or Et$_2$O (3 mL/1 mmol of 1), 30 min. $^b$Reaction conditions: 3 (1–3 mmol), B$_2$pin$_2$ (1 equiv), reagents, solvent (2 mL/1 mmol of 3) under N$_2$. $^c$Isolated yield. $^d$The reaction was conducted under air.
Scheme 1: Borylation of aryldiazonium tetrafluoroborates 3. Reaction conditions: 3 (1 mmol), B$_2$pin$_2$ (1 mmol), pyridine (4 mmol), MeCN (2 mL), 2 h.

Scheme 2: Proposed reaction mechanism.

Starting from aniline derivative 1b, a one pot diazotization–borylation sequence using different acids afforded the corresponding borylated product 2b in good yields (Table 3).

Suzuki–Miyaura cross-coupling reactions of boronates 2a and 2b with aryl iodides using a simple system without any optimization proceeded in satisfactory yields considering the electron-deficient character of the boronates and consequently less efficient transmetallation step (Scheme 4).

Transformation to SF$_5$-phenylboronic acid 8b and potassium trifluoroborates 9 was straightforward under standard conditions (Scheme 5). Similar potassium SF$_5$-phenyltrifluoroborates were found to be highly reactive with a variety of aryl bromides and iodides in the presence of catalytic amounts of...
Scheme 4: Suzuki–Miyaura reaction of boronates 2a and 2b with aryl iodides. Reaction conditions: 2 (1 mmol), ArI (1.1 mmol), Pd(PPh$_3$)$_4$ (5 mol %), LiOH·H$_2$O (4 mmol), 1,4-dioxane (2 mL), water (1 mL), 3.5 h.

Scheme 5: Synthesis of boronic acid 8b and trifluoroborates 9. Reaction conditions for the synthesis of 8b: 2 (2 mmol), NaIO$_4$ (8 mmol), THF (8 mL), H$_2$O (2 mL), rt, 1 h. Reaction conditions for the synthesis of 9: 2 (2 mmol), KHF$_2$ (10 mmol), MeOH (8 mL), H$_2$O (3.6 mL), rt, 20 min.

Scheme 6: Iodination of aryldiazonium tetrafluoroborates 3. Reaction conditions: 3 (1 mmol), I$_2$ (1.1 mmol), pyridine (4 mmol), MeCN (3 mL), 2 h. aYields in the presence of collidine instead of pyridine.

PdCl$_2$(dppf)-CH$_2$Cl$_2$ or Pd(OAc)$_2$ [72]. The recently published synthesis of arylboronic acids from anilines or aryldiazonium tetrafluoroborates using B$_2$(OH)$_4$ [68] applied to 3b provided 8b in only 25% $^{19}$F NMR yield.

To extend the synthetic utility of the pyridine-mediated derivatization of aryldiazonium tetrafluoroborates we investigated the reaction with iodobenzene and iodine as efficient scavengers of aryl radicals [83,84]. A competitive experiment starting from 3a and equimolar amounts of B$_2$pin$_2$ and iodobenzene in the presence of pyridine (4 equiv) in MeCN afforded a mixture of 2a (72% yield) and 1-iodo-3-(pentafluorosulfanyl)benzene (10a, 23% yield). Additionally, a reaction of 3b with PhI (4 equiv) in the absence of B$_2$pin$_2$ gave 1-iodo-4-(pentafluorosulfanyl)benzene (10b) in 35% yield. Both experiments point to the formation of aryl radicals during the reaction and suggest a possibility to conduct practical aromatic iodination. Indeed, the iodination reaction with I$_2$ proved to be more efficient than with PhI (Scheme 6). In contrast to borylation, iodination with I$_2$ shows a higher sensitivity to electronic properties of substituents on the aromatic ring. Electron-acceptor substituted aryldiazonium compounds are excellent substrates while those with electron-
donor groups react much less efficiently. The substitution of pyridine with collidine (2,4,6-trimethylpyridine) gave similar yields. Unlike borylations, the iodination reactions were not sensitive to ortho substitutions. In the case of 3i, compound 10i was the sole product; no product of hydrogen atom transfer or cyclization was observed, demonstrating that the reaction with I$_2$ is much faster than with B$_3$pin$_2$. Importantly, the yields of SF$_5$-phenyl iodides 10a and 10b using our two-step diazotization–iodination method significantly exceed those obtained by classical Sandmeyer reaction (ca. 80% yield over two steps compared to 63% for 10a and 50% for 10b by one-pot Sandmeyer procedure requiring 10 fold excess of KI) [14]. The side-product in the iodination of 3 was bis(pyridine)iodonium tetrafluoroborate, which can be easily isolated from the reaction mixture by precipitation upon addition of diethyl ether. This iodonium salt was first synthesized by Barluenga [85] and later used for mild iodination of alkenes, alkynes and aromatics [85-87]. Its formation can be explained by the reaction of the pyridinium tetrafluoroborate radical (Scheme 2), pyridine and I$_2$ or iodine radical. Bromination of 3b with Br$_2$ was attempted under conditions similar to iodination but the reaction was slow and inefficient resulting in a mixture of products with expected 1-bromo-4-(pentafluorosulfonyl)benzene as a minor product. With equimolar NBS instead of bromine, the reaction is much cleaner but slow; after overnight at ambient temperature the bromo product was isolated in 35% yield.

Finally, hydrodediazoniation using tributyltin hydride or THF was tested and THF proved to be a more efficient hydrogen atom donor. The addition of excess pyridine to MeCN/THF solution of diazonium tetrafluoroborates 3a or 3b led to an efficient hydrodediazoniation and the formation of (pentafluorosulfonyl)benzene (6). Deuteration experiments established that the hydrogen atom in the product comes exclusively from THF and not from pyridine or MeCN (Table 4). The observed deuterium enrichment using THF-d$_8$ was around 80%. Thermal decomposition of aryldiazonium salts prepared from immobilized triazene precursors and the formation of deuterated aromatics using THF-d$_8$ was reported [88]. We explain the reduced yield of 6-D (48% yield) and the formation of tar products by hydrogen atom abstraction from 3 or 6 and subsequent polymerization. No significant amounts of double deuterated products were detected. The kinetic isotope effect was determined from intermolecular competition experiment using 3b and a 1:1 mixture of THF and THF-d$_8$ giving KIE = 5.5 (6-D ratio determined by GC–MS) and combined yield of 62%. This means that the hydrogen abstraction is much faster than the deuterium abstraction and suggests the C–H(D) bond formation as the rate-limiting step. For unambiguous identification of the rate-limiting step, individual rate constants $k_H$ and $k_D$ in two parallel reactions would have to be determined [89]. Dihydrofuran (11) and pyridinium tetrafluoroborate were identified as byproducts of the dediazonation reactions. Similarly to the previous processes, we presume the formation of aryldiazopyridinium 4 and its decomposition to an aryl radical and the pyridinium tetrafluoroborate radical. The aryl radical abstracts a hydrogen atom from THF forming 6 and a THF radical. The THF radical then transfers the hydrogen atom to the pyridinium tetrafluoroborate radical giving dihydrofuran (11) and pyridinium salt.

### Conclusion

In conclusion, a novel dediazonation–borylation methodology was developed based on the reaction of aryldiazonium tetrafluoroborates with pyridine and B$_3$pin$_2$ to give arylpinacolborates. Particular emphasis was on the synthesis of SF$_5$-phenylboronates where our methodology represents a considerable improvement in reaction efficiency compared to previously published syntheses. Furthermore, no transition metals are needed and mild reaction conditions are used. The borylation is applicable to a variety of aryldiazonium tetrafluoroborates with electron-donor or acceptor groups while ortho-substituted substrates are less reactive. A mechanism involving aryl radicals is suggested. The Suzuki–Miyaura reaction of SF$_3$-phenylboronates with aryl iodides provided the cross-coupling biaryl products. In analogy to the borylation reaction, iodination of aryldiazonium tetrafluoroborates with pyridine and iodine resulted in aryl iodides. An efficient reaction was observed with electron-acceptor substituted aromatic compounds even with ortho-substituted derivatives. In the case of SF$_5$-substituted

<table>
<thead>
<tr>
<th>Entry</th>
<th>3 (mmol)</th>
<th>D source</th>
<th>D enrichment$^0$</th>
<th>6, Yield (%)$^c$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3a (0.5)</td>
<td>—</td>
<td>n/a</td>
<td>6, 75</td>
</tr>
<tr>
<td>2</td>
<td>3b (0.5)</td>
<td>—</td>
<td>n/a</td>
<td>6, 70</td>
</tr>
<tr>
<td>3</td>
<td>3b (0.5)</td>
<td>THF-d$_8$ (0.5 mL)</td>
<td>77–82</td>
<td>6-D, 48</td>
</tr>
<tr>
<td>4</td>
<td>3b (0.25)</td>
<td>C$_9$H$_7$N (4 mmol)</td>
<td>0</td>
<td>6, 70</td>
</tr>
<tr>
<td>5</td>
<td>3b (0.25)</td>
<td>CD$_3$CN (0.75 mL)</td>
<td>0</td>
<td>6, 67</td>
</tr>
</tbody>
</table>

$^0$Reaction conditions: 3 (0.25–0.5 mmol), pyridine (4 equiv), THF (1 mL/1 mmol of 3), MeCN (3–4 mL/1 mmol of 3); 2 h. $^c$Based on GC–MS. $^c$Based on $^{19}$F NMR using 1-nitro-4-(pentafluorosulfanyl)-benzene as an internal standard.
iodobenzenes, the method is much more efficient than the classical Sandmeyer reaction starting from SF$_5$-containing aniline derivatives. Finally, hydrodediazoniation of SF$_5$-phenylidazonium tetrafluoroborates by hydrogen atom abstraction from THF in the presence of pyridine provided (pentafluorosulfanyl)-benzene.

Supporting Information
Synthesis and characterization of all products, copies of $^1$H, $^{13}$C, and $^{31}$P NMR spectra of newly synthesized products, and X-ray crystallographic files of the compounds 3a and 3b.

Supporting Information File 1
Experimental part.
[http://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-11-162-S1.pdf]

Supporting Information File 2
Crystal structure of compound 3a.
[http://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-11-162-S2.cif]

Supporting Information File 3
Crystal structure of compound 3b.
[http://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-11-162-S3.cif]

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References

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