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Boron Compounds

Synthesis of Boron-Substituted Diaryliodonium Salts and Selective Transformation into Functionalized Aryl Boronates[**]

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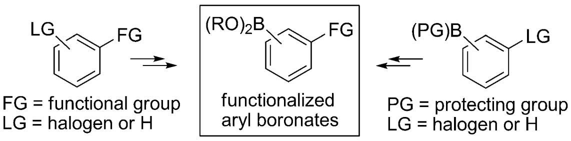
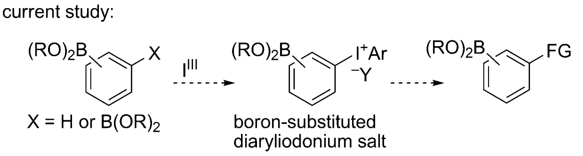
Functionalized aryl boronates are highly important building blocks for the construction of complex and valuable molecules, such as natural products, pharmaceuticals, and optoelectric materials.[1] For the synthesis of these compounds, the boronate group has usually been introduced into a prefunctionalized arene during the last step of the synthesis, traditionally by a two-step transformation involving metalation or recently by catalytic borylation [Eq. (1), left].[2] In contrast, another possible approach, the postfunctionalization of aryl boronates, has been rarely investigated [Eq. (1), right] owing to the sensitivity of boronate groups to common organic reagents. However, this strategy would enable rapid access to complex aryl boronates because their molecular diversity and complexity could be readily increased by coupling with a range of partners. For example, a recent advancement in the boron-protection strategy with remarkable advantages was the concise synthesis of oligoarenes by iterative Suzuki–Miyaura coupling and deprotection processes.[3] However, the protective functionalization of a conventional aryl boronate for later straightforward deprotection and further transformations is still limited.[4]



(1)

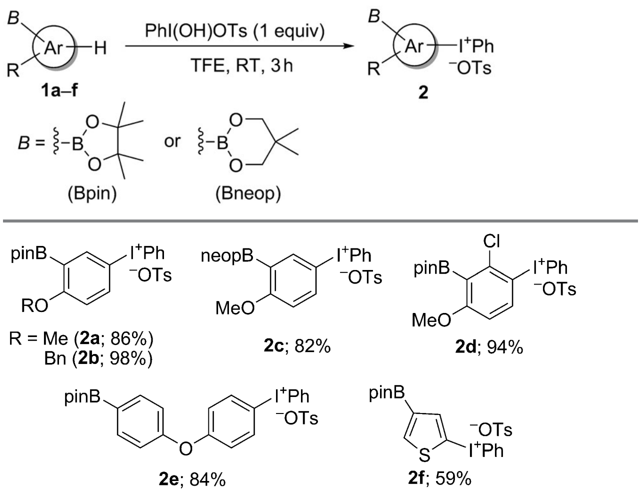
To develop a new precursor that would permit the postfunctionalization of aryl boronates, we focused on novel boron-substituted[5] diaryliodonium salts [Eq. (2)]. These unique hypervalent iodine(III) species were expected to be efficient synthetic modules for the preparation of functionalized aryl boronates owing to their accessibility from various arenes, their stability, and the ability to convert the iodonium moiety into a wide range of functional groups by catalyst-free aromatic nucleophilic substitution (S_NAr) or metal-catalyzed coupling.[6]



(2)

We previously reported the direct and efficient synthesis of diaryliodonium salts from electron-rich aromatic substrates with iodine(III) reagents, such as $PhI(OCOCF_3)_2$ (PIFA) or PhI(OH)OTs, in high-polarity and low-nucleophilicity fluoroalcohol solvents, CF_3CH_2OH (TFE) or $(CF_3)_2CHOH$ (HFIP).[7] We attempted to apply this method to boron-substituted aromatic substrates containing reactive C–H bonds, such as aryl boronates **1a–f** (Table 1). The selective C–H transformation of the aryl boronate pinacol esters **1a**,**b** and neopentylglycol ester **1c** successfully proceeded at the *para* position to the oxygen atom, and the boron-substituted salts **2a–c** were obtained in excellent yields without the loss of the boronate group.[8] Substrate **1d** was converted into the salt **2d** with an additional chlorine functionality. Salt **2e** was obtained as the sole product from substrate **1e**, in which the

Table 1: Direct synthesis of boron-substituted iodonium salts.[a]



[a] The yield based on substrate **1** is reported in each case for the pure product. Bn = benzyl, Ts = *p*-tosyl.

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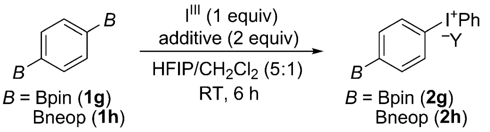
boronate group, like the C–H bond cleaved in the reaction, was located in a *para* position to the activating oxygen atom. Thiophene **1f** was also transformed into the desired salt **2f**; the reaction proceeded at the α position of the thiophene ring.[9] This C–H transformation was quite straightforward, and the boron-substituted salts obtained were highly stable.

We considered a partial boron–iodine(III) exchange[10] of aryl diboronates with iodine(III) reagents as an efficient alternative route to boron-substituted iodonium salts. Such an approach would expand the range of possible substrates and enable the control of regioselectivity. However, the aryl diboronate **1g** was unexpectedly inert to PhI(OH)OTs. The reaction did not proceed in various ordinary solvents (CH_2Cl_2, CH_3CN, and MeOH)[11] or even in HFIP (Table 2, entry 1). Upon further investigation, we found that the addition of acetic acid to HFIP led to the production of **2g** ($Y^- = TsO^-$) as the sole product (Table 2, entry 2). Overreaction leading to the bisiodonium salt should be suppressed by the strong deactivation effect of the introduced electron-withdrawing iodonium moiety. The much stronger acids CF_3CO_2H and TsOH were less effective than acetic acid (Table 2, entries 3 and 4). When TFE was used instead of HFIP, the yield decreased (Table 2, entry 5). The reaction did not proceed in acetic acid as the solvent, although acetic acid was not only an efficient activator in HFIP, but is also the classically used solvent to promote the formation of iodonium salts (Table 2, entry 6). This result indicated that both acetic acid and HFIP play a crucial role in the reaction. The use of PIFA gave a superior result to that observed with PhI(OH)OTs (Table 2, entry 7). The selection of the boronate was also important: the use of the less bulky neopentylglycol ester **1h** significantly improved the yield (Table 2, entries 8 and 9).

Table 2: Synthesis of boron-substituted salts **2g** and **2h** from aryl diboronates **1g** and **1h**.

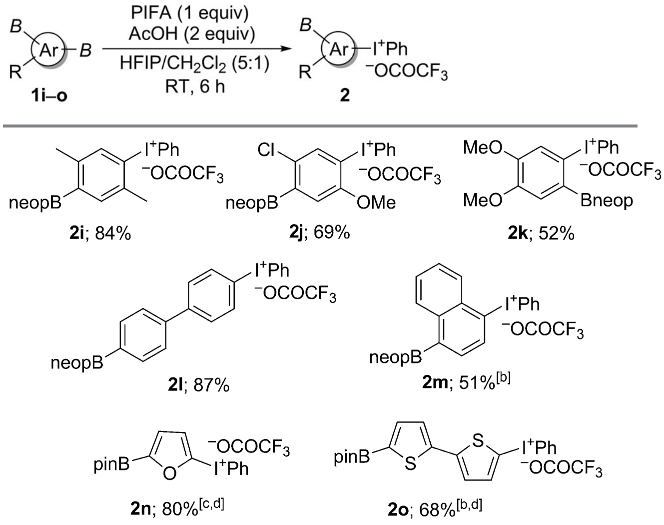


Entry	1	I^{III} reagent	Additive	Product	Yield [%][a]
1	**1g**	PhI(OH)OTs	none	ND	
2	**1g**	PhI(OH)OTs	AcOH	**2g** (Y = OTs)	52
3	**1g**	PhI(OH)OTs	CF_3CO_2H	**2g** (Y = OTs)	44
4	**1g**	PhI(OH)OTs	TsOH	**2g** (Y = OTs)	11
5[b]	**1g**	PhI(OH)OTs	AcOH	**2g** (Y = OTs)	13
6[c]	**1g**	PhI(OH)OTs	none	NR[d]	
7	**1g**	PIFA	AcOH	**2g** (Y = $OCOCF_3$)	62
8	**1h**	PhI(OH)OTs	AcOH	**2h** (Y = OTs)	77
9	**1h**	PIFA	AcOH	**2h** (Y = $OCOCF_3$)	89

[a] Yield of the pure product with respect to substrate **1**. [b] TFE was used instead of HFIP. [c] AcOH was used as the solvent. [d] A large amount of PhI(OH)OTs (80%) was recovered. ND = not determined, NR = no reaction.

The optimized conditions were subsequently applied to other substrates (Table 3). Methyl-substituted **1i** was converted into the sterically hindered salt **2i** in excellent yield. The salt **2j** with methoxy and chlorine substituents was obtained from the diboronate **1j** with complete regioselectivity.[12] The *ortho*-boronated salt **2k** was obtained from a dimethoxy-substituted diboronate **1k**. A symmetrical biphenyl substrate **1l** was transformed into the monoiodonium salt **2l** without any overreaction. Salts with other aromatic backbones, such as naphthalene (compound **2m**) or heteroaromatic structures (compounds **2n** and **2o**), were also obtained in good yields.

Table 3: Generality of iodonium salt formation from (hetero)aryl diboronates.[a]

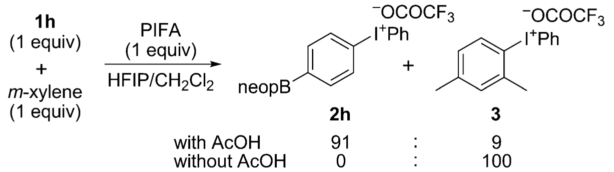


2i; 84%
2j; 69%
2k; 52%
2l; 87%
2m; 51%[b]
2n; 80%[c,d]
2o; 68%[b,d]

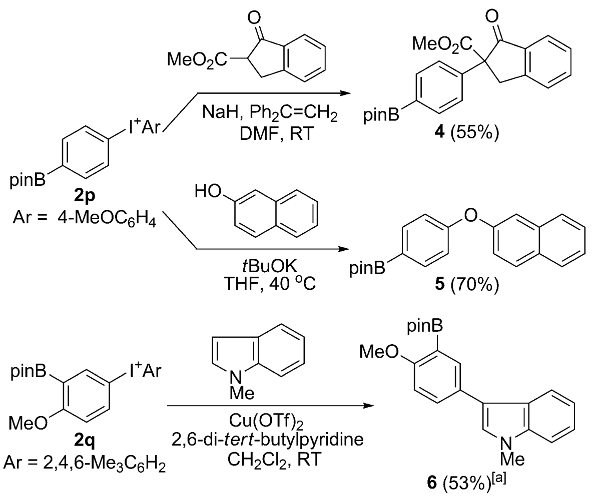
[a] The yield based on substrate **1** is reported in each case for the pure product. [b] TFE was used instead of HFIP. [c] A larger amount of substrate **1n** was used (1.2 equiv with respect to PIFA). [d] Pinacol esters were used instead of neopentylglycol esters, because the neopentylglycol esters were difficult to synthesize.

Although the effect of acetic acid is still unclear, we propose that the acid activates diboronates **1** by coordination to the boron atom. This coordination counteracts the electron-withdrawing resonance effect of the boronate groups.[4b,c] A competition experiment with a 1:1 mixture of **1h** and *m*-xylene provided support for this hypothesis (Scheme 1). Under the optimized conditions with acetic acid, the reaction gave the salt **2h** as the major product, along with a small amount of the *m*-xylyliodonium salt **3**. In contrast, the reaction in the absence of acetic acid gave **3** as the sole product. Therefore, the boronate **1h** must be specifically activated by the acid.

To demonstrate the utility of the boron-substituted salts as precursors to functionalized boronates, we examined their reactivity with various reaction partners (Scheme 2). We tested synthetically valuable C–C bond formation in an S_NAr



Scheme 1. Competitive iodonium-salt formation with substrates **1h** and *m*-xylene.



Scheme 2. Transformation of boron-substituted iodonium salts. [a] The product included a small amount of the compound resulting from arylation at the 2-position of the indole. Tf = trifluoromethanesulfonyl.

reaction of the salt **2g** with a 1,3-dicarbonyl compound and obtained the desired boron-functionalized product **4** as the major product (32%). Thus, the reaction was confirmed to proceed without any loss of the boronate moiety, but the yield was low owing to the formation of an undesired phenylated product. In unsymmetrical iodonium salts, S_NAr reactions are known to occur preferentially at the more electron deficient ring of the two aromatic rings bound to an iodine atom.[13] Therefore, we synthesized the salt **2p** with an electron-rich 4-methoxyphenyl dummy aromatic ring from **1g**[14] and used it in the α arylation. With **2p**, the selectivity was completely controlled, and the yield of **4** was improved to a satisfactory level. Similarly, the coupling of **2p** with 2-naphthol as an oxygen nucleophile proceeded to give the diaryl ether **5** in good yield.[15] Furthermore, a copper-catalyzed C–H coupling with *N*-methylindole led to the biaryl compound **6** without the loss of the boronate group even in the presence of a metal catalyst.[16] As metal catalysts are reported to transfer the less sterically hindered ring of unsymmetrical iodonium salts, we facilitated the selective transfer of the boron-substituted ring by employing the highly congested mesityl-substituted substrate **2q**, which was prepared by the C–H transformation of **1a** with the corresponding iodine reagent in 80% yield.[14]

In conclusion, we have developed the first efficient synthesis of boron-substituted diaryliodonium salts. The iodonium moiety of the synthesized salts underwent various catalyst-free and metal-catalyzed organic reactions, and the retained boronate group is suitable for further transformation. Therefore, this series of iodonium salts is expected to be remarkably useful for the construction of complex functionalized compounds.

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Keywords: aromatic nucleophilic substitution · boron · cross-coupling · hypervalent iodine · iodonium salts

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[12] For the regioselective transformation of unsymmetrical aryl diboronates, a strong donating group, such as a methoxy group, was necessary to direct the reaction at the *ortho* or *para* position.

Other examples concerning the regioselectivity of the reaction will be reported at a later date.

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