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# Synthesis, characterization and catalytic activity of palladium complexes with α-imino–amidos ligands

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ABSTRACT

In the present work, a series of steric substituted α-imino–amido palladium complexes, {[Ar–N=C($CH_3$)–C($CH_3$)(R)–NH–Ar]$PdCl_2$} (**C1**, R = Me, Ar = 2,6-dimethylphenyl; **C2**, R = Me, Ar = 2,6-diisopropylphenyl; **C3**, R = $CH_2$Ph, Ar = 2,6-dimethylphenyl; **C4**, R = $CH_2$Ph, Ar = 2,6-diisopropylphenyl), were synthesized and characterized. The structures of palladium complexes **C3** and **C4** were elucidated by X-ray diffraction. These bidentate nitrogen ligands were applied in palladium-catalyzed Suzuki–Miyaura cross-coupling reactions. The effect of ligand substitution as well as reaction conditions on catalytic activity was evaluated. Under the optimization process, the less bulky and electron-donating ligand were successfully used to catalyze the reaction of a variety of aryl bromides and chlorides with arylboronic acids, giving the desired biaryl products in high yields.



## 1. Introduction

$C_{Ar}$–$C_{Ar}$ bond-forming reactions facilitated by palladium-catalyzed cross-coupling are a useful methodology in organic synthesis [1–6]. Among these reactions, the Suzuki–Miyaura reaction involving the cross-coupling of aryl halides with organoboron reagents has proven to be the most effective for its simplicity and high tolerance toward various functional groups [7–10]. Over the past several decades, considerable efforts have been devoted to improving the efficiency of the catalyst for this cross-coupling reaction [11–13]. The previous research has been focused primarily on phosphine ligands, which are sterically bulky and electron-rich ligands that facilitate the catalytic transformation [14–17]. However, most of these ligands are air/moisture sensitive and toxic and are therefore difficult to handle. To overcome the disadvantage of using phosphine as a ligand, researchers have attempted to develop stable and environmentally friendly phosphine-free ligands, and this research area continues to be the subject of intense investigation. Palladium catalysts derived from bidentate N,N-ligands (Fig. 1) have been shown to produce inspiring results, where steric restriction and a strong electron-donating ability are of the highest importance. For example, the α-diimine (**I**) and pyridylimine (**II**) palladium catalysts exhibited good catalytic activities towards aryl bromides [18–23]. Di-2-pyridylmethylamine (**III**) [24–26], pyridylbenzamidine (**IV**) [27,28], pyridylmethylamines (**V**) [29,30] and other [N,N]-based palladium complexes have also demonstrated broad applicability and efficiency toward a wide range of aryl bromides under mild and simple reaction conditions [31–39]. Nevertheless, the more economical and readily available aryl chlorides have rarely been used as coupling partners in these protocols because of the low reactivity of chlorides under the conditions employed to couple bromides and iodides [9,40,41].

In the cases where N,N-ligands have been used, conjugated molecular structures were found, in general, to reduce the σ-electron donation while increasing the π-acceptor ability, which was unfavorable to the cross-coupling reaction. However, the pyridyl moiety in pyridyl-based ligands is not sufficiently bulky. We surmised that non-conjugated ligands, combined with steric substitutions, can not only furnish adequate electron donation to the metal center to promote the oxidative addition process but also favor reductive elimination. Therefore, a further improvement in catalytic activity could be achieved. Because of our ongoing research on phosphine-free catalysts and their catalytic activity toward Suzuki–Miyaura cross-coupling reactions [27,28,42–44], we became interested in a family of α-imino–amido palladium complexes (Scheme 1) whose steric environments can be easily tuned. Here, we report the results of α-imino–amido compounds as ligands for the palladium-catalyzed Suzuki–Miyaura reaction of aryl bromides and chlorides with arylboronic acids.

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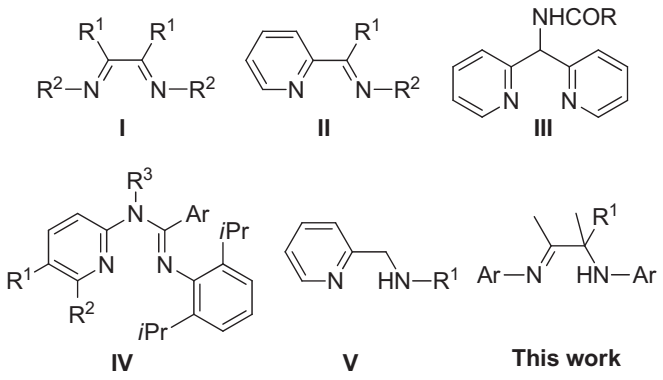



**Fig. 1.** Types of N,N-bidentate ligands.

## 2. Experimental section

### 2.1. Physical measurements and materials

2,6-Dimethylaniline and 2,6-diisopropylaniline were purchased from Aldrich Chemical and were distilled under reduced pressure before being used. Palladium chloride and trimethylaluminium (1 M, hexane) was purchased from Aldrich Chemical. 2,3-Butanedione and benzyl chloride was purchased from Guangzhou Chemical Reagent Factory and was used as received. Toluene was refluxed over metallic sodium for 24 h before being used. 2,6-$(CH_3)_2C_6H_3$–N=C($CH_3$)–C($CH_3$)=N–2,6-$(CH_3)_2C_6H_3$ (**1a**), 2,6-$(^iPr)_2C_6H_3$–N=C($CH_3$)–C($CH_3$)=N–2,6-$(^iPr)_2C_6H_3$ (**1b**), 2,6-$(CH_3)_2C_6H_3$–N=C($CH_3$)–C($CH_3$)($CH_3$)–NH–2,6-$(CH_3)_2C_6H_3$ (**L1**) and 2,6-$(^iPr)_2C_6H_3$–N=C($CH_3$)–C($CH_3$)–NH–2,6-$(^iPr)_2C_6H_3$ (**L2**) [45,46], were prepared according to literature methods.

The NMR data of compounds were obtained on a Varian Mercury-Plus 300 MHz spectrometer at ambient temperature, using $CDCl_3$ as solvent and referenced *versus* TMS as standard. Elemental analyses were determined with a Vario EL Series Elemental Analyzer from Elementar. The X-ray diffraction data of single crystals were obtained with the $\omega$-$2\theta$ scan mode on a Bruker SMART 1000 CCD diffractometer with graphite-monochromated Mo K$\alpha$ radiation ($\lambda$ = 0.71073 Å) at 173 K. The structure was solved using direct methods, and further refinement with full-matrix least squares on $F^2$ was obtained with the SHELXTL program package. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were introduced in calculated positions with the displacement factors of the host carbon atoms.

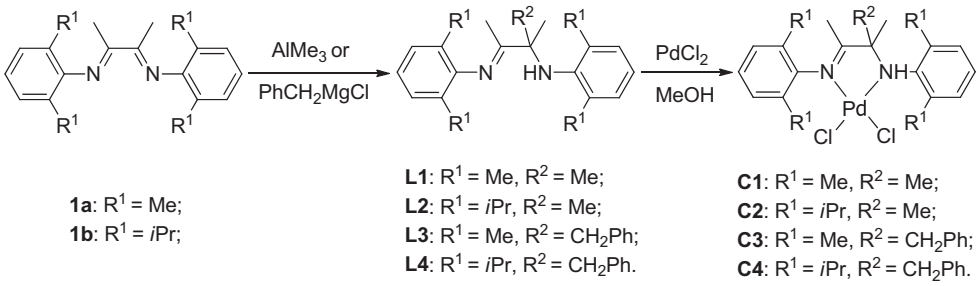
### 2.2. Syntheses and characterization

#### 2.2.1. Synthesis of 2,6-$(CH_3)_2C_6H_3$–N=C($CH_3$)–C($CH_3$)($CH_2Ph$)–NH–2,6-$(CH_3)_2C_6H_3$ (*L3*)

Under nitrogen atmosphere, a mixture of powdered magnesium (25 mmol) in anhydrous ether (45 mL) was stirred at 35 °C. Benzyl chloride (20 mmol) was added to the reaction mixture in the presence of iodine catalyst. After the reaction finished (*ca* 1.5 h), the reaction mixture was cooled to room temperature, then a solution of 2,6-$(CH_3)_2C_6H_3$–N=C($CH_3$)–C($CH_3$)=N-2,6-$(CH_3)_2C_6H_3$ (**1a**, 20 mmol) in anhydrous ether (10 mL) was injected slowly through a syringe. The mixture was allowed to stir for 24 h at room temperature, and then the mixture was filtered. The filtrate was carefully hydrolyzed with 5% aqueous NaOH solution, and the organic layer was separated, dried over $Na_2SO_4$ and concentrated to give the crude product. The pure ligand was recrystallized from ethanol to afford the white solid in 51% yield. There are two isomers found in solution sate (the ratio is *ca* 1:1). Isomer **1**: $^1$H NMR (300 MHz, $CDCl_3$), $\delta$ (ppm): 7.52–7.50 (m, 2H, Ar–*H*), 7.17–7.13 (m, 3H, Ar–*H*), 6.94–6.75 (m, 6H, Ar–*H*), 5.35 (s, 1H, N*H*), 3.71 (s, 2H, C$H_2$Ph), 2.32 (s, 6H, C$H_3$), 1.92 (s, 3H, C$H_3$), 1.66 (s, 3H, C$H_3$), 1.33 (s, 6H, C$H_3$). $^{13}$C NMR (75 MHz, $CDCl_3$), $\delta$ (ppm): 174.14 (*C*=N), 147.76, 144.65, 138.24, 133.90, 130.26, 128.63, 127.91, 126.61, 126.35, 124.76, 122.54, 65.80, 44.22, 24.91, 21.47, 18.08, 16.75. Isomer **2**: $^1$H NMR (300 MHz, $CDCl_3$), $\delta$ (ppm): 7.52–7.50 (m, 2H, Ar–*H*), 7.17–7.13 (m, 3H, Ar–*H*), 6.94–6.75 (m, 6H, Ar–*H*), 5.35 (s, 1H, N*H*), 2.88 (s, 2H, C$H_2$Ph), 2.32 (s, 6H, C$H_3$), 1.92 (s, 3H, C$H_3$), 1.66 (s, 3H, C$H_3$), 1.24 (s, 6H, C$H_3$). $^{13}$C NMR (75 MHz, $CDCl_3$), $\delta$ (ppm): 174.14 (*C*=N), 147.76, 144.65, 138.24, 133.90, 130.26, 128.63, 127.91, 126.61, 126.35, 124.76, 122.54, 65.80, 44.22, 24.91, 21.47, 18.08, 16.75. Elemental analysis calculated for $C_{27}H_{32}N_2$: C, 84.33; H, 8.39; N, 7.28. Found: C, 84.17; H, 8.45; N, 7.15.

#### 2.2.2. Synthesis of 2,6-$(^iPr)_2C_6H_3$–N=C($CH_3$)–C($CH_3$)($CH_2Ph$)–NH–2,6-$(^iPr)_2C_6H_3$ (*L4*)

Following the similar procedure, **L4** was received as white crystal in 54% yield. There are two isomers found in solution sate (the ratio is *ca* 1:1). Isomer **1**: $^1$H NMR (300 MHz, $CDCl_3$), $\delta$ (ppm): 7.64–7.61 (m, 2H, Ar–*H*), 7.21–7.13 (m, 3H, Ar–*H*), 7.07–7.02 (m, 4H, Ar–*H*), 6.95–6.93 (m, 2H, Ar–*H*), 5.30 (s, 1H, N*H*), 3.67 (m, 2H, C*H*($CH_3$)$_2$), 3.52 (s, 2H, C$H_2$Ph), 2.75 (m, 2H, C*H*($CH_3$)$_2$), 1.58 (s, 3H, C$H_3$), 1.16 (d, $J$ = 6.6 Hz, 12H, C$H_3$), 1.10 (d, $J$ = 6.6 Hz, 12H, C$H_3$), 0.73 (s, 3H, C$H_3$). $^{13}$C NMR (75 MHz, $CDCl_3$), $\delta$ (ppm): 174.51(*C*=N), 147.11, 145.51, 140.27, 138.84, 136.65, 135.91, 129.79, 127.86, 126.34, 124.53, 123.30, 122.85, 65.93, 43.69, 28.99, 27.76, 25.53, 24.22, 23.77, 22.32, 17.37. Isomer **2**: $^1$H NMR (300 MHz, $CDCl_3$), $\delta$ (ppm): 7.64–7.61 (m, 2H, Ar–*H*), 7.21–7.13 (m, 3H, Ar–*H*), 7.07–7.02 (m, 4H, Ar–*H*), 6.95–6.93 (m, 2H, Ar–*H*), 5.30 (s, 1H, N*H*), 3.67 (m, 2H, C*H*($CH_3$)$_2$), 3.50 (s, 2H, C$H_2$Ph), 1.98 (m, 1H, C*H*($CH_3$)$_2$), 1.58 (s, 3H, C$H_3$), 1.16 (d, $J$ = 6.6 Hz, 12H, C$H_3$), 1.10 (d, $J$ = 6.6 Hz, 12H, C$H_3$), 0.73 (s, 3H, C$H_3$). $^{13}$C NMR (75 MHz, $CDCl_3$), $\delta$ (ppm): 174.51(*C*=N), 147.11, 145.51, 140.27, 138.84, 136.65, 135.91, 129.79, 127.86, 126.34, 124.53, 123.30, 122.85, 65.93, 43.69, 28.99, 27.76, 25.53, 24.22, 23.77, 22.32, 17.37. Elemental analysis calculated for $C_{35}H_{48}N_2$: C, 84.62; H, 9.74; N, 5.64. Found: C, 84.45; H, 9.81; N, 5.56.




**1a**: $R^1$ = Me;
**1b**: $R^1$ = *i*Pr;

**L1**: $R^1$ = Me, $R^2$ = Me;
**L2**: $R^1$ = *i*Pr, $R^2$ = Me;
**L3**: $R^1$ = Me, $R^2$ = $CH_2Ph$;
**L4**: $R^1$ = *i*Pr, $R^2$ = $CH_2Ph$.

**C1**: $R^1$ = Me, $R^2$ = Me;
**C2**: $R^1$ = *i*Pr, $R^2$ = Me;
**C3**: $R^1$ = Me, $R^2$ = $CH_2Ph$;
**C4**: $R^1$ = *i*Pr, $R^2$ = $CH_2Ph$.

**Scheme 1.** The synthetic route of α-imino–amido ligands and palladium complexes.