



Accepted Article

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This manuscript has been accepted and appears as an Accepted Article online.

This work may now be cited as: *Chin. J. Chem.* **2020**, *38*, 10.1002/cjoc.202000237.

The final Version of Record (VoR) of it with formal page numbers will soon be published online in Early View: http://dx.doi.org/10.1002/cjoc.202000237.

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ISSN 1001-604X • CN 31-1547/O6 mc.manuscriptcentral.com/cjoc www.cjc.wiley-vch.de Cite this paper: Chin. J. Chem. 2021, 39, XXX-XXX. DOI: 10.1002/cjoc.202100XXX

Synthesis of NHC Silver(I) and Palladium(II) Complexes with Acylated Piperazine Linker and Catalytic Activity in Three Types of C-C Coupling Reactions

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Keywords

VCCED

Silver | Palladium | N-Heterocyclic carbine | Catalytic activity | C-C Coupling reaction

Main observation and conclusion

Two bis-imidazolium salts $LH_2 \cdot CI_2$ and $LH_2 \cdot (PF_6)_2$ with acylated piperazine linker and two *N*-heterocyclic carbene (NHC) silver(I) and palladium(II) complexes [L₂Ag₂](PF₆)₂ (1) and [L₂Pd₂Cl₄] (2) were prepared. The crystal structures of $LH_2 \cdot CI_2$ and 1 were confirmed by X-ray analysis. In 1, one 26-membered macrometallocycle was generated through two silver(I) ions and two bidentate ligands L. The catalytic activity of 2 was investigated in Sonogashira, Heck-Mizoroki and Suzuki-Miyaura reactions. The results displayed that these C-C coupling reactions can be smoothly carried out under the catalysis of 2.

Comprehensive Graphic Content



This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/cjoc.202000237

Background and Originality Content

After the first free stable N-heterocyclic carbene (NHC) was discovered.^[1] the metal complexes based on N-heterocyclic carbenes have drawn considerable attention owing to their easy access and structural variety.^[2] Various kinds of relevant metal complexes have been prepared via deprotonation of benzimidazolium (or imidazolium) salts.^[3] Because N-heterocyclic carbenes possess the strong σ -donating ability, the metal complexes of them have high stability to air, moisture and heat.^[4] Among NHC r etal complexes, NHC silver(I) complexes play an important part. On one hand, NHC silver(I) complexes can be used as carbene transfer reagent to synthesize NHC-Ni(II), -Pd(II), -Cu(II), -Au(I), -Rh(I), and -Ru(II) complexes.^[5,6] On the other hand, NHC silver(I) complexes are of biological activities as antimicrobial and anti-Incer agents.^[7,8] In addition, NHC palladium(II) complexes also attracted extensive attention due to their importance as catalysts organic synthesis. NHC palladium(II) complexes have multiple types of structures.^[9] Among them, NHC-Pd(II) complexes with 'o coordinated halogen atoms (Cl, Br or I) are a common kind of catalyst, and they mainly contain six classes of structures as shown in Scheme 1. (1) Mono-palladium(II) complexes bearing vo monodentate ligands (namely, two NHC ligands, or one NHC ligand and one other ligand with heteroatom E (N, P, O, As and)),^[10] (2) mono-palladium(II) complexes bearing one bidentate cnelating ligand (II),^[11] (3) open bi-palladium(II) complexes bearing one bis-NHC ligand (III),^[12] (4) open bi-palladium(II) complexer bearing one bis-NHC ligand using B as bridge linker (IV), [13] (5) cyclic bi-palladium(II) complexes bearing two bidentate chelating ligands (V)^[14] and (6) open tri-palladium(II) complexes bearing he tri-NHC ligand (VI).[15] These catalysts have been widely applied in some organic reactions such as Suzuki-Miyaura, eck-Mizorokim, olefin metathesis and Sonogashira reactions.^[16] Over the past two decades, the organic reactions in aqueous n edia have been concerned by more and more researchers for nvironmentally friendly and safe purposes. A number of related reactions using P-Pd(II)^[17] or NHC-Pd(II)^[18] complexes as catalysts

ave been reported. However, the application of P-Pd(II) complexes was limited due to their toxicity and air-instability. By conast, NHC-Pd(II) complexes are more favored by researchers due to their small toxicity and good air-stability. NHC-Pd(II) catalyzed cue. ons in aqueous media are relatively rare, and the main problem is that water-solubility of most NHC-Pd(II) complexes is poor. To solve this problem, it is necessary that introducing some sood water-soluble groups in the preparation of ligand. For example, Huynh reported the complexes with -NR3⁺ (type I in S heme 1), and these catalysts can catalyze Suzuki-Miyaura and Mizoroki-Heck coupling reactions using PrOH/H2O as solvent to give excellent yields for aromatic bromide, and good yields for omatic chloride.^[19] Peris reported complexes with -SO₃ (type I and type II in Scheme 1), and these catalysts can catalyze Suzuki-Miyaura coupling reactions using H₂O as solvent to give modate to high yields.^[20] Also, Cetinkaya and co-workers developed a series of NHC-Pd(II) complexes with one carboxylate and two carboxylates (type I in Scheme 1), and these catalysts can catalyze Suzuki-Miyaura coupling reactions in water to give moderate to high yields.^[21] Even so, the preparation of water-soluble and

highly effective NHC-Pd(II) catalyst is still a challenge.

Additionally, Sonogashira reaction under copper-free is one of the things that researchers focused on. In a typical Sonogashira procedure, the reaction is conducted using a Pd catalyst with a copper additive (like Cul) as cocatalyst. Although the copper additive can increase the cross-coupling rate, it can also promote the occurrence of Glaser-Hay coupling as a side reaction.^[22] Moreover, Cu-acetylide generated in situ is extremely sensitive to air and moisture, so inert atmospheric conditions are required.^[23] To overcome these drawbacks, some palladium catalysts containing phosphine^[24] or NHC^[25] ligands have been developed in the absence of Cu. However, NHC-Pd(II) catalyzed Sonogashira couplings under copper-free remain tiny compared to P-Pd(II) complexes. Here are a few related examples, such as Ghosh reported the complexes [(NHC)PyPdI₂] (type I in Scheme 1), and these catalysts can catalyze Sonogashira coupling reactions to give moderate to high yields for aromatic bromide and aromatic iodide.[26] Yasar reported the mixed P/NHC-Pd(II) complexes [(NHC)(PPh₃)PdCl₂] (type I in Scheme 1), and good to excellent yields for aromatic bromide and iodide were obtained.[27] Also, Cao reported the complexes [(NHC)PyPdBr₂] (type I in Scheme 1), and the yields of 55-91% for aromatic bromide and iodide were gained.^[28] Although some good results were obtained in these Sonogashira reactions, the most of cases suffer from the problem of high catalyst loadings.

In view of this, further developing environmentally friendly, air-stable and highly efficient catalysts for C-C cross-coupling reactions is still highly desired. We are interested in bis-NHC ligands and their metal complexes, several open bi-Pd(II) complexes ([(NHC)(CH₃CN)(PdCl₂)]₂) with different bridging linkers (such as alkyl, aryl or aryl ether) have been reported by us (type IV in Scheme 1),^[29] in which NHC-Pd(II) complexes were synthesized via the metal exchange reaction of NHC-Ag(I) complexes with PdCl₂(CH₃CN)₂. The catalytic activities of these complexes in Suzuki-Miyaura or Heck-Mizoroki reactions were investigated using MeOH/H₂O or H₂O as solvents with the catalyst dosages of 0.1-0.2%. In most cases, the moderate to high yields for aromatic bromide and iodide were obtained. To explore more efficient catalysts for C-C coupling reactions in aqueous media, herein, we report the synthesis of two bis-imidazolium salts LH2·Cl2 and LH₂·(PF₆)₂ and two N-heterocyclic carbene silver(I) and palladium(II) complexes $[L_2Ag_2](PF_6)_2$ (1) and $[L_2Pd_2Cl_4]$ (2) (type V in Scheme 1). Particularly, the catalytic performance of complex 2 was studied in Suzuki-Miyaura, Heck-Mizoroki and Sonogashira reactions. During investigation, we paid special attention to three aspects below. Firstly, the water-soluble acylated piperazine as bridging group was introduced in the synthesis of ligands, which was a new attempt for the preparation of NHC metal complexes. As expected, above three types of C-C coupling reactions can be smoothly carried out in $H_2O/EtOH$ (1:1) under the catalysis of 2. Secondly, we did not add any copper additive in Sonogashira reactions, but good cross-coupling yields were obtained. Thirdly, although the low catalyst loading (0.1 mol%) in these coupling reactions were used, the similar yields were obtained in comparison with other traditional NHC-Pd(II) catalyst using high catalyst dosages.^[30] These results indicated that complex 2 was an effective catalyst for promoting the formation of C-C bond.

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Scheme 1 Structures of some NHC-Pd(II) complexes with two coordinated halogen atoms (Cl, Br or I)

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Report

Results and Discussion

Preparation and characterization of bis-imidazolium salts $LH_2 \cdot Cl_2$ and $LH_2 \cdot (PF_6)_2$ and NHC metal complexes $[L_2Ag_2](PF_6)_2$ (1) and $[L_2Pd_2Cl_4]$ (2)

The piperazine as a starting material was treated with chloroacetyl chloride in the presence of Na₂CO₃ to generate 1,4-bis(2'-chloroacetyl)piperazine as shown in Scheme 2, followed by the reaction with *N*-nbutylimidazole to afford b s-imidazolium salt LH₂·Cl₂. Subsequent anion exchange reaction sing NH₄PF₆ in CH₃OH was conducted to generate 1,4-bis[2'-(*N*-nbutylimidazoliumyl)acetyl]piperazine hexafluoronosphate LH₂·(PF₆)₂, which reacted further with Ag₂O in acetonitrile under N₂ for 24 h to afford NHC silver(I) complex [I₂Ag₂](PF₆)₂ (1). NHC palladium(II) complex [L₂Pd₂Cl₄] (2) was prepared via the metal exchange reaction of [L₂Ag₂](PF₆)₂ (1) with PdCl₂(CH₃CN)₂ (2 equiv.) in CH₃CN under N₂.

Precursor LH₂·(PF₆)₂ has good stability in air, and it is soluble in CH₃CN, CH₂Cl₂ and DMSO, and hardly soluble in petroleum cher, diethyl ether and benzene. In the ¹H NMR spectrum of LH2·(PF6)2 (Figure S7), the proton signal of imidazolium (NCHN) was at δ = 9.07 ppm, and this value was similar to the signals of nown imidazolium salts.^[2,3] Complexes 1 and 2 were stable in the air, soluble in DMSO, but nearly insoluble in petroleum ether nd diethyl ether. From the ¹H NMR spectra of **1** and **2** (Figure S9 and Figure S11), the proton signals of imidazolium (NCHN) have disappeared, which indicated the formation of NHC-metal complexes, and the signals of other protons were similar to those of LH2·(PF6)2. [31-35] In the ¹³C NMR spectra of 1 and 2 (Figure S10 and Figure S12), the signals of the carbonyl carbon were observed at _30.4 ppm and 179.9 ppm. The signal of carbene carbons for 1 d d not observed, and this phenomenon has been reported in some literatures of carbene-silver(I) complexes.^[32] The signal of carbene carbons for 2 was observed at 171.9 ppm, and this value as similar to the signals of known carbene-palladium(II) complexes.^[5] In ESI-MS of [L₂Pd₂Cl₄] (2) (Figure S13(a)-(c)), the signals o^c losing 2Cl⁻, 3Cl⁻ and 4Cl⁻ (m/z [(M - 2Cl⁻)²⁺/2] = 556.5267, m/z $_{11}M - 3Cl^{-})^{3+}/3$ = 359.0568 and m/z [(M - 4Cl^{-})^{4+}/4] = 260.0894) were observed, which further indicated that the structure of N HC-Pd(II) complex 2 was a macrocycle as shown in Scheme 2. Additionally, the carbene-silver(I) complex as an intermediate of preparing carbene-palladium(II) complex via metal exchange reaction has been reported in some literatures, [36-38] in which the ructure of carbene-palladium(II) complexes were similar to the structure of carbene-silver(I) complexes. We attempted to obtain c ystal structure of 2, unfortunately, it was unsuccessful.

structures of $LH_2 \cdot Cl_2$ and $[L_2Ag_2](PF_6)_2(1)$

The single crystals of LH_2 · Cl_2 and $[L_2Ag_2](PF_6)_2$ (1) were gained rough diffusing diethyl ether to their solution of CH_3CN . In the cation of LH_2 · Cl_2 (Figure 1), the N-C-N angle at imidazole ring is 1)8.4(1)°, and this value is similar to those in the literatures of known imidazolium salts.^[39-42] In LH_2 · Cl_2 , two imidazole rings were parallel, and an inverse symmetric center was observed.

The crystal structure of **1** was displayed in Figure 2, where two ligands **L** and two silver(I) ions formed a 26-membered macrocycle. The Ag(1) \cdots Ag(1A) separation was 11.506(8) Å, which

showed no metal-metal interactions between two $Ag^{+,[43]}$ The piperazine rings exhibited chair configuration and an inverse symmetric center was observed in **1**.





Figure 1 Perspective view of LH₂·Cl₂ and anisotropic displacement parameters depicting 50% probability. Some bond angles (°) and lengths (Å): N(2)-C(7)-N(1) 108.4(1), C(9)-N(3)-C(10) 120.0(1); C(7)-N(1) 1.323(2), C(7)-N(2) 1.329(1), C(9)-N(3) 1.341(2), C(10)-N(3) 1.464(2). Sym. code: i: -*x*, 1 - *y*, 1 - *z*. Monoclinic, space group *P*2₁/c with cell dimensions of *a* = 0.759(4) nm, *b* = 1.588(8) nm, *c* = 1.069(5) nm, *b* = 98.14(1)°, V = 1.2765 nm³, *Z* = 2, μ = 2.84 cm⁻¹.



Figure 2 Perspective view of 1 and anisotropic displacement parame-

ters depicting 50% probability. Some bond angles (°) and lengths (Å): N(2)-C(7)-N(1) 104.0(3), C(7A)-Ag(1)-C(17) 174.5(1), N(5)-C(17)-N(6) 103.9(3); C(7A)-Ag(1) 2.079(4), C(17)-Ag(1) 2.084(3), C(7)-N(1) 1.355(5), C(7)-N(2) 1.354(5). Sym. code: i: -1 + x, 1 + y, -1 + z. Triclinic, space group *P*-1 with cell dimensions of *a* = 1.027(7) nm, *b* = 1.306(1) nm, *c* = 1.341(1) nm, β = 93.05(1)°, *V* = 1.6140 nm³, *Z* = 1, μ = 7.72 cm⁻¹.

Catalytic performance of $\left[L_2 P d_2 C l_4\right]$ (2) in Suzuki-Miyaura reaction

The cross-coupling of phenylboronic acid with 4-bromotoluene was used to test the different reaction conditions (Table S2, see the supporting information). The reactions were detected through GC analysis after the suitable intervals. Using K_2CO_3 as base and $H_2O/EtOH$ (1:1) as solvent with the catalyst loading of 0.1 mol% at 40 °C in air gave the same



 Table 1
 Suzuki-Miyaura reaction with different aryl halides catalyzed by complex 2^a

eaction conditions: Aryl halide (0.50 mmol), phenylboronic acid (0.60 mmol), K₂CO₃ (1.0 mmol), complex **2** (0.1 mol%), TBAB (10% mol), H₂O/EtOH (1:1) (3 mL), 40 °C, in air.

yield of 92% in 14 h or 16 h (entries 10 and 20). When the temperature of reaction was changed to 25 °C or 60 °C, the yields of 56% or 92% were obtained (entries 21 and 22). When time was reduced, the yields also descended (entries 17-19). When the catalyst dosages were reduced, the catalytic performance was bviously decreased (entry 24). Under the same conditions as entry 10, the yield of 96% was obtained after adding 10 mol% trabutylamonium bromide (TBAB) (entry 23, see the supporting information). In this reaction, the palladium(0) species was genera ed in the catalytic process, and this substance may be the actual atalyst. The addition of TBAB can stabilize palladium(0) and improve catalytic activity of the catalyst.[44-48] Water, MeOH, EtOH, 2O/EtOH (5:1), H2O/EtOH (1:5), DMF, 1,4-dioxane, THF and CH₃CN as solvents have also been tested, and the yields of 11-61% rere obtained (entries 1-9). By contrast, the solvent H₂O/MeOH (1:1) gave a high yield of 90% (entry 11). Different bases (Na₂CO₃, D_3 , Et₃N, K₃PO₄·3H₂O, and NaOAc) have also been tested to lead to poor to medium yields (entries 12-16). According to the a ove results, the optimal conditions for this reaction were 12O/EtOH (1:1) and K2CO3 as solvent and base, TBAB (10 mol%) as co-catalyst with the catalyst loading of 0.1 mol% at 40 °C in air (ntry 23, see the supporting information). In entry 25, the coupling reaction was carried out without the precursor, and other conditions were the same as the optimal conditions to afford the v eld of 49%, which illustrated that the precursor played a key role in the catalytic reaction.

As shown in Table 1, the different aryl halides as substrates ere used. In most cases, phenylboronic acid can react with the aryl halides. 4-Nitrobromobenzene or 4-bromoacetophenone gave the excellent yields of 99% or 96% (**2b**(1) and **2d**). 4-Bromoanisole or 3-bromoanisole gave the good yields of 93% or 92% (**2a** and **2c**). The catalyst was highly effective to the coupling of iodobenzene with phenylboronic acid to gave the yield of 100% (**2m**(3)). Relative low yields (trace-36%) were gained in the cases of aryl chlorides as substrates (**2b**(2), **2e**(2), **2j**, **2k**, **2l**, **2m**(2)).

Catalytic performance of $\left[L_2 P d_2 C I_4\right]$ (2) in Heck-Mizoroki reaction

Over the years, the Heck-Mizoroki reaction has been widely concerned and developed.^[49-53] The cross-coupling of styrene with phenyl bromide was used to test the different reaction conditions (Table S3, see the supporting information). Use of H₂O/EtOH (1:1) and K₂CO₃ as solvent and base with the catalyst loading of 0.1 mol% at 110 °C in 12 h gave the yield of 87% (entry 17). Under the same conditions, the yield of 92% was gained after adding 10 mol% TBAB (entry 8, see the supporting information). The results of entry 8 (the yield of 92% in air) and entry 20 (the yield of 92% in N₂) showed that the catalytic system had good tolerance to air. Namely, the atmosphere had no obvious effect on the yield. When the catalyst dosages were reduced, the catalytic performance was obviously decreased (entry 18). Other solvents such as water, MeOH, EtOH, DMF, 1,4-dioxane, THF and CH₃CN were also tested, and the yields of 11-45% were gained (entries 1-7). Some usual bases (K₃PO₄·3H₂O, NaOAc, Et₃N, Na₂CO₃ and NaHCO₃) were also used to give poor to medium yields (entries 9-13). By analyzing above results, the optimal conditions were H₂O/EtOH (1:1) and K₂CO₃ as solvent and base, TBAB (10 mol%) as co-catalyst with the catalyst loading of 0.1 mol% at 110 °C in air (entry 8, see the supporting information). In entry 19, the coupling reaction was carried out without the precursor, and other conditions were same as the optimal conditions to afford the yield of 38%, which illustrated that the precursor played a key role in the reaction.

As displayed in Table 2, other aryl halides as substrates were also used to test the catalytic activity. 4-Bromoacetophenone,

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3-bromoanisole, 4-bromoanisole, 4-nitrobromobenzene and 1-bromonaphthalene can react easily with styrene to afford yields of 90-95% (**3a-3c**, **3d**(1) and **3f**). 4-Bromoaniline gave the yield of 85% (**3e**(1)). Aryl dibromides (9,10-dibromoanthracene, 4,4-dibromobiphenyl and 1,4-dibromonaphthalene) gave yields of 91-95% (**3g-3i**). Iodobenzene and bromobenzene afforded the yields of 98% in 6 h and 92% in 12 h (**3**j(1) and **3**j(2)). Aryl chlorides gave unsatisfactory yields (from trace to 39% for **3d**(2), **3e**(2), **3**j(3), **3k** and **3l**). Notably, only *trans* products were obtained in the catalytic system.





eaction conditions: aryl halide (0.50 mmol), styrene (0.75 mmol), K₂CO₃ (1.0 mmol), complex 2 (0.1 mol%), TBAB (10% mol), H₂O/EtOH (1:1) (3 mL), 110 °C, in air.



e Reaction conditions: aryl halide (0.50 mmol), styrene (0.75 mmol), Cs₂CO₃ (1.0 mmol), complex **2** (0.1 mol%), TBAB (10% mol), H₂O/EtOH (1:1) (3 mL), 80

Catalytic performance of [L₂Pd₂Cl₄] (2) in Sonogashira react^{*}on

Phenylacetylene and 4-bromoacetophenone were chosen to screen the optimal conditions.^[54,55] As illustrated in Table S4 (see t¹ e supporting information), using single solvent (such as CH₃CN, 1,4-dioxane, DMSO, H₂O, DMF, MeOH, EtOH and THF) and using Cs₂CO₃ as base with the catalyst loading of 0.1 mol% at 80 °C in 10

h gave the yields of 24-75% (entries 1-8). However, when mixed solvents such as $H_2O/MeOH$ (1:1) or $H_2O/EtOH$ (1:1) were used in the presence of Cs_2CO_3 at 80 °C in 10 h, the coupling yields of 87% or 88% were obtained (entries 9 and 10). Other bases such as K_2CO_3 , NaOAc, K_3PO_4 ·3 H_2O , Et₃N or NaHCO₃ were also tested upon using $H_2O/EtOH$ (1:1) as solvent at 80 °C in 10 h, and the yields of 26-77% were obtained (entries 11-15). When 10 mol% of TBAB

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was added and other conditions were the same as entries 9 and 10, the yields of 90% and 92% were gained (entry 16 and entry 17, see the supporting information). According to above experimental results, the optimal conditions for this reaction were $H_2O/EtOH$ (1:1) and Cs_2CO_3 as solvent and base, TBAB (10 mol%) as co-catalyst with the catalyst loading of 0.1 mol% at 80 °C in air (entry 17, see the supporting information). In entry 18, the coupling reaction was carried out without the precursor, and other conditions were the same as the optimal conditions to afford the yield of 47%, which illustrated the precursor played a key role in the reaction.

In Table 3, the different aryl halides were tested. ²-Bromoanisole, 4-bromoanisole or 4-bromoaniline coupled with phenylacetylene to give the yields of 89-94% (**4a-4c**). 4-Nitrobromobenzene or 4-bromoacetophenone gave the yields f 96% or 92% (4d(1) and 4h(1)). The couplings of 1-bromonaphthalene, 2-methylbromobenzene or bromobenzene fforded the yields of 85-94% (4g, 4j(1), 4k(1)). The couplings of aryl dibromides (4,4'-dibromobiphenyl or ,10-dibromoanthracene) afforded same yield of 91% (4e and 4f). Coupling of aryl chlorides gave the yields of 55% and 66% (4i and 4-nitrochlorobenzene, **4I**). While 4-chloroacetophenone. -chlorobenzaldehyde or 2-chlorotoluene afforded the poor yields of 36-44% (4d(2), 4h(2), 4m, 4j(2)). Iodobenzene gave the excelent yield of 98% (4k(2)).

Kinetic studies

The kinetic experiments of the three coupling reactions were carried out to research the mechanisms of reactions under the optimal conditions (Table S2: entry 23, Table S3: entry 8 and Table S4: entry 17, see the supporting information). The induction periods of 2 or 3 hours were observed in Figure 3. These reactions rogressed fast from 0 h, Suzuki-Miyaura and Heck-Mizoroki reactions gave the yields of 82% and 78% after 8 h, and Sonogashira reactions progressed slowly, and afforded the final yields of 96% in 14 h, 92% in 12 h and 92% in 10 h. These experimental results howed that the active catalytic species may be Pd(0) and the precatalyst may be complex **2**.^[56, 57]

To understand whether these reactions were homogeneous cr heterogeneous, Hg drop experiments were carried out. These

kinds of reactions were all suppressed. According to the experimental results, Pd(0) was further confirmed to be the actual (atalytic species and these reactions were heterogeneous.^[58, 59]



Figure 3 Kinetic experiments of Sonogashira, Heck-Mizoroki and Suzuki-Miyaura reactions.

Conclusions

In summary, two piperazine-bridging NHC metal complexes $[L_2Ag_2](PF_6)_2$ (1) and $[L_2Pd_2Cl_4]$ (2) have been prepared and characterized. One 26-membered macrometallocycle in complex 1 was formed by two silver(I) ions and two ligand L. Additionally, the catalytic performance of complex 2 was studied in three types of C-C coupling reactions. In the synthesis of ligand, the introduction of acylated piperazine improved water solubility of complex 2. Thus, three types of C-C coupling reactions (Sonogashira, Heck-Mizoroki and Suzuki-Miyaura reactions) can be smoothly carried out in H₂O/EtOH (1:1) under the conditions of low catalyst loading (0.1 mol%). In Sonogashira reaction, although no copper additive was used, good cross-coupling yields were obtained. These results indicated that complex 2 was an effective catalyst for the formation of C-C bonds. Some further researches are underway.

Experimental

General procedures

The solvents and chemicals for experiment were analytical grade by purchasing commercially. ¹H NMR and ¹³C NMR spectra were collected using a Varian spectrometer. A Focus DSQI GC-MS equipped with an integrator (C-R8A) was applied in GC analysis. Elemental analyses were measured to apply Perkin-Elmer 2400C Elemental Analyzer. The Accurate-Mass Q-TOF LC/MS (Agilent) at 220 °C was applied for recording ESI-MS spectra.

Preparation of 1,4-bis(2'-chloroacetyl)piperazine

Chloroacetyl chloride (2.010 g, 17.8 mmol) was added dropwise into a H_2O (100 mL) solution of piperazine (0.765 g, 8.9 mmol) and Na_2CO_3 (1.886 g, 17.8 mmol) under ice-water bath. The mixture was stirred at room temperature for 1 h and a white precipitate was formed. After the mixture was cooled for 0.5 h under ice-water bath, the solid was collected through filtration to give

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Preparation of LH₂·Cl₂ and LH₂·(PF₆)₂

1,4-Bis(2'-chloroacetyl)piperazine (0.956 g, 4.0 mmol) and N-ⁿbutylimidazole (1.104 g, 8.9 mmol) were dissolved in 50 mL of T IF, and heated to reflux with stirring. After 72 h, 1,4-bis[2'-(N-ⁿbutylimidazoliumyl)acetyl]piperazine dichloride (**LH₂·Cl**₂) as a white solid was formed, and it was obtained through intration. Yield: 1.637 g (84%). M.p.: 150-152 °C. ¹H NMR (400 MHz, DMSO-d₆) δ : 9.07 (s, 2H, 2-imiH), 7.81 (s, 2H, ArH), 7.63 (s, 1, ArH), 5.38 (d, *J* = 10.8 Hz, 4H, CH₂), 4.26 (t, *J* = 7.2 Hz, 4H, CH₂), 3.59 (s, *J* = 5.4 Hz, 4H, CH₂), 3.52 (s, 4H, CH₂), 1.79 (s, *J* = 7.2 Hz, 4H, CH₂), 0.93 (t, *J* = 7.2 Hz, 6H, CH₃). ¹³C NMR (100 MHz, DMSO-d₆) δ : 163.9 (*C*=O), 137.3 (imiC), 124.1 (ⁿhC), 121.8 (PhC), 48.6 (CH₂), 31.3 (CH₂), 18.6 (CH₂), 13.2 (CH₃). Anal. Calcd for C₂₂H₃₆O₂N₆Cl₂: C, 54.20; H, 7.44; N, 17.24%. Found: C, 54.33; H, 7.51; N, 17.32%.

The methanol (20 mL) solution of NH₄PF₆ (0.619 g, 3.8 mmol) and the methanol (20 mL) solution of LH₂·Cl₂ (0.974 g, 2.0 mmol) were mixed. The mixture was stirred for 72 h at 25 °C, and 1,4-bis[2'-(N-ⁿbutylimidazoliumyl)acetyl]piperazine hexafluorophosphate (LH₂·(PF₆)₂) as a white solid was formed. LH₂·(PF₆)₂ was obtained through filtration. Yield: 1.235 g (87%). M.p.: 96-98 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ : 9.07 (s, 2H, 2-imiH), 7.81 (s, 2H, PhH), 7.63 (s, 2H, PhH), 5.38 (d, *J* = 10.4 Hz, 4H, CH₂), 4.26 (t, *J* = 6 0 Hz, 4H, CH₂), 3.61 (d, *J* = 6.4 Hz, 4H, CH₂), 3.52 (s, 4H, CH₂), 1.82 (m, *J* = 6.6 Hz, 4H, CH₂), 1.28 (m, *J* = 6.9 Hz, 4H, CH₂), 0.93 (t, *J* 7.0 Hz, 6H, CH₃). ¹³C NMR (100 MHz, DMSO-*d*₆) δ : 163.9 (*C*=O), 137.3 (imiC), 124.1 (PhC), 121.7 (PhC), 48.6 (CH₂), 31.3 (CH₂), 18.7 (CH₂), 13.2 (CH₃). Anal. Calcd for C₂₂H₃₆O₂N₆P₂F₁₂: C, 37.40; H, 5.13; , 11.89%. Found: C, 37.55; H, 5.28; N, 11.78%.

Preparation of complex $[L_2Ag_2](PF_6)_2(1)$

Silver oxide (0.069 g, 0.30 mmol) reacted with 1,4-bis[2'-(*N*-ⁿbutylimidazoliumyl)acetyl]piperazine hexafluorophosphate (0.212 g, 0.30 mmol) in acetonitrile (30 mL) at 40 °C in ter 12 h, the suspension was filtered and the filtrate was concentrated to 5 mL. Upon the addition of 5 mL Et₂O, a white powder was precipitated. Isolation by filtration yields complex ₋₂Ag₂](PF₆)₂ (**1**). Yield: 0.131 g (65%). M.p.: 212-214 °C. ¹H NMR (400 MHz, DMSO-d₆) δ: 7.50 (s, 4H, PhH), 7.36 (s, 4H, PhH), 5.31 (d, J = 10.4 Hz, 8H, CH2), 4.17 (d, J = 6.0 Hz, 8H, CH2), 3.62 (t, J 11.0 Hz, 16H, CH₂), 1.79 (s, 8H, CH₂), 1.30 (q, J = 6.9 Hz, 8H, CH₂), 0.93 (t, J = 7.0 Hz, 12H, CH₃). ¹³C NMR (100 MHz, DMSO- d_6) δ : 130.4 (C=O), 123.8 (PhC), 121.3 (PhC), 50.7 (CH₂), 33.2 (CH₂), 19.2 CH₂), 13.5 (CH₃). Anal. Calcd for C₄₄H₆₈O₄N₁₂Ag₂P₂F₁₂: C, 39.59; H, 5.13; N, 12.59%. Found: C, 39.44; H, 5.35; N, 12.46%.

rreparation of $[L_2Pd_2Cl_4](2)$

 $Pd(CH_3CN)_2Cl_2$ (0.026 g, 0.10 mmol) was added to a solution of $[t_2Ag_2](PF_6)_2$ (1) (0.067 g, 0.05 mmol) in CH₃CN (25 mL) under N₂, and the suspension solution was stirred for 24 h at ambient temperature. After filtering, the solvent in the filtrate was re-

moved by rotary evaporator to afford a yellow powder. This powder was recrystallized through adding diethyl ether into its CH₃CN solution to give [L₂Pd₂Cl₄] (**2**) as a pale yellow powder. Yield: 0.049 g (83%). M.p.: 272-275 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ : 7.81 (s, 4H, ArH), 7.62 (s, 4H, ArH), 5.37 (d, *J* = 10.0 Hz, 8H, CH₂), 4.26 (t, *J* = 6.0 Hz, 8H, CH₂), 3.60 (d, *J* = 6.0 Hz, 8H, CH₂), 3.51 (s, 8H, CH₂), 1.82 (m, 8H, CH₂), 1.28 (m, 8H, CH₂), 0.92 (t, *J* = 7.0 Hz, 12H, CH₃). ¹³C NMR (100 MHz, DMSO-*d*₆) δ : 179.9 (*C*=O), 171.9 (*C*_{carben}), 126.6 (PhC), 122.6 (PhC), 50.1 (CH₂), 47.9 (CH₂), 33.5 (CH₂), 19.8 (CH₂), 13.7 (CH₃). ESI-MS: m/z [(M - 2Cl·)²⁺/2] = 556.5267, m/z [(M - 3Cl·)³⁺/3] = 359.0568, m/z [(M - 4Cl·)⁴⁺/4] = 260.0894.

General method of Suzuki-Miyaura reaction

For a representative reaction, 4-nitrobromobenzene (0.101 g, 0.50 mmol), phenylboronic acid (0.073 g, 0.60 mmol), TBAB (0.016 g, 10 mol%), K₂CO₃ (0.165 g, 1.2 mmol) and [L₂Pd₂Cl₄] (**2**) (0.5 mg, 0.1 mol%) were added into the solvent (3 mL, H₂O:C₂H₅OH = 1:1, v:v), and stirred at 40 °C in air. After the predetermined time, 10 mL of water was added to the reaction mixture, which was extracted three times using CH₂Cl₂ (8 mL × 3). The oil layer was washed three times with water (8 mL × 3), which was dried over MgSO₄. After filtration, the solution was concentrated to 3 mL. The solution was separated through a column chromatography to give 4-nitrobiphenyl (**2b**). Yield: 0.099 g (99%). ¹H NMR (400 MHz, CDCl₃) δ : 8.31 (d, *J* = 8.8 Hz, 2H, ArH), 7.75 (d, *J* = 8.8 Hz, 2H, ArH), 7.64 (t, *J* = 4.2 Hz, 2H, ArH), 7.45 (m, 3H, ArH). ¹³C NMR (100 MHz, CDCl₃) δ : 147.6, 147.1, 138.7, 129.1, 128.9, 127.8, 127.3, 124.1.

General method of Heck-Mizoroki reaction

A mixture of bromobenzene (0.078 g, 0.50 mmol), styrene (0.078 g, 0.75 mmol), TBAB (0.016 g, 10 mol%), K₂CO₃ (0.165 g, 1.2 mmol) and [L₂Pd₂Cl₄] (**2**) (0.5 mg, 0.1 mol%) in solvent (3 mL, H₂O:C₂H₅OH = 1:1, v:v) was stirred at 110 °C in air. The other operations were similar to that in Suzuki reactions, and stilbene (**3**) was obtained. Yield: 0.082 g (92%). ¹H NMR (400 MHz, CDCl₃) δ : 7.60 (d, *J* = 7.6 Hz, 4H, ArH), 7.45 (t, *J* = 7.6 Hz, 4H, ArH), 7.19 (s, 2H, ArH). ¹³C NMR (100 MHz, CDCl₃) δ : 137.3, 128.6, 127.6, 126.5.

General method of Sonogashira reaction

A mixture of 4-bromoacetophenone (0.078 g, 0.50 mmol), phenylacetylene (0.076 g, 0.75 mmol), TBAB (0.016 g, 10 mol%), Cs₂CO₃ (0.390 g, 1.2 mmol) and [L₂Pd₂Cl₄] (**2**) (0.5 mg, 0.1 mol%) in solvent (3 mL, H₂O:C₂H₅OH = 1:1, v:v) was stirred at 80 °C in air. The other operations were similar to that in Suzuki reactions, and 1-(4-acetylphenyl)-2-phenylacetylene (**4h**) was obtained. Yield: 0.101 g (92%). ¹H NMR (400 MHz, CDCl₃) δ : 7.95 (d, *J* = 8.4 Hz, 2H, Ar*H*), 7.62 (d, *J* = 8.4 Hz, 2H, Ar*H*), 7.56 (m, 2H, Ar*H*), 7.37 (t, *J* = 3.2 Hz, 3H, Ar*H*), 2.61 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ : 197.2, 136.2, 131.7, 131.7, 128.8, 128.4, 128.2, 128.2, 122.7, 92.7, 88.6, 26.6.

X-ray data collection and structural determinations

The collection of diffraction data of **1** and **LH₂·Cl₂** was carried out applying a Bruker Apex II CCD diffractometer.^[60] The structures were solved with the SHELXS program.^[61] Figures 1 and 2 were formed via employing Crystal-Maker.^[62]

Supporting Information

The supporting information for this article is available on the WWW under https://doi.org/10.1002/cjoc.2021xxxxx.

Acknowledgements

This work was financially supported by Tianjin Natural Science Foundation (No. 18JCZDJC99600), the National Natural Science Foundation of China (No. 21572159) and the Program for novative Research Team in University of Tianjin (TD13-5074).

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(The following will be filled in by the editorial staff) Manuscript received: XXXX, 2021 Manuscript revised: XXXX, 2021 Manuscript accepted: XXXX, 2021 Accepted manuscript online: XXXX, 2021 Version of record online: XXXX, 2021

Accept

Entry for the Table of Contents

Synthesis of NHC Silver(I) and Palladium(II) Complexes with Acylated Piperazine Linker and Catalytic Activity in Three Types of C-C Coupling Reactions

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NHC silver(I) and palladium(II) complexes were prepared, and the catalytic activity of NHC palladium(II) complex in C-C coupling reactions were invesigated.