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N-Heterocyclic Carbene-Tricyclohexylphosphine Palladium(II) Complex: Synthesis, Crystal Structure and Application in Suzuki Reaction of Aryl Chlorides

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Palladium-catalyzed coupling reactions such as the Suzuki reaction have become an extremely powerful method for the construction of carbon-carbon bonds.[1,2] Employing aryl chlorides for this reaction has been a focused because they are cheaper and more available than their bromides and iodide counterparts.[3] Recently, great progress has been obtained for this transformation by using palladium(II) complexes associated with bulky and electron-rich phosphine ligands.[4,5] As an alternative, *N*-heterocyclic carbenes (NHCs) palladium(II) complexes are one of the most active catalysts for the coupling reactions.[6,7] An earlier work by Herrmann and co-workers reported that mixed palladium(II) complexes [(NHC)Pd(PR_3)I_2] were efficient catalysts for the coupling reactions.[8] Consequently, many NHC-phosphine palladium(II) complexes have been prepared and studied.[9-16]

In recent years, part of our research effort has focused on the palladium-catalyzed coupling reactions.[17-20] In a preliminary communication,[21] we reported two new *trans*/*cis* NHC-phosphine palladium(II) complexes, which displayed good activity in the Suzuki reaction of aryl bromides although they were not particularly useful for aryl chlorides. In view of these findings and our continuous interest in the synthesis and application of NHC palladium(II) complexes, we prepared a new NHC-phosphine palladium(II) complex Pd(IMeo)PCy_3I_2 (**2**) (IMeo = 1,3-di-4-methoxyphenylimidazolin-2-ylidene; PCy_3 = tricyclo-hexylphosphine) *in situ* from the reaction of the corresponding iodide-bridged NHC dimer **1** with PCy_3 (Scheme 1) and examined its catalytic activity in the Suzuki reaction. Here, we report that **2** is an extremely effective catalyst for the Suzuki reaction of aryl chlorides.

Complex **2** was prepared according to the published procedures.[21] It is very soluble in chloroform, dichloromethane and acetone, but insoluble in petroleum ether and *n*-hexane. The new complex was characterized by elemental analysis, IR, ^{1}H NMR. These spectra were well consistent with the title complex. The ^{1}H NMR spectrum of complex **2** showed only one of signals in a symmetrical environment indicating the exclusive formation of the isomer. For example, the two doublets at δ 7.93 and 6.98 are assigned to the signals of benzene protons of the NHC. The two singlets at δ 7.30 and 3.84 are assigned to the signals of backbone protons (-NC*HCH*N-) and -OCH_3 of the NHC. The signals of PCy_3 are observed at δ 2.48, 1.75, 1.42, 1.21. Finally, its detailed structure has been determined by X-ray single-crystal diffraction.

The crystals were obtained by recrystallization from CH_2Cl_2-petroleum ether solution at room temperature. The molecule is shown in Figure 1. As can be seen, the molecule

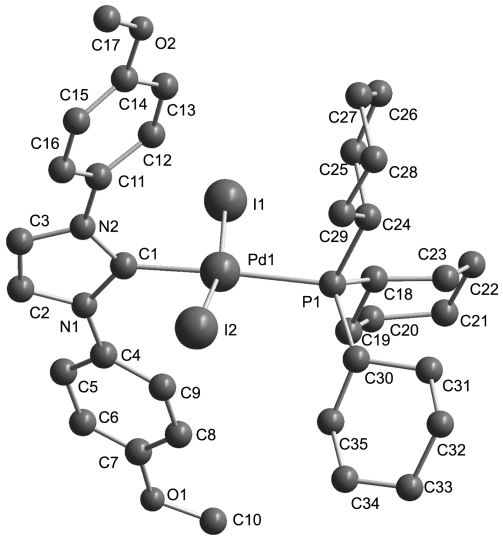
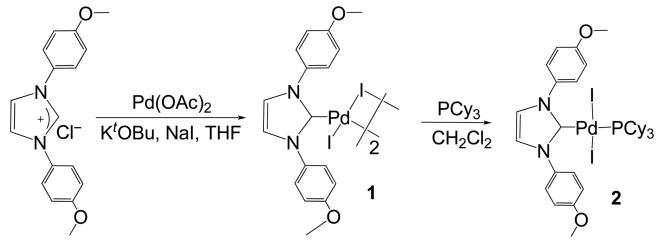


Figure 1. Molecular structure of complex **2**. H atoms are omitted for clarity. Selected bond lengths (Å) and angles (°) are as follows (corresponding values for the unshown second structure are given in brackets): Pd(1)–C(1) 2.020(16) [2.008(17)], Pd(1)–P(1) 2.362(5) [2.341(5)], Pd(1)–I(1) 2.625(19) [2.6148(19)], Pd(1)–I(2) 2.626(2) [2.639(2)] and C(1)–Pd(1)–I(2) 85.5(4) [85.0(5)], I(2)–Pd(1)–P(1) 94.23(13) [95.43(13)], P(1)–Pd(1)–I(1) 94.49(13) [95.58(13)], C(1)–Pd(1)–I(1) 86.2(4) [84.2(5)].



Scheme 1. Synthesis of **2**.

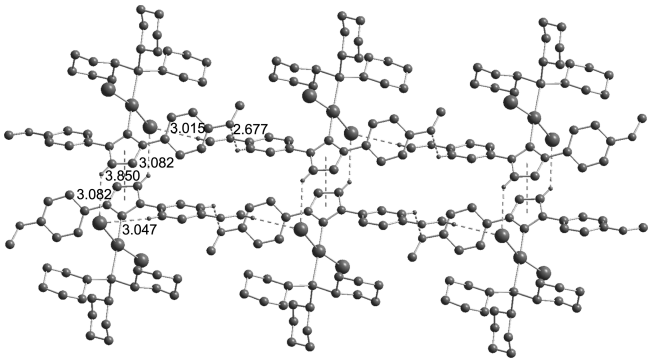


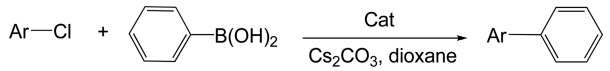
Figure 2. Two-dimensional network structure of complex **2**. Non-hydrogen bonding H atoms are omitted for clarity.

of **2** adopts a *trans* configuration of the coordinated phosphine to the C atom of NHC. The Pd atom is in a slightly distorted square-planar environment bonded to the phosphorus atom, the iodine atoms, the C atom of NHC. The Pd–P [2.362(5) Å and 2.341(5) Å] bond lengths of **2** are longer than those of the related NHC-PPh_3 [$P(C_6H_4$-*p*-$Me)_3$] palladium(II) complexes [2.3396(9) Å and 2.2782(15) Å] possibly due to the steric bulk of the PCy_3 ligand.[21] In the crystal of **2** there exist two types of intermolecular C–H···I and C–H···O hydrogen bonds.[22,23] Furthermore, there also exist intermolecular π–π stacking interactions between the imidazole rings of the two nearest complexes (the interplane distance is about 3.850 Å),[24] which link the molecules into a 2D network structure (Figure 2).

In the present study, our initial exploration of the reaction focused on the coupling of chlorobenzene with phenyl boronic acid (Table 1, entries 1-3). Based on our previous experiments in palladium-catalyzed Suzuki reactions,[21] the reaction was performed under nitrogen atmosphere in dioxane in the presence of Cs_2CO_3 as base at 110 °C for 12 h. The dimer **1** and the related NHC-PPh_3 [$P(C_6H_4$-*p*-$Me)_3$] palladium(II) complexes[21] were almost inactive under the above reaction conditions (entry 1) and the yield was greatly improved by the addition of PCy_3 (49%, entry 2) suggesting that PCy_3 was an excellent ligand for the Suzuki reactions of aryl chlorides. The complex **2** exhibited high activity and produced the coupled product in 99% yield with a catalyst loading of 0.5 mol % (entry 3). Under otherwise conditions using xylene as the solvent[8] provided the product in 72% yield (entry 4). Similar to the result of chlorobenzene, good yields (91-95%) were also obtained in the cases of electron-rich and *ortho*-substituent aryl chlorides (entries 5-8). For activated aryl chlorides 4-chloronitro-benzene and 4-chloro-benzonitrile, they could be coupled very efficiently with a catalytic loading as low as 0.1 mol % (entries 9-10). In addition, heterocyclic chlorides were also found to be efficient coupling partners in this system (entries 11-13).

In contrast to Suzuki coupling of aryl monochlorides, the double coupling of aryl dichlorides have been relatively less reported.[25] In the following experiments, the Suzuki coupling of aryl dichlorides with aryl boronic acids was investigated (Table 2). Complex **2** showed high catalytic activity for the double coupling of 1,4-dichlorobenzene, the teraryl derivatives were isolated in high yields (87-92%) by using a 3 equimolar amount of aryl boronic acids and catalyst loading of 1 mol % (entries 1-3). However, the yields (62-73%) of the double coupling reactions of 1,4-dichlorobenzene with heteroarylboronic acids are lower than those of aryl boronic acids (entries 4-6). It is known that palladium-catalyzed Suzuki reaction of heterocyclic chlorides with aryl boronic acids was an extremely practical method in synthesis for the substituted heterocyclic compound.[26-28] When heterocyclic dichlorides such as 2,6-dichloropyridine was employed, the coupling of aryl boronic acids could proceed in 85-95% good yields (entries 7-9). Finally, the

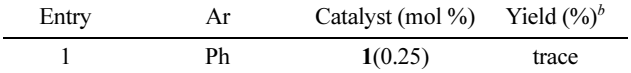
Table 1. Suzuki coupling of aryl chlorides with phenyl boronic acid[a]



Entry	Ar	Catalyst (mol %)	Yield (%)[b]
1	Ph	**1**(0.25)	trace
2	Ph	**1**/PCy_3(0.25/1)	49
3	Ph	**2**(0.5)	99
4[c]	Ph	**2**(0.5)	72
5	*p*-MeC_6H_4	**2**(0.5)	95
6	*o*-MeC_6H_4	**2**(0.5)	92
7	*p*-$OMeC_6H_4$	**2**(0.5)	93
8	*o*-$OMeC_6H_4$	**2**(0.5)	91
9	*p*-$NO_2C_6H_4$	**2**(0.1)	97
10	*p*-CNC_6H_4	**2**(0.1)	95
11	pyridin-2-yl	**2**(0.5)	94
12	pyridin-3-yl	**2**(0.5)	89
13	thiophen-2-yl	**2**(0.5)	83

[a]Reaction conditions: aryl chlorides (1.0 mmol), $PhB(OH)_2$ (1.5 mmol), Cs_2CO_3 (1.5 mmol), dioxane (5 mL), 110 °C, 12 h. [b]Isolated yields. [c]Using xylene as the solvent, 130 °C.

Table 2. Suzuki coupling of aryl dichlorides with aryl boronic acids catalyzed by **2**[a]



Entry	Ar	Ar_1	Yield (%)[b]
1	1,4-C_6H_4	Ph	87
2	1,4-C_6H_4	*p*-tolyl	89
3	1,4-C_6H_4	*p*-$OMeC_6H_4$	92
4	1,4-C_6H_4	pyridin-4-yl	73
5	1,4-C_6H_4	pyridin-3-yl	68
6	1,4-C_6H_4	thiophen-2-yl	62
7	2,6-pyridyl	Ph	93
8	2,6-pyridyl	*p*-tolyl	95
9	2,6-pyridyl	pyridin-4-yl	85
10	4,6-pyrimidyl	Ph	97
11	4,6-pyrimidyl	*p*-FC_6H_4	91

[a]Reaction conditions: aryl dichlorides (1.0 mmol), $PhB(OH)_2$ (3.0 mmol), Cs_2CO_3 (3.0 mmol), dioxane (5 mL), 110 °C, 12 h. [b]Isolated yields.

couplings of 4,6-dichloropyrimidine with aryl boronic acids also gave excellent yields (entries 10-11).

In conclusion, we have prepared and characterized a new NHC-phosphine palladium(II) complex **2**. Its catalytic activity was evaluated in the Suzuki reaction. **2** was found to be very efficient catalyst for this reaction of aryl chlorides.

Experimental Section

Materials and Measurement. The dimer **1** was prepared according to published procedures.[16] All other chemicals were used as purchased. Elemental analyses were determined with a Thermo Flash EA 1112 elemental analyzer. IR spectra were collected on a Bruker VECTOR22 spectrophotometer using KBr pellets. ^{1}H NMR spectra were recorded on a Bruker DPX-400 spectrometer in $CDCl_3$ with TMS as an internal standard. Crystallographic data were collected on a Bruker SMART APEX-II CCD diffractometer. **CCDC** reference number 886745 for **2**. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_ request/cif.

Pd[($C_3N_2H_2$)-(C_6H_4-OCH_3)$_2$]PCy_3I_2 (2): A solution of **1** (0.1 mmol) and ligand PCy_3 (0.22 mmol) in CH_2Cl_2 (10 mL) was stirred at room temperature for 1 hour. The product was separated by passing through a short silica gel column with CH_2Cl_2 as eluent. The second band was collected and afforded complex **2**. Yield 70%. IR (KBr, cm^{-1}): 2922, 2847, 1614, 1513, 1459, 1441, 1343, 1287, 1251, 1174, 1089, 1028, 941, 915, 835, 736, 688. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.4 Hz, 4H, Ar-H), 7.30 (s, 2H, NCHCHN), 6.98 (d, J = 8.4 Hz, 4H, Ar-H), 3.84 (s, 6H, -OCH_3), 2.48 (m, 3H, P(C*H*$C_5H_{10})_3$), 1.75 (m, 15H, P($C_6H_{11})_3$), 1.42 (m, 6H, P($C_6H_{11})_3$), 1.21 (m, 9H, P($C_6H_{11})_3$). Anal. Calc. for $C_{35}H_{49}I_2N_2O_2PPd$: C, 45.64; H, 5.36; N, 3.04. Found: C, 45.89; H, 5.17; N, 3.23.

General Procedure for the Coupling Reaction of Aryl Chlorides. In a Schlenk tube, a mixture of the prescribed amount of catalyst, aryl chloride (1.0 mmol), aryl boronic acid (1.5-3.0 mmol) and the selected Cs_2CO_3 (1.5-3.0 mmol) in solvent (5 mL) was evacuated and charged with nitrogen. The reaction mixture was then placed in an oil bath and heated at 110 °C for 12 h. After being cooled, the mixture was extracted with dry diethyl ether and evaporated, the pure products were isolated by flash chromatography on silica gel and identified by comparing melting points or ^{1}H NMR spectra.

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