DOI: 10.1002/jccs.201800145

ARTICLE



Synthesis of a palladium complex bearing 2-phenylbenzothiazole and its application to Suzuki–Miyaura coupling reaction

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Funding information

Kaohsiung Medical University, Grant/Award Number: NSYSUKMU 107-P010; Ministry of Science and Technology, Taiwan, Grant/Award Number: MOST 106-2113-M-037 -002

1 | INTRODUCTION

Transition-metal-mediated catalytic cross-coupling reactions, Mizoroki-Heck,[1d] such as Negishi,[1f] Suzuki-Miyaura,[1e] Sonogashira,[1g] Kumada–Corriu,[1h] Hiyama,[1i] and Stille[1c] coupling reactions, are powerful methods for the construction of Caryl-Caryl or Caryl-Calkyl bonds^[1] and other functions.[1b] Among these crosscoupling reactions, Suzuki coupling reaction[1e,2] is one of the most important methods for the synthesis of biaryl compounds because boronic acids, which are less toxic and safer to the environment, are used as the precursor under mild reaction conditions. Phosphines^[3] and N-heterocyclic carbenes (NHCs)^[4] are the commonly employed ligands for Suzuki coupling reactions because they adjust the electron density surrounding the metal center, facilitating steps such as oxidative addition and reductive elimination (through steric bulk). Recently, cyclometalated Pd complexes^[5] were used as catalysts for the Suzuki coupling reaction, and they

The palladacycle complex $[L^{s}PdOAc]_{2}$ bearing 2-phenyl benzothiazole was synthesized and characterized by NMR and X-ray crystallography. $[L^{s}PdOAc]_{2}$ was used as a catalyst in the Suzuki–Miyaura cross coupling reaction of 4-bromotoluene with phenylboronic acid, which resulted in a conversion of >90% with 5 mol% of the Pd complex within 10 min at 60°C.

KEYWORDS

palladium, Suzuki-Miyaura cross coupling reaction

revealed great catalytic activity. A palladacycle complex^[6] bearing benzothiazole was reported, but no catalytic activity toward the Suzuki coupling reaction was studied. In this paper, we report the synthesis of a 2-phenyl benzothiazole-derived Pd complex [L^sPdOAc]₂ and its application toward Suzuki coupling reactions (Figure 1).

2 | RESULTS AND DISCUSSION

2.1 | Synthesis and characterization of [L^sPdOAc]₂

 $[L^{s}PdOAc]_{2}$ was synthesized from Pd(OAc)_{2} and 2-phenyl benzothiazole in acetic acid at 60°C and crystalized in THF at -20° C. The *anti* and *syn* isomers of $[L^{s}PdOAc]_{2}$ were clearly observed by ¹H NMR spectroscopy (Figure 2), which were consistent with those reported in the literature.^[6] In Figure 2, the *anti* isomer shows a larger ratio than the *syn* isomer. The crystal structure of $[L^{s}PdOAc]_{2}$ (Figure 3) was analyzed by X-ray crystallography, which revealed a square-

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FIGURE 1 Synthesis of palladacycle complex ([L^sPdOAc]₂)



FIGURE 2 ¹H NMR spectrum of [L^sPdOAc]₂

planar geometry of the dinuclear Pd complex with two 2-phenyl benzothiazoles and two bridging acetates. The bond lengths and bond angles were compared with those of 2-phenyl benzoxazole-derived Pd complex $[L^{o}PdOAc]_{2}^{[5]}$ (Figure 4). The data revealed that the two complexes have similar geometry. The only differences are that the angles $\angle N-Pd-C$ of $[L^{s}PdOAc]_{2}$ (81.02° and 81.82°) are smaller than those of $[L^{o}PdOAc]_{2}$ (90.50, 90.47, 90.59, and 89.24), and the distances between the phenyl and benzothiazolyl groups of $[L^{s}PdOAc]_{2}$ (d(C(10)-C(11)) = 1.450(6) Å, d(C (23) -C(24)) = 1.441(6) Å in Figure 4) are smaller than those of $[L^{o}PdOAc]_{2}$ (1.389–1.409 Å).

2.2 | Suzuki coupling reaction

 $[L^{s}PdOAc]_{2}$ was tested as a catalyst for the Suzuki crosscoupling reaction of 4-bromotoluene with phenylbronic acid to synthesize 4-methyl-1,1'-biphenyl. We first performed the optimization of solvents and bases for the coupling reaction of 4-bomotoluene and phenylboronic acid with 5 mol% of $[L^{s}PdOAc]_{2}$ as catalyst (Table 1). As shown in entries 1–5 in Table 1, $Cs_{2}CO_{3}$ was used as the base and the solvent system was varied. The mixed solvents DMF + H₂O (1:1, entry 4) and CH₃CN + H₂O (1:1, entry 5) both revealed the highest catalytic activity with conversions of >90% at 60°C after 3 hr. However, performing the coupling reaction in the



FIGURE 3 Molecular structure of $[L^{\circ}PdOAc]_{2}$ (CCDC 1826155) as 20% ellipsoids and all hydrogen atoms were omitted for clarity. Selected distances and angles: d(C(5)-Pd(1)) = 1.960(4) Å, d(C(18)-Pd(2)) = 1.972 (4) Å, d(N(1)-Pd(1)) = 2.023(3) Å, d(N(2)-Pd(2)) = 2.043(3) Å, d(O(1)-Pd(1)) = 2.132(3) Å, d(O(2)-Pd(2)) = 2.046(3) Å, d(O(3)-Pd(2)) = 2.153 (3) Å, d(O(4)-Pd(1)) = 2.035(3) Å, d(Pd(1)-Pd(2)) = 2.8577(5) Å, d(C(10)-C(11)) = 1.450(6) Å, d(C(23)-C(24)) = 1.441(6) Å, $\angle C(5)-Pd(1)-N$ (1) = 81.03(16)°, $\angle C(18)-Pd(2)-N(2) = 81.82(16)°$, $\angle O(4)-Pd(1)-O$ (1) = 87.31(13)°, $\angle O(2)-Pd(2)-O(3) = 88.55(12)°$



FIGURE 4 Select bond distances (Å) and bond angles (°) of [L*PdOAc]₂ and [L*PdOAc]₂

mixed solvent $CH_3CN + H_2O$ [1:1] with NaOH as the base showed lower catalytic activity (conversion 66%, entry 7 in Table 1) than in the mixed solvent DMF + H_2O (1:1, conversion 91%, entry 6 in Table 1). Using the mixed solvent system reduced the reaction time to 10 min (conversion 90% for the mixed solvent DMF + H_2O (entry 8) and 86% for $CH_3CN + H_2O$ (entry 9)). When the reaction temperature was brought down to 30°C, the conversion was 85% in a 1:1 mixture of DMF + H₂O after 60 min (entry 10), 80% after 30 min (entry 11), and 68% after 10 min (entry 12). However, the conversion was only 17% while using a 1:1 mixture of CH₃CN + H₂O at 30°C after 60 min (entry 13). With reduced Pd loading of 1 mol% in the solvent mixture $DMF + H_2O$, the conversion was 62%. It showed that [L^sPdOAc]₂ was a great catalyst for the Suzuki coupling reaction. [L^sPdOAc]₂ was tested as the catalyst of choice for an entire set of substrates (Table 2). In the condition of entry 8 of Table 1, [L^sPdOAc]₂ was also effective with various substrates in Table 2. However, aryl chlorides were inactive when using [L^sPdOAc]₂ as catalyst in this reaction condition, and therefore their results are not reported.

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TABLE 1 Suzuki coupling reaction of 4-bromotoluene and phenylboronic acid by using the complex [L^sPdOAc]₂ as catalyst

Entry	Base	Solvent	Time (min)	Temperature (°C)	Yield (%) ^a
1	Cs ₂ CO ₃	DMSO	360	60	Trace
2	Cs ₂ CO ₃	DMF	360	60	79/60
3	Cs ₂ CO ₃	1,4-Dioxane	360	60	34/20
4	Cs ₂ CO ₃	$DMF + H_2O$	180	60	91/85
5	Cs ₂ CO ₃	$CH_3CN + H_2O$	180	60	91/83
6	NaOH	$DMF + H_2O$	180	60	91/86
7	NaOH	$CH_3CN + H_2O$	180	60	66/50
8	Cs ₂ CO ₃	$DMF + H_2O$	10	60	90/80
9	Cs ₂ CO ₃	CH ₃ CN+ H ₂ O	10	60	86/79
10	Cs ₂ CO ₃	$DMF + H_2O$	60	30	85/75
11	Cs ₂ CO ₃	$DMF + H_2O$	30	30	80/70
12	Cs ₂ CO ₃	$DMF + H_2O$	10	30	68/55
13	Cs ₂ CO ₃	$CH_3CN + H_2O$	60	30	17/ – ^c
14 ^b	Cs ₂ CO ₃	$DMF + H_2O$	10	30	62/50

Reaction conditions: 4-Bromotoluene 0.5 mmol, phenylboronic acid 0.5 mmol, base 1 mmol, and [L*PdOAc]₂ 5 mol% in solvent (3 mL).

^a GC yield/isolated yield.

^b [L^sPdOAc]₂ 1 mmol%.

^c Not available.

TABLE 2	Suzuki coupling reaction of	various aryl halides and	phenylboronic acid b	y using the com	plex [L ^s PdOAc] ₂ as a catal	lyst
		2			1 6 32	~

Entry	Aryl halide	Product	Conversion yield (%) ^a	Isolated yield (%)
1	CF ₃	CF ₃ Ph	95	91
2	CHO Br	CHO	90	85
3	ІОН	Ph-OH	95	91
4	IF	Ph-F	86	80
5	Br	Ph-Ph	90	83
6	Br	Ph	90	85

Reaction conditions: aryl halide 0.5 mmol, phenylboronic acid 0.5 mmol, Cs_2CO_3 1 mmol, and $[L^sPdOAc]_2$ 5 mol% in solvent (3 mL, DMF + H₂O (1:1)) at 60°C in 10 min.

^{a 1}H NMR yield.

3 | CONCLUSIONS

The palladacycle $[L^{s}PdOAc]_{2}$ was synthesized and characterized. Its structure was identified by X-ray crystallography. The exceptional catalytic reactivity of $[L^{s}PdOAc]_{2}$ was demonstrated with the Suzuki cross-coupling reaction of 4-bromotoluene with phenylboronic acid, with 80% conversion at 30°C after 1 hr.

4 | EXPERIMENTAL

4.1 | General

Standard Schlenk techniques and a N₂-filled glove box were used throughout the isolation and handling of all the compounds. Solvents and deuterated solvents were purified prior to use. Deuterated chloroform was purchased from Acros. 3-Iodobenzotrifluoride, 2-bromobenzaldehyde, 4-iodophenol, 4-fluoroiodobenzene, 1,4-dibromobenzene, 4-bromoanisole, 4-bromotoluene, phenylboronic acid, 2-aminothiophenol, benzaldehyde, and palladium acetate were purchased from Aldrich. Cesium carbonate and sodium hydroxide were purchased from Alfa. ¹H and ¹³C NMR spectra were recorded on a Varian Gemini2000-200 (200 MHz for ¹H and 50 MHz for ¹³C) spectrometer with chemical shifts given in ppm from the internal TMS or center line of CDCl₃. 2-Phenylbenzothiazole was prepared following literature procedures.^[7]

4.2 | General procedure for the Suzuki–Miyaura crosscoupling reaction of 4-bromotoluene with phenylbronic acid

A typical procedure is exemplified by the synthesis of entry 1 (Table 1). 4-Bromotoluene (0.5 mmol), phenylboronic acid (0.5 mmol), and Cs_2CO_3 (1 mmol) with $[L^sPdOAc]_2$ (5 mol %) as a catalyst were stirred at 60°C in DMSO (3 mL). After 360 min, the solution was cooled to room temperature, diluted with CH_2Cl_2 , and filtered through silica gel with copious washing (CH_2Cl_2). The yield was determined by gas chromatography (GC).

ACKNOWLEDGMENTS

This study was supported by Kaohsiung Medical University, NSYSU-KMU Joint Research Project (#NSYSUKMU 107-P010), and the Ministry of Science and Technology (Grant MOST 106-2113-M-037-002). We thank the Center for Research Resources and Development, Kaohsiung Medical University, for instrumentation and equipment support.

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How to cite this article: Kosuru SR, Lai H-Y, Yang C-Y, Senadi GC, Lai Y-C, Chen H-Y. Synthesis of a palladium complex bearing 2phenylbenzothiazole and its application to Suzuki– Miyaura coupling reaction. *J Chin Chem Soc.* 2018; 1–4. https://doi.org/10.1002/jccs.201800145