α-Hydroxyimine palladium complexes: Synthesis, molecular structure, and their activities towards the Suzuki–Miyaura cross-coupling reaction

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ABSTRACT

An activity-promoting strategy for phosphine-free catalytic systems is presented in this study. The strategy is based on a series of non-conjugated *N,O* ligands with bulky substituents, [Ar−N=C(R)−(R)C(CH$_3$)OH] (**L1**, R = Acenaphthyl, Ar = 2,6-diisopropylphenyl; **L2**, R = Ph, Ar = 2,6-dimethylphenyl; **L3**, R = Ph, Ar = 2,6-diisopropylphenyl). The reaction of PdCl$_2$ with 1 equiv of the ligand **L1−3** in methanol affords the four-coordinate palladium complex with the general formula **LPdCl$_2$** (**1−3**). The molecular structures of **L3**, as well as the palladium complexes **1** and **3**, were established by single-crystal X-ray diffraction studies. The application of these palladium complexes as precatalysts was examined for the Suzuki–Miyaura cross-coupling of a range of aryl bromides with arylboronic acids. **3**, which incorporates bulky substituents, was shown to be effective in the cross-coupling reactions at 0.01 mol% palladium loading, affording the corresponding biaryls in high yields.

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1. Introduction

Biaryls are widely found in the synthesis of natural products, pharmaceuticals, and functional polymer materials [1–3]. Therefore, it is important to develop general methods to construct such compounds. One such path is the palladium-catalysed Suzuki–Miyaura reaction, which involves the cross-coupling of an aryl halide with an arylboronic acid to form the respective biaryl structure [4–21]. In the past few decades, there have been numerous efforts to develop efficient phosphine-based catalysts for this transformation [16,18]. The key feature of these catalysts lies in the sterically bulky and electron-rich ligands that have great facility in the catalytic cycle. As a result, they exhibit outstanding performance in the synthesis of biaryls, even using sterically hindered substrates under mild conditions [22–25]. However, most phosphines are air sensitive, toxic, and therefore difficult to handle.

The development of stable and environmentally friendly phosphine-free ligands for the preparation of biaryls has been intensely investigated in recent years [14,15,26–40]. Among the ligands investigated, the *N,O*-based ligands have exhibited good activity for the Suzuki–Miyaura cross-coupling, which is often attributed to their σ-donating ability that allows for the formation of a strong palladium–imine bond that helps to prevent catalyst decomposition [26]. Moreover, other attractive features are that these phosphine-free ligands are easily accessible synthetically and that they have rather flexible architectures. These properties allow for the steric and electronic effects to be tuned to a large extent, giving the possibility of screening these compounds for their catalytic properties. For example, salicylaldimine (**I**) (Fig. 1) palladium complexes exhibited fine catalytic activities [26–30]. In addition, β-ketoamine (**II**) and quinoline-8-carboxylate (**III**) (Fig. 1) demonstrated broad applicability and efficiency towards a wide range of aryl bromide substrates under mild and simple reaction conditions [26,32,33]. Despite this, very few examples of these catalysts were running at a low (≤0.01 mol%) palladium loadings. Thus, the design of new and readily available phosphine-free catalyst, which can significantly lower the catalyst loading and improve the reactivity with broad substrate generality, is still in high demand.

Previous investigations using calculations and kinetic measurements suggested that the strong σ-donor ability of the ligands would accelerate the oxidative addition, which is believed to be the rate determining step in the catalytic cycle [38–42]. It is reasonable that the discrimination between the phosphine-free and phosphine-based ligands can be primarily attributed to electronic factors. To enhance the activities of the *N,O* ligands, some ancillary ligand such as triphenylphosphine was added, which provides more electron donation towards the metal centre. As a result, highly active catalysts were obtained [43–45]. In view of the *N,O* ligands reported, conjugated molecular structures were found in

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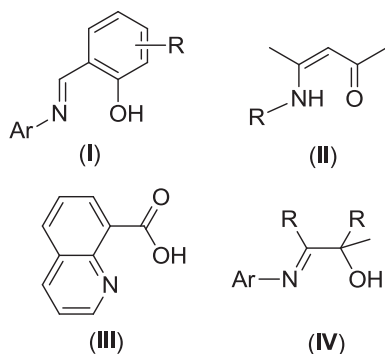
Fig. 1. *N,O*-Bidentate ligands.

most cases to generally reduce the electron donation ability. We surmised that non-conjugated ligands, combined with steric substitutions, can not only furnish adequate electron donation to the metal centre, to promote the oxidative addition process, but also favour the reductive elimination. Therefore, a further improvement in catalytic activity could be achieved without the addition of any ancillary ligand. In this regard, we have become interested in the non-conjugated α-hydroxyimine ligand (**IV**) (Fig. 1) where its steric and electronic properties can be easily modified. The arylimine moiety is anticipated to be perpendicular to the coordination plane. While the substituents on the backbone of the ligand are directed away from the metal centre, it would hinder the rotation of the arylimine moiety, and thus provide stability to the catalytic centre in further catalytic steps. Herein, we report the synthesis of the ligands and palladium complexes and their structural characterisation and describe the catalytic properties of these precatalysts for the Suzuki–Miyaura cross-coupling reaction.

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. TMA (1 M, hexane) was purchased from Aldrich Chemical. Acenaphthenequinone and benzil were purchased from Alfa Aesar Chemical and used as received. Toluene was refluxed over metallic sodium for 24 h before being used. 2,6-(*i*-Pr)$_2$C$_6$H$_3$–N=C(An)–C(An)=O [46], and 2,6-(*i*-Pr)$_2$C$_6$H$_3$–N=C(Ph)–C(Ph)=O [47], were prepared according to literature procedures.

The NMR data of ligands and biaryls were obtained on a Varian Mercury-Plus 300 MHz spectrometer at ambient temperature, using CDCl$_3$ as solvent and referenced *versus* TMS as standard. The NMR data of palladium complexes were obtained on a Varian Mercury-Plus 300 MHz spectrometer, using DMSO-d$_6$ as solvent. Elemental analyses were determined with a Vario EL Series Elemental Analyser 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 Kα 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. TEM observations were performed on a TEM (JEM100CX, Japan) with an accelerating voltage of 100 kV. A drop of solution was deposited onto a carbon coated copper grid, dried at room temperature.

2.2. Syntheses and characterization

2.2.1. Synthesis of 2,6-(*i*Pr)$_2$C$_6$H$_3$–N=C(acenaphthyl)–C(acenaphthyl)(Me)-OH (**L1**)

2,6-(*i*Pr)$_2$C$_6$H$_3$–N=C(acenaphthyl)–C(acenaphthyl)=O (**1a**, 5 mmol) was dissolved in 10 ml toluene under a nitrogen atmosphere, and trimethylaluminum (7 ml, 1.0 M) was added slowly through a syringe at room temperature, and then the reaction was heated to reflux for 4 h. When having reached the determined time, the solution was cooled to 0 °C, and the reaction mixture was carefully hydrolysed with 5% aqueous NaOH solution. The organic product was extracted with ethyl acetate, dried over MgSO$_4$, and evaporated the solvent. The desired product obtained as yellow solid. The crude material was crystallized from ethanol as light yellow crystal in 92% yield. Non enantioselective donation was observed with the compound, which suggested a completely racemic ligand. Moreover, isomers were detected by NMR in 1:1 ratio. ^{1}H NMR (300 MHz, CDCl$_3$), δ (ppm): Isomer 1: ^{1}H NMR: (CDCl$_3$, 300 MHz), δ (ppm): 7.86–7.62 (m, 4H, Ar–H), 7.29–7.20 (m, 4H, Ar–H), 6.51–6.49 (m, 1H, Ar–H), 3.13 (s, 1H, OH), 2.98 (m, 2H, C*H*(CH$_3$)$_2$), 1.90 (s, 3H, CH$_3$), 1.25 (d, *J* = 6.9 Hz, 6H, CH$_3$), 1.15 (d, *J* = 6.9 Hz, 6H, CH$_3$). ^{13}C NMR: (CDCl$_3$, 75 MHz), δ (ppm): 174.34, 146.01, 142.68, 138.43, 136.24, 135.65, 130.92, 129.37, 128.89, 128.41, 127.85, 124.91, 124.10, 123.51, 119.49, 78.69, 28.41, 27.61, 23.43. Isomer 2: ^{1}H NMR: (CDCl$_3$, 300 MHz), δ (ppm): 7.86–7.62 (m, 4H, Ar–H), 7.29–7.20 (m, 4H, Ar–H), 6.51–6.49 (m, 1H, Ar–H), 3.13 (s, 1H, OH), 2.98 (m, 2H, C*H*(CH$_3$)$_2$), 1.90 (s, 3H, CH$_3$), 1.02 (d, *J* = 6.9 Hz, 6H, CH$_3$), 0.83 (d, *J* = 6.9 Hz, 6H, CH$_3$). ^{13}C NMR: (CDCl$_3$, 75 MHz), δ (ppm): 174.34, 146.01, 142.68, 138.43, 136.24, 135.65, 130.92, 129.37, 128.89, 128.41, 127.85, 124.91, 124.10, 123.16, 119.49, 78.69, 27.94, 27.61, 23.09. Elemental analysis calculated for C$_{25}$H$_{27}$NO: C, 83.99; H, 7.61; N, 3.92. Found: C, 83.91; H, 7.56; N, 3.87.

2.2.2. Synthesis of 2,6-(CH$_3$)$_2$C$_6$H$_3$–N=C(Ph)–C(Ph)(Me)-OH (**L2**)

Following the above procedure, **L2** was isolated as white crystal in 87% yield. Isomers were detected by NMR in 1:1 ratio. Isomer 1: ^{1}H NMR: (CDCl$_3$, 300 MHz), δ (ppm): 7.48–7.46 (m, 2H, Ar–H), 7.38–7.30 (m, 3H, Ar–H), 7.13–7.08 (m, 1H, Ar–H), 7.00–6.89 (m, 3H, Ar–H), 6.78–6.74 (m, 2H, Ar–H), 6.46–6.44 (m, 2H, Ar–H), 2.22 (s, 3H, CH$_3$), 1.81 (s, 6H, CH$_3$). ^{13}C NMR: (75 MHz), δ (ppm): 174.47 (C=N), 145.55, 142.80, 134.43, 128.59, 128.04, 127.84, 127.57, 127.23, 126.90, 126.52, 125.39, 123.42, 76.68, 25.89, 18.66. Isomer 2: ^{1}H NMR: (CDCl$_3$, 300 MHz), δ (ppm): 7.48–7.46 (m, 2H, Ar–H), 7.38–7.30 (m, 3H, Ar–H), 7.13–7.08 (m, 1H, Ar–H), 7.00–6.89 (m, 3H, Ar–H), 6.78–6.74 (m, 2H, Ar–H), 6.46–6.44 (m, 2H, Ar–H), 2.22 (s, 3H, CH$_3$), 1.80 (s, 6H, CH$_3$). ^{13}C NMR: (75 MHz), δ (ppm): 174.47 (C=N), 145.55, 142.80, 134.43, 128.59, 128.04, 127.74, 127.57, 127.23, 126.90, 126.42, 125.39, 123.42, 76.68, 25.89, 18.48. Elemental analysis calculated for C$_{23}$H$_{23}$NO: C, 83.85; H, 7.04; N, 4.25. Found: C, 83.73; H, 7.01; N, 4.16.

2.2.3. Synthesis of 2,6-(*i*Pr)$_2$C$_6$H$_3$–N=C(Ph)–C(Ph)(Me)-OH (**L3**)

Following the above procedure, **L3** was isolated as white crystal in 95% yield. Isomers were detected by NMR in 1:1 ratio. Isomer 1: ^{1}H NMR: (CDCl$_3$, 300 MHz), δ (ppm): 7.51–7.36 (m, 4H, Ar–H), 7.13–7.08 (m, 1H, Ar–H), 7.02–6.74 (m, 6H, Ar–H), 6.45–6.42 (m, 2H, Ar–H), 3.05 (m, 2H, C*H*(CH$_3$)$_2$), 1.82 (s, 3H, CH$_3$), 1.54 (br, 1H, OH), 1.30 (d, *J* = 3 Hz, 6H, CH$_3$), 1.12 (d, *J* = 6.9 Hz, 6H, CH$_3$). ^{13}C NMR: (CDCl$_3$, 75 MHz), δ (ppm): 174.34, 146.01, 142.68, 138.43, 136.24, 135.65, 130.92, 129.37, 128.89, 128.41, 127.85, 124.91, 124.10, 123.51, 119.49, 78.69, 28.41, 27.61, 23.43. Isomer 2: ^{1}H NMR: (CDCl$_3$, 300 MHz), δ (ppm): 7.51–7.36 (m, 4H, Ar–H), 7.13–7.08 (m, 1H, Ar–H), 7.02–6.74 (m, 6H, Ar–H), 6.45–6.42 (m, 2H, Ar–H), 2.53 (m, 2H, C*H*(CH$_3$)$_2$), 1.82 (s, 3H, CH$_3$), 1.54 (br, 1H, OH), 1.27 (d, *J* = 3 Hz, 6H, CH$_3$), 0.71 (d, *J* = 6.9 Hz, 6H, CH$_3$). ^{13}C NMR: (CDCl$_3$, 75 MHz),