

COMMUNICATION

Air-Stable, Well-Defined Palladium–BIAN–NHC Chloro Dimer: Fast-Activating, Highly Efficient Catalyst for Cross-Coupling

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Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

We report the synthesis, characterization and reactivity of an air-stable, well-defined acenaphthoimidazolylidene palladium–BIAN–NHC chloro dimer complex, $[\text{Pd}(\text{BIAN-IPr})(\mu\text{-Cl})\text{Cl}]_2$. This rapidly activating catalyst merges the reactive properties of palladium chloro dimers, $[\text{Pd}(\text{NHC})(\mu\text{-Cl})\text{Cl}]_2$, with the attractive structural features of BIAN framework. $[\text{Pd}(\text{BIAN-IPr})(\mu\text{-Cl})\text{Cl}]_2$ is the most reactive Pd(II)–NHC precatalyst discovered to date undergoing fast activation under both inert atmosphere and aerobic conditions. The catalyst features bulky-yet-flexible sterics that render the C–H substituents closer to the metal center in combination with rapid dissociation to monomers and strong σ -donor properties. $[\text{Pd}(\text{BIAN-IPr})(\mu\text{-Cl})\text{Cl}]_2$ should be considered as a catalyst for reactions using well-defined Pd(II)–NHCs.

Palladium-catalyzed cross-couplings play a central role in organic synthesis as evidenced by the 2010 Nobel Prize in Chemistry and the tremendous progress in the cross-coupling arena.^{1,2} The continuous impact on academic and industrial research makes cross-couplings one of the most powerful tools for carbon–carbon and carbon–heteroatom bond construction for the synthesis of small molecules, agrochemicals and functional materials.^{3,4} Although significant progress has been made using electron-rich phosphines as ancillary ligands to palladium, N-heterocyclic carbenes (NHCs) have become a major direction in ligand development in the cross-coupling arena.^{5–7} The combination of readily-tuneable sterics and availability of various ligand scaffolds with strong σ -donation of the carbene center in the absence of air-sensitive phosphines enables a range of challenging cross-coupling reactions.^{5–7} In particular, the development of well-defined Pd(II)–NHC precatalysts has gained major attention due to high-reactivity,

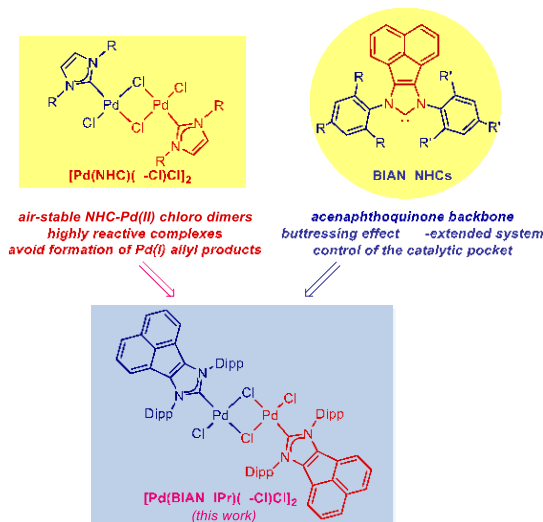


Figure 1. Well-defined $[\text{Pd}(\text{NHC})(\mu\text{-Cl})\text{Cl}]_2$ chloro dimers and BIAN–NHCs: fast-activating, highly active palladium–BIAN–NHC chloro dimer complex, $[\text{Pd}(\text{BIAN-IPr})(\mu\text{-Cl})\text{Cl}]_2$.

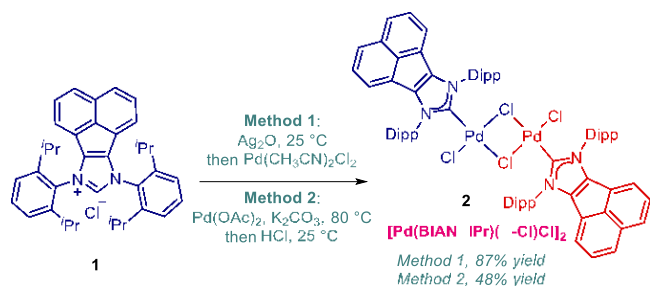
operational-simplicity in handling well-defined, air-stable Pd(II) precatalysts and the synthetically preferred 1:1 ligand/palladium ratio.^{8,9} The most successful in this regard are $[\text{Pd}(\text{NHC})(\text{allyl})\text{Cl}]$ complexes, which have found many cross-coupling applications and are now commercially available from different suppliers.¹⁰ However, recent studies demonstrate the formation of inactive bridging Pd(I) allyl complexes during activation of Pd–allyl complexes.¹¹ In this context, recently imidazol-2-ylidene Pd(II)–NHC chloro dimers have been identified as the most reactive Pd(II)–NHC precatalysts owing to facile dimer dissociation, while simultaneously rendering an attractive solution to deactivation of $[\text{Pd}(\text{NHC})(\text{allyl})\text{Cl}]$ complexes through bridging Pd(I) allyls.¹² In these catalysts, the replacement of the allyl ligand with the bridging chloride permits for fast activation, while preventing the formation of off-cycle Pd(I) allyl complexes.^{5a,13}

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Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x



Scheme 1. Synthesis of $[\text{Pd}(\text{BIAN-IPr})(\mu\text{-Cl})\text{Cl}]_2$. Conditions: (1) BIAN-IPr-HCl , Ag_2O (1.5 equiv), CH_2Cl_2 , 25 °C, 48 h; (ii) $\text{Pd}(\text{MeCN})_2\text{Cl}_2$ (2.0 equiv), CH_2Cl_2 , 25 °C, 24 h. (2) (i) BIAN-IPr-HCl , $\text{Pd}(\text{OAc})_2$ (1.2 equiv), K_2CO_3 (4.0 equiv), toluene, 80 °C, 15 h; (ii) HCl , 25 °C, 1 h.

In the meantime, significant progress has been made in using BIAN-NHC (BIAN = bis(imino)acenaphthene) complexes (Figure 1).¹⁴ In particular, the presence of bis(imino)acenaphthene backbone enforces a buttressing effect by pushing N-wingtip substituents towards the metal center, which permits for a better control of the catalytic pocket than in classical imidazol-2-ylidenes. The presence of the extended backbone results in strong σ -donor and π -acceptor properties.¹⁵ Altogether, these features render a highly attractive BIAN framework that enables variation of bulky-yet-flexible sterics, while protecting the metal-center during the cross-coupling, which is not easily possible using classical imidazol-2-ylidenes.¹⁴⁻¹⁷

Inspired by our studies in Pd-NHC catalysis,^{12,14,18} herein we report the synthesis, characterization and reactivity of an air-stable, well-defined acenaphthoimidazolydene palladium BIAN-NHC chloro dimer complex, $[\text{Pd}(\text{BIAN-IPr})(\mu\text{-Cl})\text{Cl}]_2$ (Figure 1). This rapidly activating catalyst merges the attractive properties of (1) palladium chloro dimers with (2) the structural and electronic features of BIAN framework. Considering high reactivity of Pd(II)-NHC chloro dimers,¹² $[\text{Pd}(\text{BIAN-IPr})(\mu\text{-Cl})\text{Cl}]_2$ is the most reactive Pd(II)-NHC precatalyst discovered to date undergoing fast activation under both inert atmosphere and aerobic conditions. $[\text{Pd}(\text{BIAN-IPr})(\mu\text{-Cl})\text{Cl}]_2$ should be considered as a catalyst for reactions using air-stable, well-defined Pd(II)-NHCs .

Our investigation commenced with the synthesis of BIAN-IPr chloro dimer, $[\text{Pd}(\text{BIAN-IPr})(\mu\text{-Cl})\text{Cl}]_2$, as the parent complex in this class. We determined that the desired complex could be synthesized by two routes: (1) from the corresponding BIAN-NHC-HCl salt by transmetalation of $[(\text{BIAN-NHC})\text{AgCl}]$ with $\text{Pd}(\text{MeCN})_2\text{Cl}_2$ in CH_2Cl_2 at room temperature (87% yield) or (2) by the direct, one-pot, two-step synthesis using $\text{Pd}(\text{OAc})_2/\text{K}_2\text{CO}_3$ and HCl (48% yield) (Scheme 1). The complex was found to be air- and moisture-stable. The structure was confirmed by X-ray crystallography (Figure 2). The geometry of palladium is distorted square planar; the bond lengths of Pd1-C : 1.946 Å; Pd1-Cl : 2.268 Å; Pd1-(m)Cl : 2.331 Å, 2.389 Å (Pd2-C : 1.951 Å; Pd2-Cl : 2.275 Å; Pd2-(m)Cl : 2.399 Å, 2.328 Å) in $[\text{Pd}(\text{BIAN-IPr})\text{Cl}_2]_2$ are in the range for the IPr congener (Pd-C : 1.953 Å; Pd-Cl : 2.272 Å; Pd-(m)Cl : 2.403 Å, 2.315 Å). The N-C(carbene)-N angles (avg) in $[\text{Pd}(\text{BIAN-IPr})(\mu\text{-Cl})\text{Cl}]_2$ of 126.0° are much smaller than in the IPr congener (128.3°), indicating closer steric impact of N-Ar wingtips on the metal center, consistent with the C1-H/N-Ar steric repulsion by the naphthalene framework.¹³

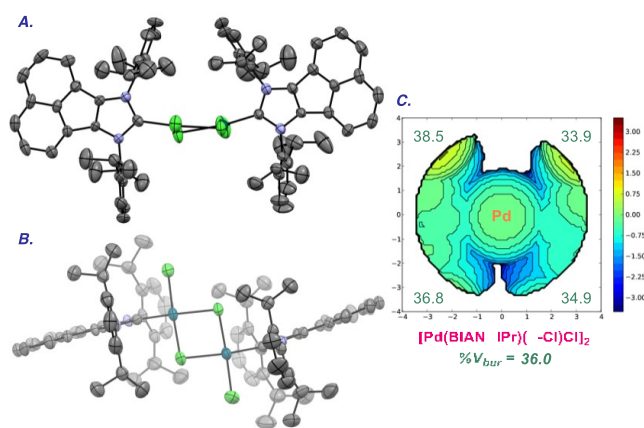


Figure 2. X-ray crystal structure of complex **2**. Two views: front (A); side (B). Hydrogen atoms have been omitted for clarity. Selected bond lengths [Å] and angles [°], see SI. (C) Topographical steric map of complex **2** showing $\%V_{\text{bur}}$ per quadrant. **2**: CCDC 2159737.

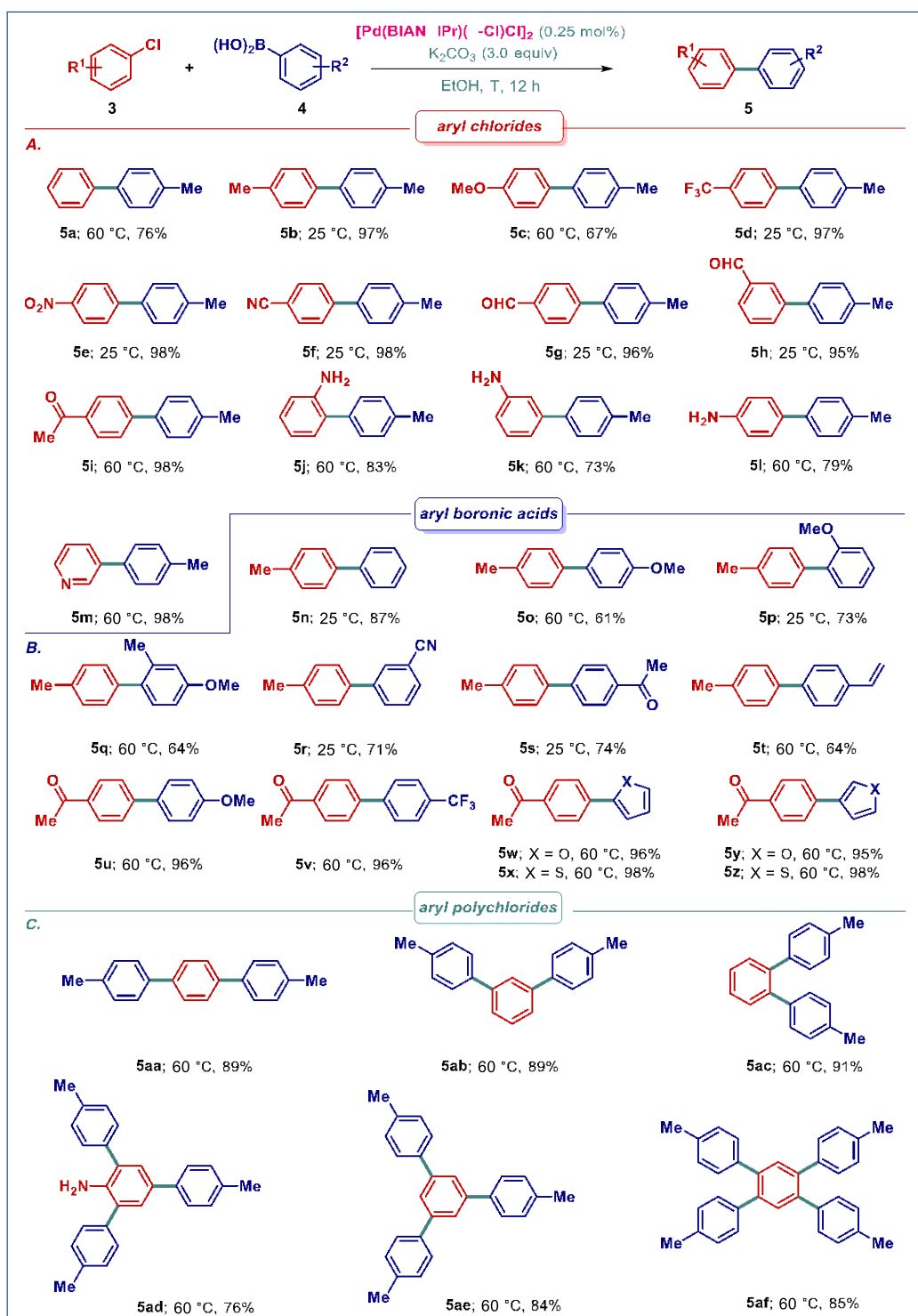
Table 1. Optimization Studies.^a

Entry	Base [equiv]	Solvent	T [°C]	Yield [%]
1 ^{b,c}	KO^tBu (1.1)	EtOH	25	95
2 ^{b,d}	KO^tBu (1.1)	EtOH	25	84
3 ^b	KO^tBu (1.1)	EtOH	25	52
4	KO^tBu (1.1)	EtOH	25	80
5	KO^tBu (1.1)	i PrOH	25	35
6	KO^tBu (1.1)	THF	25	62
7	KO^tBu (1.1)	1,4-dioxane	25	63
8	KO^tBu (1.1)	MeOH	25	72
9	Cs_2CO_3 (1.5)	EtOH	25	73
10	K_2CO_3 (1.5)	EtOH	25	84
11	K_2CO_3 (3.0)	EtOH	25	87
12	K_2CO_3 (3.0)	EtOH	60	92

^aConditions: ArCl (1.0 equiv), Ph-B(OH)_2 (2.0 equiv), $[\text{Pd}(\text{BIAN-IPr})(\mu\text{-Cl})\text{Cl}]_2$ (0.25 mol%), base (1.1-3 equiv), solvent (0.5 M), 25-60 °C, 12 h. ^b Ph-B(OH)_2 (1.2 equiv). ^c $[\text{Pd}(\text{BIAN-IPr})(\mu\text{-Cl})\text{Cl}]_2$ (1.5 mol%). ^d $[\text{Pd}(\text{BIAN-IPr})(\mu\text{-Cl})\text{Cl}]_2$ (0.5 mol%).

The palladium and chlorine atoms are coplanar. The steric map approach developed by Cavallo revealed the ($\%V_{\text{bur}}$) of 36.0% with 36.8%, 38.5%, 33.9%, 34.9% for each quadrant (Figure 2; Pd2 : ($\%V_{\text{bur}}$) of 34.9% with 32.1%, 34.3%, 34.8%, 38.3% for each quadrant).¹⁹ The values can be compared with the ($\%V_{\text{bur}}$) of 38.1% (avg) for the IPr congener with 48.3%, 28.9%, 47.6%, 27.4% for each quadrant.¹³

With the access to this novel bench-stable BIAN-NHC chloro dimer, we investigated its reactivity in a Suzuki cross-coupling involving aryl chlorides (Table 1). Although solubility of acenaphthoimidazolydene is a consideration in the reactions catalyzed by BIAN-NHCs ,¹⁴⁻¹⁷ we found that the model Suzuki cross-coupling could be efficiently performed using either strong base (Table 1, entries 1-8) or weak base conditions (Table 1, entries 9-12) using a range of solvents.⁵ The optimal conditions involve K_2CO_3 as a base and EtOH as a solvent (Table 1, entry 12). It is important to note that these reactions can be performed with commercial grade ethanol.

Table 2. Scope of the Suzuki Cross-Coupling Catalyzed by $[\text{Pd}(\text{BIAN-IPr})(\mu\text{-Cl})\text{Cl}]_2$ ^a

^aConditions: ArCl (1.0 equiv), Ph-B(OH)₂ (2.0 equiv), $[\text{Pd}(\text{BIAN-IPr})(\mu\text{-Cl})\text{Cl}]_2$ (0.25 mol%), K_2CO_3 (3.0 equiv), EtOH (0.5 M), 25–60 °C, 12 h.

Encouraged by the high activity of the $[\text{Pd}(\text{BIAN-IPr})(\mu\text{-Cl})\text{Cl}]_2$ catalyst, we next investigate the scope of the Suzuki cross-coupling of aryl chlorides (Table 2). As shown, the scope of this method is broad and encompasses a range of neutral (5a–5b), electron-rich (5c, 5j–5l), electron-deficient (5d–5f, 5i) and heterocyclic (5m) aryl chlorides (Table 2A). Importantly, various sensitive functional groups, such as nitro (5e), cyano (5f), formyl

(5g, 5h), acetyl (5i) and unprotected amino (5j–5l) are well-tolerated by this BIAN catalyst. Furthermore, the scope of boronic acids is also broad and accommodates electron-neutral (5n), electron-rich (5o–5q, 5t, 5u), electron-deficient (5r–5s, 5v) and heterocyclic (5w–5z) boronic acids (Table 2B). Further, this catalyst could be applied to the challenging cross-coupling of polychlorinated arenes (Table 2C). It is important to note that in

addition to better kinetics, $[\text{Pd}(\text{BIAN-IPr})(\mu\text{-Cl})\text{Cl}]_2$ catalyses the coupling of sterically-hindered substrates and polyhalogenated arenes in much higher yields than the IPr congener, which is likely due to increased bulkiness around the metal facilitating reductive elimination (see SI). $[\text{Pd}(\text{BIAN-IPr})(\mu\text{-Cl})\text{Cl}]_2$ is stable on the benchtop (solid) and in solution (CDCl_3 , C_6D_6 , $\text{DMSO-}d_6$). We have not observed any decomposition after 6 months (solid) and 5 days (solution). Under basic conditions, catalyst decomposition pathway involves dissociation of Pd and oxidation to cyclic urea. This is similar to the related catalysts.¹²

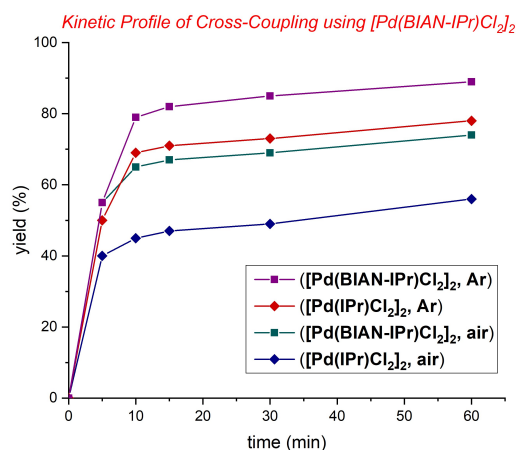


Figure 3. Kinetic profile of the Suzuki-Miyaura cross-coupling catalyzed by $[\text{Pd}(\text{BIAN-IPr})(\mu\text{-Cl})\text{Cl}]_2$ and $[\text{Pd}(\text{IPr})(\mu\text{-Cl})\text{Cl}]_2$ at 25 °C. Conditions: $[\text{Pd}(\text{NHC})\text{Cl}_2]_2$ (0.25 mol%), 4-CHO- $\text{C}_6\text{H}_4\text{-Cl}$ (1.0 equiv), 4-Tol-B(OH) $_2$ (2.0 equiv), K_2CO_3 (3.0 equiv), EtOH (0.5 M), 25 °C, 0–60 min, Ar or air.

Polyphenyls such as **5aa–5af** have broad applications in materials science and organic synthesis. Overall, the scope of the cross-coupling catalyzed by $[\text{Pd}(\text{BIAN-IPr})(\mu\text{-Cl})\text{Cl}]_2$ compares very favourably with other Pd(II)–NHC systems.^{5,6}

To gain further insight into the reactivity of $[\text{Pd}(\text{BIAN-IPr})(\mu\text{-Cl})\text{Cl}]_2$ preliminary kinetic studies were conducted (Figure 3). The reactions were benchmarked against the most reactive to date¹² imidazol-2-ylidene IPr congener. As indicated in Figure 3, $[\text{Pd}(\text{BIAN-IPr})(\mu\text{-Cl})\text{Cl}]_2$ showed favorable kinetic profile over the IPr analogue, $[\text{Pd}(\text{IPr})(\mu\text{-Cl})\text{Cl}]_2$, under inert and aerobic^{14–17} conditions. The kinetic profile of $[\text{Pd}(\text{BIAN-IPr})(\mu\text{-Cl})\text{Cl}]_2$ is consistent with the fast activation of the metal center enabled by the BIAN framework.

In conclusion, we have reported an air-stable, well-defined acenaphthoimidazolylidene palladium BIAN–NHC chloro dimer complex, $[\text{Pd}(\text{BIAN-IPr})(\mu\text{-Cl})\text{Cl}]_2$. This novel catalyst combines the benefits of palladium chloro dimers with the structural features of the BIAN framework. Considering high reactivity of Pd(II)–NHC chloro dimers, $[\text{Pd}(\text{BIAN-IPr})(\mu\text{-Cl})\text{Cl}]_2$ is the most reactive Pd(II)–NHC precatalyst discovered to date. $[\text{Pd}(\text{BIAN-IPr})(\mu\text{-Cl})\text{Cl}]_2$ should be routinely utilized for cross-coupling and C–H activation^{6h} reactions using well-defined Pd(II)–NHCs.

We thank Rutgers University (M.S.), the NSF (CAREER CHE-1650766, M.S.), and National Natural Science Foundation of China (22179075, J.Z.) for support.

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