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An N-Heterocyclic Carbene-Nickel Half-Sandwich Complex as a Precatalyst for Suzuki–Miyaura Coupling of Aryl/Heteroaryl Halides with Aryl/Heteroarylboronic Acids

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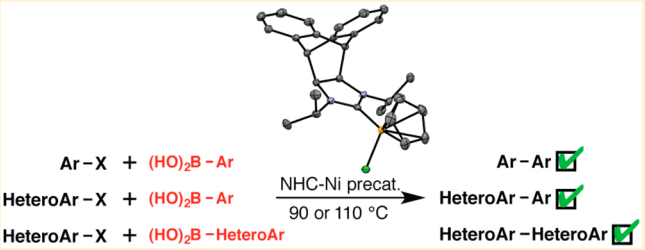
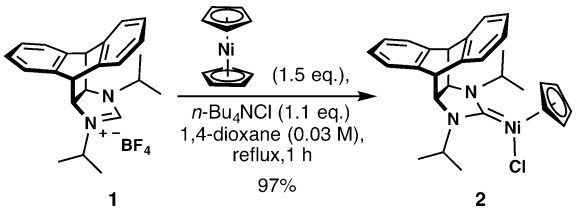
Supporting Information

ABSTRACT: A nickel half-sandwich complex supported by our original NHC ligand was developed as a robust precatalyst for Suzuki–Miyaura cross-coupling. The addition of PPh_3 was a crucial element in the suppression of side reactions and in accelerating the cross-coupling reaction. By employing the optimal conditions, aryl–aryl, heteroaryl–aryl, and heteroaryl–heteroaryl couplings were achieved.



The development of stable precatalysts under air and moisture, which can be readily activated in a reaction vessel, is an attractive area for chemists due to their ease of handling. A number of such precatalysts that contain palladium as an active transition metal have already been developed and are often commercially available, but the first low counterpart, nickel, is much less frequently mentioned in the literature. The addition to powerful Ni catalysts supported by phosphine ligands,[1] and more recently N-heterocyclic carbene (NHC) ligands, has been actively applied in Ni-based catalysis, which has revealed unique reactivities of NHC-Ni catalysts.[2] Current NHC-Ni-based catalysts, however, are traditionally formed using air- and moisture-sensitive $Ni(COD)_2$ as a Ni(0) source, along with isolated or *in situ*-formed NHC ligands,[1b,3] which means that the development of a stable source of NHC-based Ni precatalysts remains a highly sought accomplishment.

Among some types of the air- and moisture-stable NHC-Ni complexes, [Ni(NHC)CpCl] half-sandwich versions are good examples of easily accessible NHC-Ni complexes, which can be prepared via a simple heating of the NHC precursor in the presence of nickelocene.[3−11] After the seminal report by Cowley and co-workers,[4] most of the ubiquitous NHC ligands were investigated to demonstrate their usefulness in this type of complex. During these investigations, some groups discovered that organometallic reagents such as Grignard reagents,[5] bases such as sodium *tert*-butoxide,[6] and arylboronic acids[7] could activate a Ni(II) complex and produce catalytically active species. At this point, several reactions were reported with the use of [Ni(NHC)CpCl] complexes as a precatalyst: Buchwald–Hartwig type amination,[6] Kumada–Tamao–Corriu (KTC) coupling,[5] ketone α-arylation,[8] hydrosilylation,[9] hydrothiolation,[10] and polymerization of a styrene.[11] Although some examples of Suzuki–Miyaura cross-coupling[12] with these types of complexes have also been reported,[7,11a] their substrate scope was limited to only electron-deficient *para*-substituted aryl halides. Here, we present a [Ni(NHC)CpCl] complex with our original bicyclic NHC ligand, which can catalyze the Suzuki–Miyaura cross-coupling of sterically and/or electronically challenging aryl chlorides with arylboronic acids. This precatalyst was even applicable to the coupling of heteroaryl halides with aryl and heteroarylboronic acids.



1 2 (1)

Our group designed and synthesized original bicyclic NHCs equipped with a bicyclic architecture on the non-carbenic carbons,[13] and this type of NHC ligand, which we refer to as DHASI, is characterized by a stabilizing effect on the metal complexes that is caused by the bulkiness of the DHASI ligands. Recently, we found that a DHASI*i*Pr-supported copper catalyst was more amenable to the borylation of sterically hindered substrates than ubiquitous NHCs, which suggested that DHASI ligands are bulky but accessible.[14] We envisioned that the bulkiness would facilitate the activation of [Ni(NHC)CpCl] precatalysts[15] and that their accessibility would result in a much wider scope of substrates for Suzuki–Miyaura coupling. Motivated by this hypothesis, we began the synthesis of a [Ni(NHC)CpCl] complex using a DHASI*i*Pr ligand. With a small modification to the method reported by Albrecht and co-workers,[7c] we heated a mixture of DHASI*i*Pr·HBF_4 **1**,[14] freshly sublimed nickelocene, and *n*-Bu_4NCl in degassed 1,4-dioxane at reflux for 1 h in an oil bath and obtained [Ni(DHASI*i*Pr)CpCl]

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2 in a 97% yield as an air- and moisture-stable solid (eq 1). As far as we could ascertain, this is the first example of a [Ni(NHC)CpCl] complex supported by a *N*,*N*′-dialkylated imidazolinylidene ligand. The structure of [Ni(DHASI*i*Pr)-CpCl] was confirmed by X-ray crystallography, and a thermal ellipsoid representation at the 50% probability level is shown in Figure 1.

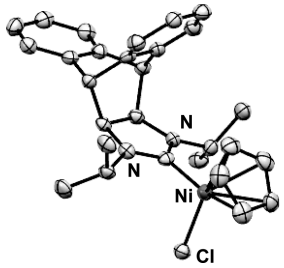
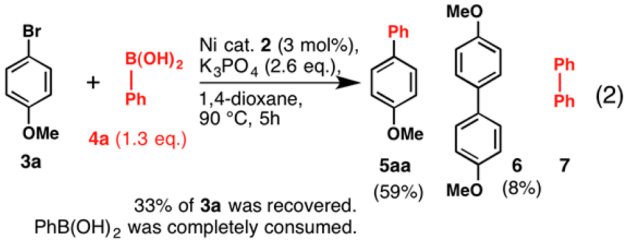


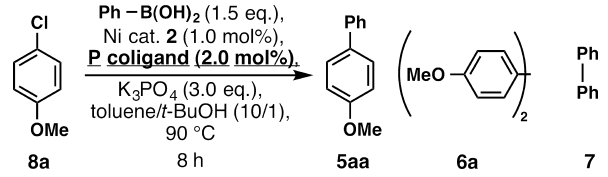
Figure 1. ORTEP diagram of [Ni(DHASI*i*Pr)CpCl] **2**; thermal ellipsoids are shown at the 50% probability level (CCDC 1512438). H atoms and solvents are omitted for clarity.

For a preliminary trial of this stable NHC-Ni complex **2**, we tried the Suzuki–Miyaura coupling of 4-bromoanisole **3a**, which is an electronically deactivated arylbromide, with phenylboronic acid **4a**. Under a representative condition for a similar transformation, we obtained 59% of the cross-coupled product **5aa** with 8% of the homocoupled product **6** and 33% of recovered S.M. **3a** (based on ^{1}H NMR of the crude product) after 5 h at 90 °C (eq 2). Although these were the same level as the highest activity of the related complexes reported to date,[7a] we noticed that a significant amount of biphenyl **7** was formed via the homocoupling of phenylboronic acid **4a**, which resulted in the complete consumption of **4a**.[16] This indicated that a loss in the activity of the nickel catalyst was not the reason that the cross-coupling of challenging substrates resulted in a poor yield.



Encouraged by the above-mentioned promising results, we extensively studied the reaction conditions to accomplish the coupling of 4-chloroanisole **8a**, which is a somewhat more challenging substrate, with 1.5 equiv of phenylboronic acid **4a** using 1.0 mol % of [Ni(DHASI*i*Pr)CpCl] **2** (Table 1). We then found that the phosphine coligand, particularly PPh_3,[17] was effective in suppressing the undesired homocoupling of phenylboronic acid **4a** and that a toluene/*tert*-BuOH (10/1) solvent system was superior to 1,4-dioxane for this coupling (see the Supporting Information for other optimizations). Among the phosphine ligands we tested, PPh_3 was the only effective coligand that could reduce the formation of biphenyl **7** with a high conversion to cross-coupling (Table 1, entries 1–5). Intriguingly, an increased PPh_3 accelerated the reaction, and the reaction using 20 mol % of PPh_3 with 1.0 mol % of Ni precatalyst **2** at 90 °C was completed within 8 h to give the coupled product **5aa** in a 95% yield (entry 6). To obtain more information about the effects of PPh_3, we heated a mixture of

Table 1. Effects of a Phosphine Coligand in Suzuki–Miyaura Coupling



		products ratio in a crude mixture[a]			
entry	P coligand	**5aa**	**6a**	**8a**	consumed $PhB(OH)_2$ (equiv)
1	PPh_3	55	5	40	0.74
2	$P(o\text{-tol})_3$	20	trace	80	0.47
3	$P(OPh)_3$	0	0	100	0.28
4	dppe	0	0	100	0
5	$PCy_3{\cdot}HBF_4$	14	1	85	0.59
6[b]	PPh_3	95 (95)	5	0	1.13

[a]Calculated using ^{1}H NMR. [b]20 mol % of PPh_3 was used. Yield after isolation by chromatography is shown in parentheses.

$PhB(OH)_2$, K_3PO_4, and the Ni catalyst **2** in the absence of aryl halide. Interestingly, under these conditions, biphenyl was formed in a ca. 3% yield regardless of the addition of PPh_3.[18] These results suggested that another active pathway would be generated in the presence of an aryl halide[19] and would result in the homocoupling of $PhB(OH)_2$. The addition of PPh_3 seems to prioritize the cross-coupling over the homocoupling, and the acceleration of the reaction by an excess amount of PPh_3 would be caused by increasing the rate of the reductive elimination step.

With the optimal reaction conditions (condition A) in hand, we tested a scope of substrates for a [Ni(DHASI*i*Pr)CpCl] precatalyst and focused on *ortho*-substituted versions to establish steric capacity (Figure 2). A variety of EWG- and EDG-substituted arylchlorides were coupled with phenylboronic acid in an efficient manner (**5ba**–**5ia**). The catalyst worked in nondistilled standard solvents on a 70 mmol scale with 0.25 mol % loading to give the coupled product in a 90% yield (10.6 g of **5ea**; see Table S6 in the Supporting Information). For the coupling of more bulky substrates, a somewhat higher temperature in toluene/*tert*-amylalcohol (condition B) was required in order to accomplish the reaction in 24 h (**5ja** to **5na**). Although free aniline showed better reactivity (**5ha**), BOC protected and acetylated aniline derivatives were also reacted in moderate yields with 2 mol % of catalyst **2** (**5la** and **5ma**). Unfortunately, di-*ortho*-methylated arylchloride was not tolerated, and only 37% of the product was observed in the ^{1}H NMR of a crude mixture even with 2-bromo-*m*-xylene as a substrate. When we tested the coupling with *ortho*-methyl- and methoxy-phenylboronic acids (**4b** and **4c**), the coupling reactions of arylchlorides possessing EWG and EDG with **4b** smoothly proceeded, while reactions with **4c** required a higher level of catalyst loading (**5ab**–**5ec**). In particular, a comparison between **5cb** and **5ec** clearly showed that a methoxy group at the 2-position of arylboronic acid caused a severe bottleneck, which was effectively alleviated by switching the coupling partner.

We subsequently addressed the coupling of heteroaryl halide with phenylboronic acid and found that our catalytic system successfully catalyzed the coupling (Figure 3). In these coupling reactions, the rate was generally faster than that shown in

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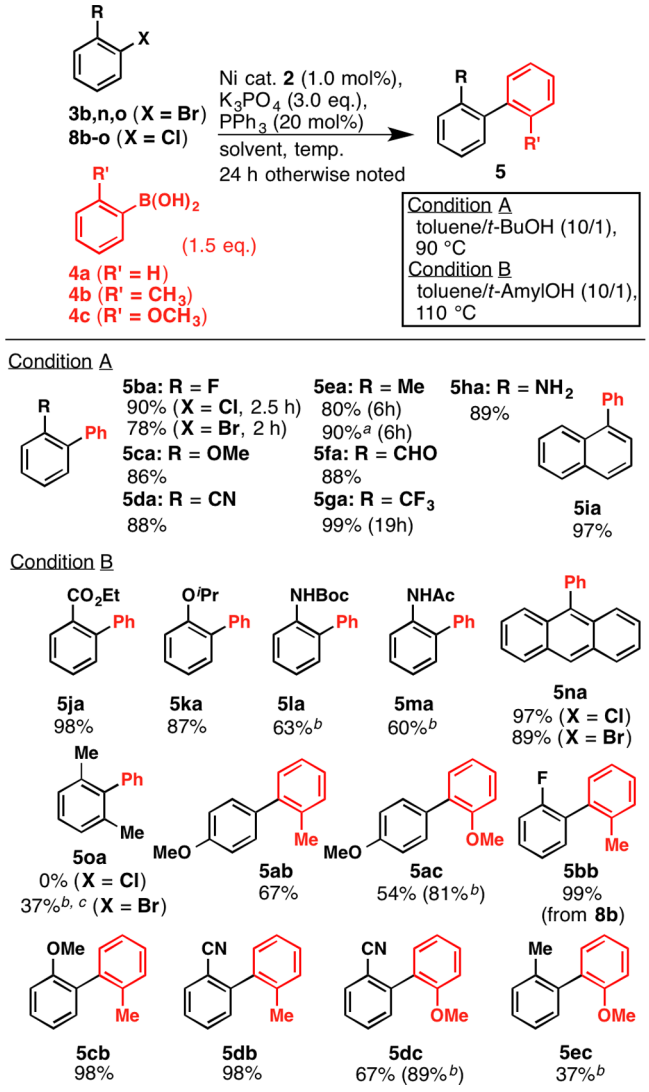

Figure 2. Coupling of aryl halides with arylboronic acids using [Ni(DHASI*i*Pr)CpCl] **2**. [a]The reaction was attempted on a 70 mmol scale. 0.25 mol % of Ni cat. **2** and 20 mol % of PPh_3 were used. [b]2.0 mol % of Ni cat. **2** and 40 mol % of PPh_3 were used. [c]Calculated using ^1H NMR of a crude mixture.

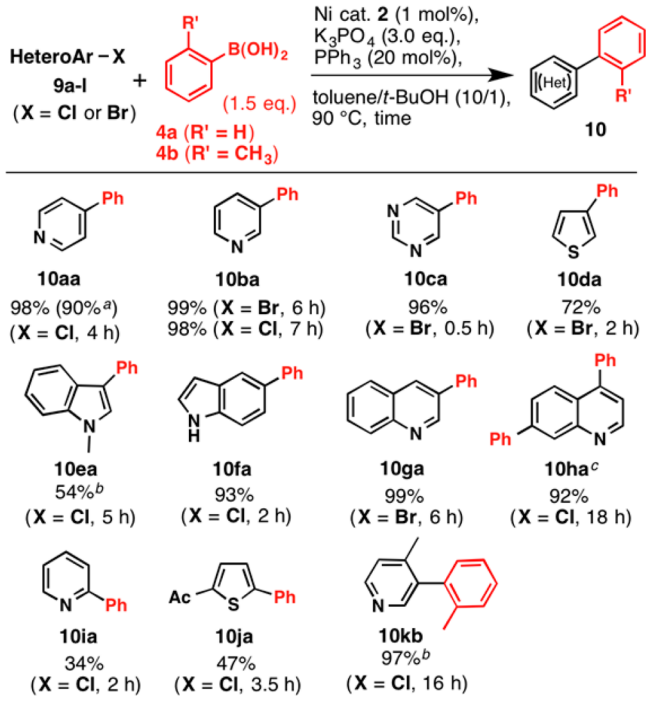

Figure 3. Coupling of heteroaryl halides with arylboronic acids using [Ni(DHASI*i*Pr)CpCl] **2**. [a]0.25 mol % of Ni cat. **2** was used. [b]The coupling was run at 110 °C in toluene/*tert*-AmylOH (10/1). [c]3.0 equiv of $PhB(OH)_2$ and 6.0 equiv of K_3PO_4 were used.

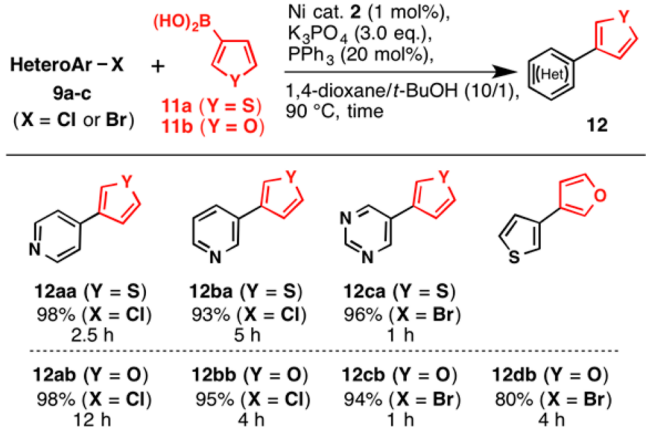

Figure 4. Coupling of heteroaryl halides with heteroarylboronic acids using [Ni(DHASI*i*Pr)CpCl] **2**.

Figure 2, and the phenylated heteroarenes (**10aa**−**10ha**) were isolated in good to excellent yields. However, the reaction at the reactive 2-position of heteroarene resulted in an incompletion, which was not helped by increasing the catalyst with protracted heating (**10ia** and **10ja**).[20] The catalyst loading for the coupling between 4-chloropyridine and phenylboronic acid (**10aa**) was reduced to 0.25 mol %. Even for the heteroaryl−aryl coupling, steric hindrance caused no problem (**10kb**).

We finally attempted the most challenging coupling between heteroaryl halides (**9a**−**c**) and heteroarylboronic acids (**11a** and **11b**),[1h,21] and a 10:1 mixture of 1,4-dioxane and *tert*-BuOH proved to be an optimal solvent system (Figure 4). The couplings of 3-chloropyridine, 4-chloropyridine, and 5-bromopyrimidine with 3-thiophene and 3-furanboronic acids were sufficiently catalyzed by [Ni(DHASI*i*Pr)CpCl] (**12aa**−**12cb**). Also, 3-bromothiophene was coupled with 3-furanboronic acid under this catalysis (**12db**), even though couplings at the 2-positions of heteroarylboronic acids were fruitless.

In addition to the typical Suzuki−Miyaura cross-coupling, we applied [Ni(DHASI*i*Pr)CpCl] **2** to the Ni-NHC catalyzed Suzuki−Miyaura coupling of amide, which was recently reported by Garg and co-workers.[2a] This reaction is a powerful method for ketone syntheses, but the active catalyst was formed using $Ni(COD)_2$ along with an isolated NHC ligand. As a result, [Ni(DHASI*i*Pr)CpCl] **2** worked for the coupling between amide **13** and phenylboronic acid **4a** to give benzophenone **14** in an 85% yield (eq 3).[22] This result suggested that [Ni(DHASI*i*Pr)CpCl] **2** would be a useful precatalyst to seek reactions, wherein NHC-Ni complexes could demonstrate their characteristic effects.

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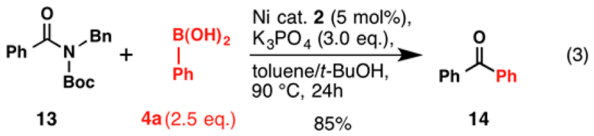

(3)

In conclusion, the [Ni(NHC)CpCl] complex supported by our original DHASI*i*Pr ligand covered a much wider scope of substrates during Suzuki−Miyaura coupling compared with that of related nickel complexes. This robust complex is the first example of a [Ni(NHC)CpCl] complex supported by *N*,*N*′-dialkylated imidazolinylidene ligands, and its structure was confirmed by X-ray crystallography. In the Suzuki−Miyaura coupling using [Ni(DHASI*i*Pr)CpCl] as a precatalyst, PPh_3 was found to be a crucial coligand to suppress the problematic homocoupling of phenylboronic acid and also to accelerate the reaction. The established catalytic system successfully catalyzed the coupling reaction of aryl and heteroaryl halides with aryl and heteroarylboronic acids with 0.25−2 mol % of catalyst loading. Further investigations into the application of this robust precatalyst to other useful reactions are being conducted in our laboratory.

EXPERIMENTAL SECTION

General Procedure and Chemicals. All reactions were carried out under an argon atmosphere with freshly distilled solvents under anhydrous conditions, unless otherwise noted. 1,4-Dioxane was distilled from sodium benzophenone ketyl. Toluene was distilled from CaH_2. *tert*-BuOH was distilled from CaH_2. *tert*-Amylalcohol was distilled from K_2CO_3. Nickelocene was sublimed at 100 °C prior to use. Reagents were used without further purification. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous materials, unless otherwise stated. ^{1}H and ^{13}C NMR spectra were recorded at 600 and 151 MHz, respectively. Chemical shifts are reported in δ ppm referenced to an internal tetramethylsilane or solvent peaks. High-resolution mass spectra were recorded on a double-focusing magnetic-sector mass analyzer operating in a FAB mode.

[Ni(DHASI*i*Pr)CpCl] 2. 1,4-Dioxane was degassed via the freeze−thaw technique prior to use. A flask was charged with DHASI*i*Pr·HBF_4 **1** (74 mg, 177 mmol),[14] freshly sublimed nickelocene (50 mg, 265 mmol), *n*-Bu_4NCl (54 mg, 194 mmol), and a magnetic stir bar at 25 °C. The flask was evacuated and backfilled with argon (repeated this sequence three times). 1,4-Dioxane (5.6 mL) was then added to the resulting flask at 25 °C, and the reaction mixture was stirred at reflux for 1 h. The reaction solution was cooled to 25 °C, and the solvent was removed under reduced pressure. The residue was treated with boiling toluene (10 mL), and the resulting red solution was filtered. This process was repeated three times, and the combined filtrates were transferred to a separatory funnel and washed with H_2O (20 mL × 3). The organic layer was dried over Na_2SO_4 and filtered, and the volume of the resulting solution was reduced to ca. 2 mL under reduced pressure. *n*-Hexane was slowly added to this solution to precipitate the title complex [Ni(DHASI*i*Pr)CpCl] **2** (84 mg, 97%) as a reddish orange solid. A single crystalline for X-ray diffraction analysis was grown by the slow vapor diffusion of *n*-hexane into a toluene solution. mp 199−201 °C (decomp.); ^{1}H NMR (600 MHz, $CDCl_3$, 297 K): δ = 7.29 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.28−7.25 (m, 2H), 7.16 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.14 (dd, *J* = 5.4, 3.0 Hz, 2H), 6.48 (sep, *J* = 7.2 Hz, 2H), 4.75 (s, 5H), 4.58 (s, 2H), 4.39 (dd, *J* = 1.2, 1.2 Hz, 2H), 1.60 (d, *J* = 7.2 Hz, 6H), 1.40 (d, *J* = 7.2 Hz, 6H) ppm; ^{13}C{^{1}H} NMR (151 MHz, CD_2Cl_2, 303 K): δ = 199.0, 139.9, 138.7, 126.5, 126.1, 125.6, 124.5, 91.0, 63.7, 53.5, 48.2, 23.0, 19.6 ppm; IR (KBr pellet): ν_{max} = 3040, 2972, 2938, 2873, 1470, 1459, 1368, 1297, 1269, 1184, 1126, 1085, 1035, 833, 779, 759 cm^{-1}; HRMS (FAB+) calcd. for $C_{28}H_{31}ClN_2Ni$ (M^+) 488.1529, found 488.1533.

Typical Procedure for the Ni(NHC)CpCl Catalyzed Suzuki−Miyaura Cross-Coupling. A test tube with screw cap was charged with [Ni(DHASI*i*Pr)CpCl] **2** (2.0 mg, 4.0 μmol), K_3PO_4 (255 mg, 1.2 mmol), PPh_3 (21 mg, 80 μmol), phenylboronic acid (73 mg, 0.60 mmol), and magnetic stir bar at 25 °C (if an aryl chloride was solid, the aryl chloride was added to this test tube at this point), and the resulting test tube was capped with a rubber septum. The test tube was evacuated and backfilled with argon (repeated this sequence three times). Degassed solvent (1.0 mL, (2.0 mL in the case of solid aryl chloride)) was then added to the resulting vessel at 25 °C, and the reaction mixture was stirred at 25 °C until the color of the solution changed from red to yellow. Aryl chloride (0.40 mmol) in degassed solvent (0.5 mL) was added by a syringe through the septum, and an additional 0.5 mL of degassed solvent was used to rinse the flask which had been charged with the aryl chloride (skipped this process in the case of solid aryl chloride). The rubber septum was replaced with a screw cap promptly, and the reaction solution was then heated at 90 °C for 24 h. The reaction was quenched with H_2O (20 mL) at 0 °C, and the resulting mixture was extracted with EtOAc (10 mL × 3). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by flash column chromatography on silica gel (30 mL) to afford the cross-coupled product. The coupling reaction using 1-chloro-2-(1-methylethoxy)benzene or ethyl 2-chlorobenzoate was heated at 110 °C in toluene/*tert*-amylalcohol.

*4-Methoxybiphenyl (**5aa**).*[23] Eluent for column chromatography: 1−5% EtOAc/*n*-hexane; Yield: 71 mg (96%); State of the product: colorless solid; ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 7.55 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.53 (d, *J* = 8.4, 2H), 7.41 (dd, *J* = 7.2, 7.2 Hz, 2H), 7.30 (dddd, *J* = 7.2, 7.2, 1.2, 1.2 Hz, 1H), 6.98 (d, *J* = 8.4 Hz, 2H), 3.85 (s, 3H) ppm.

*2-Fluorobiphenyl (**5ba**; Obtained as an Inseparable Mixture with Biphenyl).*[23] Eluent for column chromatography: *n*-hexane; Yield: 66 mg (90% yield based on ^{1}H NMR); State of the product: colorless solid; ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 7.56−7.53 (m, 2H), 7.46−7.41 (m, 3H), 7.36 (dddd, *J* = 7.2, 7.2, 1.2, 1.2 Hz, 1H), 7.33−7.28 (m, 1H), 7.20 (ddd, *J* = 7.2, 7.2, 1.2 Hz, 1H), 7.15 (ddd, *J* = 10.8, 7.2, 1.2 Hz, 1H) ppm.

*2-Methoxybiphenyl (**5ca**).*[23] Eluent for column chromatography: 1−5% EtOAc/*n*-hexane; Yield: 64 mg (86%); State of the product: colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 7.53−7.51 (m, 2H), 7.40 (dddd, *J* = 7.2, 7.2, 1.2, 1.2 Hz, 2H), 7.33−7.29 (m, 3H), 7.02 (ddd, *J* = 7.2, 7.2, 1.2 Hz, 1H), 6.97 (d, *J* = 7.8 Hz, 1H), 3.79 (s, 3H) ppm.

*2-Phenylbenzonitrile (**5da**).*[23] Eluent for column chromatography: 5−9% EtOAc/*n*-hexane; Yield: 63 mg (88%); State of the product: colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$, 299 K): δ = 7.76 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.64 (ddd, *J* = 7.2, 7.2, 1.2 Hz, 1H), 7.57−7.54 (m, 2H), 7.52 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.51−7.47 (m, 2H), 7.46−7.42 (m, 2H) ppm.

*2-Methylbiphenyl (**5ea**; Obtained as an Inseparable Mixture with Biphenyl).*[23] Eluent for column chromatography: *n*-hexane; Yield: 59 mg of mixture (80% yield based on ^{1}H NMR); State of the product: colorless liquid; ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 7.41−7.38 (m, 2H), 7.34−7.30 (m, 3H), 7.27−7.21 (m, 4H), 2.27 (s, 3H) ppm.

*Biphenyl-2-carboxaldehyde (**5fa**).*[23] Eluent for column chromatography: 1−3% EtOAc/*n*-hexane; Yield: 64 mg (88%); State of the product: colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 9.99 (d, *J* = 0.6 Hz, 1H), 8.03 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.64 (ddd, *J* = 7.2, 7.2, 1.2 Hz, 1H), 7.52−7.44 (m, 5H), 7.40−7.36 (m, 2H) ppm.

*2-(Trifluoromethyl)biphenyl (**5ga**; Obtained as an Inseparable Mixture with Biphenyl).*[23] Eluent for column chromatography: *n*-hexane; Yield: 88 mg (99% yield based on ^{1}H NMR); State of the product: colorless liquid; ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 7.74 (d, *J* = 7.8 Hz, 1H), 7.55 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.46 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.41−7.37 (m, 3H), 7.34−7.31 (m, 3H) ppm.

*2-Aminobiphenyl (**5ha**).*[23] Eluent for column chromatography: 10% EtOAc/*n*-hexane; Yield: 60 mg (89%); State of the product: pale yellow solid; ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 7.47−7.42 (m, 4H), 7.34 (dddd, *J* = 6.6, 6.6, 1.2, 1.2 Hz, 1H), 7.15 (ddd, *J* = 7.8, 7.8, 1.2 Hz, 1H), 7.13 (dd, *J* = 7.2, 1.2 Hz, 1H), 6.82 (ddd, *J* = 7.8, 7.8, 1.2 Hz, 1H), 6.76 (dd, *J* = 7.8, 1.2 Hz, 1H), 3.74 (br s, 2H) ppm.

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*1-Phenylnaphthalene (**5ia**; Obtained as an Inseparable Mixture with a Trace Amount of Biphenyl).*[23] Eluent for column chromatography: *n*-hexane; Yield: 79 mg (97%); State of the product: colorless liquid; ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 7.90 (d, *J* = 9.6 Hz, 2H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.53−7.46 (m, 6H), 7.44−7.40 (m, 3H) ppm.

*Ethyl 2-Phenylbenzoate (**5ja**).*[23] Eluent for column chromatography: 5% EtOAc/*n*-hexane; Yield: 89 mg (98%); State of the product: colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 7.82 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.51 (ddd, *J* = 7.8, 7.8, 1.2 Hz, 1H), 7.42−7.33 (m, 5H), 7.32−7.30 (m, 2H), 4.08 (q, *J* = 7.2 Hz, 2H), 0.98 (t, *J* = 7.2 Hz, 3H) ppm.

*2-(1-Methylethoxy)biphenyl (**5ka**).*[23] Eluent for column chromatography: 0−1% Et_2O/*n*-hexane; Yield: 74 mg (87%); State of the product: colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 7.57−7.54 (m, 2H), 7.39 (dd, *J* = 7.2, 7.2 Hz, 2H), 7.33 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.32−7.25 (m, 2H), 7.01 (ddd, *J* = 7.2, 7.2, 1.2 Hz, 1H), 6.99 (d, *J* = 7.8 Hz, 1H), 4.42 (sep, *J* = 6.0 Hz, 1H), 1.24 (d, *J* = 6.0 Hz, 6H) ppm.

*1,1-Dimethylethyl N-Biphenyl-2-ylcarbamate (**5la**).*[23] Eluent for column chromatography: 1−5% EtOAc/*n*-hexane; Yield: 68 mg (63%; 13% of Boc cleaved product **5ha** was also isolated); State of the product: colorless solid; ^{1}H NMR (600 MHz, $CDCl_3$, 297 K): δ = 8.11 (d, *J* = 6.6 Hz, 1H), 7.49 (dd, *J* = 7.2, 7.2 Hz, 2H), 7.41 (dddd, *J* = 7.2, 7.2, 1.2, 1.2 Hz, 1H), 7.39−7.36 (m, 2H), 7.34 (ddd, *J* = 7.2, 7.2, 1.2 Hz, 1H), 7.20 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.08 (ddd, *J* = 7.2, 7.2, 1.2 Hz, 1H), 6.50 (br s, 1H), 1.46 (s, 9H) ppm.

*N-Biphenyl-2-ylacetamide (**5ma**).*[23] Eluent for column chromatography: 20−50% EtOAc/*n*-hexane; Yield: 51 mg (60%; 22% of acetanilide was also isolated); State of the product: colorless crystalline; ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 8.27 (d, *J* = 8.4 Hz, 1H), 7.49 (dd, *J* = 7.2, 7.2 Hz, 2H), 7.42 (dd, *J* = 7.2, 7.2 Hz, 1H), 7.40−7.36 (m, 3H), 7.24 (d, *J* = 7.2 Hz, 1H), 7.18 (dd, *J* = 7.2, 7.2 Hz, 1H), 7.12 (br s, 1H), 2.02 (s, 3H) ppm.

*9-Phenylanthracene (**5na**).*[23] Eluent for column chromatography: *n*-hexane; Yield: 99 mg (97%); State of the product: colorless crystalline; ^{1}H NMR (600 MHz, $CDCl_3$, 299 K): δ = 8.49 (s, 1H), 8.04 (d, *J* = 8.4 Hz, 2H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.57 (dddd, *J* = 7.2, 7.2, 1.2, 1.2 Hz, 2H), 7.52 (dddd, *J* = 7.2, 7.2, 1.2, 1.2 Hz, 1H), 7.47−7.41 (m, 4H), 7.35 (dd, 7.8, 1.2 Hz, 1H), 7.33 (dd, 6.6, 1.2 Hz, 1H) ppm.

*4-Methoxy-2′-methylbiphenyl (**5ab**).*[23] Eluent for column chromatography: 0−2% Et_2O/*n*-hexane; Yield: 53 mg (67%); State of the product: pale yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 7.26−7.20 (m, 6H), 6.95 (d, *J* = 9.0 Hz, 2H), 3.84 (s, 3H), 2.27 (s, 3H) ppm.

*2,4′-Dimethoxy-biphenyl (**5ac**).*[23] Eluent for column chromatography: 2−4% EtOAc/*n*-hexane; Yield: 69 mg (81%); State of the product: colorless solid; ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 7.47 (d, *J* = 9.0 Hz, 2H), 7.31−7.27 (m, 2H), 7.01 (ddd, *J* = 7.2, 7.2, 1.2 Hz, 1H), 6.97 (d, *J* = 7.2 Hz, 1H), 6.95 (d, *J* = 9.0 Hz, 2H), 3.84 (s, 3H), 3.81 (s, 3H) ppm.

*2-Fluoro-2′-methylbiphenyl (**5bb**; Obtained as an Inseparable Mixture with 2,2′-Dimethylbiphenyl).*[23] Eluent for column chromatography: *n*-hexane; Yield: 76 mg (99% yield based on ^{1}H NMR); State of the product: colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 7.33 (dddd, *J* = 7.8, 7.2, 4.8, 1.8 Hz, 1H), 7.31−7.27 (m, 2H), 7.24 (ddd, *J* = 7.2, 7.2, 1.8 Hz, 1H), 7.22 (ddd, *J* = 7.2, 7.2, 1.2 Hz, 1H), 7.19 (ddd, *J* = 7.2, 7.2, 1.2 Hz, 1H), 7.13 (ddd, *J* = 9.6, 8.4, 1.2 Hz, 1H), 2.20 (s, 3H) ppm.

*2-Methoxy-2′-methylbiphenyl (**5cb**, **5ec**).*[23] Eluent for column chromatography: 0−1% Et_2O/*n*-hexane; Yield: 78 mg (98%); State of the product: colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 7.34 (ddd, *J* = 8.4, 7.8, 1.2 Hz, 1H), 7.26−7.21 (m, 3H), 7.18 (d, *J* = 7.2 Hz, 1H), 7.14 (dd, *J* = 7.2, 1.8 Hz, 1H), 7.01 (ddd, *J* = 7.2, 7.2, 1.2 Hz, 1H), 6.96 (d, *J* = 7.8 Hz, 1H), 3.76 (s, 3H), 2.14 (s, 3H) ppm.

*2-(2-Methylphenyl)benzonitrile (**5db**).*[23] Eluent for column chromatography: 5−7% EtOAc/*n*-hexane; Yield: 76 mg (98%); State of the product: colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 7.75 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.63 (ddd, *J* = 7.8, 7.8, 1.2 Hz, 1H), 7.45 (ddd, *J* = 7.8, 7.8, 1.2 Hz, 1H), 7.37 (d, *J* = 7.2 Hz, 1H), 7.34 (ddd, *J* = 7.2, 7.2, 1.2 Hz, 1H), 7.31 (d, *J* = 7.2 Hz, 1H), 7.27 (ddd, *J* = 7.2, 7.2, 1.2 Hz, 1H), 7.20 (dd, *J* = 7.8, 1.2 Hz, 1H), 2.19 (s, 3H) ppm.

*2-(2-Methoxyphenyl)benzonitrile (**5dc**).*[23] Eluent for column chromatography: 5−7% EtOAc/*n*-hexane; Yield: 74 mg (89%); State of the product: colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 7.72 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.62 (ddd, *J* = 7.8, 7.8, 1.2 Hz, 1H), 7.45 (d, *J* = 7.2 Hz, 1H), 7.43−7.39 (m, 2H), 7.25 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.06 (ddd, *J* = 7.2, 7.2, 1.2 Hz, 1H), 7.03 (d, *J* = 7.8 Hz, 1H), 3.84 (s, 3H) ppm.

*4-Phenylpyridine (**10aa**).*[23] Reaction time: 4 h; Eluent for column chromatography: 40% EtOAc/*n*-hexane; Yield: 61 mg (98%); State of the product: colorless solid; ^{1}H NMR (600 MHz, $CDCl_3$, 299 K): δ = 8.65 (dd, *J* = 4.2, 1.2 Hz, 2H), 7.64−7.62 (m, 2H), 7.51−7.46 (m, 4H), 7.43 (dddd, *J* = 7.2, 7.2, 1.2, 1.2 Hz, 1H) ppm.

*3-Phenylpyridine (**10ba**).*[21e] Reaction time: 7 h; Eluent for column chromatography: 40% EtOAc/*n*-hexane; Yield: 61 mg (98%); State of the product: pale yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$, 299 K): δ = 8.85 (d, *J* = 1.8 Hz, 1H), 8.58 (dd, *J* = 4.8, 1.8 Hz, 1H), 7.86 (ddd, *J* = 7.8, 1.8, 1.2 Hz, 1H), 7.59−7.56 (m, 2H), 7.47 (dddd, *J* = 8.4, 8.4, 1.8, 1.8 Hz, 2H), 7.40 (dddd, *J* = 8.4, 8.4, 1.8, 1.8 Hz, 1H), 7.35 (ddd, *J* = 7.8, 4.8, 0.6 Hz, 1H) ppm.

*5-Phenylpyrimidine (**10ca**).*[23] Reaction time: 0.5 h; Eluent for column chromatography: 30% EtOAc/*n*-hexane; Yield: 60 mg (96%); State of the product: colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$, 297 K): δ = 9.21 (s, 1H), 8.96 (s, 2H), 7.60−7.57 (m, 2H), 7.53 (dddd, *J* = 7.8, 7.8, 1.2, 1.2 Hz, 2H), 7.48 (dddd, *J* = 7.2, 7.2, 1.2, 1.2 Hz, 1H) ppm.

*3-Phenylthiophene (**10da**; Obtained as an Inseparable Mixture with Biphenyl).*[23] Reaction time: 2 h; Eluent for column chromatography: *n*-hexane; Yield: 49 mg (72% yield based on ^{1}H NMR); State of the product: colorless solid; ^{1}H NMR (600 MHz, $CDCl_3$, 299 K): δ = 7.59 (dd, *J* = 7.2, 1.2 Hz, 2H), 7.45−7.43 (m, 1H), 7.39−7.36 (m, 4H), 7.28 (dddd, *J* = 7.2, 7.2, 1.2, 1.2 Hz, 1H) ppm.

*1-Methyl-3-phenylindole (**10ea**).*[23] Reaction time: 5 h; Eluent for column chromatography: 0−10% CH_2Cl_2/*n*-hexane; Yield: 45 mg (54%); State of the product: colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 7.94 (ddd, *J* = 7.8, 0.6, 0.6 Hz, 1H), 7.65 (dd, *J* = 7.8, 1.2 Hz, 2H), 7.43 (dddd, *J* = 7.2, 7.2, 1.2, 1.2 Hz, 2H), 7.36 (d, *J* = 8.4 Hz, 1H), 7.28 (ddd, *J* = 7.8, 7.2, 1.2 Hz, 1H), 7.26 (dddd, *J* = 7.2, 7.2, 1.2, 1.2 Hz, 1H), 7.22 (s, 1H), 7.19 (ddd, *J* = 7.8, 7.2, 1.2 Hz, 1H), 3.83 (s, 3H) ppm.

*5-Phenylindole (**10fa**).*[23] Reaction time: 2 h; Eluent for column chromatography: 15−20% EtOAc/*n*-hexane; Yield: 72 mg (93%); State of the product: pale yellow solid; ^{1}H NMR (600 MHz, $CDCl_3$, 297 K): δ = 8.20 (brs, 1H), 7.86 (d, *J* = 0.6 Hz, 1H), 7.65 (dd, *J* = 7.8, 1.2 Hz, 2H), 7.46−7.45 (m, 2H), 7.44 (dddd, *J* = 8.4, 8.4, 1.8, 1.8 Hz, 2H), 7.31 (dddd, *J* = 7.2, 7.2, 1.2, 1.2 Hz, 1H), 7.24 (dd, *J* = 3.0, 2.4 Hz, 1H), 6.61 (dd, *J* = 3.0, 2.4 Hz, 1H) ppm.

*3-Phenylquinoline (**10ga**).*[21e] Reaction time: 6 h; Eluent for column chromatography: 30% EtOAc/*n*-hexane; Yield: 81 mg (99%); State of the product: colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$, 297 K): δ = 9.18 (d, *J* = 1.8 Hz, 1H), 8.29 (d, *J* = 2.4 Hz, 1H), 8.15 (d, *J* = 8.4 Hz, 1H), 7.87 (dd, *J* = 7.8, 0.6 Hz, 1H), 7.73−7.69 (m, 3H), 7.57 (ddd, *J* = 7.8, 7.2, 1.2 Hz, 1H), 7.52 (dddd, *J* = 7.2, 7.2, 1.2, 1.2 Hz, 2H), 7.43 (dddd, *J* = 7.2, 7.2, 1.2, 1.2 Hz, 1H) ppm.

*4,7-Diphenylquinoline (**10ha**).*[23] Reaction time: 18 h; Eluent for column chromatography: 20−30% EtOAc/*n*-hexane; Yield: 104 mg (92%); State of the product: colorless solid; ^{1}H NMR (600 MHz, $CDCl_3$, 299 K): δ = 8.97 (d, *J* = 4.8 Hz, 1H), 8.40 (d, *J* = 1.8 Hz, 1H), 7.99 (d, *J* = 9.0 Hz, 1H), 7.79−7.76 (m, 3H), 7.56−7.49 (m, 7H), 7.41 (dddd, *J* = 7.2, 7.2, 1.2, 1.2 Hz, 1H), 7.33 (d, *J* = 4.2 Hz, 1H) ppm.

*2-Phenylpyridine (**10ia**).*[23] Reaction time: 2 h; Eluent for column chromatography: 5−10% EtOAc/*n*-hexane, pure product for the analysis was obtained after the removal of residual S.M via distillation under reduced pressure; Yield: 21 mg (34%); State of the product: pale yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 8.69 (ddd, *J* = 5.4, 1.2, 1.2 Hz, 1H), 8.00−7.97 (m, 2H), 7.76−7.71 (m, 2H), 7.47 (dddd, *J* = 7.2, 7.2, 1.2, 1.2 Hz, 2H), 7.41 (dddd, *J* = 7.2, 7.2, 1.2, 1.2 Hz, 1H), 7.22 (ddd, *J* = 6.6, 4.8, 1.8 Hz, 1H) ppm.

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1-(5-Phenylthiophen-2-yl)ethan-1-one (**10ja**).[23] Reaction time: 3.5 h; Eluent for column chromatography: 5−7% EtOAc/*n*-hexane; Yield: 38 mg (47%; 51% of S.M. was recovered); State of the product: pale yellow solid; ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 7.67−7.64 (m, 3H), 7.42 (dddd, *J* = 7.2, 7.2, 1.2, 1.2 Hz, 2H), 7.37 (dddd, *J* = 7.2, 7.2, 1.2, 1.2 Hz, 1H), 7.32 (d, *J* = 4.2 Hz, 1H), 2.57 (s, 3H) ppm.

4-Methyl-3-(2-methylphenyl)pyridine (**10kb**).[21a] Reaction time: 16 h; Eluent for column chromatography: 30−40% EtOAc/*n*-hexane; Yield: 71 mg (97%); State of the product: colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$, 300 K): δ = 8.46 (d, *J* = 5.4 Hz, 1H), 8.33 (s, 1H), 7.31−7.29 (m, 2H), 7.25 (ddd, *J* = 7.2, 7.2, 1.2 Hz, 1H), 7.21 (d, *J* = 4.8 Hz, 1H), 7.09 (d, *J* = 7.8 Hz, 1H), 2.09 (s, 3H), 2.06 (s, 3H) ppm.

4-(Thiophen-3-yl)pyridine (**12aa**).[23] Reaction time: 2.5 h; Eluent for column chromatography: 20−40% EtOAc/*n*-hexane; Yield: 63 mg (98%); State of the product: off-white solid; ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 8.65 (app d, *J* = 6.0 Hz, 2H), 7.68 (dd, *J* = 3.0, 1.2 Hz, 1H), 7.51 (dd, *J* = 4.2, 1.2 Hz, 2H), 7.46−7.43 (m, 2H) ppm.

4-(Furan-3-yl)pyridine (**12ab**).[23] Reaction time: 12 h; Eluent for column chromatography: 30−50% EtOAc/*n*-hexane; Yield: 57 mg (98%); State of the product: beige oil; ^{1}H NMR (600 MHz, $CDCl_3$, 297 K): δ = 8.58 (dd, *J* = 4.2, 1.2 Hz, 2H), 7.88 (dd, *J* = 1.2, 1.2 Hz, 1H), 7.53 (dd, *J* = 1.2, 1.2 Hz, 1H), 7.37 (dd, *J* = 4.2, 1.2 Hz, 2H), 6.74 (dd, *J* = 1.8, 0.6 Hz, 1H) ppm.

3-(Thiophen-3-yl)pyridine (**12ba**).[1h,21e] Reaction time: 5 h; Eluent for column chromatography: 30−40% EtOAc/*n*-hexane; Yield: 60 mg (93%); State of the product: pale yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$, 300 K): δ = 8.88 (s, 1H), 8.54 (d, *J* = 3.0 Hz, 1H), 7.88 (ddd, *J* = 7.8, 1.8, 1.8 Hz, 1H), 7.53 (dd, *J* = 3.0, 1.2 Hz, 1H), 7.45 (dd, *J* = 4.8, 3.0 Hz, 1H), 7.40 (dd, *J* = 5.4, 1.2 Hz, 1H), 7.34 (dd, *J* = 7.8, 4.8 Hz, 1H) ppm.

3-(Furan-3-yl)pyridine (**12bb**).[1h] Reaction time: 12 h; Eluent for column chromatography: 30−40% EtOAc/*n*-hexane; Yield: 55 mg (95%); State of the product: yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$, 298 K): δ = 8.77 (d, *J* = 1.8 Hz, 1H), 8.50 (dd, *J* = 4.8, 1.8 Hz, 1H), 7.78 (dd, *J* = 1.2, 1.2 Hz, 1H), 7.76 (ddd, *J* = 7.8, 1.8, 1.8 Hz, 1H), 7.53 (dd, *J* = 1.8, 1.8 Hz, 1H), 7.31 (ddd, *J* = 7.8, 4.8, 1.2 Hz, 1H), 6.72 (dd, *J* = 1.8, 1.2 Hz, 1H) ppm.

5-(Thiophen-3-yl)pyrimidine (**12ca**).[1h,21e] Reaction time: 1 h; Eluent for column chromatography: 30−40% EtOAc/*n*-hexane; Yield: 62 mg (96%); State of the product: pale yellow solid; ^{1}H NMR (600 MHz, $CDCl_3$, 300 K): δ = 9.14 (s, 1H), 8.96 (s, 2H), 7.61 (dd, *J* = 3.0, 1.2 Hz, 1H), 7.51 (dd, *J* = 4.8, 3.0 Hz, 1H), 7.41 (dd, *J* = 4.8, 1.2 Hz, 1H) ppm.

5-(Furan-3-yl)pyrimidine (**12cb**).[1h,21e] Reaction time: 1 h; Eluent for column chromatography: 30% EtOAc/*n*-hexane; Yield: 55 mg (94%); State of the product: colorless needle; ^{1}H NMR (600 MHz, $CDCl_3$, 297 K): δ = 9.12 (s, 1H), 8.86 (s, 2H), 7.85 (dd, *J* = 1.2, 1.2 Hz, 1H), 7.58 (dd, *J* = 1.8, 1.8 Hz, 1H), 6.74 (dd, *J* = 1.8, 0.6 Hz, 1H) ppm.

3-(Thiophen-3-yl)furan (**12db**).[23] Reaction time: 4 h; Eluent for column chromatography: *n*-hexane; Yield: 48 mg (80%); State of the product: colorless solid; ^{1}H NMR (600 MHz, $CDCl_3$, 297 K): δ = 7.67 (br dd, *J* = 1.2, 1.2 Hz, 1H), 7.44 (dd, *J* = 1.8, 1.8 Hz, 1H), 7.34 (dd, *J* = 4.8, 3.0 Hz, 1H), 7.27 (dd, *J* = 3.0, 1.2 Hz, 1H), 7.21 (dd, *J* = 4.8, 1.2 Hz, 1H), 6.63 (dd, *J* = 1.8, 0.6 Hz, 1H) ppm.

Coupling of Amide with Phenylboronic Acid.[2a] Toluene and *tert*-butylalcohol (10:1) were mixed and degassed via the sonication under reduced pressure prior to use. A test tube with a screw cap was charged with [Ni(DHASI*i*Pr)CpCl] **2** (4.9 mg, 10 mmol), K_3PO_4 (127 mg, 0.6 mmol), amide substrate **13** (62 mg, 0.2 mmol),[2a] phenylboronic acid (61 mg, 0.50 mmol), and a magnetic stir bar at 25 °C, and the resulting test tube was capped with a rubber septum. The test tube was evacuated and backfilled with argon (repeated this sequence three times). Degassed solvent (1.0 mL) was then added to the resulting vessel at 25 °C, and the rubber septum was then replaced with a screw cap promptly. The reaction solution was then heated at 90 °C for 24 h. The reaction was quenched with H_2O (20 mL) at 0 °C, and the resulting mixture was extracted with EtOAc (10 mL × 3). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by flash column chromatography (5% EtOAc/*n*-hexane) on silica gel (30 mL) to afford the benzophenone **14** (31 mg, 85%) as a colorless solid. ^{1}H NMR (600 MHz, $CDCl_3$, 297 K): δ = 7.81 (dd, *J* = 7.2, 1.2 Hz, 4H), 7.59 (dddd, *J* = 7.2, 7.2, 1.2, 1.2 Hz, 2H), 7.48 (dd, *J* = 7.2, 7.2 Hz, 4H) ppm.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02666.

Miscellaneous data from the optimization of the reaction conditions, characterization data, copies of NMR spectra, and crystallographic data of complex **2** (PDF)

Crystallographic data of complex **2** (CIF)

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Notes

The authors declare no competing financial interest.

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(23) See the Supporting Information for the list of references for the characterization data of known compounds.

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