Suzuki–Miyaura Cross-Coupling of Aryl Fluorosulfonates Mediated by Air- and Moisture-Stable [Pd(NHC)(μ-Cl)Cl]$_2$ Precatalysts: Broad Platform for C–O Cross-Coupling of Stable Phenolic Electrophiles

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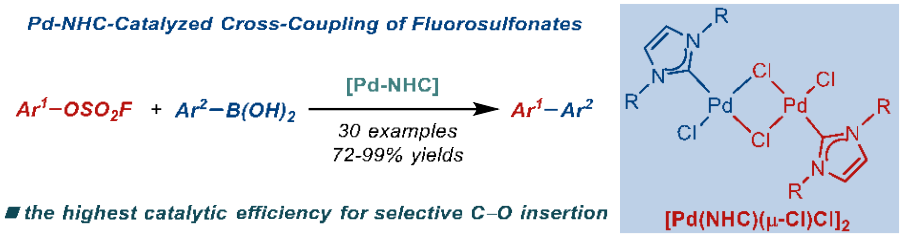
Supporting Information



ABSTRACT: A highly efficient protocol for the Suzuki–Miyaura cross-coupling of aryl fluorosulfonates by selective –OFs cleavage using well-defined, air- and moisture-stable NHC–Pd(II) chloro dimers is presented. The reaction proceeds in excellent yields and with broad functional group tolerance using 0.10-0.20 mol% of [Pd] in the presence of mild K_3PO_4 base under aqueous conditions. A variety of sensitive functional groups are tolerated in this operationally-trivial protocol for C–O bond activation. Selectivity studies and gram scale cross-coupling are presented. The method advances well-defined and highly reactive Pd(II)–NHCs to the cross-cou-pling of readily available, orthogonal and bench-stable fluorosulfonates as aryl halide surrogates.

Introduction

Transition-metal-catalyzed cross-couplings are the most prevalent methodology commonly utilized in academic and industrial research.[1-3] In particular, the Suzuki cross-coupling is the most powerful protocol for the synthesis of biaryl motifs that are present in pharmaceuticals, agrochemicals and synthetic intermediates in all facets of modern chemistry.[3,4] In this regard, in contrast to aryl halides (Ar–X), phenolic electrophiles (Ar–OX) have attracted significant interest owing to several major benefits as orthogonal and environmentally-friendly electrophiles in cross-coupling research (Figure 1A).[5,6] The utility of C–O electrophiles stems from natural abundance of phenolic precursors, orthogonal reactivity in cross-coupling protocols due to different rates of oxidative addition, capacity for prefunctionalization by S_EAr mechanism, and availability of phenols from orthogonal pool of substrates than aryl halides.[3-6]

In this context, recently there has been a resurgence of fluorosulfonates (R–OSO_2F) owing to the "click" synthesis from the corresponding phenols.[7] First, the availability of protocols by the reaction of phenols with mainstream, cheap and non-toxic insecticide SO_2F_2 (sulfuryl fluoride) produced by Dow and Maui (Hangzou) on a multi-ton scale annually renders aryl fluorosulfonates particularly appealing electrophiles in organic synthesis.[8] Second, despite electronic activation of the C–O moiety, aryl fluorosulfonates are significantly more stable than structurally related aryl triflates, with >10 days stability under mild basic conditions (pH = 10).[7] Adding the fact that other known C–O electrophiles are either unstable, expensive to prepare or suffer from high C–O bond dissociation energy making oxidative addition difficult,[5,6] thus limiting the scope of the cross-coupling methods, aryl fluorosulfonates may represent a breakthrough in the common utilization of C–O electrophiles in cross-coupling research in modern chemistry.[5,6] Seminal studies by Hanley[9] and Roth[10] established the capacity of aryl fuorosulfonates as cross-coupling partners under Pd catalysis in Suzuki,[9] Negishi[10] and Stille[10] coupling. However, protocols for cross-coupling of aryl fluorosulfonates are scarce, which is a major limitation for the considerable use of these highly appealing "click" electrophiles.[9-11]

Herein, we report a highly efficient protocol for the Suzuki–Miyaura cross-coupling of aryl fluorosulfonates by selective –OFs cleavage using well-defined, air- and moisture-stable NHC–Pd(II) chloro dimers (Figure 1B).[12-14] The following features of our study are noteworthy: (1) the present catalyst is much superior to the system developed previously,[9] the reaction proceeds in excellent yields and with broad functional group tolerance at low Pd loading in the presence of mild K_3PO_4 base under aqueous conditions; (2) this green phosphine-free catalyst system operates using fast-activating Pd(II)–NHCs, which outperform Pd–phosphines in terms of catalyst loading and substrate scope including a variety of sensitive functional groups; (3) selectivity studies demonstrate high selectivity of –OFs cross-coupling using versatile Pd(II)–NHCs. We anticipate that well-defined [Pd(NHC)(μ-Cl)Cl]$_2$ will become the catalysts of

choice for Pd-catalyzed cross-coupling of fluorosulfonates as phenolic aryl halide surrogates of broad synthetic interest.

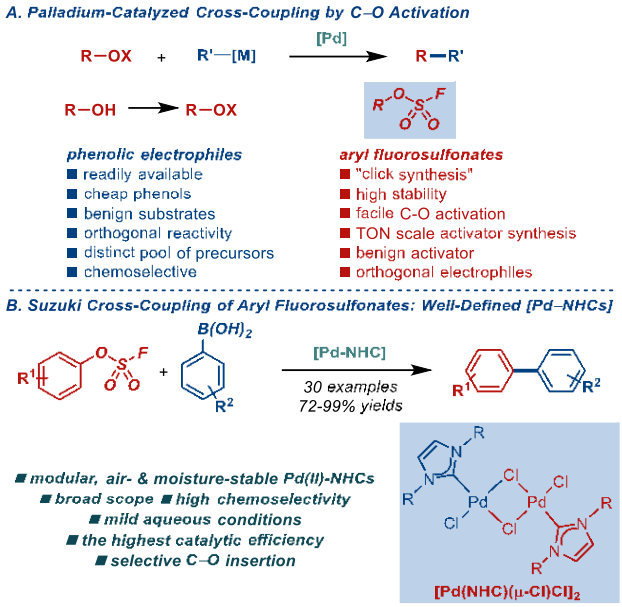


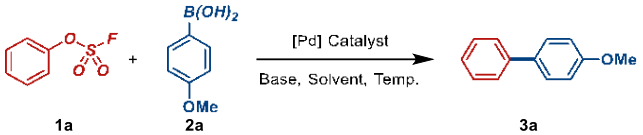
Figure 1. (a) Cross-coupling of C–O electrophiles. (b) This work: Suzuki cross-coupling of aryl fluorosulfonates using well-defined Pd–NHCs by selective C–O activation.

Results and Discussion

Our investigation commenced by evaluating the cross-coupling of phenyl fluorosulfonate (**1a**) with *p*-methoxyphenylboronic acid (**2a**) (Table 1). From the outset, we interrogated [Pd(NHC)(μ-Cl)Cl]$_2$ chloro dimers as by far the most preferred Pd(II)–NHC precatalysts for generating the monoligated Pd(0)–NHC active species owing to the ease of synthesis, fast dissociation to monomers, high air- and moisture stability and the ease of catalyst diversification by NHC scaffold alteration.[13,14] In early studies, we determined that NHC ligand is required for efficient coupling (Table 1, entries 1-2), and that, as expected, well-defined Pd(II)–NHC catalysts are preferred over in situ formed catalysts (Table 1, entries 3-4). As expected, no reaction occurred in the absence of a base (Table 1, entry 5). Significant efforts were made to improve the efficiency of the cross-coupling. We found that decreasing the catalyst loading to 0.50 mol% [Pd] was feasible at 60 °C (Table 1, entry 6); however, these conditions were not compatible with room temperature (Table 1, entry 7). We found that changing the solvent system to an aqueous solution to improve the solubility of boronic acid and activation of the catalyst, dramatically improved the efficiency of the cross-coupling (Table 1, entries 8-10). By careful optimization of solvents, we were able to decrease the catalyst loading to 0.10 mol% [Pd] at 60 °C (Table 1, entries 11-14). Examination of different bases (Table 1, entries 15-20) revealed that K_3PO_4 is the optimal base for this cross-coupling. Different Pd(II)–NHC precatalysts were screened (Chart 1), including the change of NHC ancillary ligand in the chloro dimer series to saturated imidazolinylidene SIPr as well as steric variation to the less sterically-hindered IMes and more sterically-demanding IPr* ([[Pd(SIPr)(μ-Cl)Cl]$_2$], [Pd(IMes)(μ-Cl)Cl]$_2$, [Pd(IPr*)(μ-Cl)Cl]$_2$) (Table 1, entries 21-23) revealing that IPr is the most suitable NHC ancillary ligand. Furthermore, allyl-type and heterocycle-type throw-away ligands ([Pd(IPr)(cin)Cl], [Pd(IPr)(3-Cl-py)Cl$_2$], Table 2, entries 24-25) were less effective, consistent with the ease of activation to mono-ligated Pd(0)–NHC. Control experiments using Pd(OAc)$_2$/phosphine[9a] and Pd(OAc)$_2$[9b] according to the previous protocols (Table 1, entries 26-27) gave no conversion, indicating superior performance of the current catalyst system. We have tested [Pd(IPr)(μ-Cl)Cl]$_2$ under the same reaction conditions as previously reported using Pd-phosphines and non-ligated Pd. Under the tested reaction conditions, there is full conversion using the present catalyst (>98% conversion, 98% yield), while no reaction (<2% conversion, >95% recovery) is observed using the previously reported systems. These features make this class of [Pd(NHC)(μ-Cl)Cl]$_2$ catalysts of general interest to the synthetic community.

The present catalyst is much superior to the system developed by Dow.[9] Specifically, we performed studies under the reaction conditions reported previously[9] using Pd(OAc)$_2$/PPh$_3$ system, which resulted in <2% conversion (Table 1, entry 26) vs. >98% yield using the present catalyst system (Table 1, entry 12).

Table 1. Optimization of the Reaction Conditions[a]



1a 2a 3a

entry	[Pd]	[Pd] (mol%)	base	solvent	*T* (°C)	yield (%)
1	[Pd(IPr)(μ-Cl)Cl]$_2$	5	K_3PO_4	dioxane	120	>98
2	Pd(OAc)$_2$	5	K_3PO_4	dioxane	120	11
3	Pd(OAc)$_2$/IPrHCl	5	K_3PO_4	dioxane	120	64
4	Pd(OAc)$_2$/IMesHCl	5	K_3PO_4	dioxane	120	30
5	[Pd(IPr)(μ-Cl)Cl]$_2$	5	-	dioxane	120	0
6	[Pd(IPr)(μ-Cl)Cl]$_2$	0.5	K_3PO_4	dioxane	60	>98
7	[Pd(IPr)(μ-Cl)Cl]$_2$	0.5	K_3PO_4	dioxane	23	<2
8	[Pd(IPr)(μ-Cl)Cl]$_2$	0.5	K_3PO_4	dioxane/H_2O, 2:1 (v/v)	23	>98
9	[Pd(IPr)(μ-Cl)Cl]$_2$	0.5	K_3PO_4	dioxane/H_2O, 1:1 (v/v)	23	40
10	[Pd(IPr)(μ-Cl)Cl]$_2$	0.5	K_3PO_4	dioxane/H_2O, 4:1 (v/v)	23	66
11	[Pd(IPr)(μ-Cl)Cl]$_2$	0.1	K_3PO_4	dioxane/H_2O, 2:1 (v/v)	60	67
12	[Pd(IPr)(μ-Cl)Cl]$_2$	0.1	K_3PO_4	THF/H_2O, 2:1 (v/v)	60	>98
13	[Pd(IPr)(μ-Cl)Cl]$_2$	0.1	K_3PO_4	MeCN/H_2O, 2:1 (v/v)	60	42
14	[Pd(IPr)(μ-Cl)Cl]$_2$	0.1	K_3PO_4	EtOH/H_2O, 2:1 (v/v)	60	38
15	[Pd(IPr)(μ-Cl)Cl]$_2$	0.1	K_2HPO_4	THF/H_2O, 2:1 (v/v)	60	95
16	[Pd(IPr)(μ-Cl)Cl]$_2$	0.1	Cs_2CO_3	THF/H_2O, 2:1 (v/v)	60	82
17	[Pd(IPr)(μ-Cl)Cl]$_2$	0.1	K_2CO_3	THF/H_2O, 2:1 (v/v)	60	75
18	[Pd(IPr)(μ-Cl)Cl]$_2$	0.1	Na_3PO_4	THF/H_2O, 2:1 (v/v)	60	48
19	[Pd(IPr)(μ-Cl)Cl]$_2$	0.1	KF	THF/H_2O, 2:1 (v/v)	60	57
20	[Pd(IPr)(μ-Cl)Cl]$_2$	0.1	KOAc	THF/H_2O, 2:1 (v/v)	60	5
21	[Pd(SIPr)(μ-Cl)Cl]$_2$	0.1	K_3PO_4	THF/H_2O, 2:1 (v/v)	60	85
22	[Pd(IPr*)(μ-Cl)Cl]$_2$	0.1	K_3PO_4	THF/H_2O, 2:1 (v/v)	60	53
23	[Pd(IMes)(μ-Cl)Cl]$_2$	0.1	K_3PO_4	THF/H_2O, 2:1 (v/v)	60	65
24	[Pd(IPr)(cin)Cl]	0.1	K_3PO_4	THF/H_2O, 2:1 (v/v)	60	80
25	[Pd(IPr)(3-Clpy)Cl$_2$]	0.1	K_3PO_4	THF/H_2O, 2:1 (v/v)	60	62
26	Pd(OAc)$_2$/PPh$_3$	0.1	K_3PO_4	THF/H_2O, 2:1 (v/v)	60	<2
27	Pd(OAc)$_2$	0.1	Et_3N	H_2O	60	<2

[a]Conditions: PhOFs (1.0 equiv), Ar-B(OH)$_2$ (2.0 equiv), base (3.0 equiv), [Pd] (0.10-5 mol%), ligand (none or 2 x [Pd]), solvent (0.25 M), *T*, 12 h.

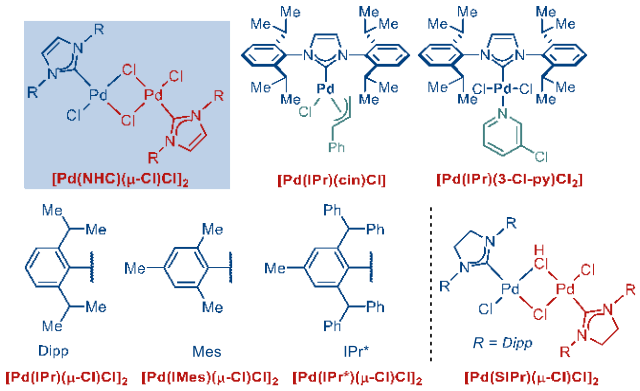
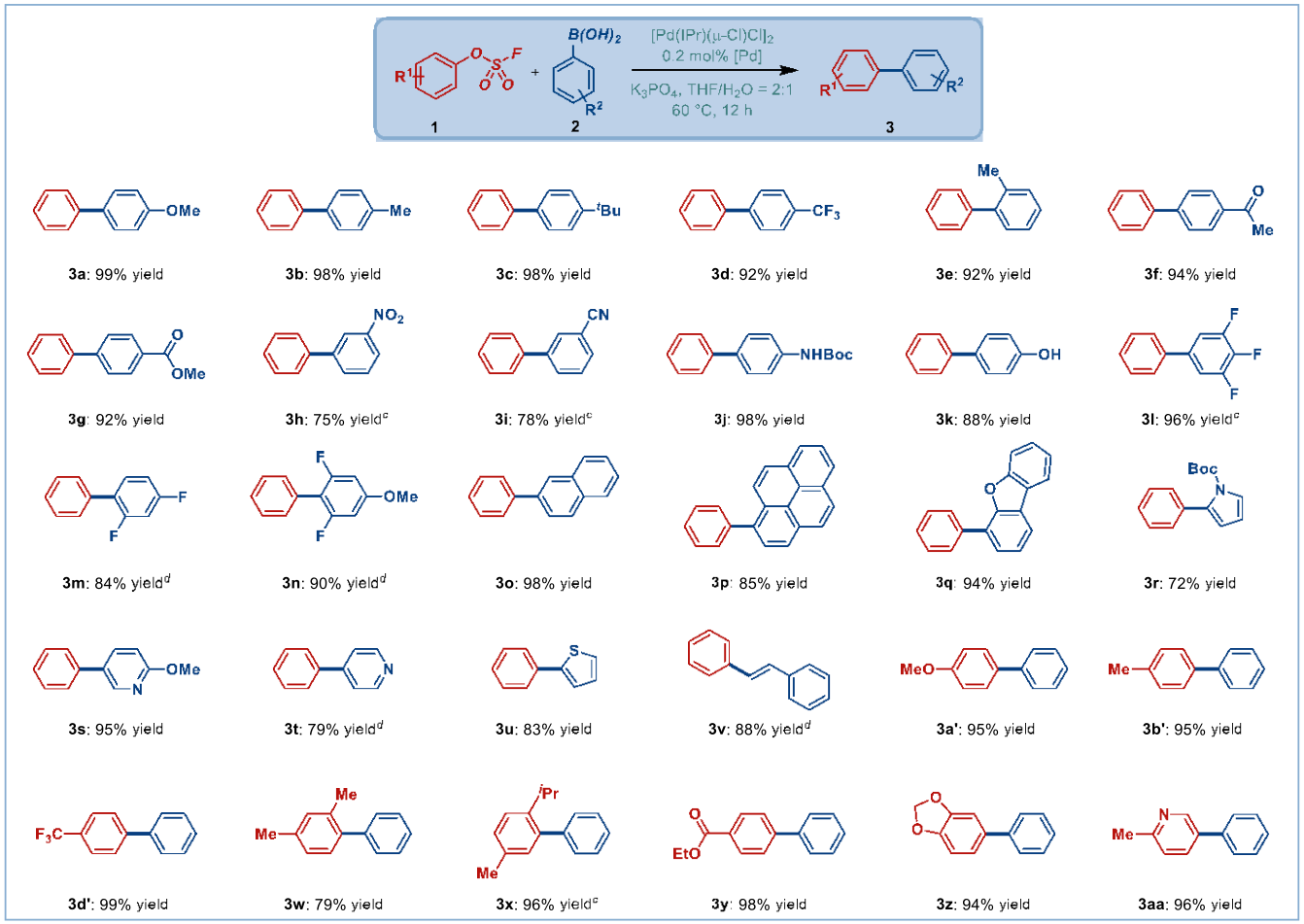


Chart 1. Structures of Pd–NHC catalysts.

Scheme 1. Suzuki–Miyaura Cross-Coupling of Aryl Fluorosulfonates[a,b]



[a]Conditions: ArOFs (1.0 equiv), Ar'B(OH)$_2$ (2.0 equiv), [Pd(IPr)(μ-Cl)Cl]$_2$] (0.10 mol%), K_3PO_4 (3.0 equiv), THF/H_2O (2/1 v/vol, 0.25 M), 60 °C, 12 h. [b]Isolated yields. [c][Pd] 0.6 mol% was used. [d][Pd] 1.0 mol% was used. See SI for details.

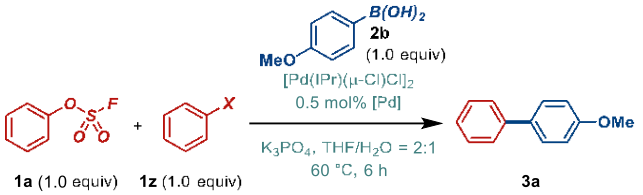
With the optimized conditions in hand, the scope of the cross-coupling was next investigated (Scheme 1). We found the scope to be remarkably broad delivering the cross-coupling products in excellent yields and tolerating a variety of sensitive functional groups. As such, electronically-differentiated aryl boronic acids such as methoxy (**3a**), alkyl (**3b–3c**) and trifluoromethyl (**3d**) furnished the products in excellent yields. Steric hindrance was well-tolerated (**3e**). Notably, various aryl boronic acids decorated with electrophilic groups, such as ketone (**3f**), ester (**3g**), nitro (**3h**), cyano (**3i**) proved to be excellent coupling partners. This mild Pd(II)–NHC catalyst system can tolerate amino (**3j**) and free hydroxyl groups (**3k**). Furthermore, challenging fluorinated arylboronic acids prone to protodeboronation are readily accommodated providing access to fluorinated biaryls (**3l–3n**). Note that this includes the notoriously challenging 2,6-F_2-disubsitition (**3n**). Moreover, polyaromatic boronic acids, such as naphthyl (**3o**) and pyrenyl (**3p**) can be employed. Notably, heterocyclic boronic acids are also excellent substrates, including benzofuran (**3q**), pyrrole (**3r**), pyridines (**3s–3t**) and thiophene (**3u**) delivering valuable heterobiaryl products. Note that 4-pyridyl boronic acid (**3t**) is one of the most challenging boronic acids for cross-coupling and

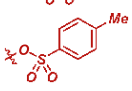
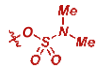
routinely used as a test for the efficiency of cross-coupling reactions. Furthermore, alkenyl boronic acids are also compatible as demonstrated in the cross-coupling of β-styrenyl boronic acid (**3v**). The scope of aryl fluorosulfonates is equally broad and encompasses electronically-diverse substrates, such as methoxy (**3a'**), alkyl (**3b'**) and trifluoromethyl (**3d'**). Steric hindrance is well-tolerated as demonstrated in the cross-coupling of a naturally-occurring monoterpenoid *thymol* (**3w**) and a fragrance agent 2,5-xylenol (**3x**). Furthermore, electrophilic functional groups are compatible, such as esters (**3x**), derived from naturally-occurring 4-hydroxybenzoic acid. Finally, heterocycles are excellent substrates, such as *sesamol* (**3z**), an antioxidant found in sesame seeds, and pharmaceutical intermediate 5-hydroxy-2-methylpyridine (**3aa**).

The scalability of this cross-coupling was evaluated (Scheme 2). We were pleased to find that the cross-coupling proceeded on gram scale in 98% isolated yield, attesting to the utility of this C–O cross-coupling protocol in organic synthesis.

We were further interested to probe the selectivity of the fluorosulfonate cross-coupling (Table 2). In this selectivity study, we followed the study reported previously by Dow using Pd-phosphines.[9] It is now well-stablished that Suzuki–Miyaura cross-coupling using Pd–NHCs involves oxidative addition or transmetallation as the most common rate determining steps, which are often distinct from Pd/phosphine systems.[12,13] We found that the reaction is selective vs. chlorides, sulfonates and sulfamates (Table 3, entries 4, 6-8). However, between 4-12% of $ArOSO_2F$ is consumed in the reaction vs. aryl chloride and aryl sulfonate (Table 3, entries 4 and 6). Furthermore, cross-coupling of aryl iodides is selective in the presence of aryl fluorosulfonates (Table 3, entry 2). Note that aryl bromides couple preferentially over fluorosulfonates (Table 3, entry 3), while triflates show similar reactivity to fluorosulfonates using Pd–NHCs. Overall, this allows to establish the following order of reactivity of fluorosulfonates using Pd–NHCs: (1) OFs >> Cl, OMs, OTs, OSO_2NMe_2; (2) I > Br > OFs, and (3) OFs ≈ OTf. The observed trend of reactivity parallels the selectivity observed using Pd-phosphines.[9] Note that fluorosulfonates are significantly more stable than triflates.

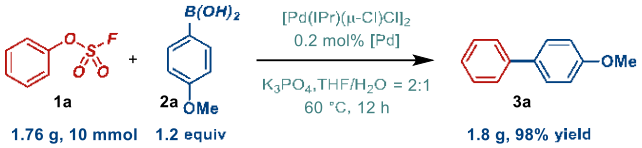
Table 2. Selectivity Studies[a]



entry	X	conversion of **1a** (%)	conversion of **PhX** (%)	yield of **3a** (%)
1[b]		98	/	92
2		32	98	91
3		56	75	85
4		88	<5	87
5		46	50	88
6		96	<2	90
7		95	<2	89
8		92	<2	92

[a]Conditions: PhOFs (1.0 equiv), PhX (1.0 equiv), Ar-$B(OH)_2$ (1.0 equiv), K_3PO_4 (3.0 equiv), [Pd(IPr)(μ-Cl)Cl]$_2$] (0.5 mol%), THF/H_2O (2/1 v/vol, 0.25 M), 60 °C, 12 h. [b]In the absence of PhX.

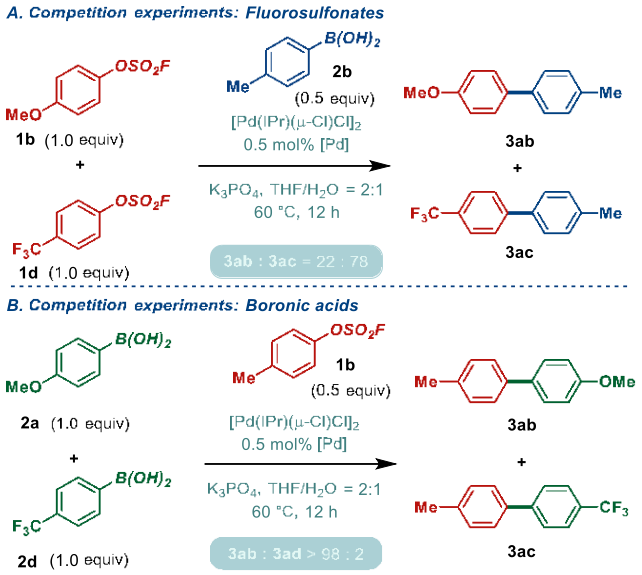
Scheme 2. Gram Scale Cross-Coupling



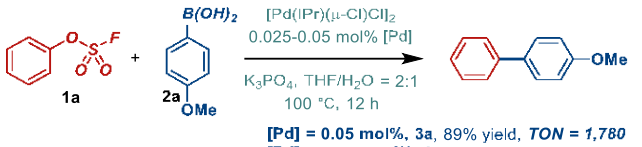
Preliminary studies were conducted to gain insight into the reaction mechanism (Scheme 3). (1) Intermolecular competition experiments with differently substituted aryl fluorosulfonates revealed electron-deficient arenes to be inherently more reactive (4-CF_3:4-MeO = 78:22); (2) Further competitions with differently substituted boronic acids revealed a significant preference for electron-donating boronic acids (4-MeO:4-CF_3 >98:2). These results are consistent with transmetallation as the kinetically relevant step. Further studies are underway.

Turnover numbers of 1,780 and 2,320 were determined for the cross-coupling of **1a** (K_3PO_4, 100 °C) at 0.05 mol% and 0.025 mol% [Pd] loading under standard conditions (Scheme 4), indicating high reactivity of the catalyst system.

Scheme 3. Mechanistic Studies



Scheme 4. Determination of TON



Conclusions

In conclusion, we have reported a highly efficient protocol for the Suzuki–Miyaura cross-coupling of aryl fluorosulfonates mediated by well-defined, air- and moisture-stable NHC–Pd(II) chloro dimers. The scope of this operationally-trivial method

has been found to be excellent. These phosphine-free conditions feature low catalyst loading in the presence of a mild phosphate base in aqueous solution. The protocol tolerates a variety of sensitive substituents and can be applied to challenging aryl boronic acids. In a broader sense, 'click' fluorosulfonates balance high –O–X stability and accessible C–O dissociation energy that renders them highly attractive substrates for cross-coupling of phenolic bonds. Fast-activating, well-defined and highly reactive Pd(II)–NHCs offer major practical advantage in activation of –OFs group as phenolic aryl halide surrogates.

Experimental Section

List of Known Compounds/General Methods

All starting materials reported in the manuscript have been previously described in literature or prepared by the method reported previously unless stated otherwise. Aryl fluorosulfonates were prepared by standard methods.[9-11] All experiments were performed using standard Schlenk techniques under nitrogen or argon unless stated otherwise. All solvents were purchased at the highest commercial grade and used as received or after purification by passing through activated alumina columns or distillation from sodium/benzophenone under nitrogen. All solvents were deoxygenated prior to use. All other chemicals were purchased at the highest commercial grade and used as received. All other general methods have been published.[14a] ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded in $CDCl_3$ on Bruker spectrometer at 500 MHz (^{1}H NMR), 126 MHz (^{13}C NMR) and 471 MHz (^{19}F NMR). ^{1}H NMR and ^{13}C NMR shifts are reported in parts per million (ppm) relative to residual $CHCl_3$ peak. All coupling constants (*J*) are reported in Hertz (Hz). ^{1}H NMR, ^{13}C NMR and ^{19}F NMR data are given for all starting materials for characterization purposes.

General Procedure for the Synthesis of Starting Materials. All aryl fluorosulfonates used in this study were prepared by procedures reported in the literature.[9-11] Spectroscopic data matched those reported in the literature. Pd–NHC complexes were synthesized according to the literature[14] or purchased from Sigma-Aldrich. $[Pd(NHC)(\mu\text{-}Cl)Cl]_2$ was purchased from Sigma-Aldrich.

General Procedure for the Synthesis of Aryl Sulfonates. To a solution of phenol (20.0 mmol, 1.00 equiv) and Et_3N (20.0 mmol, 1.00 equiv) in CH_2Cl_2 (25.0 mL), SO_2F_2 was introduced by a needle from balloon filled with SO_2F_2. For large scale reactions such as described in this procedure, depletion of the sulfuryl fluoride from the balloon is easily observed, and more SO_2F_2 can be added when required. The reaction mixture was stirred vigorously overnight at room temperature. The solvent was removed in vacuo and the crude product was purified by flash chromatography on silica gel (EtOAc/hexanes). **Cautionary Note:** Care should be taken when handling SO_2F_2. Nevertheless, it should be noted that SO_2F_2 is relatively safe and not toxic as determined by cell and animal in vivo experiments.[7a]

Phenyl sulfurofluoridate (1a)[9a]

According to general procedure, 2.82 g of **1a** was obtained as a colorless oil after chromatography (EtOAc/hexanes = 1:10). Yield, 80%. 1H NMR (500 MHz, $CDCl_3$) δ 7.49 (t, *J* = 7.8 Hz, 2H), 7.42 (t, *J* = 7.4 Hz, 1H), 7.35 (d, *J* = 7.9 Hz, 3H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 150.1, 130.4, 128.7, 120.9. 19F NMR (471 MHz, $CDCl_3$): δ 37.49.

4-Methoxyphenyl sulfurofluoridate (1b)[9a]

According to general procedure, 3.01 g of **1b** was obtained as a colorless oil after chromatography (EtOAc/hexanes = 1:10). Yield, 73%. 1H NMR (500 MHz, $CDCl_3$) δ 7.13 (d, *J* = 9.3 Hz, 2H), 6.82 (d, *J* = 9.3 Hz, 2H), 3.69 (s, 3H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 159.3, 143.6, 122.0, 115.2, 55.7. 19F NMR (471 MHz, $CDCl_3$) δ 36.26.

***p*-Tolyl sulfurofluoridate (1c)**[9a]

According to general procedure, 2.85 g of **1c** was obtained as a colorless oil after chromatography (EtOAc/hexanes = 1:10). Yield, 75%. 1H NMR (500 MHz, $CDCl_3$) δ 7.16 (d, *J* = 8.7 Hz, 2H), 7.12 (d, *J* = 8.7 Hz, 2H), 2.35 (s, 3H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 148.1, 138.8, 130.8, 120.5, 20.9. 19F NMR (471 MHz, $CDCl_3$) δ 37.05.

4-(Trifluoromethyl)phenyl sulfurofluoridate (1d)[9a]

According to general procedure, 3.79 g of **1d** was obtained as a colorless oil after chromatography (EtOAc/hexanes = 1:10). Yield, 78%. 1H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.8 Hz, 2H), 7.49 (d, *J* = 8.5 Hz, 2H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 152.0, 131.1 (q, *J* = 33.8 Hz), 127.9 (q, *J* = 3.6 Hz), 123.3 (q, *J* = 273.4 Hz), 121.60. 19F NMR (471 MHz, $CDCl_3$) δ 38.65, -62.71.

2,4-Dimethylphenyl sulfurofluoridate (1e)[9a]

According to general procedure, 3.26 g of **1e** was obtained as a colorless oil after chromatography (EtOAc/hexanes = 1:10). Yield, 80%. 1H NMR (500 MHz, $CDCl_3$) δ 7.20 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.12 (s, 1H), 7.08 (dd, *J* = 8.4, 2.3 Hz, 1H), 2.35 (s, 6H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 147.1, 138.6, 132.8, 130.1, 128.2, 120.6, 20.8, 16.2. 19F NMR (471 MHz, $CDCl_3$) δ 38.58.

2-Isopropyl-5-methylphenyl sulfurofluoridate (1f)[9a]

According to general procedure, 3.80 g of **1f** was obtained as a colorless oil after chromatography (EtOAc/hexanes = 1:10). Yield, 82%. 1H NMR (500 MHz, $CDCl_3$) δ 7.16 (d, *J* = 8.7 Hz, 2H), 7.12 (d, *J* = 8.7 Hz, 2H), 2.35 (s, 3H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 148.1, 138.8, 130.8, 120.5, 20.9. 19F NMR (471 MHz, $CDCl_3$) δ 37.05.

Ethyl 4-((fluorosulfonyl)oxy)benzoate (1g)[9a]

According to general procedure, 3.72 g of **1g** was obtained as a colorless oil after chromatography (EtOAc/hexanes = 1:10). Yield, 75%. 1H NMR (500 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.9 Hz, 2H), 7.38 (d, *J* = 9.0 Hz, 2H), 4.37 (q, *J* = 7.2 Hz, 2H), 1.37 (t, *J* = 7.2 Hz, 3H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 164.9, 152.8, 132.0, 131.0, 120.9, 61.6, 14.3. ^{19}F NMR (471 MHz, $CDCl_3$) δ 38.49.

Benzo[*d*][1,3]dioxol-5-yl sulfurofluoridate (1h)[9a]

According to general procedure, 3.52 g of **1h** was obtained as a colorless oil after chromatography (EtOAc/hexanes = 1:10). Yield, 80%. 1H NMR (500 MHz, $CDCl_3$) δ 6.85 – 6.79 (m, 3H), 6.04 (d, *J* = 1.3 Hz, 2H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 148.6, 147.6, 144.0, 114.0, 108.3, 103.0, 102.5. ^{19}F NMR (471 MHz, $CDCl_3$) δ 36.51.

6-Methylpyridin-3-yl sulfurofluoridate (1i)[9a]

According to general procedure, 2.90 g of **1i** was obtained as a colorless oil after chromatography (EtOAc/hexanes = 1:3). Yield, 76%. 1H NMR (500 MHz, $CDCl_3$) δ 8.46 (d, *J* = 3.0 Hz, 1H), 7.51 (dd, *J* = 8.6, 2.9 Hz, 1H), 7.21 (d, *J* = 8.6 Hz, 1H),

2.54 (s, 3H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 159.0, 145.2, 141.6, 128.7, 124.2, 23.9. ^{19}F NMR (471 MHz, $CDCl_3$) δ 37.90.

General Procedure for the Suzuki-Miyaura Cross-Coupling of Aryl Fluorosulfonates. An oven-dried vial equipped with a stir bar was charged with an aryl fluorosulfonate (typically, 0.2 mmol, 1.0 equiv), potassium phosphate (typically, 0.6 mmol, 3.0 equiv), boronic acid (typically, 0.4 mmol, 2.0 equiv), $[(IPr)Pd(\mu\text{-}Cl)Cl]_2$ (typically, 0.10 mol%), placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. THF and H_2O (typically, 0.25 M as 2:1 (v/vol)) were added. The reaction was placed in a preheated oil bath and stirred at 60 °C for 12 h. After the indicated time, the reaction mixture was cooled down, diluted with ethyl acetate (5 mL), washed with H_2O, extracted with ethyl acetate (3 x 2 mL) and concentrated. The sample was analyzed by ^1H NMR ($CDCl_3$, 500 MHz) and GC-MS to obtain conversion and yield using internal standard and comparison with authentic samples. Purification by chromatography on silica gel (EtOAc/hexanes) afforded the title products.

Procedure for the Suzuki-Miyaura Cross-Coupling of Aryl Fluorosulfonates. Gram Scale. An oven-dried 100 mL flask equipped with a stir bar was charged with phenyl sulfurofluoridate (10.0 mmol, 1.76 g, 1.0 equiv), 4-methoxyphenylboronic acid (12.0 mmol, 1.82 g, 1.2 equiv), potassium phosphate (15.0 mmol, 3.18 g, 1.5 equiv), and $[(IPr)Pd(\mu\text{-}Cl)Cl]_2$ (0.01 mmol, 12 mg, 0.10 mol%) placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. THF (30 mL) and H_2O (15 mL) were added (0.67 M). The reaction was placed in a preheated oil bath at 60 °C and stirred for 12 h. After the indicated time, the reaction mixture was cooled down, diluted with ethyl acetate (50 mL), washed with H_2O, extracted with ethyl acetate (3 x 20 mL) and concentrated. Purification by flash chromatography on silica gel (EtOAc/hexanes = 1:20) afforded the title product **3a** in 98% yield (1.8 g). Spectroscopic data are included in the section below.

4-Methoxy-1,1'-biphenyl (3a)

According to the general procedure, the reaction of **1a** (0.20 mmol, 35.2 mg), **2a** (4-methoxyphenylboronic acid, 0.40 mmol, 60.8 mg), K_3PO_4 (0.60 mmol, 127.2 mg), and $[(IPr)Pd(\mu\text{-}Cl)Cl]_2$ (0.0002 mmol, 0.23 mg) in THF/H_2O = 2:1 (v/vol) mix solution (0.8 mL in all, 0.25M) for 12 h at 60 °C, afforded after work-up and chromatography (EtOAc/hexanes = 1:20) the title product in 99 % yield (36 mg). White solid. 1H NMR (500 MHz, $CDCl_3$) δ 7.58-7.52 (m, 4H), 7.42 (t, *J* = 7.7 Hz, 2H), 7.31 (t, *J* = 7.3 Hz, 1H), 6.99 (d, *J* = 8.7 Hz, 2H), 3.86 (s, 3H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 159.2, 140.9, 133.8, 128.7, 128.2, 126.8, 126.7, 114.2, 55.4. NMR spectroscopic data agreed with literature values.[9a]

4-Methyl-1,1'-biphenyl (3b)

According to the general procedure, the reaction of **1a** (0.20 mmol, 35.2 mg), **2b** (4-Methylphenylboronic acid, 0.40 mmol, 54.4 mg), K_3PO_4 (0.60 mmol, 127.2 mg), and $[(IPr)Pd(\mu\text{-}Cl)Cl]_2$ (0.0002 mmol, 0.23 mg) in THF/H_2O = 2:1 (v/vol) mix solution (0.8 mL in all, 0.25M) for 12 h at 60 °C, afforded after work-up and chromatography (EtOAc/hexanes = 1:20) the title product in 98 % yield (33 mg). White solid. 1H NMR (500 MHz, $CDCl_3$) δ 7.59 (d, *J* = 6.8 Hz, 2H), 7.50 (d, *J* = 8.1 Hz, 2H), 7.43 (t, *J* = 7.7 Hz, 2H), 7.33 (t, *J* = 7.4 Hz, 1H), 7.28 – 7.25 (m, 2H), 2.40 (s, 3H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 141.2, 138.4, 137.0, 136.7, 129.5, 128.7, 127.0, 127.0, 21.1. NMR spectroscopic data agreed with literature values.[9a]

4-(*tert*-Butyl)-1,1'-biphenyl (3c)

According to the general procedure, the reaction of **1a** (0.20 mmol, 35.2 mg), **2c** (4-*tert*-Butylphenylboronic acid, 0.40 mmol, 71.2 mg), K_3PO_4 (0.60 mmol, 127.2 mg), and $[(IPr)Pd(\mu\text{-}Cl)Cl]_2$ (0.0002 mmol, 0.23 mg) in THF/H_2O = 2:1 (v/vol) mix solution (0.8 mL in all, 0.25M) for 12 h at 60 °C, afforded after work-up and chromatography (EtOAc/hexanes = 1:20) the title product in 98 % yield (41 mg). Colorless oil. 1H NMR (500 MHz, $CDCl_3$) δ 7.61 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.56 (d, *J* = 8.4 Hz, 2H), 7.48 (d, *J* = 8.5 Hz, 2H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.34 (t, *J* = 7.4 Hz, 1H), 1.38 (s, 9H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 150.3, 141.1, 138.4, 128.7, 127.1, 127.0, 126.8, 125.7, 34.6, 31.4. NMR spectroscopic data agreed with literature values.[15]

4-(Trifluoromethyl)-1,1'-biphenyl (3d)

According to the general procedure, the reaction of **1a** (0.20 mmol, 35.2 mg), **2d** (4-Trifluoromethylphenylboronic acid, 0.40 mmol, 76.0 mg), K_3PO_4 (0.60 mmol, 127.2 mg), and $[(IPr)Pd(\mu\text{-}Cl)Cl]_2$ (0.0002 mmol, 0.23 mg) in THF/H_2O = 2:1 (v/vol) mix solution (0.8 mL in all, 0.25M) for 12 h at 60 °C, afforded after work-up and chromatography (EtOAc/hexanes = 1:20) the title product in 92 % yield (42 mg). White solid. 1H NMR (500 MHz, $CDCl_3$) δ 7.70 (s, 4H), 7.61 (d, *J* = 6.9 Hz, 2H), 7.48 (t, *J* = 7.5 Hz, 2H), 7.44 – 7.38 (m, 1H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 144.8, 139.8, 129.4 (q, *J* = 32.4 Hz), 129.0, 128.2, 127.4, 127.3, 125.7 (q, *J* = 3.7 Hz), 124.3 (q, *J* = 272.0 Hz). 19F NMR (471 MHz, $CDCl_3$) δ -62.39. NMR spectroscopic data agreed with literature values.[9a]

2-Methyl-1,1'-biphenyl (3e)

According to the general procedure, the reaction of **1a** (0.20 mmol, 35.2 mg), **2e** (2-Methylphenylboronic acid, 0.40 mmol, 54.4 mg), K_3PO_4 (0.60 mmol, 127.2 mg), and $[(IPr)Pd(\mu\text{-}Cl)Cl]_2$ (0.0002 mmol, 0.23 mg) in THF/H_2O = 2:1 (v/vol) mix solution (0.8 mL in all, 0.25M) for 12 h at 60 °C, afforded after work-up and chromatography (EtOAc/hexanes = 1:20) the title product in 92 % yield (31 mg). Colorless oil. 1H NMR (500 MHz, $CDCl_3$) δ 7.41 (t, *J* = 7.4 Hz, 2H), 7.36 – 7.31 (m, 3H), 7.28 – 7.27 (m, 1H), 7.24 (t, *J* = 2.6 Hz, 2H), 2.28 (s, 3H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 142.0, 141.9, 135.3, 130.3, 129.8, 129.2, 128.1, 127.2, 126.8, 125.7, 20.5. NMR spectroscopic data agreed with literature values.[16]

1-([1,1'-Biphenyl]-4-yl)ethan-1-one (3f)

According to the general procedure, the reaction of **1a** (0.20 mmol, 35.2 mg), **2f** (4-Acetylphenylboronic acid, 0.40 mmol, 65.6 mg), K_3PO_4 (0.60 mmol, 127.2 mg), and $[(IPr)Pd(\mu\text{-}Cl)Cl]_2$ (0.0002 mmol, 0.23 mg) in THF/H_2O = 2:1 (v/vol) mix solution (0.8 mL in all, 0.25M) for 12 h at 60 °C, afforded after work-up and chromatography (EtOAc/hexanes = 1:10) the title product in 94 % yield (37 mg). White solid. 1H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.3 Hz, 2H), 7.69 (d, *J* = 8.2 Hz, 2H), 7.63 (d, *J* = 7.1 Hz, 2H), 7.48 (t, *J* = 7.7 Hz, 2H), 7.41 (t, *J* = 7.2 Hz, 1H), 2.64 (s, 2H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 197.8, 145.8, 139.9, 135.9, 129.0, 128.9, 128.2, 127.3, 127.2, 26.7. NMR spectroscopic data agreed with literature values.[9a]

Methyl [1,1'-biphenyl]-4-carboxylate (3g)

According to the general procedure, the reaction of **1a** (0.20 mmol, 35.2 mg), **2g** (4-(Methoxycarbonyl)phenylboronic acid, 0.40 mmol, 72.0 mg), K_3PO_4 (0.60 mmol, 127.2 mg), and $[(IPr)Pd(\mu\text{-}Cl)Cl]_2$ (0.0002 mmol, 0.23 mg) in THF/H_2O = 2:1 (v/vol) mix solution (0.8 mL in all, 0.25M) for 12 h at 60 °C, afforded after work-up and chromatography (EtOAc/hexanes = 1:20) the title product in 92 % yield (39 mg). White solid. 1H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.4 Hz, 2H), 7.74 – 7.53 (m, 4H), 7.47 (t, *J* = 7.5 Hz, 2H), 7.43 – 7.37 (m, 1H), 3.95 (s, 3H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 167.0, 145.7, 140.0, 130.1, 128.95, 128.92, 128.2, 127.3, 127.1, 52.1. NMR spectroscopic data agreed with literature values.[17]

3-Nitro-1,1'-biphenyl (3h)

According to the general procedure, the reaction of **1a** (0.20 mmol, 35.2 mg), **2h** (3-Nitrophenylboronic acid, 0.40 mmol, 66.8 mg), K_3PO_4 (0.60 mmol, 127.2 mg), and $[(IPr)Pd(\mu\text{-}Cl)Cl]_2$ (0.0006 mmol, 0.67 mg) in THF/H_2O = 2:1 (v/vol) mix solution (0.8 mL in all, 0.25M) for 12 h at 60 °C, afforded after work-up and chromatography (EtOAc/hexanes = 1:20) the title product in 75 % yield (29 mg). Pale yellow solid. 1H NMR (500 MHz, $CDCl_3$) δ 8.46 (s, 1H), 8.20 (dd, *J* = 8.3, 2.3 Hz, 1H), 7.92 (d, *J* = 7.6 Hz, 1H), 7.71 – 7.57 (m, 3H), 7.50 (t, *J* = 7.6 Hz, 2H), 7.44 (t, *J* = 7.3 Hz, 1H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 148.8, 142.9, 138.7, 133.1, 129.7, 129.2, 128.6, 127.2, 122.1, 122.0. NMR spectroscopic data agreed with literature values.[18]

[1,1'-Biphenyl]-3-carbonitrile (3i)

According to the general procedure, the reaction of **1a** (0.20 mmol, 35.2 mg), **2i** (3-Cyanophenylboronic acid phenylboronic acid, 0.40 mmol, 59.6 mg), K_3PO_4 (0.60 mmol, 127.2 mg), and $[(IPr)Pd(\mu\text{-}Cl)Cl]_2$ (0.0006 mmol, 0.67 mg) in THF/H_2O = 2:1 (v/vol) mix solution (0.8 mL in all, 0.25M) for 12 h at 60 °C, afforded after work-up and chromatography (EtOAc/hexanes = 1:20) the title product in 78 % yield (28 mg). White solid. 1H NMR (500 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.82 (d, *J* = 7.9 Hz, 1H), 7.63 (d, *J* = 7.7 Hz, 1H), 7.59 – 7.52 (m, 6H), 7.48 (t, *J* = 7.5 Hz, 2H), 7.42 (t, *J* = 7.3 Hz, 1H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 142.5, 138.9, 131.5, 130.7, 130.7, 129.6, 129.2, 128.4, 127.1, 118.9, 113.1. NMR spectroscopic data agreed with literature values.[19]

***tert*-Butyl [1,1'-biphenyl]-4-ylcarbamate (3j)**

According to the general procedure, the reaction of **1a** (0.20 mmol, 35.2 mg), **2j** (4-*tert*-butoxycarbonylamino phenylboronic acid, 0.40 mmol, 94.8 mg), K_3PO_4 (0.60 mmol, 127.2 mg), and $[(IPr)Pd(\mu\text{-}Cl)Cl]_2$ (0.0002 mmol, 0.23 mg) in THF/H_2O = 2:1 (v/vol) mix solution (0.8 mL in all, 0.25M) for 12 h at 60 °C, afforded after work-up and chromatography (EtOAc/hexanes = 1:10) the title product in 98 % yield (53 mg). Pale yellow oil. 1H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.6 Hz, 2H), 7.53 (d, *J* = 8.6 Hz, 2H), 7.47 – 7.39 (m, 4H), 7.32 (t, *J* = 7.4 Hz, 1H), 6.54 (s, 1H), 1.54 (s, 9H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 152.7, 140.7, 137.7, 136.0, 128.8, 127.6, 126.9, 126.8, 118.8, 28.4. NMR spectroscopic data agreed with literature values.[20]

[1,1'-Biphenyl]-4-ol (3k)

According to the general procedure, the reaction of **1a** (0.20 mmol, 35.2 mg), **2k** (4-hydroxyl phenylboronic acid, 0.40 mmol, 55.2 mg), K_3PO_4 (0.60 mmol, 127.2 mg), and $[(IPr)Pd(\mu\text{-}Cl)Cl]_2$ (0.0002 mmol, 0.23 mg) in THF/H_2O = 2:1 (v/vol) mix solution (0.8 mL in all, 0.25M) for 12 h at 60 °C, after work-up (with 1N HCl instead of H_2O) and chromatography (EtOAc/hexanes = 1:5) the corresponding compound was afforded in 88 % yield (30 mg). White crystal. 1H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.5 Hz, 2H), 7.48 (d, *J* = 6.8 Hz, 2H), 7.42 (t, *J* = 7.3 Hz, 2H), 7.33 – 7.28 (m, 1H), 6.91 (d, *J* = 6.8 Hz, 2H), 4.83 (s, 1H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 155.1, 140.8, 134.1, 128.7, 128.4, 126.74, 126.73, 115.7. NMR spectroscopic data agreed with literature values.[21]

3,4,5-Trifluoro-1,1'-biphenyl (3l)

According to the general procedure, the reaction of **1a** (0.20 mmol, 35.2 mg), **2l** (3,4,5-Trifluoro phenylboronic acid, 0.40 mmol, 70.4 mg), K_3PO_4 (0.60 mmol, 127.2 mg), and $[(IPr)Pd(\mu\text{-}Cl)Cl]_2$ (0.0006 mmol, 0.67 mg) in THF/H_2O = 2:1 (v/vol) mix solution (0.8 mL in all, 0.25M) for 12 h at 60 °C, afforded after work-up and chromatography (EtOAc/hexanes = 1:20) the title product in 96 % yield (40 mg). Colorless oil. 1H NMR (500 MHz, $CDCl_3$) δ 7.52 – 7.49 (m, 2H), 7.46 (t, *J* = 7.4 Hz, 1H), 7.42 – 7.37 (m, 1H), 7.23 – 7.15 (m, 2H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 152.4 (dd, *J* = 10.0, 4.4 Hz), 150.5 (dd, *J* = 10.1, 4.3 Hz), 140.3 (t, *J* = 15.4 Hz), 138.2 (dd, *J* = 3.1 Hz, 2.5 Hz), 137.4 (td, *J* = 7.8, 4.6 Hz). 129.1, 128.4, 126.9. 19F NMR (471 MHz, $CDCl_3$) δ -134.22, -162.78. NMR spectroscopic data agreed with literature values.[22]

2,4-Difluoro-1,1'-biphenyl (3m)

According to the general procedure, the reaction of **1a** (0.20 mmol, 35.2 mg), **2m** (2,4-Difluoro phenylboronic acid, 0.40 mmol, 55.2 mg), K_3PO_4 (0.60 mmol, 127.2 mg), and $[(IPr)Pd(\mu\text{-}Cl)Cl]_2$ (0.001 mmol, 1.15 mg) in THF/H_2O = 2:1 (v/vol) mix solution (0.8 mL in all, 0.25M) for 12 h at 80 °C, afforded after work-up and chromatography (EtOAc/hexanes = 1:20) the title product in 84 % yield (32 mg). Colorless oil. 1H NMR (500 MHz, $CDCl_3$) δ 7.53 – 7.47 (m, 2H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.41 – 7.35 (m, 2H), 7.00 – 6.87 (m, 2H). 128.93 (d, *J* = 2.9 Hz), 111.54 (dd, *J* = 21.0, 3.8 Hz). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 162.3 (d, *J* = 249.5 Hz, 11.8 Hz), 159.7 (d, *J* = 251.5 Hz, 11.8 Hz), 135.0, 131.5 (dd, *J* = 9.5, 5.0 Hz), 128.9 (d, *J* = 2.9 Hz), 128.5, 127.8, 125.4, 111.5 (dd, *J* = 21.0, 3.8 Hz), 104.4 (dd, *J* = 26.7, 25.5 Hz). 19F NMR (471 MHz, $CDCl_3$) δ -111.59, -113.64. NMR spectroscopic data agreed with literature values.[23]

2,6-Difluoro-4-methoxy-1,1'-biphenyl (3n)

According to the general procedure, the reaction of **1a** (0.20 mmol, 35.2 mg), **2n** (2,6-Difluoro-4-methoxy phenylboronic acid, 0.40 mmol, 75.2 mg), K_3PO_4 (0.60 mmol, 127.2 mg), and $[(IPr)Pd(\mu\text{-}Cl)Cl]_2$ (0.001 mmol, 1.15 mg) in THF/H_2O = 2:1 (v/vol) mix solution (0.8 mL in all, 0.25M) for 12 h at 80 °C, afforded after work-up and chromatography (EtOAc/hexanes = 1:20) the title product in 90 % yield (40 mg). White solid. ^1H NMR (500 MHz, $CDCl_3$) δ 1H NMR (500 MHz, $CDCl_3$) δ 7.46 – 7.41 (m, 4H), 7.37 (heptet, *J* = 4.3 Hz, 1H), 6.60 – 6.50 (m, 2H), 3.83 (s, 3H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 160.6 (dd, *J* = 246.6, 10.4 Hz), 160.0 (t, *J* = 14.2 Hz),130.4, 130.4, 129.4, 128.2, 127.8, 110.9 (d, *J* = 19.7 Hz), 98.2 (d, *J* = 30.2 Hz), 55.8. 19F NMR (471 MHz, $CDCl_3$) δ -113.68. NMR spec-troscopic data agreed with literature values.[23]

2-Phenylnaphthalene (3o)

According to the general procedure, the reaction of **1a** (0.20 mmol, 35.2 mg), **2o** (Naphthalen-2-ylboronic acid, 0.40 mmol,

68.8 mg), K_3PO_4 (0.60 mmol, 127.2 mg), and [(IPr)Pd(μ-Cl)Cl]$_2$ (0.0002 mmol, 0.23 mg) in THF/H_2O = 2:1 (v/vol) mix solution (0.8 mL in all, 0.25M) for 12 h at 60 °C, afforded after work-up and chromatography (EtOAc/hexanes = 1:25) the title product in 98 % yield (40 mg). White solid. 1H NMR (500 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.92 (t, *J* = 8.7 Hz, 2H), 7.88 (d, *J* = 7.9 Hz, 1H), 7.79 – 7.70 (m, 3H), 7.55 – 7.46 (m, 3H), 7.39 (t, *J* = 7.3 Hz, 1H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 140.1, 137.5, 132.6, 131.6, 127.8, 127.4, 127.2, 126.6, 126.4, 126.3, 125.3, 124.9, 124.8, 124.6. NMR spectroscopic data agreed with literature values.[9a]

1-Phenylpyrene (3p)

According to the general procedure, the reaction of **1a** (0.20 mmol, 35.2 mg), **2p** (Pyren-1-ylboronic acid, 0.40 mmol, 98.4 mg), K_3PO_4 (0.60 mmol, 127.2 mg), and [(IPr)Pd(μ-Cl)Cl]$_2$ (0.0002 mmol, 0.23 mg) in THF/H_2O = 2:1 (v/vol) mix solution (0.8 mL in all, 0.25M) for 12 h at 60 °C, afforded after work-up and chromatography (EtOAc/hexanes = 1:25) the title product in 85 % yield (47 mg). Pale yellow solid. 1H NMR (500 MHz, $CDCl_3$) δ 8.25 – 8.16 (m, 4H), 8.10 (d, *J* = 8.5 Hz, 2H), 8.05 – 7.98 (m, 3H), 7.66 (d, *J* = 7.5 Hz, 2H), 7.59 (t, *J* = 7.7 Hz, 2H), 7.54 – 7.48 (m, 1H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 141.3, 137.8, 131.5, 131.2, 131.0, 130.6, 128.4, 127.6, 127.5, 127.5, 127.4, 127.3, 126.0, 125.9, 125.3, 125.1, 125.0, 124.9, 124.7. NMR spectroscopic data agreed with literature values.[24]

4-Phenyldibenzo[*b*,*d*]furan (3q)

According to the general procedure, the reaction of **1a** (0.20 mmol, 35.2 mg), **2q** (dibenzo[b,d]furan-4-ylboronic acid, 0.40 mmol, 84.8 mg), K_3PO_4 (0.60 mmol, 127.2 mg), and [(IPr)Pd(μ-Cl)Cl]$_2$ (0.0002 mmol, 0.23 mg) in THF/H_2O = 2:1 (v/vol) mix solution (0.8 mL in all, 0.25M) for 12 h at 60 °C, afforded after work-up and chromatography (EtOAc/hexanes = 1:20) the title product in 94 % yield (52 mg). White solid. 1H NMR (500 MHz, CDCl3) δ 8.01 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.97 – 7.91 (m, 3H), 7.64 – 7.60 (m, 2H), 7.56 (t, *J* = 7.7 Hz, 2H), 7.51-7.42 (m, 3H), 7.41 – 7.35 (m, 1H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 156.2, 153.4, 136.5, 128.9, 128.7, 127.8, 127.3, 126.9, 125.9, 125.0, 124.3, 123.2, 122.8, 120.7, 119.7, 111.9. NMR spectroscopic data agreed with literature values.[25]

***tert*-Butyl 2-phenyl-1*H*-pyrrole-1-carboxylate (3r)**

According to the general procedure, the reaction of **1a** (0.20 mmol, 35.2 mg), **2r** (1-*tert*-butoxycarbonyl-1H-pyrrol-2-yl-boronic acid 0.4 mmol, 84.4 mg), K_3PO_4 (0.60 mmol, 127.2 mg), and [(IPr)Pd(μ-Cl)Cl]$_2$ (0.0002 mmol, 0.23 mg) in THF/H_2O = 2:1 (v/vol) mix solution (0.8 mL in all, 0.25M) for 12 h at 60 °C, afforded after work-up and chromatography (EtOAc/hexanes = 1:20) the title product in 72 % yield (35 mg). Pale yellow oil. 1H NMR (500 MHz, $CDCl_3$) δ 7.36 – 7.33 (m, 5H), 7.32 – 7.27 (m, 1H), 6.23 (t, *J* = 3.3 Hz, 1H), 6.19 (dd, *J* = 3.3, 1.8 Hz, 1H), 1.35 (s, 9H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 149.4, 135.0, 134.5, 129.2, 127.6, 127.2, 122.5, 114.4, 110.6, 83.6, 27.6. NMR spectroscopic data agreed with literature values.[26]

2-Methoxy-5-phenylpyridine (3s)

According to the general procedure, the reaction of **1a** (0.20 mmol, 35.2 mg), **2s** (6-methoxypyridin-3-yl-boronic acid, 0.40 mmol, 71.2 mg), K_3PO_4 (0.60 mmol, 127.2 mg), and [(IPr)Pd(μ-Cl)Cl]$_2$ (0.0002 mmol, 0.23 mg) in THF/H_2O = 2:1 (v/vol) mix solution (0.8 mL in all, 0.25M) for 12 h at 60 °C, afforded after work-up and chromatography (EtOAc/hexanes = 1:5) the title product in 95 % yield (29 mg). White solid. 1H NMR (500 MHz, $CDCl_3$) δ 8.40 (s, 1H), 7.79 (dd, *J* = 8.6, 2.5 Hz, 1H), 7.53 (d, *J* = 7.6 Hz, 2H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.35 (t, *J* = 7.6 Hz, 1H), 6.82 (d, *J* = 8.6 Hz, 1H), 3.99 (s, 3H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 1127.2, 145.0, 137.9, 137.5, 130.1, 129.0, 127.3, 126.7, 110.8, 53.6. NMR spectroscopic data agreed with literature values.[27]

4-Phenylpyridine (3t)

According to the general procedure, the reaction of **1a** (0.20 mmol, 35.2 mg), **2t** (Pyridin-4-ylboronic acid, 0.40 mmol, 49.2 mg), K_3PO_4 (0.60 mmol, 127.2 mg), and [(IPr)Pd(μ-Cl)Cl]$_2$ (0.001 mmol, 1.15 mg) in THF/H_2O = 2:1 (v/vol) mix solution (0.8 mL in all, 0.25M) for 12 h at 80 °C, afforded after work-up and chromatography (EtOAc/hexanes = 1:5) the title product in 79 % yield (24 mg). White solid. 1H NMR (500 MHz, $CDCl_3$) δ 8.60 (d, *J* = 5.1 Hz, 2H), 7.58 (d, *J* = 7.3 Hz, 2H), 7.50 (d, *J* = 4.9 Hz, 2H), 7.46-7.36 (m, 3H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 149.4, 149.2, 137.8, 129.4, 129.2, 127.1, 121.9. NMR spectroscopic data agreed with literature values.[28]

2-Phenylthiophene (3u)

According to the general procedure, the reaction of **1a** (0.20 mmol, 35.2 mg), **2u** (thiophen-2-ylboronic acid, 0.40 mmol, 51.2 mg), K_3PO_4 (0.60 mmol, 127.2 mg), and [(IPr)Pd(μ-Cl)Cl]$_2$ (0.0002 mmol, 0.23 mg) in THF/H_2O = 2:1 (v/vol) mix solution (0.8 mL in all, 0.25M) for 12 h at 60 °C, afforded after work-up and chromatography (EtOAc/hexanes = 1:20) the title product in 83 % yield (26 mg). Pale yellow oil. 1H NMR (500 MHz, $CDCl_3$) δ 7.61 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.46 (dd, *J* = 2.6, 1.7 Hz, 1H), 7.43 – 7.37 (m, 4H), 7.34 – 7.27 (m, 1H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 142.4, 135.9, 128.8, 127.2, 126.48, 126.37, 126.21, 120.29. NMR spectroscopic data agreed with literature values.[29]

(*E*)-1,2-Diphenylethene (3v)

According to the general procedure, the reaction of **1a** (0.20 mmol, 35.2 mg), **2v** ((E)-Styrylboronic acid, 0.40 mmol, 59.2 mg), K_3PO_4 (0.60 mmol, 127.2 mg), and [(IPr)Pd(μ-Cl)Cl]$_2$ (0.001 mmol, 1.15 mg) in THF/H_2O = 2:1 (v/vol) mix solution (0.8 mL in all, 0.25M) for 12 h at 80 °C, afforded after work-up and chromatography (EtOAc/hexanes = 1:20) the title product in 88 % yield (31 mg). White solid. 1H NMR (500 MHz, $CDCl_3$) δ 7.63 – 7.48 (m, 4H), 7.39 (ddt, *J* = 8.0, 3.7, 1.9 Hz, 4H), 7.33 – 7.26 (m, 4H), 7.14 (d, *J* = 1.7 Hz, 2H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 137.4, 128.7, 127.7, 126.6. NMR spectroscopic data agreed with literature values.[30]

4-Methoxy-1,1'-biphenyl (3a')

According to the general procedure, the reaction of **1b** (0.20 mmol, 41.2 mg), **2w** (Phenylboronic acid, 0.40 mmol, 48.8 mg), K_3PO_4 (0.60 mmol, 127.2 mg), and [(IPr)Pd(μ-Cl)Cl]$_2$ (0.0002 mmol, 0.23 mg) in THF/H_2O = 2:1 (v/vol) mix solution (0.8 mL in all, 0.25M) for 12 h at 60 °C, afforded after work-up and chromatography (EtOAc/hexanes = 1:20) the title product in 95 % yield (34 mg). White solid. 1H NMR (500 MHz, $CDCl_3$) δ 7.60 – 7.51 (m, 4H), 7.42 (t, *J* = 7.7 Hz, 2H), 7.31 (t, *J* = 7.4 Hz, 1H), 6.86 (s, 3H), 3.86 (s, 4H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 159.2, 140.9, 133.8, 128.7, 128.2, 126.8, 126.7, 114.2, 55.4. NMR spectroscopic data agreed with literature values.[9a]

4-Methyl-1,1'-biphenyl (3b')

According to the general procedure, the reaction of **1c** (0.20 mmol, 38.0 mg), **2w** (Phenylboronic acid, 0.40 mmol, 48.8 mg), K_3PO_4 (0.60 mmol, 127.2 mg), and [(IPr)Pd(μ-Cl)Cl]$_2$ (0.0002 mmol, 0.23 mg) in THF/H_2O = 2:1 (v/vol) mix solution (0.8 mL in all, 0.25M) for 12 h at 60 °C, afforded after work-up and chromatography (EtOAc/hexanes = 1:20) the title product in 95 % yield (32 mg). White solid. 1H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 6.9 Hz, 2H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.43 (t, *J* = 7.7 Hz, 2H), 7.33 (t, *J* = 7.5 Hz, 1H), 7.28 – 7.23 (m, 2H), 2.40 (s, 3H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 141.2, 138.4, 137.0, 129.5, 128.7, 127.0, 126.8, 21.1. NMR spectroscopic data agreed with literature values.[9a]

4-(Trifluoromethyl)-1,1'-biphenyl (3d')

According to the general procedure, the reaction of **1d** (0.20 mmol, 48.8 mg), **2w** (Phenylboronic acid, 0.40 mmol, 48.8 mg), K_3PO_4 (0.60 mmol, 127.2 mg), and [(IPr)Pd(μ-Cl)Cl]$_2$ (0.0002 mmol, 0.23 mg) in THF/H_2O = 2:1 (v/vol) mix solution (0.8 mL in all, 0.25M) for 12 h at 60 °C, afforded after work-up and chromatography (EtOAc/hexanes = 1:20) the title product in 99 % yield (45 mg). White solid. 1H NMR (500 MHz, $CDCl_3$) δ 7.70 (s, 4H), 7.60 (d, *J* = 6.9 Hz, 2H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.44 – 7.38 (m, 1H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 144.8, 139.8, 129.4 (q, *J* = 32.4 Hz), 129.0, 128.2, 127.4, 127.3, 125.7 (q, *J* = 3.8 Hz), 124.3 (q, *J* = 272.2 Hz). 19F NMR (471 MHz, $CDCl_3$) δ -62.40. NMR spectroscopic data agreed with literature values.[9a]

2,4-Dimethyl-1,1'-biphenyl (3w)

According to the general procedure, the reaction of **1e** (0.20 mmol, 40.8 mg), **2w** (Phenylboronic acid, 0.40 mmol, 48.8 mg), K_3PO_4 (0.60 mmol, 127.2 mg), and [(IPr)Pd(μ-Cl)Cl]$_2$ (0.0002 mmol, 0.23 mg) in THF/H_2O = 2:1 (v/vol) mix solution (0.8 mL in all, 0.25M) for 12 h at 60 °C, afforded after work-up and chromatography (EtOAc/hexanes = 1:20) the title product in 79 % yield (28 mg). Colorless oil. 1H NMR (500 MHz, $CDCl_3$) δ 7.41 (t, *J* = 7.4 Hz, 2H), 7.33 (td, *J* = 6.9, 1.6 Hz, 3H), 7.15 (d, *J* = 7.7 Hz, 1H), 7.11 (d, *J* = 1.8 Hz, 1H), 7.07 (d, *J* = 7.7 Hz, 1H), 2.38 (s, 3H), 2.26 (s, 3H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 142.0, 139.1, 136.9, 135.2, 131.1, 129.8, 129.3, 128.0, 126.6, 126.5, 21.1, 20.4. NMR spectroscopic data agreed with literature values.[9a]

2-Isopropyl-5-methyl-1,1'-biphenyl (3x)

According to the general procedure, the reaction of **1f** (0.20 mmol, 42.0 mg), **2w** (Phenylboronic acid, 0.40 mmol, 48.8 mg), K_3PO_4 (0.60 mmol, 127.2 mg), and [(IPr)Pd(μ-Cl)Cl]$_2$ (0.0006 mmol, 0.67 mg) in THF/H_2O = 2:1 (v/vol) mix solution (0.8 mL in all, 0.25M) for 12 h at 60 °C, afforded after work-up and chromatography (EtOAc/hexanes = 1:20) the title product in 96 % yield (40 mg). Colorless oil. 1H NMR (500 MHz, $CDCl_3$) δ 7.42 (t, *J* = 7.1 Hz, 2H), 7.36 (t, *J* = 7.4 Hz, 1H), 7.31 (dd, *J* = 8.5, 2.4 Hz, 3H), 7.19 (d, *J* = 7.9 Hz, 1H), 7.03 (s, 1H), 3.04 (hept, *J* = 6.8 Hz, 1H), 2.36 (s, 3H), 1.17 (d, *J* = 6.9 Hz, 6H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 143.4, 142.2, 141.0, 134.7, 130.7, 129.3, 128.5, 128.0, 126.7, 125.5, 29.0, 24.4, 20.9. NMR spectroscopic data agreed with literature values.[9a]

Ethyl [1,1'-biphenyl]-4-carboxylate (3y)

According to the general procedure, the reaction of **1g** (0.20 mmol, 49.6 mg), **2w** (Phenylboronic acid, 0.40 mmol, 48.8 mg), K_3PO_4 (0.60 mmol, 127.2 mg), and [(IPr)Pd(μ-Cl)Cl]$_2$ (0.0002 mmol, 0.23 mg) in THF/H_2O = 2:1 (v/vol) mix solution (0.8 mL in all, 0.25M) for 12 h at 60 °C, afforded after work-up and chromatography (EtOAc/hexanes = 1:20) the title product in 98 % yield (44 mg). White solid. 1H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.5 Hz, 2H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.63 (d, *J* = 7.1 Hz, 2H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.40 (t, *J* = 7.3 Hz, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H). 13C{1H} NMR (126 MHz, CDCl3) δ 166.6, 145.6, 140.1, 130.1, 129.3, 128.9, 128.1, 127.3, 127.0, 61.0, 14.4. NMR spectroscopic data agreed with literature values.[9a]

5-Phenylbenzo[*d*][1,3]dioxole (3z)

According to the general procedure, the reaction of **1h** (0.20 mmol, 44.0 mg), **2w** (Phenylboronic acid, 0.40 mmol, 48.8 mg), K_3PO_4 (0.60 mmol, 127.2 mg), and [(IPr)Pd(μ-Cl)Cl]$_2$ (0.0002 mmol, 0.23 mg) in THF/H_2O = 2:1 (v/vol) mix solution (0.8 mL in all, 0.25M) for 12 h at 60 °C, afforded after work-up and chromatography (EtOAc/hexanes = 1:20) the title product in 94 % yield (37 mg). White solid. 1H NMR (500 MHz, $CDCl_3$) δ 7.59 – 7.49 (m, 2H), 7.41 (t, *J* = 7.7 Hz, 2H), 7.31 (t, *J* = 7.3 Hz, 1H), 7.14 – 6.99 (m, 2H), 6.89 (d, *J* = 7.9 Hz, 1H), 6.00 (s, 2H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 148.1, 147.1, 141.0, 135.6, 128.8, 126.9, 126.9, 120.7, 108.6, 107.7, 101.2. NMR spectroscopic data agreed with literature values. NMR spectroscopic data agreed with literature values.[9a]

2-Methyl-5-phenylpyridine (3aa)

According to the general procedure, the reaction of **1i** (0.20 mmol, 38.2 mg), **2w** (Phenylboronic acid, 0.40 mmol, 48.8 mg), K_3PO_4 (0.60 mmol, 127.2 mg), and [(IPr)Pd(μ-Cl)Cl]$_2$ (0.0002 mmol, 0.23 mg) in THF/H_2O = 2:1 (v/vol) mix solution (0.8 mL in all, 0.25M) for 12 h at 60 °C, afforded after work-up and chromatography (EtOAc/hexanes = 1:5) the title product in 96 % yield (32 mg). White solid. 1H NMR (500 MHz, $CDCl_3$) δ 8.66 (s, 1H), 7.70 (dd, *J* = 8.1, 2.4 Hz, 1H), 7.49 (d, *J* = 7.0 Hz, 2H), 7.39 (t, *J* = 7.6 Hz, 2H), 7.31 (t, *J* = 7.4 Hz, 1H), 7.15 (d, *J* = 8.0 Hz, 1H), 2.53 (s, 3H). 13C{1H} NMR (126 MHz, $CDCl_3$) δ 157.2, 147.5, 137.9, 134.8, 133.8, 129.0, 127.8, 127.0, 123.2, 24.1. NMR spectroscopic data agreed with literature values.[9a]

Procedure for Competition Studies. An oven-dried vial equipped with a stir bar was charged with phenyl sulfurofluoridate (1.0 equiv, 0.2 mmol), aryl electrophile (1.0 equiv, 0.2 mmol), 4-methoxyphenylboronic acid (**2a**, 1.0 equiv, 0.2 mmol), K_3PO_4 (3.0 equiv, 0.6 mmol), [(IPr)Pd(μ-Cl)Cl]$_2$ (0.25 mol%, 0.0005 mmol) placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. THF and H_2O (0.25 M in all as 2:1 (v/vol)) were added. The reaction was placed in a preheated oil bath at 60 °C for 6 h. After the indicated time, the reaction mixture was cooled down, diluted with ethyl acetate (10 mL), washed with H_2O, extracted with ethyl acetate (5 x 2 mL) and concentrated. The sample was analyzed by ^{1}HNMR ($CDCl_3$, 500 MHz) to obtain conversion, selectivity and yield using internal standard and comparison with authentic samples.

Procedure for Selectivity Studies.

A. Fluorosulfonates. An oven-dried vial equipped with a stir bar was charged with two fluorosulfonate substrates (1.0 equiv, 0.2 mmol each), boronic acid (0.5 equiv, 0.1 mmol), K_3PO_4 (3.0 equiv, 0.6 mmol), [(IPr)Pd(μ-Cl)Cl]$_2$ (0.25 mol%, 0.0005 mmol) placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. THF

and H_2O (0.25 M in all as 2:1 (v/vol)) were added. The reaction was placed in a preheated oil bath at 60 °C for 6 h. After the indicated time, the reaction mixture was cooled down, diluted with ethyl acetate (10 mL), washed with H_2O, extracted with ethyl acetate (5 x 2 mL) and concentrated. The sample was analyzed by ^{1}HNMR ($CDCl_3$, 500 MHz) to obtain conversion, selectivity and yield using internal standard and comparison with authentic samples.

B. Boronic Acids. An oven-dried vial equipped with a stir bar was charged with two boronic acid substrates (1.0 equiv, 0.2 mmol each), fluorosulfonate (0.5 equiv, 0.1 mmol), K_3PO_4 (3.0 equiv, 0.6 mmol), $[(IPr)Pd(\mu\text{-}Cl)Cl]_2$ (0.25 mol%, 0.0005 mmol) placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. THF and H_2O (0.25 M in all as 2:1 (v/vol)) were added. The reaction was placed in a preheated oil bath at 60 °C for 6 h. After the indicated time, the reaction mixture was cooled down, diluted with ethyl acetate (10 mL), washed with H_2O, extracted with ethyl acetate (5 x 2 mL) and concentrated. The sample was analyzed by ^{1}HNMR ($CDCl_3$, 500 MHz) to obtain conversion, selectivity and yield using internal standard and comparison with authentic samples.

Procedure for Determining Turnover Number. An oven-dried vial equipped with a stir bar was charged with phenyl sulfurofluoridate (1.0 equiv, 0.2 mmol), 4-methoxyphenylboronic acid (**2a**, 2.0 equiv, 0.4 mmol), K_3PO_4 (3.0 equiv, 0.6 mmol), $[(IPr)Pd(\mu\text{-}Cl)Cl]_2$ ([Pd] 0.025-0.05 mol%) placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. THF and H_2O (0.25 M in all as 2:1 (v/vol)) were added. The reaction was placed in a preheated oil bath at 100 °C for 12 h. After the indicated time, the reaction mixture was cooled down, diluted with ethyl acetate (10 mL), washed with H_2O, extracted with ethyl acetate (5 x 2 mL) and concentrated. The sample was analyzed by ^{1}HNMR ($CDCl_3$, 500 MHz) to obtain conversion, selectivity and yield using internal standard and comparison with authentic samples.

ASSOCIATED CONTENT

Supporting Information

^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra for all products. This material is available free of charge via the Internet at http://pubs.acs.org.

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REFERENCES

(1) For representative books and chapters, see: (a) Molander, G. A.; Wolfe, J. P.; Larhed, M. *Science of Synthesis: Cross-Coupling and Heck-Type Reactions*, 1st ed. Thieme: Stuttgart, **2013**. (b) Molnar, A. *Palladium-Catalyzed Coupling Reactions: Practical Aspects and Future Developments*; Wiley: Weinheim: **2013**. (c) Meijere, A. D.; Brase, S.; Oestreich, M. *Metal Catalyzed Cross-Coupling Reactions and More, 3 Vol. Set.;* Wiley: Weinheim: **2014**. (d) Colacot, T. J. *New Trends in Cross-Coupling*; 1st ed. RSC: Cambridge, **2015**.

(2) For representative perspectives, see: (a) Wu, X. F.; Anbarasan, P.; Neumann, H.; Beller, M. From Noble Metal to Nobel Prize: Palladium-Catalyzed Coupling Reactions as Key Methods in Organic Synthesis. *Angew. Chem. Int. Ed.* **2010**, *49*, 9047-9050. (b) Johansson Seechurn, C. C. C.; Kitching, M. O.; Colacot, T. J.; Snieckus, V. Palladium-Catalyzed Cross-Coupling: A Historical Contextual Perspective to the 2010 Nobel Prize. *Angew. Chem., Int. Ed.* **2012**, *51*, 5062-5085. (c) Li, H.; Johansson Seechurn, C. C. C.; Colacot, T. J. Development of Preformed Pd Catalysts for Cross-Coupling Reactions Beyond the 2010 Nobel Prize. *ACS Catal.* **2012**, *2*, 1147-1164.

(3) For representative reviews, see: (a) Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. Palladium-catalyzed cross-coupling reactions in total synthesis. *Angew. Chem. Int. Ed.* **2005**, *44*, 4442-4489. (b) Torborg, C.; Beller, M. Recent Applications of Palladium-Catalyzed Coupling Reactions in the Pharmaceutical, Agrochemical, and Fine Chemical Industries. *Adv. Synth. Catal.* **2009**, *351*, 3027-3043. (c) Magano, J.; Dunetz, J. R. Large-Scale Applications of Transition Metal-Catalyzed Couplings for the Synthesis of Pharmaceuticals. *Chem. Rev.* **2011**, *111*, 2177-2250. (d) Cross-Coupling Reactions in Organic Synthesis Themed Issue. *Chem. Soc. Rev.* **2011**, 40, 4877-5208. (e) Gildner, P. G.; Colacot, T. J. Reactions of the 21st Century: Two Decades of Innovative Catalyst Design for Palladium-Catalyzed Cross-Couplings. *Organometallics* **2015**, *34*, 5497-5508. (f) Campeau, L. C.; Hazari, N. Cross-Coupling and Related Reactions: Connecting Past Successes to the Development of New Reactions for the Future. *Organometallics* **2019**, *38*, 3-35 (g) Zhang, Y. F.; Shi, Z. J. Upgrading Cross-Coupling Reactions for Biaryl Syntheses. *Acc. Chem. Res.* **2019**, *52*, 161-169. (h) Korch, K. M.; Watson, D. A. Cross-Coupling of Heteroaromatic Electrophiles. *Chem. Rev.* **2019**, *119*, 8129-8228.

(4) (a) Miyaura, N.; Suzuki, A. Palladium-Catalyzed Cross-Coupling Reactions of Organoboron Compounds. *Chem. Rev.* **1995**, *95*, 2457-2483. (b) Han, F. S. Transition-Metal-Catalyzed Suzuki-Miyaura Cross-Coupling Reactions: A Remarkable Advance from Palladium to Nickel Catalysts. *Chem. Soc. Rev.* **2013**, *42*, 5270-5298. (c) Beletskaya, I. P.; Alonso, F.; Tyurin, V. The Suzuki–Miyaura reaction after the Nobel prize. *Coord. Chem. Rev.* **2019**, *385*, 137-173. (d) Hooshmand, S. E.; Heidari, B.; Sedghi, R.; Varma, R. Recent Advances in the Suzuki–Miyaura Cross-coupling Reaction Using Efficient Catalysts in Eco-Friendly Media. *Green Chem.* **2019**, *21*, 381-405.

(5) (a) Rappoport, Z. *The Chemistry of Phenols*, Wiley: Chichester, **2003**. (b) Goossen, L. J.; Goossen, K.; Stanciu, C. C(aryl)-O Activation of Aryl Carboxylates in Nickel-Catalyzed Biaryl Syntheses. *Angew. Chem. Int. Ed.* **2009**, *48*, 3569-3571. (c) Quasdorf, K. W.; Riener, M.; Petrova, K. V.; Garg, N. K. Suzuki−Miyaura Coupling of Aryl Carbamates, Carbonates, and Sulfamates. *J. Am. Chem. Soc.* **2009**, *131*, 49, 17748-17749. (d) Agarwal, T.; Cook, S. P. Iron-Catalyzed Coupling of Aryl Sulfamates and Aryl/Vinyl Tosylates with Aryl Grignards. *Org. Lett.* **2014**, *16*, 5080-5083.

(6) For representative reviews, see: (a) Yu, D.-G.; Li, B.-J.; Shi, Z.-J. Exploration of New C−O Electrophiles in Cross-Coupling Reactions. *Acc. Chem. Res.* **2010**, *43*, 12, 1486–1495. (b) So, C. M.; Kwong, F. Y. Palladium-Catalyzed Cross-Coupling Reactions of Aryl Mesylates. *Chem. Soc. Rev.* **2011**, *40*, 4963-4972. (c) Tollefson, E. J.; Hanna, L. E.; Jarvo, E. R. Stereospecific Nickel-Catalyzed Cross-Coupling Reactions of Benzylic Ethers and Esters. *Acc. Chem. Res.* **2015**, *48*, 2344-2353. (d) Zhou, T.; Szostak, M. Palladium-Catalyzed Cross-Couplings by C-O Bond Activation. *Catal. Sci. Technol.* **2020**, *10*, 5702-5739.

(7) (a) Dong, J.; Krasnova, L.; Finn, M. G.; Sharpless, K. B. Sulfur (VI) Fluoride Exchange (SuFEx): Another Good Reaction for Click Chemistry. *Angew. Chem. Int. Ed.* **2014**, *53*, 9430-9448. (b) Dong, J.; Sharpless, K. B.; Kwisnek, L.; Oakdale, J. S.; Fokin, V. V. SuFEx-Based Synthesis of Polysulfates. *Angew. Chem. Int. Ed.* **2014**, *53*, 9466-9470.

(8) Andersen, S. P. S.; Blake, D. R.; Rowland, F. S.; Hurley, M. D.; Wallington, T. J. Atmospheric Chemistry of Sulfuryl Fluoride: Reaction with OH Radicals, Cl Atoms and O_3, Atmospheric Lifetime, IR Spectrum, and Global Warming Potential. *Environ. Sci. Technol.* **2009**, *43*, 1067-1070.

(9) (a) Hanley, P. S.; Ober, M. S.; Krasovskiy, A. L.; Whiteker, G. T.; Kruper, W. J. Nickel- and Palladium-Catalyzed Coupling of Aryl

Fluorosulfonates with Aryl Boronic Acids Enabled by Sulfuryl Fluoride. *ACS Catal.* **2015**, *5*, 5041-5046. (b) Liang, Q.; Xing, P.; Huang, Z.; Dong, J.; Sharpless, K. B.; Li, X.; Jiang, B. Palladium-catalyzed, Ligand-free Suzuki Reaction in Water Using Aryl Fluorosulfates. *Org. Lett.* **2015**, *17*, 1942-1945. (c) Zhang, E.; Tang, J.; Li, S.; Wu, P.; Moses, J. E.; Sharpless, K. B. Chemoselective Synthesis of Polysubstituted Pyridines from Heteroaryl Fluorosulfates. *Chem. Eur. J.* **2016**, *22*, 5692-5697. (d) Hanley, P. S.; Clark, T. P.; Krasovskiy, A. L.; Ober, M. S.; O'Brien, J. P.; Staton, T. S. Palladium- and Nickel-Catalyzed Amination of Aryl Fluorosulfonates. *ACS Catal.* **2016**, *6*, 3515-3519.

(10) (a) Roth, G. P.; Fuller, C. E. Palladium Cross-coupling Reactions of Aryl Fluorosulfonates: an Alternative to Triflate Chemistry. *J. Org. Chem.* **1991**, *56*, 3493–3496. (b) McGuire, M. A.; Sorenson, E.; Owings, F. W.; Resnick, T. M.; Fox, M.; Baine, N. H. A Novel, Practical Synthesis of Estra-1,3,5(10)-triene-3,17b-dicarboxylic Acid 17-tert-Butylamide (SK&F 105656) from Estrone, via a Palladium-Catalyzed Methoxycarbonylation of a 3-Fluorosulfonate. *J. Org. Chem.* **1994**, *59*, 6683-6686. (c) Clark, W. M.; Tickner-Eldridge, A. M.; Huang, G. K.; Pridgen, L. N.; Olsen, M. A.; Mills, R. J.; Lantos, I.; Baine, N. H. A Catalytic Enantioselective Synthesis of the Endothelin Receptor Antagonists SB-209670 and SB-217242. *J. Am. Chem. Soc.* **1998**, *120*, 4550-4551.

(11) For selected recent studies, see: (a) Domino, K.; Veryser, C.; Wahlqvist, B. A.; Gaardbo, C.; Neumann, K. T.; Daasbjerg, K.; De Borggraeve, W. M.; Skrydstrup, T. Direct Access to Aryl Bis(trifluoromethyl)carbinols from Aryl Bromides or Fluorosulfates: Palladium-Catalyzed Carbonylation. *Angew. Chem. Int. Ed.* **2018**, *57*, 6858-6862. (b) Ma, C.; Zhao, C. Q.; Xu, X. T.; Li, Z. M.; Wang, X. Y.; Zhang, K.; Mei, T. S. Nickel-Catalyzed Carboxylation of Aryl and Heteroaryl Fluorosulfates Using Carbon Dioxide. *Org. Lett.* **2019**, *21*, 2464-2467. (c) Lekkala, R.; Lekkala, R.; Moku, B.; Rakesh, K. P.; Qin, H.-L. Applications of Sulfuryl Fluoride (SO_2F_2) in Chemical Transformations. *Org. Chem. Front.* **2019**, *6*, 3490-3516. (d) Fang, W. Y.; Zha, G. F.; Qin, H. L. Making Carbonyls of Amides Nucleophilic and Hydroxyls of Alcohols Electrophilic Mediated by SO_2F_2 for Synthesis of Esters from Amides. *Org. Lett.* **2019**, *21*, 8657-8661. (e) Wei, M.; Liang, D.; Cao, X.; Luo, W.; Ma, G.; Liu, Z.; Li, L. A Broad-Spectrum Catalytic Amidation of Sulfonyl Fluorides and Fluorosulfates. *Angew. Chem. Int. Ed.* **2021**, *60*, 7397-7404. (f) Mendel, M.; Kalvet, I.; Hupperich, D.; Magnin, G.; Schoenebeck, F. Site-Selective, Modular Diversification of Polyhalogenated Aryl Fluorosulfates ($ArOSO_2F$) Enabled by an Air-Stable Pd(I) Dimer. *Angew. Chem. Int. Ed.* **2020**, *59*, 2115-2119.

(12) Marion, N.; Nolan, S. P. Well-defined N-heterocyclic carbenes-palladium(II) precatalysts for cross-coupling reactions. *Acc. Chem. Res.* **2008**, *41*, 1440-1449.

(13) For select reviews on NHCs, see: (a) *N-Heterocyclic Carbenes*, Nolan, S. P., Ed.; Wiley: Weinheim, **2014**. (b) Diez-Gonzalez, S.; Marion, N.; Nolan, S. P. N-Heterocyclic Carbenes in Late Transition Metal Catalysis. *Chem. Rev.* **2009**, *109*, 3612-3676. (c) Fortman, G. C.; Nolan, S. P. N-Heterocyclic carbene (NHC) ligands and palladium in homogeneous cross-coupling catalysis: a perfect union. *Chem. Soc. Rev.* **2011**, *40*, 5151-5169. (d) Froese, R. D. J.; Lombardi, C.; Pompeo, M.; Rucker, R. P.; Organ, M. G. Designing Pd–N-Heterocyclic Carbene Complexes for High Reactivity and Selectivity for Cross-Coupling Applications. *Acc. Chem. Res.* **2017**, *50*, 2244-2253. (e) Zhao, Q.; Meng, G.; Nolan, S. P.; Szostak, M. N-Heterocyclic Carbene Complexes in C–H Activation Reactions. *Chem. Rev.* **2020**, *120*, 1981-2048.

(14) (a) Lei, P.; Meng, G.; Szostak, M. General Method for the Suzuki-Miyaura Cross-Coupling of Amides Using Commercially Available, Air- and Moisture-Stable Palladium/NHC (NHC = N-Heterocyclic Carbene) Complexes. *ACS Catal.* **2017**, *7*, 1960-1965. (b) Lei, P.; Meng, G.; Shi, S.; Ling, Y.; An, J.; Szostak, R.; Szostak, M. Suzuki–Miyaura Cross-Coupling of Amides and Esters at Room Temperature: Correlation with Barriers to Rotation around C–N and C–O Bonds. *Chem. Sci.* **2017**, *8*, 6525-6530. (c) Shi, S.; Nolan, S. P.; Szostak, M. Well-Defined Palladium(II)-NHC (NHC = N-Heterocyclic Carbene) Precatalysts for Cross- Coupling Reactions of Amides and Esters by Selective Acyl CO–X (X = N, O) Cleavage. *Acc. Chem. Res.* **2018**, *51*, 2589-2599. (d) Zhou, T.; Ma, S.; Nahra, F.; Obled, A. M. C.; Poater, A.; Cavallo, L.; Cazin, C. S. J.; Nolan, S. P.; Szostak, M. $[Pd(NHC)(\mu\text{-}Cl)Cl]_2$: Versatile and Highly Reactive Complexes for Cross-Coupling Reactions that Avoid Formation of Inactive Pd(I) Off-Cycle Products. *iScience* **2020**, *23*, 101377. (e) Zhao, Q.; Meng, G.; Li, G.; Flach, C.; Mendelsohn, R.; Lalancette, R.; Szostak, R.; Szostak, M. $IPr^{\#}$ – Highly Hindered, Broadly Applicable N-Heterocyclic Carbenes. *Chem. Sci.* **2021**, *12*, 10583-10589. (f) Xia, Q.; Shi, S.; Gao, P.; Lalancette, R.; Szostak, R.; Szostak, M. $[(NHC)PdCl_2(Aniline)]$ Complexes: Easily Synthesized, Highly Active Pd(II)–NHC Precatalysts for Cross-Coupling Reactions. *J. Org. Chem.* **2021**, *86*, 15648-15657. (g) Yang, S.; Zhou, T.; Poater, A.; Cavallo, L.; Nolan, S. P.; Szostak, M. Suzuki-Miyaura Cross-Coupling of Esters by Selective O-C(O) Cleavage Mediated by Air- and Moisture-Stable $[Pd(NHC)(\mu\text{-}Cl)Cl]_2$ Precatalysts: Catalyst Evaluation and Mechanism. *Catal. Sci. Technol.* **2021**, *11*, 3189-3197.

(15) Zhou, C.; Liu, Q.; Li, Y.; Zhang, R.; Fu, X.; Duan, C. Palladium-Catalyzed Desulfitative Arylation by C–O Bond Cleavage of Aryl Triflates with Sodium Arylsulfinates. *J. Org. Chem.* **2012**, *77*, 10468-10472.

(16) Raders, S. M.; Moore, J. N.; Parks, J. K.; Miller, A. D.; Leissing, T. M.; Kelley, S. P.; Rogers, R. D.; Shaughnessy, K. H. Trineopentylphosphine: A Conformationally Flexible Ligand for the Coupling of Sterically Demanding Substrates in the Buchwald–Hartwig Amination and Suzuki–Miyaura Reaction. *J. Org. Chem.* **2013**, *78*, 4649-4664.

(17) Mita, T.; Suga, K.; Sato, K.; Sato, Y. A Strained Disilane-Promoted Carboxylation of Organic Halides with CO2 under Transition-Metal-Free Conditions. *Org. Lett.* **2015**, *17*, 5276-5279.

(18) Peng, Z.; Hu, G.; Qiao, H.; Xu, P.; Gao, Y.; Zhao, Y. Palladium-Catalyzed Suzuki Cross-Coupling of Arylhydrazines via C–N Bond Cleavage. *J. Org. Chem.* **2014**, *79*, 2733-2738.

(19) Mattiello, S.; Rooney, M.; Sanzone, A.; Brazzo, P.; Sassi, M.; Beverina, L. Suzuki–Miyaura Micellar Cross-Coupling in Water, at Room Temperature, and under Aerobic Atmosphere. *Org. Lett.* **2017**, *19*, 654-657.

(20) Dai, Q.; Li, P.; Ma, N.; Hu, C. Palladium-Catalyzed Decarboxylative Synthesis of Arylamines. Suzuki–Miyaura Coupling of Halophenols and Phenol Boronic Acids: Systematic Investigation of Positional Isomer Effects and Conclusions for the Synthesis of Phytoalexins from Pyrinae. *Org. Lett.* **2016**, *18*, 5560-5563.

(21) Schmidt, B.; Riemer, M. Suzuki–Miyaura Coupling of Halophenols and Phenol Boronic Acids: Systematic Investigation of Positional Isomer Effects and Conclusions for the Synthesis of Phytoalexins from Pyrinae. *J. Org. Chem.* **2014**, *79*, 4104-4118

(22) Yin, L.; Zhang, Z.-H.; Wang, Y.-M. PEG (300)–PdCl2 promoted efficient and convenient Suzuki–Miyaura coupling of aryl chlorides with arylboronic acids. *Tetrahedron* **2006**, *62*, 9359-9364.

(23) Kandathil, V.; Fahlman, B. D.; Sasidhar, B. S.; Patil, S. A.; Patil, S. A. A convenient, efficient and reusable N-heterocyclic carbene-palladium(II) based catalyst supported on magnetite for Suzuki–Miyaura and Mizoroki–Heck cross-coupling reactions. *New J. Chem.* **2017**, *41*, 9531-9545.

(24) Dwadnia, N.; Roger, J.; Pirio, N.; Cattey, H.; Ben Salem, R.; Hierso, J.-C. Gold-Catalyzed Suzuki Coupling of ortho-Substituted Hindered Aryl Substrates. *Chem. Asian J.* **2017**, *12*, 459-464.

(25) Ye, W.; Naohiko, Y. Oxidative Cyclization of 2-Arylphenols to Dibenzofurans under Pd(II)/Peroxybenzoate Catalysis. *Org. Lett.* **2011**, *13*, 5504-5507.

(26) Zhang, S.; Tang, Z.; Bao, W.; Li, J.; Guo, B.; Huang, S.; Zhang, Y.; Rao, Y. Perylenequinonoid-catalyzed photoredox activation for the direct arylation of (het)arenes with sunlight. *Org. Biomol. Chem* **2019**, *17*, 4364-4369.

(27) Molander, G. A.; Iannazzo, L. Palladium-Catalyzed Hiyama Cross-Coupling of Aryltrifluorosilanes with Aryl and Heteroaryl Chlorides. *J. Org. Chem.* **2011**, *76*, 9182-9187.

(28) Liu, Y.; Luo, W.; Wang, Z.; Zhao, Y.; Zhao, J.; Xu, X.; Wang, C.; Li, P. Visible-Light Photoredox-Catalyzed Formal [5 + 1] Cycloaddition of N-Tosyl Vinylaziridines with Difluoroalkyl Halides. *Org. Lett.* **2020**, *22*, 9658-9664.

(29) Martinez-Solorio, D.; Melillo, B.; Sanchez, L.; Liang, Y.; Lam, E.; Houk, K. N.; Smith, A. B. Design, Synthesis, and Validation of an Effective, Reusable Silicon-Based Transfer Agent for Room-Temperature Pd-Catalyzed Cross-Coupling Reactions of Aryl and Heteroaryl Chlorides with Readily Available Aryl Lithium Reagents. *J. Am. Chem. Soc.* **2016**, *138*, 1836-1839.

(30) Vaddula, B. R.; Saha, A.; Leazer, J.; Varma, R. S. A simple and facile Heck-type arylation of alkenes with diaryliodonium salts using magnetically recoverable Pd-catalyst. *Green. Chem.* **2012**, *14*, 2133-2136.