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Synthesis and characterization of *N*-heterocyclic carbene-palladium(II) chlorides-1-methylindazole and -1-methylpyrazole complexes and their catalytic activity toward C-N coupling of aryl chlorides

Xiao-Yun Zhao,[a] Quan Zhou[a] and Jian-Mei Lu*[a]

A series of *N*-heterocyclic carbene-palladium(II) chlorides-1-methylindazole and -1-methylpyrazole complexes was successfully synthesized and fully characterized by X-ray single crystal diffraction. In addition, initial investigations of their catalytic activity showed that they were efficient catalysts in the C-N coupling of primary and secondary amines with aryl chlorides at low catalyst loadings.

Introduction

Aryl amines are very important compounds in organic synthesis because of their potential applications in chemistry, pharmaceuticals, materials sciences and industries.[1] Besides the abundant traditional methods for the synthesis of such compounds,[2] the palladium-catalysed C-N cross-coupling reactions have become one of the most powerful methods due to their high efficiency of diverse substrates under mild conditions.[3] Among the organic electrophiles invovled, aryl chlorides seem to be the most desirable ones due to their lower cost, easy availability and higher stability compared to their iodide and bromide counterparts in spite of their lower reactivity.[4] To achieve efficient coupling of aryl chlorides, kinds of tertiary phosphine ligands, which are usually air- and thermal-sensitive, have been synthesized to date.[5] On the other hand, during the past years, *N*-heterocyclic carbenes (NHCs), which usually are air- and thermal-insensitive compared to phosphine ligands, have also been developed and successfully applied in the palladium-catalysed C-N coupling of aryl chlorides.[6] It may be noted here that in the palladium-phosphine catalytic systems, usually excess ligands over palladium salts are mandatory; while different from free phosphine ligands, NHCs are usually used as their palladium complexes, which thus have strict NHC/Pd ratio. In addition, the palladium salts and NHCs are in the same molecule, both of which can be added simultaneously, thus will also simplify the experimental procedures to some extent. However, their applications toward ideal practicality are still hampered by at least one of the following facts: (1) lengthy pathways are necessary for the synthesis of NHC precursors and the corresponding palladium complexes, especially for the synthesis of NHC precursors; (2) toxic pyridine derivatives are used as the solvents and ancillary ligands; (3) high catalyst loadings are required (usually 1.0-5.0 mol%). Therefore, great room still remains for the NHC-Pd(II) complexes-catalysed C-N coupling of aryl chlorides, especially with respect to the easy availability of the complexes and the lower loadings in catalysis.

Recently, we have developed a series of novel NHC-Pd(II)-2-aryl-4,5-dihydro-oxazole complexes from commercially available imidazolium salts such as IPr·HCl [1,3-bis-(2,6-diisopropylphenyl)imidazolium chloride], IMes·HCl [1,3-bis-(2,4,6-trimethylphenyl)imidazolium chloride], and IXy·HCl [1,3-bis-(2,6-dimethylphenyl)imidazolium chloride], $PdCl_2$ and 2-aryl-4,5-dihydrooxazoles in a one-pot procedure under mild conditions and have showed that they were efficient catalysts in the C-N coupling of primary and secondary amines with aryl chlorides at the catalyst loading of 0.5 mol%.[6c] The reported method includes the advantages of easy availability of the NHC-Pd(II) complexes and high efficiency in C-N coupling of aryl chlorides. These results thus prompted us to further develop new NHC-Pd(II)

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† Electronic Supplementary Information (ESI) available: [CCDC references numbers 1445502-1445505 for complexes **3a**-**d**, respectively. For crystallographic data in CIF and experimental details]. See DOI: 10.1039/x0xx00000x

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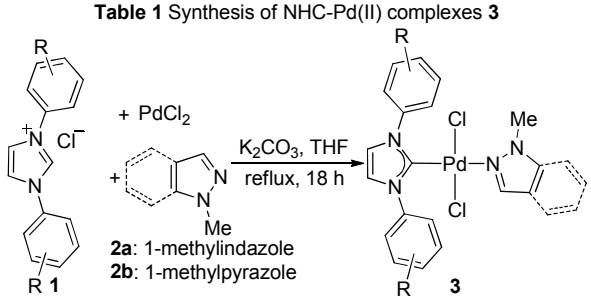
complexes and investigate their applications toward C-N coupling of aryl chlorides. In this case, a new series of NHC-Pd(II)-1-methylindazole and -1-methylpyrazole complexes was successfully obtained in good to high yields, and they demonstrated efficient catalytic activity toward C-N coupling of primary and secondary amines with aryl chlorides at lower catalyst loadings to 0.03 mol%. Herein, we report these results in detail.

Results and discussion

Synthesis of NHC-Pd(II) complexes

The NHC-Pd(II) complexes were achieved by slightly modifying our previous process.[6c] In the general one-pot procedure, a mixture of commercially available imidazolium salts **1** (1.1 mmol), $PdCl_2$ (1.0 mmol), 1-methylindazole **2a** or 1-methylpyrazole **2b** and K_2CO_3 (1.04 mmol) in THF (3.0 mL) was stirred at 80 °C for 18 h. After normal flash chromatography by SiO_2 column, pure products **3** can then be obtained in acceptable to high yields (Table 1).

Table 1 Synthesis of NHC-Pd(II) complexes **3**



Entry[a]	**1** (R)	**2** (equiv)	Yield (%)[b]
1	**1a** (2,6-^{i}Pr$_2$)	**2a** (2.0)	**3a**, 51
2	**1a**	**2a** (3.0)	**3a**, 76
3	**1a**	**2b** (3.0)	**3b**, 25
4	**1a**	**2b** (4.0)	**3b**, 91
5	**1b** (2,6-Me$_2$)	**2b** (3.0)	**3c**, 9
6	**1b**	**2b** (4.0)	**3c**, 83
7	**1c** (2,4,6-Me$_3$)	**2b** (3.0)	**3d**, 21
8	**1c**	**2b** (4.0)	**3d**, 70

[a]All reactions were carried out using **1** (1.1 mmol), $PdCl_2$ (1.0 mmol), **2** and K_2CO_3 (1.04 mmol) in THF (3.0 mL) at 80 °C for 18 h. [b]Isolated yields.

All these four complexes were fully characterized by NMR, MS, and elemental analysis. In addition, all of them are stable enough in open air under ambient conditions. Crystals of **3a**-**d** were grown in the mixture of ethyl acetate and dichloromethane, which were then characterized by X-ray single crystal diffraction analysis. The molecular structures of them are shown in Figures 1-4, including representative bond lengths and bond angles, and selected crystallographic data of them are shown in Table 2. As expected, all complexes showed slightly distorted square-planar geometries around all palladium centers, which are coordinated by four ligands such as one carbene carbon atom, one N atom and two chlorine atoms, with the carbene carbon atom and N atom in the *trans*-configuration. The two chlorine atoms are almost perpendicular to the plane of NHC and 1-methylindazole or 1-methylpyrazole.

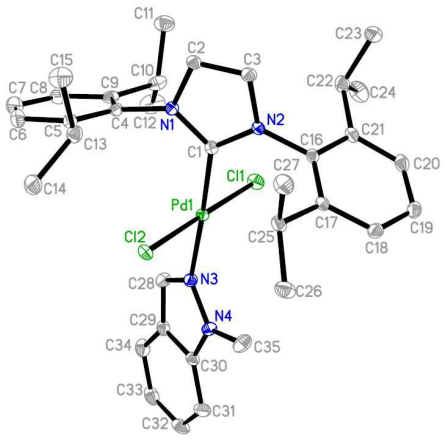


Fig. 1 The molecular structure of complex **3a** showing 30% probability ellipsoids; all hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and bond angles (°): Pd(1)-C(1) = 1.9680(19), Pd(1)-N(3) = 2.0862(16), Pd(1)-Cl(2) = 2.2892(5), Pd(1)-Cl(1) = 2.2938(5), N(1)-C(1) = 1.358(2), N(2)-C(1) = 1.348(2); C(1)-Pd(1)-N(3) = 177.25(7), C(1)-Pd(1)-Cl(2) = 90.15(5), N(3)-Pd(1)-Cl(2) = 90.06(5), C(1)-Pd(1)-Cl(1) = 90.55(5), N(3)-Pd(1)-Cl(1) = 89.27(5), Cl(2)-Pd(1)-Cl(1) = 178.975(19).

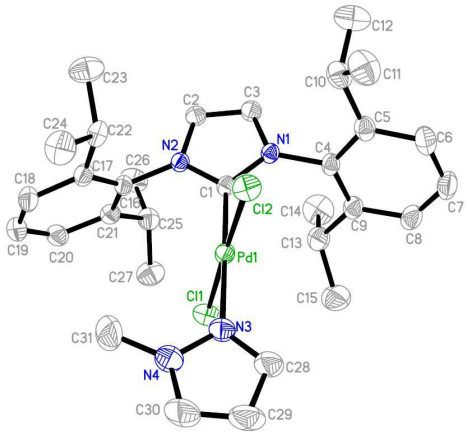


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Fig. 2 The molecular structure of complex **3b** showing 30% probability ellipsoids; all hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and bond angles (°): Pd(1)-C(1) = 1.972(3), Pd(1)-N(3) = 2.093(3), Pd(1)-Cl(2) = 2.2938(10), Pd(1)-Cl(1) = 2.3020(10), N(1)-C(1) = 1.349(4), N(2)-C(1) = 1.352(4); C(1)-Pd(1)-N(3) = 178.06(13), C(1)-Pd(1)-Cl(2) = 88.69(9), N(3)-Pd(1)-Cl(2) = 89.84(10), C(1)-Pd(1)-Cl(1) = 92.82(9), N(3)-Pd(1)-Cl(1) = 88.68(10), Cl(2)-Pd(1)-Cl(1) = 178.18(4).

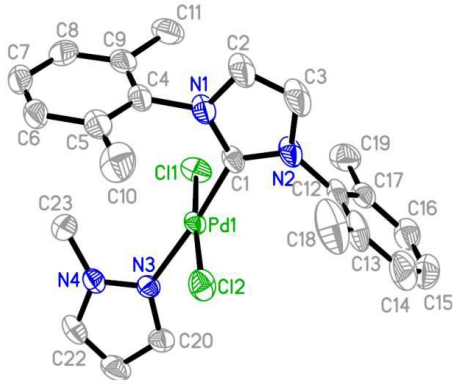

Fig. 3 The molecular structure of complex **3c** showing 30% probability ellipsoids; all hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and bond angles (°): Pd(1)-C(1) = 1.968(3), Pd(1)-N(3) = 2.088(3), Pd(1)-Cl(2) = 2.2948(11), Pd(1)-Cl(1) = 2.3178(11), N(1)-C(1) = 1.367(4), N(2)-C(1) = 1.358(4); C(1)-Pd(1)-N(3) = 173.78(11), C(1)-Pd(1)-Cl(2) = 89.40(12), N(3)-Pd(1)-Cl(2) = 88.60(8), C(1)-Pd(1)-Cl(1) = 91.73(11), N(3)-Pd(1)-Cl(1) = 90.84(8), Cl(2)-Pd(1)-Cl(1) = 174.30(4).

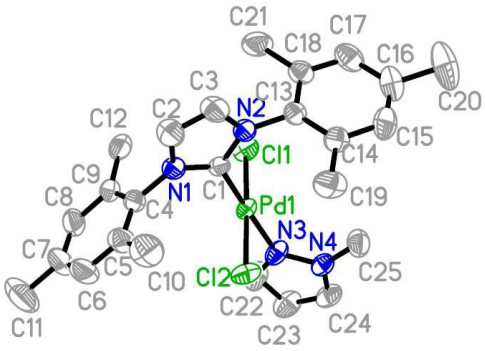

Fig. 4 The molecular structure of complex **3d** showing 30% probability ellipsoids; all hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and bond angles (°): Pd(1)-C(1) = 1.972(4), Pd(1)-N(3) = 2.089(3), Pd(1)-Cl(1) = 2.2931(13), Pd(1)-Cl(2) = 2.3048(13), N(1)-C(1) = 1.352(5), N(2)-C(1) = 1.349(5); C(1)-Pd(1)-N(3) = 177.35(16), C(1)-Pd(1)-Cl(1) = 92.65(11), N(3)-Pd(1)-Cl(1) = 89.06(12), C(1)-Pd(1)-Cl(2) = 88.96(11), N(3)-Pd(1)-Cl(2) = 89.40(12), Cl(1)-Pd(1)-Cl(2) = 177.57(5).

Table 2 Crystal data and structure refinement details for complexes **3a**-**d**

Complex	**3a**	**3b**	**3c**	**3d**
Formula	$C_{35}H_{44}Cl_2N_4Pd$	$C_{31}H_{42}Cl_2N_4Pd{\cdot}CH_3CO_2Et{\cdot}H_2O$	$C_{23}H_{26}Cl_2N_4Pd$	$C_{25}H_{30}Cl_2N_4Pd$
Formula weight	698.04	754.11	535.78	563.83
Temperature of measurement (K)	100(2)	100(2)	100(2)	100(2)
Crystal system	Monoclinic	Monoclinic	Triclinic	Monoclinic
Space group	P21/C	P21/n	P-1	P21/n
a (Å)	10.5287(11)	15.909(3)	9.1155(18)	16.484(4)
b (Å)	12.2427(12)	14.083(2)	13.036(3)	16.074(4)
c (Å)	26.839(3)	17.085(3)	20.075(4)	21.788(6)
α (°)	90	90	87.103(4)	90
β (°)	94.179(2)	92.674(3)	89.823(4)	109.467(4)
γ (°)	90	90	89.630(4)	90
Volumn (Å^3)	3450.3(6)	3823.4(10)	2382.4(9)	5443(2)
Z	4	4	4	8
Crystal size (mm)	0.29x0.25x0.22	0.29x0.23x0.21	0.31x0.25x0.22	0.32x0.26x0.23
F(000)	1448	1576	1088	2034
Theta range for data collection (°)	1.52-26.00	1.71-26.00	1.02-26.00	1.35-26.00
Goodness-of-fit on F^2	1.008	1.107	1.047	1.086
Final R indices [$I>2\sigma(I)$]	R_1 = 0.0228	R_1 = 0.0418	R_1 = 0.0321	R_1 = 0.0464

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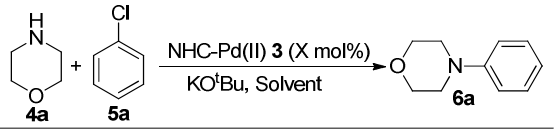
	wR_2 = 0.0737	wR_2 = 0.1325	wR_2 = 0.0890	wR_2 = 0.1399
R indices (all data)	R_1 = 0.0250 wR_2 = 0.0824	R_1 = 0.0505 wR_2 = 0.1428	R_1 = 0.0456 wR_2 = 0.1006	R_1 = 0.0712 wR_2 = 0.1626

C-N coupling reactions

Once the structures of the above NHC-Pd(II) complexes **3** were fully characterized, their activity toward C-N coupling of aryl chlorides was then investigated systematically. The representative results are illustrated in Table 3. Initially, using morpholine **4a** (1.2 mmol) and chlorobenzene **5a** (1.0 mmol) as the substrates, **3a** (0.1 mol%) as the catalyst, a variety of bases (1.3 equiv) were tested in THF (1.0 mL) at 90 °C for 1 h. In these cases, KO^{t}Bu gave the best yield (93%) (Table 3, entry 1) over NaO^{t}Bu (84%) and KOH (20%). In the presence of other bases such as LiO^{t}Bu, NaOH, K_2CO_3, Na_2CO_3, $KHCO_3$, Cs_2CO_3, K_3PO_4 and CH_3COOK, almost no desired product can be detected. In the presence of KO^{t}Bu, some common solvents were tested, and the same yield was obtained in toluene (Table 3, entry 2), while in polar solvents such as DMF and DMSO, very low yields were observed in both cases (4% and 16%, respectively). Based on the above results, the catalytic activity of complex **3a** was further tested in decreased loading of 0.05 mol% using KO^{t}Bu as the base in THF and toluene, respectively. It was found that by elevating the temperature to 110 °C, somewhat higher yield can still be achieved in THF within 1 h (Table 3, entry 4), while that in toluene became very low (Table 3, entry 5). Upon further decreasing the catalyst loading to 0.03 mol%, similar high yield can still be achieved when the reaction was performed in THF at 130 °C for 12 h (Table 3, entry 7). Based on the above results, other NHC-Pd(II) complexes **3** were also examined (Table 3, entries 10-12). For example, in the presence of NHC-Pd(II) complex **3b**, product **6a** can be obtained in 85% yield (Table 3, entry 10); however, very low yields were observed when complexes **3c** and **3d** were used as the catalysts under identical conditions (Table 3, entries 11 and 12).

Table 3 Optimization for the C-N coupling reaction



4a **5a** **6a**

Entry[a]	**3** (X)	Temp. (°C)	Time (h)	Yield (%)[b]
1	**3a** (0.1)	90	1	93
2[c]	**3a** (0.1)	90	1	93
3	**3a** (0.05)	100	1	67
4	**3a** (0.05)	110	1	97
5[c]	**3a** (0.05)	110	1	6
6	**3a** (0.03)	110	12	69
7	**3a** (0.03)	130	12	93
8	**3a** (0.01)	110	12	22
9	**3a** (0.01)	130	12	37
10	**3b** (0.05)	110	1	87
11	**3c** (0.05)	110	1	5
12	**3d** (0.05)	110	1	15

[a]Otherwise specified, all reactions were carried out using **4a** (1.2 mmol), **5a** (1.0 mmol), **3** (X mol%), KO^{t}Bu (1.3 equiv) in THF (1.0 mL). [b]Isolated yields. [c]Toluene instead of THF.

With the optimal conditions established, the generality and limitation of the reactions between a variety of secondary amines and aryl chlorides was first tested. The results are shown in Table 4. Most reactions performed well enough in the presence of 0.05 mol% **3a** at 110 °C within 1 h or 0.03 mol% **3a** at 130 °C within 12 h, giving the corresponding coupling products **6** in good to almost quantitative yields. Diverse electronic and sterically-hindered substituents on the aryl chlorides are all tolerated in such transformation. For instance, electron-rich groups such as methoxy and methyl group and electron-poor group such as fluorine atom are all tolerated to give the corresponding products in good to almost quantitative yields. Sterically-hindered substituted 2-methylphenyl chloride **5d** was also a suitable substrate to give products **6d**, **6k** and **6p** in 83-99% yields (Table 4, entries 4, 5, 14 and 22). It seems that the relative position of the same substituents on the phenyl groups of aryl chlorides affected the reactions to some extent. For example, *meta*-substituted aryl chlorides are better than *para*-ones, giving higher yields in all cases (Table 4, entries 1 *vs* 3, 6 *vs* 8 and 10 *vs* 9). To our pleasure, heterocyclic chloride such as 2-chloropyridine **5j** was also a good substrate, giving products **6s**-**6u** in good to high yields (Table 4, entries 25-27). In addition, these three reactions were also tested in the presence of PEPPSI[6af] under identical conditions, similar or a litter lower yields were observed in these cases.

Usually, primary amines were thought to be more poor organonucleophiles in the palladium-catalysed C-N coupling reactions. Based on the above satisfactory

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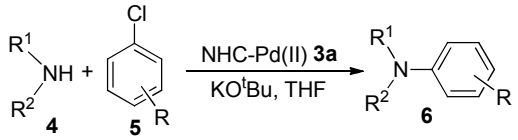
Table 4 NHC-Pd(II) complex **3a**-catalysed C-N coupling of secondary amines with aryl chlorides

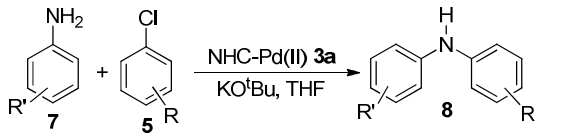


Entry[a]	4	5	Conditions	Yield (%)[b]
1	**4a**	**5b** (3-OMe)	**A**	**6b**, 95
2	**4a**	**5b**	**B**	**6b**, 90
3	**4a**	**5c** (4-OMe)	**A**	**6c**, 84
4	**4a**	**5d** (2-Me)	**A**	**6d**, 91
5	**4a**	**5d**	**B**	**6d**, 94
6	**4a**	**5e** (3-Me)	**A**	**6e**, 94
7	**4a**	**5e**	**B**	**6e**, 88
8[c]	**4a**	**5f** (4-Me)	**A**	**6f**, 89
9	**4a**	**5g** (4-F)	**A**	**6g**, 81
10	**4a**	**5h** (3-F)	**A**	**6h**, 93
11	**4a**	**5h**	**B**	**6h**, 82
12	**4a**	**5i** (4-vinyl)	**A**	**6i**, 86
13	**4b**	**5b**	**B**	**6j**, 95
14	**4b**	**5d**	**B**	**6k**, 99
15	**4b**	**5e**	**B**	**6l**, 86
16	**4c**	**5b**	**A**	**6m**, 90
17	**4c**	**5b**	**B**	**6m**, 96
18	**4c**	**5e**	**A**	**6n**, 80
19	**4c**	**5e**	**B**	**6n**, 96
20	**4d**	**5b**	**A**	**6o**, 91
21	**4d**	**5b**	**B**	**6o**, 99
22	**4d**	**5d**	**B**	**6p**, 83
23	**4d**	**5e**	**B**	**6q**, 99
24	**4d**	**5f**	**B**	**6r**, 99
25[d]	**4a**	**5j**	**A**	**6s**, 96 (89)
26[d]	**4c**	**5j**	**A**	**6t**, 80 (77)
27[d]	**4d**	**5j**	**A**	**6u**, 85 (85)

[a]Otherwise specified, the reaction conditions were as follows: **4** (0.84 mmol), **5** (0.7 mmol), KO^{t}Bu (1.3 equiv), THF (1.0 mL) and (**A**) **3a** (0.05 mol%), 110 °C, 1 h or (**B**) **3a** (0.03 mol%), 130 °C, 12 h. [b]Isolated yields. [c]The time was prolonged to 3 h. [d]The time was prolonged to 6 h and the yields in the parathesis were obtained catalysed by PEPPSI (Ref. 6af).

results on the NHC-Pd(II) complex **3a** catalysed C-N coupling between secondary amines and aryl chlorides, kinds of primary amines were also subjected to the optimal conditions to test the generality and limitations. The results are shown in Table 5. To our delight, it was found that the desired mono-arylated products **8** can also be achieved in good to almost quantitative yields under identical conditions. For instance, electron-rich, -poor and sterically-hindered groups substituted anilines are all tolerated to give the corresponding products in good to almost quantitative yields. The amination reactions between sterically-encumbered substrates seem to be a challenge in the previously reported methods, especially at low catalyst loadings. However, to our delight, both anilines and aryl chlorides bearing sterically-hindered substituents are suitable substrates under identical conditions. For example, 2-methylaniline **7b**, 2-methoxyaniline **7c**, 2,4-dimethylaniline **7e**, 2,4,6-trimethylaniline **7f**, 2,6-dimethylaniline **7g** and 2,6-di-isopropylaniline **7i** are all good substrates under the optimal conditions. In addition, 2-methylphenyl chloride **5d**, 2,6-dimethylphenyl chloride **5k** and 2,6-di-isopropylphenyl chloride **5l** are all compatible.

Table 5 NHC-Pd(II) complex **3a**-catalysed C-N coupling of primary amines with aryl chlorides



Entry[a]	7 (R')	5	Conditions	Yield (%)[b]
1[c]	**7a** (H)	**5d** (2-Me)	**A**	**8a**, 98
2	**7b** (2-Me)	**5d**	**A**	**8b**, 98
3[c]	**7c** (2-OMe)	**5d**	**A**	**8c**, 99
4	**7c**	**5d**	**B**	**8c**, 98
5	**7d** (4-Me)	**5d**	**A**	**8d**, 98
6	**7d** (4-Me)	**5d**	**B**	**8d**, 98
7	**7e** (2,4-Me$_2$)	**5d**	**A**	**8e**, 98
8	**7e**	**5d**	**B**	**8e**, 98
9	**7f** (2,4,6-Me$_3$)	**5d**	**A**	**8f**, 98
10	**7g** (2,6-Me$_2$)	**5d**	**A**	**8g**, 98
11	**7g**	**5d**	**B**	**8g**, 98
12	**7h** (4-OMe)	**5d**	**A**	**8h**, 98
13[c]	**7i** (2,6-^{i}Pr$_2$)	**5d**	**A**	**8i**, 92
14	**7j** (4-F)	**5d**	**A**	**8j**, 84
15	**7j**	**5d**	**B**	**8j**, 98
16	**7b**	**5k** (2,6-Me$_2$)	**A**	**8g**, 97
17	**7f**	**5k**	**A**	**8k**, 96
18	**7g**	**5k**	**A**	**8l**, 97
19[c]	**7f**	**5l** (2,6-^{i}Pr$_2$)	**A**	**8m**, 95

[a]Otherwise specified, the reaction conditions were as follows: **7** (0.84 mmol), **5** (0.7 mmol), KO^{t}Bu (1.3 equiv), THF (1.0 mL) and (**A**) **3a** (0.05 mol%), 110 °C, 1 h or (**B**) **3a** (0.03 mol%), 130 °C, 12 h. [b]Isolated yields. [c]The time was prolonged to 3 h.

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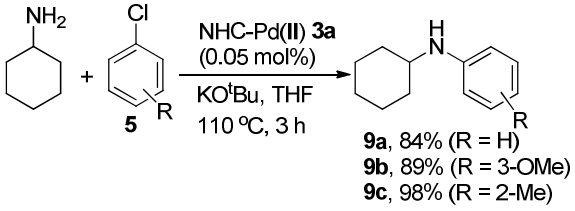
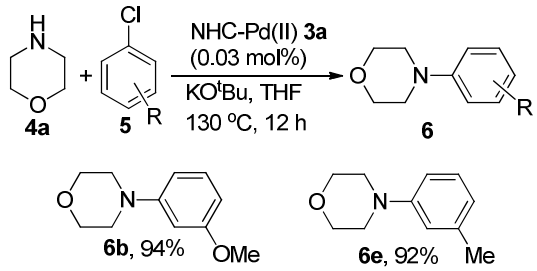
To make the complex more practicable in organic synthesis, the reactions of alkyl amine such as cyclohexylamine with aryl chlorides were also investigated under the optimal conditions. It was found that all reactions performed well enough to give the desired mono-arylated amines **9** in good to high yields (Scheme 1).

Scheme 1. Complex **3a** catalysed coupling of cyclohexylamine with aryl chlorides



In addition, gram-scale reactions between morpholine (42 mmol) and aryl chlorides (35 mmol) were also carried out in the presence of KO^tBu (1.3 equiv) and complex **3a** (0.03 mol%) in THF (10.0 mL) at 130 °C for 12 h, also giving the corresponding coupling products in high yields in both cases (Scheme 2).

Scheme 2. Complex **3a** catalysed gram-scale reactions



Experimental

General procedures

NMR spectra were recorded at 500 MHz (for ^{1}H NMR) or 125 MHz (for ^{13}C NMR), respectively. ^{1}H and ^{13}C NMR spectra recorded in $CDCl_3$ solutions were referenced to TMS (0.00 ppm) and the residual solvent peak (77.0 ppm), respectively. J values are given in Hz. The organic solvents used were dried by standard methods. The mass analyzer type for the high resolution mass spectra (HRMS) is quadrupole (for ESI). All amines were distilled prior to using. Other commercially obtained reagents were used without further purification. Flash column chromatography was performed on silica gel (300−400 mesh). X-ray single crystallography was performed on a Bruker APEX II area-detector graphite-monochromated Mo Kα radiation (λ = 0.71073 Å). The crystal data collection and refinement parameters are summarized in Table 2. Absorption correction was performed by SADABS (Bruker, 2002) program. The structures were solved by direct methods using the SHELXS-97 program and refined by full-matrix least squares techniques on F^2.

General procedure for the synthesis of NHC-Pd(II) complexes 3

Under a N_2 atmosphere, a mixture of imidazolium salts **1** (1.1 mmol), $PdCl_2$ (1.0 mmol), K_2CO_3 (1.04 mmol), the indicated amounts of **2** (Table 1) and anhydrous THF (3.0 mL) in a sealed tube was stirred at 80 °C for 18 h. Then the solvent was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 60:1 to 10:1) to give the pure NHC-Pd(II) complexes **3** as yellow solids.

Compound **3a**: yellow solid. m.p. 287 °C (decomposed). ^{1}H NMR ($CDCl_3$, 500 MHz, TMS) δ 7.82 (s, 1H), 7.56-7.52 (m, 3H), 7.40 (d, *J* = 8.0 Hz, 4H), 7.28 (d, *J* = 7.5 Hz, 1H), 7.17-7.15 (m, 3H), 7.02 (t, *J* = 7.5 Hz, 1H), 3.97 (s, 3H), 3.19 (hept, *J* = 6.5 Hz, 4H), 1.48 (d, *J* = 6.5 Hz, 12H), 1.12 (d, *J* = 6.5 Hz, 12H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 154.9, 146.9, 140.3, 135.1, 134.6, 130.2, 127.4, 125.0, 123.9, 122.9, 121.11, 121.08, 108.8, 36.0, 28.8, 26.4, 23.0. MS (ESI): 661 $[M\text{-}Cl]^+$. HRMS (ESI) calcd. for $C_{35}H_{44}ClN_4Pd$ $[M\text{-}Cl]^+$: 661.2294; found: 661.2281. Anal. calcd. for $C_{35}H_{44}Cl_2N_4Pd$: C, 60.22%; H, 6.53%; N, 8.03%; found: C, 60.09%; H, 6.24%; N, 8.04%. IR (neat) ν 2960, 2925, 2860, 1618, 1506, 1464, 1441, 1413, 1379, 1351, 1329, 1211, 1155, 1121, 1056, 1031, 972, 944, 911, 816, 802, 783 cm^{-1}.

Compound **3b**: yellow solid. m.p. 295 °C (decomposed). ^{1}H NMR ($CDCl_3$, 500 MHz, TMS) δ 7.51 (t, *J* = 7.5 Hz, 2H), 7.37 (d, *J* = 8.0 Hz, 4H), 7.27 (d, *J* = 2.5 Hz, 1H), 7.13 (s, 2H), 7.11 (d, *J* = 2.5 Hz, 1H), 6.04 (t, *J* = 2.5 Hz, 1H), 3.80 (s, 3H), 3.17 (hept, *J* = 7.0 Hz, 4H), 1.46 (d, *J* = 7.0 Hz, 12H), 1.10 (d, *J* = 7.0 Hz, 12H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 155.2, 146.9, 140.6, 135.1, 132.1, 130.2, 124.9, 123.9, 106.3, 39.4, 28.8, 26.3, 23.0. MS (ESI): 611 $[M\text{-}Cl]^+$. HRMS (ESI): calcd for $C_{31}H_{42}ClN_4Pd$ $[M\text{-}Cl]^+$: 611.2136; found: 611.2154. Anal. Calcd for $C_{31}H_{42}Cl_2N_4Pd$: C, 57.46; H, 6.53; N, 8.65. Found: C, 57.50; H, 6.61; N, 8.71. IR (neat) ν 2960, 2921, 2866, 1522, 1468, 1457, 1411, 1382, 1346, 1330, 1284, 1208, 1120, 1105, 1083, 1060, 937, 889, 801, 764 cm^{-1}.

Compound **3c**: yellow solid. m.p. 287 °C (decomposed). ^{1}H NMR ($CDCl_3$, 500 MHz, TMS) δ 7.36 (t, *J* = 7.5 Hz, 2H), 7.27 (s, 2H), 7.25 (s, 2H), 7.24 (dd, *J* = 2.5, 0.5 Hz, 1H), 7.14-7.13 (m, 3H), 6.05 (t, *J* = 2.5 Hz, 1H), 3.74 (s, 3H), 2.41 (s, 12H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 150.3, 140.5, 137.5,

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137.0, 132.2, 129.4, 128.4, 123.9, 106.4, 39.2, 19.2. HRMS (ESI): calcd for $C_{23}H_{26}ClN_4Pd$ $[M\text{-}Cl]^+$, 499.0811; found, 499.0899. Anal. Calcd for $C_{23}H_{26}Cl_2N_4Pd$: C, 51.56; H, 4.89; N, 10.46. Found: C, 51.60; H, 4.98; N, 10.26. MS (ESI): 499 $[M\text{-}Cl]^+$. HRMS (ESI) calcd. for $C_{23}H_{26}ClN_4Pd$ $[M\text{-}Cl]^+$: 499.0881; found: 499.0899. IR (neat) ν 2963, 1523, 1475, 1406, 1361, 1331, 1285, 1261, 1224, 1159, 1098, 1019, 945, 866, 797, 779, 760 cm^{-1}.

Compound **3d**: yellow solid. m.p. 291 °C (decomposed). ^1H NMR ($CDCl_3$, 500 MHz, TMS) δ 7.26 (d, *J* = 2.5 Hz, 1H), 7.14 (d, *J* = 2.5 Hz, 1H), 7.08 (s, 2H), 7.06 (s, 4H), 6.05 (t, *J* = 2.5 Hz, 1H), 3.78 (s, 3H), 2.39 (s, 6H), 2.35 (s, 12H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 153.1, 140.5, 139.1, 136.6, 135.1, 132.1, 129.1, 124.0, 106.3, 39.2, 21.1, 19.1. MS (ESI): 527 $[M\text{-}Cl]^+$. HRMS (ESI): calcd for $C_{25}H_{30}ClN_4Pd$ $[M\text{-}Cl]^+$, 527.1214; found, 527.1195. Anal. Calcd for $C_{25}H_{30}Cl_2N_4Pd$: C, 53.25; H, 5.36; N, 9.94. Found: C, 52.99; H, 5.32; N, 9.83. IR (neat) ν 3523, 2968, 2921, 2855, 1609, 1520, 1486, 1438, 1425, 1410, 1374, 1338, 1281, 1261, 1224, 1162, 1101, 1076, 1039, 992, 928, 868, 853, 801, 750 cm^{-1}.

General procedure for the NHC-Pd(II) complex 3a catalysed C-N coupling reactions

Under a N_2 atmosphere, NHC-Pd(II) complex **3a** (0.05 or 0.03 mol %), KO^tBu (1.3 equiv), THF (1.0 mL), amines (0.84 mmol) and aryl chlorides (0.7 mmol) were successively added into a sealed tube. The mixture was stirred vigorously at the indicated temperature and specified time shown in Tables 3-5. Then the solvent was removed under reduced pressure and the residue was purified by flash column chromatography (SiO_2) to give the pure products.

Conclusions

In conclusion, from easily available starting materials such as NHC·HCl, $PdCl_2$ and 1-methylindazole and 1-methylpyrazole, a new type of NHC-$PdCl_2$ complexes was obtained in acceptable to high yields in a one-pot procedure under mild conditions, and the structures of all of them were unambiguously determined by X-ray single crystal diffraction. Their catalytic activity was initially tested by the C-N coupling between secondary and primary amines with aryl chlorides. It was found that low catalyst loadings such as 0.03 mol% are sufficient for such transformation. Compared to other well-defined NHC-Pd(II) complexes such as PEPPSI-type complexes, they have at least one of the following advantages such as easy availability, lower cost and lower toxicity of the ancillary ligands, and small amounts of them in the synthesis of the complexes, easy synthesis, and lower catalyst loading. Catalytic activities of these complexes in other transformations are underway in this laboratory.

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Graphic Abstract

Synthesis and characterization of *N*-heterocyclic carbene-palladium-1-methylindazole and -1-methylpyrazole complexes and their catalytic activity toward C-N coupling of aryl chlorides

Xiao-Yun Zhao, Quan Zhou and Jian-Mei Lu*

A series of *N*-heterocyclic carbene-palladium(II) chlorides-1-methylindazole and -1-methylpyrazole complexes was successfully synthesized and fully characterized by X-ray single crystal diffraction. In addition, initial investigations of their catalytic activity showed that they were efficient catalysts in the C-N coupling of primary and secondary amines with aryl chlorides at low catalyst loadings.