

# Nickel-Catalyzed Suzuki–Miyaura Reaction of Aryl Fluorides

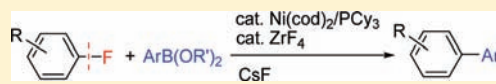
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**S** Supporting Information

**ABSTRACT:** Two protocols for the nickel-catalyzed cross-coupling of aryl fluorides with aryl boronic esters have been developed. The first employs metal fluoride cocatalysts, such as ZrF<sub>4</sub> and TiF<sub>4</sub>, which enable Suzuki–Miyaura reactions of aryl fluorides bearing electron-withdrawing (ketones, esters, and CF<sub>3</sub>), aryl and alkenyl groups as well as those comprising fused aromatic rings, such as fluoronaphthalenes and fluoroquinolines. The second protocol employs aryl fluorides bearing ortho-directing groups, which facilitate the difficult C–F bond activation process via cyclometalation. N-heterocycles, such as pyridines, quinolines, pyrazoles, and oxazolines, can successfully promote cross-coupling with an array of organoboronic esters. A study into the substituent effects with respect to both coupling components has provided fundamental insights into the mechanism of the nickel-catalyzed cross-coupling of aryl fluorides.

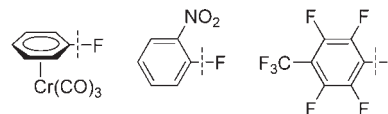


## INTRODUCTION

Over the past few decades, the Suzuki–Miyaura reaction has emerged as one of the most powerful carbon–carbon bond-forming methodologies available.<sup>1</sup> Typical protocols employ organic iodides, bromides, chlorides, and sulfonates, but catalytic systems that allow the use of more inert, but widely available, electrophiles would be of great value to practitioners of chemical synthesis.<sup>2</sup> Such processes would enable the assembly of complicated molecules via sequential cross-coupling reactions or late-stage diversification.<sup>3</sup> Aryl fluorides represent an attractive choice of electrophile owing to their commercial availability of diverse derivatives.<sup>4</sup> Furthermore, the carbon–fluorine bond is robust under a range of synthetic conditions, including palladium catalysis.<sup>5</sup> Nevertheless, the Suzuki–Miyaura reaction of aryl fluorides has only been successfully applied to a limited number of extremely electron-deficient fluorides, including chromium-bound,<sup>6</sup> ortho-nitro<sup>7</sup> and perfluorinated<sup>8</sup> substrates (Figure 1).<sup>9</sup> This paucity is notable, in light of successful fluoride cross-couplings with Grignard<sup>10</sup> and organozinc<sup>11</sup> reagents. In these cases, Lewis acidic magnesium or zinc ions may assist fluoride elimination throughout the oxidative addition and/or transmetalation processes.<sup>10d,f,g</sup> The absence of such an assistance, due to the lower Lewis acidity of boronic acids, renders the fluoride Suzuki–Miyaura reaction a significant challenge. Herein, we report a nickel-catalyzed Suzuki–Miyaura reaction that is applicable to a wide range of aryl fluorides.

## RESULTS AND DISCUSSION

From preliminary studies, Ni(0)/PCy<sub>3</sub> was identified as a promising catalyst system for the fluoride Suzuki–Miyaura reaction (See Supporting Information for detailed optimization studies). The reaction of 4-fluorobiphenyl (**1a**) with boronic acid **2**, in the presence of Ni(cod)<sub>2</sub>/PCy<sub>3</sub> as a catalyst and CsF as a base, afforded the corresponding biaryl product in 38% yield



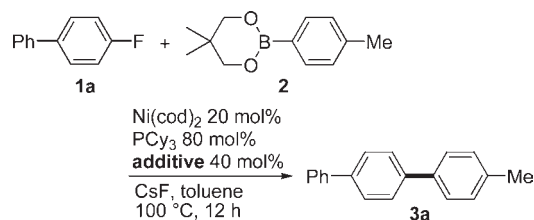
**Figure 1.** Highly electron-deficient aryl fluorides applicable to the Suzuki–Miyaura reaction.

(entry 1, Table 1). Based on the successful application of Grignard reagents in the nickel-catalyzed cross-coupling of aryl fluorides,<sup>10</sup> the addition of magnesium salts was examined. While MgBr<sub>2</sub> impeded the formation of **3a** (0% yield), the yield was slightly increased upon the addition of MgF<sub>2</sub> (entry 2, Table 1). This fluoride salt-specific effect led us to screen other metal fluoride additives. Interestingly, all the metal fluorides examined imposed a positive effect on the yields of **3a**. Of those examined, ZrF<sub>4</sub> proved to be the optimal additive, generating a yield of 80% (entry 7, Table 1). The application of ZrCl<sub>4</sub> afforded no cross-coupling product, reflecting the importance of metal fluorides. The cross-coupling reaction did not proceed at all in the absence of CsF, even in the presence of ZrF<sub>4</sub>, ruling out a mechanistic scenario whereby the ZrF<sub>4</sub> simply serves as a fluoride donor, to convert boronic ester **2** into an activated tetra-coordinated borate species.

To evaluate the potency of the Ni(0)/ZrF<sub>4</sub> catalyst system, the scope with respect to aryl fluoride was investigated (Table 2). Under standard conditions, fluorobenzene (**1b**) underwent cross-coupling to produce the biaryl product in modest yield. As expected, the electronic nature of aryl fluorides had a significant impact on reaction efficiency. Not unlike cross-couplings with other halides,<sup>12</sup> substrates bearing an electron-withdrawing group, such as CF<sub>3</sub> **1c**, ester **1d**, and ketones **1e–1g**, successfully coupled with **2**. Remarkably, the ketone-containing

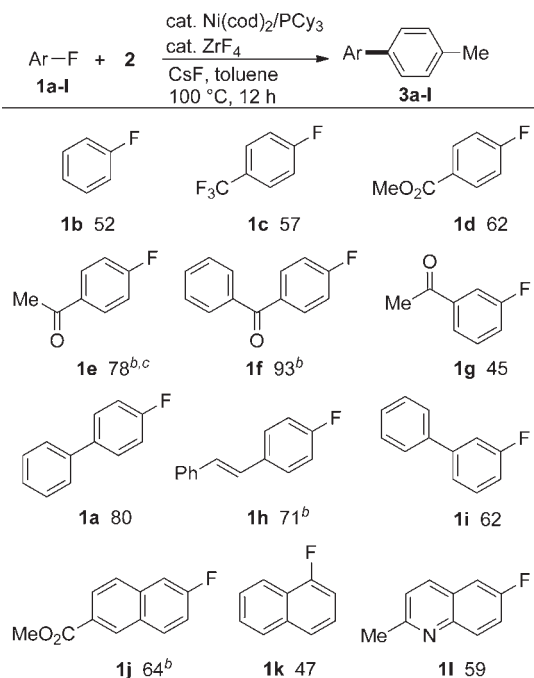
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**Table 1. Ni-Catalyzed Suzuki–Miyaura Reaction of Aryl Fluorides: Effect of Additives<sup>a</sup>**

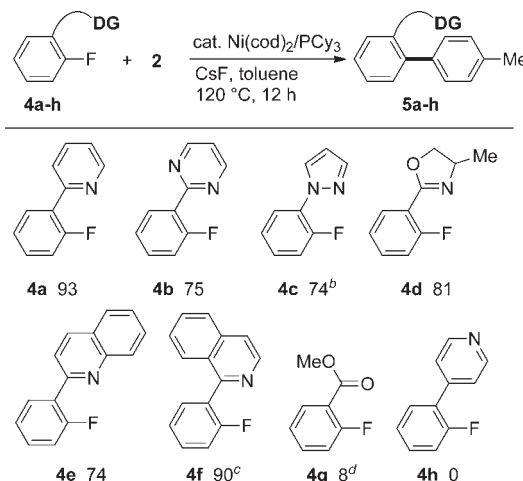
entry	additive	yield (%) <sup>b</sup>	entry	additive	yield (%) <sup>b</sup>
1	none	38	6	TiF <sub>4</sub>	77
2	MgF <sub>2</sub>	47	7	ZnF <sub>4</sub>	80
3	ZnF <sub>2</sub>	56	8	FeF <sub>3</sub>	48
4	CeF <sub>3</sub>	52	9	NiF <sub>2</sub>	44
5	TiF <sub>3</sub>	61	10	AlF <sub>3</sub>	43

<sup>a</sup> Reaction conditions: **1a** (0.25 mmol), **2** (0.75 mmol), Ni(cod)<sub>2</sub> (0.05 mmol), PCy<sub>3</sub> (0.20 mmol), CsF (0.75 mmol), additive (0.10 mmol), and toluene (0.75 mL) in a screw-capped vial under N<sub>2</sub> at 100 °C for 12 h. <sup>b</sup> Isolated yield based on **1a**.

**Table 2. Ni-Catalyzed Cross-Coupling of Aryl Fluorides with 2<sup>a</sup>**

<sup>a</sup> Reaction conditions: **1a** (0.25 mmol), **2** (0.75 mmol), Ni(cod)<sub>2</sub> (0.05 mmol), PCy<sub>3</sub> (0.20 mmol), CsF (0.75 mmol), ZrF<sub>4</sub> (0.10 mmol), and toluene (0.75 mL) in a screw-capped vial under N<sub>2</sub> at 100 °C for 12 h. Isolated yields based on aryl fluorides are shown. <sup>b</sup> Run in the absence of ZrF<sub>4</sub>. <sup>c</sup> Run at 80 °C.

substrates **1e** and **1f** exhibited reactivities superior to that of CF<sub>3</sub>-substituted **1c**, delivering the corresponding products in good yield, even in the absence of ZrF<sub>4</sub>.<sup>13</sup> These results suggest that resonance effects, rather than the inductive effects, play a critical



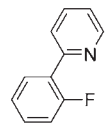
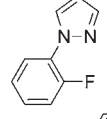
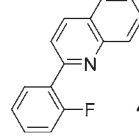
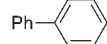
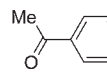
**Table 3. Effect of Directing Groups<sup>a</sup>**

<sup>a</sup> Reaction conditions: substrate (0.50 mmol), **2** (0.60 mmol), Ni(cod)<sub>2</sub> (0.05 mmol), PCy<sub>3</sub> (0.20 mmol), CsF (0.6 mmol), and toluene (1.5 mL) in a screw-capped vial under N<sub>2</sub> at 120 °C for 12 h. Isolated yields based on aryl fluorides are shown unless otherwise noted. <sup>b</sup> Run using **2** (1.50 mmol) for 44 h. <sup>c</sup> Run using Ni(cod)<sub>2</sub> (0.10 mmol) and **2** (2.0 mmol). <sup>d</sup> GC yield.

role in the present catalytic reaction (vide infra). This view is further supported by the higher yield obtained for para-substituted isomer **1e** compared to that for the meta-isomer **1g**. As shown in Table 1, a para-phenyl group, which is expected to exert a negligible electronic effect at the reaction center ( $\sigma_p = -0.01$ ,  $\sigma_p^- = 0.02$ ),<sup>14</sup> dramatically accelerates the reaction. Similarly, aryl fluorides bearing para-styrenyl **1h** and meta-phenyl **1i** groups serve as suitable substrates in this nickel-catalyzed cross-coupling. Moreover, fluorine atoms on the polyaromatic rings, including naphthalene **1j** and **1k** and quinoline **1l**, can be arylated under these conditions. In contrast, electron-rich aryl fluorides are less reactive under these conditions (i.e., a yield of only 28% was obtained upon coupling 4-fluoroanisole).

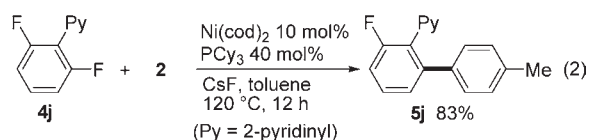
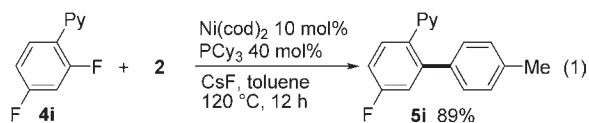
Metal fluoride salts, especially ZrF<sub>4</sub>, have been identified as effective cocatalysts to promote the nickel-catalyzed Suzuki–Miyaura reaction of aryl fluorides and allow a significant expansion to the scope of the reaction. An alternative approach to facilitate the difficult C–F bond oxidative addition process involves the use of chelation assistance.<sup>15</sup> The nickel-mediated activation of unreactive bonds is reported to be promoted by neighboring coordinating groups.<sup>16</sup> Inspired by these reports, we investigated the nickel-catalyzed Suzuki–Miyaura reaction of aryl fluorides bearing ortho-directing groups (Table 3). The treatment of 2-(2-fluorophenyl)pyridine (**4a**) with boronic ester **2**, in the presence of catalytic Ni(cod)<sub>2</sub> and PCy<sub>3</sub>, afforded biaryl **5a** in 88% isolated yield, even in the absence of metal fluoride salts. During the preparation of this manuscript, Love and co-workers reported a similar imine-directed Suzuki–Miyaura reaction of aryl fluorides.<sup>17</sup> The isomeric 4-pyridinyl derivative **4h** did not afford any cross-coupling product, suggesting the 2-pyridinyl moiety serves to facilitate the oxidative addition of C–F bonds, not simply via an electron-withdrawing inductive effect but by forming a stable cyclometalated intermediate. Although carbonyl groups, like that in **4g**, were poor directors, N-heteroaromatics, such as pyrimidine **4b**, pyrazole **4c**, quinoline **4e**, and isoquinoline **4f**, afforded the corresponding

Table 4. Use of NiCl<sub>2</sub>(PCy<sub>3</sub>)<sub>2</sub> as a Catalyst Precursor<sup>a</sup>

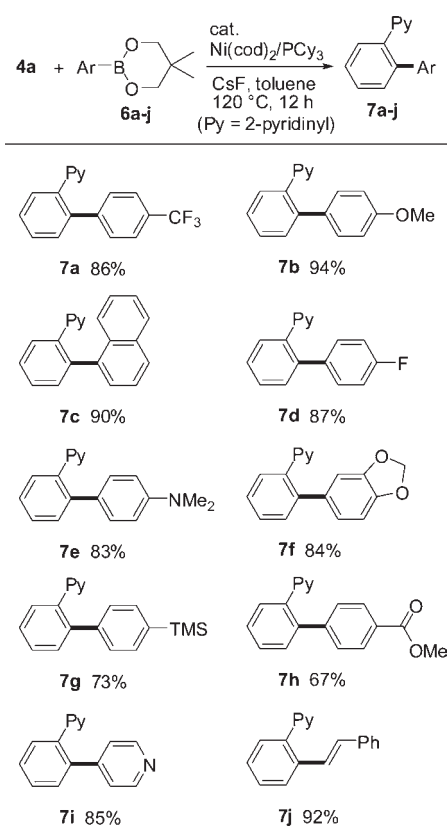
Ar-F + (HO) <sub>2</sub> B- 		5.0 mol% NiCl <sub>2</sub> (PCy <sub>3</sub> ) <sub>2</sub> K <sub>3</sub> PO <sub>4</sub> , toluene 120 °C, 12 h		Ar- 	
entry	Ar-F	product	yield (%) <sup>b</sup>		
1	 <b>4a</b>	<b>5a</b>	98 (48) <sup>c</sup>		
2	 <b>4c</b>	<b>5c</b>	71		
3	 <b>4e</b>	<b>5e</b>	99		
4 <sup>d</sup>	 <b>1a</b>	<b>3a</b>	trace		
5 <sup>e</sup>	 <b>1e</b>	<b>3e</b>	0		

<sup>a</sup> Reaction conditions: substrate (0.30 mmol), 4-tolylboronic acid (0.75 mmol), NiCl<sub>2</sub>(PCy<sub>3</sub>)<sub>2</sub> (0.015 mmol), K<sub>3</sub>PO<sub>4</sub> (1.4 mmol), and toluene (0.90 mL) in a screw-capped vial under N<sub>2</sub> at 120 °C for 12 h. <sup>b</sup> Isolated yield based on aryl fluorides. <sup>c</sup> Yield using 4-tolylboronic acid (0.36 mmol) and K<sub>3</sub>PO<sub>4</sub> (0.66 mmol). <sup>d</sup> Run at 100 °C. <sup>e</sup> Run using 4-tolylboronic acid (0.90 mmol) and K<sub>3</sub>PO<sub>4</sub> (1.7 mmol) at 80 °C.

cross-coupling products in good yield. The observed reaction insensitivity to electronics and sterics of coordinating sp<sup>2</sup>-hybridized nitrogen atoms is notable.<sup>18</sup> The successful application of a nonaromatic oxazoline ring, as in **4d**, is also of synthetic value, as it can be postmodified for further functionalization.<sup>19</sup> Pyridine derivatives are typical directing groups in C–H bond activation reactions,<sup>15</sup> but no corresponding C–H arylation products were observed in any examples. The accelerating effect of a pyridinyl group allows for the regioselective arylation of difluorinated substrate **4i** (eq 1). Moreover, the ortho-difluoro substrate **4j** also produced a monoarylated product in a selective manner (eq 2).



We typically used a Ni(cod)<sub>2</sub>/PCy<sub>3</sub> catalyst system in our studies, but the reaction can also be performed with NiCl<sub>2</sub>(PCy<sub>3</sub>)<sub>2</sub>, which is more conveniently handled.<sup>20</sup> For example, the reaction of **4a** with 4-tolylboronic acid (2.5 equiv) in the presence of 5 mol % NiCl<sub>2</sub>(PCy<sub>3</sub>)<sub>2</sub> and K<sub>3</sub>PO<sub>4</sub> (4.5 equiv) in

Table 5. Scope of Boronic Esters<sup>a</sup>

<sup>a</sup> Reaction conditions: **4a** (0.50 mmol), boronic ester (0.6 mmol), Ni(cod)<sub>2</sub> (0.05 mmol), PCy<sub>3</sub> (0.20 mmol), CsF (0.6 mmol), and toluene (1.5 mL) in a screw-capped vial under N<sub>2</sub> at 120 °C for 12 h. Isolated yield based on aryl fluorides is shown.

toluene at 120 °C for 12 h afforded **5a** in 98% yield (entry 1, Table 4). While this practical protocol proved to be applicable to several aryl fluorides bearing directing groups (entries 2 and 3, Table 4), aryl fluorides **1a** and **1e** generated no cross-coupling products with the NiCl<sub>2</sub>(PCy<sub>3</sub>)<sub>2</sub> catalyst (entries 4 and 5, Table 4).

We also discovered that a broad range of aryl and heteroaryl rings could be coupled with aryl fluoride **4a** (Table 5). Both electron-rich and electron-poor aryl groups could be introduced efficiently. Functional groups, including methoxy **7b**,<sup>21</sup> fluoro **7d**,<sup>10</sup> ester **7h**, and pyridine **7i**, that are potentially reactive toward Grignard reagents remained intact under these conditions. This highlights the advantage of using boronic esters as mild nucleophiles. It should be noted that biaryl products **7b** and **7d** could further be elaborated via C–OMe<sup>22</sup> and C–F<sup>5</sup> bond functionalization reactions, respectively. Sterically hindered (**6c**) and alkenyl (**6j**) boronic esters also proved to be suitable coupling partners in this fluoride Suzuki–Miyaura reaction.

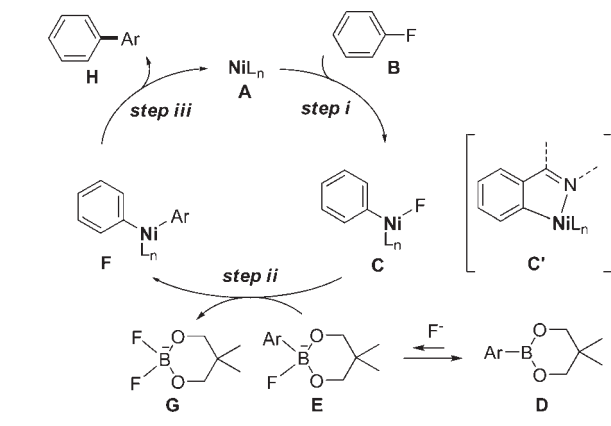
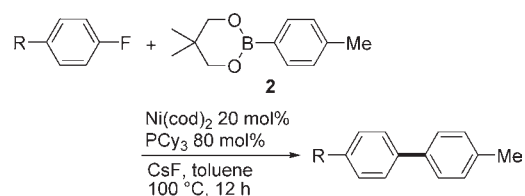
To gain insight into the mechanism of the present fluoride Suzuki–Miyaura reaction, the electronic effect characteristics of the boronic ester component were investigated via intermolecular competition experiments (Table 6). The Ni(0)/ZrF<sub>4</sub>-catalyzed reaction of fluorobenzene (**1b**) with a mixture of electron-deficient (**6a**) and electron-rich (**6e**) boronic esters was conducted (5 equiv each). The corresponding biaryls were produced in a ratio of 51:49, suggesting the electronic nature of the boronic

**Table 6. Comparing the Electronic Effects of the Boronic Esters in the Suzuki–Miyaura Couplings of Aryl Halides<sup>a</sup>**

entry	Ar-X	ligand	total yield <sup>b</sup>	ratio (CF <sub>3</sub> :NMe <sub>2</sub> ) <sup>b</sup>
1 <sup>c</sup>		PCy <sub>3</sub> /ZrF <sub>4</sub>	55%	51:49
2		PCy <sub>3</sub>	99%	70:30
3 <sup>d</sup>		dppf	55%	60:40
4		PCy <sub>3</sub>	32%	78:22
5		PCy <sub>3</sub>	37%	78:22

<sup>a</sup> Reaction conditions: ArX (0.30 mmol), **6a** (1.5 mmol), **6e** (1.5 mmol), Ni(cod)<sub>2</sub> (0.030 mmol), ligand (0.12 mmol), CsF (3.0 mmol), and toluene (1.5 mL) in a screw-capped vial under N<sub>2</sub> at 120 °C for 2–3 h. <sup>b</sup> Determined by GC. <sup>c</sup> ZrF<sub>4</sub> (0.12 mmol) was also added. <sup>d</sup> Dppf (0.06 mmol) was used.

esters has a negligible impact on the cross-coupling (entry 1, Table 6). In contrast, a similar competition reaction using an aryl fluoride bearing a directing group, as in **4a**, predominantly furnished the coupling product with electron-deficient **6a**, rather than that derived from electron-rich **6e** (ratio = 70:30, entry 2, Table 6). This discrepancy in the product ratio, between the nondirected and directed Suzuki–Miyaura reactions of aryl fluorides, may be attributed to a change in the turnover-limiting step. Scheme 1 illustrates a proposed mechanism for the nickel-catalyzed cross-coupling of aryl fluorides. Similar to the mechanisms for typical cross-coupling reactions, the catalytic cycle consists of three main processes: oxidative addition of the C–F bond (step i), transmetalation (step ii), and reductive elimination (step iii). The results obtained with aryl fluorides bearing no directing group (entry 1, Table 6) are best accommodated by a mechanism in which step (i) is kinetically the most difficult step in the catalytic cycle. Miyaura reported a similar insensitivity to the electronics of boronic acids in the nickel-catalyzed cross-coupling of aryl chlorides, in which the oxidative addition of the C–Cl bond was rate-determining.<sup>23</sup> Indeed, the electronics of the boronic ester component did not significantly influence the cross-coupling of chlorobenzene under Miyaura's catalytic conditions (Ni(0)/dppf) (entry 3, Table 6). For substrates bearing a directing group, the formation of a stable cyclometalated intermediate, such as **C'**, drives the oxidative addition process forward, compared to simple aryl fluorides. This chelation assistance renders steps (ii and iii) kinetically more important. Since transmetalation is often proposed as the rate-limiting step in the nickel-catalyzed Suzuki–Miyaura reaction of

**Scheme 1. Possible Mechanism****Table 7. Ni-Catalyzed Suzuki–Miyaura Reaction of Aryl Fluorides: Effects of Substituents<sup>a</sup>**

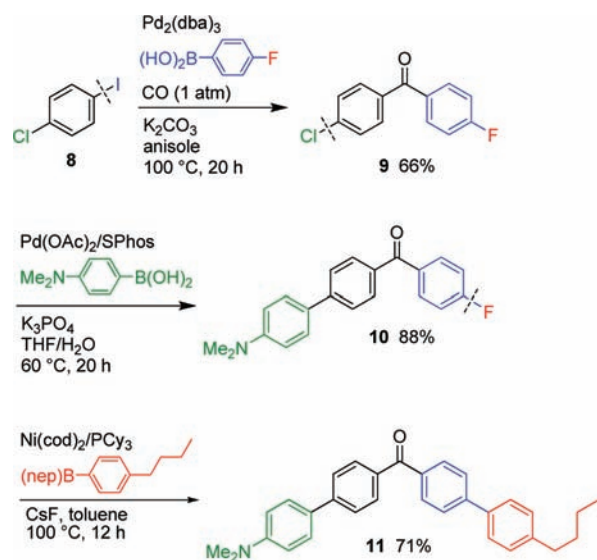
entry	R	$\sigma_p^b$	$\sigma_p^{-b}$	yield (%) <sup>b</sup>
1	Ac	0.50	0.84	78
2	CO <sub>2</sub> Me	0.45	0.74	45
3	CF <sub>3</sub>	0.54	0.65	39
4	Ph	0.01	0.02	38
5	H	0	0	10
6	OMe	−0.28	−0.12	8 <sup>d</sup>

<sup>a</sup> Reaction conditions: aryl fluoride (0.25 mmol), **2** (0.75 mmol), Ni(cod)<sub>2</sub> (0.05 mmol), PCy<sub>3</sub> (0.20 mmol), CsF (0.75 mmol), ZrF<sub>4</sub> (0.10 mmol), and toluene (0.75 mL) in a screw-capped vial under N<sub>2</sub> at 100 °C for 12 h. <sup>b</sup> See ref 14. <sup>c</sup> Isolated yield based on aryl fluorides. <sup>d</sup> GC yield.

aryl halides and their equivalents,<sup>2m,23,24</sup> it is reasonable to assume that step (ii), which requires the cleavage of an inert Ni–F bond, limits the overall rate of the reaction most significantly when a directing group is present. In accordance with this rationale, the cross-couplings of bromo- and iodobenzene, in which transmetalation is expected to be rate-limiting, afforded the biaryl products from electron-deficient boronic ester **6a** significantly faster than those from **6e** (entries 4 and 5, Table 6). Although the electronics of the arylboron reagent have a profound influence on the efficiency of the transmetalation process (step ii), an explanation for the high reactivities associated with electron-deficient boronic esters remains elusive. Opposing electronic effects have been reported for a set of catalytic reactions that involve the rate-limiting transmetalation of boronic acid derivatives.<sup>25</sup> Electron-rich boronic acids react faster in nickel-catalyzed Suzuki–Miyaura reactions with aryl sulfamates,<sup>2m</sup> whereas electron-deficient boron reagents are more reactive in nickel-catalyzed cross-couplings with aryl



## Scheme 2. Sequential Cross-Couplings of Aryl Iodide/Chloride/Fluoride

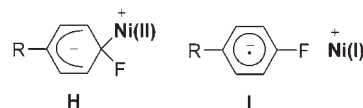


tosylates<sup>20</sup> and in other palladium<sup>26</sup> and ruthenium<sup>2v</sup> catalyzed methodologies. One possible explanation for the faster reactions with electron-deficient boronic esters is that the higher Lewis acidity of the boron center favors the formation of activated boronate E.

The addition of metal fluoride salts, such as ZrF<sub>4</sub>, remarkably accelerates the nondirected Suzuki–Miyaura reactions of aryl fluorides (Table 1). As mentioned above, ZrF<sub>4</sub> is unlikely to act as a fluoride donor to assist the formation of boronate E, since both CsF and ZrF<sub>4</sub> are required for an efficient reaction. We currently believe that ZrF<sub>4</sub> acts as a Lewis acid to facilitate the elimination of the fluorine atom in an oxidative addition and/or transmetalation process, as we initially envisioned.<sup>10d,f,g,27,28</sup>

Based on the electronic effects of the boronic ester component, the relative reactivities of aryl fluorides without directing groups, toward the nickel-catalyzed cross-coupling, primarily reflect the relative reactivities of their C–F bonds toward oxidative addition. To understand the nature of the C–F bond oxidative addition to the nickel complex, the substituent effects of aryl fluorides were investigated. The yields for cross-coupling reactions, using a series of para-substituted aryl fluorides in the absence of ZrF<sub>4</sub>, are listed in Table 7. As expected, the yields of biaryl products increased with more electron-deficient substrates (entries 1–3, Table 7). Electron-rich fluorides produced only a trace levels of corresponding biaryl (entry 6, Table 7). Among the substituents examined, the acetyl group promoted the reaction most significantly (78% yield, entry 1, Table 7), whereas the more electron-withdrawing CF<sub>3</sub> group only improved the yield modestly (39%, entry 3, Table 7). Therefore, the accelerating effect cannot be interpreted as a simple inductive effect represented by the Hammett  $\sigma_p$  values. There is, however, a good correlation with the  $\sigma_p^-$  values, which are often applied to reactions that involve direct resonance interactions between the electron acceptor and the anionic reaction site.<sup>29</sup> Although more kinetic studies are necessary to fully interpret these results, a charged intermediate/transition state, such as a Meisenheimer-type  $\sigma$  complex H<sup>7c,30</sup> or a radical anion I via single electron transfer (SET) from Ni(0),<sup>31</sup> may be involved in the C–F bond

oxidative addition.<sup>10b,32</sup> The current analysis cannot explain the exceptionally high reactivities of the *p*-phenyl- and *p*-styrenyl-substituted aryl fluorides.<sup>33</sup> The extended conjugation of the aryl system may favor the prerequisite formation of a  $\eta^2$ -nickel complex prior to the rate-limiting oxidative addition.<sup>34</sup>



To demonstrate the synthetic utility of the fluoride Suzuki–Miyaura reaction, tandem cross-couplings were performed (Scheme 2). The palladium-catalyzed reaction of 4-chloroiodobenzene (8) with 4-fluorophenyl boronic acid, under an atmospheric pressure of carbon monoxide, afforded the benzophenone derivative 9. The cross-coupling proceeded selectively at the iodide site. The chloride moiety in 9 was then arylated under Buchwald's ligand-accelerated palladium catalysis to form 10. The  $\pi$ -conjugation in 10 was further extended using the nickel-catalyzed Suzuki–Miyaura reaction at the fluoride site to furnish 11. The orthogonal reactivity of the three halides (F, Cl and I) allows three cross-coupling events to be accomplished in a straightforward manner. The functional group tolerance with organoboron nucleophiles is also essential for the preparation of ketone 11 in this synthetic sequence.

## CONCLUSION

We have developed two protocols for the nickel-catalyzed Suzuki–Miyaura cross-coupling of aryl fluorides. The first uses metal fluoride cocatalysts, including ZrF<sub>4</sub> and TiF<sub>4</sub>, to significantly accelerate the reaction and thus expand the substrate scope. A range of electron-deficient aryl fluorides and those bearing extended  $\pi$ -systems, such as biaryl-, stilbene-, and naphthalene-based fluorides, can be arylated using Ni/Zr bimetallic catalysis. The second protocol utilizes aryl fluorides bearing a directing group, which facilitate the difficult C–F bond oxidative addition by forming stable cyclometalated intermediates. Directing groups that contain an sp<sup>2</sup>-hybridized nitrogen atom, including pyridine, pyrazole, and oxazoline, can successfully promote the cross-coupling reaction with an array of aryl and alkenylboronic esters. The electronic characteristics of the boronic esters have little impact in the nondirected cross-coupling of aryl fluorides, whereas electron-deficient boronic esters exhibited a superior reactivity in the chelation-assisted reactions. We propose that the turnover-limiting step changes from being the oxidative addition to the transmetalation, through the introduction of directing groups. We hope that the fundamental insights from these studies will guide the further development of catalytic transformations via C–F bond activation. Further investigations are currently underway in our laboratory.

## ASSOCIATED CONTENT

**S Supporting Information.** Detailed experimental procedures and characterization of products are provided. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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