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Palladium-catalyzed borylation of aryldiazonium tetrafluoroborate salts. A new synthesis of arylboronic esters

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Abstract

The first synthesis of arylboronic esters via the coupling of bis(pinacolato)diboron with easily prepared aryldiazonium tetrafluoroborate salts is reported. The palladium-catalyzed borylation reaction proceeds efficiently under mild reaction conditions in the absence of a base to afford various functionalized arylboronic esters in moderate to high yields. © 2000 Elsevier Science Ltd. All rights reserved.

Boronic acids and esters are used in a wide variety of research applications.[1] They also continue to attract attention as versatile functional group tolerant cross-coupling substrates in organic synthesis.[2] Synthetic methodology allowing for the direct attachment of boron to aromatics to afford arylboronates is thus an important challenge.[3] Arylboronic esters are generally purified more easily than arylboronic acids, can be synthesized without organolithium or Grignard reagents and promote one-pot cross-couplings.[4] Aryl borylation reactions, which directly afford arylboronic esters, have been successfully performed using aryl halides and triflates.[3]

Aryldiazonium tetrafluoroborate salts are highly attractive synthetic alternatives to the corresponding halides and triflates. They can be prepared from relatively inexpensive, readily available anilines.[5] They are more reactive than halides or triflates in cross-coupling reactions.[6] Recently, we demonstrated the first palladium-catalyzed cross-coupling of aryldiazonium tetrafluoroborate salts with arylboronic esters.[7] As part of our program also entails the efficient synthesis of well-defined oligoaromatic materials[8] for boronic acid-based sensory applications,[9] we herein report the first synthesis of arylboronic esters using aryldiazonium tetrafluoroborate salts as substrates (Scheme 1).

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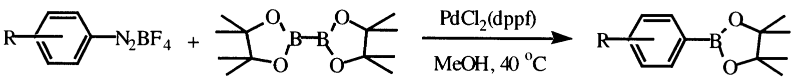


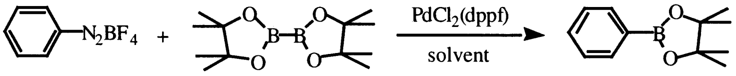
1 **2** **3**

a R = H
b R = *p*-Br
c R = *p*-Me
d R = *p*-I
e R = *p*-CO_2Me
f R = *p*-OMe
g R = *p*-NO_2
h R = *p*-Br,*o*-Me
i α-naphthyl

Scheme 1.

We initially screened the reaction of **1a** (0.50 mmol) and **2** (0.55 mmol) in 2 mL of solvent in the presence or absence of base (Table 1). KOAc and DMF had been used previously in borylation reactions of aryl halides.[3a] Our best results were observed using MeOH rather than DMF as solvent (entry 3). In addition, we observed a comparable yield in the absence of base (entry 4). Unfortunately, no reaction occurred using dialkoxyhydroborane as the borylation reagent.[3b,3d] Similar results were obtained using MeOH in the presence and absence of Et_3N. Commonly used dioxane[3b–d] was not suitable for converting **1a** to **3a** regardless of the borylation reagent employed. We thus decided to further study the palladium-catalyzed coupling of **1a** and **2** in MeOH without base.

Table 1
Effect of solvent and base on the borylation of **1a**[a]



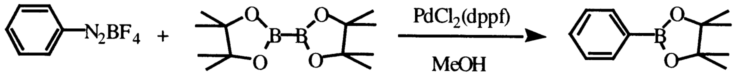
1a **2** **3a**

Entry	Solvent	Base (equiv.)	% **3a**
1	DMF	KOAc (3)	54
2	DMF	–	17
3	MeOH	KOAc (3)	70
4	MeOH	–	68
5	Dioxane	–	–

[a] Reactions were performed over 24 h at 60°C using 3 mol% catalyst (dppf = 1,1′-bis(diphenylphosphino)ferrocene) and anhydrous solvents. Isolated yields are reported.

Optimization studies began with the investigation of the effect of stoichiometry and temperature on the course of the reaction (Table 2). The use of 1 equiv. of **1a** to **2** resulted in a 56% conversion to **3a** at 60°C (entry 1). Adding additional aliquots of **1a** (0.5 equiv.) in 1 h intervals resulted in 65 and 75% conversion to **3a**, respectively; however, adding 2 equiv. of **1a** at once did not improve the conversion (entry 2) and afforded partial decomposition of **1a**. Couplings conducted at rt with varying amounts of **1a** (entries 3–6) afforded conversions comparable to the runs at 60°C. We thus decided to allow the borylation to proceed at rt for 1 h and then add aliquots of **1** at a slightly elevated temperature to push the reaction to completion.[10]

Table 2
Effect of temperature and stoichiometry on the borylation of **1a**[a]



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

Entry	Equiv. **1a** used	Temp. (°C)	Time (h)	% **3**[b]
1	1.0	60	1.75	56
2	2.0	60	1.00	75
3	1.0	Rt	1.25	56
4	2.0	Rt	1.25	60
5	3.0	Rt	1.25	56
6	4.0	Rt	1.25	54

[a] Reactions performed in 2 mL of anhydrous MeOH under nitrogen using 0.125 mmol **2**.

[b] Conversion yields based on NMR integration.

As shown in Table 3, the borylation reactions, performed in the absence of added base, afforded arylboronic esters **3** in moderate to high yields.[11] Sterically encumbered aryldiazonium tetrafluoroborate salt **1h** (entry 8) furnished multi-substituted arylboronic ester **3h** in moderate yield. Direct borylation of α-naphthyldiazonium tetrafluoroborate salt (entry 9) afforded naphthylboronate **3i** in high yield. Aryldiazonium tetrafluoroborate salt **1f** (entry 6) provided only a moderate yield of functionalized arylboronic ester **3f**. Successful regioselective borylation at the diazonium site was accomplished in the presence of both C–I (entry 4) and C–Br (entries 2 and 8) bonds, affording two novel functionalized arylboronates **3d** and **3h**, respectively.

Table 3
Synthesis of arylboronic esters **3**

Entry	Ar–N_2BF_4	Equiv. **1** used	Time (h)	Product **3**	% Yield[a]
1	$C_6H_5N_2BF_4$	3.0	3.0	**3a**	96
2	4–$BrC_6H_5N_2BF_4$	3.0	5.0	**3b**	80
3	4-$MeC_6H_5N_2BF_4$	3.0	5.0	**3c**	87
4	4-$IC_6H_5N_2BF_4$	3.0	5.0	**3d**	58
5	4-$CO_2MeC_6H_5N_2BF_4$	4.5	8.0	**3e**	81
6	4-$OMeC_6H_5N_2BF_4$	4.5	8.0	**3f**	51
7	4-$NO_2C_6H_5N_2BF_4$	3.5	6.0	**3g**	61
8	4-Br, 2-$MeC_6H_5N_2BF_4$	3.0	5.0	**3h**	42
9	α-$C_{10}H_7N_2BF_4$	3.0	5.0	**3i**	73

[a] Isolated yield.

In conclusion, aryldiazonium tetrafluoroborate salts, which are synthesized from economical and readily available anilines, are useful substrates for the synthesis of arylboronic esters. The new methodology features relatively mild conditions, an environmentally benign alcohol solvent and no added base. To the best of our knowledge, this is the first example of a direct carbon–nitrogen to carbon–boron bond transformation.

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10. Inert atmosphere was essential for reaction success.
11. General procedure for the borylation of aryldiazonium tetrafluoroborate salts **1**. Bis(pinacolato) diboron **2** (1.0 mmol), aryldiazonium tetrafluoroborate salt **1** (1.0 mmol) and PdCl$_2$(dppf) (0.03 mmol) were added to a reaction vessel which was purged thoroughly with N$_2$. Deoxygenated anhydrous MeOH (2–10 mL) was added via syringe and the reaction was allowed to proceed at rt for 1 h. Additional 0.5 and 0.0075 equiv. aliquots of **1** and PdCl$_2$(dppf), respectively, were then added in 1 h intervals and the solution was heated to 40°C in a sand bath until reaction completion. The solution was then cooled to room temperature and concentrated. The residue was dissolved in 0–20% EtOAc/Hex, decolorized, passed through celite and concentrated. Kugelrohr distillation or silica gel chromatography (0–20% EtOAc/hexanes) afforded the respective arylboronic esters **3**. The borylation of 1,4-phenylenebisdiazonium tetrafluoroborate salt was unsuccessful to date, affording phenylboronic pinacol ester and a trace amount of bisborylated product. Spectral data for arylboronic esters **3a**, **3c**, and **3e**–**g** was consistent with that found in Ref. 3b. Spectral data for arylboronic esters **3b** and **3i** was consistent with that found in Refs. 3a and 3d, respectively. Physical data for novel arylboronic esters is as follows: **3d**: white solid, mp 86–88°C. ^{1}H NMR (CDCl$_3$, 250 MHz): δ 7.70 (2H, d, $J=8.0$ Hz), 7.49 (2H, d, $J=8.0$ Hz), 1.33 (12H, s); ^{13}C NMR (CDCl$_3$, 62 MHz) δ 136.9, 136.3, 98.8, 84.0, 24.8; GC/MS (m/z): 330 (M$^+$), 315, 244 (100%), 230 (100%), 161, 117, 104. **3h**: clear yellow oil, Kugelrohr distilled ^{1}H NMR (CDCl$_3$, 250 MHz): δ 7.59 (1H, d, $J=8.0$ Hz), 7.31–7.33 (2H, m), 2.50 (3H, s), 1.32 (12H, s); ^{13}C NMR (CDCl$_3$, 62 MHz): δ 147.0, 137.3, 132.6, 127.8, 125.5, 83.6, 24.8, 21.9; GC/MS (m/z): 255 (M$^+$, 100%), 239, 210, 196, 182, 168, 155.