The Impact of the N-heterocyclic carbene (NHC) ligand on the *trans*-[Pd(NHC)($NH_2{}^nBu$)Cl_2] precatalyst architecture in C-N bond-forming reactions

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KEYWORDS. Buchwald-Hartwig amination • N-heterocyclic carbenes • Palladium

ABSTRACT: Two straightforward synthetic procedures leading to air- and moisture-stable *trans*-[Pd(NHC)($NH_2{}^nBu$)Cl_2] precatalysts are presented. These complexes, obtained by adding *n*-butylamine to [Pd(NHC)(μ-Cl)Cl]$_2$ or *trans*-[Pd(NHC)(DMS)Cl_2] precursors (DMS = dimethyl sulfide), demonstrate superior catalytic activity compared to their DMS counterparts in Buchwald-Hartwig amination reactions. Utilizing a more sustainable solvent (2-MeTHF), the catalyst loading was halved to 0.1 mol%, establishing this new system as a highly efficient and environmentally more friendly alternative to previous systems.

Introduction

Amines represent important building blocks in organic chemistry as C-N bonds are commonly encountered in pharmaceutical and agrochemical compounds, dyes, and plastics.[1-4] More than 80% of currently marketed drugs contain at least one C-N bond.[5] Over the years, numerous catalytic solutions, especially those mediated by transition metal catalysts, have allowed for new assembly strategies in the construction of various functional C-N bonds.[6, 7] Among these strategies, the palladium-mediated Buchwald-Hartwig amination (BHA) reaction stands out as an important tool for C-N bond installation.[2, 8, 9]

The generation of C-N bonds through Pd was first reported by Buchwald and Hartwig in 1995,[10,11] with following industrial applications exhibiting excellent performance at relatively low catalyst loading.[12] Through the deployment of meticulously designed and stable Pd precatalysts, reaction efficiencies have been substantially enhanced over time. Consequently, reduction of the catalyst loading, milder reaction conditions and wider substrate scopes have resulted from focused catalyst design efforts.[13,14] Pd cross-coupling reactions and catalyst design are continuously improving, fueled by an unprecedented demand and important contributions from researchers worldwide.[15] The utilization of key ligands such as phosphines and N-heterocyclic carbenes (NHCs) has been crucial for this accelerated growth.[16, 17] Pd complexes bearing NHC ligands have shown to be excellent partners for these reactions, exhibiting in most cases superior performance due to the great stability of the Pd-NHC bond.[17] The generally observed trend is that the straightforward molecular construction of the N-heterocyclic carbenes and their superior stabilization enhance the catalytic activity of the metal core.[13, 18]

Designing air-stable and easy to synthesize Pd^{II} precatalysts is a challenging and crucial factor in accessing active catalyst species in most cross-coupling reaction. Historically, the approach used has consisted of adding ligand to a metal precursor to generate (hopefully) active M-L containing species and enough of it to lead to catalytic efficient systems. The approach has evolved overtime and now well-defined species have become the norm as only the activation of the pre-catalyst (and not questions as to whether the M-L bond is formed or not) remains the key mechanistic question.[14,19,20]

In the context of well-defined palladium precatalytic species, effective complexes require labile sacrificial ligands (a.k.a throwaway ligands), that do not perturb or hinder the catalytic reaction cycle. Some of the most successful sacrificial ligands to date include the palladacycles reported by Buchwald,[16] PEPPSI complexes (Pyridine Enhanced Pre-catalyst Preparation Stabilization and Initiation) reported by Organ[21] and the allyl-based systems reported by Nolan.[22]

By incorporating Organ's PEPPSI or Nolan's cinnamyl ligand strategies with palladium and specially decorated NHCs, the groups of Xu[23] and Qiu,[24] independently designed effective catalysts that operate efficiently at very low catalyst loading (0.05 - 4 mol%) for the Buchwald-Hartwig amination reaction of challenging substrates. In these studies, focusing on NHC optimization, identical conclusions were reached as in our initial reports where the IPr* ligand, first reported by Markó,[25] proved an exceptionally effective supporting ligand (see the top two structures presented in Figure 1 for graphical representation of IPr*).[26,27]

More recently, in efforts to examine the role of the throwaway/stabilizing ligand, Cazin and co-workers reported in 2022

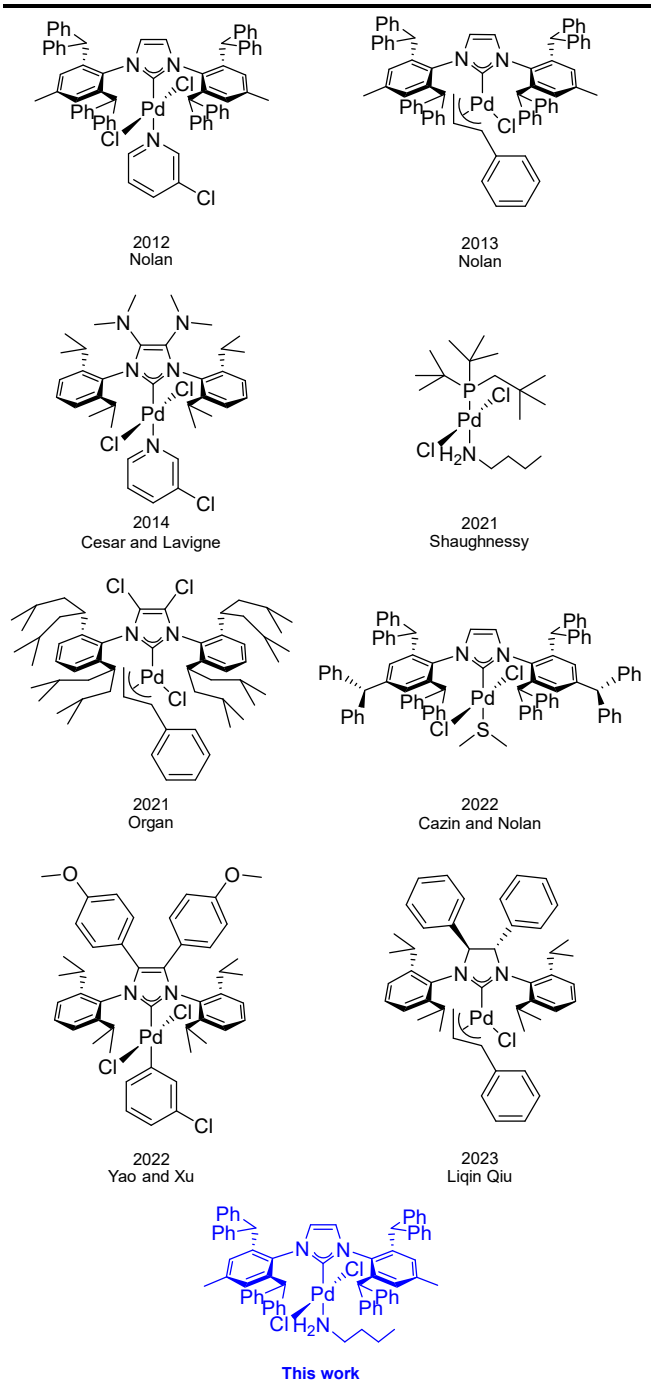


Figure 1. Selected examples of robust Pd-precatalysts in the BHA reaction working at mild temperature or low catalyst loading or both.

on the use of DMS (dimethyl sulfide) in [Pd(NHC)] containing complexes. Such system facilitated the Buchwald-Hartwig and Suzuki-Miyaura couplings under quite mild, greener conditions, operating respectively at 0.2 and 0.5 mol% catalyst loadings.[28] Shaughnessy has also explored the effects of such throw-away ligands and has made use of *n*-butylamine as a sacrificial ligand in combination with Pd-phosphine architectures,[29] operating at 0.5 mol% for Buchwald-Hartwig amination between RT to 80 °C. Previous report of Chen and Hsu on Pd-NHC complexes bearing various designs of primary arylamines and only one alkylamine (i.e.ethylamine), highlighted the higher efficiency of 2,6-diisopropylaniline as throwaway ligand in the BHA reaction, with ethylamine being the least efficient.[30] Even though several iterations of primary arylamines have been investigated as throwaway ligands to Pd-NHC precatalysts, ethylamine from the previously mentioned report remains the only example of a primary alkylamine acting in such a role.[30] Shaughnessy's approach with Pd-phosphine complexes using the bulkier *n*-butylamine sacrificial ligand (and non-rebinding as it is transformed under catalytic conditions)[31] represents an intriguing alternative to the small ethylamine ligand,[30] and to date this approach has not yet been reported in combination with [Pd(NHC)] complexes. Therefore, we herein bridge this gap by reporting on the design and synthesis of several Pd^{II} precatalysts bearing NHC ligands as well as *n*-butylamine, and evaluating their performance in the BHA reaction to examine whether such a throw-away ligand might also prove beneficial when NHC ligands are present as supporting ligands.

Results and Discussion

We began our investigation by synthesizing [Pd(NHC)(cin)Cl] complexes (**1**) using the $[Pd(cin)Cl]_2$ dimer and adopting the weak base route (Scheme 1).[32-34] Furthermore, we made use of the TMSCl route to synthesize the palladium dimers: $[Pd(NHC)(\mu\text{-}Cl)Cl]_2$ (**2**). Adding *n*-butylamine (NBA) to **2** afforded the products $[Pd(NHC)(NBA)Cl_2]$ (**4**) in quantitative yields. An alternative route proceeds via $[Pd(NHC)(DMS)Cl_2]$ precursors (**3**) for complexes **4** that were not accessible using the previously mentioned methodology (Scheme 1). The substitution of DMS with *n*-butylamine proved successful, and with straightforward purification, afforded the desired products in good yields. Note that all reactions were carried out overnight (16 hrs) in dichloromethane or ethyl acetate at room temperature and consistently yielded a single product. A total of 8 complexes were synthesized using the mentioned routes and produced the desired product **4** in good to excellent yields (Scheme 2). The molecular structures of **4d** and **4e**, bearing IPr^* and IPr^{*OMe} ligands respectively, were unambiguously confirmed by X-ray diffraction studies performed on single crystals. Their graphical representation along with their corresponding percent buried volumes ($\%V_{bur}$) and spatial occupation maps, these calculated using the SambVca web application[35] are presented in Figure 2.

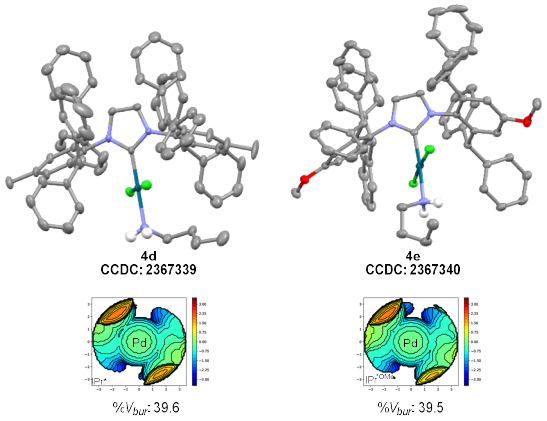
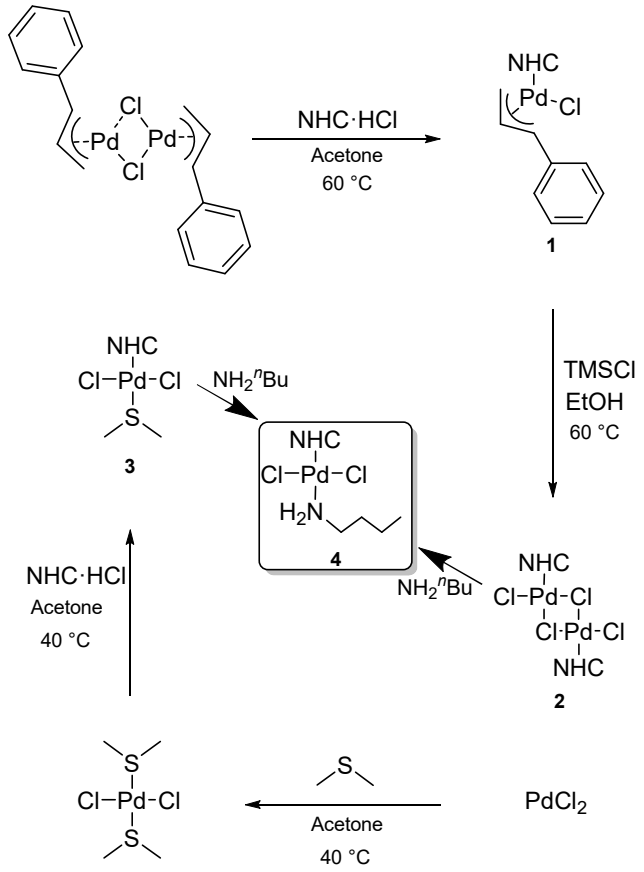
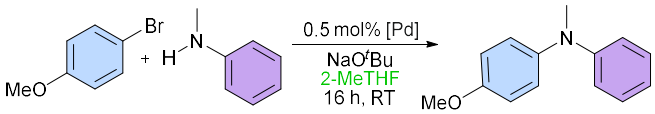


Figure 2. X-ray molecular structures of 4d and 4e, showing thermal displacement ellipsoids at 50% probability level and corresponding calculated $\%V_{bur}$. Hydrogen atoms have been omitted for clarity.



Scheme 1. Synthetic routes to [Pd(NHC)(NH$_2^n$Bu)Cl$_2$] complexes.

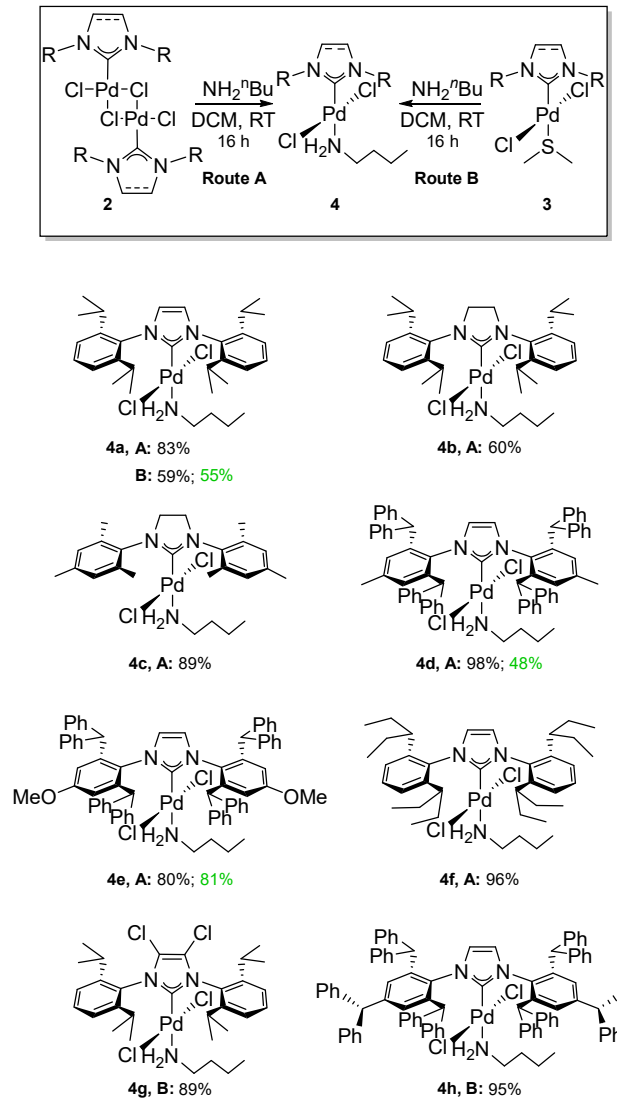
Table 1. Catalyst screening for Buchwald-Hartwig amination[a]



Entry	Catalyst	Conversion [%]
1	[Pd(**IPr**)(NH$_2^n$Bu)Cl$_2$] (**4a**)	69
2	[Pd(**SIPr**)(NH$_2^n$Bu)Cl$_2$] (**4b**)	25
3	[Pd(**SIMes**)(NH$_2^n$Bu)Cl$_2$] (**4c**)	0
4	[Pd(**IPr***)(NH$_2^n$Bu)Cl$_2$] (**4d**)	100
5	[Pd(**IPr***$^{\mathbf{OMe}}$)(NH$_2^n$Bu)Cl$_2$] (**4e**)	100
6	[Pd(**IPent**)(NH$_2^n$Bu)Cl$_2$] (**4f**)	100
7	[Pd(**IPr**$^{\mathbf{Cl}}$)(NH$_2^n$Bu)Cl$_2$] (**4g**)	100
8	[Pd(**IPr**$^{\#}$)(NH$_2^n$Bu)Cl$_2$] (**4h**)	100

[a] 4-bromoanisole (1 eq), N-methylaniline (1.2 eq), NaO^{t}Bu (1.5eq) in anhydrous 2-MeTHF. Data are the average of two independent runs and analyzed by GC. Conversion of 4-bromoanisole.

Next, the catalytic activity of the synthesized complexes was evaluated in the Buchwald-Hartwig amination reaction. Initially, several parameters (such as catalyst loading, temperature,



Scheme 2. Pd catalysts prepared in this study; A: yield from route A. B: yield from route B. Yields in green when EtOAc was used as solvent instead of DCM.

reaction time, base, and solvent) were varied using different amines as coupling partners with p-bromoanisole to determine the best conditions under which to evaluate the synthesized complexes (See ESI, Table S1). Among the solvents evaluated, 2-MeTHF and dioxane excelled, with the first one chosen as the preferred solvent due to its greener profile (Table S1).[36]

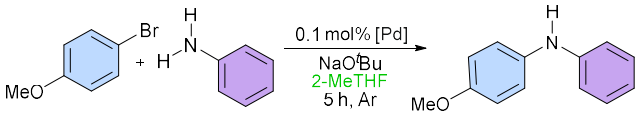
NaO^{t}Bu proved to be the base of choice for reaction performed at room temperature using 0.5 mol% of catalyst under Argon. All complexes were initially evaluated in reactions lasting 16 h under these conditions (Table 1). Results highlight a higher efficiency when bulkier NHCs were used (Table 1, entries 4-8). The presence of unsaturated NHCs lead to the poorest activities (Table 1, entries 2-3).Subsequently, the reaction profiles employing 0.2 mol% loading of the most promising catalysts (**4d-h**) were monitored over a 16 h reaction period, at room temperature (Figure S1). The reactivity of the newly

synthesized catalysts was also evaluated against [Pd(IPr#)(DMS)Cl] (used as a control due to its known efficacy under similar conditions, but at 80 °C)[28] under our optimized protocol at room temperature. All *n*-butylamine bearing catalysts (**4d-h**) performed significantly better than the control complex, [Pd(IPr#)(DMS)Cl]. The bulky IPr*, IPr*^{OMe}, and IPr# based complexes (**4d**, **4e**, **4h**, respectively) exhibited the best performance, achieving full completion within 5 hours at room temperature. The [Pd(NHC)($NH_2{}^nBu$)Cl_2] complexes proved to be more effective than the previously reported [Pd(IPr#)(DMS)Cl_2][28] when used at room temperature (Figure S1). This increased reactivity can likely be attributed to the ability of the *n*-butylamine ability to act as a throwaway ligand through base activation and conversion into a non-returning ligand, unlike DMS which is simply temperature activated.[29]

Further optimisation showed that the best three catalysts (**4d**, **4e**, **4h**) can afford good yields of the desired product (84-85%) even at 0.1 mol% catalyst loading (Table S1). Increasing the temperature allows for the IPr*-based complex (**4d**) to achieve full conversion with 95% GC yield of the desired arylated product (Table S1, entry 33).

In the case of primary amines, the most significant challenge is the prevention of diarylation byproduct formation. We reoptimized the amination reaction using aniline, instead of N-methylaniline, along with the best bulky catalysts found in the previous optimization (Table 2). No diarylation products were detected in any case under the current conditions. A slight increase in temperature was necessary to achieve full conversion, with the best result obtained using complex **4d** at 50°C (Table 2, entry 4). Further increase in temperature resulted in a drop of yield (Table 2, entry 5). This result is noteworthy as primary amine monoarylation has, for a longtime, represented an undesired parasitic side-reaction and a key challenge in BHA.[37]

Table 2. Optimization reaction for Buchwald-Hartwig amination of aniline



Entry	Catalyst	T [°C]	Yield^{GC} [%]
1	[Pd(**IPr***)($NH_2{}^nBu$)Cl_2] (**4d**)	40	78
2	[Pd(**IPr***^{OMe})($NH_2{}^nBu$)Cl_2] (**4e**)	40	73
3	[Pd(**IPr#**)($NH_2{}^nBu$)Cl_2] (**4h**)	40	56
4	[Pd(**IPr***)($NH_2{}^nBu$)Cl_2] (**4d**)	50	95
5	[Pd(**IPr***)($NH_2{}^nBu$)Cl_2] (**4d**)	80	89

4-bromoanisole (1 eq), aniline (1.2 eq), NaO^{t}Bu (1.5 eq) in anhydrous 2-MeTHF. Data are the average of two independent runs.

Next, the scope of the BHA reaction was investigated using primary and secondary anilines under the optimal conditions (0.1 mol% of complex **4d** in 2-MeTHF for 5 h) at different temperatures depending on substrate reactivity. For some products (**5n**, **5r**, **5s**) a change in base to KO^{t}Bu was necessary. This catalytic system exhibited robust performance with challenging coupling partners, including heteroaryl chlorides and sterically hindered di-ortho-substituted substrates (**5f**, **5i**, **5j**, **5n** and **5o**). Noteworthy, additional time and higher temperatures were required for some of these reactions to achieve 100% conversion. N-methylaniline proved to be a reactive substrate, being successfully integrated into our conditions at 40 °C. On the other hand, morpholine was not as reactive under these conditions. Instead, the simple substrate required changing the base to KO^{t}Bu and heating the reaction at 80 °C to afford the product (**5s**) in quantitative yield. Reaction with diphenyl amine did not proceed at all even at higher temperature which was not surprising considering the steric demand exhibited by the IPr* ligand and agrees with previous reports.[26,27] Here it is interesting to note that the lack of diarylation in our successful trials to perform monoarylation hint at the large steric influence of the IPr* ligand, for one, but as a result the arylation of primary amines is stopped at this degree of arylation, and this selectively.

With these optimized conditions in hand, a wide range of substrates with diverse electronic and steric properties were successfully evaluated (Scheme 3). Notably, no palladium black formation was observed during these reactions, further highlighting the ability of the IPr* ligand to stabilize the active Pd^0 catalyst in a wide range of temperatures preventing its decomposition.[31]As expected, hindered, and inactivated substrates required higher temperatures but reactions still lead to products in 5 h without the need for an increase in catalyst loading. The present system operates efficiently at low concentrations, achieving excellent performance. It is noteworthy that our system performs exceptionally well at relatively low temperatures in green solvents. High activities are achieved, and the observations made by Shaughnessy[19,29] in a related phosphine-based systems hold when very sterically demanding NHCs serve as supporting ligands in the BHA reactions.

The complexes remained stable when stored in air at room temperature for over 3 months, with no signs of decomposition as confirmed by NMR. However, when stored in a 2-MeTHF stock solution, only complex **4g** showed decomposition when examined after one week, while the others retained their entity.

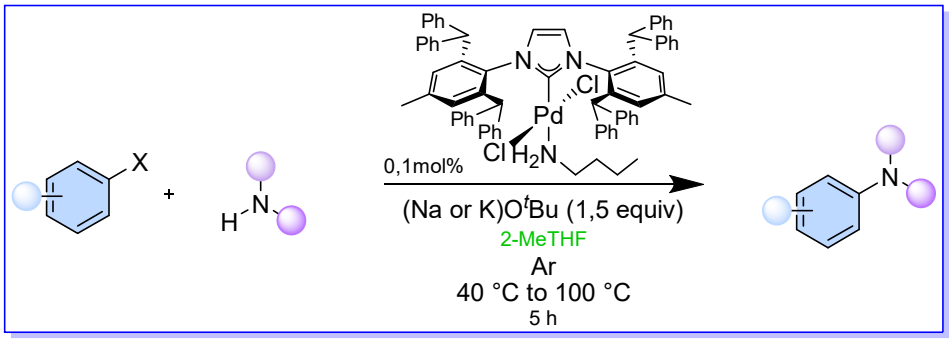
Conclusion

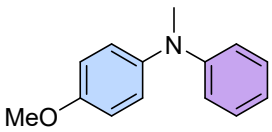
This study presents a series of novel *trans*-[Pd(NHC)($NH_2{}^nBu$)Cl_2] complexes, synthesized by reacting the [Pd(NHC)(μ-Cl)Cl]$_2$ dimer or *trans*-[Pd(NHC)(DMS)Cl_2] complexes with *n*-butylamine under aerobic conditions at room temperature. Notably, in the Buchwald-Hartwig amination reactions, the novel complexes exhibit superior performance compared to similar systems bearing the throwaway DMS ligand. The present systems disply remarkable efficiency at low catalyst loading at mild temperatures and in a green solvent.

In particular, [Pd(IPr*)($NH_2{}^nBu$)Cl_2] exhibited the highest catalytic activity for the Buchwald-Hartwig amination of various (hetero)aryl chlorides in 2-MeTHF using a 0.1 mol% catalyst loading. The scope of C-N couplings examined includes several challenging electrophiles and nucleophiles, with the corresponding final products isolated in good to excellent yields. The selective monoarylation of primary amines is noteworthy among the substrates examined and highlights the spatial selective reactivity displayed by this most active catalyst. The lack of reactivity of secondary amines leading to tertiary amines is also a consequence of the demanding steric environment.

This sacrificial ligand combination with sterically larger NHC family members appears as an ideal combination leading to high and selective catalytic activity in the Buchwald-Hartwig

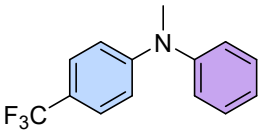
amination reaction. The ease of synthetic access is also noteworthy. Future studies aimed at testing the activity of this specific catalyst in challenging synthetic applications are ongoing in our laboratories.





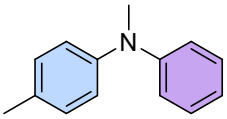
5a

Br: 82(95)%[a]
Cl: (96)%[a]



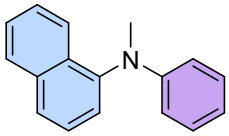
5b

Br: 87(90)%[a]
Cl: (94)%[a]



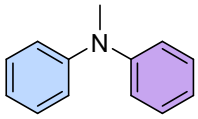
5c

Br: 72(91)%[a]
Cl: (93)%[a]



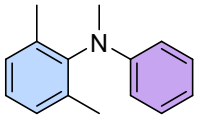
5d

Br: 85(90)%[a]
Cl: (83)%[a]



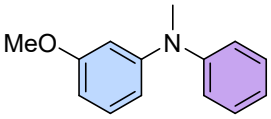
5e

Br: 80%[a]



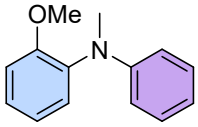
5f

Br: 71(96)%[b]



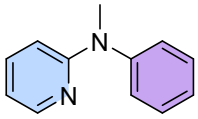
5g

Br: 85%(96%)[a]



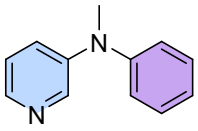
5h

Br: 91(92)%[a]



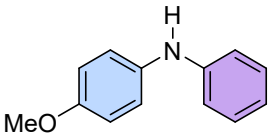
5i

Cl: 79%[b]



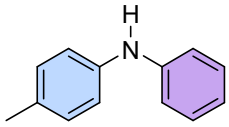
5j

Cl: 53%[c]



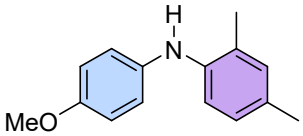
5k

Br: 84(95)%[d]



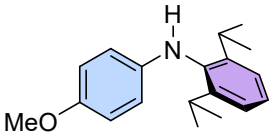
5l

Br: 71(95)%[d]



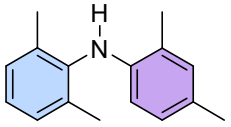
5m

Br: 47(91)%[b]



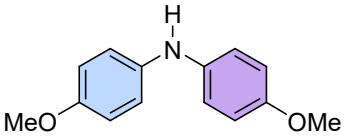
5n

Br: 62(93)%[e]



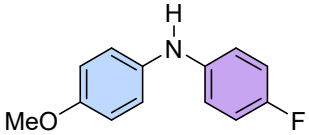
5o

Br: 80(91)%[b]



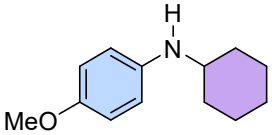
5p

Br: 52(92)%[d]



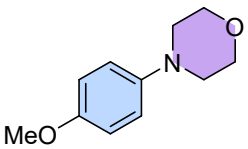
5q

Br: 65(97)%[b]



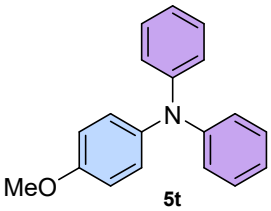
5r

Br: 86(99)%[e]



5s

Br: 94(96)%[e]
Cl: (99)%[e]



5t

Br: **NR**[b]

Scheme 3. BHA reaction scope. a: 40 °C/NaO^{t}Bu ; b: 80 °C/NaO^{t}Bu; c: 100 °C/NaO^{t}Bu/16 h; d: 50 °C/NaO^{t}Bu; e: 80 °C/KO^{t}Bu; isolated yields; GC yields in parenthesis

Experimental

General considerations. Elemental analyses were performed at Université de Namur, rue de Bruxelles 61, B-5000 Namur, Belgium and VITO (Flemish Institute for Technological Research), Separation and Conversion Technology, Boeretang 200, Mol 2400, Belgium. ^{1}H, ^{13}C-{^{1}H} Nuclear Magnetic Resonance (NMR) spectra were recorded on a Bruker Avance 400 Ultrashield or a Bruker Avance 300 Ultrashield at 298K using the residual solvent peak as reference ($CDCl_3$: δ_H=7.26ppm, δ_C=77.1ppm). Synthesis of the complexes were carried out in air. Solvents and all other reagents were purchased and used as received without further purification unless otherwise stated. 2-Methyltetrahydrofuran was dried over molecular sieves at least for a minimum of 3 days and bubbled under argon for at least 10min prior to use. Air sensitive reactions were performed under argon in a glovebox. GC samples were measured using hexadecane as internal standard. Purification of the compounds by filtration was performed using silica gel or celite purchased from Sigma Aldrich. Unless otherwise noted, absolute ethanol, HPLC acetone and freshly crushed potassium carbonate were used. X-ray intensity data of the products were collected at 100K, on a Rigaku Oxford Diffraction Supernova Dual Source (Cu or Mo). Complexes **4d** and **4e** have been crystallized; characterized through XRD and show a tetrahedral Pd^{II} coordination sphere. Crystallographic data have been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number ***CCDC 2367339*** (**4d** at 100 K) and ***CCDC 2367340*** (**4e** at 100 K). These data can be obtained free of charge via https://www.ccdc.cam.ac.uk/structures.

$[\mathbf{Pd(SIMes)(\eta^3-cin)(Cl)}]$ (**1b**)[32];$[\mathbf{Pd(IPent)(\eta^3-cin)(Cl)}]$(**1f**)[38]; $[\mathbf{Pd(IPr^{*OMe})(\eta^3-cin)(Cl)}]$ (**1e**)[32]; were prepared according to reported procedures. $[\mathbf{Pd(NHC)(\eta^3-cin)(Cl)}]$ complexes were prepared from $[\mathbf{Pd(\eta^3-cin)(Cl)}]_2$ which was supplied by Umicore. $[\mathbf{Pd(IPr)(\mu-Cl)(Cl)}]_2$ (**2a**) and $[\mathbf{Pd(SIPr)(\mu-Cl)(Cl)}]_2$ (**2b**) dimers were supplied by Umicore

General procedure for the synthesis of Pd dimers (2) using the TMSCl route. $[Pd(NHC)(\eta^3-cin)(Cl)]$ (**1**) and TMSCl (4 to 10 eq) were charged in a vial equipped with a magnetic stirring. EtOH was added and the mixture was allowed to stir at 60°C for the indicated time. Afterwards Solvents were removed, and dichloromethane was added. The mixture was microfiltered and passed through a 3 cm pad of silica gel or celite; then the pad was washed with more solvent; the clear solution was concentrated, and the product was precipitated with pentane. The powder was washed and sonicated with pentane (3x5mL). The compound was left to dry under a high vacuum to afford the pure product.

$[\mathbf{Pd(SIMes)(\mu-Cl)(Cl)}]_2$ (**2c**). $[Pd(SIMes)(\eta^3-cin)(Cl)]$ (**1c**) (200mg, 0.309mmol) and TMSCl (156.6µL, 1.234mmol) were charged in a 10 mL vial equipped with a magnetic stirring bar. 4.0mL of EtOH were added and the mixture was allowed to stir at 60°C for 16h. Afterwards Solvents were removed, and 4mL of dichloromethane were added. The mixture was microfiltered and passed through a 3cm pad of celite; then the pad was washed with more solvent (10mL); the clear solution was concentrated, and the product was precipitated with 10mL of pentane. The yellow powder was washed and sonicated with pentane (3x5mL). The compound was left to dry under high vacuum to afford the pure product in 56% (82.8mg) yield. ^{1}H NMR (300 MHz, Chloroform-d) δ 7.00 (s, 2H), 3.87 (s, 2H), 2.36 (d, J = 32.3 Hz, 9H) ppm. In agreement with the reported data.[39]

$[\mathbf{Pd(IPr^*)(\mu-Cl)(Cl)}]_2$ (**2d**). $[Pd(IPr^*)(\eta^3-cin)(Cl)]$ (**1d**) (200mg, 0.171mmol) and TMSCl (217µL, 1.706mmol) were charged in a 10 mL vial equipped with a magnetic stirring bar. 4.0 mL of EtOH were added and the mixture was allowed to stir at 60°C for 72 h. Afterwards Solvents were removed, and 4 mL of dichloromethane were added. The mixture was microfiltered and passed through a 3 cm pad of celite; then the pad was washed with more solvent (10mL); the clear solution was concentrated, and the product was precipitated with 10mL of pentane. The yellow powder was washed and sonicated with pentane (3x5 mL). The compound was left to dry under a high vacuum to afford the pure product in 70% (261.1mg) yield. ^{1}H NMR (300 MHz, Chloroform-d) δ 7.49 (d, J = 7.5 Hz, 8H), 7.23 (s, 4H), 7.15 – 6.83 (m, 56H), 6.76 (s, 4H), 6.69 (d, J = 5.4 Hz, 8H), 6.57 (d, J = 7.1 Hz, 8H), 6.30 (s, 4H), 5.50 (s, 4H), 4.64 (s, 4H), 2.07 (s, 12H) ppm. In agreement with the reported data.[40]

$[\mathbf{Pd(IPr^{*OMe})(\mu-Cl)(Cl)}]_2$ (**2e**). $[Pd(IPr^{*OMe})(\eta^3-cin)(Cl)]$ (**1e**) (150mg, 0.125mmol) and TMSCl (316µL, 2.490mmol) were charged in a 4 mL vial equipped with a magnetic stirring bar. 2.0 mL of EtOH were added and the mixture was allowed to stir at 60°C for 72 h. Afterwards Solvents were removed, and 4 mL of dichloromethane were added. The mixture was microfiltered and passed through a 3 cm pad of silica gel; then the pad was washed with more solvent (10mL); the clear solution was concentrated, and the product was precipitated with 10 mL of pentane. The yellow powder was washed and sonicated with pentane (3x5 mL). The compound was left to dry under a high vacuum to afford the pure product in 70% (94.7mg) yield. ^{1}H NMR (300 MHz, Chloroform-d) δ 7.49 (d, J = 7.5 Hz, 8H), 7.31 (d, J = 7.7 Hz, 8H), 7.12 – 6.87 (m, 48H), 6.76 (dd, J = 6.4, 3.0 Hz, 8H), 6.64 – 6.56 (m, 12H), 6.49 (d, J = 2.9 Hz, 4H), 6.35 (s, 4H), 5.47 (s, 4H), 4.60 (s, 4H), 3.38 (s, 12H) ppm.

$[\mathbf{Pd(IPent)(\mu-Cl)(Cl)}]_2$ (**2f**). $[Pd(IPent)(\eta^3-cin)(Cl)]$ (**1f**) (150mg, 0.197mmol) and TMSCl (100µL, 0.790mmol) were charged in a 4 mL vial equipped with a magnetic stirring bar. 2.6 mL of EtOH were added and the mixture was allowed to stir at 60°C for 16 h. Afterwards Solvents were removed, and 4 mL of dichloromethane were added. The mixture was microfiltered and passed through a 3cm pad of silica gel; then the pad was washed with more solvent (10 mL); the solvent was removed, and the compound was left to dry under high vacuum to afford the product in (126.9mg) 95% yield. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.45 (t, J = 7.7 Hz, 4H), 7.20 (d, J = 7.8 Hz, 8H), 6.90 (s, 4H), 2.33 (s, 8H), 2.01 (dtd, J = 14.7, 7.3, 4.1 Hz, 8H), 1.68 (ddt, J = 16.6, 13.9, 7.1 Hz, 8H), 1.42 (tp, J = 13.8, 6.7 Hz, 16H), 0.92 (t, J = 7.3 Hz, 24H), 0.67 (t, J = 7.4 Hz, 24H) ppm. In agreement with the reported data.[41]

$[Pd(IPr)(DMS)Cl_2]$ (**3a**), **$[Pd(IPr^{Cl})(DMS)Cl_2]$** (**3g**) and **$[Pd(IPr^{\#})(DMS)Cl_2]$** (**3h**) were prepared according to reported procedures.[28]

General procedure for the synthesis of $[Pd(NHC)(NH_2{}^nBu)Cl_2]$. Route A. Starting from Pd-dimer complexes: In a 4 mL scintillation vial equipped with a magnetic stirring bar, $[Pd(NHC)Cl_2]_2$ (**2**) (1eq) was dissolved in dichloromethane or ethyl acetate prior to the addition of *n*-Butylamine (1.1eq). The mixture was stirred at RT for 16h. After completion, the solvent was removed, and the products were worked up as indicated. The product was left to dry under a high vacuum to afford the pure catalyst. **Route B.** Starting from Pd-DMS complexes: In a 4 mL scintillation vial equipped with a magnetic stirring bar, $[Pd(NHC)(DMS)Cl_2]$ (**3**) (1eq) was dissolved in dichloromethane or ethyl acetate prior to the addition of *n*-Butylamine (1.1eq). The mixture was stirred at RT for 16 h. After completion, the solvent was removed, and the resulting solid was worked up as indicated. The product was left to dry under high vacuum to afford the pure catalyst.

[Pd(IPr)($NH_2{}^nBu$)Cl_2] (4a). Following the **route A** from DCM: In a 4 mL scintillation vial equipped with a magnetic stirring bar, $[Pd(IPr)(Cl)_2]_2$(**2a**) (100.4mg, 0.089mmol) was dissolved in dichloromethane (1.7mL) prior to the addition of *n*-Butylamine (17.7µL, 0.179mmol). The mixture was stirred at RT for 16 h. After completion, DCM was removed, and the resulting solid was washed and sonicated with hexane (3x5 mL). The product was left to dry under high vacuum to afford the pure catalyst in (93.7mg) 83% yield. Following the **route B** from DCM: In a 4 mL scintillation vial equipped with a magnetic stirring bar, $[Pd(IPr)(DMS)Cl_2]$ (**3a**) (25mg, 0.040mmol) was dissolved in dichloromethane (0.8mL) prior to the addition of *n*-Butylamine (4.0µL, 0.040mmol). The mixture was stirred at RT for 16 h. After completion, DCM was removed, and the resulting solid was washed and sonicated with hexane (3x5 mL). The product was left to dry under a high vacuum to afford the pure catalyst in (14.7mg) 59% yield. Following the **route B** from EtOAc: In a 4 mL scintillation vial equipped with a magnetic stirring bar, $[Pd(IPr)(DMS)Cl_2]$ (**3a**) (100mg, 0.159mmol) was dissolved in EtOAc (3 mL) prior to the addition of *n*-Butylamine (15.9 µL, 0.161 mmol). The mixture was stirred at RT for 16 h. After completion, EtOAc was removed, and the resulting solid was recrystallized from DCM/Hexane washed and sonicated with hexane (3x5mL). The product was left to dry under high vacuum at 45°C to afford the pure catalyst in (55mg) 55% yield. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.51 (t, 2H, $H_{Ar(IPr)}$), 7.35 (d, J = 7.8 Hz, 4H, $H_{Ar(IPr)}$), 7.09 (s, 2H, $H_{(backbone)}$), 3.06 (hept, J = 6.8 Hz, 4H, $H_{(IPr)}$), 2.45 (p, 2H, $CH_{2(NH_2{}^nBu)}$), 1.82 (t, J = 6.9 Hz, 2H, $NH_{2(NH_2{}^nBu)}$), 1.43 (d, J = 6.6 Hz, 12H, $H_{(IPr)}$), 1.26 (p, 2H, $CH_{2(NH_2{}^nBu)}$), 1.16 – 1.11 (m, 2H, $CH_{2(NH_2{}^nBu)}$), 1.09 (d, J = 6.9 Hz, 12H, $H_{(IPr)}$), 0.74 (t, J = 7.3 Hz, 3H, $CH_{3(NH_2{}^nBu)}$) ppm. ^{13}C NMR (101 MHz, Chloroform-d) δ 158.5(N**C**N), 146.9($C_{Ar(IPr)}$), 135.2($C_{Ar(IPr)}$), 130.3($CH_{Ar(IPr)}$), 124.9($CH_{(Backbone)}$), 124.0($CH_{Ar(IPr)}$), 42.8($CH_{2(NH_2{}^nBu)}$), 33.6($CH_{2(NH_2{}^nBu)}$), 28.8($CH_{(IPr)}$), 26.5($CH_{3(IPr)}$), 23.1($CH3_{(IPr)}$), 19.8($CH_{2(NH_2{}^nBu)}$), 13.8($CH_{3(NH_2{}^nBu)}$) ppm. Elemental Anal. Calcd for $[C_{31}H_{47}Cl_2N_3Pd]$: C, 58.26; H, 7.41; N, 6.58. Found: C, 58.34; H, 7.56; N, 6.89.

[Pd(SIPr)($NH_2{}^nBu$)Cl_2] (4b). Following the **route A**: In a 4 mL scintillation vial equipped with a magnetic stirring bar, $[Pd(SIPr)(Cl)_2]_2$ (**2b**) (100.0mg, 0.088mmol) was dissolved in dichloromethane (1.7mL) prior to the addition of *n*-Butylamine (17.6µL, 0.178mmol). The mixture was stirred at RT for 16h. After completion, DCM was concentrated, 10mL of hexane were added and the solution was placed in the fridge to precipitate the product. Solvent was decantated and the resulting solid was washed and sonicated with hexane (3x5mL). The product was left to dry under high vacuum to afford the pure catalyst in (67.3mg) 60% yield. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.42 (dd, J = 8.3, 7.1 Hz, 2H, $H_{Ar(SIPr)}$), 7.30 (d, J = 7.7 Hz, 4H, $H_{Ar(SIPr)}$), 4.03 (s, 4H, $H_{(backbone)}$), 3.48 (hept, J = 6.7 Hz, 4H, $H_{(SIPr)}$), 2.41 (p, J = 7.1 Hz, 2H, $CH_{2(NH_2{}^nBu)}$), 1.72 (t, J = 7.0 Hz, 2H, $NH_{2(NH_2{}^nBu)}$), 1.51 (d, J = 6.6 Hz, 12H, $H_{(SIPr)}$), 1.23 (d, J = 6.9 Hz, 12H, $H_{(SIPr)}$), 1.21 – 1.15 (overlap. m, 2H, $CH_{2(NH_2{}^nBu)}$), 1.08 (dq, J = 13.8, 7.1 Hz, 2H, $CH_{2(NH_2{}^nBu)}$), 0.72 (t, J = 7.2 Hz, 3H, $CH_{3(NH_2{}^nBu)}$). ^{13}C NMR (101 MHz, Chloroform-d) δ 189.1(N**C**N), 147.8(CAr$_{(SIPr)}$), 135.4(CAr$_{(SIPr)}$), 129.5($CH_{Ar(SIPr)}$), 124.4($CH_{Ar(SIPr)}$), 53.7($CH_{2(Backbone)}$), 42.7($CH_{2(NH_2{}^nBu)}$), 33.7($CH_{2(NH_2{}^nBu)}$), 28.8($CH_{(SIPr)}$), 27.0($CH_{3(SIPr)}$), 24.1($CH_{3(SIPr)}$), 19.8($CH_{2(NH_2{}^nBu)}$), 13.7($CH_{3(NH_2{}^nBu)}$) ppm. Elemental Anal. Calcd for $[C_{31}H_{49}Cl_2N_3Pd]$: C, 58.08; H, 7.70; N, 6.55. Found: C, 58.15; H, 7.99; N, 6.82.

[Pd(SIMes)($NH_2{}^nBu$)Cl_2] (4c). Following the **route A**: In a 4 mL scintillation vial equipped with a magnetic stirring bar, $[Pd(SIMes)(Cl)_2]_2$ (**2c**) (73.1mg, 0.076mmol) was dissolved in dichloromethane (1.5mL) prior to the addition of *n*-Butylamine (15.1µL, 0.153mmol). The mixture was stirred at RT for 16 h. After completion, DCM was concentrated, 10 mL of hexane were added, and the solution was placed in the fridge to precipitate the product. Solvent was decantated and the resulting solid was washed and sonicated with hexane (3x5mL). The product was left to dry under high vacuum to afford the pure catalyst in (74.8mg) 89 % yield. ^{1}H NMR (400 MHz, Chloroform-d) δ 7.00 (s, 4H, $H_{Ar(SIMes)}$), 3.97 (s, 4H, $CH_{2(Backbone)}$), 2.52 (s, 12H, $CH_{3(SIMes)}$), 2.40 (s, 2H, $CH_{2(NH_2{}^nBu)}$), 2.33 (s, 6H, $CH_{3(SIMes)}$), 1.73 (s, 2H, $NH_{2(NH_2{}^nBu)}$), 1.27 (s, 2H, $CH_{2(NH_2{}^nBu)}$), 1.11 (d, J = 7.4 Hz, 2H, $CH_{2(NH_2{}^nBu)}$), 0.77 (s, 3H, $CH_{3(NH_2{}^nBu)}$). ^{13}C NMR (101 MHz, Chloroform-d) δ 187.4(N**C**N), 138.5($C_{Ar(SIMes)}$), 137.4($C_{Ar(SIMes)}$), 135.1($C_{Ar(SIMes)}$), 129.6($C_{Ar(SIMes)}$), 51.1($CH_{2(Backbone)}$), 42.5($CH_{2(NH_2{}^nBu)}$), 33.2($CH_{2(NH_2{}^nBu)}$), 21.2($CH_{3(SIMes)}$), 19.9($CH_{2(NH_2{}^nBu)}$), 19.3($CH_{3(SIMes)}$), 13.7($CH_{3(NH_2{}^nBu)}$). Elemental Anal. Calcd for $[C_{25}H_{37}Cl_2N_3Pd]$: C, 53.92; H, 6.70; N, 7.55. Found: C, 53.98; H, 6.90; N, 7.49.

[Pd(IPr*)($NH_2{}^nBu$)Cl_2] (4d). Following **the route A***:* From DCM: In a 4 mL scintillation vial equipped with a magnetic stirring bar, $[Pd(IPr^*)(Cl)_2]_2$ (**2d**) (250.0mg, 0.115mmol) was dissolved in dichloromethane (5mL) prior to the addition of *n*-Butylamine (22.9µL, 0.232mmol). The mixture was stirred at RT for 16 h. After completion, DCM was removed, and the product was left to dry under high vacuum at 40°C to afford the pure catalyst in (262mg) 98% yield. From EtOAc: In a 4 mL scintillation vial equipped with a magnetic stirring bar, $[Pd(IPr^*)(Cl)_2]_2$ (**2d**) (100.0mg, 0.046mmol) was dissolved in ethyl acetate (1.5mL) prior to the addition of *n*-Butylamine (9.2µL, 0.093mmol). The mixture was stirred at RT for 16h. After completion, EtOAc was removed, and the product crude was recrystallized by slow evaporation of DCM. Then it was dried under high vacuum at 40°C the pure catalyst in (52mg) 48% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.44 (d, *J* = 7.4 Hz, 8H, $H_{Ar(IPr^*)}$), 7.26 (d, *J* = 14.7 Hz, 8H, $H_{Ar(IPr^*)}$), 7.19 (t, *J* = 7.2 Hz, 4H, $H_{Ar(IPr^*)}$), 7.08 – 6.96 (m, 12H, $H_{Ar(IPr^*)}$), 6.78 (s, 4H, $H_{Ar(IPr^*)}$), 6.73 – 6.67 (m, 8H, $H_{Ar(IPr^*)}$), 6.11 (s, 4H, $CH_{(IPr^*)}$), 4.71 (s, 2H, $CH_{(Backbone)}$), 2.83 (p, *J* = 7.5 Hz, 2H, $CH_{2(NH_2{}^nBu)}$), 2.22 (s, 8H, $CH_{3(IPr^*)}$+ $NH_{2(NH_2{}^nBu)}$), 1.52 – 1.40 (m, 2H, $CH_{2(NH_2{}^nBu)}$), 1.34 – 1.22 (m, 2H, $CH_{2(NH_2{}^nBu)}$), 0.82 (t, *J* = 7.3 Hz, 3H, $CH_{3(NH_2{}^nBu)}$) ppm. ^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.6(N**C**N), 144.7($C_{Ar(IPr^*)}$), 144.3($C_{Ar(IPr^*)}$), 142.0($C_{Ar(IPr^*)}$), 138.4($C_{Ar(IPr^*)}$), 135.1($C_{Ar(IPr^*)}$), 130.8($CH_{Ar(IPr^*)}$), 130.6($CH_{Ar(IPr^*)}$), 129.5($CH_{Ar(IPr^*)}$), 128.2($CH_{Ar(IPr^*)}$), 128.0($CH_{Ar(IPr^*)}$), 126.2($CH_{Ar(IPr^*)}$), 126.1($CH_{Ar(IPr^*)}$), 123.6($CH_{(Backbone)}$), 51.0($CH_{(IPr^*)}$), 43.5($CH_{2(NH_2{}^nBu)}$), 34.5($CH_{2(NH_2{}^nBu)}$), 22.0($CH_{3(IPr^*)}$), 20.1($CH_{2(NH_2{}^nBu)}$), 13.8($CH_{3(NH_2{}^nBu)}$) ppm. Elemental Anal. Calcd for $[C_{73}H_{67}Cl_2N_3Pd]$: C, 75.35; H, 5.80; N, 3.61. Found: C, 75.34; H, 6.26; N, 4.04.

[Pd(IPr*^{OMe})($NH_2{}^nBu$)Cl_2] (4e).Following the **route A**, from DCM: In a 4 mL scintillation vial equipped with a magnetic stirring bar, $[Pd(IPr^{*OMe})(Cl)_2]_2$ (**2e**) (50.2mg, 0.0224mmol) was dissolved in dichloromethane (0.4mL) prior to the addition

of *n*-Butylamine (4.5µL, 0.0452mmol). The mixture was stirred at RT for 16h. After completion, DCM was removed, and the resulting solid was recrystallized from DCM/Pentane, washed and sonicated with pentane (3x5mL). The product was left to dry under high vacuum to afford the pure catalyst in (42.5mg) 80% yield. Following the **route A**, from ethyl acetate: In a 4 mL scintillation vial equipped with a magnetic stirring bar, $[Pd(IPr^{*OMe})(Cl)_2]_2$ (**2e**) (65.9mg, 0.029mmol) was dissolved in ethyl acetate (1 mL) prior to the addition of *n*-Butylamine (5.7 µL, 0.059 mmol). The mixture was stirred at RT for 16 h. After completion, it was passed through a plug of celite and then the solvent was removed. The resulting solid was washed and sonicated with pentane (3x5mL). The product was left to dry under high vacuum at 70°C and then at 40°C for 60 h to afford the pure catalyst in (57mg) 81% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45 (d, 8H, $CH_{Ar(IPr^{*OMe})}$), 7.29 – 7.23 (m, 8H, $CH_{Ar(IPr^{*OMe})}$), 7.21 – 7.16 (m, 4H, $CH_{Ar(IPr^{*OMe})}$), 7.06 – 6.97 (m, 12H, $CH_{Ar(IPr^{*OMe})}$), 6.73 (d, *J* = 5.9 Hz, 8H, $CH_{Ar(IPr^{*OMe})}$), 6.50 (s, 4H, $CH_{Ar(IPr^{*OMe})}$), 6.10 (s, 4H, $CH_{(IPr^{*OMe})}$), 4.65 (s, 2H, $CH_{(backbone)}$), 3.54 (s, 6H, $CH_{3(IPr^{*OMe})}$), 2.84 (p, *J* = 7.4 Hz, 2H, $CH_{2(NH_2{}^nBu)}$), 2.20 (t, *J* = 7.2 Hz, 2H, $NH_{2(NH_2{}^nBu)}$), 1.48 (p, *J* = 7.8, 6.2 Hz, 2H, $CH_{2(NH_2{}^nBu)}$), 1.28 (h, *J* = 7.3 Hz, 2H, $CH_{2(NH_2{}^nBu)}$), 0.82 (t, *J* = 7.3 Hz, 3H, $CH_{3(NH_2{}^nBu)}$) ppm. ^{13}C NMR (101 MHz, Chloroform-*d*) δ 159.1($C_{Ar(IPr^{*OMe})}$), 156.2(N**C**N), 144.5($C_{Ar(IPr^{*OMe})}$), 144.1($C_{Ar(IPr^{*OMe})}$), 144.0($C_{Ar(IPr^{*OMe})}$), 130.8($CH_{Ar(IPr^{*OMe})}$), 130.6($C_{Ar(IPr^{*OMe})}$), 129.4($CH_{Ar(IPr^{*OMe})}$), 128.2($CH_{Ar(IPr^{*OMe})}$), 128.1($CH_{Ar(IPr^{*OMe})}$), 126.4($CH_{Ar(IPr^{*OMe})}$), 126.2($CH_{Ar(IPr^{*OMe})}$), 123.6($CH_{(Backbone)}$), 115.2($CH_{Ar(IPr^{*OMe})}$), 55.0($CH_{3(IPr^{*OMe})}$), 51.3($CH_{(IPr^{*OMe})}$), 43.5($CH_{2(NH_2{}^nBu)}$), 34.5($CH_{2(NH_2{}^nBu)}$), 20.1($CH_{2(NH_2{}^nBu)}$), 13.8($CH_{3(NH_2{}^nBu)}$) ppm. Elemental Anal. Calcd for $[C_{73}H_{67}Cl_2N_3O_2Pd]+1.2H_2O$: C, 72.03; H, 5.75; N, 3.45. Found: C, 72.04; H, 5.88; N, 3.30.

[Pd(SIPr)(NH$_2{}^n$Bu)Cl$_2$] (4f). Following the **route A**: In a 4 mL scintillation vial equipped with a magnetic stirring bar, $[Pd(IPent)(Cl)_2]_2$ (**2f**) (100.0mg, 0.30mmol) was dissolved in dichloromethane (1.7mL) prior to the addition of *n*-Butylamine (29.8µL, 0.30mmol). The mixture was stirred at RT for 16 h. After completion, DCM was removed, and the resulting solid was left to dry for 2 weeks to afford the pure catalyst in (106.0mg) 96% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.44 (t, *J* = 7.8 Hz, 2H, $H_{Ar(IPent)}$), 7.23 (d, *J* = 7.8 Hz, 4H, $H_{Ar(IPent)}$), 7.02 (s, 2H, $H_{(Backbone)}$), 2.70 (dq, *J* = 10.2, 5.3 Hz, 4H, $CH_{(IPent)}$), 2.49 (p, *J* = 7.3 Hz, 2H, $CH_{2(NH_2{}^nBu)}$), 2.09 (ddd, *J* = 13.2, 7.5, 4.6 Hz, 4H, $CH_{2(IPent)}$), 1.90 – 1.76 (m, 6H, $CH_{2(IPent)}$ +$NH_{2(NH_2{}^nBu)}$), 1.51 (qd, *J* = 7.5, 5.6 Hz, 8H, $CH_{2(IPent)}$), 1.24 (dt, *J* = 14.2, 6.9 Hz, 2H, $CH_{2(NH_2{}^nBu)}$), 1.08 (t, *J* = 7.3 Hz, 14H, $CH_{3(IPent)}$+ $CH_{2(NH_2{}^nBu)}$), 0.76 (t, *J* = 7.5 Hz, 15H, $CH_{3(IPent)}$+ $CH_{3(NH_2{}^nBu)}$) ppm. ^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.1(N**C**N), 144.8($C_{Ar(IPent)}$), 136.7($C_{Ar(IPent)}$), 129.1($CH_{Ar(IPent)}$), 125.3($CH_{Ar(IPent)}$), 125.1($CH_{(Backbone)}$), 42.9($CH_{2(NH_2{}^nBu)}$), 41.1($CH_{(IPent)}$), 34.2($CH_{2(NH_2{}^nBu)}$), 28.6($CH_{2(IPent)}$), 27.0($CH_{2(IPent)}$), 19.8($CH_{2(NH_2{}^nBu)}$), 13.8($CH_{3(NH_2{}^nBu)}$), 12.9($CH_{3(IPent)}$), 11.1($CH_{3(IPent)}$). Elemental Anal. Calcd for $[C_{39}H_{63}Cl_2N_3Pd]$: C, 62.35; H, 8.45; N, 5.59. Found: C, 62.49; H, 8.13; N, 5.42.

[Pd(IPr^{Cl})(NH$_2{}^n$Bu)Cl$_2$] (4g) Following the **route B**: In a 4 mL scintillation vial equipped with a magnetic stirring bar, $[Pd(IPr^{Cl})(DMS)(Cl)_2]$ (**3g**) (91.2mg, 0.0626mmol) was dissolved in dichloromethane (1.2mL) prior to the addition of *n*-Butylamine (6.3µL, 0.0632mmol). The mixture was stirred at RT for 16h. After completion, DCM was concentrated, and pentane was added to crashed out the product. The resulting solid was left to dry to afford the catalyst in (82mg) 89% yield. (The compound shows decomposition in solution). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 – 7.54 (m, 2H, H_{Ar}), 7.40 (d, *J* = 7.7 Hz, 4H, H_{Ar}), 2.96 (hept, *J* = 6.6 Hz, 4H, $CH_{(IPr)}$), 2.49 – 2.40 (m, 2H, $CH_{2(NH_2{}^nBu)}$), 1.90 (t, *J* = 6.6 Hz, 2H, $NH_{2(NH_2{}^nBu)}$), 1.43 (d, *J* = 6.6 Hz, 12H, $CH_{3(IPr)}$), 1.30 – 1.21 (m, 2H, $CH_{2(NH_2{}^nBu)}$), 1.20 – 1.04 (m, 14H, $CH_{2(NH_2{}^nBu)}$+$CH_{3(IPr)}$), 0.72 (t, *J* = 7.3 Hz, 3H, $CH_{3(NH_2{}^nBu)}$) ppm. ^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.9(N**C**N), 147.9(C_{Ar}), 132.3(C_{Ar}), 131.2(C_{Ar}), 124.8(C_{Ar}), 120.5(C_{Ar}), 43.0($CH_{2(NH_2{}^nBu)}$), 33.3($CH_{2(NH_2{}^nBu)}$), 29.0(CH), 25.5(CH_3), 24.6(CH_3), 19.8($CH_{2(NH_2{}^nBu)}$), 13.8($CH_{3(NH_2{}^nBu)}$) ppm. Elemental Anal. Calcd for $[C_{31}H_{45}Cl_4N_3Pd]$: C, 52.59; H, 6.41; N, 5.94. Found: C, 52.30; H, 6.48; N, 5.80. m/z (TOF): $[C_{27}H_{35}Cl_2N_2]^+$ Calc: 457.2172; Found: 457.2174.

[Pd(IPr$^{\#}$)(NH$_2{}^n$Bu)Cl$_2$] (4h). Following the **route B**: In a 4 mL scintillation vial equipped with a magnetic stirring bar, $[Pd(IPr^{\#})(DMS)]$ (**3h**) (100mg, 0.0686mmol) was dissolved in dichloromethane (1.4mL) prior to the addition of *n*-Butylamine (6.9µL, 0.0693mmol). The mixture was stirred at RT for 16h. After completion, DCM was removed, and the resulting solid was left to dry to afford the pure catalyst in (95.6mg) 95% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.29 (d, *J* = 6.4 Hz, 8H, $CH_{Ar(IPr^{\#})}$), 7.19 – 7.07 (m, 24H, $CH_{Ar(IPr^{\#})}$), 7.03 – 6.95 (m, 20H, $CH_{Ar(IPr^{\#})}$), 6.78 (s, 4H, $CH_{Ar(IPr^{\#})}$), 6.68 – 6.62 (m, 8H, $CH_{Ar(IPr^{\#})}$), 6.10 (s, 4H, $CH_{Ar(IPr^{\#})}$), 5.37 (s, 2H, $CH_{(IPr^{\#})}$), 4.80 (s, 2H, $CH_{(Backbone)}$), 2.77 (p, *J* = 7.5 Hz, 2H, $CH_{2(NH_2{}^nBu)}$), 2.17 (t, *J* = 7.4 Hz, 2H, $NH_{2(NH_2{}^nBu)}$), 1.44 (tt, *J* = 7.8, 6.4 Hz, 2H, $CH_{2(NH_2{}^nBu)}$), 1.20 (h, *J* = 7.4 Hz, 2H, $CH_{2(NH_2{}^nBu)}$), 0.78 (t, *J* = 7.4 Hz, 3H, $CH_{3(NH_2{}^nBu)}$) ppm. ^{13}C NMR (101 MHz, Chloroform-*d*) δ 156.2(N**C**N), 144.7($C_{Ar(IPr^{\#})}$), 144.0($C_{Ar(IPr^{\#})}$), 143.9($C_{Ar(IPr^{\#})}$), 143.7($C_{Ar(IPr^{\#})}$), 142.0($C_{Ar(IPr^{\#})}$), 135.7($C_{Ar(IPr^{\#})}$), 131.1($CH_{Ar(IPr^{\#})}$), 130.5($CH_{Ar(IPr^{\#})}$), 129.4 (d, *J* = 2.1 Hz, $CH_{Ar(IPr^{\#})}$), 128.3($CH_{Ar(IPr^{\#})}$), 128.2($CH_{Ar(IPr^{\#})}$), 127.9($CH_{Ar(IPr^{\#})}$), 126.3($CH_{Ar(IPr^{\#})}$), 126.1($CH_{Ar(IPr^{\#})}$), 123.5($CH_{(Backbone)}$), 56.5($CH_{(IPr^{\#})}$), 51.2($CH_{(IPr^{\#})}$), 43.4($CH_{2(NH_2{}^nBu)}$), 34.5($CH_{2(NH_2{}^nBu)}$), 19.9($CH_{2(NH_2{}^nBu)}$), 13.8($CH_{3(NH_2{}^nBu)}$) ppm. Elemental Anal. Calcd for $[C_{97}H_{83}Cl_2N_3Pd]$: C, 79.36; H, 5.70; N, 2.86. Found: C, 79.08; H, 6.12; N, 2.68.

General procedure for the Buchwald-Hartwig amination. In a glovebox, a vial equipped with a stirring bar and sealed with a screw cap fitted with a septum was charged with NaO^{t}Bu or KO^{t}Bu (1.5 eq), the aryl-halide (0.5mmol, 1eq) and the amine (1,2eq). the [Pd(IPr*)(NH$_2{}^n$Bu)Cl$_2$] precatalyst (0.1mol%) already dissolved in a stock solution of dried 2-MeTHF was added into the vial to reach 1.5mL of its volume with content of solvent. The vial was taken outside of the glovebox and was allowed to stir (1000rpm) at the convenient temperature. After 5h, the crude mixture was charged onto celite and chromatographed on silica gel from ethyl acetate and hexanes dilutions to yield the desired product.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.
Supporting information with experimental details and spectra (PDF); Crystallographic data for **4d** (CIF) and Crystallographic data for **4e** (CIF).

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Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript

Notes

The authors declare no competing financial interests.

ACKNOWLEDGMENTS

We gratefully thank the Research Foundation – Flanders (FWO grant no: G0A6823N to SPN; GOC5423N to CSJC and G0A8723N to KVH) for support. Umicore AG is gratefully thanked for gifts of materials. UGent is gratefully acknowledged for the doctoral assistantship awarded to N. B. P.

ABBREVIATIONS

NHC N-heterocyclic carbene; BHA Buchwald-Hartwig amination; DMS Dimethyl sulfide; PEPPSI pyridine enhanced precatalyst preparation, stabilization and initiation. Pd Palladium; Ni Nickel.

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SYNOPSIS TOC