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Short Communication

A functionalized ionic liquid containing phosphine-ligated palladium complex for the Sonogashira reactions under aerobic and CuI-free conditions

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ABSTRACT

A Pd-complex functionalized ionic liquid (IL), di-(1-butyl-2-diphenylphosphino-3-methylimidazolium)-dichloropalladium(II) hexafluorophosphate (**2**), was synthesized and used as the highly efficient and recyclable catalyst for the Sonogashira reactions of aryl iodides and aryl bromides with several terminal acetylenes, under aerobic and CuI-free conditions. The activity loss, Pd black precipitation, and Pd leaching were not observed even after 7 runs in **2**-catalyzed Sonogashira reactions using the room temperature IL of [Bmim]PF_6 as the reaction medium.

1. Introduction

The Sonogashira reaction is a powerful tool for the formation of Csp^2-Csp bond, and the most important method for the synthesis of internal acetylenes, which finds its applications in the preparation of natural products, pharmaceuticals, biologically active molecules, liquid crystalline materials and conducting polymers, or molecular electronics in general [1–3]. In the conventional method, the Sonogashira coupling is performed in the presence of base, copper(I) iodide as co-catalyst, and palladium catalyst such as $PdCl_2(PPh_3)_2$, $[Pd(allyl)Cl]_2/PPh_3$, $PdCl_2/PPh_3$, or $Pd(PPh_3)_4$ in organic solvents under inert atmosphere [4–6]. The inert atmosphere is required for the Sonogashira reaction due to the following reasons: 1) most of phosphine-containing palladium catalysts are moisture- and air-sensitive; 2) the *in situ* formed copper(I) acetylides derived from copper(I) iodide, undergo homocoupling upon exposure to air, yielding the side-products (Glaser coupling); and 3) the copper(I) acetylides are featured with the extremely high reactivity and the explosive nature in open air [1–3,7,8].

From environmental and economic points of view, the development of more efficient, recoverable and recyclable, but moisture- and air-insensitive palladium catalysts, which allow the manipulation of the Sonogashira reaction with low catalyst loadings under copper-free conditions and without the need of exclusion of air and moisture, is highly demanded. Recent researches have led to many alternatives for more efficient and clean Sonogashira reactions, including copper- and ligand-free reactions [9,10], new palladium catalyst systems [11], as well as significant changes in the reaction conditions and solvents [12–17]. Non-volatile ionic liquids (ILs) have been recognized as promising alternative solvents, which also can immobilize homogenous palladium catalysts and then prevent their leaching and deactivation [15–17]. On the other hand, ILs can be functionalized flexibly by varying the cation and/or anion that constitute IL structure with specific functionalities. Thus, it is possible to develop abundant functionalized ILs (FILs) dually possessing the characters of the incorporated functionalities as well as that of the ILs. As a part of our continued activities in the functionalization of ILs for homogeneous catalysis [18–22], herein, for the first time we report the synthesis of a phosphine-ligated palladium complex FIL, di-(1-butyl-2-diphenylphosphino-3-methylimidazolium)-dichloridopalladium(II) hexafluorophosphate (**2**), which was applied as the efficient and recyclable catalyst for the clean Sonogashira reactions under aerobic and CuI-free conditions (Scheme 1). Due to high polarity of **2** and its compatibility with the room temperature IL of 1-*n*-butyl-3-methylimidazolium hexafluorophosphate ([Bmim]PF_6), the latter was selected as the solvent to assure the homogeneous catalysis. The performed Sonogashira reactions are expected with advantages of no need of inert atmosphere, CuI-free condition, as well as the available recyclability of **2** in [Bmim]PF_6.

2. Results and discussion

2.1. Synthesis and characterization of 2

When $PdCl_2(CH_3CN)_2$ was treated with ligand **1** (**1**, 1-butyl-2-diphenylphosphino-3-methylimidazolium hexafluorophosphate [23])

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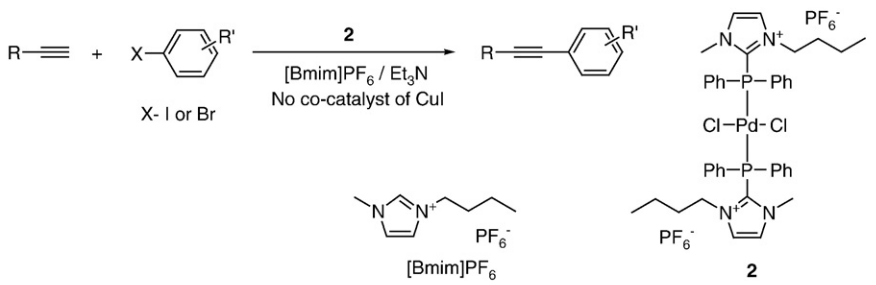


Scheme 1. The Sonogashira reactions of aryl halides with terminal acetylenes catalyzed by **2** in [Bmim]PF_6.

in ethanol, **2** was obtained as a yellow solid in good yield (75 wt.%) which was fully characterized by ^1H NMR, ^{31}P NMR, TG/DTA, and elemental analysis. It is moisture- and air-stable both in solid state and in organic solvent at room temperature. The crystals suitable for single-crystal X-ray analysis were obtained by re-crystallization from acetone/benzene.

The molecular structure of **2**, depicted in Fig. 1, is very similar to that of the neutral palladium complex of *trans*-$PdCl_2(PPh_3)_3$ [24]. **2** is composed of the Pd complex cations and PF_6^- anions. The Pd complex cation possesses square-planar geometry. The Pd center, lying at the center of inversion, is coordinated by two chloride ions and two imidazolium-tailed phosphine ligands. The bond angles of P1 – Pd1 – P1A and Cl1 – Pd1 – Cl1A are 180°. The same bond distances of 2.3203(7) Å for Pd – P and 2.2967(7) Å for Pd – Cl are observed. The bond distances of Pd – P and Pd – Cl in **2** (Table 1) are slightly shorter than those observed in *trans*-$PdCl_2(PPh_3)_3$ (Pd – P, 2.3721(10) Å; Pd – Cl, 2.3111(13) Å) [24].

In comparison with PPh_3, ligand **1** is a relatively weaker electron-donor featured with moisture- and air-insensitive character, due to the intensive delocalization of the lone-pair electrons in the P atom to the adjacent positive imidazolium ring. Consequently, **2** is also a moisture- and air-insensitive complex endowed with strong tolerance against oxidative degradation, which facilitates the manipulation in open air.

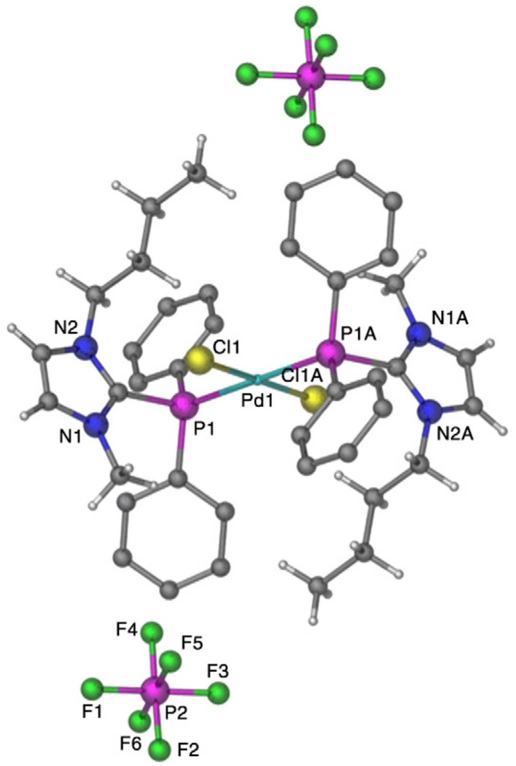


Fig. 1. Molecular structure of **2** (the solvent molecule of benzene has been omitted for clarity).

2.2. Catalytic performance of 2 for the Sonogashira reaction

The coupling of phenylacetylene with iodobenzene was first studied as a model reaction under CuI-free conditions. A typical reaction was carried out by mixing 1 mmol iodobenzene, 1.5 mmol phenylacetylene, 2 mmol base, and 0.02 mmol **2** in 2 mL of [Bmim]PF_6 under the appointed conditions. The selection of [Bmim]PF_6 as the solvent is made on the comparison of its same ionophilicity and the structural similarity with **2**. Through screening the bases, Et_3N was found to be the best choice. Under the optimal condition (2 h, 80 °C), the complete conversion of iodobenzene into the cross-coupling product was obtained.

The purpose of incorporating the palladium complex into the IL structure is to integrate the advantageous characters of the palladium complex as the catalyst and the IL like recyclability. To demonstrate that issue, the recovery and recycling experiments were conducted over **2** in [Bmim]PF_6 for the coupling of phenylacetylene with iodobenzene. Upon completion of each run, the reaction slurry was extracted with diethyl ether to separate the substrate and the products out of the IL phase. The residues were reused without further treatment if not specified. As shown in Table 2, the activity of **2** decreased gradually although the precipitation of Pd black was not observed during the recycling. After six runs, the yield of 1,2-diphenylethyne decreased from 100% to 66%. However, when the residues were washed with water to remove the cumulative ammonium salts, the recovered IL phase exhibited the activity as well as the fresh one. These results indicated that the activity loss was due to the capsulation of **2** by the formed slurry of ammonium salts, thus leading to the inefficient accessibility of the catalytic site to the substrate and then the limited transformation. In this method, the hydrophobicity of [Bmim]PF_6 and **2** facilitated the removal of the formed ammonium salts by water from the IL system, leading to the convenient refreshment of the activity of **2**. On the other hand, after the seven-run recycling uses, the total loss of **2** in term of Pd amount in the combined organic and water phase was below the ICP detection limit (<0.1 μg/g on the basis of the ICP analysis). This revealed that **2** was tightly locked in the structurally similar [Bmim]PF_6 medium without leaching during the process of ether extraction or water washing. In contrast, when CH_3CN was used as the solvent, the activity of **2** lost rapidly due to the

Table 1
The selected bond distances (Å) and bond angles (o) for **2** and *trans*-$PdCl_2(PPh_3)_2$.

2	Pd1–Cl	2.297(7)	Pd1–P	2.320(7)
	Cl1–Pd1–P1	92.62(3)	Cl1A–Pd1–P1	87.38(3)
	Cl1–Pd1–Cl1A	180.0	P1–Pd1–P1A	180.0
trans-$PdCl_2(PPh_3)_2$[24]	Pd1–Cl	2.311(1)	Pd1–P	2.372 (1)
	Cl1–Pd–P1	92.38(4)	Cl1A–Pd–P1	87.62(4)
	Cl1–Pd1–Cl1A	180.0	P1–Pd1–P1A	180.0

Table 2
The recycling uses of **2** as catalyst for the Sonogashira reaction of phenylacetylene with iodobenzene[a].

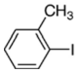
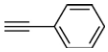
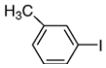
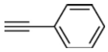
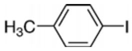
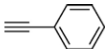
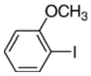
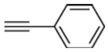
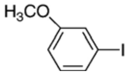
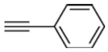
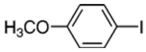
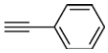
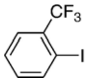
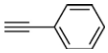
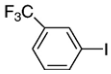
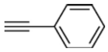
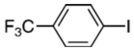
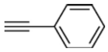
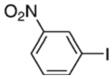
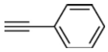
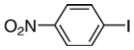
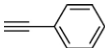
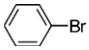
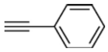
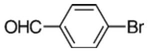
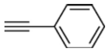
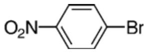
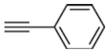
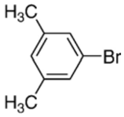
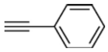
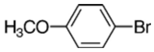
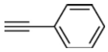
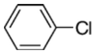
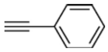
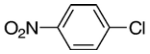
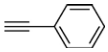
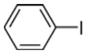
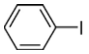
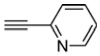
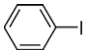
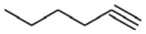
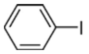
Run	Yield (%)	
	[Bmim]PF_6[b]	CH_3CN[c]
1	100	98
2	98	89
3	94	78
4	79	70
5	78	48
6	66	Undone
7[d]	92	Undone

[a] **2** 2 mol% (0.02 mmol), iodobenzene 1 mmol, phenylacetylene 1.5 mmol, Et_3N 2 mmol, reaction time 2 h, temperature 80 °C, time 2 h, solvent 2 mL.
[b] The total loss of Pd was undetectable by ICP analysis.
[c] The concentration of Pd in the combined organic phase after 5 runs was 7.2 μg/g.
[d] The residues after the sixth run were washed with water to remove the cumulative ammonium salts.

serious leaching of the Pd catalyst into the organic phase. After 5 runs, it was found that the concentration of Pd in the combined organic solution was 7.2 μg/g (ICP analysis), indicating 34% loss of Pd into the organic phase.

The generality of **2** as catalyst in [Bmim]PF_6 for the Sonogashira reaction was shown in Table 3, in which a wide range of the substrates with different electronic and steric effects were investigated. The results showed that the catalytic system of **2**-[Bmim]PF_6 was generally efficient to the coupling of aryl iodides with phenylacetylene. The electronic and steric properties of the substituents also showed the obvious influences on the reaction rate. The aryl iodides with electron-donating substituents, such as methyl and methoxyl, reacted with phenylacetylene to generate the corresponding coupling products in good to moderate yields (Entries 1–6). The substituent located at *meta*- or *para*-position gave rise to the reaction in comparison to that at *ortho*-position due to the steric effect. The activated aryl iodides with electron-withdrawing substituent such as $-CF_3$ or $-NO_2$, coupled with phenylacetylene in excellent yields when the substituent was located at *meta*- or *para*-position (Entries 8–11). As for the aryl bromides with relatively low reactivity, the activated substrates with electron-deficient character, such as 4-bromobenzaldehyde and 4-bromonitrobenzene, coupled with phenylacetylene in better yields than non-activated bromobenzene as the reaction temperature was raised to 120 °C (Entries 13, 14 *vs* 12). The deactivated substrates (1-bromo-3,5-dimethylbenzene and 1-bromo-4-methoxybenzene) were converted to the corresponding coupling products in relatively low yields even harsh reaction conditions were applied (Entries 15 and 16). All attempts by using chlorobenzene or 4-chloronitrobenzene to perform the Sonogashira coupling under the applied conditions have failed so far (Entries 17 and 18). When other terminal acetylenes were examined to couple with iodobenzene, the excellent yields of the products were obtained without obvious electronic and steric discrimination as shown in Entries 19–22.

Table 3
The generality of **2** as catalyst for the Sonogashira reactions of terminal acetylenes with aryl halides in [Bmim]PF_6[a].

Entry	Aryl halide	Terminal acetylenes	Time (h)	Yield (%)[c]
1			3	38
2			3	82
3			3	71
4			3	36
5			3	63
6			3	57
7			3	36
8			3	93
9			3	97
10			2	98
11			2	100
12[b]			2	71
13[b]			2	81
14[b]			2	83
15[b]			2.5	24
16[b]			2	25
17[b]			6	3
18[b]			6	5
19			2	99
20			2	93
21			2	90
22			2	96

[a] **2** 2 mol% (0.02 mmol), aryl halide 1 mmol, terminal acetylene 1.5 mmol, Et_3N 2 mmol, temperature 80 °C, [Bmim]PF_6 2 mL.
[b] Temperature 120 °C.
[c] GC and GC-mass analysis.

3. Conclusions

The novel functionalized IL (**2**) containing the phosphine-ligated Pd(II) complex, featured with ionophilicity, hydrophobicity, and moisture- and air-insensitivity, was proved to be a highly efficient, recoverable and recyclable catalyst for the Sonogashira reaction of phenylacetylene with iodobenzene under aerobic and CuI-free conditions when the structurally similar room temperature IL of [Bmim]PF_6 was used as the solvent. Due to their compatibility, **2** was tightly locked in [Bmim]PF_6, thus avoiding the Pd leaching and facilitating the reuses of **2**. **2**-[Bmim]PF_6 IL systems could successfully catalyze the Sonogashira reactions available for a wide range of substrates including sterically hindered and electron-rich aryl iodides and aryl bromides, and several terminal acetylenes.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at doi:10.1016/j.catcom.2011.10.031.

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