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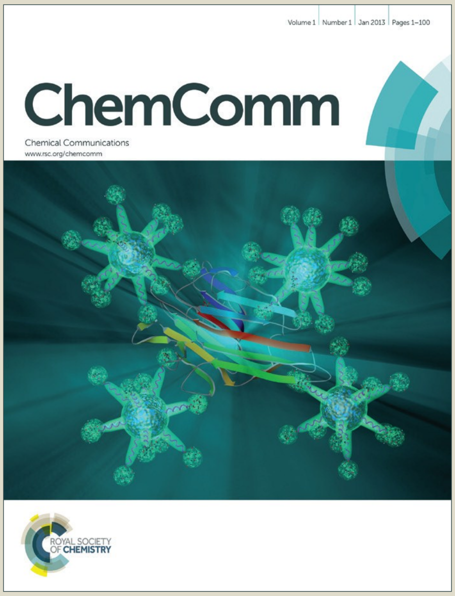

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A mild carbon-boron bond formation from diaryliodonium salts

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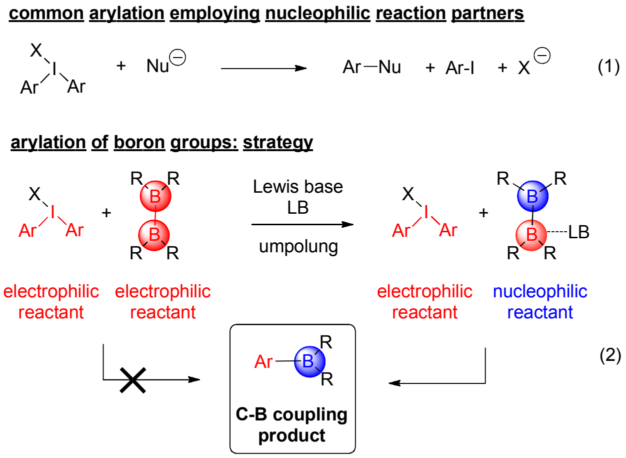
The direct metal-free borylation of diaryliodonium salts with diboron reagents is now demonstrated to be a feasible process toward aryl boronic esters formation without any additive or catalysts, and it can be extended to a two-step C-C coupling of both aryl groups of the initial diaryliodonium reagent.

Due to their ready availability and high stability, diaryliodonium salts **1** constitute an attractive class of compounds that have been recognized as particularly versatile aryl transfer reagents.[1] Consequently, they have been involved in a series of arylation reactions, which have been mostly aided by the presence of transition metal catalysts. While initially C-C bond forming reactions had been explored to a larger extent, carbonheteroatom bond forming events based on diaryliodonium salts have been investigated in greater detail in recent years (Scheme 1, eq. 1).[2-10] Among all these accomplishments, carbon-boron bond formation toward aryl boronic acid derivatives is notably absent.

Arylboronic acids and esters are key components for modern cross-coupling reactions and advanced synthetic transformations.[11] Their high versatility has made C-C coupling events based on them one of the most versatile themes in the field,[12] which was recognized by the Nobel prize for Suzuki in 2010.[13] Common approaches to this type of reagents employ the original Miyaura-type borylation reaction between aryl halides and bis(pinacolato)diboron (pinB–Bpin, **2a**) in the presence of catalytic amounts of palladium complexes. The key intermediate [LPd(Ar)(OAc)] undergoes a transmetallation process with **2a**.[14] Other transition metal complexes have catalyzed the aryl halide borylation[15] complementing the C-H activation of arenes by borane reagents.[16] We here report the unprecedented direct formation of aryl boronic esters, in particular aryl pinacolboranes, through an effective coupling between diaryliodonium salts and bis(pinacolato)diboron **2a** under mild conditions and without any requirement for a metal promoter. In principal, the synthetic approach to such a type of direct C-B bond formation appears unconventional at first sight, as it involves the combination of two reactants that are of exceedingly electrophilic nature (Scheme 1, eq. 2).



Scheme 1. Conceptual approaches to carbon-heteroatom bond formation using diaryliodonium salts

To accomplish the targeted carbon-boron bond formation, we envisioned that presence of Lewis base could be employed for the activation of the diboron reactant. Such an interaction should be favorable as it provides an umpolung of the native electrophilic boron atom. The resulting nucleophilic character[17] at one of the boron centers then ensures for effective C-B bond formation with the electrophilic iodine(III) reagent. This approach is reminiscent of previous alkoxide base mediated reactions developed by some of us[18,19] and others.[20,21] A subsequent screening between various diphenyliodonium salts **1a-d** and bis(pinacolato)diboron (**2a**) was undertaken and for the acetate derivative **1d** confirmed the correctness of the initial hypothesis (Scheme 2). In agreement with previous experience,[18,19] methanol was identified as the best solvent.[22] For the reaction between acetate derivative **1d** and **2a**, the expected product **3a** was formed in high yield and isolated in

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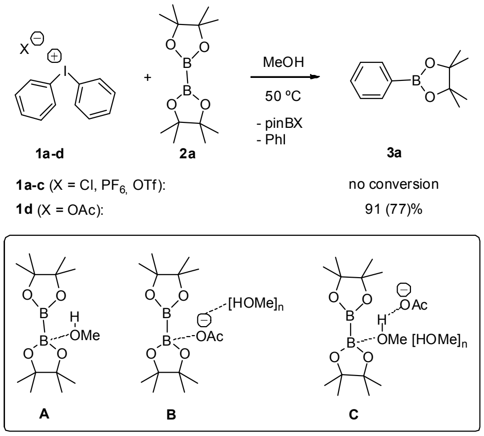
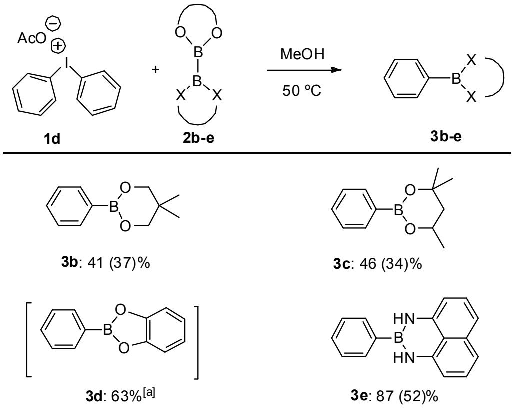
77%. This successful transformation leads to two important conclusions: First, methanol as solvent may play a crucial role in activating the diboron reagent through a state such as **A**. Secondly, the pronounced dependence of the reaction on the counterion of the diphenyliodonium reagent suggests a crucial participation of this anion as well. This may include a direct interaction between the solvated acetate with the diboron reagent (state **B**) or a participation of its negative charge throughout the hydrogen-bonding network of the protic solvent (state **C**). For the latter scenario, the activation is reminiscent of the more common activation with methoxide base. Obviously, the anions from compounds **1a-c** do not display sufficient basicity to induce activation of the diboron reagent. The importance of the polar protic solvent is evident from a comparison of a reaction in polar unprotic THF, which led to a significantly lower yield of 39% of **3a**.[22]

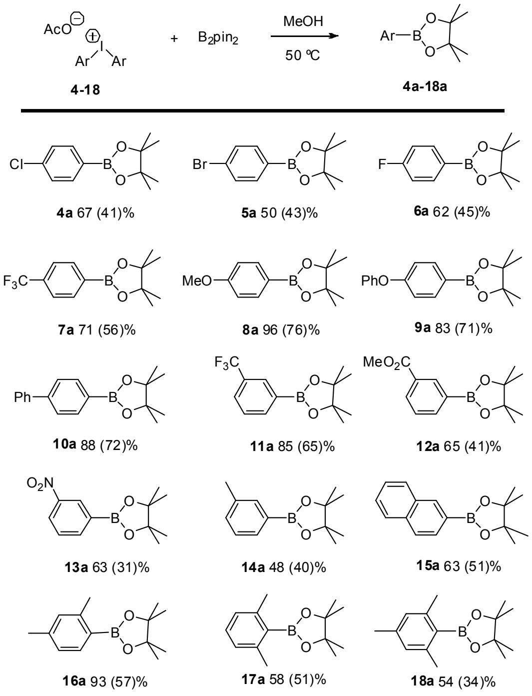


Scheme 2. Borylation of diphenyliodonium salts: optimization with B_2pin_2. [a] Reaction conditions: $(C_6H_5)_2I^+X^-$ (0.2 mmol), B_2pin_2 (0.3 mmol), 50 ºC, 1.25 mL solvent, 24 h; average yield from two independent runs calculated by GC spectroscopy with mesitylene as internal standard; the value in parenthesis refers to an isolated yield based on $(C_6H_5)_2IOAc$

With the conceptual verification of the C-B bond formation in hand, the reaction was further extended to various diboron compounds for aryl-boron coupling (Scheme 3). For example, products **3b** and **3c** are conveniently generated from treatment between diphenyliodonium acetate and bis(neopentylglycolato) diboron (**2b**) and bis(hexyleneglycolato)diboron (**2c**), respectively, as in the case of the parent transformation with bis(pinacolato)diboron (**2a**). The same protocol was also applicable for the related bis(catecholato)diboron (**2d**) to furnish the coupling product **3d**. Due to the notorious instability of the catecholboryl derivative, the boronic ester was transformed into phenol upon oxidative work-up.[22a] Finally, an excellent result was obtained using the mixed diboron reagent Bpin-Bdan (**2e**) (dan = 1,8-diaminonaphthalene),[23] which underwent selective activation at the more electrophilic Bpin center.[19] This promotes the transfer of the Bdan entity to selectively generate C-B coupling product **3e** in 87% conversion and 52% isolated yield. There is only one precedence on borylation of aryl halides with Bpin-Bdan (**2e**), which required the presence of a palladium- XPhos catalyst under basic conditions.[24]



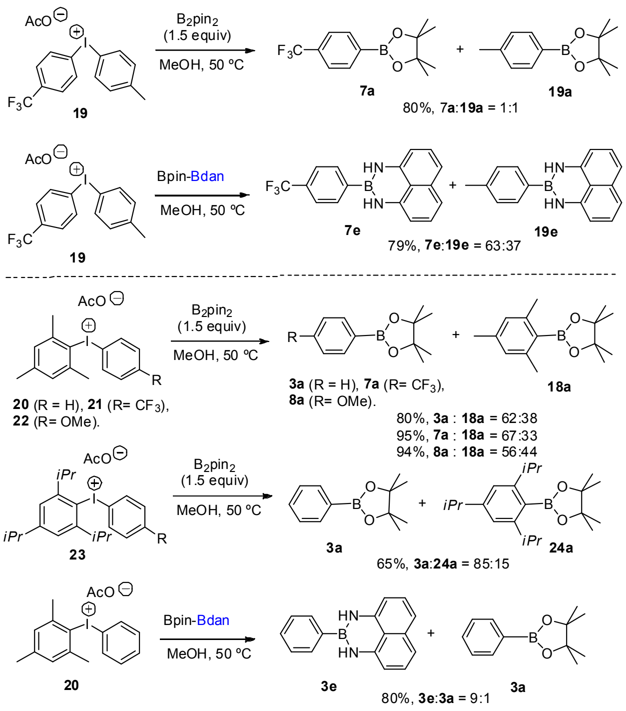
Scheme 3. Borylation of diphenyliodonium salts: influence of the diboron reagent X = O, NH. Reaction conditions: $(C_6H_5)_2IOAc$ (0.2 mmol), diboron reagent (0.3 mmol), 50 ºC, 1.25 mL methanol, 24 h; yield calculated by GC spectroscopy with mesitylene as internal standard as an average of two reactions; isolated yields given in brackets calculated from $(C_6H_5)_2IOAc$; [a] Isolated yield of the corresponding alcohol after oxidative work up.[22]



Scheme 4. Borylation of diphenyliodonium salts: reaction scope with B_2pin_2. Reaction conditions: Ar_2IOAc (0.2 mmol), B_2pin_2 (0.3 mmol), 50 ºC, 1.25 mL methanol, 24 h; average yield from two independent runs calculated by GC spectroscopy with mesitylene as internal standard; values in brackets refer to isolated yields based on Ar_2IOAc.

The scope of the reaction has been evaluated for a number of symmetric diaryliodonium salts, which includes *ortho*-, *meta* and *para*-substitution pattern as well as higher substituted aromatic entities (Scheme 4). As to a general trend, electron releasing groups on the 4-substituted aryls of Ar_2IOAc contribute to a higher percentage of borylated product formation (**8a**-**10a**) in comparison with the electron-withdrawing functional groups (products **4a**-**7a**). On the contrary, 3-substituted aryl groups in Ar_2IOAc bearing electron-withdrawing substituents favor the borylation with the activated B_2pin_2 (products **11a**-**13a**), while the corresponding diaryliodonoum salt with 3-tolyl groups is transformed into coupling product **14a** in moderate yield. As regularly encountered in arylboronates, yields can diminish during the purification step, being comparable to the most recent achievement in Zn catalyzed borylation of aryl halides.[25]

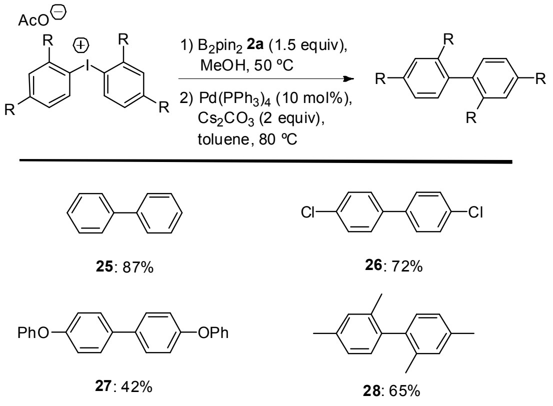
Interestingly, the highly substituted aryl(pinacolboronate) esters **15a**-**18a** are quantitatively formed demonstrating that the present method provides a great tolerance to formation of sterically encumbered aryl boronates.



Scheme 5. Borylation of non-symmetric diphenyliodonium salts.

With the aim to explore a selective mixed borylation we conducted two parallel strategies: i) the reactivity of the novel non-symmetric diaryliodonium salts **19**-**23** with B_2pin_2 and ii) the reactivity of electronically and sterically mixed diaryliodonium salts **19** and **20** with the mixed diboron reagent Bpin-Bdan (**2e**). Scheme 5 demonstrates that sterically encumbered aryl boronates exert the higher degree of selective borylation when reacted with both symmetrical and mixed diboron compounds. Therefore, the diaryliodonium salt **19** reacts with **2a** to give **7a** and **19a** in a 1:1-ratio, which is comparable to the reaction with **2e** providing **7e** and **19e** in a ratio of 63:37. However, the higher the steric hindrance on one of the aryl groups, the more pronounced chemoselectivity favoring **3a** is observed, regardless the electronic nature of the substituents on the neighboring aryl group. Interestingly, the reaction of **23** with **2e** is conducted towards the formation of **3e** and **3a** in 9:1-ratio, showing that steric factors are predominant.

Finally, the successful development of the C-B bond forming reaction was extended to an *in situ* cross coupling reaction. Since the borylation reaction of the diaryliodonium salts **1** generates an equimolar amount of free aryl iodides, submission of the crude reaction mixture to Suzuki-Miyaura cross-coupling should result in an overall diaryl synthesis. Such a process would make economic use of both of the aryl groups of the diaryliodonium precursor. Transformations of this kind are rare. Within this context, Beletskaya reported an exhaustive Suzuki-Miyaura coupling between diaryliodonium salts and sodium tetraphenylborate,[26] Nachtsheim developed two sequential C-N bond forming events of cyclic diaryliodonium salts with anilines to yield *N*-arylated carbazoles[27] and Greaney recently reported on the use of both aryl groups of diaryliodonium salts in 1,3- difunctionalization of indoles.[28] Indeed, the anticipated reaction sequence comprising the C-B bond formation as a transient path to C-C coupling could be realized. After the borylation reaction, the solvent was changed from MeOH to toluene followed by addition of the palladium catalyst $Pd(PPh_3)_4$ and carbonate base (Scheme 6). By this, the mentioned product mixtures from C-B bond formation with symmetric diaryliodonium salts engage in the desired direct Suzuki-Miyaura coupling to provide the corresponding diaryl compounds **25-28** as the only C-C coupling products.



Scheme 6. One pot cross coupling from diaryliodonium salts via B_2pin_2. Reaction conditions for activation: Ar_1Ar_2IOAc (0.2 mmol), B_2pin_2 (0.3 mmol), 50 ºC, 1.25 mL MeOH, 24 h, reaction conditions for cross-coupling: $Pd(PPh_3)_4$ (10 mol%), Cs_2CO_3 (2 eq), 80 ºC, 2 mL toluene, 16 h. Yields refer to isolated yields based on Ar_1Ar_2IOAc.

Conclusions

In summary, we have developed a new protocol for the metal-free formation of aryl-boron bonds. It employs readily available diaryliodonium acetates and commercially available diboron reagents, which in methanol solution engage in direct aryl-boron bond formation through a formal umpolung of the electrophilic boron center. The reaction is selective, proceeds under mild conditions and does not require any metal reagent or other promoter. It opens a new methodological venue for the use of hypervalent diaryliodonium reagents in carbon-heteroatom bond formation. By simply adding a palladium source, the reaction can be directly expanded to biaryl synthesis through the cross coupling of symmetric diaryliodonium salts.

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