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Dimetallic Palladium–NHC Complexes: Synthesis, Characterization, and Catalytic Application for Direct C–H Arylation Reaction of Heteroaromatics with Aryl Chlorides

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Abstract. A series of dimetallic palladium(II)–NHC complexes comprised of 1,4-naphthalenyl or 9,10-anthracenyl spacer sandwiched between two imidazole rings was successfully synthesized. These complexes were characterized by ^{1}H and $^{13}C\{^{1}H\}$ NMR spectroscopy and elemental analysis. The structures of two dimetallic palladium complexes and a related mononuclear palladium complex to be used for comparative studies were further characterized by X-ray diffraction. The dimetallic palladium complex with the 9,10-anthracenyl linker was very efficient in catalyzing direct C–H arylation reactions of heteroaromatic compounds (imidazoles, imidazo[1,2-*a*]pyridine, and thioazole) with a broad range of aryl chlorides, employing a mild monopalladium loading of 1.5 mol%. It allows for the effective use of aryl chlorides to prepare arylated heterocycles, previously only accessible with the more reactive bromide counterparts. Importantly, the catalytic activity of the dimetallic precatalyst was found to be higher than that of an analogous mononuclear complex.

Keywords: Carbene ligands; Palladium; C−H activation ; Heterocycles; Aryl halides; Dinuclear palladium complex

Introduction

Palladium-catalyzed direct C–H arylation reactions of heteroarenes with aryl halides offer an economical and environmental-friendly approach for the construction of heterobiaryls as they do not require stoichiometric amounts of preliminary organometallic reagents, thereby streamlining synthetic routes and reducing waste.[1] We have been interested in the preparation of aryl imidazoles because these heterocyclic compounds exhibit interesting biological activities[2] and they are important structural units in organic materials.[3] Arylated imidazoles can be conveniently prepared by the direct arylation reaction of azoles. Palladium in combination with phosphine and related ligands represents the typical catalytic conditions in earlier works,[4] where a high palladium loading in the range of 2.0–10 mol% was required. *N*-heterocyclic carbene (NHC) ligands have attracted much attention in the past two decades because they offer many advantages over phosphine ligands such as superior activity, stronger σ-donating properties, and better stability and structural versatility.[5] Recently, much effort has been directed toward the use of preformed palladium–NHC complexes for catalyzing the C5-direct arylation reaction of imidazoles with aryl halides.[6] Although these palladium–NHC complexes were generally effective in catalyzing the reaction with aryl iodides and bromides, general catalyst systems capable of utilizing a broad range of less reactive but inexpensive aryl chlorides remain elusive. Ke and Liu *et al.* reported on some highly bulky PEPPSI-themed palladium–NHC complexes which enabled aryl bromides to be effectively coupled under aerobic conditions with a low Pd loading of 1 mol%.[6d] However, they were not efficient catalysts for aryl chloride substrates such as 4-chlorobenzonitrile and 4-chlorobenzaldehyde, giving low yields in the range of 22–29%. Recently, Singh *et. al.* developed palladium complexes with chalcogenated amidate NHC ligands, also capable of facilitating the direct arylation of imidazoles with aryl bromides under aerobic conditions and a mild Pd loading of 0.5–1 mol%.[6g] Nevertheless, only a single aryl chloride substrate was successfully employed in the coupling reaction. It is noteworthy that reports on palladium–NHC precatalysts were based predominantly on mononuclear complexes. Compared to mononuclear complexes, dinuclear palladium–NHC complexes exhibited improved catalytic activity in cross-coupling reactions.[7] Their superior activity may be attributable

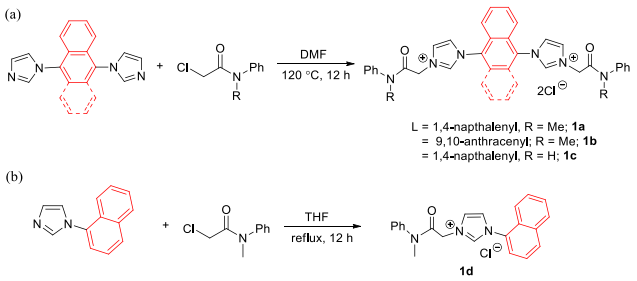
to a higher local concentration of the metal in the dimetallic systems, or in some cases, to favorable supramolecular interactions between ligand and substrate.[7b,7d] An earlier study by Huynh *et.al* demonstrated superior catalytic performance of dinuclear palladium–NHC complexes in comparison to those of their mononuclear equivalents in the direct C5-arylation of 1-methylimidazoles.[6c] The activity with aryl chloride substrates was however still unsatisfactory.

In view of possibly superior activities of dimetallic precatalysts, in this study we develop new dimetallic PEPPSI-themed[8] palladium–NHC complexes and investigate their potential in catalyzing direct arylation reactions using aryl chlorides as substrates. Fortunately, one of our new dimetallic palladium complexes is highly effective in catalyzing the coupling reaction between imidazoles and aryl halides. Our studies show that compared to a similar mononuclear palladium complex, a dimetallic palladium complex exhibits superior catalytic activity. The dimetallic complex requires a mild monopalladium loading of 1.5 mol% to catalyze reactions with a range of aryl chlorides, thus yielding arylated imidazoles and related heterocycles which were previously only accessible with the use of more reactive aryl bromides or iodides.

Results and Discussion

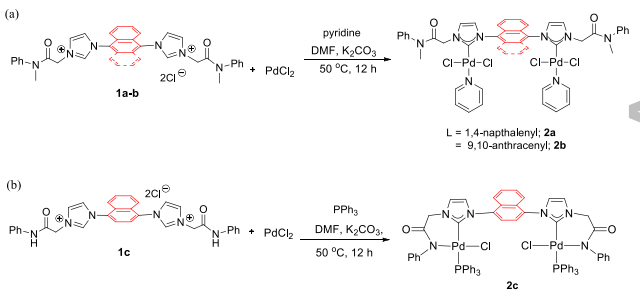
We began by exploring a new NHC-based ditopic ligand scaffold for the preparation of dimetallic palladium complexes. Synthetic routes for all new ligand precursors are shown in Scheme 1. Target compounds were accessed by means of straightforward synthetic steps, employing cheap starting materials. A key feature of ligand scaffolds **1a**–**c** is the 9,10-anthracenyl or 1,4-naphthalenyl spacer sandwiched between two imidazole rings. For comparison, ligand precursor **1d**, needed for the preparation of an analogous mononuclear complex was also developed. Imidazolium salts **1a**,**b** possess *N*-methyl groups, which exclude the possibility of bidentate chelation by the ligand. In contrast, the amide functional groups in **1c** offer the possibility of N*H* deprotonation and consequently bidentate chelation of the NHC ligand. Palladium complexes with donor-functionalized NHC ligands had been used in direct C–H arylation reactions of heterocycles.[6e-g,9]

To obtain imidazolium salts **1a-d**, the key quaternization reaction between a *N*-substituted imidazole and 2-chloro-*N*-phenylacetamide or its derivative was achieved under reflux conditions. Products were obtained as white solids of excellent purity and in moderate to high yields (67–96%). They were characterized by NMR spectroscopy, elemental analysis, and high-resolution mass spectrometry. The characteristic C2-proton signals were visible at *ca.* 10 ppm in the ^{1}H NMR spectrum. The N*H* signal for the imidazolium chloride **1c** was observed at *ca*. 11 ppm.



Scheme 1. Synthesis of ligand precursors.

The imidazolium salt precursors were reacted with $PdCl_2$ in the presence of pyridine in DMF at 50 °C to afford new palladium complexes **2a,b** and **2d** (Scheme 2 and 3). Dimetallic palladium(II) complexes **2a**,**b** featuring monodentate NHC moieties were obtained in 48–73% yields. For the dimetallic complex **2c**, featuring bidentate amidate/NHC groups, addition of PPh_3 was essential for the formation of pure compound in 65% yield. The PPh_3 ligand is *trans* to NHC moiety as confirmed by X-ray structural analysis (*vide infra*). The mononuclear complex **2d** was similarly prepared from imidazolium salt **1d** in a good yield of 87%. The successful coordination by ligands of **2a**–**b** and **2d** was reflected by the absence of downfield NC*H*N signals in their ^{1}H NMR spectra. For complex **2c**, the disappearance of both the NC*H*N and N*H* proton signals at ca. 10 and 11 pm, respectively, confirmed the bidentate ligand coordination. Notably, the ^{1}H NMR signals in **2a**–**c** are broad, reflecting the possibility of fluxional behavior of these complexes. In fact, the ^{1}H NMR of **2a** suggests a symmetric nature of the complex in solution, but a subsequent X-ray structural analysis revealed that the two palladium centers adopt different *cis* and *trans* coordination environments in the solid-state. The pyridine ligand in **2d** can be easily replaced by PPh_3, forming **3d** in 60% yield. Interestingly, unlike **2c**, **3d** adopts a *cis* geometry as revealed by X-ray structural analysis. Nevertheless, for both complexes, the ^{31}P NMR signals were observed at ca. 27 ppm. These new solids are all air-stable and readily soluble in solvents of high polarity such as dichloromethane and DMF.



Scheme 2. Synthesis of Dinuclear Palladium–NHC Complexes.

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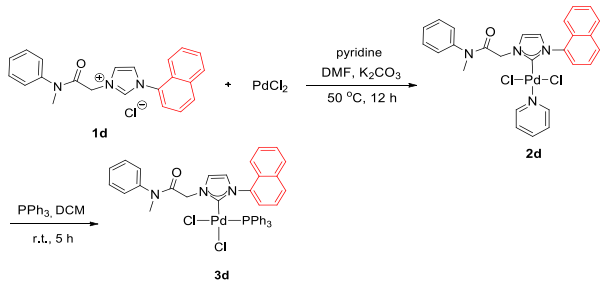


Scheme 3. Synthesis of Mononuclear Palladium–NHC Complexes.

Crystals of **2a**, **2c**, and **3d** suitable for single-crystal X-ray diffraction were grown from vapor diffusion using the solvent combinations of acetonitrile/ether, DMF/ether, and dichloromethane/ether respectively. The crystallographic data are tabulated in Table S1 in the supplementary electronic information. Interestingly, the coordination environments around the two palladium centers of **2a** are different (Figure 1); one adopts *trans* geometry, while the other is *cis*. Such a structural arrangement can be explained by the presence of a non-classical hydrogen bonding interaction between Cl3 atoms in the *trans* $PdCl_2$ unit and the proton on the C36 atom of the pyridine ligand in the *cis* $PdCl_2$ unit (∠C—H···Cl = 142.8(4); C—H···Cl = 2.796(2) Å). Further stabilization of the structure comes from the weak π — π stacking interaction between the 1,4-naphthalenyl group and the pyridine ring (centroid to centroid distance = 4.1 Å; interplanar angle = 22°).[10] In the structure of **2c**, the dimetallic complex is situated on a crystallographic two-fold rotation axis. In contrast to the structure of **2a**, the two NHC moieties in **2c** exhibit an *anti* conformation (Figure 2). The bidentate NHC/amidate coordination around the palladium centers is confirmed. The steric effect imposed by the bidentate ligand leads to a cis disposition of the PPh_3 ligand in relation to the NHC group. No significant intramolecular nonbonding interactions were observed. The NHC and PPh_3 moieties in **3d** are also *cis* to each other (Figure 3). The preference for the *cis* configuration in mixed NHC/phosphine complexes is well documented in the literature.[6a,11] The palladium center adopts a slightly distorted square planar coordination environment with ∠P1—Pd1—Cl1 (168.7(2)°) and ∠C1—Pd—Cl2 (171.5(2)°), significantly distorted from linearity.

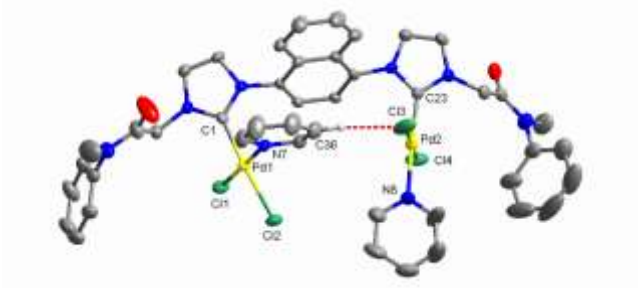


Figure 1. Molecular structure of **2a** at 35 % probability level. Hydrogen atoms except that on C36 are omitted for clarity. The intramolecular non-hydrogen bonding interaction is shown. Selected bond distances and angles (°): Pd1—C1, 1.959(5); Pd1—N7, 2.027(5); Pd1—Cl1, 2.2891(16); Pd1—Cl2, 2.3578(15); Pd2—C23, 1.946(6); Pd2—N8, 2.064(5); Pd2—Cl3, 2.283(2); Pd2—Cl4, 2.294(2); C1—Pd1—N7, 90.01(19); C1—Pd1—Cl1, 89.35(15); Cl1—Pd1—Cl2, 93.00(6); N7—Pd1—Cl2, 87.67(13); C1—Pd1—Cl2, 176.29(16); N7—Pd1—Cl1, 179.22(14); C23—Pd2—N8, 177.6(2); C23—Pd2—Cl3, 89.52(19); N8—Pd2—Cl3, 90.71(19); C23—Pd2—Cl4, 88.56(19); N8—Pd2—Cl4, 91.30(19); Cl3—Pd2—Cl4, 177.15(7).

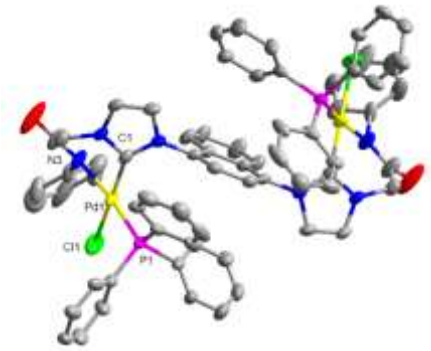


Figure 2. Molecular structure of **2c** at 35 % probability level. Hydrogen atoms are omitted for clarity. Only one of the two disordered *N*-phenyl ring orientations is shown. Selected bond distances and angles (°): Pd1—C1, 1.961(6); Pd1—P1, 2.3268(17); Pd1—Cl1, 2.3268(17); Pd1—N3, 2.109(5); C1—Pd1—P1, 98.42(16); C1—Pd1—N3, 83.4(2); Cl1—Pd1—N3, 91.77(16); Cl1—Pd1—P1, 86.86(7); C1—Pd1—Cl1, 174.03(18); N3—Pd1—P1, 171.59(16).

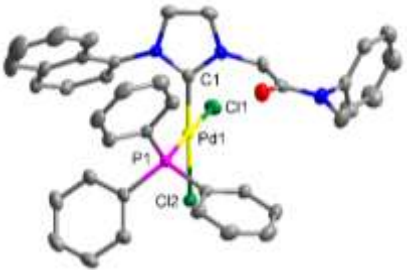
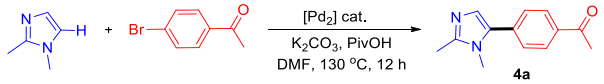


Figure 3. Molecular structure of **3d** at 50 % probability level. Hydrogen atoms are omitted for clarity. The intramolecular non-hydrogen bonding interaction is shown. Selected bond distances and angles (°): Pd1—C1, 1.981(2); Pd1—P1, 2.2593(5); Pd1—Cl1, 2.3773(5); Pd1—Cl2, 2.3426(5); C1—Pd1—P1, 95.61(6); C1—Pd1—Cl1, 88.07(6); Cl1—Pd1—Cl2, 91.173(19); Cl2—Pd1—P1, 85.137(19); C1—Pd1—Cl, 178.59(6); Cl1—Pd1—P1, 176.300(19).

The catalytic potential of these new complexes in direct arylation reactions of imidazoles and aryl halides was investigated. The reaction between 1,2-dimethylimidazole and 4-bromoacetophenone was

chosen as the benchmark reaction (Table 1). Based on previous work reported by others and ourselves,[6i] initial conditions of 1 mol% monopalladium loading, K_2CO_3 as the base, pivalic acid (PivOH) as the additive, DMF as the solvent, and a reaction temperature of 130 °C for 12 h were employed to screen for the most active precatalyst. Different catalysts including mononuclear and dinuclear complexes were tested; the monopalladium loading was fixed at 1 mol% and thus for mononuclear complex, the catalyst loading was 1 mol% and that for dimetallic complex was 0.5 mol%. As shown in entry 2, the dimetallic Pd complex **2b** was the most active precatalyst, affording a quantitative yield of product. Somewhat surprisingly, although complex **2a** bearing a 1,4-naphthalenyl spacer is structurally similar to complex **2b** featuring a 9,10-anthracenyl linker, it gave a much poorer product yield of 38% (entry 1), reflecting probably the importance of steric effects. Complex **2c** bearing bidentate amidate/NHC moieties gave a similar poor yield of 40% (entry 3), reflecting the importance of vacant coordination sites around the Pd atom in the catalytic cycle. Significantly, both mononuclear complexes **2d** and **3d** produced inferior yields to that of **2b** (entries 4 and 5), justifying the use of dimetallic Pd precatalyst. Complex **3d**, with a PPh_3 ligand delivered a good yield of 74% (entry 5) compared to a poor product yield of 18% from complex **2d** bearing a pyridine ligand (entry 4). The superiority of dimetallic complex **2b** over mononuclear complex **3d** in catalyzing the reaction was confirmed by the respective time-yield reaction profiles (Figure S1 in ESI). Simple NHC-free $Pd(OAc)_2$ was shown to catalyze the reaction effectively. Indeed, a quantitative yield of product was also obtained with $Pd(OAc)_2$ under our conditions (entry 6). The NHC-free system was, however, ineffective when applied to aryl chloride substrates (*vide infra*). In contrast, free $PdCl_2$ was ineffective in catalyzing the reaction (entry 7).

Table 1. Screening of Palladium Complexes [a)]

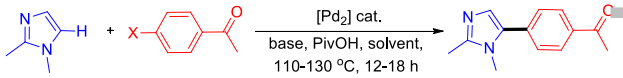


Entry	Complex	Yields
1	**2a**	38
2	**2b**	>99
3	**2c**	40
4	**2d**	18
5	**3d**	74
6	$Pd(OAc)_2$	>99
7	$PdCl_2$	2

a) Reaction conditions: 1,2-dimethylimidazole (2 mmol), 4-bromoacetophenone (1 mmol), K_2CO_3 (2 mmol), PivOH (0.3 mmol), DMF (3 mL), [Pd_2] cat. (0.5 mol%) or PdX_2 (1.0 mol%), 130 °C, 12 h. GC yield using benzophenone as an internal standard.

After identifying the best dimetallic complex as precatalyst, efforts were made to further optimize the reaction conditions (Table 2). K_2CO_3 was found to be the best choice of base as other commonly used inorganic bases gave inferior yields (entries 1 – 4). Both DMF and DMA were suitable reaction solvents (entries 4 – 5), whereas other high polarity solvents such as DMSO and NMP were not (entries 6 – 8). The addition of pivalic acid (PivOH), which generated potassium pivalate *in situ*, was essential for the reaction evidenced by a drastic reduction in yield in its absence (entry 5 vs 8). The use of *in situ* generated potassium pivalate was an established procedure in the literature.[4f] Entries 9 and 10 revealed that at a lower monopalladium loading of 0.5 mol% (catalyst loading of **2b** = 0.25 mol%), DMA was preferable to DMF as the solvent. Entries 10 and 11 indicate that free $Pd(OAc)_2$ was more effective than **2b** when utilizing an aryl bromide substrate. In sharp contrast, complex **2b** was much more efficient than free $Pd(OAc)_2$ in catalyzing the reaction with 4-chloroacetophenone as the substrate, delivering the coupled product in a fair yield of 62% (entry 12 vs. 13). The optimal temperature for the 4-chloroacetophenone reaction was 130 °C and no catalytic activity was observed when the temperature was lowered to 110 °C (entry 14). Increasing the monopalladium loading to 1.5 mol% (catalyst loading of **2b** = 0.75 mol%) and prolonging the reaction time to 18 h gave an optimal yield of 95 % (entry 16). The higher catalytic activity of the dimeric complex **2b** compared with that of mononuclear complex **3d** was further confirmed as the latter complex was totally inactive in the activation of 4-chloroacetophenone (entry 17). Hence, the optimal reaction conditions were established as follows: 1.5 mol% monopalladium loading of **2b** (catalyst loading = 0.75 mol%), K_2CO_3 as the base, PivOH as an additive, DMA as the solvent, and a reaction temperature of 130 °C for 18 h.

Table 2. Optimizing Conditions [a)]



Entry	Cat.	Solvent	Base	X	mono-Pd loading (mol%)	Yield (%)
1	**2b**	DMF	Cs_2CO_3	Br	1	20
2	**2b**	DMF	K_3PO_4	Br	1	0
3	**2b**	DMF	KOAc	Br	1	0
4	**2b**	DMF	K_2CO_3	Br	1	>99
5	**2b**	DMA	K_2CO_3	Br	1	>99
6	**2b**	DMSO	K_2CO_3	Br	1	2
7	**2b**	NMP	K_2CO_3	Br	1	43
8	**2b**	DMA	K_2CO_3	Br	1	16 [d)]
9	**2b**	DMF	K_2CO_3	Br	0.5	20
10	**2b**	DMA	K_2CO_3	Br	0.5	70
11	$Pd(OAc)_2$	DMA	K_2CO_3	Br	0.5	90
12	**2b**	DMA	K_2CO_3	Cl	1	62
13	$Pd(OAc)_2$	DMA	K_2CO_3	Cl	1	9
14	**2b**	DMA	K_2CO_3	Cl	1	0 [b)]
15	**2b**	DMA	K_2CO_3	Cl	1.5	83
16	**2b**	DMA	K_2CO_3	Cl	1.5	95 [c)]
17	**3d**	DMA	K_2CO_3	Cl	1.5	0 [c)]

a) Reaction conditions: 1,2-dimethylimidazole (2 mmol), aryl halide (1 mmol), K_2CO_3 (2 mmol), PivOH (0.3 mmol), solvent (3 mL), catalyst (0.5 – 1.5 mol% monopalladium loading; for $Pd(OAc)_2$, the catalyst loading equals the monopalladium loading; for dimeric complex **2b**, the catalyst loading equals the monopalladium loading divided by 2), 130 °C, 12 h. GC yield using benzophenone as an internal standard.

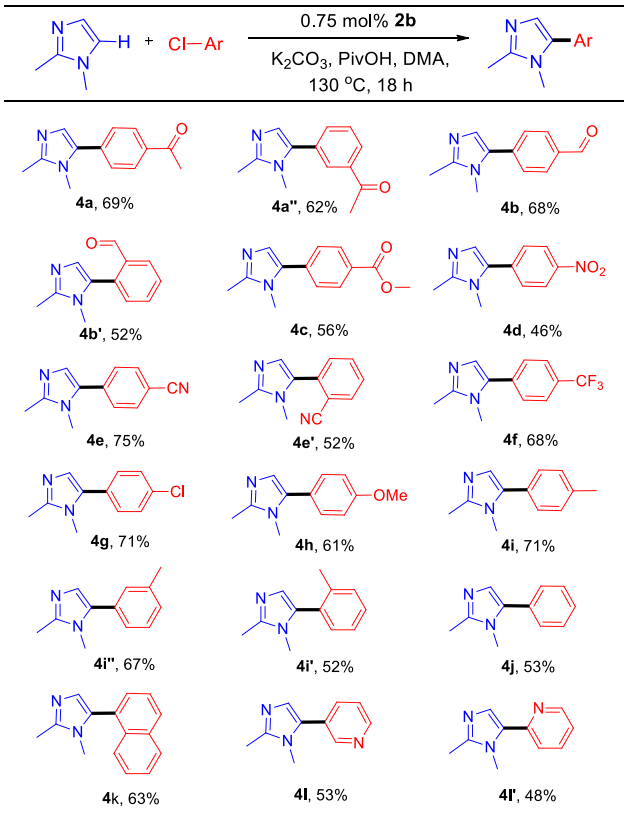
b) 110 °C.

[c] 18 h.

[d] In the absence of PivOH.

After the establishment of optimized conditions, the substrate scope of our catalyst system with respect to aryl chlorides was explored (Table 3). To demonstrate the catalytic efficiency of our catalyst system, most of the selected substrates were aimed at products which in the literature had generally been prepared from aryl bromides, but were inaccessible from the less reactive aryl chlorides (*vide infra*). In general, activated aryl chlorides such as 4-chloroacetopheone, 4-chlorobenzaldehyde, methyl 4-chlorobenzoate, 4-nitrochlorobenzene, 4-chlorobenzonitrile, and 4-chlorobenzotrifluoride were able to couple smoothly with 1,2-dimethylimidazole, affording 1,2,5-trisubstituted imidazoles **4a-f** with yields in a range of 46-75%. The arylation is highly regioselective, predominantly affording only the C5-arylated products. Desirably, deactivated electron-donating aryl chloride substrates can be employed, exemplified by a satisfactory yield of 61% for product **4h** obtained from 4-chloroanisole. The slightly electron-donating 4-chlorotoluene gave **4i** in a good yield of 71%. Somewhat surprisingly, an inferior yield of 53% for **4j** was obtained with electron-neutral chlorobenzene. Even though 1,2-dimethylimidazole was in two-fold excess, only one of the C−Cl bonds was activated when 1,4-dichlorobenzene was used as the substrate, giving **4 g** in a 71% yield.

Table 3. Substrate Scope of Aryl Chlorides in the Reaction with 1,2-Dimethylimidzole [a]

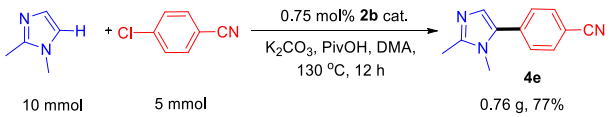


a) Reaction conditions: 1,2-dimethylimidazole (2 mmol), aryl halide (1 mmol), K_2CO_3 (2 mmol), PivOH (0.3 mmol), DMA (3 mL), **2b** (0.75 mol%), 130 °C, 18 h. Isolated yield.

Interestingly, the yields from 4-chloroacetophenone and its *meta* isomer were comparable (69% for **4a** vs. 62% for **4a''**), reflecting some tolerance for increased steric crowding in the palladium species. However, the steric hindrance from *ortho*-substituted aryl chloride substrates became significant such that inferior product yields were obtained (68% for **4b** vs. 52% for **4b′** and 75% for **4e** vs. 52% for **4e′**). Consistently, the *para* isomer of chlorotoluene afforded the best yield of 71%, followed by a slightly lower yield of 67% for **4i′′** from the *meta* isomer and an inferior yield of 52% for **4i′,** derived from the *ortho* isomer. The compound **4i′′** with a *meta*-substituted methyl group is a new compound. Besides substituted chlorobenzenes, other aryl chlorides can also be employed as substrates. For example, 1-chloronaphthalene gave **4k** in a reasonable yield of 63%, and 2- and 3-chloropyridines afforded the products **4l** and **4l′** in yields of 53% and 48%, respectively.

It is worth mentioning that literature reported catalyst systems required the use of more reactive aryl bromides for the preparation of **4a′′**,[12] **4b'**,[12-13] **4c**,[6d,6i,12] **4d**,[6d,6g,6h,12-14] **4e′**,[6f,12] **4f**,[6d,12,15] **4i**,[6f,6h,6i,12-13,15b] **4i′**,[6f,12-13] **4k**, [6d,6g,6i,12-13,16] **4l**,[6g,6h,12-13,15a,16] and **4l′**.[14] The use of chloride analogs as reported herein is unprecedented. In the case of **4e**, **4g**, and **4h**, the only previous example using aryl chlorides instead of bromo analogs was likewise reported by us.[6a] However, our earlier reported palladium–NHC/phosphine complex required the expensive and air-sensitive PCy_3 ligand, a high Pd loading (2.5 mol%), and MW irradiation to afford **4e**, **4g**, and **4h** in comparable yields of 63%, 55%, and 56%, respectively. Even though chlorobenzene was successfully applied in the formation of **4j**, again high Pd loading (2.5–5.0 mol%) and the PCy_3 ligand were required in the reported catalyst systems.[6a,17]

To confirm the practicability of the catalyst system in synthetic organic chemistry, the direct arylation reaction between 1,2-dimethylimidazole and 4-chlorobenzonitrile was successfully scaled up from 1 to 5 mmol, yielding 0.76 g, 77% of **4e** (Scheme 4).



Scheme 4. The direct arylation reaction between 1,2-dimethylimidazole and 4-chlorobenzonitrile in a preparative scale.

In addition, heterocycles other than 1,2-dimethylimidazole were tested (Table 4). Entries 1-3 indicate that 1-methylimidazoles can be applied as substrates in the coupling reaction with aryl chlorides. Despite the presence of an apparent acidic hydrogen

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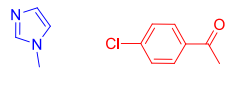
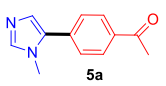
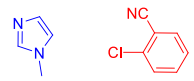
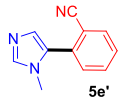
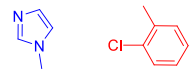
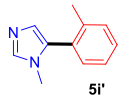
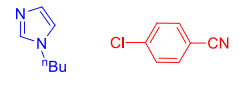
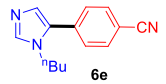
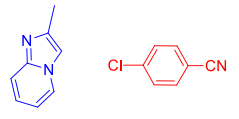
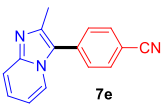
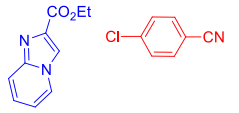
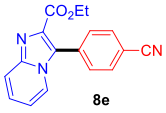
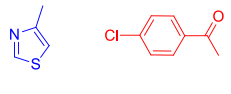
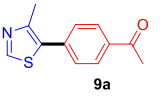
on the C2 position of the heterocycle, the arylation is regioselective, producing exclusively C5-arylated products. **5a** was obtained in a good yield of 73% when electron-deficient 4-chloroacetophenone was used as the substrate (entry 1). Interestingly, replacing the Me group with an H in the C2 position of 1-methylimidazole reduced both the electron-richness of the heterocyclic ring and the steric hindrance around the palladium species, leading to an increase in yield. Specifically, the reaction between sterically hindered 2-chlorobenzonitrile and 1-methylimidazole gave **5e'** in a good yield of 68% (entry 2), whereas a lower yield of 52% was obtained for **4e'** in the reaction with 1,2-dimethylimidazole and the same aryl chloride (Table 3). This observation is further confirmed when 2-chlorotoluene was used as a substrate; a good yield of 71% for **5i'** was obtained with 1-methylimidazole (entry 3), but the yield was reduced to 52% when 1,2-dimethylimidazole was used (see **4i'** in Table 3). Entry 4 shows that 1-butylimidazole also reacted smoothly with 4-chlorobenzonitrile to produce **6e,** a new compound, in a good yield of 82%. Imidazo[1,2-*a*]pyridine derivatives are important heterocycles displaying a range of biological activities.[18] The new catalyst system also allows for the use of 2-substituted imidazo[1,2-*a*]pyridines in the coupling reaction with activated 4-chlorobenzonitrile, affording 2,3-disubstituted imidazo[1,2-*a*]pyridine **7e** and a new compound, **8e** in good yields (entries 5 and 6). However, the catalyst system failed to give any coupling product when unsubstituted imidazo[1,2-*a*]pyridine was employed. Arylthiazole derivatives are also important heterocyclic compounds with a wide range of biological and material applications.[19] 4-Methyl-thiazole was successfully employed as a substrate in the reaction with 4-chloroacetophenone, producing the 4,5-disubstituted-thiazole **9a** in a mediocre yield of 45% (entry 7).

The superior catalytic performance of **2b** was again demonstrated in our preparation of **5i′**, [6c, 20] **5e′**,[21] and **9a**,[6h,15a,19,22] which were previously prepared exclusively from the corresponding aryl bromides, not chlorides. In a literature example, 2-bromotoluene was used for the preparation of **5i′** in the presence of 2.5—5.0 mol% Pd loading and gave yields in the range of 35–68%, compared to a 71% yield for our reaction conditions (see entry 3).[6c,20] There were only two catalyst systems reported for the preparation of **5a** from the less reactive 4-chloroacetophenone.[6a,6c] However, both these catalyst systems require 2.5 mol% of Pd loading and phosphine ligands, giving 32–70% yields, compared to a 73% yield catalyzed by **2b** (see entry 1). Similarly, compound **7e** was reported to arise from 4-chlorobenzonitrile; however a 2.5 mol% loading of Pd and the expensive PAd_2Bu ligand were required to produce the same yield of 75% (see entry 5).[23]

Table 4. Direct Arylation Reaction of Heterocycles with Aryl Chlorides [a)]

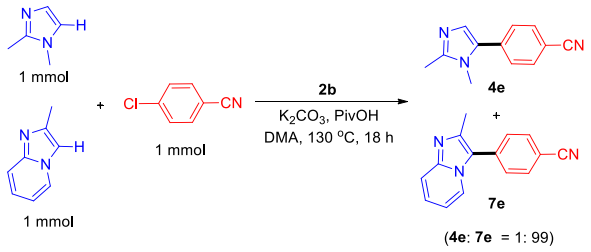
Entry	Substrate	Product	Yield (%)
1			73%
2			68%
3			71%
4			82%
5			75%
6			64%
7			45%

[a)] Reaction conditions: heterocycle (2 mmol), aryl halide (1 mmol), K_2CO_3 (2 mmol), PivOH (0.3 mmol), DMA (3 mL), [Pd_2] cat. (0.75 mol%), 130 °C, 18 h. Isolated yield.

For palladium-catalyzed direct arylation reactions of heteroaromatics with aryl halides, electrophilic aromatic substitution (S_EAr)[4a,24], and concerted metalation-deprotonation (CMD)[15b,25] pathways have the most experimental and theoretical support. The absence of discrimination in the reactions of 1,2-dimethylimidazole with aryl chlorides containing a *para* electron-donating and electron-withdrawing groups (see Table 3, **4h**: –OMe, 61%; **4i**: –CH_3, 71%; **4a**: –$COCH_3$, 69%; **4e**: –CN, 75%) seems to exclude the S_EAr pathway.[26] In addition, the general trend of higher activity observed for 1-methylimidazole compared to that for the more electron-rich 1,2-dimethylimidazole (see Table 3 and Table 4) is consistent with the CMD pathway. However, this difference could be attributed to the steric bulk of an additional methyl group (*vide supra*). To provide further evidence, a competition experiment was performed; electron-rich 1,2-dimethylimidazole was allowed to compete with 2-methylimidazo[1,2-*a*]pyridine in the reaction with 4-chlorobenzonitrile (Scheme 5). For the electrophilic aromatic substitution pathway, the more electron-rich 1,2-dimethylimidazole should be favored; but the product ratio of 1:99 of **4e**:**7e** suggests that the less-electron rich 2-methylimidazo[1,2-*a*]pyridine is a superior substrate, which is compatible with the CMD mechanistic pathway. Furthermore, the crucial role of the in situ generated potassium pivalate, which served as a soluble proton transfer agent,[4f,27] in the

enhancement of catalytic activity also implies the involvement of this pathway (see Table 2, entry 8).

It has been shown that palladium-catalyzed cross-coupling reactions can also proceed via heterogeneous mechanistic pathways.[28] A mercury drop test[29] was performed on the benchmark reaction between 1,2-dimethylimidazole and 4-bromoacetophenone catalyzed by **2b** in order to understand the possible involvement of heterogeneous species. In the presence of mercury, the product yield was markedly reduced from quantitative (see entry 2 in Table 1) to 37%. This suggested that beside homogeneous pathways, the possible involvement of heterogeneous species in the catalytic cycle cannot be excluded.



Scheme 5. Competition experiment.

Conclusion

A series of new ditopic bis(NHC) ligand precursors with aromatic linkers and their dimetallic PEPPSI-themed palladium complexes was successfully synthesized. We demonstrated that a dimetallic palladium complex was more effective than the related mononuclear palladium complex in catalyzing C5-direct arylation reactions of heterocycles with aryl halides. The dimetallic palladium–NHC complex bearing 9,10-anthracenyl spacer was the most efficient precatalyst, enabling effective utilization of a broad range of aryl chlorides. The catalyst system allows for the effective use of aryl chlorides to prepare arylated heterocycles which were previously accessible only with the use of more reactive bromide or iodide analogs. This work demonstrates the tractability of dimetallic palladium catalyst motifs for use in direct arylation reactions.

Experimental Section

General Information

All manipulations were performed under a dry nitrogen atmosphere using standard Schlenk techniques. Solvents were dried with standard procedures. Starting chemicals were purchased from commercial source and used as received. ^{1}H, ^{13}C{^{1}H} and ^{31}P{^{1}H} NMR spectra were recorded at 300.13, 75.47 and 121.49 MHz, respectively, on a Bruker AV-300 spectrometer. Elemental analyses were performed on a Thermo Flash 2000 CHN-O elemental analyzer. HRESI and HREI were carried out on a Thermo Fisher LTQ Orbitrap XL mass spectrometer and a Thermo Q Exactive Plus mass spectrometer, respectively, at Instrument Center of National Chung Hsing University (Taiwan). 1-(Naphthalen-1-yl)-*1H*-imidazole[30] and 9,10-di(*1H*-imidazol-1-yl)anthracene,[31] 1-(4-bromophenyl)-1*H*-imidazole[32] were prepared according to the literature procedures.

Synthesis of 1,4-di(1*H*-imidazol-1-yl)naphthalene

To a 50 mL Schlenk flask, 1,4-dibromonaphthalene (2.0 g, 6.99 mmol), 1*H*-imidazole (1.19 g, 17.5 mmol), CuI (0.4 g, 2.09 mmol), and Cs_2CO_3 (9.11 g, 28.0 mmol) were dissolved in dry DMF (20 mL) under nitrogen atmosphere. The solution was allowed to stir at 120 °C for 40 h. Solvent was removed under vacuum and the residue was washed with water and extracted with DCM. The extract was dried over anhydrous $MgSO_4$ and then purified by column chromatography (MeOH/ethyl acetate). Yield: 0.93 g (51 %). Mp = 215.1–215.8 °C. ^{1}H NMR ($CDCl_3$): δ 6.95-7.03 (m, 5H, Ar *H*), 7.30-7.40 (m, 5H, Ar *H*), 7.50 (s, 2H, NC*H*N). ^{13}C{^{1}H} NMR (DMSO-d_6): δ 122.9, 123.9, 128.6 (quaternary *C*), 128.9, 129.9, 131.0 (quaternary *C*), 140.4 (N*C*HN). HRMS (EI) *m*/*z* calcd for $C_{16}H_{12}N_4$ $[M]^+$ 260.1061, found 260.1064.

Synthesis of 1,1'-(Naphthalene-1,4-diyl)bis(3-(2-(methyl(phenyl)amino)-2-oxoethyl)-1*H*-imidazol-3-ium) (1a)

A mixture of 1,4-di(1*H*-imidazol-1-yl)naphthalene (0.5 g, 1.92 mmol) and 2-chloro-*N*-methyl-*N*-phenylacetamide (1.06 g, 5.76 mmol) in DMF (30 mL) was placed in a Schlenk flask. The mixture was heated at 120 °C for 12 h. After cooling, the white solid was collected on a frit, washed with DCM, and dried under vacuum.Yield: 1.16 g (96 %). Mp = 271.3–272.5 °C. ^{1}H NMR (DMSO-d_6): δ 3.30 (s, 6H, C*H*$_3$), 5.18 (s, 2H, C*H*$_2$), 7.52-7.72 (m, 12H, Ar *H*), 7.91 (s, 2H, Ar *H*), 8.12 (d, *J* = 15.0 Hz, 4H, Ar *H*), 8.25 (s, 2H, Ar *H*), 9.87 (s, 2H, NC*H*N). ^{13}C{^{1}H} NMR (DMSO-d_6): δ 38.1 (*C*H$_3$), 51.8 (*C*H$_2$), 122.8, 124.5, 125.5, 125.6, 128.3, 129.2, 129.3 (quaternary *C*), 130.8, 134.0 (quaternary *C*), 140.3 (N*C*HN), 141.9 (quaternary *C*), 165.1 (*C*=O). HRMS (ESI) *m*/*z* calcd for $C_{34}H_{32}N_6O_2$ $[M–2Cl]^{2+}$ 278.1293, found 278.1287.

Synthesis of 1,1'-(Anthracene-9,10-diyl)bis(3-(2-(methyl(phenyl)amino)-2-oxoethyl)-1*H*-imidazol-3-ium) (1b)

The compound was prepared with a similar procedure to that of **1a**. A mixture of 9,10-di(*1H*-imidazol-1-yl)anthracene (0.5 g, 1.61 mmol) and 2-chloro-*N*-methyl-*N*-phenylacetamide (0.59 g, 3.22 mmol) were used. Yield: 1.1 g (70 %). Mp = 307–308 °C. ^{1}H NMR (DMSO-d_6): δ 3.33 (s, 6H, C*H*$_3$), 5.29 (s, 4H, C*H*$_2$), 7.53–7.62 (m, 14H, Ar *H*), 7.89–7.93 (m, 4H, Ar *H*), 8.28–8.33 (m, 4H, imi *H*, Ar *H*), 10.06 (s, 2H, NC*H*N). ^{13}C{^{1}H} NMR (DMSO-d_6): δ 37.9 (*C*H$_3$), 52.0 (*C*H$_2$), 122.3, 125.3, 126.1, 127.8 (quaternary *C*), 128.2, 129.2, 129.4 (quaternary *C*), 130.3, 130.6, 141.4 (N*C*HN), 141.8 (quaternary *C*), 165.0 (*C*=O). HRMS (ESI) *m*/*z* calcd for $C_{38}H_{34}N_6O_2$ $[M–2Cl]^{2+}$ 303.1371, found 303.1358.

Synthesis of 1,1'-(Naphthalene-1,4-diyl)bis(3-(2-oxo-2-(phenylamino)ethyl)-1*H*-imidazol-3-ium) Chloride (1c)

The compound was prepared with a similar procedure to that of **1a**. A mixture of 1,4-di(1*H*-imidazol-1-yl)naphthalene (0.5 g, 1.92 mmol) and 2-chloro-*N*-phenylacetamide (0.65 g, 3.84 mmol) were used. Yield: 1.15 g (94 %). Mp = 213–214 °C. ^{1}H NMR (DMSO-d_6): δ 5.52 (s, 4H, C*H*$_2$), 7.12 (t, *J* = 6.0 Hz, 2H, Ar *H*), 7.37 (t, *J* = 9.0 Hz, 4H, Ar *H*), 7.71 (d, *J* = 6.0 Hz, 4H, Ar *H*), 7.80–7.83 (m, 2H, Ar *H*), 7.94–7.96 (m, 2H, Ar *H*), 8.20 (s, 2H, Ar *H*), 8.25 (s, 2H, imi *H*), 8.32 (s, 2H, imi *H*), 9.96 (s, 2H, NC*H*N), 11.22 (s, 2H, N*H*). ^{13}C{^{1}H} NMR (DMSO-d_6): δ 52.3 (*C*H$_2$), 119.7, 122.8, 124.3, 124.6, 125.3, 125.4, 129.0 (quaternary *C*), 129.4, 130.5, 133.8 (quaternary *C*), 139.0 (quaternary *C*), 140.1 (N*C*HN), 164.0 (*C*=O). HRMS (ESI) *m*/*z* calcd for $C_{32}H_{28}N_6O_2$ $[M–2Cl]^{2+}$ 264.1136, found 264.1127.

Synthesis of 1-(2-(Methyl(phenyl)amino)-2-oxoethyl)-3-(naphthalen-1-yl)-1*H*-imidazol-3-ium Chloride (1d)

A mixture 1-(naphthalen-1-yl)-*1H*-imidazole (1.0 g, 5.2 mmol) and 2-chloro-*N*-methyl-*N*-phenylacetamide (0.95 g, 5.2 mmol) in THF (30 mL) was placed in a Schlenk flask. The mixture was heated under reflux for 24 h. After cooling, the white solid was collected on a frit, washed with THF, and dried under vacuum. Yield: 1.5 g (78 %). Mp = 188.3–189.4 °C. ^{1}H NMR (DMSO-d_6): δ 3.29 (s, 3H, CH_3), 5.18 (s, 2H, CH_2), 7.51-7.85 (m, 10H, Ar *H*), 8.07 (s, 1H, imi *H*), 8.20-8.30 (m, 3H, imi *H*, Ar *H*), 9.79 (s, 1H, NC*H*N). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 37.9 (*C*H$_3$), 51.8 (*C*H$_2$), 120.7, 123.0, 124.5, 124.6, 125.2, 127.7, 128.7, 128.8, 130.3, 130.7 (quaternary *C*), 131.5, 134.0 (quaternary *C*), 139.6 (N*C*HN), 140.9 (quaternary *C*), 164.5 (*C*=O). HRMS (ESI) *m*/*z* calcd for $C_{22}H_{20}N_3O$ [M–Cl]$^+$ 342.1606, found 342.1595.

Synthesis of Dinuclear Palladium Complex 2a

To a 20 mL Schlenk flask containing $PdCl_2$ (0.056 g, 0.32 mmol), **1a** (0.1 g, 0.16 mmol), pyridine (25.7 µL and potassium carbonate (0.13 g, 0.96 mmol) was added dry DMF (8 mL). The mixture was allowed to stir at 50 ºC for 12 h. The solvent was completely removed under vacuum. The residue was dissolved in dichloromethane. The organic layer was then washed twice with water. After drying with anhydrous magnesium sulfate, the solvent was completely removed under vacuum. The residue was washed with diethyl ether and filtered on a frit and dried under vacuum. Air stable yellow solid was obtained. Yield: 0.12 g (73 %); Mp 183.6-184.5 °C (dec.). ^{1}H NMR ($CDCl_3$): δ 3.37 (s, 6H, CH_3), 5.26-5.45 (m, 4H, CH_2), 7.22-7.80 (m, 26H, imi *H*, Py *H*, Ar *H*), 8.33-8.39 (m, 2H, Py *H*), 8.63 (d, *J* = 3.0 Hz, 2H, Py *H*). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 37.9 (*C*H$_3$), 51.8 (*C*H$_2$), 123.7, 124.1, 124.3 (Py *C*), 124.9, 126.5, 127.8, 128.0, 128.7 (quaternary *C*), 130.2, 130.3, 136.4 (quaternary *C*), 138.0 (Py *C*), 142.4 (quaternary *C*), 151.1 (Py *C*), 166.0 (*C*=O), 166.1 (Pd—*C*). Anal. Calc. for $C_{44}H_{40}Cl_4N_8O_2Pd_2$: C, 49.50; H, 3.77; N, 10.49. Found: C, 49.33; H, 3.66; N, 10.38 %.

Synthesis of Dinuclear Palladium Complex 2b

The compound was prepared with a similar procedure to that of **2a**. A mixture of $PdCl_2$ (0.052 g, 0.30 mmol), **1b** (0.1 g, 0.15 mmol), pyridine (23.8 µL, 0.30 mmol), and K_2CO_3 (0.12 g, 0.88 mmol) were used. Yield: 0.11 g (67 %). Mp =190.3–191.5 °C. (dec.) ^{1}H NMR (DMSO-d_6): δ 3.46 (s, 6H, CH_3), 5.61 (s, 4H, CH_2), 7.31-8.31 (m, 30H, imi *H*, Py *H*, Ar *H*), 8.75 (d, *J* = 6.0 Hz, 2H, Py *H*). ^{13}C{^{1}H} NMR (DMSO-d_6): δ 37.8 (*C*H$_3$), 52.4 (*C*H$_2$), 125.1 (Py *C*), 125.3, 126.0, 127.3, 127.7 (quaternary *C*), 128.3, 128.4, 128.9, 130.4 (quaternary *C*), 130.6, 139.3 (Py *C*), 143.0 (quaternary *C*), 151.0 (Py *C*), 166.1 (*C*=O), 166.2 (Pd—*C*). Anal. Calc. for $C_{48}H_{42}Cl_4N_8O_2Pd_2$: C, 51.58; H, 3.78; N, 10.02. Found: C, 51.52; H, 4.02; N, 10.47 %.

Synthesis of Dinuclear Palladium Complex 2c

The compound was prepared with a similar procedure to that of **2a**. A mixture of $PdCl_2$ (0.059 g, 0.34 mmol), **1c** (0.10 g, 0.17 mmol), PPh_3 (0.088 g, 0.34 mmol), and K_2CO_3 (0.18 g, 1.3 mmol) were used. Yield: 0.10 g (65 %). Mp =194.4–195.1 °C (dec.). ^{1}H NMR (DMSO-d_6): δ 4.83 (d, *J* = 15.0 Hz, 2H, CH_aH$_b$), 5.77 (d, *J* = 12.0 Hz, 2H, CH$_a$*H*$_b$), 6.78-7.56 (m, 46H, imi *H*, Ar *H*), 7.83-8.20 (m, 4H, Ar *H*). ^{13}C{^{1}H} NMR (DMSO-d_6): δ 58.8 (*C*H$_2$), 119.9, 122.5, 123.7, 124.2, 124.4, 124.9, 127.3, 127.6, 128.6 (d, *J* = 9.8 Hz, Ar *C*), 129.2 (d, *J* = 12.1 Hz, Ar *C*), 130.0 (quaternary *C*), 131.2, 132.9 (d, *J* = 9.8 Hz, Ar *C*), 132.4, 132.5, 133.8 (quaternary *C*), 134.3 (d, *J* = 18.0 Hz, Ar *C*), 148.9 (quaternary *C*), 161.6 (Pd—*C*), 168.4 (*C*=O). ^{31}P{^{1}H} NMR (DMSO–d_6): δ 26.6. Anal. Calc. for $C_{68}H_{54}Cl_2N_6O_2P_2Pd_2$: C, 61.27; H, 4.08; N, 6.30. Found: C, 61.62; H, 3.99; N, 6.11 %.

Synthesis of Palladium Complex 2d

The compound was prepared with a similar procedure to that of **2a**. A mixture of $PdCl_2$ (0.051 g, 0.29 mmol), **1d** (0.11 g, 0.29 mmol), pyridine (23.0 µL, 0.29 mmol), and K_2CO_3 (0.080 g, 0.58 mmol) were used. Yield: 0.15 g (87 %). Mp =176.3–177.1 °C (dec.). ^{1}H NMR ($CDCl_3$): δ 3.37 (s, 3H, CH_3), 5.38 (s, 2H, CH_2), 7.15-7.21 (m, 3H, Ar *H*), 7.35-7.65 (m, 11H, imi *H*, Py *H*, Ar *H*), 7.91 (t, *J* = 6.0 Hz, 1H, Py *H*), 7.97 (d, *J* = 9.0 Hz, 1H, Ar *H*), 8.09 (d, *J* = 6.0 Hz, 1H, Ar *H*), 8.57 (d, *J* = 3.0 Hz, 1H, Py *H*). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 37.9 (*C*H$_3$), 51.8 (*C*H$_2$), 123.5, 124.2 (Py *C*), 124.6, 125.1, 126.8, 127.0, 127.3, 127.8, 128.0, 128.7, 129.8, 130.2, 134.2 (quaternary *C*), 135.2 (quaternary *C*), 137.9 (Py *C*), 142.4 (quaternary *C*), 151.1 (Py *C*), 152.4 (Pd—*C*), 166.1 (*C*=O). Anal. Calc. for $C_{27}H_{24}Cl_2N_4OPd$: C, 54.24; H, 4.04; N, 9.37. Found: C, 54.35; H, 4.12; N, 8.98 %.

Synthesis of Palladium Complex 3d

To a 20 mL Schlenk flask containing **2d** (0.11 g, 0.18 mmol) and PPh_3 (0.056 g, 0.21 mmol) in dichloromethane (10 mL) was stirred at ambient temperature for 5h. The solvent was removed completely under vacuum. The residue was washed thoroughly with THF to afford a pale yellow solid. Yield: 0.084 g (60 %). Mp = 267.7–268.4 °C. ^{1}H NMR ($CDCl_3$): δ 3.24 (s, 3H, CH_3), 5.18 (d, *J* = 6.0 Hz, 2H, CH_2), 6.45 (d, *J* = 9.0 Hz, 1H, imi *H*), 6.82–8.01 (m, 27H, imi *H*, Ar *H*), 9.05 (d, *J* = 9.0 Hz, 1H, Ar *H*). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 37.9 (*C*H$_3$), 52.4 (*C*H$_2$), 121.1, 124.2, 126.0, 126.2, 127.3, 127.4, 127.7, 128.0, 128.2 (d, *J* = 11.3 Hz, Ar *C*), 128.6, 129.0, 129.5 (quaternary *C*), 129.7 (quaternary *C*), 130.6 (d, *J* = 14.3 Hz, Ar *C*), 133.8 (d, *J* = 10.6 Hz, Ar *C*), 134.3 (quaternary *C*), 141.8 (quaternary *C*), 163.9 (Pd—*C*), 165.4 (*C*=O). ^{31}P{^{1}H} NMR ($CDCl_3$): δ 26.9. Anal. Calc. for $C_{40}H_{34}Cl_2N_3OPPd$: C, 61.61; H, 4.39; N, 5.39. Found: C, 61.97; H, 4.43; N, 5.40 %.

General Procedure for Palladium-Catalyzed Direct C-H Arylation Reaction of Heteroaromatic Compounds

In a Schlenk tube was charged with aryl chloride (1 mmol), heteroaromatic (2 mmol), K_2CO_3 (276 mg, 2.0 mmol), PivOH (30 mol%), Pd precatalyst (0.5–1.5 mmol% of monopalladium loading), and DMA (3 mL) under nitrogen atmosphere. The reaction mixture was sealed and heated at 130 °C for 18 h. The reaction mixture was cooled to ambient temperature, and H_2O (5 mL) was added, followed by extraction with ethyl acetate (3 × 10 mL). The organic phases were collected and dried over $MgSO_4$. All the volatiles were removed in vacuo, and the crude product was analyzed by GC chromatography using benzophenone as internal standard or purified by column chromatography. Each catalytic yield was an average of two runs.

1,2-Dimethyl-5-(*m*-tolyl)-1*H*-imidazole (4i'')

Yellow liquid (124 mg, 67 %), ethyl acetate:hexane = 2:1, R_f = 0.3; ^{1}H NMR (300MHz, $CDCl_3$) δ 7.34-7.29 (m, 1H), 7.17 (br s, 3H), 6.94 (s, 1H), 3.53 (s, 3H), 2.45 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (75MHz, $CDCl_3$) δ 145.9, 138.4, 133.7, 130.5, 129.3, 128.6, 128.4, 125.7, 125.6, 31.4, 21.5, 13.7. HRMS (EI) calcd for $C_{12}H_{14}N_2$ [M]$^+$: 186.1157, found: 186.1154.

4-(1-Butyl-1*H*-imidazol-5-yl)benzonitrile (6e)

Yellow oil, (184 mg, 82 %), ethyl acetate:hexane = 3:1, R_f = 0.3; ^{1}H NMR (300MHz, $CDCl_3$) δ 7.75 (d, *J* = 9.0Hz, 2H), 7.62 (s, 1H), 7.51 (d, *J* = 6.0Hz, 2H), 7.17 (s, 1H), 4.02 (t, *J* = 9.0Hz, 2H), 1.68-1.59 (m, 2H), 1.31-1.19 (m,2H), 0.84 (t, *J* = 9.0Hz, 3H); ^{13}C NMR (75MHz, $CDCl_3$) δ 139.6, 134.9, 132.6, 131.1, 129.8, 128.6, 118.6, 111.4, 45.5, 32.9, 19.6, 13.4. HRMS (EI) calcd for $C_{14}H_{15}N_3$ [M]$^+$: 225.1266, found: 225.1265.

Ethyl 3-(4-cyanophenyl)imidazo[1,2-*a*]pyridine-2-carboxylate (8e).

Off-white solid (186 mg, 64 %), Mp: 189.5-190.8 °C, ethyl acetate:hexane = 1:3, R_f = 0.2; ^{1}H NMR (300MHz, $CDCl_3$) δ 7.94 (d, *J* = 6.0Hz, 1H), 7.86 (d, *J* = 9.0Hz, 2H), 7.76 (d, *J* = 9.0Hz, 1H), 7.68 (d, *J* = 9.0Hz, 2H), 7.36-7.28 (m, 1H), 6.90 (t, *J* = 6.0Hz, 1H), 4.41-4.34 (m, 2H), 1.34 (t, *J* = 6.0Hz, 3H); ^{13}C NMR (75MHz, $CDCl_3$) δ 163.1, 144.8, 133.8, 132.9, 132.5, 131.5, 127.0, 126.8, 123.5, 119.4, 118.4, 114.5, 113.1, 61.3, 14.3. HRMS (EI) calcd for $C_{17}H_{13}N_3O_2$ $[M]^+$: 291.1008, found: 291.1011.

Mercury-drop test

In a Schlenk tube was charged with 4-bromoacetophene (1 mmol), 1,2-dimethylimidzole (2 mmol), K_2CO_3 (276 mg, 2.0 mmol), PivOH (30 mol%), Pd precatalyst **2b** (0.5 mmol%), and a drop of Hg in DMF (1 mL) under nitrogen atmosphere. The reaction mixture was sealed and heated at 130 °C for 12 h. The workup procedure was the same of the general procedure for the direct C—H arylation reaction. The product yield was analyzed by GC chromatography using benzophenone as internal standard. The catalytic yield was an average of two runs.

Single-crystal X-ray Diffraction

Samples were collected at 150(2) on a Bruker APEX II equipped with a CCD area detector and a graphite monochromator utilizing Mo Kα radiation (λ = 0.71073 Å). The unit cell parameters were obtained by least-squares refinement. Data collection and reduction were performed using the Bruker APEX2 and SAINT software.[33] Absorption corrections were performed using the SADABS program.[34] All the structures were solved by direct methods and refined by full-matrix least squares methods against F^2 with the SHELXTL software package.[35] All non-H atoms were refined anisotropically. All H atoms were fixed at calculated positions and refined with the use of a riding model. Disordered ether molecules in **2a** was refined using a rigid model. Heavily disordered DMF solvent molecules were found in an asymmetric unit of **2c** and a satisfactory refinement model was unable to achieve. Hence, SQUEEZE procedure implemented in the PLATON program suite was applied to remove the disordered solvent contribution to the structural factors.[36] Removing the DMF molecules led to a total accessible void of 3174.0 Å and 972 electrons in the unit cell. These results were in good agreement with the volume occupied by 24 DMF molecules in the unit cell (127 Å^3 and 40 electrons per DMF[37]). The *N*-phenyl ring in **2c** was disordered over two orientations of equal occupancy, which were refined with rigid group constraints. CCDC-1554094 (**2a**), -1554095 (**2c**), and -1554096 (**3d**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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FULL PAPER

Dimetallic Palladium–NHC Complexes: Synthesis, Characterization and Catalytic Application for Direct C—H Arylation Reaction of Heteroaromatics with Aryl Chlorides

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Jhen-Yi Lee, Debalina Ghosh, Ya-Ting Kuo and Hon Man Lee*