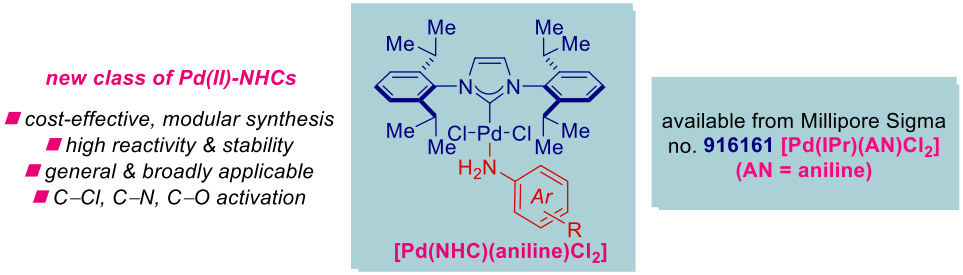
[(NHC)PdCl$_2$(Aniline)] Complexes: Easily Synthesized, Highly Active Pd(II)–NHC Precatalysts for Cross-Coupling Reactions

Qinqin Xia,[†,§] Shicheng Shi,[†] Pengcheng Gao,[†] Roger Lalancette,[†] Roman Szostak,[‡] and Michal Szostak*,[†]

[§]School of Pharmaceutical Sciences, Wenzhou Medical University, Wenzhou 325035, China
[†]Department of Chemistry, Rutgers University, 73 Warren Street, Newark, New Jersey 07102, United States
[‡]Department of Chemistry, Wroclaw University, F. Joliot-Curie 14, Wroclaw 50-383, Poland

Supporting Information



ABSTRACT: We report the synthesis, characterization and reactivity of [(NHC)PdCl$_2$(aniline)] complexes. These well-defined, air- and moisture-stable catalysts are highly active in the Suzuki–Miyaura cross-coupling of amides by N–C(O) activation as well as in the Suzuki–Miyaura cross-coupling of esters, aryl chlorides and Buchwald–Hartwig amination. Most crucially, this study introduces broadly available anilines as stabilizing ligands for well-defined Pd(II)-NHC catalysts. The availability of various aniline scaffolds, including structural and electronic diversity, has a significant potential in fine-tuning of challenging cross-couplings by Pd-NHCs. The parent catalyst in this class, [Pd(IPr)(AN)Cl$_2$], has been commercialized in collaboration with Millipore Sigma, offering broad access for reaction screening and optimization.

1. Introduction

Palladium-catalyzed cross-coupling reactions have revolutionized the synthesis of small molecules and are among the most important methods for the construction of diverse chemicals.[1,2] In particular, the recent years have witnessed the emergence of well-defined Pd(II) precatalysts, which allow to use the optimal 1:1 Pd to ligand ratio in operationally-convenient protocols (Figure 1, **1-5**).[3,4] A number of these precatalysts, including [Pd(NHC)(allyl)Cl] and [Pd(NHC)(cin)Cl] complexes,[5] Pd-PEPPSI systems,[6] SingaCycle catalysts[7] or G1-G4 palladacycles[8] are now commercially available, enabling straightforward application and reaction optimization by synthetic chemists.

In this context, NHCs (NHC = N-heterocyclic carbenes) have shown significant advantages as ancillary ligands in Pd catalysis, including strong σ-donation and steric tuning around the metal center.[9,10] Stabilization of palladium by the amine-type nitrogen is a key feature of palladacycles (Figure 1, **4-5**).[11,12] As catalyst design criteria, the stabilizing ligand should be easily removed during the activation step to yield the active monoligated Pd(0) complex,[13] while its re-association could stabilize the active metal species, leading to a longer catalyst lifetime.

Our laboratory has been interested in Pd-NHC catalysis[14] and the synthesis of N-containing molecules.[15] In this context, we sought to take advantage of anilines as an unexplored class of weakly coordinating ligands in Pd(II)-NHC catalysis.[16] Herein, we report the synthesis, characterization and reactivity of [(NHC)PdCl$_2$(aniline)] complexes (Figure 1, **6**). The study introduces broadly available anilines as stabilizing ligands for well-defined Pd(II)-NHC catalysis. The availability of various aniline scaffolds, including structural and electronic diversity, offers significant potential in the optimization and fine-tuning of cross-coupling reactions.

There are several additional points that should be addressed:

(1) In particular, it should be pointed out that similar reactions have been effected with related Pd(II)-NHC precatalysts.[14,16–19] In our experience, the use of different ancillary ligands on Pd in this class of precatalysts leads to changes in performance of specific substrates, and thus it is recommended that various Pd(II)-NHC precatalysts are screened to achieve optimum performance. In this respect, anilines as ancillary ligands are expected to be complementary to other systems, while the broad availability of anilines should enable further catalyst tuning that is not

easily possible with other ancillary ligands. As an additional advantage, [(NHC)PdCl$_2$(aniline)] catalysts are readily synthesized and a representative catalyst has been made available to allow other researchers utilize this class of catalysts in their research.

(2) A common terminology used in Pd(II)-NHC catalysis to define a ligand that does not participate in catalysis, but enables stability of Pd(II) precatalysts is "throw-away" ligand.[16–19]

(3) It is important to discuss the potential utility of amides as cross-coupling reagents.[14,15] Ni(0)-NHC systems in N–C(O) cross-coupling have been pioneered by Garg and co-workers.[14g] These systems are less practical because they utilize air-sensitive reagents, although several elegant solutions have been devised, including paraffin capsules. In contrast, Pd(II)-NHC systems have now been shown to be more reactive than Ni-NHC systems in amide cross-coupling owing to the combination of catalyst stability and strong σ-donation of NHC ligands. Furthermore, the use of amides in cross-coupling raises a question about the utility of these reactions.[14h] In general, there are two advantages of amides as cross-coupling electrophiles over acid chlorides or anhydrides: (1) amides are typically more stable than acid chlorides owing to the amidic resonance across the N–C(O) bond, which allows for late-stage functionalization not easily available with more sensitive functional groups as well as for the use of less functional group tolerant catalysts that often result in decomposition of acid chlorides; (2) more importantly, the use of amides as cross-coupling partners may enable biomolecule functionalization at the N–C(O) bond by acyl cross-coupling.

(4) It is also important to point out the difference between Pd(II)-NHC catalysts bearing stabilizing ligands and Pd(0)-NHC systems. The most known examples of Pd(0)-NHC catalysts are by Beller stabilized by naphthoquinone ligands,[16e] however, these catalysts are rarely used due to their air-sensitivity. While the use of monoligated Pd(0)-NHCs would be optimal or even catalysts prepared in situ, these catalysts are too sensitive or unreactive enough to be commonly used.[16-19]

2. Results and Discussion

Our investigation began with the synthesis of [(NHC)PdCl$_2$(aniline)] complexes (Scheme 1). IPr was selected as a model NHC ancillary ligand because it is a privileged motif in Pd-NHC catalysis (**6**).[17] In addition, a representative imidazolinylidene complex, Pd-SIPr, was synthesized (**7**). The synthesis of [(NHC)PdCl$_2$(aniline)] complexes was readily achieved by reacting anilines with [{Pd(NHC)(Cl)(μ-Cl)}$_2$] dimers in CH_2Cl_2 at room temperature in excellent yields. [(NHC)PdCl$_2$(aniline)] complexes were isolated after trituration with cold pentanes. All complexes were found to be stable to air and moisture.

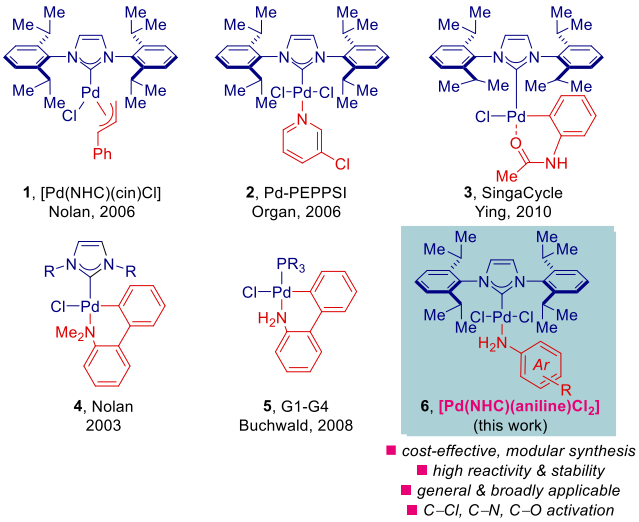
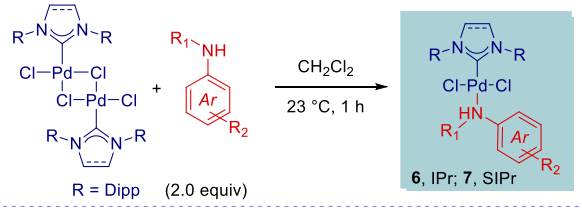


Figure 1. Structures of well-defined Pd(II) precatalysts.

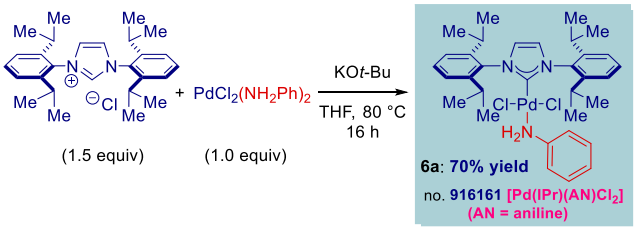
Scheme 1. Synthesis of (NHC)PdCl$_2$(AN) Complexes[a]



6a, R_1 = H, R_2 = H, 91%
6b, R_1 = H, R_2 = 4-MeO, 92%
6c, R_1 = H, R_2 = 4-CF_3, 86%
6d, R_1 = H, R_2 = 2,6-Me_2, 90%
6e, R_1 = H, R_2 = 2,6-i-Pr_2, 82%
6f, R_1 = H, R_2 = 3-CF_3, 84%
6g, R_1 = Me, R_2 = H, 85%
6h, R_1 = Me, R_2 = 4-CF_3, 82%
7a, R_1 = H, R_2 = H, 88%

[a][{Pd(NHC)(Cl)(μ-Cl)}$_2$] (1.0 equiv), aniline (2.0 equiv), CH_2Cl_2 23 °C.

Scheme 2. Direct Synthesis of (IPr)PdCl$_2$(AN)[a]



[a]IPrHCl (1.5 equiv), PdCl$_2$(AN)$_2$ (1.0 equiv), KO*t*-Bu (1.5 equiv), THF, 80 °C. AN = $PhNH_2$.

Note that if required [(NHC)PdCl$_2$(aniline)] complexes are also amenable to chromatographic purification, which should facilitate their use. Complexes **6a** and **7a** were fully characterized by X-ray crystallography (Figure 2 and SI).

In consideration of the utility of PdCl$_2$(aniline)$_2$ precursors[18] for rapid screening of various NHCs, we also developed a direct synthesis [(IPr)PdCl$_2$(AN)] (AN = aniline) (Scheme 2). Under the optimized conditions, IPrHCl (1.5 equiv) is reacted with Pd(PhNH$_2$)$_2$Cl$_2$ (1.0 equiv) and KO*t*-Bu (1.5 equiv) in THF at 80 °C to afford the well-defined [(IPr)PdCl$_2$(AN)] complex in 70% yield.

To evaluate the steric impact in [(NHC)PdCl$_2$(aniline)] complexes, the % buried volume (%V_{bur}) and steric maps in **6a** and **7a** were calculated (Figure 3).[20] With the (%V_{bur}) of 36.1% and 40.7% **6a** and **7a** represent bulky [Pd-NHC]

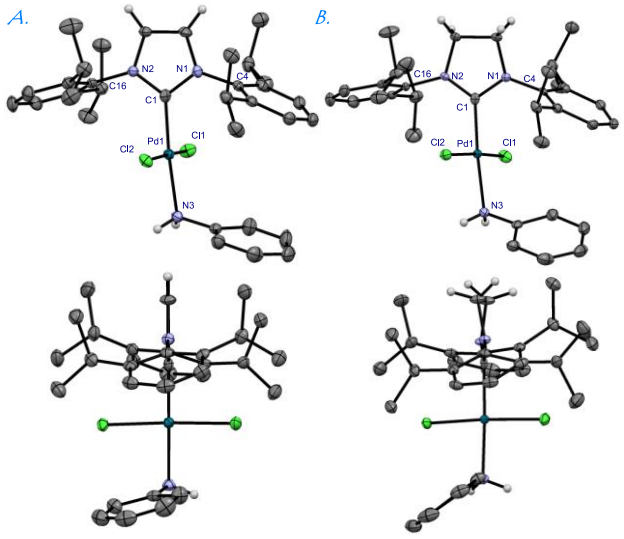


Figure 2. X-ray crystal structure of complex **6a** (a) and **7a** (b). Two views: front (top); side (bottom). Hydrogen atoms have been omitted for clarity except the atoms in the NHC backbone and the $ArNH_2$ moiety. See SI for selected bond lengths and angles. Crystallographic data have been deposited with the CCDC (2077379 and 2077380).

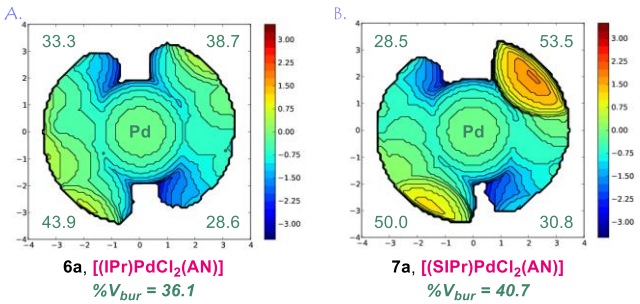


Figure 3. Topographical steric maps of [(IPr)$PdCl_2$(AN)] (**6a**) and [(SIPr)$PdCl_2$(AN)] (**7a**) showing % V_{bur} per quadrant.

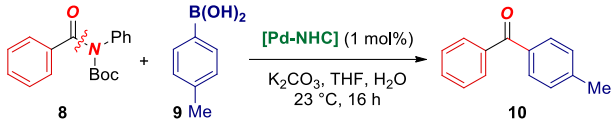
complexes. These values can be compared with the (%V_{bur}) of 34.8% and 39.2% for [Pd(IPr)(3-Cl-py)Cl_2] and [Pd(SIPr)(3-Cl-py)Cl_2] complexes.

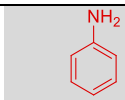
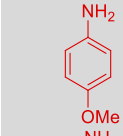
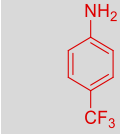
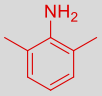
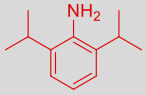
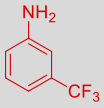
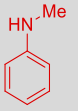
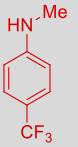
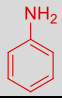
Next, the reactivity of these new Pd(II)-NHC precatalysts was explored. For the initial screen, we selected the Suzuki–Miyaura cross-coupling of amides by N–C(O) activation (Table 1).[14b,c] The reactions performed at 1.0 mol% of (IPr)$PdCl_2$(aniline) (K_2CO_3, H_2O, THF, 16 h) using a series of electronically- and sterically-differentiated precatalysts **6a-h** demonstrate high reactivity in the cross-coupling at mild room temperature (Table 1, column A).

Next, the cross-coupling was performed at 0.25 mol% loading to differentiate the activity of these new precatalysts (Table 1, column B). In this more discriminating screen, we found that electron-neutral (**6a**) and electron-withdrawing (**6c**) substituents are preferred over electron-donating substituents (**6b**), while steric hindrance on the aniline ring (**6d-e**) resulted in lower efficiency.

To gain insight into the activation of these new precatalysts, the reactions were performed at 1.0 mol% of (IPr)$PdCl_2$(aniline) for shorter reaction time (Table 1, column C, RT, 3 h). This led to the identification of 3-

Table 1. Activity of (NHC)$PdCl_2$(Aniline) Complexes in the Suzuki-Miyaura Cross-Coupling of Amides



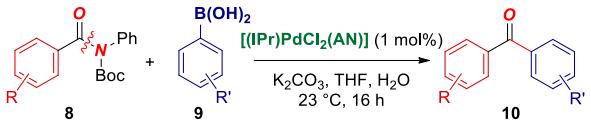
entry	aniline	[Pd-NHC]	NHC	A yield (%)[a]	B yield (%)[b]	C yield (%)[c]
1		**6a**	IPr	>98	>98	52
2		**6b**	IPr	>98	90	22
3		**6c**	IPr	>98	>98	58
4		**6d**	IPr	>98	37	37
5		**6e**	IPr	54	11	<5
6		**6f**	IPr	>98	>98	84
7		**6g**	IPr	>98	>98	46
8		**6h**	IPr	>98	>98	31
9		**7a**	SIPr	>98	62	8

[a][Pd] (1.0 mol%), amide (1.0 equiv), Ar-$B(OH)_2$ (2.0 equiv), K_2CO_3 (3.0 equiv), H_2O (5.0 equiv), THF (0.25 M), 23 °C, 16 h. [b][Pd] (0.25 mol%). [c][Pd] (1.0 mol%), 3 h.

trifluoromethylaniline (**6f**) as the optimal ligand, with the neutral aniline (**6a**) as an inexpensive variant available in bulk.

The generality of the Suzuki–Miyaura cross-coupling of amides using (IPr)$PdCl_2$(AN) is shown in Table 2. We were further pleased to find that the Suzuki–Miyaura cross-coupling of esters by C–O activation is feasible using this new catalyst system (Scheme 3).[14d] We found that the Pd–NHC catalyst bearing 3-trifluoromethylaniline (**6f**) is more efficient than the neutral aniline (**6a**) ligand in this more challenging C–O cross-coupling, mirroring the reactivity trend observed in the amide C–N bond activation. We found that the now available (NHC)$PdCl_2$(AN)[24] also showed excellent reactivity in the Suzuki–Miyaura

Table 2. [(IPr)PdCl$_2$(AN)]-Catalyzed Suzuki-Miyaura Cross-Coupling of Amides by C–N Cleavage[a]

entry	amide (Ar$_1$)	Ar$_2$-B(OH)$_2$	yield (%)
			
1	Ph	R' = 4-Me	98
2	Ph	R' = 4-MeO	95
3	Ph	R' = 4-CF_3	97
4	Ph	R' = 4-CO_2Me	91
5	Ph	R' = 2-Me	90
6	4-MeO-C_6H_4	R' = H	94
7	4-CF_3-C_6H_4	R' = H	95
8	2-Me-C_6H_4	R' = H	79

[a]Conditions: [Pd] (1.0 mol%), amide (1.0 equiv), Ar-B(OH)$_2$ (2.0 equiv), K_2CO_3 (3.0 equiv), H_2O (5.0 equiv), THF (0.25 M), 23 °C, 16 h.

Scheme 3. [(IPr)PdCl$_2$(Aniline)]-Catalyzed Suzuki-Miyaura Cross-Coupling of Esters by C–O Cleavage

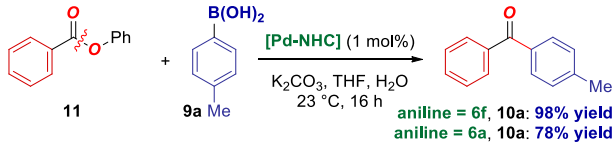
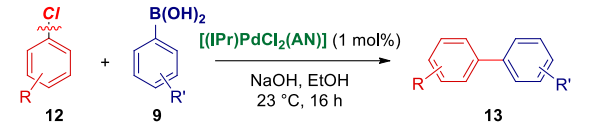
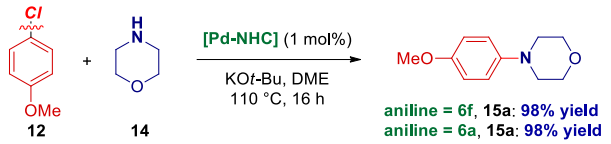


Table 3. [(IPr)PdCl$_2$(AN)]-Catalyzed Suzuki-Miyaura Cross-Coupling of Aryl Chlorides[a]

entry	aryl chloride (Ar$_1$)	Ar$_2$-B(OH)$_2$	yield (%)
			
1	4-MeO-C_6H_4	R' = 4-Me	98
2	4-MeO-C_6H_4	R' = H	98
3	4-CF_3-C_6H_4	R' = H	98
4	4-CN-C_6H_4	R' = H	88
5	4-COMe-C_6H_4	R' = H	98
6	2-C_5H_4N	R' = H	89
7	2-Me-C_6H_4	R' = H	90
8	Ph	R' = 4-MeO	98
9	Ph	R' = 4-CF_3	93
10	Ph	R' = 4-COMe	94
11	Ph	R' = 2-Me	87
12	2-Me-C_6H_4	R' = 2-Me	78

[a]Conditions: [Pd] (1.0 mol%), aryl chloride (1.0 equiv), Ar-B(OH)$_2$ (2.0 equiv), NaOH (2.0 equiv), EtOH (0.25 M), 23 °C, 16 h.

Scheme 4. [(IPr)PdCl$_2$(Aniline)]-Catalyzed Buchwald-Hartwig Cross-Coupling of Aryl Chlorides



cross-coupling of aryl chlorides (Table 3).[5] Only one example of the Buchwald-Hartwig cross-coupling has been studied at this point (Scheme 4).[8] Despite high temperature, this example demonstrates the capacity of these catalysts in N–C coupling.

Finally, to gain insight into the properties of (NHC)PdCl$_2$(aniline) complexes, HOMO and LUMO energy levels of (IPr)PdCl$_2$(AN) (**6a**) were determined at the B3LYP 6-311++g(d,p) level (Figure 4 and Table S3).[9e,f] Determination of HOMO (-6.08 eV) and LUMO (-1.76 eV) of (**6a**) shows that HOMO is located on palladium, while the LUMO is located on the carbene ligand, chlorides, and the aniline ligand. This can be compared with the analogous Pd-PEPPSI system (-6.06 eV; -1.88 eV) and imidazolinylidene system (**7a**) (-6.07 eV; -1.75 eV).

To further understand properties of the Pd–C(carbene) bond in (NHC)PdCl$_2$(aniline), we performed NBO analysis.[21,22] The Wiberg bond orders for the Pd–C(carbene) and Pd–N bonds in (**6a**) are 0.6776 and 0.3142 (Pd–C_1, 0.6299; Pd–Cl_2, 0.6305), which can be compared with the analogous [Pd(IPr)(3-Cl-py)Cl$_2$] system (Pd–C, 0.6871; Pd–N, 0.3267; Pd–Cl_1, 0.6302; Pd–Cl_2, 0.6278) and imidazolinylidene system (**7a**) (Pd–C, 0.6745; Pd–N, 0.3024). Thus, aniline ligands will be applicable to redistribute the electron density along the metal–NHC axis.

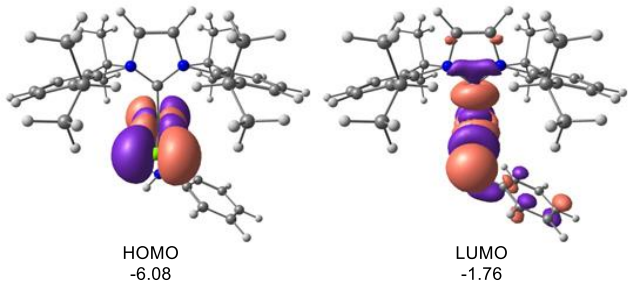


Figure 4. HOMO and LUMO and energies (eV) of (IPr)PdCl$_2$(AN) (**6a**) calculated at B3LYP 6-311++g(d,p). See SI for details.

3. Conclusions

In summary, we have developed a new class of highly active Pd(II)–NHC complexes bearing anilines as stabilizing ligands. These catalysts are well-defined, air- and moisture-stable and can be easily purified by chromatographic techniques. The broad availability of aniline scaffolds offers significant potential in the development of active Pd(II)–NHC catalysts and should prove useful in the design and optimization of novel cross-couplings.[23,24] The parent catalyst in this class, [(IPr)PdCl$_2$(AN)], has been commercialized in collaboration with Millipore Sigma (no 916161)[24], offering broad access for reaction screening

and optimization. Further studies expanding the utility of Pd–NHCs are ongoing in our laboratory and will be reported in due course.[25]

4. Experimental Section

General Methods. All compounds reported in the manuscript have been previously described in literature or prepared by the method reported previously unless stated otherwise. **11**,[14d] **14**,[14c] *tert*-butyl benzoyl(phenyl)carbamate,[14f] $Pd(PhNH_2)_2Cl_2$,[12d] and amide series of compounds[14c] have been previously reported in the literature. Spectroscopic properties matched literature data. Compounds **12**, **14**, aryl chlorides and aniline series of compounds are commercially available and have been purchased from Oakwood Chemical. All boronic acids are commercially available and have been purchased from Oakwood Chemical. All experiments involving palladium 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 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.[14c]

General Procedure for the Suzuki-Miyaura Cross-Coupling of Amides. An oven-dried vial equipped with a stir bar was charged with an amide substrate (neat, 0.10 mmol, 1.0 equiv), potassium carbonate (typically, 0.30 mmol, 3.0 equiv), boronic acid (typically, 0.20 mmol, 2.0 equiv), Pd-NHC (typically, 1.0 mol%), placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. THF (typically, 0.25 M) and water (typically, 0.50 mmol, 5.0 equiv) were added with vigorous stirring at room temperature, and the reaction was stirred at room temperature. After the indicated time, the reaction mixture was diluted with CH_2Cl_2 (10 mL), filtered, and concentrated. The sample was analyzed by ^1H NMR ($CDCl_3$, 500 MHz) and GC-MS to obtain conversion, selectivity and yield using internal standard and comparison with authentic samples. Purification by chromatography on silica gel (EtOAc/hexanes) afforded the title product.

General Procedure for the Suzuki-Miyaura Cross-Coupling of Esters. An oven-dried vial equipped with a stir bar was charged with an ester substrate (neat, 0.10 mmol, 1.0 equiv), potassium carbonate (typically, 0.30 mmol, 3.0 equiv), boronic acid (typically, 0.20 mmol, 2.0 equiv), Pd-NHC (typically, 1.0 mol%), placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. THF (typically, 0.25 M) and water (typically, 0.50 mmol, 5.0 equiv) were added with vigorous stirring at room temperature, and the reaction was stirred at room temperature. After the indicated time, the reaction mixture was diluted with CH_2Cl_2 (10 mL), filtered, and concentrated. The sample was analyzed by ^1H NMR ($CDCl_3$, 500 MHz) and GC-MS to obtain conversion, selectivity and yield using internal standard and comparison with authentic samples. Purification by chromatography on silica gel (EtOAc/hexanes) afforded the title product.

General Procedure for the Suzuki-Miyaura Cross-Coupling of Aryl Chlorides. An oven-dried vial equipped with a stir bar was charged with an aryl chloride substrate (neat, 0.10 mmol, 1.0 equiv), sodium hydroxide (typically, 0.20 mmol, 2.0 equiv), boronic acid (typically, 0.20 mmol, 2.0 equiv), Pd-NHC (typically, 1.0 mol%), placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. EtOH (typically, 0.25 M) was added with vigorous stirring at room temperature, and the reaction was stirred at room temperature. After the indicated time, the reaction mixture was diluted with CH_2Cl_2 (10 mL), filtered, and concentrated. The sample was analyzed by ^1H NMR ($CDCl_3$, 500 MHz) and GC-MS to obtain conversion, selectivity and yield using internal standard and comparison with authentic samples. Purification by chromatography on silica gel (EtOAc/hexanes) afforded the title product.

General Procedure for the Buchwald-Hartwig Cross-Coupling. An oven-dried vial equipped with a stir bar was charged with an aryl chloride substrate (neat, 0.10 mmol, 1.0 equiv), potassium *tert*-butoxide (0.20 mmol, 2.0 equiv), Pd-NHC (typically, 1.0 mol%), placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. 1,2-Dimethoxyethane (typically, 0.25 M) and amine (0.20 mmol, 2.0 equiv) were added with vigorous stirring at room temperature, the reaction mixture was placed in a preheated oil bath and stirred at 110 °C. After the indicated time, the reaction mixture was cooled down to room temperature, diluted with CH_2Cl_2 (10 mL), filtered, and concentrated. The sample was analyzed by ^1H NMR ($CDCl_3$, 500 MHz) and GC-MS to obtain conversion, selectivity and yield using internal standard and comparison with authentic samples. Purification by chromatography on silica gel (EtOAc/hexanes) afforded the title product.

Representative Procedure for the Suzuki-Miyaura Cross-Coupling. 1.0 Mmol Scale. An oven-dried vial equipped with a stir bar was charged with *tert*-butyl benzoyl(phenyl)carbamate (neat, 1.0 mmol, 297.4 mg, 1.0 equiv), potassium carbonate (3.0 mmol, 414.6 mg, 3.0 equiv), *p*-tolylboronic acid (2.0 mmol, 272.0 mg, 2.0 equiv), $(IPr)PdCl_2(AN)$ (1.0 mol%, 6.8 mg), placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. THF (0.25 M) and water (5.0 mmol, 90 mg, 5.0 equiv) were added with vigorous stirring at room temperature, and the reaction was stirred at room temperature for 16 h. After the indicated time, the reaction mixture was diluted with CH_2Cl_2 (30 mL), filtered, and concentrated. The sample was analyzed by ^1H NMR ($CDCl_3$, 500 MHz) and GC-MS to obtain conversion, selectivity and yield using internal standard and comparison with authentic samples. Purification by chromatography on silica gel (EtOAc/hexanes) afforded the title product. Yield 98% (191.5 mg). White solid. Characterization data are included in the section below.

Synthesis of $(NHC)PdCl_2(Aniline)$ Complexes. Pd-NHC complexes **6a-h**, and **7a** were prepared from the corresponding

[{Pd(NHC)(Cl)(μ-Cl)}$_2$] dimers.[12b] In addition, we developed a modified method from readily available ligand-free precursor $PdCl_2$(aniline)$_2$ to facilitate screening of NHC salts and avoid preparation of the chloro bridged Pd(NHC) dimers.

(IPr)PdCl$_2$(AN) (6a). Yellow solid. Yield 91% (60 mg). Crystals suitable for X-ray diffraction were obtained by slow evaporation of a CH_2Cl_2/hexane solution of the complex. **^{1}H NMR (500 MHz, CDCl$_3$)** δ 7.49 (t, *J* = 7.7 Hz, 2H), 7.29 (d, *J* = 4.9 Hz, 4H), 7.10 (s, 2H), 7.07 (t, *J* = 7.4 Hz, 2H), 7.02 (t, *J* = 7.2 Hz, 1H), 6.94 (d, *J* = 7.9 Hz, 2H), 3.95 (s, 2H), 3.02-2.95 (m, 4H), 1.29 (d, *J* = 6.6 Hz, 12H), 1.07 (d, *J* = 6.9 Hz, 12H). **^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$)** δ 155.7, 146.6, 139.9, 135.0, 130.1, 128.7, 124.8, 124.2, 123.8, 121.4, 28.7, 26.3, 22.7. **HRMS** calcd for $C_{33}H_{43}Cl_2N_3PdNa$ (M^++ Na) 680.1761 found 680.1804.

(IPr)PdCl$_2$(4-MeO-C$_6$H$_4$-NH$_2$) (6b). Yellow solid. Yield 92% (63 mg). **^{1}H NMR (500 MHz, CDCl$_3$)** δ 7.50 (t, *J* = 7.7 Hz, 2H), 7.31 (d, *J* = 7.8 Hz, 4H), 7.10 (s, 2H), 6.88 (d, *J* = 8.9 Hz, 2H), 6.61 (d, *J* = 8.8 Hz, 2H), 3.84 (s, 2H), 3.78 (s, 3H), 3.02–2.97 (m, 4H), 1.31 (d, *J* = 6.6 Hz, 13H), 1.07 (d, *J* = 6.9 Hz, 12H). **^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$)** δ 156.6, 156.3, 146.6, 135.0, 132.9, 130.1, 124.8, 123.8, 122.5, 114.1, 55.6, 28.7, 26.3, 22.7. **HRMS** calcd for $C_{34}H_{45}Cl_2N_3OPdNa$ (M^++ Na) 710.1867 found 710.1902.

(IPr)PdCl$_2$(4-CF$_3$-C$_6$H$_4$-NH$_2$) (6c). Yellow solid. Yield 86% (62 mg). **^{1}H NMR (500 MHz, CDCl$_3$)** δ 7.41 (t, *J* = 7.7 Hz, 2H), 7.27 (d, *J* = 8.2 Hz, 2H), 7.19 (d, *J* = 7.8 Hz, 4H), 7.05 (s, 2H), 7.01 (d, *J* = 8.2 Hz, 2H), 4.10 (s, 2H), 2.90-2.85 (m, 4H), 1.21 (d, *J* = 6.6 Hz, 12H), 1.00 (d, *J* = 6.9 Hz, 12H). **^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$)** δ 154.5, 146.6, 143.5, 134.8, 130.2, 126.1 (q, J^F = 32.8 Hz), 125.7 (q, J^F = 3.8 Hz), 124.8, 124.4 (q, J^F = 270.9 Hz), 123.8, 121.6, 28.7, 26.3, 22.6. **^{19}F NMR (471 MHz, CDCl$_3$)** δ -62.18. **HRMS** calcd for $C_{34}H_{42}Cl_2F_3N_3PdNa$ (M^++ Na) 748.1635 found 748.1678.

(IPr)PdCl$_2$(2,6-Me$_2$-C$_6$H$_3$-NH$_2$) (6d). Yellow solid. Yield 90% (62 mg). **^{1}H NMR (500 MHz, CDCl$_3$)** δ 7.56 (t, *J* = 7.7 Hz, 2H), 7.38 (d, *J* = 7.7 Hz, 4H), 7.12 (s, 2H), 6.83 (s, 3H), 3.73 (s, 2H), 3.10-3.04 (m, 4H), 2.06 (s, 6H), 1.37 (d, *J* = 6.7 Hz, 12H), 1.08 (d, *J* = 6.9 Hz, 12H). **^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$)** δ 155.4, 147.0, 137.6, 135.0, 130.2, 128.5, 127.8, 125.1, 123.9, 28.7, 26.4, 22.9, 18.7. **HRMS** calcd for $C_{35}H_{48}Cl_2N_3Pd$ (M^++ H) 686.2255 found 686.2297.

(IPr)PdCl$_2$(2,6-*i*-Pr$_2$-C$_6$H$_3$-NH$_2$) (6e). Yellow solid. Yield 82% (61 mg). **^{1}H NMR (500 MHz, CDCl$_3$)** δ 7.53 (t, *J* = 7.7 Hz, 2H), 7.37 (d, *J* = 7.8 Hz, 4H), 7.10 (s, 2H), 7.00-6.92 (m, 3H), 3.87 (s, 2H), 3.12-3.07 (m, 4H), 3.05-2.98 (m, 2H), 1.40 (d, *J* = 6.6 Hz, 12H), 1.09 (d, *J* = 6.9 Hz, 12H), 1.05 (d, *J* = 6.8 Hz, 12H). **^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$)** δ 155.5, 146.9, 138.7, 135.1, 133.7, 130.2, 125.2, 124.5, 124.0, 122.7, 28.6, 27.8, 26.3, 23.2, 22.9. **HRMS** calcd for $C_{39}H_{56}Cl_2N_3Pd$ (M^++ H) 742.2881 found 742.2920.

(IPr)PdCl$_2$(3-CF$_3$-C$_6$H$_4$-NH$_2$) (6f). Yellow solid. Yield 84% (61 mg). **^{1}H NMR (500 MHz, CDCl$_3$)** δ 7.45 (t, *J* = 7.8 Hz, 2H), 7.31-7.12 (m, 8H), 7.09 (s, 2H), 4.10 (s, 2H), 2.97-2.91 (m, 4H), 1.27 (d, *J* = 6.7 Hz, 12H), 1.05 (d, *J* = 6.9 Hz, 12H). **^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$)** δ 154.7, 146.6, 140.6, 134.8, 134.3, 131.0 (q, J^F = 32.8 Hz), 130.4, 130.2, 129.1, 125.2, 124.6, 124.2, 123.8, 123.7 (q, J^F = 273.4 Hz), 121.0 (q, J^F = 3.8 Hz), 117.9 (q, J^F = 3.8 Hz), 28.6, 26.3, 22.6. **^{19}F NMR (471 MHz, CDCl$_3$)** δ -62.56. **HRMS** calcd for $C_{34}H_{42}Cl_2F_3N_3PdNa$ (M^++ Na) 748.1635 found 748.1669.

(IPr)PdCl$_2$(C$_6$H$_5$-NHMe) (6g). Yellow solid. Yield 85% (57 mg). **^{1}H NMR (500 MHz, CDCl$_3$)** δ 7.41 (t, *J* = 7.7 Hz, 2H), 7.25-7.19 (m, 4H), 7.02-6.99 (m, 4H), 6.95-6.90 (m, 1H), 6.87 (dd, *J* = 7.5, 1.8 Hz, 2H), 4.52-4.36 (m, 1H), 2.99-2.94 (m, 2H), 2.88-2.81 (m, 2H), 2.50 (d, *J* = 6.2 Hz, 3H), 1.27 (d, *J* = 6.7 Hz, 6H), 1.17 (d, *J* = 6.6 Hz, 6H), 1.00 (d, *J* = 6.9 Hz, 6H), 0.96 (d, *J* = 6.9 Hz, 6H). **^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$)** δ 152.0, 147.4, 146.2, 133.4, 129.9, 128.8, 128.4, 124.4, 124.4, 124.0, 120.1, 35.6, 28.4, 28.3, 25.3, 25.3, 24.9, 24.4. **HRMS** calcd for $C_{34}H_{45}Cl_2N_3PdNa$ (M^++ Na) 694.1918 found 694.1933.

(IPr)PdCl$_2$(4-CF$_3$-C$_6$H$_4$-NHMe) (6h). Yellow solid. Yield 82% (61 mg). **^{1}H NMR (500 MHz, CDCl$_3$)** δ 7.51 (t, *J* = 7.7 Hz, 2H), 7.37-7.25 (m, 6H), 7.10 (s, 2H), 7.04 (d, *J* = 8.3 Hz, 2H), 4.73 (q, *J* = 6.1 Hz, 1H), 3.04-2.99 (m, 2H), 2.91-2.86 (m, 2H), 2.63 (d, *J* = 6.0 Hz, 3H), 1.37 (d, *J* = 6.6 Hz, 6H), 1.23 (d, *J* = 6.6 Hz, 6H), 1.10 (d, *J* = 6.9 Hz, 6H), 1.04 (d, *J* = 6.9 Hz, 6H). **^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$)** δ 153.8, 149.0, 146.6, 146.5, 134.8, 130.1, 126.3 (q, J^F = 32.8 Hz), 125.8 (q, J^F = 3.8 Hz), 125.0, 124.2 (q, J^F = 272.2 Hz), 123.8, 123.8, 120.3, 35.8, 28.8, 28.6, 26.5, 26.2, 22.9, 22.6. **^{19}F NMR (471 MHz, CDCl$_3$)** δ -62.18. **HRMS** calcd for $C_{35}H_{45}Cl_2F_3N_3Pd$ (M^++ H) 740.1972 found 740.2014.

(SIPr)PdCl$_2$(AN) (7a). Yellow solid. Yield 88% (60 mg). Crystals suitable for X-ray diffraction were obtained by slow evaporation of a CH_2Cl_2/hexane solution of the complex. **^{1}H NMR (500 MHz, CDCl$_3$)** δ 7.42 (t, *J* = 7.7 Hz, 2H), 7.25 (d, *J* = 7.7 Hz, 4H), 7.05 (t, *J* = 7.4 Hz, 2H), 7.00 (t, *J* = 7.1 Hz, 1H), 6.89 (dd, *J* = 7.6, 1.8 Hz, 2H), 4.05 (s, 4H), 3.87 (s, 2H), 3.44-3.37 (m, 4H), 1.37 (d, *J* = 6.6 Hz, 12H), 1.22 (d, *J* = 6.9 Hz, 12H). **^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$)** δ 186.6, 147.6, 139.8, 135.2, 129.3, 128.7, 124.3, 124.2, 121.2, 53.6, 28.7, 26.9, 23.6. **HRMS** calcd for $C_{33}H_{45}Cl_2N_3PdNa$ (M^++ Na) 682.1918 found 682.1946.

Modified Synthetic Route to (IPr)PdCl$_2$(AN) (6a).[12e] An oven-dried vial equipped with a stir bar was charged with $PdCl_2$ (1.0 equiv) and $PhNH_2$ (2.0 equiv, methanol solution, 0.10 M), and the reaction mixture was stirred at room temperature for 6 h. After the indicated time, the solid was collected by filtration, washed with methanol and dried under vacuum. Yield 95%. An oven-dried vial equipped with a stir bar was charged with IPrHCl (63.9 mg, 0.15 mmol, 1.5 equiv), $Pd(PhNH_2)_2Cl_2$ (36.3 mg, 0.10 mmol, 1.0 equiv), KO*t*-Bu (16.8 mg, 0.15 mmol, 1.5 equiv), placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. THF (0.05 M) was added with vigorous stirring at room temperature and the reaction mixture was stirred at 80 °C for 16 h. After the indicated time, the reaction mixture was diluted with CH_2Cl_2 (10 mL), filtered, and concentrated. The sample was analyzed by ^{1}H NMR ($CDCl_3$, 500 MHz) to obtain conversion, selectivity and yield using

internal standard and comparison with authentic samples. Purification by chromatography on silica gel (EtOAc/hexanes) afforded the title product. Yield 70% (46.0 mg). Characterization data matched those described in the section above.[12e] **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.49 (t, *J* = 7.7 Hz, 2H), 7.29 (d, *J* = 4.9 Hz, 4H), 7.10 (s, 2H), 7.07 (t, *J* = 7.4 Hz, 2H), 7.02 (t, *J* = 7.2 Hz, 1H), 6.94 (d, *J* = 7.9 Hz, 2H), 3.95 (s, 2H), 3.02-2.95 (m, 4H), 1.29 (d, *J* = 6.6 Hz, 12H), 1.07 (d, *J* = 6.9 Hz, 12H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 155.7, 146.6, 139.9, 135.0, 130.1, 128.7, 124.8, 124.2, 123.8, 121.4, 28.7, 26.3, 22.7.

Characterization Data of Cross-Coupling Products.

Phenyl(*p*-tolyl)methanone (10a) (Table 2, Entry 1).[14c] According to the general procedure, the reaction of *tert*-butyl benzoyl(phenyl)carbamate (0.10 mmol, 1.0 equiv), 4-methylphenylboronic acid (2.0 equiv), H_2O (5.0 equiv), K_2CO_3 (3.0 equiv) and [(IPr)$PdCl_2$(AN)] (1.0 mol%) in THF (0.25 M) for 16 h at room temperature, afforded after filtration and chromatography the title compound in 98% yield (19.2 mg). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.78 (d, *J* = 7.2 Hz, 2H), 7.73 (d, *J* = 8.0 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.28 (d, *J* = 7.8 Hz, 2H), 2.44 (s, 3H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 196.7, 143.4, 138.1, 135.0, 132.3, 130.4, 130.1, 129.1, 128.3, 21.8.

(4-Methoxyphenyl)(phenyl)methanone (10b) (Table 2, Entry 2).[14c] According to the general procedure, the reaction of *tert*-butyl benzoyl(phenyl)carbamate (0.10 mmol, 1.0 equiv), 4-methoxylphenylboronic acid (2.0 equiv), H_2O (5.0 equiv), K_2CO_3 (3.0 equiv) and [(IPr)$PdCl_2$(AN)] (1.0 mol%) in THF (0.25 M) for 16 h at room temperature, afforded after filtration nd chromatography the title compound in 95% yield (20.1 mg). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.76 (d, *J* = 8.8 Hz, 2H), 7.68 (d, *J* = 6.9 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.7 Hz, 2H), 6.89 (d, *J* = 8.8 Hz, 2H), 3.81 (s, 3H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 195.6, 163.2, 138.3, 132.6, 131.9, 130.2, 129.7, 128.2, 113.6, 55.5.

Phenyl(4-(trifluoromethyl)phenyl)methanone (10c) (Table 2, Entry 3).[14c] According to the general procedure, the reaction of *tert*-butyl benzoyl(phenyl)carbamate (0.10 mmol, 1.0 equiv), (4-trifluorophenyl)boronic acid (2.0 equiv), H_2O (5.0 equiv), K_2CO_3 (3.0 equiv) and [(IPr)$PdCl_2$(AN)] (1.0 mol%) in THF (0.25 M) for 16 h at room temperature, afforded after filtration and chromatography the title compound in 97% yield (24.2 mg). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.82 (d, *J* = 8.0 Hz, 2H), 7.73 (d, *J* = 7.2 Hz, 2H), 7.68 (d, *J* = 8.1 Hz, 2H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 2H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 195.5, 140.8, 136.8, 133.8 (q, J^F = 32.8 Hz), 133.1, 130.1, 130.1, 128.6, 125.4 (q, J^F = 3.8 Hz), 123.7 (q, J^F = 273.0 Hz).

Methyl 4-benzoylbenzoate (10d) (Table 2, Entry 4).[14c] According to the general procedure, the reaction of *tert*-butyl benzoyl(phenyl)carbamate (0.10 mmol, 1.0 equiv), (4-(methoxycarbonyl)phenyl)boronic acid (2.0 equiv), H_2O (5.0 equiv), K_2CO_3 (3.0 equiv) and [(IPr)$PdCl_2$(AN)] (1.0 mol%) in THF (0.25 M) for 16 h at room temperature, afforded after filtration and chromatography the title compound in 91% yield (21.8 mg). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.08 (d, *J* = 8.5 Hz, 2H), 7.75 (dd, *J* = 18.5, 7.6 Hz, 4H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.43 (t, *J* = 7.8 Hz, 2H), 3.90 (s, 3H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 196.0, 166.3, 141.4, 137.0, 133.2, 133.0, 130.1, 129.8, 129.5, 128.5, 52.5.

Phenyl(*o*-tolyl)methanone (10e) (Table 2, Entry 5).[14c] According to the general procedure, the reaction of *tert*-butyl benzoyl(phenyl)carbamate (0.10 mmol, 1.0 equiv), 2-methylphenylboronic acid (2.0 equiv), H_2O (5.0 equiv), K_2CO_3 (3.0 equiv) and [(IPr)$PdCl_2$(AN)] (1.0 mol%) in THF (0.25 M) for 16 h at room temperature, afforded after filtration and chromatography the title compound in 90% yield (17.6 mg). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.83 (dd, *J* = 8.1, 1.6 Hz, 2H), 7.68 – 7.56 (m, 1H), 7.48 (t, *J* = 7.7 Hz, 2H), 7.42 (td, *J* = 7.4, 1.5 Hz, 1H), 7.37 – 7.22 (m, 3H), 2.36 (s, 3H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 198.6, 138.6, 137.7, 136.7, 133.1, 131.0, 130.2, 130.1, 128.5, 128.44 125.2, 20.0.

(4-Methoxyphenyl)(phenyl)methanone (10b') (Table 2, Entry 6).[14c] According to the general procedure, the reaction of *tert*-butyl (4-methoxylbenzoyl)(phenyl) carbamate (0.10 mmol, 1.0 equiv), phenylboronic acid (2.0 equiv), H_2O (5.0 equiv), K_2CO_3 (3.0 equiv) and [(IPr)$PdCl_2$(AN)] (1.0 mol%) in THF (0.25 M) for 16 h at room temperature, afforded after filtration and chromatography the title compound in 94% yield (19.9 mg). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.76 (d, *J* = 8.8 Hz, 2H), 7.68 (d, *J* = 6.9 Hz, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.7 Hz, 2H), 6.89 (d, *J* = 8.8 Hz, 2H), 3.81 (s, 3H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 195.6, 163.2, 138.3, 132.6, 131.9, 130.2, 129.7, 128.2, 113.6, 55.5.

Phenyl(4-(trifluoromethyl)phenyl)methanone (10c') (Table 2, Entry 7).[14c] According to the general procedure, the reaction of *tert*-butyl phenyl(4-(trifluoromethyl)benzoyl) carbamate (0.10 mmol, 1.0 equiv), phenylboronic acid (2.0 equiv), H_2O (5.0 equiv), K_2CO_3 (3.0 equiv) and [(IPr)$PdCl_2$(AN)] (1.0 mol%) in THF (0.25 M) for 16 h at room temperature, afforded after filtration and chromatography the title compound in 95% yield (23.8 mg). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.82 (d, *J* = 8.0 Hz, 2H), 7.73 (d, *J* = 7.2 Hz, 2H), 7.68 (d, *J* = 8.1 Hz, 2H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 2H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 195.5, 140.8, 136.8, 133.8 (q, J^F = 32.8 Hz), 133.1, 130.1, 130.1, 128.6, 125.4 (q, J^F = 3.8 Hz), 123.7 (q, J^F = 273.0 Hz).

Phenyl(*o*-tolyl)methanone (10e') (Table 2, Entry 8).[14c] According to the general procedure, the reaction of *tert*-butyl (2-methylbenzoyl)(phenyl) carbamate (0.10 mmol, 1.0 equiv), phenylboronic acid (2.0 equiv), H_2O (5.0 equiv), K_2CO_3 (3.0 equiv) and [(IPr)$PdCl_2$(AN)] (1.0 mol%) in THF (0.25 M) for 16 h at room temperature, afforded after filtration and chromatography the title compound in 79% yield (15.5 mg). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.83 (dd, *J* = 8.1, 1.6 Hz, 2H), 7.68 – 7.56 (m, 1H), 7.48 (t, *J* = 7.7 Hz, 2H), 7.42 (td, *J* = 7.4, 1.5 Hz, 1H), 7.37 – 7.22 (m, 3H), 2.36 (s, 3H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 198.6, 138.6, 137.7, 136.7, 133.1, 131.0, 130.2, 130.1, 128.5, 128.4, 125.2, 20.0.

Phenyl(*p*-tolyl)methanone (10a) (Scheme 3).[14c] According to the general procedure, the reaction of phenyl benzoate (0.10 mmol, 1.0 equiv), phenylboronic acid (2.0 equiv), H_2O (5.0

equiv), K_2CO_3 (3.0 equiv) and [(IPr)$PdCl_2$(3-CF_3-C_6H_4-NH_2)] (1.0 mol%) in THF (0.25 M) for 16 h at room temperature, afforded after filtration and chromatography the title compound in 98% yield (19.3 mg). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.78 (d, *J* = 7.2 Hz, 2H), 7.73 (d, *J* = 8.0 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.28 (d, *J* = 7.8 Hz, 2H), 2.44 (s, 3H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 196.7, 143.4, 138.1, 135.0, 132.3, 130.4, 130.1, 129.1, 128.3, 21.8.

4-Methoxy-4'-methyl-1,1'-biphenyl (13a) (Table 3, Entry 1).[12b] According to the general procedure, the reaction of 4-chloroanisole (0.10 mmol, 1.0 equiv), 4-methylphenylboronic acid (2.0 equiv), NaOH (2.0 equiv) and [(IPr)$PdCl_2$(AN)] (1.0 mol%) in EtOH (0.25 M) for 16 h at room temperature, afforded after filtration and chromatography the title compound in 98% yield (19.4 mg). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.54 (d, *J* = 8.6 Hz, 2H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.26 (d, *J* = 7.8 Hz, 2H), 7.00 (d, *J* = 8.6 Hz, 2H), 3.88 (s, 3H), 2.41 (s, 3H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 158.9, 138.0, 136.4, 133.8, 129.5, 128.0, 126.6, 114.2, 55.4, 21.1.

4-Methoxy-1,1'-biphenyl (13b) (Table 3, Entry 2).[12b] According to the general procedure, the reaction of 4-chloroanisole (0.10 mmol, 1.0 equiv), phenylboronic acid (2.0 equiv), NaOH (2.0 equiv) and [(IPr)$PdCl_2$(AN)] (1.0 mol%) in EtOH (0.25 M) for 16 h at room temperature, afforded after filtration and chromatography the title compound in 98% yield (18.0 mg). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.46 (dd, *J* = 10.9, 7.9 Hz, 4H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.22 (d, *J* = 7.3 Hz, 1H), 6.90 (d, *J* = 8.7 Hz, 2H), 3.77 (s, 3H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 157.9, 139.6, 132.5, 127.4, 126.9, 125.5, 125.4, 112.9, 54.1.

4-(Trifluoromethyl)-1,1'-biphenyl (13c) (Table 3, Entry 3).[12b] According to the general procedure, the reaction of 1-chloro-4-(trifluoromethyl)benzene (0.10 mmol, 1.0 equiv), phenylboronic acid (2.0 equiv), NaOH (2.0 equiv) and [(IPr)$PdCl_2$(AN)] (1.0 mol%) in EtOH (0.25 M) for 16 h at room temperature, afforded after filtration and chromatography the title compound in 98% yield (21.8 mg). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.63 (s, 4H), 7.53 (d, *J* = 7.2 Hz, 2H), 7.41 (t, *J* = 7.5 Hz, 2H), 7.34 (t, *J* = 7.3 Hz, 1H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 144.8, 139.8, 129.4 (q, J^F = 37.4 Hz), 129.0, 128.2, 127.7, 127.4, 127.3, 125.7 (q, J^F = 3.7 Hz), 124.3 (q, J^F = 274.4 Hz).

[1,1'-Biphenyl]-4-carbonitrile (13d) (Table 3, Entry 4).[12b] According to the general procedure, the reaction of 4-chlorobenzonitrile (0.10 mmol, 1.0 equiv), phenylboronic acid (2.0 equiv), NaOH (2.0 equiv) and [(IPr)$PdCl_2$(AN)] (1.0 mol%) in EtOH (0.25 M) for 16 h at room temperature, afforded after filtration and chromatography the title compound in 88% yield (15.8 mg). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.68-7.58 (m, 4H), 7.52 (d, *J* = 7.2 Hz, 2H), 7.41 (d, *J* = 15.0 Hz, 2H), 7.35 (t, *J* = 7.3 Hz, 1H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 145.7, 139.2, 132.6, 129.1, 128.7, 127.8, 127.3, 119.0, 111.0.

1-([1,1'-Biphenyl]-4-yl)ethanone (13e) (Table 3, Entry 5).[12b] According to the general procedure, the reaction of 1-(4-chlorophenyl)ethanone (0.10 mmol, 1.0 equiv), phenylboronic acid (2.0 equiv), NaOH (2.0 equiv) and [(IPr)$PdCl_2$(AN)] (1.0 mol%) in EtOH (0.25 M) for 16 h at room temperature, afforded after filtration and chromatography the title compound in 98% yield (19.2 mg). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.97 (d, *J* = 8.4 Hz, 2H), 7.62 (d, *J* = 8.5 Hz, 2H), 7.56 (d, *J* = 7.4 Hz, 2H), 7.41 (t, *J* = 7.5 Hz, 2H), 7.33 (t, *J* = 7.3 Hz, 1H), 2.57 (s, 3H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 197.8, 145.8, 139.9, 135.9, 129.0, 128.9, 128.2, 127.3, 127.3, 26.7.

2-Phenylpyridine (13f) (Table 3, Entry 6).[12b] According to the general procedure, the reaction of 2-chloropyridine (0.10 mmol, 1.0 equiv), phenylboronic acid (2.0 equiv), NaOH (2.0 equiv) and [(IPr)$PdCl_2$(AN)] (1.0 mol%) in EtOH (0.25 M) for 16 h at room temperature, afforded after filtration and chromatography the title compound in 89% yield (13.8 mg). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 8.63 (d, *J* = 4.7 Hz, 1H), 7.92 (d, *J* = 8.6 Hz, 2H), 7.68 (q, *J* = 7.7 Hz, 2H), 7.41 (t, *J* = 7.4 Hz, 2H), 7.38-7.32 (m, 1H), 7.16 (d, *J* = 8.5 Hz, 1H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 156.5, 148.6, 138.3, 135.8, 128.6, 128.0, 127.7, 125.9, 121.1, 119.6, 119.4, 114.4.

2-Methyl-1,1'-biphenyl (13g) (Table 3, Entry 7).[12b] According to the general procedure, the reaction of 1-chloro-2-methylbenzene (0.10 mmol, 1.0 equiv), phenylboronic acid (2.0 equiv), NaOH (2.0 equiv) and [(IPr)$PdCl_2$(AN)] (1.0 mol%) in EtOH (0.25 M) for 16 h at room temperature, afforded after filtration and chromatography the title compound in 90% yield (15.1 mg). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.34 (t, *J* = 7.4 Hz, 2H), 7.26 (tt, *J* = 7.9, 1.3 Hz, 3H), 7.20-7.16 (m, 4H), 2.20 (s, 3H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 140.9, 140.9, 134.3, 129.3, 128.8, 128.2, 127.7, 127.0, 126.2, 126.1, 125.7, 124.7, 19.4.

4-Methoxy-1,1'-biphenyl (13b') (Table 3, Entry 8).[12b] According to the general procedure, the reaction of chlorobenzene (0.10 mmol, 1.0 equiv), 4-methoxylphenylboronic acid (2.0 equiv), NaOH (2.0 equiv) and [(IPr)$PdCl_2$(AN)] (1.0 mol%) in EtOH (0.25 M) for 16 h at room temperature, afforded after filtration and chromatography the title compound in 98% yield (18.0 mg). White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (dd, *J* = 10.9, 7.9 Hz, 4H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.22 (d, *J* = 7.3 Hz, 1H), 6.90 (d, *J* = 8.7 Hz, 2H), 3.77 (s, 3H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 157.9, 139.6, 132.5, 127.4, 126.9, 125.5, 125.4, 112.9, 54.1.

4-(Trifluoromethyl)-1,1'-biphenyl (13c') (Table 3, Entry 9).[12b] According to the general procedure, the reaction of chlorobenzene (0.10 mmol, 1.0 equiv), (4-trifluorophenyl)boronic acid (2.0 equiv), NaOH (2.0 equiv) and [(IPr)$PdCl_2$(AN)] (1.0 mol%) in EtOH (0.25 M) for 16 h at room temperature, afforded after filtration and chromatography the title compound in 93% yield (20.6 mg). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.63 (s, 4H), 7.53 (d, *J* = 7.2 Hz, 2H), 7.41 (t, *J* = 7.5 Hz, 2H), 7.34 (t, *J* = 7.3 Hz, 1H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 144.8, 139.8, 129.4 (q, J^F = 37.4 Hz), 129.0, 128.2, 127.7, 127.4, 127.3, 125.7 (q, J^F = 3.7 Hz), 124.3 (q, J^F = 274.4 Hz).

1-([1,1'-Biphenyl]-4-yl)ethanone (13e') (Table 3, Entry 10).[12b] According to the general procedure, the reaction of chlorobenzene (0.10 mmol, 1.0 equiv), 4-acetylphenylboronic acid (2.0 equiv), NaOH (2.0 equiv) and [(IPr)$PdCl_2$(AN)] (1.0 mol%) in EtOH (0.25 M) for 16 h at room temperature, afforded after filtration and chromatography the title compound in 94% yield (18.4 mg). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.97 (d, *J* = 8.4 Hz, 2H), 7.62 (d, *J* = 8.5 Hz, 2H), 7.56 (d, *J* = 7.4 Hz, 2H), 7.41 (t, *J* = 7.5 Hz, 2H), 7.33 (t, *J* = 7.3 Hz, 1H), 2.57 (s, 3H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 197.8, 145.8, 139.9, 135.9, 129.0, 128.9, 128.2, 127.3, 127.3, 26.7.

2-Methyl-1,1'-biphenyl (13g') (Table 3, Entry 11).[12b] According to the general procedure, the reaction of chlorobenzene (0.10 mmol, 1.0 equiv), 2-methylphenylboronic acid (2.0 equiv), NaOH (2.0 equiv) and [(IPr)$PdCl_2$(AN)] (1.0 mol%) in EtOH (0.25 M) for 16 h at room temperature, afforded after filtration and chromatography the title compound in 87% yield (14.6 mg). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.34 (t, *J* = 7.4 Hz, 2H), 7.26 (tt, *J* = 7.9, 1.3 Hz, 3H), 7.20-7.16 (m, 4H), 2.20 (s, 3H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 140.9, 140.9, 134.3, 129.3, 128.8, 128.126, 127.7, 127.0, 126.2, 126.1, 125.7, 124.7, 19.4.

2,2'-Dimethyl-1,1'-biphenyl (13h) (Table 3, Entry 12).[12b] According to the general procedure, the reaction of 1-chloro-2-methylbenzene (0.10 mmol, 1.0 equiv), 2-methylphenylboronic acid (2.0 equiv), NaOH (2.0 equiv) and [(IPr)$PdCl_2$(AN)] (1.0 mol%) in EtOH (0.25 M) for 16 h at room temperature, afforded after filtration and chromatography the title compound in 78% yield (14.2 mg). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.22-7.10 (m, 6H), 7.03 (d, *J* = 7.3 Hz, 2H), 1.98 (s, 6H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 141.6, 135.8, 129.8, 129.3, 127.2, 125.5, 19.8.

4-(4-Methoxyphenyl)morpholine (15) (Scheme 4).[12b] According to the general procedure, the reaction of 4-chloroanisole (0.10 mmol, 1.0 equiv), morpholine (2.0 equiv), potassium *tert*-butoxide (2.0 equiv), [(IPr)$PdCl_2$(AN)] in DME (0.25 M) for 16 h at 110 °C, afforded after filtration and chromatography the title compound in 98% yield (19.2 mg). White solid. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 6.92 (d, *J* = 8.2 Hz, 2H), 6.88 (d, *J* = 8.9 Hz, 2H), 3.89 (s, 4H), 3.80 (s, 3H), 3.08 (s, 4H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 154.0, 145.7, 117.9, 114.5, 67.1, 55.6, 50.9.

ASSOCIATED CONTENT

Supporting Information

1H NMR and 13C NMR spectra for all compounds, crystallographic and computational data. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

michal.szostak@rutgers.edu

Notes

The authors declare the following competing financial interest(s): Rutgers University has filed patent(s) on ligands and precatalysts described in this manuscript (US 62/958,583, Jan 8, 2020).

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