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New recyclable catalytic system: $PdCl_2$–$Dppc^+$ PF_6^-–[bmim][PF_6] for the Suzuki coupling reaction

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An air-stable and highly efficient $PdCl_2$–$Dppc^+$ PF_6^-–[bmim][PF_6] catalytic system has been developed for the Suzuki coupling reaction of various aryl bromides with phenylboronic acid. The catalytic system can be recycled at least 10 times with minimal loss of activity. Copyright © 2006 John Wiley & Sons, Ltd.

KEYWORDS: recyclable; $Dppc^+PF_6^-$; catalytic system; the Suzuki coupling reaction

INTRODUCTION

The palladium-catalyzed Suzuki coupling reaction is one of the most efficient methods for the construction of C–C bonds and has found widespread use in organic synthesis.[1–8] However, the separation of the products from the reaction mixture, the recovery of the catalysts and the need for organic solvents are the major disadvantages in the Suzuki cross-coupling reactions. For these reasons, many Suzuki coupling reactions are not used on an industrial scale despite their benefits. To overcome these problems, several heterogeneous Pd-catalyzed Suzuki coupling systems have been described in recent years, such as Pd–C,[9–15] polymer supported Pd-catalysts,[16–18] the use of aqueous media,[19–26] and the use of ionic liquid.[27–29] Room temperature ionic liquids are promising green alternatives to conventional solvents in transition-metal-catalyzed reactions.[30,31] The advantages of the elimination of highly toxic co-solvents, the ease of work-up, and the possibility of recycling the catalyst have already been demonstrated. One example of this strategy was the use of ionic liquids as solvents for the Suzuki coupling reaction.[27–29] The products are separated from the solvent by extraction with diethyl ether and the catalytic solution can be reused three times. Generally, the neutral phosphine ligands are used to complex the palladium species, resulting in excellent results for the palladium-catalyzed Suzuki coupling reaction. However, the separation of the products with neutral phosphine ligands and Pd-catalyst is difficult, and the catalyst can only be reused several times because neutral phosphine ligands and catalyst easily dissolve in organic solvents. To overcome these problems, use of a new catalyst system consisting of $PdCl_2$–ionic phosphine ligand–ionic liquid was suggested. $Dppc^+PF_6^-$ [1,1′-bis(diphenylphosphino) baltocenium hexafluorophosphate], an ionic ligand, proved to be a very suitable ligand for the biphasic hydroformylation in ionic liquids, with high solubility in [bmim][PF_6] (1-butyl-3-methyl imidazolium hexafluorophosphate).[32] Herein we report that $PdCl_2$–$Dppc^+PF_6^-$, in combination with [bmim][PF_6] as solvent, is an air-stable, extremely effective and recyclable catalysis system for the coupling of aryl bromides with phenylboronic acid.

RESULTS AND DISCUSSION

We found that $Dppc^+PF_6^-$ is air-stable in ionic liquid and active in the Suzuki coupling reaction. In general, the $Dppc^+PF_6^-$ and $PdCl_2$ were mixed in [bmim][PF_6] and heated at 110 °C for about 2 h, resulting in the formation of a dark brown liquid. Aryl bromide and phenylboronic acid were then added and heated for 0.5–3 h to afford the biaryl product in high yield. Our first model, bromobenzene,

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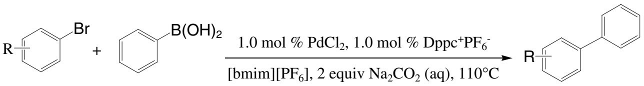
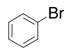
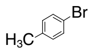
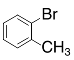
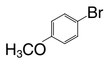
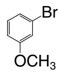
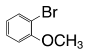
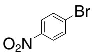
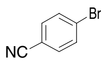
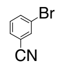
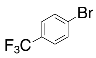
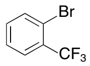
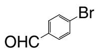
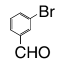
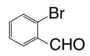
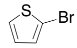
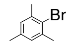
Table 1. Suzuki coupling reaction of aryl bromide with phenylboronic acid catalyzed by $PdCl_2-Dppc^+PF_6^-$ in $[bmim][PF_6]$



Entry	Substrate	Time (h)	Yield[a] (%)[b]
1		1.0	99 (92)
2		1.5	92 (85)
3		1.0	99 (93)
4		1.0	99 (94)
5		2.0	95 (87)
6		1.5	96 (91)
7		1.0	98 (92)
8		1.0	99 (95)
9		0.5	99 (92)
10		1.5	99 (93)
11		1.0	99 (93)
12		1.0	99 (92)
13		1.0	98 (90)
14		0.5	99 (93)
15		0.5	99 (91)
16		1.0	98 (89)
17		0.5	99 (92)
18		3.0	90 (84)

[a] GC yield using hexadecane as internal standard.
[b] Isolated yields are given in parentheses.

gave an excellent result of 99% conversion of starting aryl bromide and isolated purified product yield of 92%, utilizing 1.0 mol% catalyst (Table 1, entry 1). Then we tested the scope of the reaction with a range of substituted aryl bromides with varying electronic properties. The aryl halides with electron-donating groups, such as methyl (Table 1, entries 2–4) and methoxy (Table 1, entries 5–7), gave excellent yields, while aryl bromide with electron-withdrawing groups, such as nitro, trifluoromethyl and acetyl, gave the coupling products almost quantitatively. The reactivity was as expected for coupling reaction with electron-withdrawing substituents on the aryl halide achieving better conversions than electron-donating substituents. A heteroaromatic compound, 2-bromothiophene, also reacted with phenylboronic acid to give the desired product in excellent yield (entry 17). In addition, a challenging problem in the Suzuki coupling processes is the ability to combine sterically hindered substrates. This is particularly difficult when coupling partners have *ortho* substituents. We found that it was efficient to couple the sterically hindered 2-bromomesitylene with phenylboronic acid (entry 18). The above procedure could not be applied to the coupling of aryl chloride and phenylboronic acid, even heated for 3 h at 110 °C, with only a trace of biaryl being detected.

The experimental procedure is very simple. After heating for 0.5–3 h, the products could be easily separated from the catalysis system at room temperature by extraction with organic solvent such as diethyl ether or hexane. Without any apparent leaching of $PdCl_2$ and $Dppc^+PF_6^-$ into the organic solvents, the biaryl products were further purified by chromatography. The inorganic by-products were removed by washing with water, affording the recovered clean catalytic system.

The reusability of the present catalysis system was examined in the coupling reaction of bromobenzene with phenylboronic acid. As shown in Table 2, the conversion of the reactant from the first run to the fifth run remains constant (99%). We did not observe significant deterioration of activity in the recovered catalyst even after 140 uses. In contrast, the activity of the $PdCl_2-Dppf$ [1,1′-bis(diphenyl phosphino)

Table 2. Recycling experiments for the $PdCl_2-Dppc^+PF_6^--[bmim][PF_6]$-catalyzed Suzuki coupling reaction[a]

Run	Time (h)	Conversion (%)[b]	Yield (%)[c]
1	2.0	99	92
2	2.0	99	95
3	2.0	99	94
4	2.0	99	96
5	2.0	99	94
6	2.0	98	95
7	2.0	98	92
8	2.0	98	93
10	2.0	97	90

[a] Reaction conditions: 0.25 mmol of bromobenzene, 0.375 mmol of phenylboronic acid, 0.5 mmol of Na_2CO_3, $PdCl_2$ (0.0025 mmol), $Dppc^+PF_6^-$ (0.0025 mmol), 110 °C, 2 h.
[b] Conversion was determined using GC analysis with external standards.
[c] Isolated yields by column chromatography; products fully characterized by GC-MS and ^1H NMR.

ferrocene] catalyst system declined quickly after five uses (Table 3). This is likely to be due to two reasons: (1) the ionic ligands Dppc$^+$PF$_6^-$ and PdCl$_2$ are tightly complexed with the ionic liquid and therefore not easily lost during extraction of the products;[33,34] (2) and, due to the electronic-withdrawing property of cobaltocenium, the Dppc$^+$PF$_6^-$ was not easily oxidized in air.

CONCLUSION

The results of our study showed that PdCl$_2$–Dppc$^+$PF$_6^-$ catalyst not only was air-stable in ionic liquid [bmim][PF$_6$] and exhibited efficient activity for Suzuki coupling reaction, but also that it can be recycled at least 10 times without significant loss in activity. Further catalyst reuse studies on other cross-coupling reactions are being investigated.

EXPERIMENTAL SECTION

Materials

All commercially available solvents and reagents were used as supplied unless otherwise stated. Dppc$^+$PF$_6^-$[32] and [bmim][PF$_6$][35] were prepared according to the literature procedures.

Analysis

Product yields were calculated by GC, using 6890N Network GC system (Agilent Technologies). GC-MS was obtained on an Autospec Q instrument under election impact (EI) conditions at 70 eV. ^{1}H NMR was recorded on a Varian MERCURY Plus 400 MHz instrument.

Typical procedure for the PdCl$_2$–Dppc$^+$PF$_6^-$-catalyzed Suzuki coupling reaction

A 25 mL round-bottom flask, equipped with a magnetic bar and a condenser, was charged with PdCl$_2$ (0.44 mg, 0.0025 mmol), Dppc$^+$PF$_6^-$ (1.75 mg, 0.0025 mmol) and [bmim][PF$_6$] (5.0 mL). The mixture was stirred at 110 °C until a homogeneous dark brown mixture was obtained (at least 1 h); aryl halide (0.25 mmol), phenylboronic acid (45.7 mg, 0.375 mmol) and a solution of Na$_2$CO$_3$ (53.0 mg, 0.50 mmol) in water (1.0 mL) were added. The mixture was heated at 110 °C with vigorous stirring for a further 2 h, then cooled and extracted with diethyl ether; the combined extracts were washed with brine and water, and dried. After removal of the solvent in vacuum, the mixture was flushed through a silica pad to afford the diaryl products in high purity, as characterized by GC-MS, ^{1}H NMR spectroscopy.

Table 3. Recycling experiments for the PdCl$_2$–Dppf–[bmim][PF$_6$]-catalyzed Suzuki coupling reaction[a]

Run	Time (h)	Conversion (%)[b]	Yield (%)[c]
1	1.0	99	90
2	1.0	99	95
3	1.0	98	95
4	2.0	95	94
5	2.0	70	62
6	2.0	45	40

[a] Reaction conditions are as the same as those in Table 2.

[b] Conversion was determined by GC analysis with external standards.

[c] Isolated yields by column chromatography; products fully characterized by GC-MS and ^{1}H NMR.

Procedure for the catalyst recycling of the Suzuki coupling reaction

After completion of the reaction and cooling to room temperature, the products and the unreacted reagents were extracted with diethyl ether, then washed with water and dried in vacuum. The resulting viscous PdCl$_2$–Dppc$^+$PF$_6^-$–[bmim][PF$_6$] mixture was charged with fresh reagents (aryl halide, phenylboronic acid and the solution of Na$_2$CO$_3$ in water) and heated at the required temperature with stirring for the proper time.

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