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Short Communication

Room-temperature Suzuki–Miyaura coupling of aryl bromides with phenylboronic acid catalyzed by a palladium complex with an inexpensive nitrogen-containing bis(phosphinite) ligand

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ABSTRACT

A palladium(II) complex with a known inexpensive and very easily synthesized nitrogen-containing bis(phosphinite) ligand has been prepared and characterized by spectroscopic and crystallographic studies. The ligand is bound to the metal in a *P*,*P*-bidentate coordination mode with a bite angle of 98.90°. This complex was found to be an efficient catalyst for room-temperature Suzuki–Miyaura coupling of a variety of aryl bromides with phenylboronic acid. At 0.1 mol% of palladium in DMF/K_3PO_4 for 24 h, the corresponding biaryls were obtained with 75–92% yields. Activated substrates displayed high yields even within minutes.

1. Introduction

Suzuki–Miyaura cross-coupling is a powerful synthetic method for preparing biaryls, leading to agrochemicals, pharmaceuticals, polymers and materials [1]. Ambient temperature catalysis has become a challenge of high importance considering both needs for low cost energy reactions and thermal instability of several substrates. Excellent activity for room-temperature Suzuki–Miyaura coupling has been reported for particular classes of phosphanes by Buchwald [2,3], Fu [4], Hartwig [5], Beller [6], and Dai [7], and *N*-heterocyclic carbenes by Herrmann [8], Glorius [9], Organ [10], Nolan [11], Nolan/Cazin [12,13], and Dorta [14]. Recently, Zhou discovered that a combination of $Pd(OAc)_2$ and Buchwald's ligand XPhos could efficiently catalyze the room-temperature Suzuki–Miyaura coupling of heteroaryl chlorides/tosylates even within minutes [15]. High activity has also been observed for mono- and bis(phosphinites) by Balakrishna [16,17]. Moreover, phosphinites have widely been used in homogeneous catalysis due to their facile preparation and their improved catalytic activity. Excellent activity in palladium-catalyzed Suzuki–Miyaura coupling has been reported for palladacyclic monophosphinite complexes by Bedford [18,19], bis(phosphinite) PCP-pincer complexes by Bedford [20], Uozumi [21], and Protasiewicz [22], and other symmetrical and unsymmetrical pincer complexes by Gong/Song [23]. However, the efficiency of phosphinites for room-temperature Suzuki–Miyaura coupling has rarely been investigated [16,17].

Ligands bearing phosphorus and nitrogen donors are of significant interest due to the improved catalytic activity of their transition metal complexes [24]. It has also been found that the presence of nitrogen as a stabilizing group in the ligand during the course of a metal-mediated reaction, improves its catalytic efficiency despite no metal–nitrogen interaction is observed in the complex. Indeed, a nitrogen-containing bis(phosphine) displayed a much higher activity in rhodium-catalyzed hydroformylation compared to its analogous ligand containing carbon instead of nitrogen on the backbone [25], and an amino-substituted *P*,*S*-phosphinite was also found to be a more efficient ligand in palladium-catalyzed Heck reaction [26] and in rhodium-catalyzed hydroformylation [27] compared to the ligand without an amino group, although no metal–nitrogen interaction was observable in all cases. We have previously reported an easy one-pot synthesis of a nitrogen-containing bis(phosphinite) from the very cheap *N*-phenyldiethanolamine, as an efficient ligand for rhodium-catalyzed hydroformylation [28]. Herein, we report the corresponding chelate palladium complex and its evaluation in room-temperature Suzuki–Miyaura coupling.

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2. Experimental

2.1. Palladium dichloro{N,N-bis[2-[(diphenylphosphino-P)oxy]ethyl]-benzenamine} (**3**)

A solution of ligand **2** [28] (258 mg, 0.47 mmol) in dichloromethane (10 mL) was added dropwise under argon to a solution of $(PhCN)_2PdCl_2$ (180 mg, 0.47 mmol) in dichloromethane (5 mL) at ca. −70 °C or room temperature, and then stirred at room temperature overnight. The resulting solution was concentrated under reduced pressure to an approximate volume of 3 mL. Dry ether (15 mL) was added to cause precipitation of a solid, that was collected after decantation, washed with ether (2 × 10 mL) and then dried under vacuum, yielding **3** (320 mg, 94%) as a yellow-orange solid, m.p. (dec.) 160 °C. ^{1}H NMR ($CDCl_3$): δ 7.70–7.64 (m, 8H, Ar), 7.40–7.35 (m, 4H, Ar), 7.26–7.21 (m, 8H, Ar), 7.10 (t, $^3J = 8.0$ Hz, 2H, Ar), 6.68 (t, $^3J = 7.2$ Hz, 1H, Ar), 6.38 (d, $^3J = 8.1$ Hz, 2H, Ar), 3.71 (m, 4H, CH_2O), 3.56 (m, 4H, CH_2N); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 145.93–111.86 (Ar), 65.59–65.48 (m, CH_2O), 52.41–52.29 (m, CH_2N); $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ 107.37 (s); HRMS: calcd. for $C_{34}H_{33}Cl_3NO_2P_2Pd$ $[M + Cl]^-$ 760.0092, found 760.0092.

2.2. General experimental procedure for the Suzuki–Miyaura coupling

Aryl bromide (1.0 mmol), phenylboronic acid (0.183 g, 1.5 mmol), K_3PO_4 (0.425 g, 2.0 mmol), complex **3** in DMF (0.5 mM, 2 mL, 1.0 μmol) and dodecane (70 μL, 0.3 mmol) as internal standard were stirred at room temperature under argon for 24 h. After addition of water (5 mL) and extraction with dichloromethane (2 × 10 mL), the organic phase was washed with brine (10 mL), dried over Na_2SO_4, filtered, passed through celite and analyzed by GC and GC–MS. After evaporation of the volatiles, isolation of the pure biaryl was achieved by column chromatography on silica gel using hexane/AcOEt as eluent. All biaryls are known compounds and were characterized by ^{1}H and ^{13}C NMR spectra.

3. Results and discussion

3.1. Synthesis and characterization of the palladium complex

Treatment of $(PhCN)_2PdCl_2$ with one equivalent of ligand **2** yielded complex **3** as a unique species regardless of whether the addition was conducted at low or at room temperature (Scheme 1). The presence of only one singlet at δ 107.37 in the ^{31}P NMR spectrum of **3** and the absence of the signal corresponding to the free ligand at δ 114.63 [28] provided a clear evidence that both phosphorus atoms are bound to the metal and are equivalent. In the ^{1}H and ^{13}C NMR spectra of **3**, the NCH_2 resonances are almost in the same position as those in the free ligand [28], contrary to a considerable downfield shifting expected for the case of Pd–N coordination. The bidentate *P*,*P*-coordination mode of ligand **2** has also been observed towards rhodium [28] and platinum [29].

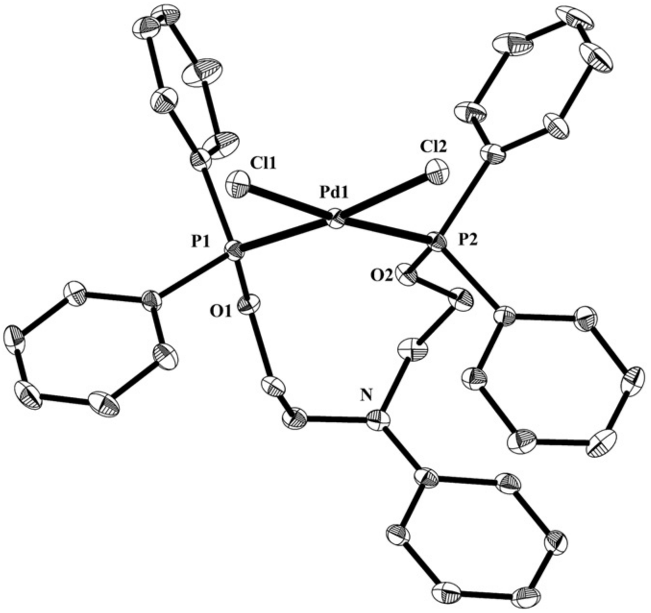
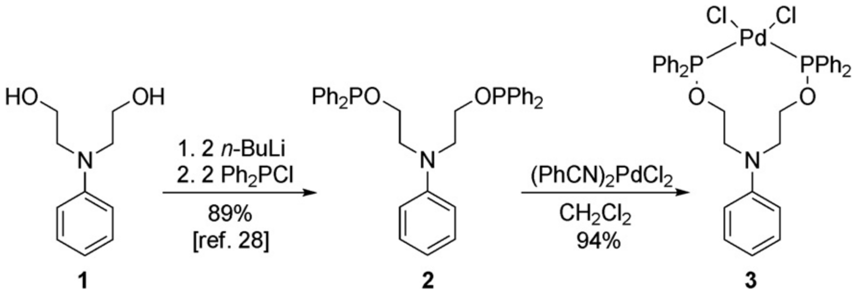


Fig. 1. Molecular structure of **3** (30% thermal probability level).

Crystals of complex $\mathbf{3}\cdot 0.5CH_2Cl_2$ were obtained by slow diffusion of ether through a solution of the complex in dichloromethane. As shown in the molecular structure (Fig. 1), the ligand is coordinated to the metal in a *P*,*P*-bidentate mode and the Pd–N distance is long enough (5.475 Å) ensuring the absence of interaction. The coordination geometry around palladium is approximately square planar. The two Pd–Cl distances are equal (2.3460(9) Å) and the two Pd–P distances are almost equal (Pd(1)–P(1), 2.2347(9) Å; Pd(1)–P(2), 2.2362(9) Å). The bite angle P–Pd–P (98.90°) is relatively large; the corresponding values in structures of $PdCl_2(dppe)$ [30] and $PdCl_2(Xantphos)$ [31] are 85.82° and 101.19°, respectively. The bite angle effects of diphosphines in cross-couplings and other reactions have been studied in details [32].

3.2. Room-temperature Suzuki–Miyaura coupling

Complex **3** is insoluble or displays a very low solubility in toluene, dioxane, acetonitrile, tetrahydrofuran, diethyl ether, methanol, and ethanol, but it is soluble in dimethylformamide, dimethylacetamide and dichloromethane. At relatively low palladium loading (0.1 mol%) [33], the latter three solvents were used in solvent optimization for room-temperature Suzuki–Miyaura coupling of the deactivated 4-bromoanisole with phenylboronic acid for 24 h (Table 1). In addition, different bases were tested, and the best system was found to be DMF/K_3PO_4 affording 92% conversion into 4-methoxybiphenyl (entry 6). In DMF, the conversion rate decreases in the base order $K_3PO_4 > K_2CO_3 > Cs_2CO_3 \gg$ MeONa > AcONa > KOH. For the three most efficient bases, the same order is also observed in the other two solvents. For the same base, the conversion decreases in the solvent order DMF > DMA ≫ dichloromethane.



Scheme 1. Synthesis of palladium complex.