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

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We report the synthesis, characterization and reactivity of an air-stable, well-defined acenaphthoimidazolydene palladium–BIAN–NHC chloro dimer complex, $[\text{Pd}(\text{BIAN-IPr})(\mu\text{-Cl})\text{Cl}]_2$. 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,

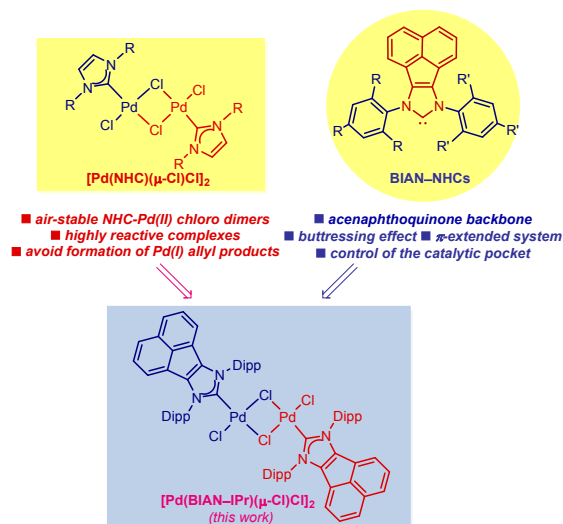


Figure 1. Well-defined $[\text{Pd}(\text{NHC})(\mu\text{-Cl})\text{Cl}]_2$ chloro dimers and BIAN–NHCs: fast-activating, highly active palladium–BIAN–NHC chloro dimer complex, $[\text{Pd}(\text{BIAN-IPr})(\mu\text{-Cl})\text{Cl}]_2$.

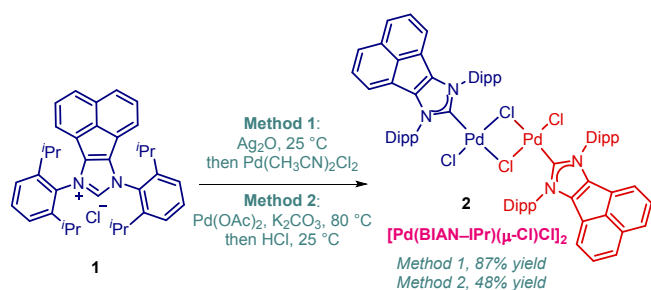
operational-simplicity in handling well-defined, air-stable Pd(II) precatalysts and the synthetically preferred 1:1 ligand/palladium ratio.^{8,9} The most successful in this regard are $[\text{Pd}(\text{NHC})(\text{allyl})\text{Cl}]$ complexes, which have found many cross-coupling applications and are 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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Scheme 1. Synthesis of [Pd(BIAN-IPr)(μ-Cl)Cl]₂. Conditions: (1) BIAN-IPr-HCl, Ag₂O (1.5 equiv), CH₂Cl₂, 25 °C, 48 h; (ii) Pd(MeCN)₂Cl₂ (2.0 equiv), CH₂Cl₂, 25 °C, 24 h. (2) (i) BIAN-IPr-HCl, Pd(OAc)₂ (1.2 equiv), K₂CO₃ (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 acenaphthoimidazolylidene palladium BIAN-NHC chloro dimer complex, [Pd(BIAN-IPr)(μ-Cl)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 [Pd(BIAN-IPr)(μ-Cl)Cl]₂ is the most reactive Pd(II)-NHC precatalyst discovered to date undergoing fast activation under both inert atmosphere and aerobic conditions. [Pd(BIAN-IPr)(μ-Cl)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, [Pd(BIAN-IPr)(μ-Cl)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 [(BIAN-NHC)AgCl] with Pd(MeCN)₂Cl₂ in CH₂Cl₂ at room temperature (87% yield) or (2) by the direct, one-pot, two-step synthesis using Pd(OAc)₂/K₂CO₃ 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 [Pd(BIAN-IPr)Cl]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 [Pd(BIAN-IPr)(μ-Cl)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 Cl-H/N-Ar steric repulsion by the naphthalene framework.¹³

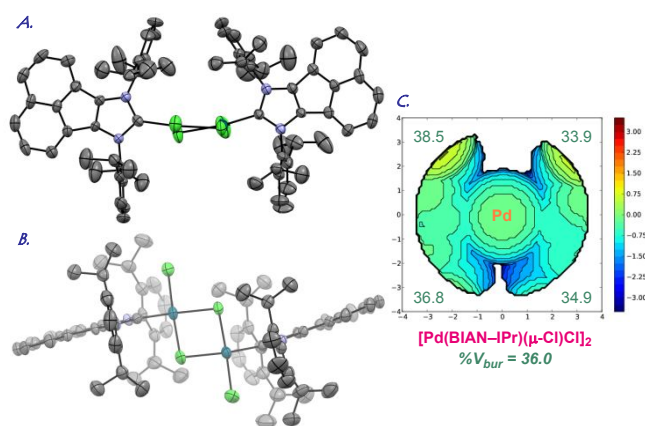


Figure 2. X-ray crystal structure of complex 2. Two views: front (A); side (B). Hydrogen atoms have been omitted for clarity. Selected bond lengths [Å] and angles [°], see SI. (C) Topographical steric map of complex 2 showing %V_{bur} per quadrant. 2: CCDC 2159737.

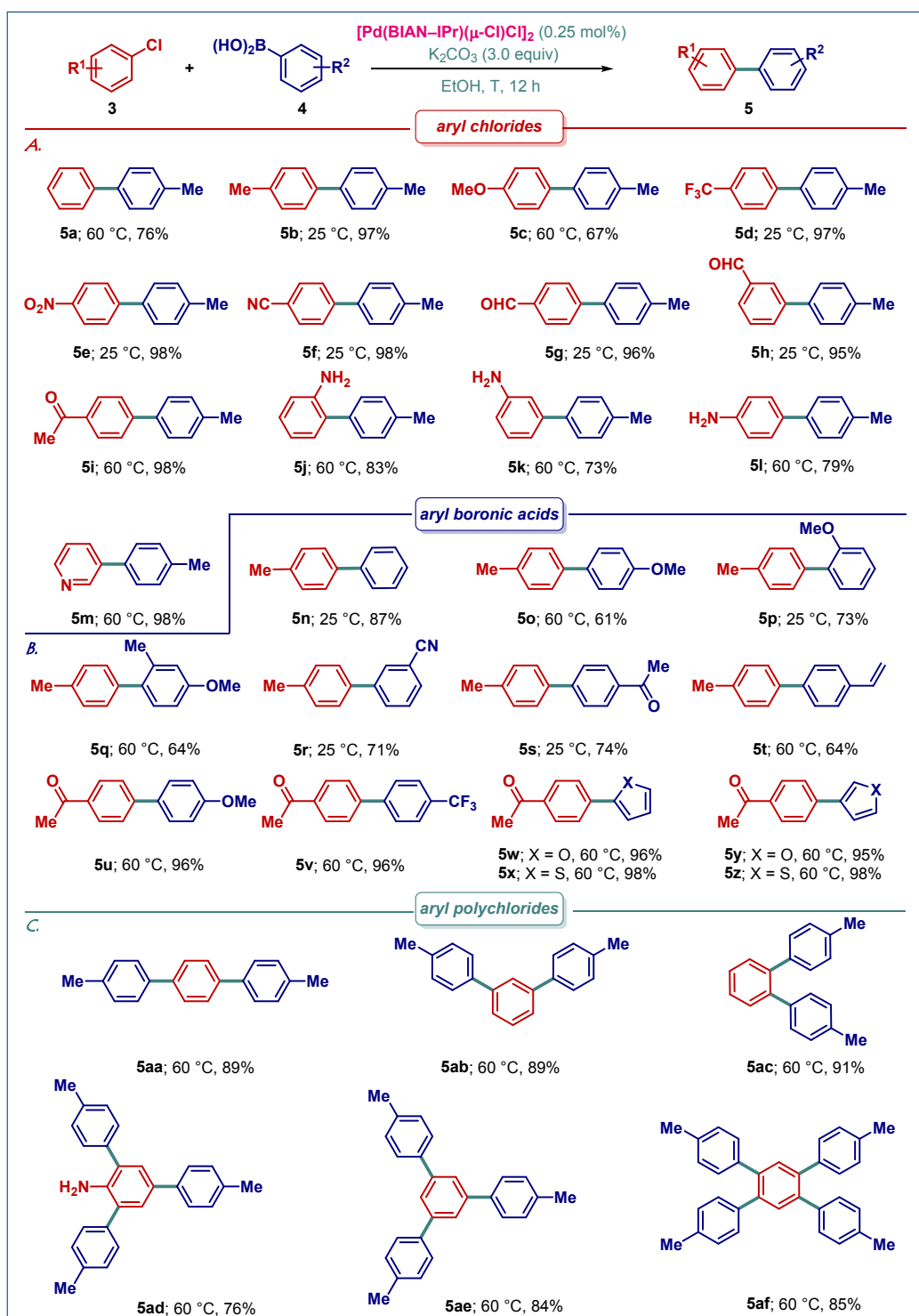
Table 1. Optimization Studies.^a

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

^aConditions: ArCl (1.0 equiv), Ph-B(OH)₂ (2.0 equiv), [Pd(BIAN-IPr)(μ-Cl)Cl]₂ (0.25 mol%), base (1.1-3 equiv), solvent (0.5 M), 25-60 °C, 12 h. ^bPh-B(OH)₂ (1.2 equiv). ^c[Pd(BIAN-IPr)(μ-Cl)Cl]₂ (1.5 mol%). ^d[Pd(BIAN-IPr)(μ-Cl)Cl]₂ (0.5 mol%).

The palladium and chlorine atoms are coplanar. The steric map approach developed by Cavallo revealed the (%V_{bur}) of 36.0% with 36.8%, 38.5%, 33.9%, 34.9% for each quadrant (Figure 2; Pd2: (%V_{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_{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 acenaphthoimidazolylidene 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 K₂CO₃ 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%), K₂CO₃ (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

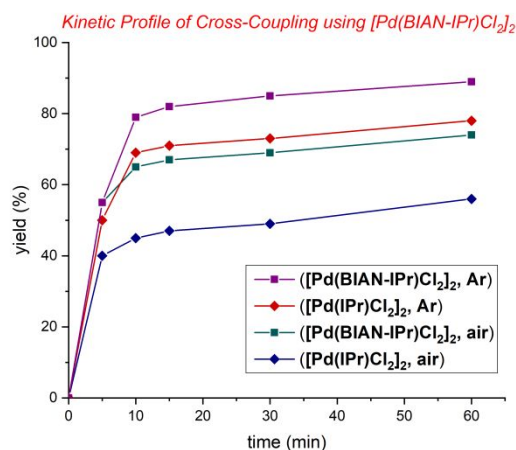


Figure 3. Kinetic profile of the Suzuki-Miyaura cross-coupling catalyzed by $[\text{Pd}(\text{BIAN-IPr})(\mu\text{-Cl})\text{Cl}]_2$ and $[\text{Pd}(\text{IPr})(\mu\text{-Cl})\text{Cl}]_2$ at 25 °C. Conditions: $[\text{Pd}(\text{NHC})\text{Cl}_2]_2$ (0.25 mol%), 4-CHO- $\text{C}_6\text{H}_4\text{-Cl}$ (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.

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. $[\text{Pd}(\text{BIAN-IPr})(\mu\text{-Cl})\text{Cl}]_2$ showed favorable kinetic profile over the IPr analogue, $[\text{Pd}(\text{IPr})(\mu\text{-Cl})\text{Cl}]_2$, under inert and aerobic¹⁴⁻¹⁷ conditions.

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. $[\text{Pd}(\text{BIAN-IPr})(\mu\text{-Cl})\text{Cl}]_2$ should be routinely utilized for cross-coupling and C-H activation^{6h} reactions using well-defined Pd(II)-NHCs.

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