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Flexible Steric Bulky Bis(Imino)acenaphthene (BIAN)-Supported *N*-Heterocyclic Carbene Palladium Precatalysts: Catalytic Application in Buchwald-Hartwig Amination in Air

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ABSTRACT:

To achieve efficient palladium-catalyzed cross-coupling reaction under mild reaction conditions with the flexible steric bulk strategy, a series of Pd-PEPPSI complexes **C1**-**C6** were synthesized and characterized, in which unsymmetric flexible steric bulk was introduced on the *N*-aryl of ancenaphthyl skeleton. These well-defined palladium complexes were found to be excellent precatalysts for Buchwald-Hartwig amination of aryl chlorides with amines in air. The electronic effect of the Pd-PEPPSI complexes and the effect of ancillary pyridine ligands were evaluated, among which complex **C3** exhibited the most efficiency. It was demonstrated that the cross-coupling products were obtained in excellent yields in the presence of 0.5-0.1 mol% palladium loading. A wide range of aryl- and heteroaryl chlorides as well as various amines were compatible. The oxidative addition of aryl chlorides is revealed to be the rate-determining step in the catalytic cycle. The catalytic activity can be enhanced by introducing electron-donating groups to the Pd-PEPPSI complexes. This type of Pd-PEPPSI precatalysts showed the most efficiency reported to date for the challenging C-N cross-coupling reactions requiring no anhydrous and inert atmosphere protections, suggesting flexible steric bulk as a promising catalyst design strategy.

Introduction

Arylamines are frequently found in the synthesis of natural products, pharmaceuticals, as well as functional materials.[1] The palladium-catalyzed Buchwald-Hartwig amination reaction, which involves the cross-coupling of aryl halide with amines to form arylamines, has emerged as one of the most valuable synthetic approaches for the construction of C(sp^2)-N bonds.[2] To achieve a high efficiency in this C-N cross-coupling reaction, much attention has been paid to the development of palladium catalysts with new ligands.[3]

Since the first isolation of 1,3-diadamantyl-imidazolylidene by Arduengo's and co-workers in 1991,[4] extensive efforts have been directed on the *N*-heterocyclic carbenes (NHCs) in the past decade, in light of their strong σ-donation toward metal center and their extraordinary utilities for promoting organic reactions.[5] Recently, an array of well-defined monoligated NHCs-palladium complexes developed by the groups of Herrmann,[6] Nolan,[7] Beller,[8] Sigman,[9] and Organ[10] exhibit excellent catalytic performance in palladium-catalyzed reactions.[11] Among these studies, the air-stable, user-friendly palladium PEPPSI complexes (PEPPSI: Pyridine-Enhanced-Precatalyst Preparation, Stabilization, and Initiation) developed by Organ and co-workers, turned out to be versatile precatalysts and can be generally applicable in numerous cross-coupling reactions.[12] It revealed that the increase of steric bulk at the *ortho* position of *N*-aryl moiety of the NHCs should benefit the Buchwald-Hartwig amination.[13] For instance, bulky palladium-based PEPPSI complexes, such as Pd-PEPPSI-IPr [IPr: 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene], Pd-PEPPSI-IPent [IPent: 1,3-bis(2,6-di-3-pentylphenyl)imidazol-2-ylidene],[10c] Pd-PEPPSI-IPr* [IPr*: 1,3-bis(2,6-bis(diphenylmethyl)-4-methylphenyl)imidazo-2-ylidene][13d], were able to conduct the most challenging amination reactions at room temperature, even with unactive aryl chlorides and

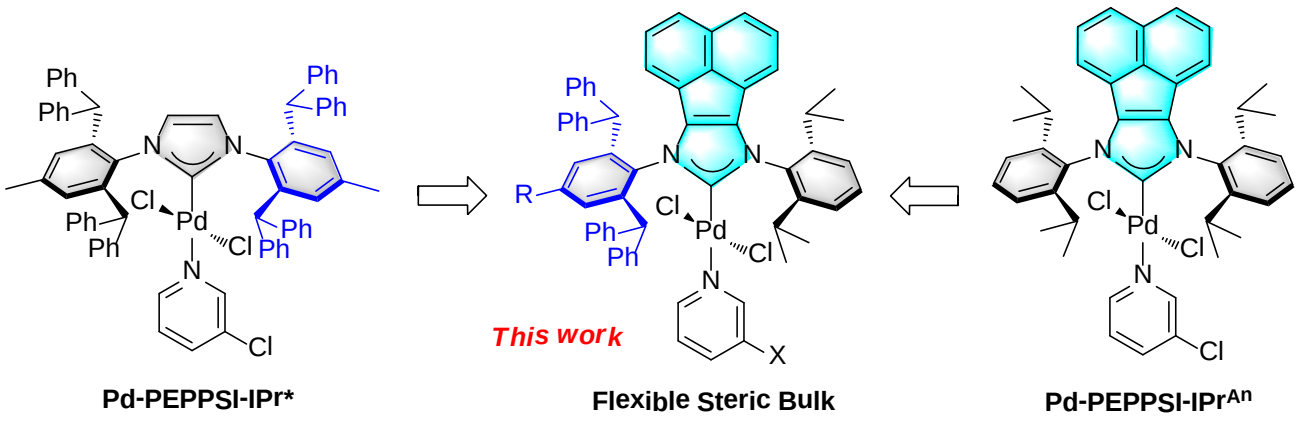
amines. In contrast, the less steric of the *N*-aryl moieties, such as Pd-PEPPSI-IMes [IMes: 1,3-bis(mesitylene) imidazol-2-ylidene] afforded much less efficiency.[10c] On the other hand, the modification on skeletons of the NHCs is another vital strategies to enhance the catalytic efficiency.[14] Tu and co-workers found that bulky acenaphthylene-substituted PEPPSI-IPr^{An} [IPr^{An}: 1,3-bis(2,6-diisopropylphenyl)ancenaphthylimidazol-2-ylidene] was highly efficient.[14a] Recently, César and Lavigne developed a new type of palladium complex with PEPPSI-IPr$^{(NMe2)2}$ [IPr$^{(NMe2)2}$: 1,3-bis(2,6-diisopropylphenyl) (N,N,N',N'-tetramethyloxalimidamide)imidazol-2- ylidene], wherein the introduction of the NMe_2 groups on the skeleton showed broad applicability and efficiency towards a wide range of aryl chloride substrates. [14c, 15]

Despite significant advances in the NHCs-palladium catalyzed cross-coupling reactions, operationally simple and generally applicable catalytic systems for cross-coupling aminations are highly desired.[16] For instance, most of these palladium complexes need multiple synthetic steps with extremely skilful workup.[17] It is noteworthy that the NHCs-Pd(II) precatalysts were rather air-stable. Unexpectedly, the catalytic species of NHCs-Pd(0) were found to be somewhat sensitive to a low level of dissolved oxygen in commercially available solvent, which could be trapped to form unreactive peroxo species.[12d, 18] To date, rare examples have been successfully achieved in the amination reactions in air.[19] Therefore, we are keenly interested in the development of NHCs palladium catalysts that do not necessitate the use of air- and moisture-free techniques in both academic and industrial applications.[14f, g]

Based on the "flexible steric bulk" strategy proposed by Glorius[20] and the extensive works above, we reasoned that the construction of palladium complexes of PEPPSI-(IPr*IPr)^{An}, PEPPSI-(IPr$^{(OMe)}$*IPr)^{An} and PEPPSI-(IPr^{F}*IPr)^{An} (Scheme 1), combined unsymmetric *N*-aryl

moieties on the bulky acenaphthyl skeleton, would benefit the cross-coupling amination reactions. Their catalytic activity for the oxidative addition of aryl chlorides will be accelerated by the strong σ donating properties of the acenaphthyl,[21] meanwhile the bulky steric hindrance can facilitate reductive elimination and can stabilize the NHCs-Pd(0) species.[22] Therefore, at a low palladium loading, an improvement of catalytic activity could be achieved in air without the need of anhydrous solvents. In order to further confirm our speculation and gain insights into the relationship between the structures and catalytic properties, herein, we report the synthesis and characterizations of the NHCs palladium complexes bearing flexible steric bulk, and describe their catalytic potentials toward Buchwald-Hartwig amination reaction in air.

Scheme1. The Design of Pd-PEPPSI Precatalysts with Flexible Bulky Steric



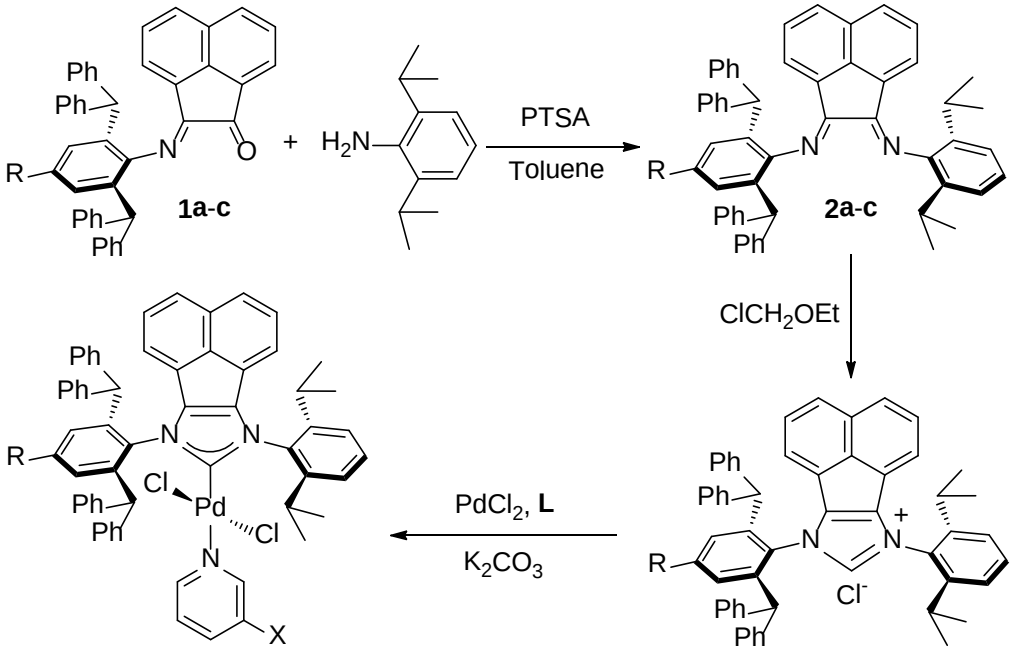
RESULTS AND DISCUSSION

Synthesis and Characterization of Ligands (L1-L3) and Their Palladium Complexes (C1-C6).

The procedures in the synthesis of Pd-PEPPSI complexes were shown in Scheme 2. Initially, the intermediates of 1-(arylimino)acenaphthylen-2-one (**1a-c**) were prepared according to the literature reports.[23] Next, the 1-(arylimino)acenaphthylen-2-one derivatives and 2,6-diisopropylaniline were mixed in toluene in the presence of catalytic amount of para-toluenesulfonic acid (Scheme 2). The

mixture was refluxed to conduct a routine condensation reaction to form the corresponding unsymmetric α-diimine compounds (**2a-c**). Subsequent cyclocondensation with chloromethyl ethyl ether provided the precipitate of the imidazolium chloride salts. These light green solids were isolated by filtration and washed with Et_2O, giving in moderate to high yields of 87%, 80% and 72% for **L1**, **L2** and **L3**, respectively. The spectroscopic properties of the imidazolium salts were investigated by ^1H NMR, in which the resonance of imidazolium C-H protons (NC*H*N) was observed downfield at δ=12.61, 12.69 and 12.71 ppm, respectively. With the imidazolium chloride salts in hand, the PEPPSI-$(IPr*IPr)^{An}$, PEPPSI-$(IPr^{(OMe)}*IPr)^{An}$ and PEPPSI-$(IPr^{F}*IPr)^{An}$ complexes (**C1-C6**) were conveniently obtained in 68-92% yields with $PdCl_2$ and K_2CO_3 in neat pyridine or 3-chloropyridine via a one-pot process.

Scheme 2. **Synthetic Route for the Pd-PEPPSI Complexes**



C1: R=Me, X=Cl; **C4**: R=OMe, X=H;
C2: R=Me, X=H; **C5**: R=F, X=Cl;
C3: R=OMe, X=Cl; **C6**: R=F, X=H;

L1: R=Me;
L2: R=OMe;
L3: R=F;

All these prepared Pd-PEPPSI complexes are air and moisture stable, and can be stored on shelf for more than a half year without noticeable decomposition or decline in catalytic efficiency. These

complexes are slightly soluble in Et_2O, hexane, and MeOH, while are well soluble in CH_2Cl_2, $CHCl_3$, and DMAc. They were fully characterized by NMR spectroscopy, mass spectrometry, and elemental analysis. The proton signal of NC*H*N from the imidazolium salts had disappeared in the ^{1}H NMR of the Pd-PEPPSI complexes, confirming the generation of Pd-$C_{carbene}$ bonds. In addition, the ^{13}C NMR of the palladium complexes revealed the direct evidence of the metalation of carbene carbon, as seen by the signal in the range of 151.7-159.4 ppm. Single crystals for the solid state structure determination could be obtained by slow diffusion of hexane into a concentrated CH_2Cl_2 solution at ambient temperature. The molecular structures of **C1**-**C4** were determined by means of X-ray diffraction studies. However, only low-quality crystal was obtained in the case for **C2** (seen in supporting information). As depicted in Figures 1-3, the solid structures of these complexes adopt slightly distorted square planar coordination geometry with the NHC and "throw away" ligands *trans* to each other. Despite bearing steric bulk on the NHC, the Pd-C(1) bond lengths turned out to be 1.960(4), 1.963(2) and 1.971(4) Å, respectively. These lengths are in the range of those observed for the closely related Pd-PEPPSI analogues for IPr* and IPr^{An}, for which values of 1.974(6) and 1.960(6) Å have been observed, respectively.[13d, 14a] Moreover, both of the *N*-aryl groups are nearly perpendicular to the plane of the NHC ring. Of particular note is that the bulky steric of the 2,6-dibenzhydryl lies above and below the coordination plane, which are oriented over the axial sites of the palladium atom. As can be expected, one direction of the axial site would be shielded by the combination of bulky steric and ancenaphthyl framework. On the other hand, the other *N*-aryl group of 2,6-diisopropyl would be much flexible as the existence of the opportunity of the rotation around the C-N bond. Therefore, these "flexible steric bulk" palladium complexes are expected to exhibit profound effect on the cross-coupling reactions.

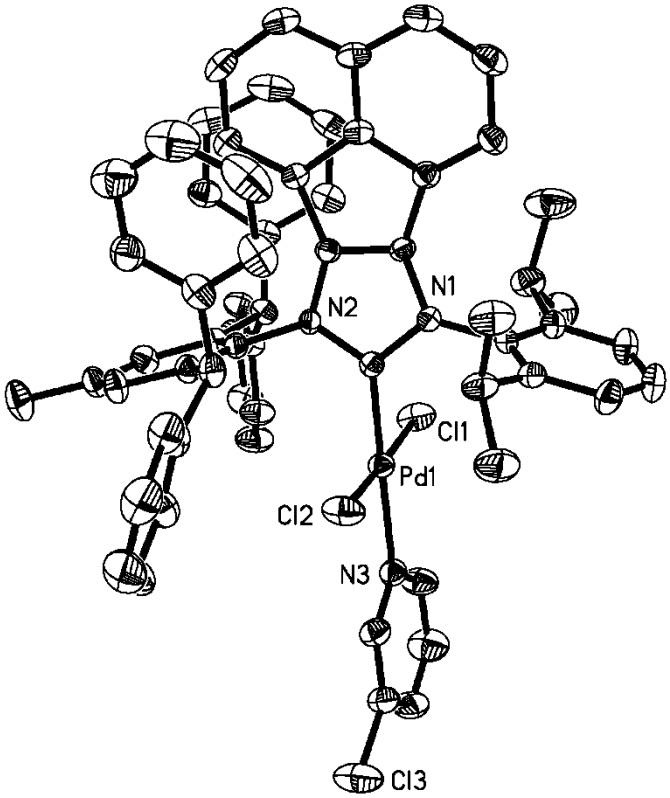


Figure 1. Molecular structure of **C1**•CH_2Cl_2 depicted with 30% thermal ellipsoids. Hydrogen atoms and uncoordinated CH_2Cl_2 molecule have been omitted for clarity. Selected bond distances (Å) and angles (^{o}): Pd(1)-C(1) 1.960(4), Pd(1)-N(3) 2.153(3), Pd(1)-Cl(1) 2.2795(11), Pd(1)-Cl(2) 2.2825(11), N(3)-Pd(1)-C(1) 178.67(14), N(3)-Pd(1)-Cl(1) 92.14(10), C(1)-Pd(1)-Cl(1) 86.61(10), N(3)-Pd(1)-Cl(2) 91.31(10), C(1)-Pd(1)-Cl(2) 89.94(10), Cl(1)-Pd(1)-Cl(2) 176.51(4).

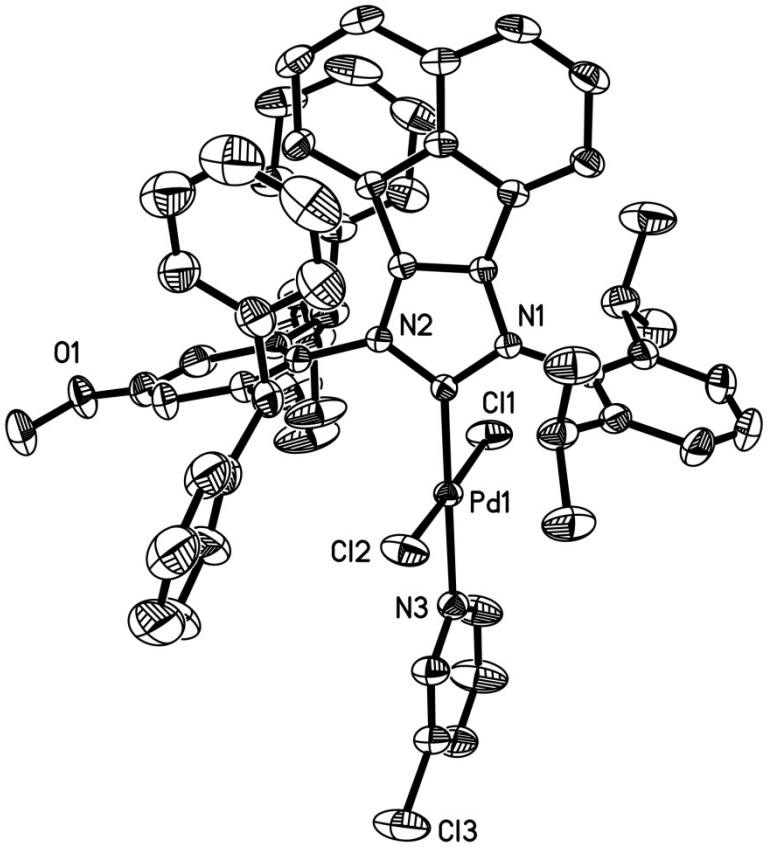


Figure 2. Molecular structure of **C3•**CH_2Cl_2 depicted with 30% thermal ellipsoids. Hydrogen atoms and uncoordinated CH_2Cl_2 molecule have been omitted for clarity. Selected bond distances (Å) and angles (°): Pd(1)-C(1) 1.963(2), Pd(1)-N(3) 2.162(2), Pd(1)-Cl(1) 2.2796(8), Pd(1)-Cl(2) 2.2836(8), N(3)-Pd(1)-C(1) 178.95(9), N(3)-Pd(1)-Cl(1) 92.23(7), C(1)-Pd(1)-Cl(1) 86.72(7), N(3)-Pd(1)-Cl(2) 91.18(7), C(1)-Pd(1)-Cl(2) 89.87(7), Cl(1)-Pd(1)-Cl(2) 176.54(3).

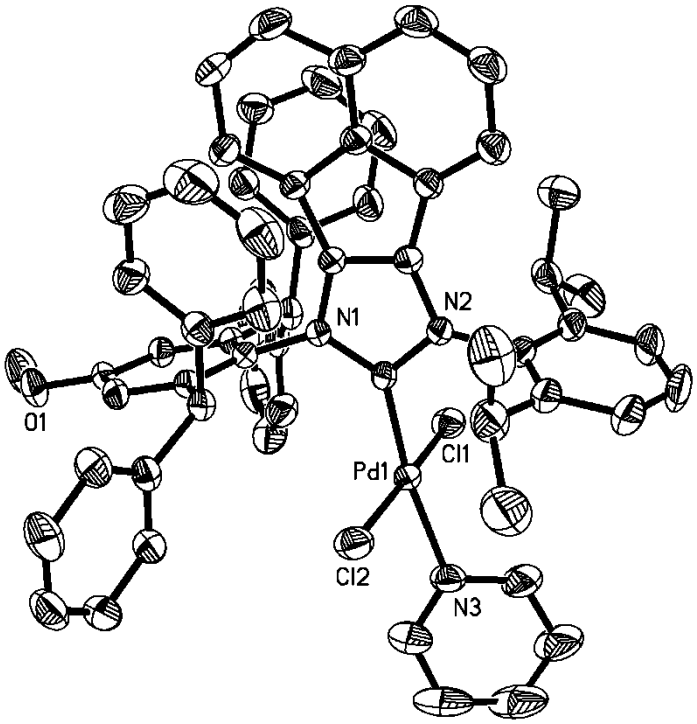


Figure 3. Molecular structure of **C4**•CH_2Cl_2•$3H_2O$ depicted with 30% thermal ellipsoids. Hydrogen atoms and uncoordinated molecules have been omitted for clarity. Selected bond distances (Å) and angles (^{o}): Pd(1)-C(1) 1.971(4), Pd(1)-N(3) 2.082(4), Pd(1)-Cl(1) 2.2945(12), Pd(1)-Cl(2) 2.2897(12), N(3)-Pd(1)-C(1) 171.15(16), N(3)-Pd(1)-Cl(1) 88.18(11), C(1)-Pd(1)-Cl(1) 91.28(11), N(3)-Pd(1)-Cl(2) 88.97(11), C(1)-Pd(1)-Cl(2) 92.38(11), Cl(1)-Pd(1)-Cl(2) 173.78(5).

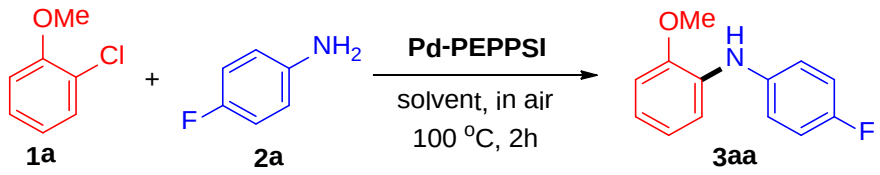
Buchwald-Hartwig Amination Reactions Catalyzed by the Pd-PEPPSI Complexes

To test the efficiency of these designed Pd-PEPPSI complexes towards C-N cross-coupling, our initial studies about the effect of ligand on the Buchwald-Hartwig reaction were performed. *It is noteworthy that all the solvents for the reactions were used without any further purification and the reactions were carried out in air.* In the presence of 0.5 mol% palladium loading, 2-chloroanisole and 4-fluoroaniline was chosen as a model reaction, using potassium *tert*-amylate (KO^tAm) as base and 1,4-dioxane as solvent at 100 ^{o}C for 2 hours. In these cases, it was found that all these precatalysts were very efficient and provided almost full conversion of the starting substrates (Runs 1-6, Table 1).

To better identify the differences in reactivity between these Pd-PEPPSI complexes, the palladium loading was then decreased to 0.1 mol%. Interestingly, dramatic changes were observed and the electronic effect of the *N*-aryl substituents has a noticeable impact on the catalytic performances. On the other hand, the effect of auxiliary ligands is insignificant (pyridine *vs.* 3-chloropyridine). As illustrated in Table 1, bearing a *para*-Me on *N*-aryl, the use of **C1** and **C2** resulted in profound efficiency, giving the GC yield of **3aa** in 86 and 90%, respectively (Runs 7 and 8, Table 1). In contrast, the introduction of *para*-OMe group (**C3** and **C4**) delivered the product in nearly quantitative yields of 100 and 96%, respectively (Runs 9 and 10, Table 1). Under the same reaction conditions, the **C5** and **C6** with *para*-F group, afford a satisfied yield of 87 and 89%, respectively (Runs 11 and 12, Table 1). To understand the relationship between the structure of the precatalysts and the active catalysts, the model reactions were monitored by GC in detail. As shown in Figure 4 and Figure S1, the **C1**-**C6** were initiated fast after a short induction period of 5 min. Significantly, the reaction rates of **C3** and **C4** were higher than those of other palladium complexes. Considering the similar steric bulk of these NHC ligands, the enhanced catalytic efficiency derived from OMe substituent would be resulted from its stronger electron donating character, which facilitates the oxidative addition of aryl chloride during the cross-coupling process.[24] To further evaluate the catalytic performance on ligand design, control experiments were conducted. As expected, in the absence of NHC ligand, the use of $Pd(OAc)_2$ as sole precatalyst furnished only trace amount of the desired product (Run 13, Table 1). This investigation proved the essential role of the NHC ligands for this cross-coupling. The commercially available Pd-PEPPSI-IPr and the Pd-PEPPSI-IPr^{An} previously reported respectively by Organ[10c] and Tu,[14a] which exhibited high efficiency in the C-N amination, were also evaluated under our reaction conditions. However, the results only showed

moderate yields of 25 and 46%, respectively (Runs 14 and 15, Table 1). The time-course of the reaction also revealed that the lifetime of Pd-PEPPSI-IPr and Pd-PEPPSI-IPr^{An} were only 10 min, which were shorter than those of **C1**-**C6**. Moreover, it was noteworthy that the Pd-PEPPSI-IPr had a long induction period of 45 min. These observations are consistent with previous results that NHCs catalysts led to much lower yields under air conditions than in inert atmosphere, which suggests the possibility of rapid capture of the palladium(0) speices by oxygen in these stances.[18d, e, g] To further shed light on this point, the reactions were performed under 1 atm of oxygen, whereas the reactions were completely shut down. Moreover, the reaction was also conducted with the most efficient precatalyst of bulky steric Pd-PEPPSI-IPr*, which bearing four bulky 2,6-dibenzhydryl groups on the *N*-aryl moieties.[13c] The desired product of **3aa** was obtained in excellent yield of 92%. Although both of the bulky *N*-aryl moieties are located in the IPr*, a slightly lower reactivity than that of **C3** was observed, indicating that both the skeleton of acenaphthyl and the steric bulk of *N*-aryl played crucial roles on the overall catalytic activity. Reasonably, the Pd-PEPPSI complex of **C3** gave the best yields as its “flexible steric bulk”, which would stabilize the Pd(0) active species with the enhancement of the lifetime, and further facilitated the oxidative addition step in this transformation due to flexible environment.

Table 1. Screening of Precatalysts and Reaction Conditions for the Buchwald−Hartwig Amination in Air[a]



Run	Pd complex	T (°C)	Pd mol%	Solvent	Base	Yield (%)
1	**C1**	100	0.5	1,4-dioxane	KO^{t}Am	96
2	**C2**	100	0.5	1,4-dioxane	KO^{t}Am	98
3	**C3**	100	0.5	1,4-dioxane	KO^{t}Am	100
4	**C4**	100	0.5	1,4-dioxane	KO^{t}Am	100
5	**C5**	100	0.5	1,4-dioxane	KO^{t}Am	97
6	**C6**	100	0.5	1,4-dioxane	KO^{t}Am	98
7	**C1**	100	0.1	1,4-dioxane	KO^{t}Am	86
8	**C2**	100	0.1	1,4-dioxane	KO^{t}Am	90
9	**C3**	100	0.1	1,4-dioxane	KO^{t}Am	100 (96)[b]
10	**C4**	100	0.1	1,4-dioxane	KO^{t}Am	97
11	**C5**	100	0.1	1,4-dioxane	KO^{t}Am	87
12	**C6**	100	0.1	1,4-dioxane	KO^{t}Am	89
13	$Pd(OAc)_2$	100	0.1	1,4-dioxane	KO^{t}Am	-[d]
14	PEPPSI-IPr	100	0.1	1,4-dioxane	KO^{t}Am	25
15	PEPPSI-(IPr)^{An}	100	0.1	1,4-dioxane	KO^{t}Am	46
16	PEPPSI-(IPr)*	100	0.1	1,4-dioxane	KO^{t}Am	92
17	**C3**	100	0.1	Toluene	KO^{t}Am	15
18	**C3**	100	0.1	DME	KO^{t}Am	12
19	**C3**	100	0.1	THF	KO^{t}Am	80
20	**C3**	100	0.1	1,4-dioxane	KO^{t}Bu	94
21	**C3**	100	0.1	1,4-dioxane	KOH	8
22	**C3**	100	0.1	1,4-dioxane	K_2CO_3	NR
23	**C3**	100	0.1	1,4-dioxane	Cs_2CO_3	13
24	**C3**	100	0.1	1,4-dioxane	NaO^{t}Bu	97
25	**C3**	100	0.05	1,4-dioxane	KO^{t}Am	88
26	**C3**	90	0.1	1,4-dioxane	KO^{t}Am	30
27	**C3**	80	0.1	1,4-dioxane	KO^{t}Am	19

[a]Reagents and conditions: 2-chloroanisole (1 mmol), 4-fluoroaniline (1.2 mmol), palladium source (0.005-0.0005 mmol), base (1.5 mmol), solvent (3 mL) under aerobic environment. All solvent was commercial and used as received. Cross-coupling product determined by GC using the (trifluoromethyl)benzene as internal standard. The cross-coupling yield was given in average twice. [b]Isolated yields in parentheses.

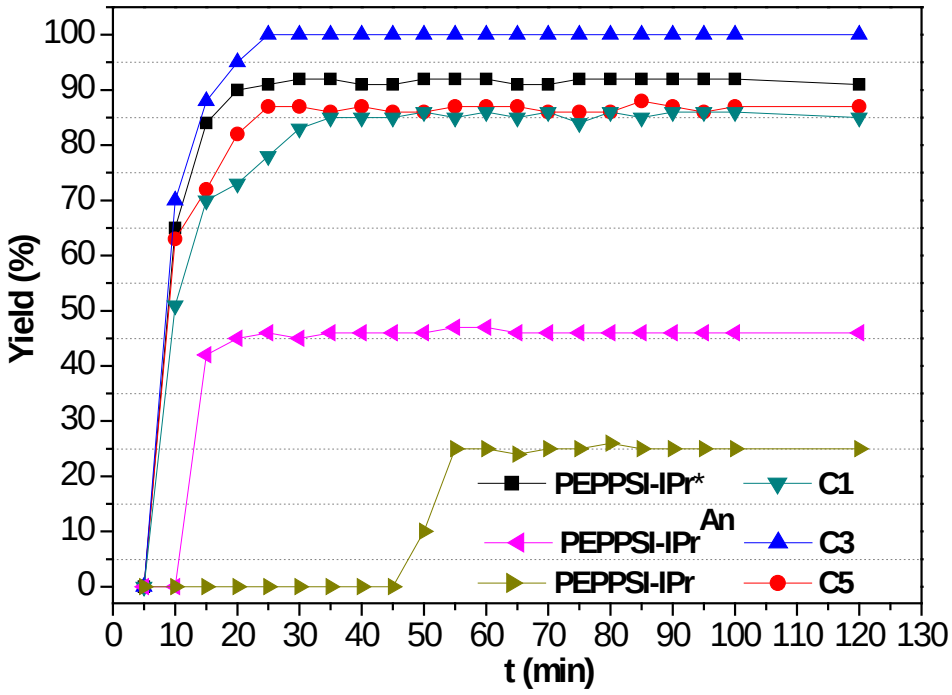


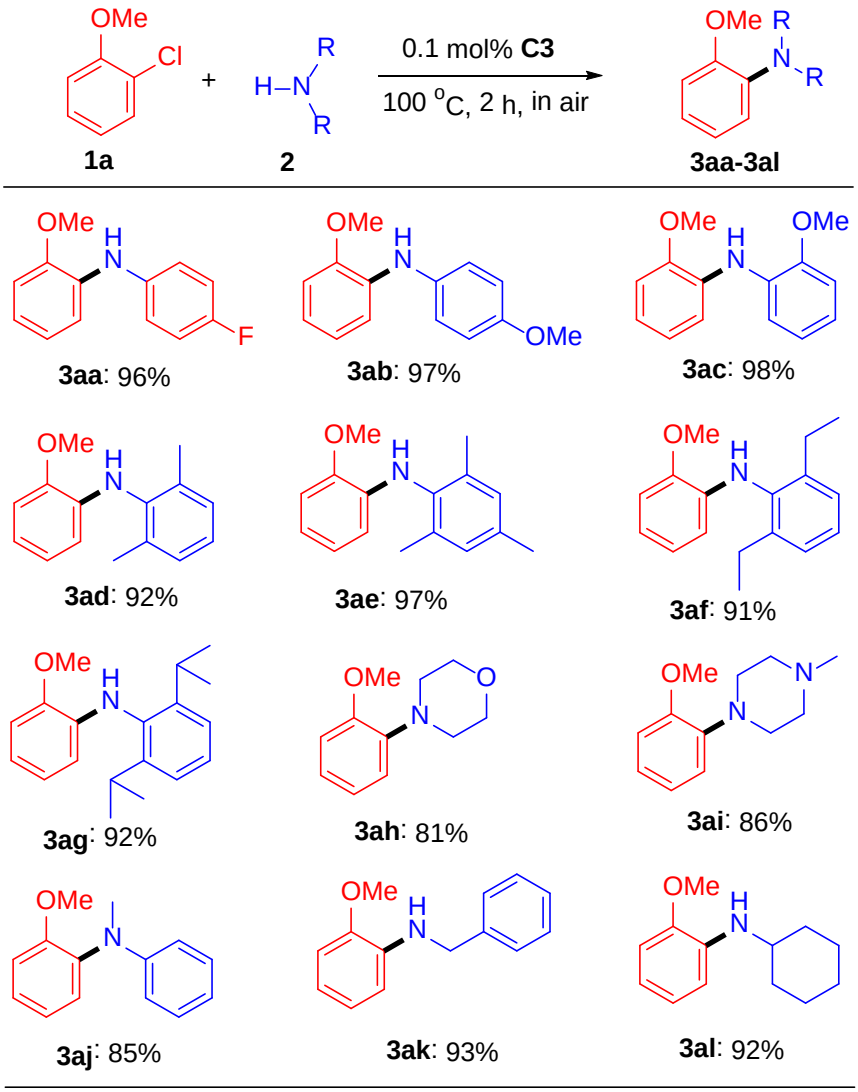
Figure 4. Kinetic profiles for Buchwald−Hartwig amination of 2-chloroanisole with 4-fluoroaniline performing in Table 1.

To investigate promising catalytic reaction conditions, different solvents and bases were subsequently screened in the amination. It revealed that the 1,4-dioxane gave the best result, affording the desired product with full conversion and a satisfied isolated yield of 96% was obtained (Run 9, Table 1). Other solvents, such as toluene, 1,2-dimethoxyethane (DME), and tetrahydrofuran (THF) afforded inferior values. The examination of bases disclosed that KO^{t}Bu and NaO^{t}Bu were very effective, while KO^{t}Am was proved to be the best choice. In contrast, the source of other bases, such as KOH, K_2CO_3, and Cs_2CO_3, gave only poor conversions (Runs 21-23, Table 1). These observations were in accordance with previous work, whereas better results were obtained using strong bases.[24] To further evaluate the catalytic efficiency, lower palladium of 0.05 mol% was conducted. To our delight, a satisfied activity of 88% yield was observed (Run 25, Table 1). Moreover, the reactions were also carried out at lower reaction temperature of 80 and 90 ^{o}C, respectively. However, a sharp decline of catalytic efficiency was investigated (Run 26 and 27, Table

1).[25]

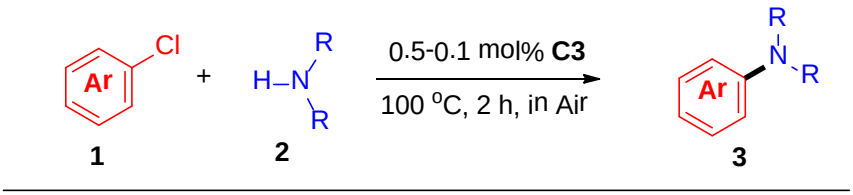
With the optimized reaction conditions in hand, the scope of the reaction was explored using 0.1 mol% of **C3** at 100 ^{o}C**,** with 1,4-dioxane as solvent and KO^{t}Am as base. As shown in Table 2, cross-coupling reactions of 2-chloroanisole (**3a**) with a range of electron-rich anilines were first examined. Anilines containing methoxyl group at *ortho*- and *para*- positions afforded the desired products in high yields of 97 and 98%, respectively (**3ab** and **3ac**). Bulky anilines bearing 2,6-dimethyl, 2,4,6-trimethyl, 2,6-diethyl, and 2,6-diisopropyl groups were well compatible, and the corresponding products (**3ad**-**3ag**) were isolated in 91-97% yields. In addition, a variety of secondary and primary amine partners, such as morpholine, *N*-methylpiperazine, *N*-methylaniline, phenylmethanamine, and cyclohexanamine all underwent highly efficient coupling, giving the products of **3ah**-**3al** in 81-95% yields. Other aryl chlorides with diverse amines were next studied and excellent results were obtained (Table 3, **3ba**-**3bh**, **3cd**-**3cj**, **3ed**). However, the catalytic performance was found to be less efficient in some cases, when steric hindrance or heteroaryl chlorides, such as 2,6-dimethyl chloride and 2- and 3-chloropyridines were used. To our delight, high yields were successfully achieved when coupling aryl chlorides between 2,6-dimethylaniline, 2,6-diisopropylaniline and *para*-fluoroaniline (**3dd**, **3fd**, **3ga**, **3gd**, and **3hg**) with an increased palladium loading of 0.5 mol%.

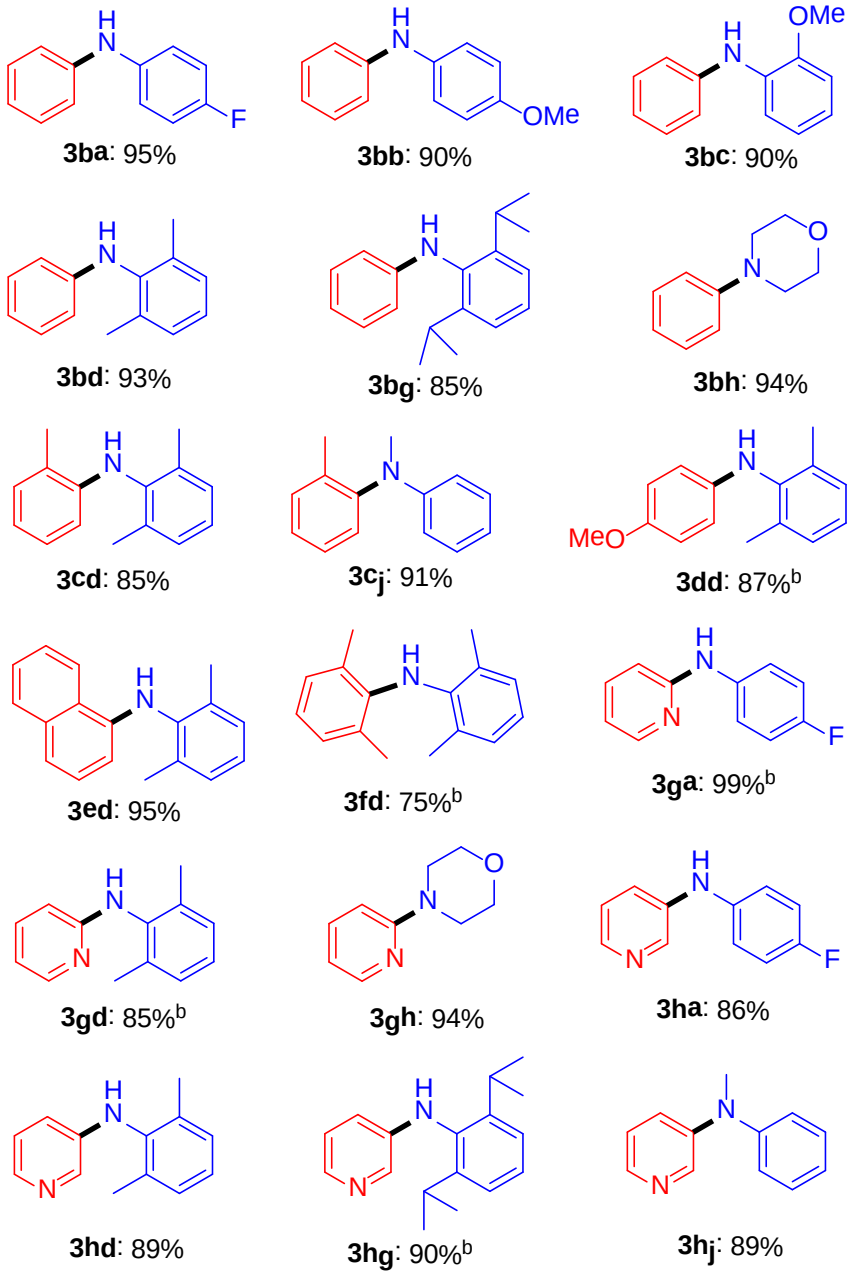
Table 2. Buchwald−Hartwig Amination of 2-Chloroanisole with Amines Catalyzed by C3.[a]



[a]Reagents and conditions: 2-chloroanisole (1 mmol), amine (1.2 mmol), **C3** (0.001 mmol), KO^{t}Am (1.5 mmol), 1,4-dioxane (3 mL) in air. Isolated yields.

Table 3. Scope of the Buchwald–Hartwig Amination of Aryl Chlorides with Amines Catalyzed by C3.[a]





[a]Reagents and conditions: (Hetero)ArCl (1 mmol), amine (1.2 mmol), **C3** (0.001 mmol), KO^{t}Am (1.5 equiv), 1,4-dioxane (3 mL) in air. Isolated yields. [b]Reagents and conditions: (1 mmol), amine (1.2 mmol), **C3** (0.005 mmol), KO^{t}Am (1.5 equiv), 1,4-dioxane (3 mL) in air. Isolated yields.

DFT Study on the Reaction Mechanism

In order to further understand the reaction mechanism and important factors for this **Pd-PEPPSI** catalyzed Buchwald-Hartwig amination reactions, DFT studies were carried out with [Pd(IPr^{OMe}*IPr)^{An}(3-Cl-pyridinyl)Cl_2] **C3** as a representative model as it has the best reaction performance. The catalytic cycle involves three mainly stages: 1) oxidative addition, 2) deprotonation, 3) reductive elimination. The obtained free energy profile and key structures for the catalytic cycle of **C3** are depicted in Figures 5 and 6, respectively. The active species Pd(0) may be generated from **C3** through a reduction elimination process, under the assistance of strong base KO^{t}Am.[26] DFT results (detailed PES is shown in Figure S48) suggested that a di-amido Pd(II) intermediate can undergo N-N coupling to generate Pd (0) species **C3-cat** ($\Delta G^{\ddagger}$ = 31.0 kcal/mol).

Oxidative Addition. The active Pd^0 species with a vacant site would be abstracted by KO^{t}Am to a resting state intermediate **C3-IM1** (-28.8 kcal/mol). By ligand exchange, the reactant aryl chloride will coordinate with Pd^0 center, to form intermediate **C3-IM2** (-7.6 kcal/mol). The oxidative addition of aryl chloride undergoes via transition state **C3-TS1** (1.5 kcal/mol), leading to a three coordinated Pd^{II} intermediate **C3-IM3** (-12.4 kcal/mol). The activation free energy of this step is calculated to be 30.3 kcal/mol relative to **C3-IM1**.

Deprotonation. In the second stage, the unsaturated **C3-IM3** would like to further coordinate with reactant aniline to form a four coordinated intermediate **C3-IM4** (-32.6 kcal/mol) with a square-planar geometry. Then the base KO^{t}Am will abstract the proton of aniline in **C3-IM4**, resulting in the deprotonated intermediate **C3-IM5** (-48.7 kcal/mol). It is worth noting that the deprotonation step from **C3-IM4** to **C3-IM5** drops in free energy by -16.1 kcal/mol without transition state, indicating a barrierless deprotonation process assisted by strong base.

Reductive elimination. The reductive elimination step initiates from intermediate **C3-IM6**, which is formed by the dissociation of chloride ligand from **C3-IM5**, uphill in free energy by 7.4 kcal/mol. In this step, C-N coupling via transition state **C3-TS2** (-23.9 kcal/mol) furnishes the PhNHPh as final product, with the regeneration of Pd^0 species from Pd^{II} center. The activation free energy of the reductive elimination step is 24.8 kcal/mol relative to intermediate **C3-IM5**.

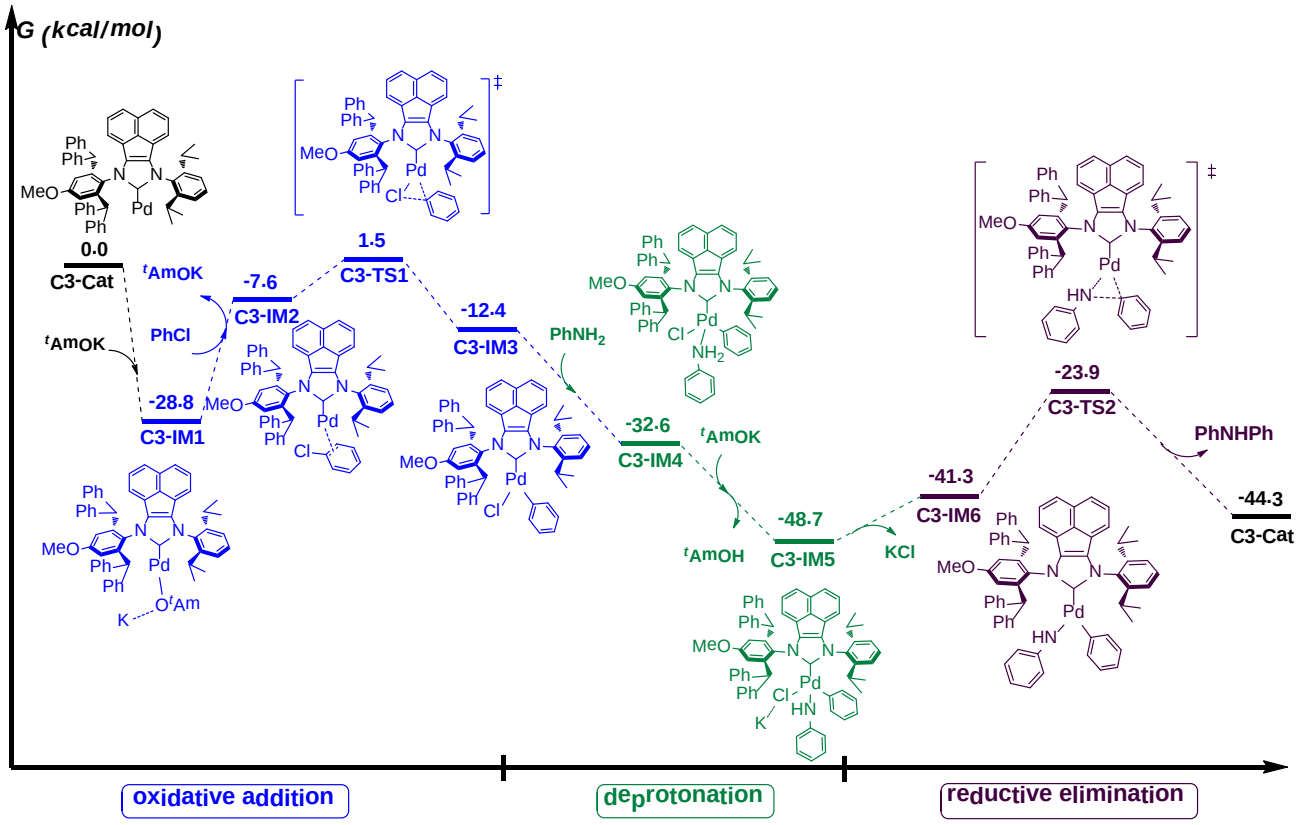


Figure 5. Free energy profile for **C3**-catalyzed Buchwald-Hartwing amination between aniline and phenyl chloride. Free energies are given in kcal/mol.

Through the DFT results above, the oxidative addition is found to be the rate-determining step for the **C3**-catalyzed Buchwald-Hartwing amination between aniline and phenyl chloride. The activation free energy of the oxidative addition step is 30.3 kcal/mol, which is 5.6 kcal/mol higher than that of the reductive elimination step. And the deprotonation step is suggested to be barrierless.

To further illustrate the electronic effect of this flexible steric bulky BIAN-Supported NHC-Pd complexes on the Buchwald-Hartwing amination, DFT studies were performed to compare the

activities of **C1**, **C3** and **C5** complexes with -CH_3, -OCH_3, and -F substituted groups, respectively. All these catalysts show accordant mechanism and similar free energy profiles. As shown in Figure **6**, the activation free energies of the rate-determining oxidative addition step are 30.3, 32.3, and 31.5 kcal/mol, for -OCH_3, -CH_3, and -F substituted NHC-Pd complexes, respectively. And the activation free energies of the reductive elimination step are 24.8, 20.9, and 13.3 kcal/mol, respectively. The electron-donating group can enhance the activity of the rate-determining oxidative addition step, although it may increase the activation free energy of the reductive elimination step. The activation free energy of the oxidative addition is composed of two parts: the ligand exchange and the C-Cl cleavage (Figure 5). Interestingly, analysis by separation of these two parts suggests that C-Cl cleavage contributes majorly to the difference in free energy barriers (Figure 6). The –OCH_3 substituted **C3** complex has lowest free energy penalty in C-Cl cleavage (9.1 kcal/mol), leading to the smallest activation free energy, exhibiting the best catalytic performance. Whereas the activities of **C1** and **C5** are relatively lower. The calculated results well explain how the electronic effect influences the catalytic activity, which is in good agreement with experimental observations.

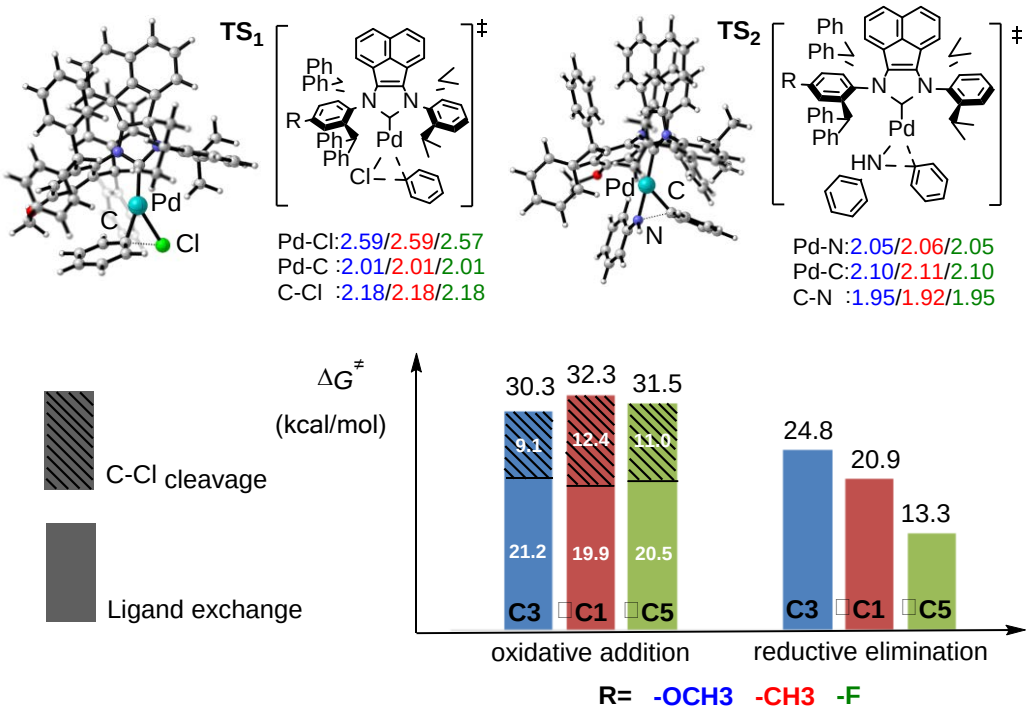


Figure 6. Activation free energies of oxidative addition and reductive elimination steps for NHCs-Pd catalysts with -OCH3, -CH_3, and -F groups.

CONCLUSION

We have developed a type of well-defined Pd-PEPPSI-(IPr*IPr)^{An}, Pd-PEPPSI-(IPr$^{(OMe)}$*IPr)^{An} and Pd-PEPPSI-(IPr^{F}*IPr)^{An} complexes for Buchwald-Hartwig cross-coupling reactions in air. The evaluation of the precatalysts confirmed that the "flexible steric bulk" and strong σ-donation nature are essential in securing high catalytic activity. Under the optimal conditions, the C-N cross-coupling products were efficiently obtained in excellent yield in the presence of 0.5-0.1 mol% palladium loading. A wide range of sterically hindered aryl, as well as heteroaryl chlorides, and various amines were compatible. DFT calculations suggest that the oxidative addition of aryl chlorides is the rate-determining step in the catalytic cycle. Electron-donating groups would benefit the catalytic activity. These results highlight a promising strategy to enhance catalytic activities under mild reaction conditions. Further synthetic program on air-stable Pd-PEPPSI complexes for cross-couplings is currently underway in our laboratories.

EXPERIMENTAL SECTION

Physical Measurements and Materials

2, 6-dibenzhydryl-4-methylaniline and 2, 6-dibenzhydryl-4-methoxyaniline were prepared according to previous report[23]. Pd-PEPPSI compounds was synthesized according to literature methods.[10a]

The 1D NMR spectra were recorded on a 400 MHz instrument at ambient temperature with the decoupled nucleus, using TMS as an internal standard and $CDCl_3$ as solvent. The X-ray diffraction data of single crystals were obtained with the ω-2θ scan mode on a CCD diffractometer with graphite-monochromated Mo Kα radiation (λ=0.71073Å) at 173K for **C1, C2** and **C4**. Cell parameters were obtained by global refinement of the positions of all collected reflections. Intensities were corrected for Lorentz and polarization effects and empirical absorption. The structures were solved by direct methods and refined by full-matrix least squares on F^2. All hydrogen atoms were placed in calculated positions. Structure solution and refinement were performed by using the SHELXL-97 package. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were introduced in calculated positions with the displacement factors of the host carbon atoms.

Computational details.

All the structures were optimized by the density functional theory (DFT)[27] at the B3LYP functional[28-30] with basis sets I (BSI, lanl2dz[31] for metal atom and 6-31G (d, p) for nonmetal atoms) in the solvent phase. Frequency analysis calculations for optimized structures were performed to characterize the structures to be minima (no imaginary frequency) or transition states (one imaginary

frequency). IRC calculations were taken to confirm the connection between two minima for a transition state. Based on B3LYP/BSI optimized geometries, the energy results were further refined by calculating the single point energy at the B3LYP/BSII level of theory (BSII designates SDD[32] for metal atom and 6-311++G**[33] for nonmetal atoms). Empirical dispersion correction has been considered in structure optimization and energy calculation. The bulky solvation effect of 1,4-Dioxane (ε= 2.2) were simulated with SMD[32] continuum solvent model at the B3LYP/BSII level of theory. Reaction temperature was corrected to 373K. All the calculations were performed with the Gaussian 09 program.[34] The 3D optimized structures were displayed by CYLview visualization program.[35]

General Procedures for the Synthesis of α-Ketoimine Compounds

Acenaphthenequinone (5 mmol) was initially suspended in acetonitrile (20 mL). After refluxing for 1h, 3 mL of acetic acid was injected and keeping refluxing until the acenaphthenequinone was completely dissolved. To this hot solution, aniline (5 mmol) was added and the reaction was refluxed for another 8 h under inert atmosphere. When reaching the determined time, the mixture was cooled and the resulting solid was filtered. The solid was washed with pentane (3 × 20 mL) and dried in air to afford the desired compound.

[2, 6-$(CHPh_2)_2$-4-(CH_3)-C_6H_2-N=C-(An)-(An)-C=O] (1a) was received as bright yellow powder (2.838 g) in 94% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (m, Ar-H, 2H), 7.71 (m, Ar-H, 2H), 7.23 (d, *J* = 7.3 Hz, Ar-H, 4H), 7.18 (d, *J* = 6.9 Hz, Ar-H, 2H), 7.05 (d, *J* = 7.5 Hz, Ar-H, 5H), 6.86 (d, *J* = 7.5 Hz, Ar-H, 4H), 6.78 (s, Ar-H, 2H), 6.60 (m, Ar-H, 4H), 6.43 (m, Ar-H, 2H), 6.13 (d, *J* = 7.1 Hz, Ar-H, 1H), 5.43 (s, C*H*$(Ph)_2$, 2H), 2.26 (s, Ar-CH_3, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.7, 162.3,

145.9, 142.9, 141.7, 133.8, 131.8, 131.7, 129.6, 129.4, 128.6, 128.4, 128.1, 127.8, 127.5, 127.2, 126.1, 125.5,123.9, 121.5, 52.1, 21.5.

[2, 6-$(CHPh_2)_2$-4-(CH_3O)-C_6H_2-N=C-(An)-(An)-C=O] (1b) was received as bright red powder (2.851 g) in 92% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 – 7.92 (m, Ar-H, 2H), 7.72 (m, Ar-H, 2H), 7.23 (d, *J* = 7.5 Hz, Ar-H, 4H), 7.18 (d, *J* = 7.1 Hz, Ar-H, 2H), 7.06 (d, *J* = 7.4 Hz, Ar-H, 5H), 6.86 (d, *J* = 7.4 Hz, Ar-H, 4H), 6.60 (m, Ar-H, 4H), 6.55 (s, Ar-H, 2H), 6.43 (m, Ar-H, 2H), 6.21 (d, *J* = 7.1 Hz,Ar-H, 1H), 5.44 (s, C*H*$(Ph)_2$, 2H), 3.62 (s, Ar-*OCH_3*, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 189.7, 162.9, 156.1, 142.5, 141.4, 133.2, 131.8, 129.6, 129.4, 128.5, 128.2, 127.8, 127.5, 127.2, 126.9, 126.3, 125.6, 123.8, 121.5, 113.7, 55.2, 52.2.

[2, 6-$(CHPh_2)_2$-4-F-C_6H_2-N=C-(An)-(An)-C=O] (1c) was received as bright yellow powder (2.674 g) in 88% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 – 7.98 (m, Ar-H, 2H), 7.83 – 7.65 (m, Ar-H, 2H), 7.21 (m, Ar-H, 5H), 7.06 (m, Ar-H, 5H), 6.85 (d, J = 7.5 Hz, Ar-H, 5H), 6.72 (d, J = 9.5 Hz, Ar-H, 2H), 6.61 (m, Ar-H, 4H), 6.44 (m, Ar-H, 2H), 6.16 (d, J = 7.0 Hz, Ar-H, 1H), 5.44 (s, C*H*$(Ph)_2$, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.4, 162.9, 142.5, 142.1, 141.0, 134.1, 131.8, 129.9, 129.6, 129.3, 128.7, 128.3, 127.9, 127.7, 127.2, 126.5, 125.8, 123.8, 121.6, 115.2, 52.2.

General Procedures for the Synthesis of α-Diimine Compounds

α-Ketoimine (5 mmol) and 2,6-diisopropylaniline (5 mmol) were mixed in toluene (20 mL) with the presence of a catalytic amount of para-toluenesulfonic acid under nitrogen atmosphere, and then the reaction was heated to 110 ^{o}C for 10 h. When having reached the determined time, the solution was cooled to room temperature and the solvent was evaporated. The rude material was crystallized from ethanol or purified by column chromatography as yellow crystals.

[2, 6-($CHPh_2$)$_2$-4-(CH_3)-C_6H_2-N=C-(An)-(An)-C=N-(2, 6-($CHCH_3$)$_2$-C_6H_3)] (2a) was received as bright yellow powder (1.984 g) in 52% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.2 Hz, Ar-H, 1H), 7.50 (d, *J* = 8.3 Hz, Ar-H, 1H), 7.29 (d, *J* = 6.6 Hz, Ar-H, 10H), 7.11 (m, Ar-H, 13H), 6.93 (d, *J* = 7.6 Hz, Ar-H, 4H), 6.81 (s, Ar-H, 2H), 5.64 (s, C*H*(Ph)$_2$, 2H), 3.17 (m, C*H*(CH_3)$_2$, 2H), 2.28 (s, Ar-*CH*$_3$, 3H), 1.29 (d, *J* = 6.7 Hz, CH_3, 6H), 1.01 (d, *J* = 6.8 Hz, CH_3, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.1, 146.8, 143.6, 142.7, 141.7, 139.6, 135.7, 132.6, 132.3, 129.6, 129.5, 129.2, 129.0, 128.8, 128.4, 128.0, 127.7, 126.8, 126.6, 126.0, 125.4, 124.4, 123.5, 122.8, 52.4, 28.5, 24.3, 23.7, 21.0.

[2, 6-($CHPh_2$)$_2$-4-(CH_3O)-C_6H_2-N=C-(An)-(An)-C=N-(2, 6-($CHCH_3$)$_2$-C_6H_3)] (2b) was received as bright yellow powder (1.753 g) in 45% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.2 Hz, Ar-H, 1H), 7.52 (d, *J* = 8.3 Hz, Ar-H, 1H), 7.28 (s, Ar-H, 5H), 7.23 (s, Ar-H, 3H), 7.19 (d, *J* = 7.1 Hz, Ar-H, 2H), 7.12 (d, *J* = 7.5 Hz, Ar-H, 4H), 6.93 (d, *J* = 7.3 Hz, Ar-H, 5H), 6.68 – 6.52 (m, Ar-H, 6H), 6.40 (m, Ar-H, 3H), 5.99 (d, *J* = 7.1 Hz, Ar-H, 1H), 5.64 (s, C*H*(Ph)$_2$, 2H), 3.64 (s, Ar-*OCH*$_3$, 3H), 3.15 (m, C*H*(CH_3)$_2$, 2H), 1.28 (d, *J* = 6.7 Hz, CH_3, 6H), 1.01 (d, *J* = 6.8 Hz, CH_3, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.0, 155.7, 145.9, 143.2, 141.3, 140.0, 135.7, 133.7, 129.7, 129.5, 128.6, 128.4, 128.1, 127.8, 127.2, 126.9, 126.8, 126.2, 125.9, 125.6, 124.4, 123.5, 122.9, 113.9, 55.2, 52.2, 28.4, 24.3, 23.7.

[2, 6-($CHPh_2$)$_2$-4-F-C_6H_2-N=C-(An)-(An)-C=N-(2, 6-($CHCH_3$)$_2$-C_6H_3)] (2c) was received as bright yellow powder (1.764 g) in 46% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (m, Ar-H, 1H), 7.51 (d, J = 8.2 Hz, Ar-H, 1H), 7.25 – 7.22 (m, Ar-H, 7H), 7.21 – 7.16 (m, Ar-H, 3H), 7.08 (d, J = 7.5 Hz, Ar-H, 4H), 6.89 (d, J = 7.3 Hz, Ar-H, 5H), 6.72 (d, J = 9.6 Hz, Ar-H, 2H), 6.56 (m, Ar-H, 4H), 6.40 (m, Ar-H, 3H), 5.92 (d, J = 7.1 Hz, Ar-H, 1H), 5.62 (s, C*H*(Ph)$_2$, 2H), 3.12 (m, C*H*(CH_3)$_2$,

2H), 1.26 (d, J = 6.7 Hz, CH_3,6H), 0.99 (d, J = 6.8 Hz, CH_3, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.9, 147.0, 142.8, 140.9, 140.0, 135.7, 134.6, 129.7, 129.5, 128.7, 128.6, 128.2, 128.1, 127.9, 127.0, 126.8, 126.4, 125.8, 124.6, 124.2, 123.6, 123.0, 115.3, 115.1, 52.2, 28.5, 24.2, 23.7.

General Procedures for the Synthesis of Imidazolium Salts

α-Diimine compounds (1 mmol) and chloromethyl ethyl (4 mL) ether were combined under a nitrogen atmosphere at room temperature, and then the reaction was heated to 100 ^{o}C overnight. When having reached the determined time, the solution was cooled to room temperature, and the reaction mixture was treated with anhydrous Et_2O and stirred for 1 h, causing the formation of a great deal of precipitate. The solid was isolated by filtration and wash with anhydrous Et_2O three times. The resulting crude was generally obtained in excellent purity and no further purification was required.

[(IPr*IPr^{Me})^{An}]$^{+}$Cl^{-} (L1) was obtained as yellowish powder (0.706 g, 87%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.61 (s, NC*H*N, 1H), 7.81 (d, *J* = 8.3 Hz, Ar-H, 1H), 7.64 (d, *J* = 8.0 Hz, Ar-H, 2H), 7.42 (m, Ar-H, 3H), 7.30 (d, *J* = 6.1 Hz, Ar-H, 8H), 7.18 (d, *J* = 6.0 Hz, Ar-H, 2H), 7.02 (m, Ar-H, 2H), 6.91 (s, Ar-H, 2H), 6.81 (d, *J* = 7.4 Hz, Ar-H, 4H), 6.70 (m, Ar-H, 4H), 6.60 (m, Ar-H, 2H), 6.22 (d, *J* = 7.0 Hz, Ar-H, 1H), 5.54 (s, C*H*$(Ph)_2$, 2H), 2.74 (m, C*H*$(CH_3)_2$, 2H), 2.29 (s, Ar-*CH_3*, 3H), 1.34 (d, *J* = 6.7 Hz, CH_3, 6H), 1.09 (d, *J* = 6.7 Hz, CH_3, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.5, 145.0, 143.9, 141.5, 140.7, 139.0, 136.8, 132.0, 130.6, 129.8, 129.7, 129.5, 129.2, 128.6, 128.2, 127.2, 127.0, 126.7, 126.5, 126.1, 124.9, 124.0, 122.7, 122.1, 121.7, 52.0, 29.4, 24.7, 23.6, 22.0. ESI-MS. *m/z*: 775.15, [**L1**]$^{+}$.

[(IPr^{OMe}*IPr)^{An}] $^{+}$Cl^{-} (**L2**) was obtained as yellowish powder (0.662 g, 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.69 (s, NC*H*N, 1H), 7.80 (d, *J* = 8.0 Hz, Ar-H, 1H), 7.64 (m, Ar-H, 2H), 7.44 (d, *J* = 7.8 Hz, Ar-H, 2H), 7.36 (m, 9.5 Hz, Ar-H, 9H), 7.18 (d, *J* = 6.1 Hz, Ar-H, 2H), 7.05 (m, Ar-H, 1H), 6.99 (d, *J* = 6.9 Hz, Ar-H, 1H), 6.84 (d, *J* = 7.4 Hz, Ar-H, 4H), 6.71 (m, Ar-H, 4H), 6.63 – 6.57 (m, Ar-H, 4H), 6.28 (d, *J* = 7.0 Hz, Ar-H, 1H), 5.58 (s, *CH*$(Ph)_2$, 2H), 3.61 (s, Ar-*OCH*$_3$, 3H), 2.73 (s, C*H*$(CH_3)_2$, 2H), 1.36 (d, *J* = 5.3 Hz, CH_3, 6H), 1.09 (d, *J* = 6.1 Hz, CH_3, 6H).^{13}C NMR (101 MHz, $CDCl_3$) δ 161.6, 148.8, 145.1, 143.5, 141.3, 139.3, 134.1, 132.0, 123.0, 129.8, 129.6, 129.4, 129.2, 128.8, 128.7, 128.6, 128.2, 127.6, 127.2, 126.9, 126.5, 124.9, 124.1, 121.7, 115.5, 55.3, 52.2, 29.4, 24.8, 23.7. ESI-MS. *m/z*: 791.15, [**L2**]$^{+}$.

[(IPr^{F}*IPr)^{An}] $^{+}$Cl^{-} (**L3**) was obtained as yellowish powder (0.587 g, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.71 (s, NC*H*N, 1H), 7.81 (d, J = 8.2 Hz, Ar-H, 1H), 7.65 (d, J = 8.0 Hz, Ar-H, 2H), 7.43 (m, Ar-H, 4H), 7.32 (m, Ar-H, 9H), 6.82 (m, Ar-H, 7H), 6.70 (m, Ar-H, 5H), 6.59 (m, Ar-H, 2H), 6.20 (d, J = 6.9 Hz, Ar-H, 1H), 5.59 (s, *CH*$(Ph)_2$, 2H), 3.48 (m, C*H*$(CH_3)_2$, 2H), 1.37 (d, J = 6.0 Hz, CH_3, 6H), 1.10 (d, J = 6.2 Hz, CH_3, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.2, 145.1, 145.0, 140.8, 134.0, 138.2, 136.9, 132.1, 129.8, 129.7, 129.5, 129.1, 128.8, 128.3, 127.2, 127.1, 127.0, 126.7, 125.0, 124.1, 122.5, 122.0, 121.8, 117.4, 117.1, 52.2, 29.5, 24.7, 23.6. ESI-MS. *m/z*: 779.30, [**L3**]$^{+}$.

General Procedures for the Synthesis of Pd-PEPPSI Compounds

In a vial equipped with a stirring bar, the mixture of $PdCl_2$ (177 mg, 1.0 mmol), imidazolium salt (1.0 mmol), K_2CO_3 (1382 mg, 10 mmol) and pyridine or 3-chloropyridine (5.0 mL) was stirred at 80°C during 24 h under a nitrogen atmosphere. After cooling to room temperature, 10 mL dichloromethane was added, and then the reaction mixture was diluted in CH_2Cl_2 and passed through

a pad of silica covered with celite and eluted with CH_2Cl_2. The solvents were removed under reduced pressure to furnish the desired product, which was recrystallized in a DCM/pentane mixture to remove completely the pyridine or 3-chloropyridine. The pure palladium complex was finally obtained after filtration and drying under high vacuum.

[Pd(IPr*IPr)^{An}(3-Cl-pyridinyl)Cl$_2$] (**C1**) was obtained as yellow powder (0.660 g, 62%).^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (s, Ar-H, 1H), 8.84 (d, *J* = 5.4 Hz, Ar-H, 1H), 7.66 (m, Ar-H, 2H), 7.49 (m, Ar-H, 3H), 7.30 (d, *J* = 7.6 Hz, Ar-H, 4H), 7.25 – 7.13 (m, Ar-H, 9H), 7.11 (s, Ar-H, 2H), 6.82 (d, *J* = 7.5 Hz, Ar-H, 4H), 6.62 (s, Ar-H, 2H), 6.56 (d, *J* = 7.0 Hz, Ar-H, 1H), 6.39 (m, 4H), 6.25 (m, Ar-H, 2H), 5.30 (s, *CH*(Ph)$_2$, 2H), 3.61 (m, C*H*(CH$_3$)$_2$, 2H), 2.38 (s, Ar-*CH$_3$*, 3H), 1.47 (d, *J* = 6.4 Hz, CH_3, 6H), 0.98 (d, *J* = 6.7 Hz, CH_3, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.5, 150.8, 149.8, 147.2, 144.5, 144.0, 141.6, 140.5, 139.1, 137.6, 135.1, 134.0, 132.0, 130.8, 130.7, 130.4, 129.7, 128.2, 127.9, 127.5, 127.2, 126.2, 125.8, 125.7, 125.4, 124.9, 124.5, 124.0, 122.4, 120.9, 51.1, 29.2, 26.1, 24.4, 21.9.Anal. Calcd for $C_{63}H_{54}Cl_3N_3Pd$: C, 70.99; H, 5.11; N, 3.94. Found: C, 70.86 ; H, 5.05; N, 3.97. ESI-MS. *m/z*: 914.95, [**L1**PdCl]$^+$; 775.15, [**L1**]$^+$.

[Pd(IPr*IPr)^{An}(pyridinyl)Cl$_2$] (**C2**) was obtained as yellow powder (0.800 g, 77%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (d, *J* = 5.0 Hz, Ar-H, 2H), 7.66 (m, Ar-H, 2H), 7.51 (d, *J* = 7.7 Hz, Ar-H, 2H), 7.46 (d, *J* = 8.2 Hz, Ar-H, 1H), 7.32 (d, *J* = 7.4 Hz, Ar-H, 4H), 7.24 – 7.13 (m, Ar-H, 9H), 7.09 (s, Ar-H, 2H), 6.83 (d, *J* = 7.4 Hz, Ar-H, 4H), 6.66 (s, Ar-H, 2H), 6.60 (t, *J* = 7.6 Hz,s Ar-H, 1H), 6.55 (d, *J* = 6.9 Hz, Ar-H, 1H), 6.40 (m, Ar-H, 4H), 6.25 (m, Ar-H, 2H), 5.30 (s, *CH*(Ph)$_2$, 2H), 3.63 (m, C*H*(CH$_3$)$_2$, 2H), 2.37 (s, Ar-*CH$_3$*, 3H), 1.48 (d, *J* = 6.4 Hz, CH_3, 6H), 0.98 (d, *J* = 6.7 Hz, CH_3, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.1, 151.7, 147.2, 144.5, 144.0, 141.5, 140.5, 139.0, 137.5, 135.1, 134.1, 130.7, 130.6, 130.4, 129.7, 128.2, 127.9, 127.5, 127.2, 127.1, 126.2, 125.7, 125.6, 125.4,

124.8, 124.1, 122.4, 120.8, 51.1, 29.1, 26.1, 24.4, 21.9.Calcd for $C_{63}H_{55}Cl_2N_3Pd$: C, 73.36; H, 5.37; N, 4.07. Found: C, 73.24; H, 5.42; N, 4.01. ESI-MS. *m/z*: 996.85, [**L1**PdClPy]$^+$; 914.60, [**L1**PdCl]$^+$; 775.15, [**L1**]$^+$.

[Pd(IPr^{OMe}*IPr)^{An}(3-Cl-pyridinyl)Cl$_2$] (**C3**) was obtained as yellow powder (0.611 g, 56%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (s, Ar-H, 1H), 8.84 (d, *J* = 5.3 Hz, Ar-H, 1H), 7.67 (m, Ar-H, 2H), 7.51 (d, *J* = 7.8 Hz, Ar-H, 2H), 7.46 (d, *J* = 8.2 Hz, Ar-H, 1H), 7.31 (d, *J* = 7.5 Hz, Ar-H, 4H), 7.21 (m, Ar-H, 6H), 7.16 (d, *J* = 6.7 Hz, Ar-H, 2H), 6.89 – 6.78 (m, Ar-H, 6H), 6.65 (s, Ar-H, 2H), 6.64 – 6.57 (m, Ar-H, 1H), 6.55 (d, *J* = 6.9 Hz, Ar-H, 1H), 6.39 (m, Ar-H, 4H), 6.24 (m, Ar-H, 2H), 5.30 (s, *CH*(Ph)$_2$, 2H), 3.69 (s, Ar-*OCH$_3$*, 3H), 3.60 (m, C*H*(CH$_3$)$_2$, 2H), 1.46 (d, *J* = 6.4 Hz, CH3, 6H), 0.97 (d, *J* = 6.7 Hz, CH3, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4, 156.8, 150.8, 149.8, 147.2, 145.9, 144.1, 141.7, 140.1, 137.6, 134.0, 132.0, 130.7, 130.4, 129.6, 127.9, 127.6, 127.3, 127.1, 126.2, 126.0, 125.8, 125.6, 125.4, 124.9, 124.5, 123.9, 122.6, 120.9, 115.5, 55.2, 51.3, 29.2, 26.1, 24.4. Calcd for $C_{63}H_{54}Cl_3N_3OPd$: C, 69.94; H, 5.03; N, 3.88. Found: C, 69.84; H, 5.07; N, 3.81. ESI-MS. *m/z*: 932.40, [**L2**PdCl]$^+$; 791.15, [**L2**]$^+$.

[Pd(IPr^{OMe}*IPr)^{An}(pyridinyl)Cl$_2$] (**C4**) was obtained as yellow powder (0.830 g, 79%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (d, *J* = 5.0 Hz, Ar-H, 2H), 7.66 (m, Ar-H, 2H), 7.51 (d, *J* = 7.8 Hz, Ar-H, 2H), 7.45 (d, *J* = 8.2 Hz, Ar-H, 1H), 7.33 (d, *J* = 7.6 Hz, Ar-H, 4H), 7.17 (m, Ar-H, 8H), 6.85 (d, *J* = 7.3 Hz, Ar-H, 4H), 6.80 (s, 2H), 6.69 (s, Ar-H, 2H), 6.66 – 6.57 (m, Ar-H, 1H), 6.55 (d, *J* = 6.9 Hz, Ar-H, 1H), 6.40 (m, Ar-H, 4H), 6.24 (m, Ar-H, 2H), 5.36 (s, *CH*(Ph)$_2$, 2H), 3.69 (s, Ar-*OCH$_3$*, 3H), 3.62 (m, C*H*(CH$_3$)$_2$, 2H), 1.48 (d, *J* = 6.5 Hz, CH$_3$, 6H), 0.98 (d, *J* = 6.8 Hz, CH$_3$, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.3, 158.5, 151.7, 147.2, 145.9, 144.2, 141.6, 140.2, 138.9, 137.5, 134.1, 130.6, 130.4, 129.7, 127.8, 127.5, 127.3, 127.1, 126.2, 125.9, 125.7, 125.6, 125.4, 124.8, 124.1,

122.6, 120.8, 115.4, 55.2, 51.3, 29.1, 26.1, 24.4.Anal. Calcd for $C_{63}H_{55}Cl_2N_3OPd$: C, 72.24; H, 5.29; N, 4.01. Found: C, 72.11; H, 5.36; N, 3.98. ESI-MS. *m/z*: 1048.80, [**L2**$PdCl_2(Py)]^+$; 933.15; [**L2**$PdCl_2]^+$, 791.15, [**L2**$]^+$.

[Pd(IPr^F*IPr)^{An}(3-Cl-pyridinyl)Cl$_2$] (**C5**) was obtained as yellow powder (0.705 g, 66%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.05 – 8.90 (m, Ar-H, 1H), 8.82 (m, Ar-H, 1H), 7.78 – 7.61 (m, Ar-H, 2H), 7.50 (m, Ar-H, 3H), 7.36 – 7.26 (m, Ar-H, 3H), 7.25 – 7.14 (m, Ar-H, 8H), 7.09 – 6.96 (m, Ar-H, 2H), 6.81 (d, J = 7.2 Hz, Ar-H, 4H), 6.68 (s, Ar-H, 2H), 6.59 (m, Ar-H, 3H), 6.40 (m, Ar-H, 4H), 6.25 (m, Ar-H, 2H), 5.30 (s, *CH*$(Ph)_2$, 2H), 3.59 (m, C*H*$(CH_3)_2$, 2H), 1.47 (d, J = 6.5 Hz, CH_3, 6H), 0.97 (d, J = 6.8 Hz, CH_3, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.1, 151.5, 150.8, 150.5, 149.7, 147.4, 147.2, 143.6, 141.4, 139.6, 139.2, 137.6, 133.9, 132.1, 130.8, 130.3, 129.6, 127.9, 127.7, 127.5, 127.3, 126.2, 126.0, 125.7, 124.9, 124.5, 122.5, 121.1, 117.2, 116.9, 51.3, 29.2, 26.1, 24.4. Anal. Calcd for $C_{62}H_{51}Cl_3FN_3Pd$: C, 69.60; H, 4.80; N, 3.93. Found: C, 69.51; H, 4.83; N, 3.89. ESI-MS. *m/z*: 921.20, [**L3**$PdCl]^+$; 779.30, [**L3**$]^+$.

[Pd(IPr^F*IPr)^{An}(pyridinyl)Cl$_2$] (**C6**) was obtained as yellow powder (0.981 g, 94%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (d, J = 5.0 Hz, 2H), 7.67 (m, Ar-H, 2H), 7.49 (m, Ar-H, 3H), 7.31 (m, Ar-H, 5H), 7.19 (m, Ar-H, 8H), 7.00 (d, J = 9.3 Hz, Ar-H, 2H), 6.82 (d, J = 7.3 Hz, Ar-H, 4H), 6.72 (s, Ar-H, 2H), 6.66 – 6.60 (m, Ar-H, 1H), 6.56 (d, J = 6.9 Hz, Ar-H, 1H), 6.41 (m, Ar-H, 4H), 6.25 (m, Ar-H, 2H), 5.33 (s, *CH*$(Ph)_2$, 2H), 3.61 (m, C*H*$(CH_3)_2$, 2H), 1.47 (d, J = 6.4 Hz, CH_3, 6H), 0.97 (d, J = 6.8 Hz, CH_3, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.7, 147.5, 147.2, 143.6, 141.4, 139.7, 139.1, 137.6, 134.0, 130.7, 130.4, 129.6, 128.2, 127.9, 127.7, 127.5, 127.3, 126.1, 125.9, 125.7, 125.3, 124.9, 124.2, 123.9, 122.5, 121.0, 117.1, 116.9, 51.3, 29.2, 26.1, 24.4. Anal. Calcd for:

$C_{62}H_{52}Cl_2FN_3Pd$: C, 71.92; H, 5.06; N, 4.06. Found: C, 71.81; H, 5.10; N, 3.98. ESI-MS. *m/z*: 1036.25, [**L3**$PdCl_2Py$]$^+$; 921.20, [**L3**PdCl]$^+$; 779.30, [**L3**]$^+$.

General Procedure for Buchwald-Hartwig Amination Reactions Promoted by Palladium Complexes

Unless otherwise noted, the amination reactions were carried out in air. The reaction temperatures are reported as the temperature of the heating vessel unless otherwise stated. All solvents were used as received and no further purification was needed. In parallel reactor containing a stirred bar was charged with Pd-PEPPSI complexes (0.001-0.005 mmol), amine (1.2 mmol), aryl chloride (1.0 mmol), base (1.5 mmol), and 3 mL of solvent. The reaction mixture was carried out at 100 ^oC for 2 h. After completion of the reaction, the reaction mixture was cooled to ambient temperature and 20 mL of water was added. The mixture was diluted with dichloromethane (5 mL), followed by extraction three times (3 × 5 mL) with dichloromethane. The organic layer was dried with anhydrous magnesium sulfate, filtered and evaporated under reduce pressure. The crude cross-coupling products were purified by silica-gel column chromatography using petroleum ether-dichloromethane (20/1) as eluent. The isolated cross-coupling products were characterized by ^1H NMR and ^{13}C NMR, and the spectrums can be found in Supporting Information.

General Information for NMR data

The NMR data of compounds were obtained on a Varian Mercury-Plus 400 MHz spectrometer at ambient temperature, using $CDCl_3$ as solvent and referenced *versus* TMS as standard. Chemical shifts are reported in ppm and coupling constants are reported in Hz.

3aa: N-(4-fluorophenyl)-2-methoxyaniline[13e] (208.6 mg, 96%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (m, Ar-H, 3H), 6.99 (m, Ar-H, 2H), 6.92 – 6.79 (m, Ar-H, 3H), 6.04 (s, NH, 1H), 3.90 (s, Ar-OCH_3, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.3, 147.9, 138.6, 133.8, 121.2, 120.9, 119.5, 115.9, 113.6, 110.4, 55.6.

3ab: 2-methoxy-N-(4-methoxyphenyl)aniline[36a] (222.3 mg, 97%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (d, *J* = 8.0 Hz, Ar-H, 2H), 7.04 (d, *J* = 7.6 Hz, Ar-H, 1H), 6.87 (d, *J* = 8.5 Hz, Ar-H, 3H), 6.84 – 6.72 (m, Ar-H, 2H), 5.97 (s, NH, 1H), 3.90 (s, Ar-OCH_3, 3H), 3.80 (s, Ar-OCH_3, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.37, 140.7, 130.5, 128.1, 122.8, 120.9, 118.5, 114.6, 112.6, 110.2, 55.6.

3ac: bis(2-methoxyphenyl)amine[36b] (224.6 mg, 98%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.0 Hz, Ar-H, 2H), 7.06 – 6.86 (m, Ar-H, 6H), 6.61 (s, NH, 1H), 3.95 (s, Ar-OCH_3, 6H).^{13}C NMR (101 MHz, $CDCl_3$) δ 148.8, 132.3, 120.6, 120.0, 115.3, 110.4, 55.5.

3ad: N-(2-methoxyphenyl)-2,6-dimethylaniline[13e] (209.1 mg, 92%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (m, Ar-H, 3H), 6.88 (m, Ar-H, 1H), 6.81 – 6.64 (m, Ar-H, 2H), 6.15 (m, Ar-H, 1H), 5.67 (s, NH, 1H), 3.97 (s, Ar-OCH_3, 3H), 2.23 (s, CH_3, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.7, 138.3, 136.1, 135.9, 128.4, 125.6, 121.1, 117.2, 111.0, 109.8, 55.6, 18.2.

3ae: N-(2-methoxyphenyl)-2,4,6-trimethylaniline[19b] (234.1 mg, 97%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.95 (s, Ar-H, 2H), 6.86 (m, Ar-H, 1H), 6.78 – 6.61 (m, Ar-H, 2H), 6.13 (m, Ar-H, 1H), 5.58 (s, NH, 1H), 3.95 (s, Ar-OCH_3, 3H), 2.31 (s, CH_3, 3H), 2.17 (s, CH_3, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.7, 136.3, 136.0, 135.6, 135.2, 129.1, 121.1, 117.0, 110.9, 109.8, 55.6, 20.9, 18.1.

3af: 2,6-diethyl-N-(2-methoxyphenyl)aniline[19b] (232.4 mg, 91%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (m, Ar-H, 3H), 6.87 (d, *J* = 7.2 Hz, Ar-H, 1H), 6.71 (m, Ar-H, 2H), 6.13 (d, *J* = 7.4 Hz, Ar-H, 1H), 5.68 (s, NH, 1H), 3.96 (s, Ar-*OCH*$_3$, 3H), 2.59 (m, CH_2, 4H), 1.16 (m, CH_3, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.5, 142.5, 137.1, 137.0, 126.5, 126.4, 121.1, 117.0, 111.0, 109.8, 55.7, 24.6, 14.7.

3ag: 2,6-diisopropyl-N-(2-methoxyphenyl)aniline[24a] (260.7 mg, 92%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.24 (m, Ar-H, 1H), 7.21 (d, *J* = 7.1 Hz, Ar-H, 2H), 6.84 (m, Ar-H, 1H), 6.74 – 6.58 (m, Ar-H, 2H), 6.11 (m, Ar-H, 1H), 5.63 (s, NH, 1H), 3.94 (s, Ar-*OCH*$_3$, 3H), 3.15 (m, CH, 2H), 1.13 (d, *J* = 6.9 Hz, CH_3, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.6, 146.2, 137.9, 135.4, 127.0, 123.7, 121.1, 116.7, 110.9, 109.7, 55.6, 28.1, 23.9.

3ah: 4-(2-methoxyphenyl)morpholine[13b] (156.5 mg, 81%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01 (m, Ar-H, 1H), 6.93 (d, *J* = 3.9 Hz, Ar-H, 2H), 6.88 (d, *J* = 7.9 Hz, Ar-H, 1H), 3.89 (s, CH_2, 4H), 3.86 (s, Ar-*OCH*$_3$, 3H), 3.07 (s, CH_2, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.2, 141.0, 123.1, 121.0, 117.9, 111.3, 67.1, 55.3, 51.1.

3ai: 1-(2-methoxyphenyl)-4-methylpiperazine[36c] (177.4 mg, 86%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.94 – 6.78 (m, Ar-H, 3H), 6.75 (d, *J* = 7.8 Hz, Ar-H, 1H), 3.74 (s, Ar-*OCH*$_3$, 3H), 3.02 (s, CH_2, 4H), 2.53 (s, CH_2, 4H), 2.26 (s, CH_3, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.7, 140.8, 122.4, 120.5, 117.7, 110.7, 54.9, 54.8, 50.1, 45.7.

3aj: 2-methoxy-N-methyl-N-phenylaniline[19b] (181.3 mg, 85%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (m, Ar-H, 4H), 6.99 (m, Ar-H, 2H), 6.74 (m, Ar-H, 1H), 6.67 (d, *J* = 8.1 Hz, Ar-H, 2H), 3.79 (s, Ar-*OCH*$_3$, 3H), 3.24 (s, CH_3, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.0, 149.4, 136.9, 129.1, 128.7, 126.9, 121.3, 117.1, 113.4, 112.7, 55.6, 39.0.

3ak: N-benzyl-2-methoxyaniline[14e] (198.4 mg, 93%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 7.4 Hz, Ar-H, 2H), 7.38 (m, Ar-H, 2H), 7.31 (m, Ar-H, 1H), 6.88 (m, Ar-H, 1H), 6.83 (d, *J* = 7.8 Hz, Ar-H, 1H), 6.72 (m, Ar-H, 1H), 6.64 (d, *J* = 7.7 Hz, Ar-H, 1H), 4.67 (s, N-H, 1H), 4.39 (s, CH_2, 2H), 3.88 (s, Ar-OCH_3, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.7, 139.6, 138.1, 128.5, 127.5, 127.1, 121.2, 116.6, 110.0, 109.4, 55.4, 48.0.

3al: N-cyclohexyl-2-methoxyaniline[36a] (188.9 mg, 92%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.94 (m, Ar-H, 1H), 6.84 (d, *J* = 7.4 Hz, Ar-H, 1H), 6.72 (d, *J* = 7.5 Hz, Ar-H, 2H), 5.31 (s, N-H, 1H), 3.90 (s, Ar-OCH_3, 3H), 3.35 (s, CH, 1H), 2.16 (d, *J* = 12.0 Hz, CH_2, 2H), 1.86 (d, *J* = 12.9 Hz, CH_2, 2H), 1.74 (d, *J* = 12.2 Hz, CH_2, 1H), 1.47 (m, CH_2, 2H), 1.40 – 1.18 (m, CH_2, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.6, 137.1, 121.1, 115.7, 110.1, 109.4, 55.2, 51.2, 33.3, 25.9, 25.0.

3ba: 4-fluoro-N-phenylaniline[36d] (177.8 mg, 95%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (m, Ar-H, 2H), 7.08 (m, Ar-H, 2H), 7.03 (m, Ar-H, 4H), 6.96 (m, Ar-H, 1H), 5.59 (s, NH, 1H).^{13}C NMR (101 MHz, CDCl3) δ 159.2, 156.8, 143.9, 138.9, 129.3, 120.5, 116.7, 116.0.

3bb: 4-methoxy-N-phenylaniline[36d] (179.3 mg, 90%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (m, Ar-H, 2H), 7.09 (d, J = 8.8 Hz, Ar-H, 2H), 6.96 – 6.84 (m, Ar-H, 5H), 5.50 (s, NH, 1H), 3.81 (s, Ar-OCH_3, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.2, 145.1, 135.7, 129.2, 122.2, 119.5, 115.6, 114.6, 55.6.

3bc: 2-methoxy-N-phenylaniline[36e] (179.3 mg, 90%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.35 (m, Ar-H, 3H), 7.27 (d, J = 7.8 Hz, Ar-H, 2H), 7.06 (m, Ar-H, 1H), 6.97 (d, J = 13.1 Hz, Ar-H, 3H), 6.28 (s, NH, 1H), 3.98 (s, Ar-OCH_3, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.2, 142.7, 132.9, 129.2, 121.0, 120.7, 119.8, 118.5, 114.6, 110.5, 55.5.

3bd: 2,6-dimethyl-N-phenylaniline[13c] (183.5 mg, 93%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 – 6.98 (m, Ar-H, 5H), 6.76 (m, Ar-H, 1H), 6.52 (d, J = 8.0 Hz, Ar-H, 2H), 5.19 (s, NH, 1H), 2.23 (s, CH_3, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.2, 138.2, 135.9, 129.2, 128.5, 125.7, 118.1, 113.5, 18.3.

3bg: 2,6-diisopropyl-N-phenylaniline[35d] (215.4 mg, 85%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, Ar-H, 1H), 7.22 (d, J = 7.4 Hz, Ar-H, 2H), 7.14 (m, Ar-H, 2H), 6.72 (m, Ar-H, 1H), 6.49 (d, J = 7.9 Hz, Ar-H, 2H), 5.12 (s, NH, 1H), 3.21 (m, CH, 2H), 1.15 (d, J = 6.9 Hz, CH_3, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.1, 147.6, 135.1, 129.2, 127.2, 123.8, 117.6, 112.9, 28.2, 23.8.

3bh: 4-phenylmorpholine[14a] (153.4 mg, 94%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (m, Ar-H, 2H), 6.91 (m, Ar-H, 3H), 4.07 – 3.74 (m, CH_2, 4H), 3.44 – 2.67 (m, CH_2, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.3, 129.2, 120.0, 115.7, 66.9, 49.3.

3cd: 2,6-dimethyl-N-(o-tolyl)aniline[24a] (179.6 mg, 85%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 – 7.06 (m, Ar-H, 4H), 6.99 (m, Ar-H, 1H), 6.73 (m, Ar-H, 1H), 6.17 (d, J = 8.0 Hz, Ar-H, 1H), 4.95 (s, NH, 1H), 2.35 (s, CH_3, 3H), 2.21 (s, CH_3, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.1, 138.7, 135.5, 130.2, 128.5, 126.9, 125.5, 122.4, 118.1, 111.7, 18.2, 17.6.

3cj: N,2-dimethyl-N-phenylaniline[24a] (179.5 mg, 91%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, J = 7.3 Hz, Ar-H, 1H), 7.19 (m, Ar-H, 5H), 6.72 (m, Ar-H, 1H), 6.55 (d, J = 8.0 Hz, Ar-H, 2H), 3.24 (s, CH_3, 3H), 2.16 (s, CH_3, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.2, 146.8, 136.8, 131.3, 128.9, 128.3, 127.5, 126.4, 116.8, 112.8, 39.0, 17.8.

3dd: N-(4-methoxyphenyl)-2,6-dimethylaniline[14a] (197.8 mg, 87%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (d, J = 7.2 Hz, Ar-H, 2H), 7.06 – 7.00 (m, Ar-H, 1H), 6.75 (d, J =

8.3 Hz, Ar-H, 2H), 6.49 (d, J = 8.1 Hz, Ar-H, 2H), 5.02 (s, NH, 1H), 3.74 (s, Ar-*OCH*$_3$, 3H), 2.19 (s, CH_3, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.7, 139.2, 137.3, 134.9, 128.6, 125.0, 115.3, 114.7, 55.7, 18.4.

3ed: N-(2,6-dimethylphenyl)naphthalen-1-amine[14a] (234.9 mg, 95%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 7.8 Hz, Ar-H, 1H), 7.88 (d, *J* = 5.9 Hz, Ar-H, 1H), 7.63 – 7.48 (m, Ar-H, 2H), 7.34 (d, *J* = 7.6 Hz, Ar-H, 1H), 7.18 (m, Ar-H, 4H), 6.26 (d, *J* = 7.1 Hz, Ar-H, 1H), 5.73 (s, NH, 1H), 2.24 (s, CH_3, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.2, 138.7, 135.1, 134.5, 128.7, 128.7, 126.5, 125.8, 125.5, 125.0, 124.0, 120.4, 118.8, 107.3, 18.2.

3fd: bis(2,6-dimethylphenyl)amine[13e] (169.1 mg, 75%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.00 (d, J = 7.4 Hz, Ar-H, 4H), 6.86 (m, Ar-H, 2H), 4.81 (s, NH, 1H), 2.03 (s, CH_3, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.7, 129.5, 128.7, 121.7, 19.1.

3ga: N-(4-fluorophenyl)pyridin-2-amine[36f] (186.3 mg, 99%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 4.5 Hz, Ar-H, 1H), 7.47 (m, Ar-H, 1H), 7.30 (m, Ar-H, 2H), 7.03 (m, Ar-H, 2H), 6.72 (m, Ar-H, 2H), 6.64 (s, NH, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.1, 156.4, 148.3, 137.7, 122.8, 116.0, 115.8, 114.9, 107.8.

3gd: N-(2,6-dimethylphenyl)pyridin-2-amine[36f] (168.5 mg, 85%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 4.5 Hz, Ar-H, 1H), 7.36 (m, Ar-H, 1H), 7.13 (s, Ar-H, 3H), 6.63 (m, Ar-H, 1H), 6.17 (s, NH, 1H), 6.00 (d, J = 8.4 Hz, Ar-H, 1H), 2.23 (s, CH_3, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.7, 148.5, 137.8, 136.7, 136.4, 128.5, 126.7, 113.6, 105.7, 18.4.

3gh: 4-(pyridin-2-yl)morpholine[14a] (154.3 mg, 94%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 4.1 Hz, Ar-H, 1H), 7.45 (m, Ar-H, 1H), 6.61 (m, 7.4 Hz, Ar-H, 2H), 3.92 – 3.66 (m, CH_2, 4H), 3.56 – 3.18 (m, CH_2, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ

159.5, 147.8, 137.3, 113.6, 106.8, 66.6, 45.5.

3ha: N-(4-fluorophenyl)pyridin-3-amine[13e] (161.9 mg, 86%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, Ar-H, 1H), 8.16 (d, *J* = 4.0 Hz, Ar-H, 1H), 7.34 – 7.27 (m, Ar-H, 1H), 7.20 – 7.15 (m, Ar-H, 1H), 7.06 (m, Ar-H, 4H), 5.73 (s, NH, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.8, 141.60, 139.3, 123.7, 122.4, 121.3, 121.2, 116.3, 116.1.

3hd: N-(2,6-dimethylphenyl)pyridin-3-amine[13b] (176.5 mg, 89%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 2.5 Hz, Ar-H, 1H), 8.00 (d, *J* = 4.5 Hz, Ar-H, 1H), 7.20 – 7.09 (m, Ar-H, 3H), 7.03 (m, Ar-H, 1H), 6.64 (d, *J* = 8.2 Hz, Ar-H, 1H), 5.33 (s, NH, 1H), 2.20 (s, CH_3, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.5, 139.5, 136.8, 136.7, 135.9, 128.7, 126.4, 123.7, 119.0, 18.2.

3hg: N-(2,6-diisopropylphenyl)pyridin-3-amine[35e] (228.9 mg, 90%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 2.3 Hz, Ar-H, 1H), 7.97 (m, Ar-H, 1H), 7.32 (m, Ar-H, 1H), 7.36 – 7.29 (d, *J* = 7.7 Hz, Ar-H, 2H), 7.01 (m, Ar-H, 1H), 6.61 (m, Ar-H, 1H), 5.21 (s, NH, 1H), 3.15 (m, CH, 2H), 1.14 (d, *J* = 6.9 Hz, CH_3, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.5, 144.2, 139.2, 136.2, 133.7, 127.8, 124.1, 123.7, 118.5, 28.2, 23.8.

3hj: N-methyl-N-phenylpyridin-3-amine[13e] (163.9 mg, 89%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, *J* = 1.5 Hz, Ar-H, 1H), 8.13 (d, *J* = 4.4 Hz, Ar-H, 1H), 7.33 (m, Ar-H, 2H), 7.22 (d, *J* = 8.4 Hz, Ar-H, 1H), 7.18 – 7.12 (m, Ar-H, 1H), 7.12 – 7.03 (m, Ar-H, 3H), 3.33 (s, CH_3, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.8, 145.1, 141.0, 140.5, 129.5, 124.7, 123.4, 123.2, 122.4, 30.0.

ASSOCIATED CONTENT

Supporting Information

The supporting information including NMR spectra and X-ray crystallographic data is available free of charge on the ACS Publications website http://pubs.acs.org.

Author Contributions

[+]*Xiao-Bing Lan and Yinwu Li* contributed equally.

Notes

The authors declare no competing financial interest.

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(25) The catalytic performance which was fluctuated to a large extent by reaction temperature, might be mainly caused by two reasons. One could be attributed to the high activation energy ($\Delta G^{\ddagger}$ = 31.0 kcal/mol) of the generation of NHC-Pd(0) in the initiaiton step, which disscussed in the subsequnt DFT calculations. The other reason might be the existence of high temperature

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Graphic picture