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Amino-salicylaldimine–palladium(II) complexes: New and efficient catalysts for Suzuki and Heck reactions

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ABSTRACT

A series of amino-salicylaldimine–palladium(II) complexes bearing 5-methyl-3-(R-1-ylmethyl)-salicylaldimine ligands (R = morpholine, piperidine, pyrrolidine, 4-methylpiperazin, diisopropylamine) have been prepared and characterized by IR, ^{1}H NMR and elemental analysis. Crystal structure details of complex **2b** have been confirmed by X-ray structure analysis. The obtained Pd(II) complexes were found to be effective catalysts for the Suzuki and Heck cross-coupling reactions which could be carried out in the undried solvent under air.

Palladium-catalyzed C–C bond forming reactions such as the Suzuki–Miyaura and Mizoroki–Heck reactions have been used extensively for the synthesis of natural products, pharmaceutical intermediates, conducting polymers, pesticides and liquid crystals [1–4]. Phosphine is generally the ligand of choice due to its superior donor capability and stabilization effects [5]. The major limitations with phosphine ligands in catalytic reactions is the oxidation of phosphines to phosphine oxides, formation of stable phosphido-bridged catalytically inactive dimers, and also the cleavage of P–C bond causing degradation of the ligand and thus the termination of the catalytic cycle. These have prompted the vigorous research on phosphine-mimics such as N-heterocyclic carbenes (NHCs) [6]. NHC complexes are largely stable, but some of them are also handicapped by the lack of coordinative flexibility, which then led to the emergence of carbine hybrids.

During the past 10 years, there has been considerable interest in the development of new phosphorus free palladium catalysts for higher activity, stability and substrate tolerance that allow reactions to be carried out under milder reaction conditions. Schiff bases are attractive ligands due to their facile preparation and simple synthetic modification, both electronic and steric, and have been used to prepare a broad range of organometallic compounds with a wide variety of applications [7]. Recently several types of salicylaldimine ligands with pendant functionality were explored to act as three-coordinate six-electron-donor. It also provides a focus of our recent work in designing new, robust and easily prepared ligands and studying their coordination behavior and catalytic applications. In this paper, we report the preparation and characterization of amino-salicylaldimine ligands 5-methyl-3-(R-1-ylmethyl)-salicylaldimine (R = morpholine, piperidine, pyrrolidine, 4-methylpiperazine, diisopropylamine) and their palladium complexes. The catalytic activities of these amino-salicylaldimine–palladium complexes toward the Suzuki and Heck reactions are investigated.

The synthetic procedures of ligands 5-methyl-3-(R-1-ylmethyl)-salicylaldimine (R = morpholine, piperidine, pyrrolidine, 4-methylpiperazin, diisopropylamine) and their palladium(II) complexes are generally shown in Scheme 1. Ligands **1a–e** were conveniently prepared in good yields (91–96%) by the condensation reaction of one equivalent of the diisopropylaniline with one equivalent of 5-methyl-3-(R-1-ylmethyl)-salicylaldehyde in ethanol, yielding yellow crystal or oil products after purified through column chromatography on Al_2O_3. All the ligands were well characterized and confirmed by IR spectrometry, ^{1}H NMR and elemental analysis.

The amino-salicylaldimine–Pd(II) complexes **2a–e** were obtained as yellow solids in reasonable yields (79–88%) by reflux of amino-salicylaldimine ligands with $PdCl_2(CH_3CN)_2$ in acetonitrile. The resulting solutions were concentrated under vacuum, and the formed complexes were precipitated by adding excessive amounts of Et_2O. Complexes **2a–e** obtained have been confirmed by IR spectra, ^{1}H NMR and elemental analysis. In comparison with the IR spectrometry of free ligands with C=N stretching frequencies in the range of 1620–1622 cm^{-1}, the C=N stretching vibrations in complexes were shifted toward lower frequencies in the range of 1614–1618 cm^{-1} with reduced peak intensity, which

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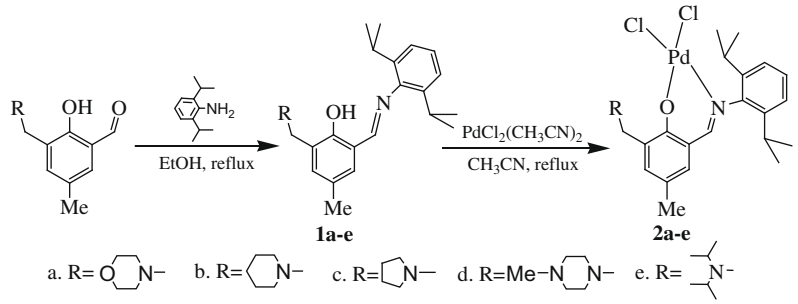


Scheme 1. Synthesis of amino-salicylaldimine ligands **1a**–**e** and their Pd(II) complexes **2a**–**e**.

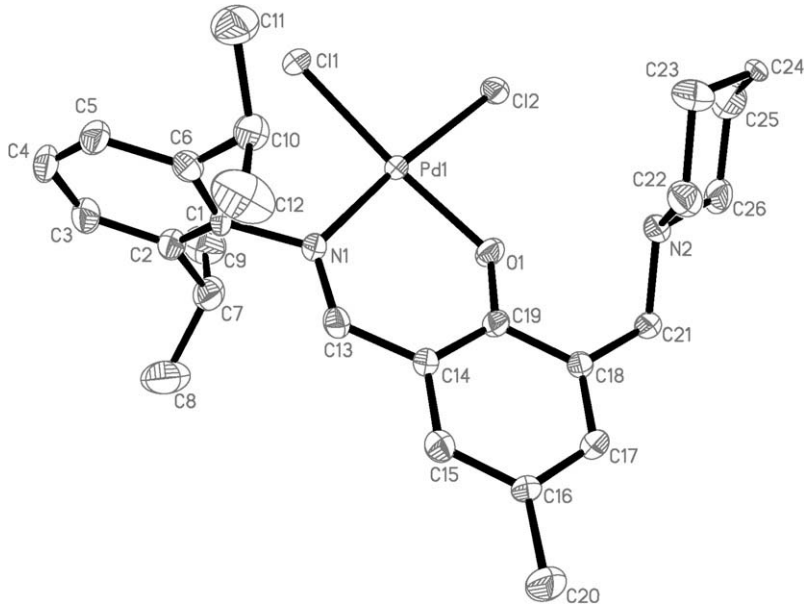
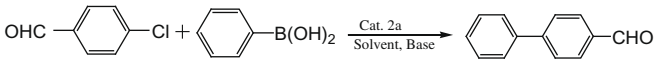


Fig. 1. Crystal structure of complex **2b**. Select bond lengths (Å) and angles (°): Pd1–Cl1 2.2939(8), Pd1–Cl2 2.3220(9), Pd1–N1 2.019(3), Pd1–O1 1.9687(19) and O1–Pd1–N1 91.03(11), O1–Pd1–Cl1 174.67(9), N1–Pd1–Cl1 94.28(8), O1–Pd1–Cl2 83.68(8), N2–Pd1–Cl2 174.66(8), Cl1–Pd1–Cl2 91.02(3).

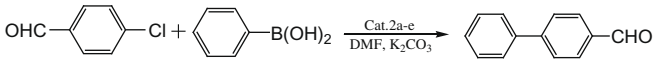
Table 1
Effect of solvents and bases on Suzuki cross-coupling reaction.[a]



Entry	Solvent	Base	Yield[b] (%)
1	Toluene	K_2CO_3	26
2	THF	K_2CO_3	46
3	Acetone	K_2CO_3	33
4	DCM	K_2CO_3	14
5	Methanol	K_2CO_3	31
6	DMF	K_2CO_3	97
7	DMF	Cs_2CO_3	81
8	DMF	$K_3PO_4{\cdot}3H_2O$	69
9	DMF	Et_3N	35
10	DMF	K_2CO_3	96[c]
11	DMF	K_2CO_3	56[c]
12	DMF	K_2CO_3	21[c]

[a] Reaction conditions: catalyst (0.5 mol%), 4-chlorobenzaldehyde (0.5 mmol), phenylboronic acid (0.7 mmol), base (1.2 mmol), and solvent (10 mL), reflux, 4 h.
[b] Conversion to the coupled product determined by GC–MS, based on 4-chlorobenzaldehyde; average of two runs.
[c] Reaction temperature: 110 °C (entry 10), 80 °C (entry 11), 50 °C (entry 12).

Table 2
Effect of complexes **2a**–**e** on Suzuki cross-coupling reaction.[a]



Entry	Catalyst	Time (h)	Yield[b] (%)
1	2a	4	96
2	2b	4	95
3	2c	4	94
4	2d	4	96
5	2e	4	92

[a] Reaction conditions: catalyst (0.5 mol%), 4-chlorobenzaldehyde (0.5 mmol), phenylboronic acid (0.7 mmol), K_2CO_3 (1.2 mmol), DMF (10 mL), 110 °C.
[b] Conversion to the coupled product determined by GC–MS, based on 4-chlorobenzaldehyde; average of two runs.

indicated an effective coordination interaction between the imino nitrogen and the Pd center. In the ^{1}H NMR spectra, the protons of substituents on the aryl ring of these complexes were almost shifted downfield compared with those of the free ligands, while the aromatic ring protons exhibited either upfield shift or remained unchanged in the range of 7.02–7.35 ppm.

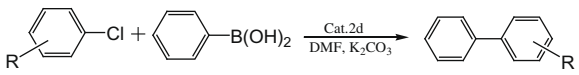
Perspective view of molecular structure of complex **2b** with atom numbering scheme is shown in Fig. 1. The yellow crystal of **2b**, suitable for X-ray diffraction analysis was obtained through slow diffusion of diethyl ether into their acetonitrile solution at room temperature. In the molecular structure of **2b**, the imino group in the solid state is in the E conformation with the typical imino C=N double-bond length of 1.293(4) Å. The dihedral angle between the two aryl rings is 82.23° and the piperidine ring possesses a stable chair configuration. The geometry around the palladium center can be described as a distorted square planar, in which the palladium was coordinated with the sp^2 N1 in the phenylimino ring instead of sp^3 N2 in the piperidine ring. The Pd1–O1 (1.969 Å) bond length is slightly shorter than that found in the related bis(phenoxyketimine) palladium complex (1.985 Å) [8] and schiff bases of 1-hydroxy-2-acetonaphthone palladium complexes (1.973–2.061 Å) [9]. The Pd1–N1 (2.019 Å) bond length is comparable to that in schiff bases of 1-hydroxy-2-acetonaphthone palladium complexes (2.010–2.019 Å), and is shorter than that in bis(phenoxyketimine) palladium complex (2.033 Å) and bis(imino)pyridine palladium complexes (2.04–2.06 Å) [10]. The angles of N1–Pd1–O1, N1–Pd1–Cl1, O1–Pd1–Cl2 and Cl1–Pd1–Cl2 are 91.03(11), 94.28(8), 83.68(8) and 91.02(3), respectively. The angles of O1–Pd1–Cl1 [174.67(9)°] and N1–Pd1–Cl2 [174.66(8)°] are both slightly less than 180 °C.

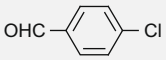
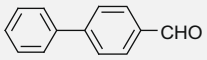
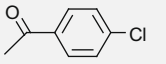
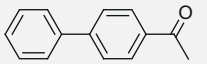
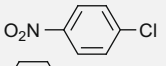
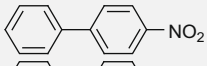
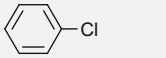
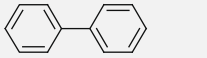
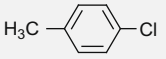
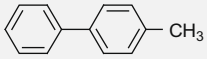
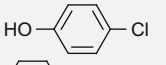
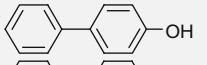
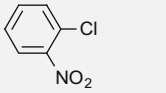
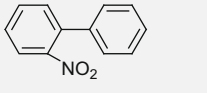
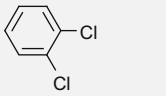
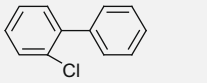
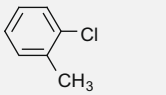
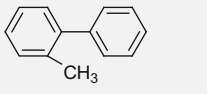
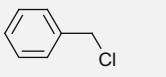
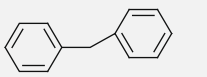
The effectiveness of amino-salicylaldimine–Pd complexes **2a–e** was first tested in the Suzuki reaction. Coupling of 4-chlorobenzaldehyde with phenylboronic acid in the presence of 0.5 mol% of **2a** for 4 h was chosen as a model to optimize the reaction conditions (Table 1). Solvent usually plays a crucial role in the rate and the product distribution of the coupling reaction, so the influence of several solvents was examined (entries 1–6). DMF was found to be much better than others (entry 6). This may be due to better solubility of the reagents and easier reduction of Pd^{2+} to Pd(0) and hence facile entry to the catalytic cycle. Similarly, several bases were employed in Suzuki reactions (entries 6–9), K_2CO_3 proving superior (entry 6). Further studies indicated that the catalytic activity could be reduced with lowering the reaction temperature (entries 10–12).

The catalytic activities of complexes **2a–e** were examined in the Suzuki reaction of 4-chlorobenzaldehyde with phenylboronic acid (Table 2). They generally gave good yields in DMF at 110 °C within 4 h under a low catalyst loading of 0.5 mol%. Complexes **2a** and **2d** showed relatively better activities towards the coupling reaction (entries 1 and 4).

Under the above optimized reaction condition, complex **2d** was applied to a representative range of aryl chlorides (Table 3). In the presence of K_2CO_3, it was effective towards the coupling of various aryl chlorides with phenylboronic acid in DMF at 110 °C within 4 h. The activated electron-deficient aryl chloride, such as 4-chloroacetophenone, 4-chlorobenzaldehyde, and 4-chloronitrobenzene efficiently coupled with phenylboronic acids to give high yields (entries 1–3). The non-activated electron neutral substrate, such as chlorobenzene afforded moderate amount of coupled product at the same condition (49%, entry 4). In the case of deactivated electron-rich substrates such as 4-chlorotoluene and 4-chlorophenol (entries 5 and 6), the yields of the desired product were very low even when prolonging the reaction time to 12 h. All these results indicated that electronic effect of substituents on the aryl

Table 3
Suzuki cross-coupling of aryl chloride with phenylboronic acid.[a]



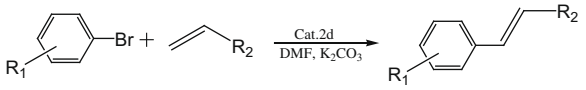
Entry	Aryl halide	product	Time (h)	Yield[b] (%)
1			4	96
2			4	95
3			4	98
4			4	49
5			12	11
6			12	6
7			4	87
8			4	13
9			12	4
10			4	45

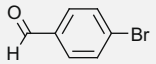
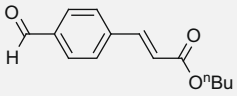
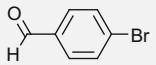
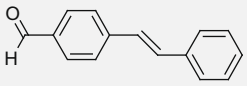
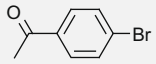
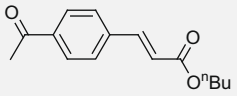
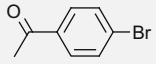
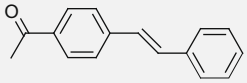
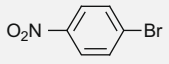
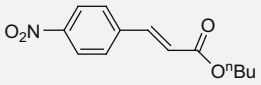
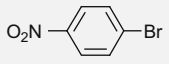
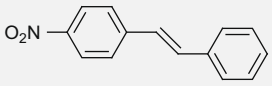
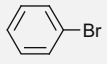
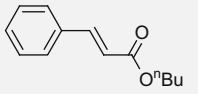
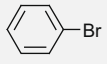
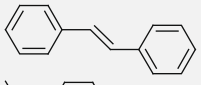
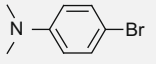
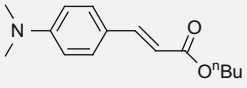
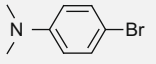
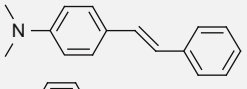
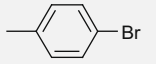
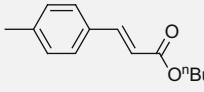
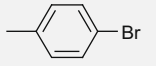
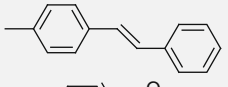
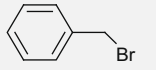
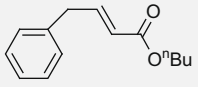
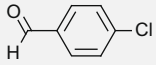
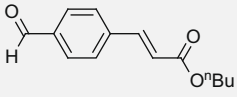
[a] Reaction conditions: complex **2d** (0.5 mol%), aryl chloride (0.5 mmol), phenylboronic acid (0.7 mmol), K_2CO_3 (1.2 mmol), DMF (10 mL), 110 °C.
[b] Conversion to the coupled product determined by GC–MS, based on aryl chloride; average of two runs.

chlorides had great influence on the reaction and the electron-withdrawing substituents were more favorable for the coupling. The sterically hindered ortho-substituted substrate 2-chloronitrobenzene could also couple efficiently giving 87% yield within 4 h (entry 7), but *o*-dichlorobenzene and 2-chlorotoluene gave very low yield. The Suzuki coupling was also extended to $C_{(sp^3)}$—$C_{(sp^2)}$ coupling by reacting benzyl chloride with phenylboronic acid, which afforded the corresponding coupling product in moderate yield (45%, entry 10). The activity of this catalyst is found to be superior to that in Pd–salen system, which catalyzes the reaction between activated aryl chlorides and phenylboronic acid in DMF/H_2O (1:1) at 110 °C giving moderate yields [11]. In comparison with other N-coordinated palladium catalysts, the catalytic activity of this catalyst is similar to those found in 1,4-bis(2-hydroxy-3,5-di-*tert*-butylbenzyl)piperazine Pd system in DMF with K_2CO_3 at 110 °C [12], in benzimidazolium–pyrazole–palladium(II) complexes in MeOH/H_2O(2:1) at room temperature [13], in diazabutadiene/palladium system in dioxane with Cs_2O_3 at 100 °C [14].

The catalytic activity of catalyst **2d** was also examined in the Heck reaction of aryl bromides with styrene or *n*-butyl acrylate

Table 4
Heck cross-coupling reactions of aryl bromide with styrene or *n*-butyl acrylate[a]



Entry	Aryl bromide	Product	Time (h)	Yield[b] (%)
1			5	94
2			5	89
3			5	92
4			5	88
5			5	100
6			5	96
7			12	44
8			12	10
9			5	46
10			5	6
11			12	42
12			12	5
13			12	55
14			24	Trace[c]

[a] Reaction conditions: complex **2d** (1 mol%), aryl bromide (0.5 mmol), olefin (1.5 mmol), K_2CO_3 (1.5 mmol), DMF (10 mL), 110 °C.
[b] Conversion to the coupled product determined by GC–MS, based on aryl bromide; average of two runs.
[c] Catalyst (complex **2d**) loading: 2 mol%.

under the optimized reaction conditions (K_2CO_3 as base, DMF as solvent at 110 °C). The results are summarized in Table 4. Under typical reaction conditions, the electron-deficient substrates 4-bromobenzaldehyde, 4-bromoacetophenone and 4-bromonitrobenzene could effectively couple with styrene and *n*-butyl acrylate providing the corresponding products in excellent yields after 5 h (entries 1–6). The electron-rich substrate 4-bromotoluene, 4-bromo-*N*,*N*′-dimethylaniline and electron neutral substrate bromobenzene gave moderate amount of products when coupling with *n*-butyl acrylate, whereas these substrates coupled with styrene to give very low yield of the coupled product which may be due to the lower activity of styrene. The substrate benzyl bromide afforded moderate amount of yield (55%) within 5 h, when reacted with *n*-butyl acrylate. Aryl chloride substrate 4-chlorobenzaldehyde coupled with *n*-butyl acrylate giving trace desired product even when prolonging the reaction time to 24 h and enlarging the catalyst loading to 2 mol%.

In conclusion, a series of new amino-salicylaldimine ligands and their Pd(II) complexes were prepared and characterized along with the single-crystal X-ray analysis. These palladium complexes were found to be active catalysts for Suzuki cross-coupling of activated aryl chlorides with phenylboronic acid using DMF as solvent. Also catalytic studies showed that these complexes exhibited good activities toward activated aryl bromides in the Heck coupling reaction. The stability of the palladium catalysts against air, moisture and temperature and the fact that they can be synthesized conveniently from inexpensive starting materials and obtained with satisfactory yields make them very promising catalysts.

Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.inoche.2009.10.023.

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