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Monophosphine-Cyclopalladated Ferrocenylpyrimidine Complex: Synthesis, Crystal Structure and Reusable Catalytic System for Coupling Reaction of Aryl Chlorides in PEG-400

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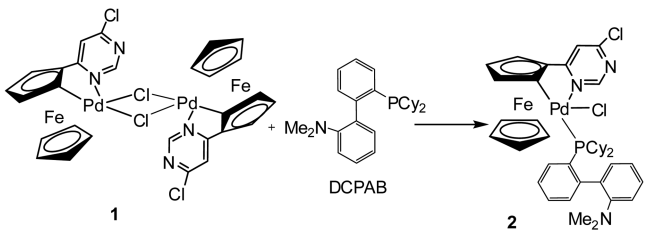
Since the first report on the use of palladacycles for the Suzuki and Heck reactions by Herrmann, Beller and co-workers in 1995,[1,2] a wide variety of known and new palladacycles have been successfully used in the coupling reactions.[3] Employing aryl chlorides for this reaction has been focused because aryl chlorides are cheaper and more available than their bromides and iodide counterparts. However, only a few palladacycles have proved to be efficient for the activation of notoriously unreactive aryl chlorides.[4-11] In most cases the catalysts employed need to be used in relatively high loadings, and poor recovery, which negated the advantages associated with the use of aryl chlorides. PEGs [poly(ethylene glycol)] have clear advantages as a solvent in organic synthesis because they are cheap, steady, readily available, and nontoxic.[12] Recently, liquid PEGs have been adopted as a new approach for catalyst recycling, in a broad range of catalytic organic reactions.[13-15]

We have also found biaryl phosphine adducts of cyclopalladated ferrocenylpyrimidine are very efficient for the amination of aryl chlorides in PEG-400.[16] These adducts combine the stability induced by the presence of a palladacycle framework with the high activity commonly associated with phosphine ligands, and were far more active than the corresponding dimeric palladacycle. As a continuation of our interest in the synthesis and application of cyclopalladated complexes,[16-18] we have prepared a new phosphine adduct of palladacycle **2** from the reaction of cyclopalladated ferrocenylpyrimidine dimer **1** with commercially available 2-dicyclohexylphosphanyl-2'-(*N*,*N*-dimethylamino)-biphenyl (DCPAB) (Scheme 1) and examined its activity in the coupling reactions.



Scheme 1. Synthesis of **2**.

Complex **2** is air- and moisture-stable, both in solid state and in solution. It is very soluble in chloroform, dichloromethane and acetone, but insoluble in petroleum ether and *n*-hexane. The new complex was fully characterized by elemental analysis, IR, ^{1}H NMR and ESI-MS. These spectra were well consistent with the title complex. Moreover, the molecular structure of **2** has been ascertained by means of X-ray studies. The molecule of **2** together with selected bond distances and angles is shown in Figure 1. The Pd atom is in a slightly distorted square-planar environment bonded to the phosphorus atom, the chlorine atom, the pyrimidinyl nitrogen atom and the carbon atom of the ferrocenyl moiety. The Pd–P bond length of **2** is similar to those of the related DCPAB-palladacycles, while the above bond length of **2** is longer than those of the related PPh_3-palladacycles possibly due to the steric bulk of the DCPAB ligand.[16-18] In the crystal of **2** there exist two types of intermolecular C–H···Cl hydrogen bonds,[19,20] which link the molecules into a 2D

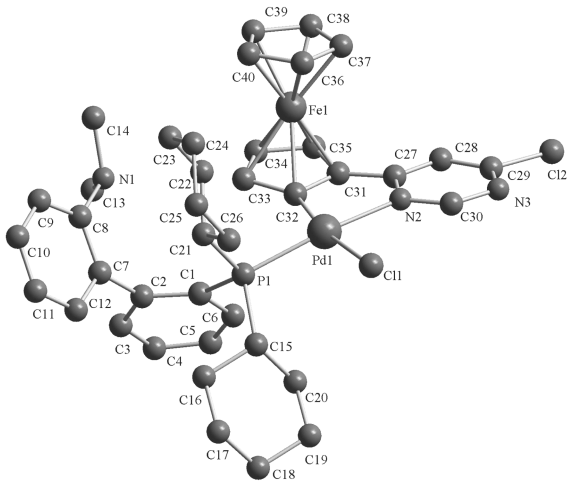


Figure 1. Molecular structure of complex **2**. H atoms are omitted for clarity. Selected bond lengths (Å) and angles (°): Pd(1)–C(32) 1.976(4), Pd(1)–N(2) 2.144(4), Pd(1)–P(1) 2.2592(12), Pd(1)–Cl(1) 2.4000(12) and C(32)–Pd(1)–N(2) 80.33(16), C(32)–Pd(1)–P(1) 94.53(12), P(1)–Pd(1)–Cl(1) 94.15(4), N(2)–Pd(1)–Cl(1) 91.62(11).

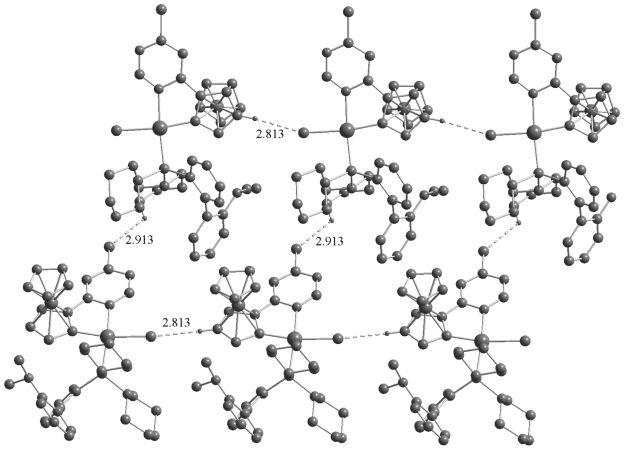
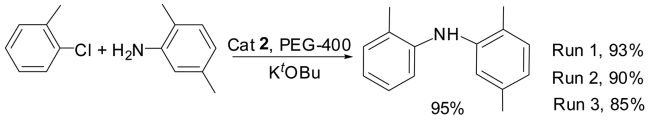


Figure 2. Two-dimensional network structure of complex **2** formed by C–H···Cl hydrogen bonds. Non-hydrogen bonding H atoms are omitted for clarity.

network structure (Figure 2).

Considering **2** is a phosphine adduct of palladacycle containing a highly active DCPAB ligand, we speculate that it would be an efficient catalyst for the coupling reactions. Based on our previous experiments,[16] we first performed the reaction of 2-chlorotoluene with 2,5-dimethylaniline under nitrogen atmosphere in PEG-400 in the presence of 1 mol % of **2** as catalyst and K^{t}OBu as base at 120 °C for 12 h (Scheme 2). **2** displayed highly catalytic activity, producing the coupled product in excellent yield (95%). We also observed that the above catalytic system could be recycled and reused three times without loss of activity for the same reaction. The high activity of **2** in the Buchwald-Hartwig amination of aryl chlorides encouraged us to examine its activity toward the Suzuki reaction.

In 2005, Li *et al.* developed a highly efficient and reusable Pd(OAc)$_2$/DABCO (triethylene-diamine)/PEG system for the Suzuki coupling.[21] However, the catalytic system could not be reused for the reaction of aryl chlorides. To our knowledge, there was no report concerning the reusable catalytic system for the Suzuki coupling of aryl chlorides in PEGs. Our initial exploration of reaction conditions focused on the coupling of 4-chlorotoluene with phenylboronic acid using 0.5 mol % of **2** in PEG-400 at 120 °C for 12h. After screening a variety of bases (Table 1, entries 1-6), K^{t}OBu was found to give the best result (97%, entry 6). The coupled product was isolated in a moderate yield at 80 °C (entry 7). However, **1** was almost inactive under the same reaction conditions (entry 8) and the yield was greatly improved by the addition of DCPAB (70%, entry 9) suggesting that DCPAB participated in the catalytic cycles. After initial experimentation, the reaction mixture was extracted with dry



Scheme 2. Amination of 2-chlorotoluene with 2,5-dimethylaniline catalyzed by **2**.

Table 1. Influence of base and catalyst on the Suzuki coupling of 4-chlorotoluene with phenyl boronic acid[a]

Entry	Catalyst (mol %)	Base	Yield (%)[b]
1	**2**(0.5)	K_3PO_4	68
2	**2**(0.5)	Na_2CO_3	51
3	**2**(0.5)	K_2CO_3	56
4	**2**(0.5)	Cs_2CO_3	65
5	**2**(0.5)	Na^{t}OBu	85
6	**2**(0.5)	K^{t}OBu	97
7[c]	**2**(0.5)	K^{t}OBu	61
8	**1**(0.5)	K^{t}OBu	trace
9	**1**/DCPAB (0.025/0.75)	K^{t}OBu	70
10	Entry 6, cycle 1, 2, 3	K^{t}OBu	95, 92, 88

[a]Reaction conditions: 4-chlorotoluene (1.0 mmol), $PhB(OH)_2$ (1.5 mmol), base (2.0 mmol), PEG-400 (3 mL), 120 °C, 12 h. [b]Isolated yields (average of two experiments). [c]80 °C.

diethyl ether, and the PEG-400 and catalyst were solidified and subjected to a second run of the amination by charging with the same substrates. The results of this experiment and two subsequent experiments were consistent in yields (95%, 92% and 88%, respectively, entry 10).

In the following experiments, the Suzuki coupling of a variety of electronically and structurally diverse aryl chlorides with aryl boronic acids was investigated under the same reaction conditions (Table 2). Similar to the result of 4-chlorotoluene, excellent yields (96-99%) were also obtained in the cases of chlorobenzene and 4-chloroanisole (entries 1-2). *Ortho*-substituents were tolerated and even the very sterically hindered 2-chloro-*m*-xylene provided the product in 89% yield (entries 3-5). For electron-deficient aryl chlorides, they could be coupled very efficiently with a catalytic loading as low as 0.1 mol % (entries 6-7). 2-

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

$$Ar_1{-}Cl + Ar_2{-}B(OH)_2 \xrightarrow[K^tOBu]{\text{Cat } \mathbf{2}, \text{ PEG-400}} Ar_1{-}Ar_2$$

Entry	Ar_1	Ar_2	Yield (%)[b]
1	Ph	Ph	99
2	*p*-$OMeC_6H_4$	Ph	96
3	*o*-MeC_6H_4	Ph	94
4	*o*-$OMeC_6H_4$	Ph	93
5	2,6-$Me_2C_6H_3$	Ph	89
6[c]	*p*-$NO_2C_6H_4$	Ph	97
7[c]	*p*-CNC_6H_4	Ph	95
8	pyridin-2-yl	Ph	94
9	Ph	pyridin-4-yl	96
10	*p*-MeC_6H_4	pyridin-4-yl	93
11	Ph	pyridin-3-yl	95
12	Ph	thiophen-2-yl	92
13	Ph	furan-2-yl	90

[a]Reaction conditions: catalyst **2** (0.5 mol %), Ar_1Cl (1.0 mmol), $Ar_2B(OH)_2$ (1.5 mmol), K^{t}OBu (2.0 mmol), PEG-400 (3 mL), 120 °C, 12 h. [b]Isolated yields (average of two experiments). [c]Catalyst **2** (0.1 mol %).

Chloropyridine was found to be an efficient coupling partner in this system giving 94% yield (entry 8). In addition, we also investigated the coupling reaction of aryl chlorides with heteroarylboronic acids. The reactions of pyridine boronic acids with chlorobenzene and 4-chlorotoluene proceeded smoothly to provide the desired products in excellent yields (entries 9-11). Finally, the couplings of thiophen-2-ylboronic acids and furan-2-ylboronic acids with chlorobenzene also gave high yields (entries 12-13)

In conclusion, we have prepared and characterized a new phosphine adduct of palladacycle **2**, which was found to be an efficient catalyst for Buchwald-Hartwig amination and Suzuki reaction of aryl chlorides. A high efficient and reusable catalytic system for these reactions has been developed.

Experimental Section

Materials and Measurement. The chloride-bridged palladacyclic dimer **1** was prepared according to published procedures.[17] 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. Mass spectra were measured on a LC-MSD-Trap-XCT instrument. Crystallographic data were collected on a Bruker SMART APEX-II CCD diffractometer. **CCDC** reference number 859776 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.

[PdCl{[(η^5-C_5H_5)]Fe[(η^5-C_5H_3)-$N_2C_4H_2$-Cl]}(DCPAB)] (2): A solution of **1** (0.1 mmol) and ligand DCPAB (0.22 mmol) in CH_2Cl_2 (10 mL) was stirred at room temperature for 30 min. The solvent was evaporated and the product was separated by passing through a short silica gel column with CH_2Cl_2/ethyl acetate (1:1, v/v) as eluent. The second band was collected and afforded complex **2** after the evaporation of the solvent. Yield 91%. IR (KBr, cm^{-1}): 2928, 1572, 1488, 1467, 1418, 1300, 1267, 1127, 1105, 1001, 943, 816, 756,731. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.62 (s, 1H, ArH), 7.16-7.51 (m, 9H, ArH), 4.57 (s, 1H, C_5H_3), 4.23 (s, H, C_5H_3), 3.92 (s, 5H, C_5H_5), 3.16 (s, 1H, C_5H_3), 2.55 (s, 6H, –NMe_2), 1.23-2.12 (m, 22H, PCy_2). MS-ESI$^+$ [*m/z*]: 797.5 (M^+-Cl). Anal. Calc. for $C_{40}H_{46}Cl_2FeN_3PPd$: C, 57.68; H, 5.57; N, 5.04. Found: C, 57.93; H, 5.28; N, 5.26.

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 mmol) or amine (1.2 mmol) and the selected base (2.0 mmol) in PEG-400 (3 mL) was evacuated and charged with nitrogen. The reaction mixture was then placed in an oil bath and heated at 120 °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. After extracting with diethyl ether, the mixture of catalyst, and PEG-400 was solidified (cooled and then evaporated under vacuo) and subjected to a second run of the coupling reaction by charging with the same substrates.

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