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Catalysis Communications

journal homepage: www.elsevier.com/locate/catcom

Short Communication

Amphiphilic ionic palladium complexes for aqueous–organic biphasic Sonogashira reactions under aerobic and CuI-free conditions $\stackrel{i}{\sim}$



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ARTICLE INFO

Article history: Received 1 April 2013 Received in revised form 3 May 2013 Accepted 4 May 2013 Available online 10 May 2013

Keywords: Sonogashira reaction Water-soluble palladium complexes Ionic complexes Biphasic catalysis

ABSTRACT

The ionic Pd(II)-complexes of **2** (ammonium-[1-(2-hydroxyethyl)-3-methylimidazolium] bis[3-(diphenylphosphino)benzenesulfonate]-dichloropalladium(II) ([(NH₄)(Hemim)][PdCl₂(TPPMS)₂])) and **3** (bis [1-*n*-butyl-3-methylimidazolium] bis[3-(diphenylphosphino)benzenesulfonate]-dichloropalladium(II) ([[Bmim]₂ [PdCl₂(TPPMS)₂])) were synthesized and fully characterized. The single crystal X-ray diffraction analyses show that **2** and **3** are composed of the imidazolium-based cations and [PdCl₂(TPPMS)₂]^{2–} anions. The properties of such imidazolium-based Pd-complexes of **2** and **3**, in terms of the aqueous solubilities and the catalytic behaviors in water, could be dramatically varied. When **2** and **3** were applied as the precatalysts for the Sonogashira coupling of iodobenzene with phenylacetylene under aerobic and Cul-free conditions, the much higher yields of 1,2-diphenylethyne were obtained due to their amphiphilicity. The wide generality of **2** was available for aqueous-organic biphasic Sonogashira reactions.

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1. Introduction

Palladium-catalyzed Sonogashira reaction is a powerful tool for the formation of Csp²–Csp bond, and the most important method for the synthesis of internal acetylenes [1]. In a typical Sonogashira procedure, the reaction is conducted using a phosphine-ligated palladium complex with a catalytic amount of copper(I) iodide as a co-catalyst in the presence of base under inert atmosphere [1,2]. However, the in situ formed copper(I) acetylides with moisture- and air-sensitivity induce unwanted homocoupling products of terminal alkynes through Glaser reaction [2-4]. In the last few decades, a variety of efficient palladium catalysts containing hindered phosphines [5-9], palladacycles [10,11] and N-heterocylic carbene (NHC) [12-15] have been developed for the copper-free Sonogashira reactions, which allow the manipulation of the Sonogashira reaction with low catalyst loadings under copper-free conditions and without exclusion of air and moisture. The absence of copper also makes the Sonogashira reactions possibly be performed in water medium [14–16].

Aqueous organometallic catalysis (AOC) by water-soluble phosphine complexes has been developed into a most successful way for product isolation and/or catalyst recycling [17–19]. The solubility of the organometallic catalysts in water is determined by the solubility

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of the ligands, and the sulfonated phosphines are generally the most important ones in AOC [20-22]. Typically, under aqueous-organic biphasic condition in AOC, the addition of a phase-transfer catalyst, such as surfactant [23,24] or cyclodextrin [25,26], is required in order to eliminate the serious mass transfer limitation observed with hydrophobic substrates. The use of amphiphilic phosphines has recently been found to be a promising alternative to suppress the mass transfer factor because the amphiphilic phosphines incorporate the surface-active property and the coordinating ability to the metal into the same compound [27-29]. Unfortunately, the syntheses of amphiphilic phosphines are often time-consuming, laborious and expensive. The activities in the functionalization of ionic liquids in our group highlight us to replace the typical counter-cation of Na⁺ or NH₄⁺ in TPPMS by the imidazolium-based cation, which can provide amphiphilicity via incorporating lipophilic organic moieties. On the basis of this conception, herein, the amphiphilic TPPMS-ligated Pd complexes of 2 and 3 were synthesized (see Supplementary Information) and fully characterized (Scheme 1), which were further studied as the precatalysts for aqueous-organic biphasic Sonogashira reactions under aerobic and Cul-free conditions.

2. Results and discussion

2.1. Synthesis and characterization of 1, 2 and 3

At room temperature, **2** and **3** were synthesized through exchanging the cation of NH_4^+ in **1** [30] by the imidazolium-based cations, which were fully characterized by ¹H NMR, ³¹P NMR, CHN-elemental analysis, and single-crystal X-ray analysis. The molecular structures of **2** and **3**



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Scheme 1. The ionic Pd-complexes of **1**, **2**, and **3** as the precatalysts for aqueous–organic biphasic Sonogashira reactions.

were depicted in Fig. 1, which were both composed of the imidazoliumbased cations and the Pd-complex anions. The Pd-complex anion possesses the square-planar geometry which is similar to that in PdCl₂(PPh₃)₂ [31]. The Pd center, lying at the center of inversion, is coordinated by two chloride ions and two mono-sulfonated phosphine ligands. The Pd–P distances observed in **2** (2.33–2.34 Å) and **3** (2.32 Å) are in the classical range, compared to those observed in the reported phosphine-ligated Pd(II) complexes with structural similarity [31,32]. As for **2**, two benzenesulfonate groups located in the Pd-complexanion ([PdCl₂(TPPMS)₂]^{2–}) are located in *cis*-position due to the strong hydrogen bond interactions between the sulfonate groups with NH₄⁴. The presence of such strong hydrogen bond interaction led to the slightly distorted square-planar [PdCl₂(TPPMS)₂]^{2–}, which is counteracted by one NH₄⁴ and one [Hemim]⁺ (1-(2-hydroxyethyl)-3methylimidazolium). Whereas in **3**, two benzenesulfonate groups are located in *trans*-position in the corresponding Pd-complex-anion with high symmetry, which is counteracted by two $[Bmim]^+$ (1-*n*-butyl-3-methylimidazolium). The ¹H NMR and ³¹P NMR spectra further supported the assigned structures of **2** and **3**. The ³¹P NMR spectra show the different resonances at 37.6 ppm for **2** and 25.1 ppm for **3**, due to the influence of the different cations on the chemical environment of $[PdCl_2(TPPMS)_2]^{2-}$ via the varied electrostatic interaction, and the additional hydrogen bond interaction in **2**.

The solubilities of **1**, **2**, and **3** in water were determined by the equilibrium method at 20 °C. It was found that, with the same Pd-complex anion, the different composition of the counter-cations could dramatically affect the solubility of the corresponding ionic compounds. When one of NH_4^+ in **1** was replaced by [Hemim]⁺, the solubility of the resultant compound of **2** was increased from 36.9 g/L to 52.9 g/L, due to the presence of – OH in the cation which developed the strong hydrogen bond interaction with water. While two of NH_4^+ in **1** were replace by [Bmim]⁺, the solubility of the resultant compound **3** was decreased to 3.4 g/L, due to the presence of the more lipophilic group of [Bmim]⁺. On the other hand, besides hydrophilicity derived from $[PdCl_2(TPPMS)_2]^{2-}$, **2** and **3** were featured with lipophilicity because of the presence of the alkyl- and imidazolium-moieties. Hence, **2** and **3** are featured with more amphiphilic character in comparison to **1**, which is purely hydrophilic due to the present of NH_4^+ as the counter-cations.

2.2. Catalytic performance of **1–3** for aqueous–organic biphasic Sonogashira reaction

The coupling of phenylacetylene with iodobenzene was studied as a model reaction to investigate the catalytic performance of 1-3 in water under Cul-free conditions (Table 1). Through screening the bases, piperidine as a strong base and effective acid-scavenger could expedite the reaction rate more rapidly than the others such as K_2CO_3 , Cs_2CO_3 ,



Fig. 1. The single crystal structures of 2 and 3 [the selected bond distances (Å) and bond angles (°): 2 Pd1-P1 2.3253(12), Pd1-P1A 2.3434(12), P1-Pd1-P1A 177.51(5), Cl1-Pd1-Cl1A 175.96(7), Cl1-Pd1-P1 91.06(5), Cl1-Pd1-P1A 89.86(4); 3 Pd1-P1 2.3326(18), Pd1-P1A 2.3326(17), P1-Pd1-P1A 180.0, Cl1-Pd1-Cl1A 180.0, Cl1-Pd1-P1 91.64(7) Cl1-Pd1-P1A 88.36(7)].

Table 1

The aqueous–organic biphasic Sonogashira reaction of phenylacetylene with iodobenzene catalyzed by **1–3**.^a

Entry	Precatalyst	Solvent	Conversion (%) ^b	Yield (%) ^b
1	1	H ₂ O	72	72
2	2	H_2O	100	100
3	3	H_2O	97	97
4 ^c	2	CH ₃ CN	40	40

 $^a\,$ Precatalyst 0.2 mol% (2 µmol), iodobenzene 1.0 mmol, phenylacetylene 1.5 mmol, piperidine 1.5 mmol, solvent 4 mL, temperature 70 °C, time 1.5 h.

^b GC analysis (with 100% selectivity to 1,2-diphenylethyne).

^c Homogeneous system.

pyridine, Et₃N, Et₂NH, (*i*-Pr)₂NH, and *n*-Bu₂NH. Under the optimized condition (1.5 h, 70 °C, piperidine as the base), the complete conversion of iodobenzene into the cross-coupling product of 1,2diphenylethyne was obtained over 2 with the best aqueous solubility (Entry 2). In comparison with 2, the lowest yield of 72% was observed over 1 (Entry 1), and the competitive yield up to 97% was obtained over 3 (Entry 3) although the aqueous solubility of 3(3.4 g/L) was much lower than those of **2** (52.9 g/L) and **1** (36.9 g/L). Actually, as precatalysts, the catalytic nature of 1-3 was basically the same, which was all derived from the anion of $[PdCl_2(TPPMS)_2]^2$. The different yields of 1,2-diphenylethyne over 1, 2, and 3 implied that the corresponding counter-cations of 1, 2, and 3 could affect aqueous-organic biphasic coupling reaction definitely. In comparison to 1 with NH₄⁺ as the counter-cations possessing the hydrophilic character, 2 and 3 were feathered with the amphiphilicity due to the presence of the imidazolium-based organic cations. As a result, the amphiphilic 2 and **3** not only behaved as the precatalysts for the Sonogashira reaction, but also acted as the quaternary ammonium surfactants to suppress the mass transfer limitation in the biphasic system. On the other hand, the timely removal of the byproduct of piperidine. HI salt from the organic phase into the aqueous one was the additional driving force to promote the coupling reaction with the expedited reaction rate, leading to the higher yield of 1,2-diphenylethyne in the biphasic system than that in the homogeneous catalysis (Entries 1-3 vs 4).

AOC was to allow the facile separation workup and/or catalyst recycling. Upon completion, the lipophilic product of 1,2-diphenylethyne was obtained simply through decantation of the upper organic phase without contamination by the by-product of piperidine HI salt, which was completely stripped into the aqueous phase. Anyway, the deactivated Pd-black was precipitated from the aqueous phase badly and the lower aqueous phase became colorless and limpid upon the 1st-run. Resultantly, the recycling use of the left aqueous phase containing the precipitated Pd-black for the coupling of Arl with phenylacetylene was unsuccessful with the yield of 1,2-diphenylethyne less than 5% in the 2nd run, which suggested that **2** suffers from serious deactivation probably due to the fragmentation by water [33].

The generality of **2** as the precatalyst for aqueous–organic biphasic Sonogashira reactions, in which a wide range of the substrates with different electronic and steric effects were investigated (see S. Table 2 in Supplementary Information). In order to obtain the acceptable yields for the coupling products, the concentration of **2** was increased up to 5 mol⁸. When the aryl iodides were used to couple with phenylacetylene over 2 under the mild conditions, generally the cross-coupling products were obtained in excellent yields without obvious discrimination for the electronic and steric properties of the substituents (Entries 1-12). Reasonably, while the substituent was located at para-position, the best coupling yields were found due to the less steric hindrance (Entries 3, 6, 9, and 12). 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 when the reaction temperature was raised to 110 °C (Entries 13 vs 14 and 15). The deactivated substrates with electron-rich character (1-bromo-4-methoxybenzene and 1-bromo-4-methylbenzene) were converted to the corresponding coupling products in moderate yields under the same conditions (Entries 16 and 17). The coupling of chlorobenzene with phenylacetylene led to the yield of 38% under the relatively harsh conditions (110 °C, 5 h). Anyway, the activated chlorobenzene with the electron-deficient substituent like – NO₂ or – CHO corresponded to the poor yields unexpectedly (Entries 19 and 20). When the other terminal acetylenes of 2-ethynylpyridine with the conjugated effect and but-3-yn-1-ol possessing hydroxyl substituent were used to couple with iodobenzene, the acceptable yields of the products were obtained (Entry 21: 78%; Entry 22: 92%). As for hex-1-yne without any other substituent, the low yield of 34% was found (Entry 23).

3. Conclusions

The ionic Pd(II)-complexes of **2** and **3** were synthesized through exchanging the cation of NH_4^+ in **1** by the imidazolium-based organic moieties. The difference of the counter-cations could dramatically change the properties of the corresponding Pd-complexes of **1–3**, in terms of the aqueous solubilities and the catalytic behaviors in water, respectively. **2** and **3** were featured with the amphiphilic character due to the dually presence of the lipophilic imidazolium-based cation and the hydrophilic anion of $[PdCl_2(TPPMS)_2]^{2-}$. When **2** and **3** were applied as the precatalysts for the coupling of iodobenzene with phenylacetylene in water under aerobic and Cul-free conditions, the much higher yields of 1,2-diphenylethyne were obtained due to their amphiphilicity. The wide generality of **2** was observed for aqueous–organic biphasic Sonogashira couplings of terminal acetylenes with aryl halides.

Acknowledgments

This work was financially supported by the National Natural Science Foundation of China (Nos. 21273077 and 21076083).

Appendix A. Supplementary data

CCDC-928534 and CCDC-928535 contain the supplementary crystallographic data of **2** and **3** for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www. ccdc.cam.ac.uk/data_request/cif. The Supplementary Information associated with this article can be found online at http://dx.doi.org/10.1016/j. catcom.2013.05.005.

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