



Synthesis of a bis(phenoxyketimine) palladium(II) complex and its activity in the Suzuki–Miyaura reaction

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ABSTRACT

The synthesis of a new charge-neutral, air- and moisture-stable fluorinated bis(phenoxyketimine) Pd(II) complex is presented. Its activity as a precatalyst in the Suzuki–Miyaura cross-coupling reaction of activated and unactivated bromides has been explored.

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1. Introduction

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 [1–4]. For instance, bis-phenoxyketimine (PHI) titanium complexes were originally reported for the polymerization of ethylene [5]. The improved activity over known metallocenes spurred further interest in these early transition metal complexes, with general formula $[M(\text{PHI})_2\text{X}_2]$ ($M = \text{Ti}, \text{Zr}; \text{X} = \text{Cl}, \text{Br}$). It was later discovered that activity increases dramatically when two or more F or CF_3 groups are introduced to the imido phenyl ring. Both synthetic and computational methods confirmed that in particular an *ortho* fluorine (or other lone pair donating substituent) can inhibit β -hydride elimination and promote living catalyst conditions [6]. It is this feature that is believed to promote high speed living polymerizations and lead to monodisperse high molecular weight polymers. A new derivative of PHI ligands with a phenyl ring on the N–O backbone, PKI-F₅ (**1**), was recently employed by Coates and co-workers, for the living, isoselective polymerization of propylene [7].

Recently, the growing interest on the development of systems for the polymerization of polar vinyl monomers, such as acrylates, has led to the synthesis of a variety of complexes of palladium and nickel for this purpose [8], because of the tolerance to functionalities that late transition metals display [9]. Many of those complexes include [N,O] chelating ligands that resemble [P,O] ligands

used for SHOP-type (SHOP = Shell Higher Olefin Process) [10]. A search of the literature uncovered several related $[\text{Pd}(\text{PHI})_2]$ and $[\text{Pd}(\text{PHI})(\text{Me})(\text{X})]$ compounds, not only for that use but for many other applications [11]. However, only one other monofluorinated example is known in the literature [12]. When attempting the synthesis of a 1:1 PdCl_2 :**1** complex, we obtained as a byproduct the new, neutral, air- and moisture-stable bis(phenoxyketimine) Pd(II) complex **2** (Fig. 1), whose synthesis we optimized and report in here. The activity of the complex in the Suzuki–Miyaura cross-coupling [13] of unactivated aryl bromides and boronic acids is also discussed.

2. Results and discussion

2.1. Complex synthesis

The ligand was prepared following the reported procedure by Mason and Coates [14], then deprotonated with *n*-butyllithium at -78°C and allowed to react with PdCl_2 at room temperature overnight. Elution of the unreacted ligand through a plug of silica with pentane, followed by elution with methylene chloride, yielded the desired complex **2** (81%) with no observable complex decomposition. X-ray quality crystals were obtained by slow diffusion of pentane into a concentrated solution of **2** in methylene chloride at room temperature, and the structure of the complex was determined by X-ray crystallography. An ORTEP plot of **2** is shown in Fig. 2, and selected crystallographic parameters are listed in Table 1. The complex displays a nearly ideal square planar geometry, with both ligands *trans* to each other. On each PKI-F₅ ligand the pentafluoro aryl ring and ketimine aryl ring have a centroid distance of

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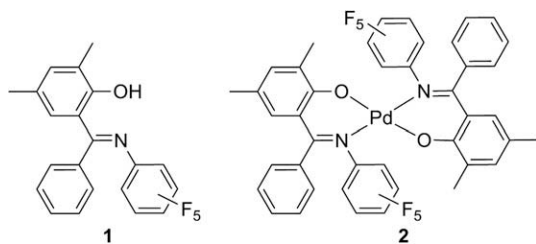


Fig. 1. Ligand PKI-F₅ (1) and (PKI-F₅)₂Pd (2).

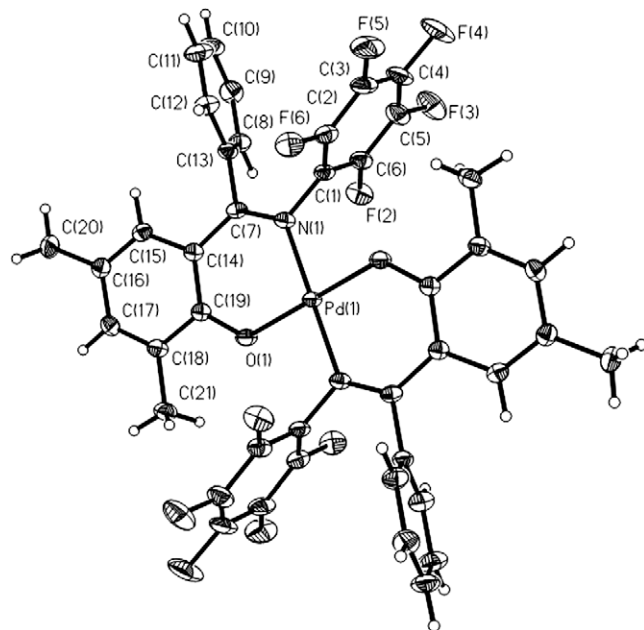


Fig. 2. ORTEP plot of **2**. Selected bond distances (Å): Pd–O1: 1.985(1) and Pd–N1: 2.033(1). Selected angles (°): O1–Pd–N1: 91.04 and O1–Pd–N2: 88.96.

3.921 Å, and a dihedral angle between their planes of 52.70°. Given this distance and angle it seems highly unlikely that any π -stacking contributes to the structure's stability. The average plane created by the phenolic aryl ring is nearly perpendicular to the both ketimine and pentafluoro rings at 81.15° and 85.29°, respectively.

A search of the literature indicated that a similar but non-fluorinated palladium(II) complex had been recently reported by Hong

Table 1
Crystallographic parameters.

Complex	2 [Pd(PKI-F ₅) ₂]
Empirical formula	PdO ₂ N ₅ F ₁₀ C ₄₂ H ₂₆
Formula weight	887.05
Crystal size (mm ³)	0.48 × 0.47 × 0.27
Crystal system	Triclinic
Space group	P1
<i>a</i> (Å)	9.047(3)
<i>b</i> (Å)	9.052(4)
<i>c</i> (Å)	12.202(5)
α (°)	77.184(6)
β (°)	83.106(5)
γ (°)	66.659(5)
Volume (Å ³)	894.053
<i>D</i> _{calc} (Mg m ⁻³)	1.647
Temperature (K)	173(2)
θ range (°)	3.29–8.07
Index ranges	–11 to <i>h</i> to 11, –11 to <i>k</i> to 11, –15 to <i>l</i> to 15
Goodness-of-fit on <i>F</i> ²	1131
Wavelength (Å)	0.71075

and co-workers [15]. The authors obtained the complex when attempting to isolate the active species involved in the in situ Suzuki–Miyaura cross-coupling of, mostly, activated aryl bromides with boronic acids. Interestingly, their isolated complex performed very poorly in these reactions, and better results were obtained when in situ systems of 1:1 free ligand: Pd(OAc)₂ were used. We decided to test the activity of our complex in the same reaction to determine whether electronic and/or steric variations in the ligand could have an effect on the performance of the complex.

2.2. Activity of **2** in the Suzuki–Miyaura reaction

The Suzuki–Miyaura reaction, involving the coupling of an organic halide or pseudo-halide with an organoboron reagent in the presence of a base and a Pd or Ni catalyst, is arguably the most used cross-coupling procedure for the formation of C–C bonds [16]. Key advantages of this reaction when compared to other cross-coupling reactions are low toxicity and ready availability of the organoboron reagents [17]. After an optimization process (Table 2), we found that our complex could perform the coupling of bromobenzene with 1-naphthaleneboronic acid using 0.6 mol% catalyst loading at 60 °C in very good yield in a couple of hours, when using technical grade isopropanol as the solvent (Table 2, entry 9). As a control reaction, we attempted the coupling of those substrates in the same conditions using nearly twice as much loading of Pd(OAc)₂ with no ligand, obtaining only 9% of the desired product after 24 h and 22% after 3 days (Table 2, entry 10). In addition, using **2**, upon decreasing the temperature to 40 °C or room temperature, product formation was still observed, but the reaction required 24–48 h for completion. Attempts to couple less reactive aryl chlorides (chlorobenzene or the more activated 4-nitrochlorobenzene) invariably failed.

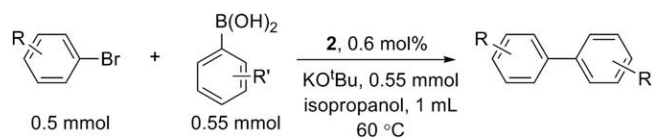
To determine the scope of the reaction, our optimized conditions were applied to a variety of aryl bromides and boronic acids (Table 3). While the complex reported by Hong and co-workers displayed very low activity even towards activated (electron-poor) aryl bromides [15], we were glad to find that our system not only also allowed for the coupling of activated deactivated (electron-rich) aryl bromides (Table 3, entries 4–9). Mono-*ortho*-substituted biaryls can be synthesized in short reaction times (Table 3, entries 2, 4, 6, 7), while more challenging di-*ortho*-substituted biaryls require longer reaction times, affording the desired coupling products in lower yields (Table 3, entries 8, 9, 10). It is worth mentioning that,

Table 2
System optimization for the Suzuki–Miyaura reaction using **2**.

Entry	Solvent	2 (mol%)	Temperature (°C)	Time (h)	Yield (%) ^a
1	Toluene	4.8	80	48	14
2	Dioxane	4.8	80	48	38
3	Ethanol	4.8	80	19	57
4	Isopropanol	4.8	80	2	92
5	Isopropanol	2.4	80	2	93
6	Isopropanol	1.2	80	2	91
7	Isopropanol	0.6	80	2	94
8	Isopropanol	0.3	80	4	39
9	Isopropanol	0.6	60	2	92
10	Isopropanol	1	60	24(72)	9(22) ^b
11	Isopropanol	0.6	40	24	91
12	Isopropanol	0.6	RT	48	89

^a GC yields using hexamethylbenzene as internal standard, average of two runs.

^b Pd(OAc)₂ instead of **2**.

Table 3Substrate scope for the Suzuki–Miyaura reaction using **2** as precatalyst.

Entry	Aryl bromide	Boronic acid	Product	Time (h)	Yield (%) ^a
1				2	89
2				2	85
3				14	86
4				2	87
5				2	82
6				2	85
7				2	89
8				24	59
9				24	60
10				24	76

^a Isolated yields, average of two runs.

in most cases, no starting aryl bromide was recovered, and the corresponding amount of dehalogenated by-product was observed in the GC traces. This competitive pathway in isopropanol-based systems has been described before [18]. As the coupling becomes more challenging because of electronic and/or steric effects, the dehalogenation path becomes favored.

3. Conclusion

The synthesis of a new air- and moisture-stable bis(phenoxyketimine) Pd(II) complex and its use in the Suzuki–Miyaura cross-coupling reaction of activated and unactivated aryl bromides is presented. We showed that simple ligand modifications from a previously reported complex [15] allowed for a dramatic increase

in performance, allowing for the coupling of unactivated aryl bromides with boronic acids to synthesize mono- and di-*ortho*-substituted biaryls in good yields, at mild temperature and short reaction times. In addition, the ligand is air- and moisture-stable and can be easily prepared. Studies on the catalyst activation and the effect of ligand modifications in this and related C–C bond forming reactions are currently ongoing in our labs.

4. Experimental

4.1. General considerations

All commercially available reagents were used as received without further purification. All synthesis and manipulations of air- and

moisture-sensitive compounds were carried out in Schlenk glassware that had been dried in an oven overnight, on dual-manifold high-vacuum/nitrogen Schlenk lines. Suzuki–Miyaura reactions were set up in oven-dried vials in an MBraun Unilab glovebox. Nuclear magnetic resonance spectra were recorded on a Varian Mercury Plus 300 MHz or on a Varian Inova 500 MHz spectrometer. Elemental analysis of **2** was performed at Columbia Analytical Services, Tucson, AZ. X-ray diffraction was performed in a Rigaku SCX-Mini CCD diffractometer. The ^{19}F NMR spectrum of **2** was reported using α,α,α -trifluorotoluene as Ref. [19].

4.2. Synthesis of bis[2,4-dimethyl-6-[phenyl(pentafluorophenylimino)methyl]-phenolato]palladium, $[\text{Pd}(\text{PKI-F}_5)_2][\text{Pd}(\text{NOF}_5\text{C}_2\text{H}_{13})_2]$ (**2**)

In a Schlenk flask, a solution of PHK-F_5 (**1**) (0.195 g, 0.5 mmol) in THF (40 mL) was cooled to -78°C using a dry ice acetone bath, and then *n*-butyllithium (0.31 mL, 0.5 mmol, 1.6 M in hexanes) was syringed in, dropwise. The reaction was allowed to warm to room temperature and stirred for another 30 min. Keeping a nitrogen flow, the septum was removed, palladium chloride (0.044 g, 0.248 mmol) was added, and the reaction was left to stir overnight. The entire solution was filtered through a Celite plug. The solvent was removed in vacuo and the resulting orange solid was placed on a silica plug. Pentane was used to elute unreacted free ligand, and then methylene chloride was used to bleed off an orange band. The solvent was removed and the resulting solid was placed on a filter frit and washed with copious amounts of pentane, yielding 0.179 g (80.7%) of **2** as an orange solid. ^1H NMR (299.84 MHz, CDCl_3): δ 7.29 (m, 6 H, Ar-H); 7.09 (m, 4 H, Ar-H), 6.90 (s, 2 H, Ar-H), 6.29 (s, 2 H, Ar-H), 1.93 (s, 6H, $-\text{CH}_3$), 1.52 (s, 6H, $-\text{CH}_3$). ^{13}C NMR (125.75 MHz, CD_2Cl_2): δ 176.21, 164.49, 138.43, 138.04, 132.65, 129.85, 129.39, 128.75, 126.11, 124.14, 120.56, 20.85, 17.09 (note: pentafluoro aryl carbons were not observed due to poor solubility and C–F coupling). ^{19}F NMR (CDCl_3 , 282.14 MHz): δ = -144.38 (m), -159.76 (t, $J = 22$ Hz), -165.10 (m). Anal. Calc. for $\text{PdO}_2\text{N}_2\text{F}_{10}\text{C}_{42}\text{H}_{26}$: C, 56.87; N, 3.16; H, 2.95. Found: C, 56.40; N, 3.03; H, 2.65%.

4.3. Suzuki–Miyaura cross-coupling of aryl bromides with boronic acids. General procedure

In a glove box, the desired boronic acid (0.55 mmol), potassium *t*-butoxide (0.55 mmol, 62 mg) and **2** (0.6 mol%, 2.7 mg) were added in turn to a vial equipped with a magnetic bar and sealed with a screw cap fitted with a septum. Outside the glovebox, technical grade isopropanol (1 mL) was syringed in the vial through the septum. After 20 min of stirring at 60°C the desired aryl bromide (0.5 mmol) was injected through the septum, and the reaction mixture was allowed to stir at that temperature. When the reaction reached completion, or no further conversion was observed, the mixture was placed in a plug of silica and eluted with hexanes,

affording the product in $>95\%$ purity. When necessary, the product was purified by flash chromatography on silica gel using mixtures ethyl acetate/hexanes as eluent. Yields reported for each substrate are the average of at least two reactions.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jorganchem.2009.04.044.

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