# Zero-Valent Metals Accelerate the Neopentylglycolborylation of Aryl Halides Catalyzed by NiCl$_2$-Based Mixed-Ligand Systems

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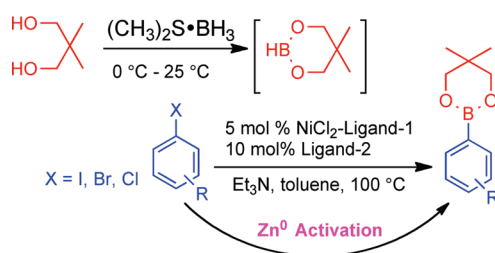
The highly active mixed-ligand catalytic system NiCl$_2$(dppp)/dppf combined with the reducing effect of zerovalent Zn and of other metals was used to demonstrate a method for the dramatic acceleration of the rate and for the enhancement of the yield of Ni-catalyzed neopentylglycolborylation of aryl halides. A diversity of electron-rich and electron-deficient aryl iodides, bromides, and chlorides were efficiently neopentylglycolborylated, typically in 1 h or less. This acceleration is particularly remarkable for the generally less reactive aryl bromides and chlorides and for all *ortho*-substituted aryl halides. By accelerating the rate of borylation and reducing its reaction time to complete conversion, pathways leading to protodeborylated or hydrodehalogenated side products have a reduced impact on the outcome of the overall reaction. Although Zn powder was the reducing agent of choice, compatibility of this technique with more readily recoverable Zn chips, as well as other metals such as Mn, Mg, Fe, Al, and Ca, has demonstrated the broad scope of this synthetic method.

Introduction

Boronic acids,[1] esters,[1] and trifluoroborate salts[2−4] are crucial intermediates for Suzuki−Miyaura coupling reactions[5] providing synthetic precursors for the medical[6] and material science[7,8] but can also serve as catalysts,[9] sensors,[10] or as therapeutics.[11] Not surprisingly, the development of efficient transition-metal-catalyzed techniques that completely obviate the need for highly

reactive organolithium or Grignard reagents have been and continue to be the subject of intense investigations. Arenes can be directly, regioselectively borylated via Re,[12] Rh,[13,14] or Ir[15−21]

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catalysis. Alternatively, Pd-catalyzed Miyaura borylation[22−29] of aryl halides and triflates has proven to be an effective regiospecific strategy. Often, these techniques involve the use of relatively expensive tetraalkoxydiborons such as bis-(pinacolato)diboron,[30,31] though recent interest has focused on the use of more practical dialkoxyboranes, such as pinacolborane.[32,33] Due in large part to the high cost of Pd, alternative methods for the borylation of aryl halides using less expensive metals such as Cu are seeing increasing use.[34−36] Analogous chemistry employing Ni-catalysis holds similar promise for process economy as well as for the ability to employ less reactive electrophiles.[37−41]

In 2000, the possibility of Ni-catalyzed borylation was demonstrated.[42] Meanwhile, we developed a novel borylating reagent, neopentylglycolborane, which can be prepared in situ[43] from neopentylglycol and borane-dimethyl sulfide. This reagent facilitated the development of Ni-catalyzed neopentylglycolborylation as an effective strategy for the preparation of aryl boronate esters. The resulting arylneopentylglycolboronate esters have been harnessed in the sequential[44] or one-pot cross-coupling[45] with aryl halides[44,45a] and aryl sulfonates[49] to form a diversity of substituted biaryls. The Ni-catalyzed borylation/cross-coupling strategy enabled the expeditious synthesis of building blocks for the construction of self-organizable supramolecular dendrimers.[46,47] The first catalyst for this neopentylglycolborylation was the single-ligand 1:1 complex of NiCl$_2$(dppp) and dppp, NiCl$_2$(dppp)/dppp, which was effective for aryl iodide and bromide substrates.[44,45a] However, it was later discovered that mixed-ligand systems, in particular NiCl$_2$(dppp)/dppf, were significantly more efficient for the catalytic neopentylglycolborylation of aryl chlorides[48] and of the less reactive aryl sulfonates.[49] While some aryl mesylates and tosylates were successfully neopentylglycolborylated in high yield with NiCl$_2$(dppp)/dppf without any additives, the addition of zerovalent Zn metal provided for very broad substrate compatibility and greatly accelerated the reaction, typically generating excellent yields within 1−2 h.[49] Recently, it was shown that NiCl$_2$(dppp)/dppf, as well as other mixed-ligand Ni complexes, are also superior catalysts for the neopentylglycolborylation of *ortho*-substituted aryl halides.[50] *ortho*-Substituted aryl iodide substrates typically reached maximum yield within a few hours. However, aryl bromides and chlorides usually required extended reaction times, often exceeding 24 h. In some cases, this longer reaction time allows for competitive protodeborylation that diminishes the yield of the reaction and generates mixtures of products. Herein, we explore the application of zerovalent metal activation to the acceleration of neopentylglycolborylation of aryl halides, including of the less reactive *ortho*-substituted aryl iodides, bromides, and chlorides.

Results and Discussion

Zero-Valent Metals Accelerate the Ni-Catalyzed Neopentylglycolborylation of Aryl Halides. The use of Zn as an accelerant for Ni-catalyzed borylation of aryl mesylates[49] was inspired by our earlier work[38a−e] where Zn was used as a

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reducing agent[37b,38a−e,51,52] in Ni-catalyzed homocoupling and cross-coupling. NiCl$_2$-phosphine complexes including NiCl$_2$(dppp) were capable to undergo oxidative addition to aryl mesylates. The catalytic cycle of Ni-catalyzed borylation of aryl halides or sulfonates has not been well elaborated. Nevertheless, the reductions of NiCl$_2$(dppp)/L precatalyst and of the oxidative addition adduct are expected to be fundamental steps in this reaction. It was hypothesized that the less efficient Ni-catalyzed neopentylglycolborylation of aryl mesylates[49] could be due to slower reduction of the precatalyst or oxidative addition adduct than for the corresponding aryl halides. The addition of Zn as reducing agent is believed to increase the rate of these processes.

Phenol-derived electrophiles such as mesylates and tosylates are often less expensive than aryl halides. Although a great diversity of phenols is commercially available, aryl halides are still extremely important intermediates in organic synthesis. Therefore, the development of rapid and efficient methods to convert aryl halides to boronic acids and boronic acid derivatives is an important technical challenge. To determine the effect of the external reducing agent, an array of zerovalent metals such as Al, Ca, Fe, Mg, Mn, and Zn were tested in the NiCl$_2$(dppp)/dppf-catalyzed neopentylglycolborylation of 4-iodo-, 4-bromo-, and 4-chloroanisole (Table 1). The results from Table 1 were obtained in the presence of a diversity of zerovalent metals and were not optimized. However, they strongly support the universality of the activation concept by zerovalent metals, and in addition they demonstrate that this process is not restricted to Zn. For the case of 4-iodoanisole (compare entries 1 and 2 with entries 3−8 in Table 1), the reaction time to 100% conversion was reduced from 1 to 0.5 h in the presence of zerovalent metals. The most significant acceleration by zerovalent metals was observed in the case of 4-bromoanisole (compare entry 9 with entries 10−17 in Table 1) and 4-chloroanisole (compare entry 18 with entries 19−26 in Table 1).

Comparison of Different Particle Sizes of Zn. In certain cases, it appears that other zerovalent metals such as Mg and Mn exhibit reducing activity comparable to that of Zn for 4-chloroanisole (compare entries 19, 20, and 25 in Table 1) but require a longer reaction time. However, considering the already demonstrated power of Zn to accelerate the neopentylglycolborylation of aryl mesylates and tosylates, it would be advantageous to develop a single universal catalytic system. Zn metal is available in many forms including powder, chips, sheets, and wire. Typically, when Zn has been employed as a reductant in Ni-catalyzed chemistry, it is supplied in the form of a nonactivated powder. In all experiments reported in this publication, nonactivated Zn or other zerovalent metals were used. Zn powder provides the largest surface area per unit mass and can be more uniformly dispersed through the reaction medium. However, monolithic Zn provides easier recovery and recycling.

The NiCl$_2$(dppp)/dppf-catalyzed neopentylglycolborylations of aryl iodides, bromides, and chlorides were performed using either 325 mesh Zn powder or Zn chips (Table 2). Both Zn powder and Zn chips accelerate the Ni-catalyzed neopentylglycolborylation.

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TABLE 1. Neopentylglycolborylation of Halogenated Anisole Catalyzed by NiCl$_2$(dppp)/dppf Activated with Different Metals

entry	X	metal[a]	time (h)	convn[b]/yield[c] (%)
1	I	**none**	**1.0**	**100/100 (85)**
2	I	**none**	**0.5**	**66/66 (40)**
3	I	Zn	0.5	100/100 (95)
4	I	Mn	0.5	100/100 (92)
5	I	Fe	1.0	100/100 (95)
6	I	Al	0.5	100/100 (78)
7	I	Mg	0.7	100/97 (82)
8	I	Ca	0.5	92/86 (76)[d]
9	Br	**none**	**1.0**	**26/26/(22)**
10	Br	Zn	0.7	100/98 (68)
11	Br	Mn	1.0	74/70
12	Br	Mn	2.0	100/97 (76)
13	Br	Fe	24	88/86 (73)
14	Br	Al	1.0	100/75 (58)
15	Br	Mg	1.0	84/84
16	Br	Mg	1.5	100/93 (67)
17	Br	Ca	14	73/73 (46)
18	Cl	**none**	**1.0**	**7/7**
19	Cl	Zn	1.0	100/98 (70)
20	Cl	Mn	2.0	100/98 (85)
21	Cl	Fe	2.0	11/11
22	Cl	Fe	22	100/100 (73)
23	Cl	Al	1.0	100/76 (49)
24	Cl	Mg	1.0	57/55
25	Cl	Mg	1.7	100/95 (84)
26	Cl	Ca	24	54/54 (30)[d]

[a]Metals are all 325 mesh. [b]Conversion determined by GC. [c]Yield determined by GC. Isolated yield in parentheses. [d]Isolated yield for potassium trifluoroborate.

As expected as a result of larger surface area, yields were generally better for Zn powder in equal or shorter reaction time. Nevertheless, in some cases comparable yields could be achieved in equivalent reaction time (Table 1, entries 3 and 6).

Ni-Catalyzed Neopentylglycolborylation of Aryl Iodides. The Zn-activated neopentylglycolborylation catalyzed by NiCl$_2$-based systems was compared using several mixed-ligand and single-ligand catalysts for a diversity of aryl iodide substrates. The neopentylglycolborylation of 4-iodoanisole using the mixed-ligand catalyst NiCl$_2$(dppp)/dppf was extremely efficient and rapid in the presence of 2 equiv of Zn, leading to 95% yield after only 30 min (entry 1 in Table 2). An extensive array of *ortho*- and *para*-substituted aryl iodides, bromides, and chlorides has been tested in the Ni-catalyzed neopentylglycolborylation. In this report, the borylation of *ortho*-substituted aryl halides will be used as the benchmark for reaction efficiency, as *para*- and *meta*-substituted aryl halides are generally more reactive. Similarly, electron-rich *ortho*-substituted aryl iodides 2-iodotoluene and 2-iodoanisole were previously borylated using NiCl$_2$(dppp)/dppf in the absence of Zn, providing 78% yield (24 h) and 80% yield (1 h), respectively.[50] Here, it is found that the presence of 2 equiv of Zn accelerates the reaction, increasing the yield to 85% for 2-iodotoluene (1 h, Table 3 Entry 1) and 96% for 2-iodoanisole (1 h, Table 3 Entry 2). It should be noted that these yields correspond to a two-step process of neopentylglycolborylation followed by conversion of the boronate ester to the more readily

TABLE 2. Neopentylglycolborylation of Aryl Halides Catalyzed by NiCl$_2$(dppp)/dppf Activated with Zn Powder and Zn Chips

entry	substrate	2	Zn chips		Zn powder	
			time (h)	convn[a]/ yield[b] (%)	time (h)	convn[a]/ yield[b] (%)
1	I-C6H4-OCH3	2a	0.5	100/89	0.5	100/95
2	Br-C6H4-OCH3	2a	5	100/77[c]	2	100/80[c]
3	(2-fluoroiodobenzene)	2b	8	90/51	1	100/91
4	(2-bromotoluene)	2c	12	100/72[c]	1	100/85[c]
5	(2-bromothiophene)	2d	1	95/90	1	100/95
6	(2,5-dibromothiophene)	2d 2e	5	100/53[d], 36	7	100/76[d], 20[e]
7	(2-chlorotoluene)	2c	7	100/87[c]	3	100/71[c]
8	(2-chlorothiophene)	2d	6	100/79	1	100/92
9	(chloro-dimethoxybenzene)	2f	12	33/13[c]	3	81/53

[a]Conversion determined by GC. [b]Isolated yield. [c]Isolated yield for potassium trifluoroborate. [d]Monoborylated product. [e]Diborylated product.

isolated potassium trifluoroborate. Therefore, the yields of the first step of this process may in fact be higher than reported as potassium trifluoroborates. The Ni-catalyzed and Zn-activated neopentylglycolborylation of 2-iodoanisole was explored using other mixed-ligand catalysts such as NiCl$_2$(dppp)/PPh$_3$, and NiCl$_2$(PPh$_3$)/dppp, and single-ligand catalysts such as NiCl$_2$-(dppp)/dppp, NiCl$_2$(PPh$_3$)/PPh$_3$, NiCl$_2$(dppp), and NiCl$_2$-(PPh$_3$)$_2$, but in all cases in significantly diminished yield. The electron-deficient aryl iodides methyl 2-iodobenzoate and 2-fluoro-1-iodobenzene were also investigated. Methyl 2-iodobenzoate was also neopentylglycolborylated in the absence of Zn using the mixed-ligand catalysts NiCl$_2$(dppp)/dppf (97% yield, 5 h) and NiCl$_2$(dppp)/PPh$_3$ (81% yield, 5 h).[50]

However, in the presence of Zn[0] the reaction reaches high yields in a very short reaction time using either NiCl$_2$(dppp)/dppf (81% yield, 0.5 h) or NiCl$_2$(dppp)/PPh$_3$ (90% yield, 1 h) (Table 3, entries 9 and 11). For 2-fluoro-1-iodobenzene, 89% yield was achieved in 1 h using NiCl$_2$(dppp)/dppf alone, whereas 80% yield was obtained in only 30 min in the presence of Zn (Table 3, entry 17).

The Ni-catalyzed neopentylglycolborylation of aryl iodides, including less reactive *ortho*-substituted aryl iodides, was generally efficient even without the use of Zn as an additive. However, more sluggish reactions were observed for aryl bromides and aryl chlorides in the absence of Zn.

TABLE 3. Neopentylglycolborylation of Aryl Iodides Catalyzed by NiCl$_2$-Based Mixed-Ligand Systems Activated with Zn Powder

entry	Substrate	Catalyst	ligand	time (h)	2	convn[a]/ yield[b] (%)
1	(2-iodotoluene)	NiCl$_2$(dppp)	dppf	1	2c	100/85[c]
2	(2-iodoanisole)	NiCl$_2$(dppp)	dppf	1	2g	100/96[c]
3	(2-iodoanisole)	NiCl$_2$(dppp)	—	1	2g	100/67
4	(2-iodoanisole)	NiCl$_2$(dppp)	PPh$_3$	1	2g	100/62
5	(2-iodoanisole)	NiCl$_2$(dppp)	dppp	24	2g	11/6[c]
6	(2-iodoanisole)	NiCl$_2$(PPh$_3$)$_3$	—	24	2g	97/16[c]
7	(2-iodoanisole)	NiCl$_2$(PPh$_3$)$_3$	PPh$_3$	25	2g	82/23[c]
8	(2-iodoanisole)	NiCl$_2$(PPh$_3$)$_3$	dppp	5	2g	100/42[c]
9	(methyl 2-iodobenzoate)	NiCl$_2$(dppp)	dppf	0.5	2h	100/81[c]
10	(methyl 2-iodobenzoate)	NiCl$_2$(dppp)	—	1	2h	100/79
11	(methyl 2-iodobenzoate)	NiCl$_2$(dppp)	PPh$_3$	1	2h	100/90
12	(methyl 2-iodobenzoate)	NiCl$_2$(dppp)	dppp	14	2h	100/12[c]
13	(methyl 2-iodobenzoate)	NiCl$_2$(PPh$_3$)$_3$	—	1	2h	100/30[c]
14	(methyl 2-iodobenzoate)	NiCl$_2$(PPh$_3$)$_3$	PPh$_3$	1	2h	100/21[c]
15	(methyl 2-iodobenzoate)	NiCl$_2$(PPh$_3$)$_3$	dppp	1	2h	100/44[c]
16	I-C6H4-OCH3	NiCl$_2$(dppp)	dppf	0.5	2a	100/95
17	(2-fluoroiodobenzene)	NiCl$_2$(dppp)	dppf	0.5	2b	100/80[c]

[a]Conversion determined by GC. [b]Isolated yield. [c]Isolated yield for potassium trifluoroborate.

Ni-Catalyzed Neopentylglycolborylation of Aryl Bromides. In an earlier report, NiCl$_2$(dppp)/dppp-catalyzed neopentylglycolborylation of 4-bromoanisole provided 90% in 18 h.[45a] Using the mixed-ligand NiCl$_2$(dppp)/dppf catalyst in the presence of Zn activator, 91% yield could be obtained in only 1 h (Table 4, entry 11). Using NiCl$_2$(dppp)/dppf and Zn activator, a similar yield could be obtained for 2-bromoanisole (95% of the trifluoroborate salt, after 1 h (Table 4, entry 3)). However, the use of single-ligand catalytic systems (Table 4, entries 4, 6−8) or other mixed-ligand systems (Table 4, entries 5 and 9) in the presence of Zn or the mixed-ligand NiCl$_2$(dppp)/dppf catalyst in the absence of Zn[50] provided significantly lower yields. Similarly high yields could be obtained in 1 h for 2-bromotoluene and

TABLE 4. Neopentylglycolborylation of Aryl Bromides Catalyzed by NiCl$_2$-Based Mixed-Ligand Systems Activated with Zn Powder
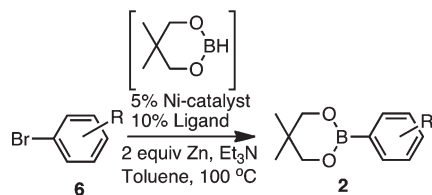
entry	substrate	Catalyst	ligand	2	time (h)	convn[a]/ yield[b] (%)
1		NiCl$_2$(dppp)	dppf	2c	1	100/85[c]
2		NiCl$_2$(dppp)	dppf	2h	1	100/87[c]
3		NiCl$_2$(dppp)	dppf	2g	1	100/95[c]
4		NiCl$_2$(dppp)	–	2g	16	72/50[c]
5		NiCl$_2$(dppp)	PPh$_3$	2g	20	70/54[c]
6		NiCl$_2$(dppp)	dppp	2g	36	71/53[c]
7		NiCl$_2$(PPh$_3$)	-	2g	21	35/9[c]
8		NiCl$_2$(PPh$_3$)	PPh$_3$	2g	21	50/5
9		NiCl$_2$(PPh$_3$)	dppp	2g	6	100/47[c]
10		NiCl$_2$(dppp)	dppf	2i	2	100/83[f]
11		NiCl$_2$(dppp)	dppf	2a	1	100/91
12		NiCl$_2$(dppp)	dppf	2j	6	100/85
13		NiCl$_2$(dppp)	dppf	2k	1	100/73
14		NiCl$_2$(dppp)	dppf	2d	1	100/95
15		NiCl$_2$(dppp)	dppf	2d, 2e	7	100/76[d], 20[e]

[a]Conversion determined by GC. [b]Isolated yield. [c]Isolated yield for potassium trifluoroborate. [d]Yield for diborylated product. [e]Yield for monoborylated product and deborylated product. [f]4 equiv of neopentylglycolborane was used.

2-bromothiophene (Table 4, entries 1, 2, 14). The true advantage of the Zn-activated system is, however, exemplified by the neopentylglycolborylation of methyl 2-bromobenzoate (Table 4, entry 2), *o*-dibromobenzene (Table 4, entry 10), 1-bromo-2-trifluoromethylbenzene (Table 4, entry 12), and 1-bromo-2,6-difluorobenzene (Table 4, entry 13). In previous work the NiCl$_2$(dppp)/dppf-catalyzed neopentylglycolborylation of methyl 2-bromobenzoate was plagued by very high levels of protodeborylation, resulting in a diminished yield (11% in 20 h).[50] Through the use of Zn additive, the borylation process was significantly accelerated, allowing for complete conversion in 1 h and obviating the need to run the reaction for longer times, where protodeborylation begins to dominate. Furthermore, the doubly *ortho*-substituted 1-bromo-2,6-difluorobenzene and the *ortho*-substituted 1-bromo-2-trifluoromethylbenzene were isolated in poor-to fair yield after only

very long reaction times (44 h) in the absence of Zn.[50] Here, in the presence of Zn, good yields could be achieved in only 1−6 h (Table 4, entries 10, 13). 1,2-Dibromobenzene could be efficiently diborylated (Table 4, entry 10), whereas in previous efforts without Zn additive only a low yield of a mixture of mono- and diborylated adducts was obtained.[50] Nevertheless, attempts to prepare diborylated 2,5-dibromothiophene were not as successful, as protodeborylation seemed to be more rapid for this system, resulting in a mixture of 2,5-diborylated thiophene and 2-borylated-thiophene (Table 4, entry 15).

Ni-Catalyzed Neopentylglycolborylation of Aryl Chlorides. The mixed-ligand NiCl$_2$(dppp)/dppf catalytic system was discovered while pursuing the neopentylglycolborylation of relatively unreactive aryl chloride electrophiles.[48a] Despite, the higher activity of the mixed-ligand NiCl$_2$(dppp)/dppf catalytic system, electron-rich aryl chlorides did not provide particularly high yields. For example, in the absence of Zn 4-chloroanisole achieved only 56% yield after 20 h[48] and 7% in 1 h (Table 1 entry18). Here, it is shown that using Zn as an additive provides 91% yield in only 1 h (Table 5, entry 9). Even 1-chloro-3,5-dimethoxy benzene could be neopentylglycolborylated in 53% yield 1-chloro-3,5-dimethoxybenzene after only 3 h (Table 5, entry 11).

Electron-rich *ortho*-substituted aryl chlorides are among the most challenging substrates for Ni-catalyzed neopentylglycolborylation.[50] Nevertheless, NiCl$_2$(dppp)/dppf in the presence of Zn provides good yields of 2-chlorotoluene (71%) and 2-chloroanisole (90%) in only 1 h (Table 5, entries 1, 2). The results from Table 5 demonstrate that both the mixed-ligand NiCl$_2$-(dppp)/dppf catalyst and the Zn activator were needed for a high catalytic performance. The single-ligand catalyst (Table 5, entries 3, 5−7) and other mixed-ligand catalysts (Table 5, entries 4, 8) were less effective. In the presence of Zn, electron-deficient *para*-substituted aryl chlorides (Table 6, entries 8−10) could be borylated in comparable yield, but in a fraction of the time required in the absence of Zn.[48a] The contrast between Ni-catalyzed borylation with and without Zn is clearer for *ortho*-substituted electron-deficient aryl chlorides. For example, using NiCl$_2$(dppp)/dppf alone, only 26% yield was obtained after 24 h.[48a] The use of this catalyst in conjunction with Zn provided 95% yield after conversion to the trifluoroborate salt in only 1 h (Table 6, entry 1). As has been shown repeatedly, this effect requires both the very efficient NiCl$_2$(dppp)/dppf mixed-ligand catalyst as well as the Zn activator. Significantly lower yields were obtained for single-ligand (Table 6, entries 2, 4−6) or other mixed-ligand (Table 6, entries 3, 7) catalysts even in the presence of Zn. Impressively, a 76% yield of *o*-diborylated benzene was obtained in 3 h from *o*-dichlorobenzene (Table 6, entry 11), and 91% borylation yield was obtained from 1-chloro-2-trifluoromethylbenzene in 4 h (Table 6, entry 12), despite worse yields under extended reaction times (24−65 h) using NiCl$_2$(dppp)/ dppf without Zn as an additive.

Conclusions

In two recent reports from our laboratory the power of the mixed-ligand systems for the Ni-catalyzed borylation of less reactive aryl chlorides[48a] and *ortho*-substituted aryl halides[50] was established. Using the particularly efficient mixed-ligand catalyst NiCl$_2$(dppp)/dppf, similar borylations of phenol-derived aryl mesylates and tosylates were shown to be feasible, and in fact the catalyst significantly accelerated the

TABLE 5. Neopentylglycolborylation of Electron-Rich Aryl Chlorides Catalyzed by NiCl$_2$-Based Mixed-Ligand Systems Activated with Zinc Powder

entry	substrate	Catalyst	ligand	2	time (h)	convn[a]/yield[b] (%)
1	Cl	NiCl$_2$(dppp)	dppf	2c	1	100/71[c]
2	H$_3$CO, Cl	NiCl$_2$(dppp)	dppf	2g	1	100/90[c]
3	H$_3$CO, Cl	NiCl$_2$(dppp)	-	2g	24	10/10[c]
4	H$_3$CO, Cl	NiCl$_2$(dppp)	PPh$_3$	2g	24	73/30[c]
5	H$_3$CO, Cl	NiCl$_2$(dppp)	dppp	2g	24	0/0
6	H$_3$CO, Cl	NiCl$_2$(PPh$_3$)$_2$	-	2g	26	0/0
7	H$_3$CO, Cl	NiCl$_2$(PPh$_3$)$_2$	PPh$_3$	2g	25	6/0
8	H$_3$CO, Cl	NiCl$_2$(PPh$_3$)$_2$	dppp	2g	23	85/41[c]
9	Cl—OCH$_3$	NiCl$_2$(dppp)	dppf	2a	1	100/91
10	Cl (thiophene)	NiCl$_2$(dppp)	dppf	2d	1	100/92
11	Cl, OCH$_3$, OCH$_3$	NiCl$_2$(dppp)	dppf	2f	3	81/53

[a]Conversion determined by GC. [b]Isolated yield. [c]Isolated yield for potassium trifluoroborate.

TABLE 6. Neopentylglycolborylation of Electron-Deficient Aryl Chlorides Catalyzed by NiCl$_2$-Based Mixed-Ligand Systems Activated with Zinc Powder

entry	substrate	Catalyst	ligand	2	time (h)	convn[a]/yield[b] (%)
1	H$_3$CO$_2$C, Cl	NiCl$_2$(dppp)	dppf	2h	1	100/95[c]
2	H$_3$CO$_2$C, Cl	NiCl$_2$(dppp)	-	2h	22	67/36[c]
3	H$_3$CO$_2$C, Cl	NiCl$_2$(dppp)	PPh$_3$	2h	12	100/40[c]
4	H$_3$CO$_2$C, Cl	NiCl$_2$(dppp)	dppp	2h	19	12/7[c]
5	H$_3$CO$_2$C, Cl	NiCl$_2$(PPh$_3$)$_2$	-	2h	17	0/0
6	H$_3$CO$_2$C, Cl	NiCl$_2$(PPh$_3$)$_2$	PPh$_3$	2h	21	46/19[c]
7	H$_3$CO$_2$C, Cl	NiCl$_2$(PPh$_3$)$_2$	dppp	2h	20	100/47[c]
8	Cl—CO$_2$CH$_3$	NiCl$_2$(dppp)	dppf	2l	1	100/79
9	Cl—CN	NiCl$_2$(dppp)	dppf	2m	1	100/79
10	Cl—CN	NiCl$_2$(dppp)	dppf	2n	1	100/77
11	Cl, Cl	NiCl$_2$(dppp)	dppf	2i	3	100/76[d]
12	F$_3$C, Cl	NiCl$_2$(dppp)	dppf	2j	4	100/91

[a]Conversion determined by GC. [b]Isolated yield. [c]Isolated yield for potassium trifluoroborate. [d]4 equiv of neopentylglycolborane was used.

reaction in the presence of Zn additive.[49] Unlike aryl sulfonates, aryl halides suffer from both protodeborylation and hydrodehalogenation side reactions, and therefore the ability to accelerate productive borylation and limit overall reaction time is of particular value. By combining the highly active mixed-ligand NiCl$_2$(dppp)/dppf catalyst with Zn activation, the neopentylglycolborylation of aryl iodides, bromides, and chlorides, including *ortho*-substituted, proceeds extremely quickly, typically achieving complete conversion and high yield in 1 h or less. Although the use of superstoichiometric Zn powder may be disadvantageous for some applications, easier product isolation due to increased yield and decreased byproduct contamination, as well as a significantly reduced reaction time, is quite compelling. Furthermore, similar efficacy with easily recoverable and recyclable Zn chips and the extension to other zerovalent metal additives has been demonstrated.

Experimental Section

Preparation of Neopentylglycolborane. To a cooled solution (0 °C) of neopentylglycol (6.0 mmol, 2.0 equiv) dissolved in toluene (3 mL) was slowly added (CH$_3$)$_2$S·BH$_3$ (6.0 mmol, 2.0 equiv) via a syringe under nitrogen. After 30 min of stirring at 0 °C, the reaction mixture was allowed to warm to 23 °C and was left stirring until the gas evolution ceased (60−90 min). Neopentylglycolborane was used directly without further purification.

General Procedure for Neopentylglycolborylation. To an oven-dried 25 mL Schlenk tube were added Zn powder or chips (6 × 10^{-3} mol), Ni-based catalyst (1.5 × 10^{-4} mol), and ligand (3 × 10^{-4} mol) (see Tables 1−6) along with the appropriate aryl halide (if it is solid) (3 × 10^{-3} mol). The *ortho*-substituted aryl halide, catalyst, and ligand were degassed by pumping and backfilling with nitrogen

three times. Toluene was added to the reaction mixture (3 mL) along with the appropiate aryl halide (if it is liquid) and Et$_3$N (1.26 mL 9 × 10^{-3} mol). Neopentylglycol borane was added dropwise to the reaction mixture. The reaction was placed into a preheated oil bath at 100 °C with stirring under an inert atmosphere. Samples were taken in time through the septum under nitrogen, and the conversion was followed by GC. After complete consumption of the starting material, the reaction was then quenched with a saturated NH$_4$Cl solution (50 mL) and extracted with ethyl acetate (3 × 25 mL). No difference between the crude GC and the last recorded GC prior quenching except for the disappearance of the in situ prepared neopentylglycolborane peak was observed. The organic fractions were combined and dried over MgSO$_4$. Following filtration the solvent was removed under reduced pressure and the crude reaction mixture was immediately purified on a silica gel column with the appropriate eluent.

2-(4-Methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (2a). White solid, mp 54−56 °C (lit.[49] 59 °C); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.74 (d, J = 8.5 Hz, 2H), 6.88 (d, J = 8.5 Hz, 2H), 3.82 (s, 3H), 3.75 (s, 4H), 1.01 (s, 6H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 161.7, 135.4, 113.0, 72.1, 55.0, 31.8, 21.8.

2-(2-Fluorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (2b)[49] Yellowish solid; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.66 (dd, J = 22.9, 7.3 Hz, 2H), 7.56−7.37 (m, J = 12.6, 7.3 Hz, 2H), 3.79 (s, 4H), 1.07 (s, 6H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 133.8, 130.6, 129.2, 121.0, 120.3, 72.6, 33.3, 21.8.

5,5-Dimethyl-2-(o-tolyl)-1,3,2-dioxaborinane (2c)[50] Colorless liquid; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.72 (d, J = 7.4 Hz, 1H), 7.27 (td, J = 7.5, 1.3 Hz, 1H), 7.14 (t, J = 7.7 Hz, 2H), 3.76 (s, 4H), 2.51 (s, 3H), 1.02 (s, 6H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 144.1, 135.0, 130.2, 130.1, 124.8, 72.4, 31.8, 22.5, 22.0.

5,5-Dimethyl-2-(thiophen-2-yl)-1,3,2-dioxaborinane (2d). White solid, mp 90−91 °C (lit. 91−92 °C);[50] ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.61−7.54 (m, 2H), 7.19−7.15 (m, 1H), 3.76 (s, 4H), 1.03 (s, 6H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 135.8, 131.5, 128.2, 72.6, 32.2, 22.1.

2,5-Bis(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)thiophene (2e). White solid, mp 155−156 °C (lit.[50] 156−157 °C); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.59 (s, 2H), 3.75 (s, 8H), 1.02 (s, 12H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 136.2, 72.3, 31.9, 21.8.

2-(3,5-Dimethoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (2f). White solid, mp 112 °C (lit.[49] 115 °C); ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.97 (d, J = 2.4 Hz, 2H), 6.55 (t, J = 2.4 Hz, 1H), 3.82 (s, 6H), 3.77 (s, 4H), 1.04 (s, 6H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 160.3, 110.7, 103.8, 72.2, 55.2, 31.8, 21.8.

2-(2-Methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (2g). White solid, mp 40 °C (lit.[50] 39−40 °C); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.65 (dd, J = 7.2, 1.3 Hz, 1H), 7.39−7.33 (m, 1H), 6.94 (t, J = 7.3 Hz, 1H), 6.86 (d, J = 8.3 Hz, 1H), 3.83 (s, 3H), 3.79 (s, 4H), 1.04 (s, 6H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 163.8, 135.9, 131.8, 120.4, 110.6, 72.6, 55.9, 31.9, 22.0.

Methyl 2-(5,5-Dimethyl-1,3,2-dioxaborinan-2-yl)benzoate (2h)[50] Colorless oil; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.92 (d, J = 7.9 Hz, 1H), 7.55−7.46 (m, 2H), 7.38 (dd, J = 8.0, 2.5 Hz, 1H), 3.92 (s, 3H), 3.80 (s, 4H), 1.12 (s, 6H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 169.0, 132.7, 131.9, 131.3, 128.6, 128.3, 72.5, 52.3, 31.7, 22.0.

1,2-Bis(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)benzene (2i)[50] White solid; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.60 (dd, J = 5.4, 3.3 Hz, 2H), 7.33 (dd, J = 5.5, 3.3 Hz, 2H), 3.76 (s, 8H), 1.07 (s, 12H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 132.3, 128.7, 72.7, 32.0, 22.1.

5,5-Dimethyl-2-(2-(trifluoromethyl)phenyl)-1,3,2-dioxaborinane (2j)[50] Colorless oil; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.68 (d, J = 7.2 Hz, 1H), 7.66−7.60 (m, 1H), 7.52−7.41 (m, 2H), 3.78 (s, 4H), 1.05 (s, 6H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 136.7, 133.8, 130.8, 129.3, 125.44, 125.40, 72.4, 31.8, 21.9.

2-(2,6-Difluorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (2k). Yellowish solid, mp 42−44 °C; ^{1}H NMR (500 MHz, CDCl$_3$) δ

7.41−7.15 (m, 1H), 6.82 (t, J = 7.5 Hz, 2H), 3.81 (s, 4H), 1.07 (d, J = 0.8 Hz, 6H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 166.0 (dd, J = 247.5, 13.5 Hz), 131.9, 111.1, 72.8, 32.0, 21.8; HRMS (CI+) calcd for C$_{11}$H$_{14}$BF$_2$O$_2$ (M$^+$ + H) 227.1055, found 227.1055.

Methyl 4-(5,5-Dimethyl-1,3,2-dioxaborinan-2-yl)benzoate (2l). White solid, mp 111−113 °C (lit.[49] 114 °C); ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.01 (d, J = 8.3 Hz, 2H), 7.86 (d, J = 8.1 Hz, 2H), 3.92 (s, 3H), 3.79 (s, 4H), 1.03 (s, 6H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 167.4, 133.9, 131.9, 128.6, 72.5, 52.2, 32.0, 22.0.

4-(5,5-Dimethyl-1,3,2-dioxaborinan-2-yl)benzonitrile (2m). White solid; mp 122 °C (lit.[49] 124−125 °C); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.87 (d, J = 8.0 Hz, 2H), 7.61 (d, J = 7.9 Hz, 2H), 3.78 (s, 4H), 1.02 (s, 6H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 134.4, 131.1, 119.2, 114.0, 72.5, 32.0, 21.9.

2-(4-(5,5-Dimethyl-1,3,2-dioxaborinan-2-yl)phenyl)acetonitrile (2n).[48a] White solid, mp 77−78 °C; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.80 (d, J = 8.0 Hz, 2H), 7.31 (d, J = 7.7 Hz, 2H), 3.77 (s, 4H), 3.75 (s, 2H), 1.02 (s, 6H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 134.8, 132.3, 127.2, 117.9, 72.5, 32.0, 23.9, 22.0.

General Procedure for Aryl Trifluoroborate Synthesis. The trifluoroborates were prepared from the corresponding crude boronic esters according to the following procedure. In a Nalgene bottle were added a stirr bar and the crude boronic ester (5 mmol, 1 equiv) dissolved in 12 mL of MeOH/H$_2$O (2:1). KHF$_2$ (15 mmol, 3 equiv) was added in one portion over the reaction mixture, and the reaction mixture was stirred at room temperature overnight. The reaction mixture was transferred to a round-bottom flask and concentrated by rotary evaporation. The crude product was recrystallized from acetone to yield the corresponding trifluoroborate.

Potassium Trifluoro(4-methoxyphenyl)borate (3a). White solid, mp > 250 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.21 (d, J = 8.0 Hz, 2H), 6.65 (d, J = 8.2 Hz, 2H), 3.67 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 157.5, 132.6, 112.2, 54.9.

Potassium Trifluoro(2-fluorophenyl)borate (3b). White solid, mp > 250 °C (lit.[53] 304−305 °C); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.34 (s, 1H), 7.16−6.99 (m, 1H), 6.91 (t, J = 6.9 Hz, 1H), 6.78 (t, J = 8.5 Hz, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 165.7 (d, J = 239.1 Hz), 134.2, 125.8, 122.5, 113.7 (d, J = 26.1).

Potassium Trifluoro(o-tolyl)borate (3c). White solid, mp 229 °C (lit.[54] 232 °C); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.31 (d, J = 5.7 Hz, 1H), 6.87 (dd, J = 15.4, 5.9 Hz, 3H), 2.28 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 140.5, 131.6, 128.2, 125.1, 123.3, 21.7.

Potassium Trifluoro(2-methoxyphenyl)borate (3g). White solid, mp > 250 °C (lit.[50] > 250 °C); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.29 (dd, J = 6.9, 1.4 Hz, 1H), 7.02 (td, J = 7.9, 1.9 Hz, 1H), 6.73−6.65 (m, 2H), 3.62 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 162.5, 133.2, 126.6, 119.1, 109.6, 54.7.

Potassium Trifluoro(2-(methoxycarbonyl)phenyl)borate (3h). White solid, mp > 260 °C (lit.[50] > 250 °C); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.45 (d, J = 7.3 Hz, 1H), 7.20 (t, J = 7.3 Hz, 1H), 7.16 (d, J = 7.3 Hz, 1H), 7.09 (t, J = 7.3 Hz, 1H), 3.65 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 172.2, 136.5, 132.7, 128.3, 125.8, 124.9, 51.3.

Supporting Information Available: ^{1}H NMR, ^{13}C NMR, and HRMS data for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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