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NICKEL-CATALYZED BOLYLATION OF ARYL HALIDES WITH 4,4,6-TRIMETHYL-1,3,2-DIOXABORINANE

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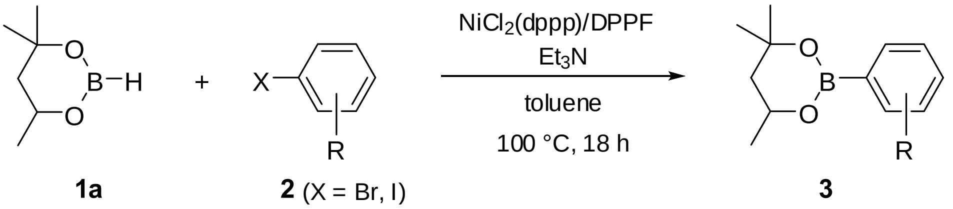
Abstract – The nickel-catalyzed borylation of aryl iodides and bromides with 4,4,6-trimethyl-1,3,2-dioxaborinane was achieved. The mild reaction conditions employed allowed for the inclusion of common functional groups in aryl halides to be tolerated. A DFT study on the catalytic cycle shows that C–B bond formation occurs through σ-bond metathesis between dialkoxyborane and arylnickel(II) halide intermediates.

Arylboronic acids and their esters are an important class of organometallics, which can be widely used as versatile building blocks in modern organic synthesis particularly with reactions involving carbon–carbon bond formation through the Suzuki–Miyaura cross-coupling.[1] As the versatility of arylboronates has made them attractive targets for synthesis, the development of transition metal-catalyzed aryl C–B bond-forming reactions has attracted considerable interest.[2] Above all, the borylation of aryl electrophiles with pinacolborane have proved to be an atom-economical and powerful method for preparation of functionalized arylboronates.[3] We have demonstrated that 4,4,6-trimethyl-1,3,2-dioxaborinane (**1a**), which is more cost-effective than pinacolborane, is an alternative boron source for the catalytic borylation of aryl electrophiles. The palladium complex coordinated with bis(2-di-*tert*-butylphosphinophenyl)ether can catalyze the reaction of aryl iodides with **1a** to afford the corresponding arylboronates in high yields.[4] However, this work was limited to aryl iodides and used the poorly available and air-sensitive phosphine ligand. After our investigation, the Chavant group has achieved the borylation of aryl iodides and bromides with **1a** by using the palladium catalyst coordinated with PPh_3 or Buchwald biaryl phosphine ligands, but these conditions resulted in somewhat low yields when aryl halides possesses electron-withdrawing groups.[5] We have also achieved the coupling of aryl arenesulfonates with **1a** by using Bu_4NI

Dedicated to Professor Dr Ei-ichi Negishi on the occasion of his 77th birthday.

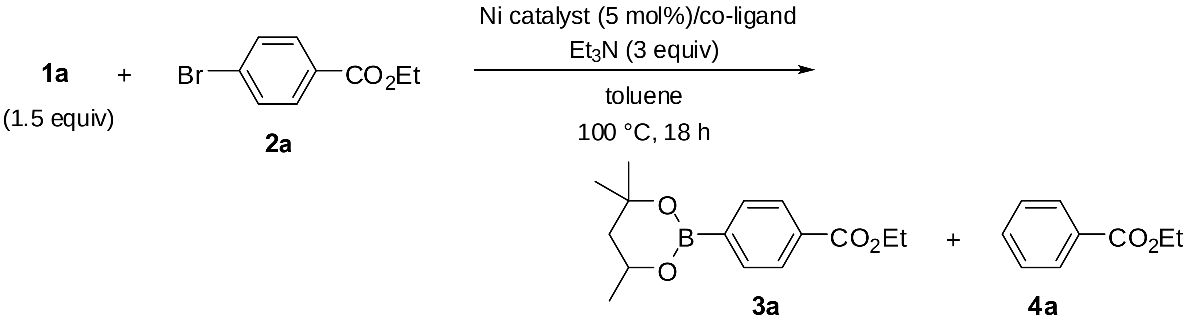
and a catalytic amount of Pd(dba)$_2$/1,1'-bis(di-*tert*-butylphosphino)ferrocene.[6] Whereas the scope of the aryl electrophiles in the palladium-catalyzed borylation with **1a** has been improved, the reaction of electron-deficient aryl bromides still had some drawbacks. In this paper, we wish to report a practical protocol for the nickel-catalyzed borylation of aryl iodides and bromides **2** using **1a** (Scheme 1). Recently, we have demonstrated that the borylation of electron-deficient aryl chlorides was achieved by the use of NiCl$_2$(dppp) catalyst with the aid of Bu$_4$NBr.[7]



Scheme 1. Borylation of Aryl Halides **2** with **1a**

As a test for the optimization of catalyst systems, ethyl 4-bromobenzoate (**2a**) was used as a substrate for the borylation using **1a**. The results are summarized in Table 1. The treatment of **2a** with **1a** (1.5 equiv) and Et$_3$N (3 equiv) with 5 mol% of NiCl$_2$(dppp) in toluene at 100 °C was found to lead to the corresponding arylboronate **3a** in a good yield (entry 1). However, the reaction suffered from small

Table 1. Screening of Co-Ligands for Borylation of **2a**

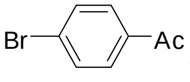
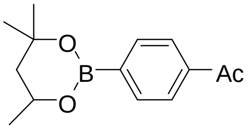
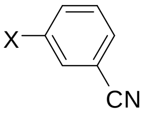
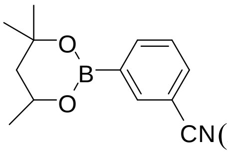
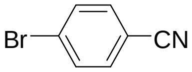
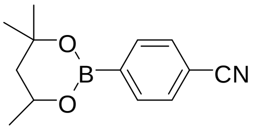
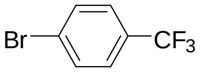
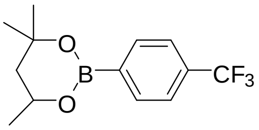
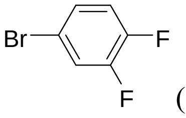
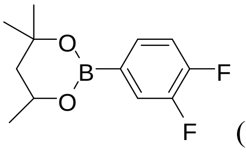
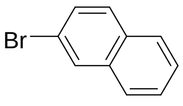
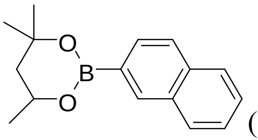
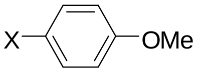
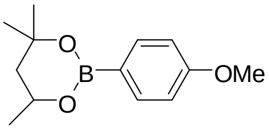
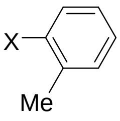
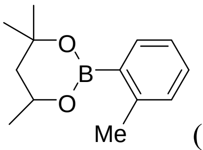


entry	catalyst	co-ligand	yield (%)[b] 3a	4a
1	NiCl$_2$(dppp)	none	78	7
2		PPh$_3$	96	4
3		DPPP	92	8
4		DPPF	100 (96)[c]	0
5	NiCl$_2$(dppf)	none	12	3
6		DPPP	6	0
7		DPPF	11	3

[a] Reaction conditions: **2a** (0.250 mmol), **1a** (0.375 mmol), Et$_3$N (0.75 mmol), catalyst (5 mol%), co-ligand (10 mol%), in toluene at 100 °C for 18 h. [b] GC yields are based on **2a**. [c] In parenthesis isolated yield.

amounts of dehalogenated arene byproducts **4a** by partially reduction of the C–Br bond. We were pleased to observe that the use of additional phosphine as a co-ligand improved the yield and selectivity (entries 2–4). Recently, Percec reported that the mixed-ligand systems provided highly active catalysts for the nickel-catalyzed borylation using in situ-prepared neopentylglycolborane.[8] As in the case of the reaction

Table 2. Borylation of Representative Aryl Halides **2** with **1a**^{a}

entry	aryl halide **2**	product **3**	yield (%)^b
1	 (**2b**)	 (**3b**)	96
2	 X = Br (**2c**)	 (**3c**)	80
3	X = I (**2d**)		99
4	 (**2e**)	 (**3e**)	73
5	 (**2f**)	 (**3f**)	86
6	 (**2g**)	 (**3g**)	88
7	 (**2h**)	 (**3h**)	98
8	 X = Br (**2i**)	 (**3i**)	14
9	X = I (**2j**)		92
10	 X = Br (**2k**)	 (**3k**)	26
11	X = I (**2l**)		98

[a] Reaction conditions: **2** (0.250 mmol), **1a** (0.375 mmol), Et_3N (0.75 mmol), $NiCl_2(dppp)$ (5 mol%), DPPF (10 mol%), in toluene at 100 °C for 18 h. [b] Isolated yields are based on **2**.

with neopentylglycolborane, DPPF above all other phosphines completely suppressed the formation of **4a** (entry 4). Additionally, $NiCl_2$(dppf)-based catalyst systems provided poor yields, indicating that the ligand exchange was limited and that the benefit of DPPF was achieved only as a co-ligand (entries 5–7).[8] Unfortunately, we still have no definitive explanation for the role of co-ligands.

With the optimized conditions in hand, we next investigated the substrate scope of the borylation of the aryl iodides and bromides **2** using **1a** (Table 2).[9] The presence of functional groups, such as not only ester (Table 1) but also ketone carbonyl (Table 2, entry 1) and cyano groups (entries 2 and 4), in the starting aryl bromides **2** (X = Br) did not interfere with the outcome of the borylation with **1a**. Unfortunately, an electron-donating (entry 8) or *ortho* substituent (entry 10) on the aromatic ring of **2** (X = Br) prevented the present reaction. In contrast to aryl bromides, the differences in the yields among iodide counterparts **2** (X = I) possessing electron-donating or -withdrawing groups were not particularly large (entries 3 and 9). Also, the yields of **3** did not depend on the steric requirement of aryl iodides (entry 11).

Our focus then turned to the mechanism of this nickel-catalyzed borylation. The proposed catalytic cycle was computationally addressed by density functional theory (DFT) calculations (Figure 1).[9] We have adopted the reaction of bromobenzene (**2m**) with 1,3,2-dioxaborolane (**1b**) as a model reaction, and the DPPP ligand was replaced by 1,2-diphosphinopropane (DHPP). Recently, Marder and Lin reported that the palladium-catalyzed borylation involves σ-bond metathesis between hydroboranes and a cationic $[L_2Pd(Ar)]^+$ species as the B–C bond-forming step.[10] Our supposition is that the present mechanism involves the oxidative addition of **2m** to Ni(0) **5** to form (η^2-dhpp)Ni(Ph)(Br) **6**;[11] however, our

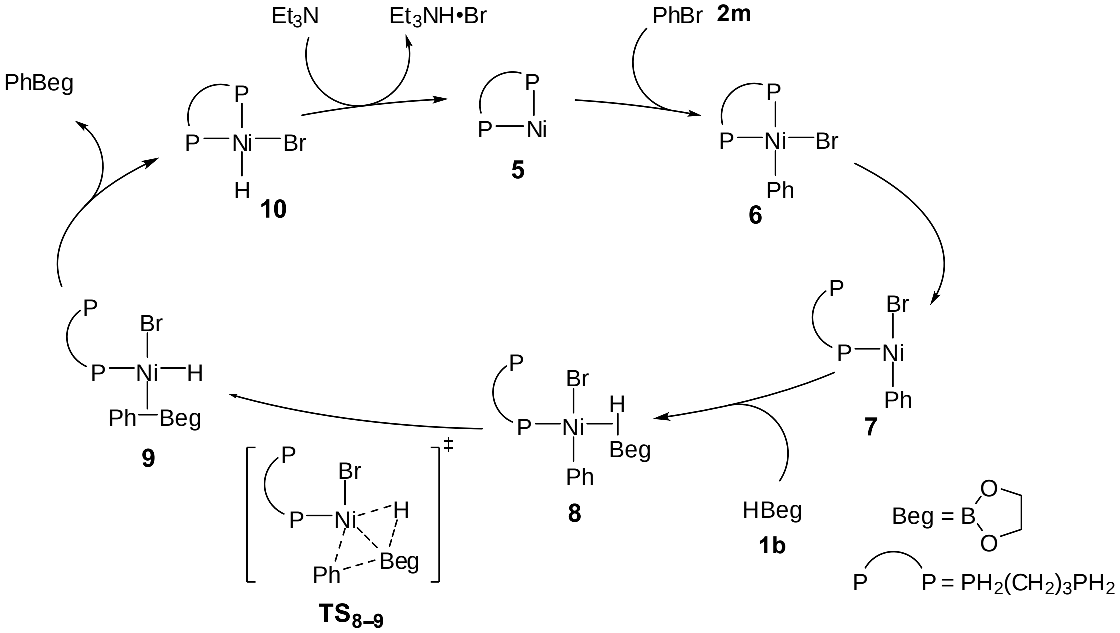


Figure 1. A Plausible Catalytic Cycle for Nickel-Catalyzed Borylation

calculations indicate that the barrier of the similar charge-separated pathway for the nickel-catalyzed borylation is significantly large even with inclusion of the solvation energies. Thus, **6** undergoes partial ligand dissociation to afford (η^1-dhpp)Ni(Ph)(Br) **7**. After the coordination of **1b** to **7**, the σ-complex-assisted metathesis (σ-CAM) with the Ni–Ph bond takes place through a transition state $\mathbf{TS_{8\text{–}9}}$, in which the boron atom is pointing toward the aryl ligand, to form the desired borylation product and a nickel(II) hydride **10**. The activation barrier of the σ-CAM is 15.6 kcal/mol, indicating that this neutral pathway is favored over the cationic one. Finally, deprotonation of **10** would regenerate the Ni(0) active species **5** with the aid of Et_3N.

In conclusion, the combination of $NiCl_2$(dppp) and DPPF was found to catalyze the borylation of aryl iodides and bromides using 4,4,6-trimethyl-1,3,2-dioxaborinane (**1**). Theoretical calculations suggest that the catalytic cycle involves the σ-bond metathesis between the Ni–C bond of neutral arylnickel(II) halide intermediate and the B–H bond of hydroborane. Further studies are currently underway to obtain detailed mechanistic insights.

ACKNOWLEDGEMENTS

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11. Treatment of Ni(Ar)(Br)(PPh_3)$_2$ (Ar = 4-EtO_2C-C_6H_4) with DPPP (1 equiv) and **1a** (20 equiv) was found to lead to the corresponding arylboronate **3a**.