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Direct Conversion of Pinacol Arylboronic Esters to Aryl Triolborates

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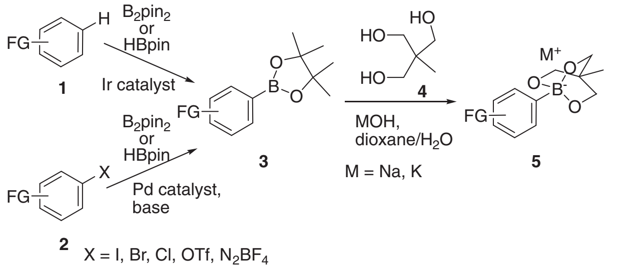
Conversion of pinacol arylboronic esters **3** to aryl triolborates **5** via transesterification with 1,1,1-tris(hydroxymethyl)ethane (**4**) was established with the advantages of tolerance to various functional groups. Transesterification was carried out at 30–60 °C in dioxane in the presence of MOH (M = Na and K) and H_2O. High yields were achieved for stable aryl triolborates **5**.

Over the past three decades, it has become increasingly clear that organoboron compounds are valuable reagents capable of undergoing many catalytic C–C bond formations in organic synthesis.[1–4] Boronic acids are convenient reagents that are generally thermally stable and are inert to water and oxygen. The C–B bond of organoboronic acids is totally covalent and inert to ionic reaction, but nucleophilicity of organic groups on a boron atom is significantly enhanced by quaternerization by an anionic ligand. Thus, tetracoordinated ate-complexes are key species that have been successfully used for addition and coupling reactions of organoboron compounds, including metal-catalyzed reactions of organoboronic acids. Recently, air- and water-stable trifluoroborates are typical ate-complexes that are advantageous over boronic acids in preparation and handling of pure and water-stable crystalline materials.[5] However, their metal-catalyzed bond-forming reactions are very slow in the absence of bases because of the low nucleophilicity of organic groups due to the high electronegativity of fluorine. We have reported novel cyclic triolborates that have exceptionally high levels of stability in air and water and higher solubility in organic solvents than that of potassium trifluoroborates.[6–9] High performance of lithium or potassium triolborates for transmetalation has been demonstrated in palladium- and copper-catalyzed C–C[7,8] and C–N[9] bond-forming reactions and rhodium-catalyzed addition reactions.[10–12]

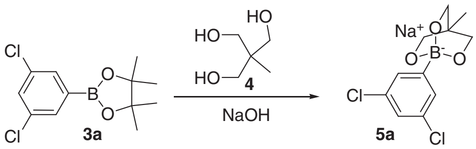
We have developed methods for the synthesis of aryl triolborates.[6] The azeotropic removal of water upon treatment of organoboronic acids with the 1,1,1-tris(hydroxymethyl)ethane (**4**) gave boronic esters, which were readily converted into triolborates by treatment with KOH. The corresponding lithium salts were synthesized by the alkylation of $B(OMe)_3$ or $B(O\textit{i}\text{-}Pr)_3$ with RLi, followed by the removal of MeOH or *i*-PrOH though ether exchange with triol **4**. Recently, synthesis of pinacol boronic esters has been achieved by palladium-,[13–15] nickel-,[16] and copper-catalyzed[17] coupling reactions between aryl halides or triflates **2** and pinacolborane[13] or diborons such as B_2pin_2 (pin: pinacol).[14,15] More recently, direct borylation of C–H bonds by HBpin or B_2pin_2 is a convenient, economical, and environmentally benign process for the synthesis of aromatic boron compounds.[18]

Herein, we report a convenient method to directly convert pinacol boronic esters **3** to aryl triolborates **5** (Scheme 1). Arylboronic esters have been converted to arylboronic acids by oxidative cleavage or displacement of pinacol by diethanolamine or KHF_2.[19,20] Matteson and co-workers reported the hydrolysis of 1,2-dicyclohexyl ethanediol (DIECHED) boronic ester to boronic acids with sodium hydroxide and tris(hydroxymethyl)methane derivative in a two-phase system.[21] We examined transesterification of pinacol boronic ester **3a** to sodium triolborate **5a**. There is a strong accelerating effect of water (Entries 1–3, Table 1). The reaction required the presence of 3 equivalents of water and proceeded smoothly in dioxane but was very slow in other solvents such as THF and DME (Entries 5, 7, and 8). Finally, the reaction took place smoothly at 30 °C in the presence of 1.0 equivalent of NaOH with 84% yield (Entry 5).



Scheme 1.

Table 1. Reaction conditions[a]

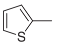
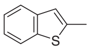
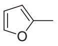
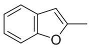
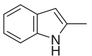
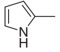
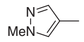


Entry	Solvent	NaOH/equiv	Temp/°C	H_2O/equiv	Yield/%[b]
1	dioxane	0.9	60	3	72
2	dioxane	0.9	60	1	27
3	dioxane	0.9	60	none	trace
4	dioxane	1.0	60	3	76
5	**dioxane**	**1.0**	**30**	**3**	**84**
6	dioxane	1.0	90	3	trace
7	THF	1.0	30	3	48
8	DME	1.0	30	3	46

[a]Reaction conditions: 2-(3,5-dichlorophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**3a**: 1.0 mmol), triol, and NaOH in solvent (5 mL) was stirred for 16 h. [b]Yields of the isolated product.

We tested the generality of this conversion of pinacol boronic esters to sodium aryl triolborates (Table 2). High yields were easily achieved in most aromatic boronic esters possessing halogens and ester substituents at para and meta carbons (Entries

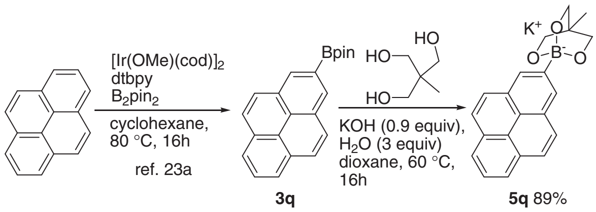
Table 2. Conversion to aryl triolborates[a]

Entry	**3** (Ar =)		Yield/%[b]
1	3,5-$Cl_2C_6H_3$	**5a**	84
2	3,4-$Cl_2C_6H_3$	**5b**	96
3	3-Cl-5-$(MeO_2C)C_6H_3$	**5c**	97
4	3-Br-5-$(CF_3)C_6H_3$	**5d**	74
5[c]		**5e**	99
6		**5f**	92
7[c]		**5g**	67
8		**5h**	85
9		**5i**	89
10[c]		**5j**	65
11[c]		**5k**	75
12	3-$(CF_3)C_6H_4$	**5l**	79
13	4-$(CF_3)C_6H_4$	**5m**	84
14	3-$(CH_3O)C_6H_4$	**5n**	73
15	4-$(CH_3O)C_6H_4$	**5o**	81
16	C_6H_5	**5p**	83

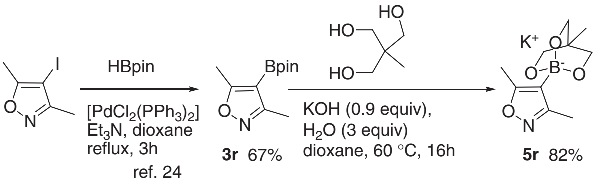
[a]All reactions were carried out at 30 °C for 16 h in dioxane in the presence of NaOH (1.0 equiv) and H_2O (3 equiv). [b]Isolated yield by chromatography. [c]At 60 °C.

1–4). Five-membered heteroarenes[22] such as thiophene, furan, pyrrole, and pyrazole provided triolborates **5** in high yields (Entries 5–11). Yields exceeding 70% were achieved when using pinacol esters having either electron-donating or electron-withdrawing substituents at the para and meta positions (Entries 12–16).

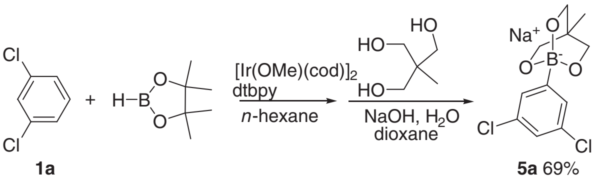
The selective Ir-catalyzed borylation of pyrene with B_2pin_2 produced 2-pyrenylboronate **3q**.[23] 2-Pyrenylboronate **3q** was converted to potassium triolborate **5q** at 60 °C in the presence of 0.9 equivalent of KOH with 89% yield (eq 1). As reported for arene C–H borylation, coupling at C–H bonds located ortho to substituents was very slow due to steric hindrance. 3,5-Dimethyl-4-isoxazolylboronic ester **3r**, which was synthesized by palladium-catalyzed cross-coupling reaction between 4-iodo-3,5-dimethylisoxazole and pinacolborane,[24] was efficiently converted to triolborate (eq 2). A direct method to convert 1,3-dichlorobenzene (**1a**) to 3,5-dichlorophenyl triolborates **5a** is shown in eq 3. The formation of **5a** from **1a** was achieved with 69% yield.



(1)

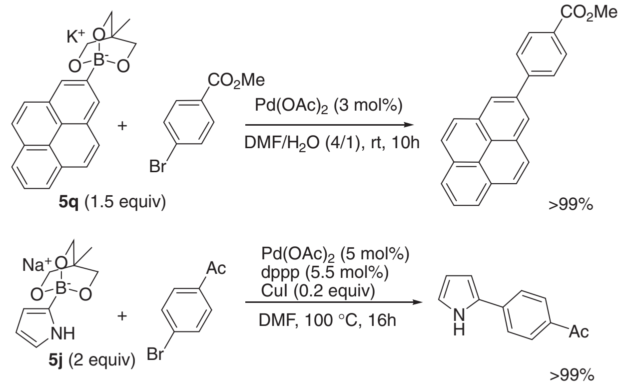


(2)



(3)

The cross-coupling reactions of arylboronic esters has often suffered from long reaction time[23b] or low yields due to competitive hydrolytic B–C bond cleavage.[25] Triolborates reacted quantitatively with bromoarenes in DMF (Scheme 2). The cross-coupling reaction of potassium 2-pyrenyl triolborate (**5q**) with methyl 4-bromobenzoate was completed at room temperature in the presence of $Pd(OAc)_2$ in aqueous DMF.[6] The presence of CuI led to an increase in the coupling yield with sodium 2-pyrrolyl triolborate (**5j**).[7]



Scheme 2. Cross-coupling reactions of triolborates **5**.

In conclusion, we have described a simple and practical synthetic method to convert pinacol boronic esters to triolborates.[26] As such complexes are key species in various metal-catalyzed C–C bond-forming reactions, studies toward their application to other addition and coupling reactions are in progress.

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