## 1-Phosphabarrelene complexes of palladium and their use in Suzuki–Miyaura coupling reactions<sup>†</sup>

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A bulky 1-phosphabarrelene, 2, was obtained from the reaction of a phosphinine with benzyne; two palladium complexes of 2 were successfully employed in the Suzuki–Miyaura coupling of several aryl chlorides with phenylboronic acid at a relatively low catalyst loading, and activated aryl chlorides were coupled at room temperature in the absence of strong bases.

Phosphorus compounds that feature P=C double bonds are a powerful synthetic tool for elaborating new classes of functional tertiary phosphines<sup>1</sup> and unsaturated heterocycles. Thus, molecules such as 2H-phospholes and phosphinines have been widely used as building blocks in the synthesis of new types of heterocycles that are difficult to obtain using classical synthetic strategies. Among these, phosphabarrelenes, which are easily produced from phosphinines through a [4 + 2] Diels-Alder reaction,<sup>2-4</sup> recently appeared as a very promising new class of ligands for homogeneous catalysis, and have already shown excellent performances in important catalytic transformations, such as the hydroformylation of olefins.<sup>3,5</sup> A great advantage in their synthesis resides in the possible use of 2,6-difunctional phosphinines, which allows the environment of the phosphorus atom to be sterically tuned.<sup>6</sup> As part of a program aimed at evaluating the activity of new phosphorus heterocycles in group 10-catalyzed C-C and C-N coupling reactions, we recently explored the synthesis of bulky substituted phosphabarrelenes and evaluated the reactivity of their Pd complexes in the Suzuki-Miyaura cross-coupling of aryl chlorides<sup>7</sup> with phenylboronic acid, a challenging transformation in which bulky phosphines are among the most efficient ligands.<sup>8–11</sup> Herein, we wish to report on these results.

The synthesis of 2,6-bis-trimethylsilyl-substituted phosphabarrelene **2** was readily achieved by the addition of *in situ*generated benzyne<sup>2</sup> to phosphinine **1** at room temperature (Scheme 1). Phosphabarrelene **2** was obtained in good yield (75%) as an air-stable, white, crystalline solid.<sup>12</sup> As anticipated, the X-ray crystal structure analysis of **2**<sup>‡</sup> revealed a



Scheme 1 The synthesis of phosphabarrelene 2.

strong pyramidalization at the phosphorus atom ( $\Sigma$ (CPC) = 288°) (see the ESI†). In order to analyze the electronic properties of **2** in theoretical terms, a charge decomposition analysis using the CDA program<sup>13</sup> was carried out on some model [LNi(CO)<sub>3</sub>] complexes (L = PPh<sub>3</sub>, **2** and PF<sub>3</sub>). This type of analysis has already been shown to provide useful data with respect to the ratio between donation and back-donation in transition metal complexes that feature different types of twoelectron donor ligands (see the ESI† for detailed information). The calculations indicated that **2** was a stronger  $\pi$ -acceptor ligand than PPh<sub>3</sub> but weaker than PF<sub>3</sub>.

To evaluate the catalytic properties of **2** in the Suzuki– Miyaura coupling process, two catalytic precursors were synthesized. We first focused on the (allyl)chloropalladium(II) derivative, because  $\pi$ -allyl–palladium–*N*-heterocyclic carbene (NHC) complexes have been shown to be very efficient catalysts in Suzuki–Miyaura couplings of poorly reactive aryl chlorides.<sup>10</sup>

Complex 3, which readily formed upon mixing  $[Pd(allyl)Cl]_2$  with 2 in  $CH_2Cl_2$  at room temperature, was structurally characterised (Fig. 1). Other important catalyst precursors for C–C coupling reactions are the 14 VE neutral  $Pd(0)L_2$ 



**Fig. 1** An ORTEP plot (50% thermal ellipsoids) of the X-ray crystal structure of **3** (hydrogen atoms, one of the two independent crystallographic units and the disorder of the allyl moiety have been omitted for clarity). Selected bond lengths (Å) and angles (°): P1–Pd1: 2.291(1), Pd1–C20a: 2.123(5), Pd1–C21a: 2.139(7), Pd1–C1: 2.374(1), Pd1–C22a: 2.210(5); P1–Pd1–C11: 86.89(4), P1–Pd1–C22a: 172.7(2),  $\Sigma$ (CPC): 294.9.‡

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<sup>†</sup> Electronic supplementary information (ESI) available: Experimental procedures and characterization data for **2**, **3** and **4**, literature references for the prepared biaryls, Cartesian coordinates and energies for the optimized structures, three lowest frequencies, detailed information of the CDA calculations, and X-ray crystal data for **2**, **3** and **4**. CCDC 699913–699915. For ESI and X-ray crystal data in CIF or other electronic format, see DOI: 10.1039/b814886d



**Fig. 2** An ORTEP plot (50% thermal ellipsoids) of the X-ray crystal structure of  $4^{+}_{+}$  (hydrogen atoms have been omitted for clarity). Selected bond lengths (Å) and angles (°): P1–Pd: 2.274(1), P2–Pd: 2.268(1); P1–Pd1–P2: 160.65(4),  $\Sigma$ (CP1C): 290.5,  $\Sigma$ (CP2C): 290.2.

complexes, where L is typically a trialkyl phosphine.<sup>9</sup> The corresponding phosphabarrelene-containing 14 VE complex, **4**, was thus conveniently prepared by the reduction of  $[(COD)PdCl_2]$  with cobaltocene in the presence of two equivalents of **2** in acetonitrile, and isolated in high yield (90%) as a white, crystalline solid (Fig. 2).

Complex 4 adopts a near linear geometry mode, with a P-Pd-P angle of *ca*. 160°. As with  $[Pd(Cy_3P)_2]$ ,<sup>14</sup> no agostic interactions between the ligands and the Pd atom were observed.

In the first series of experiments, **3** was used in the presence of a second equivalent of **1** to determine the best experimental conditions, the nature of the base being crucial in this type of coupling.<sup>11</sup> The best results were obtained when reactions were carried out in toluene at 80 °C using carbonate or phosphate as a base.§ Surprisingly, the use of alkoxides resulted in a complete loss of activity (Table 1).

Various substituted aryl chlorides were coupled with phenylboronic acid under these conditions in very good yields, using 0.2 mol% of either catalyst **3** or **4** (see Table 2).

Acceptor-substituted biphenyls were obtained in excellent yields with short reaction times. Donor-substituted aryl chlorides required somewhat longer reaction times but the coupling still proceeded smoothly and delivered the products in high yields. 2,6-Dimethylchlorobenzene, which is deactivated and also sterically hindered, was not reactive under these conditions (Table 2, entry 13). Interestingly, reduction of the aryl chlorides was not observed and only trace amounts of

 Table 1 Optimization of the reaction conditions<sup>a</sup>



Entry	Base	$T/^{\circ}\mathbf{C}$	t/h	Conversion $(\%)^b$
1	KO(t-Bu)	80	24	0
2	Et <sub>3</sub> N	80	24	17
3	KÕH	80	24	58
4	Cs <sub>2</sub> CO <sub>3</sub>	80	24	76
5	K <sub>3</sub> PO <sub>4</sub>	80	24	82
6	K <sub>2</sub> CO <sub>3</sub>	80	24	91

<sup>*a*</sup> Reaction conditions: ArCl (1.0 mmol), PhB(OH)<sub>2</sub> (1.2 mmol), base (3 mmol), toluene (2 mL), **3** (0.002 mmol), **2** (0.002 mmol), 80 °C, substrate : Pd = 500 : 1. <sup>*b*</sup> As judged by GC analysis.

Table 2The Suzuki–Miyaura cross-coupling of aryl chlorides using 3or  $4^a$ 

R	CI +	$\langle \rangle$	$-B(OH)_2 \xrightarrow{[cat]}_{K_2CO_3} R$		$\langle \rangle$
Entry	R	Cat.	Product	t/h	Yield (%) <sup>b</sup>
1 2	4-CN	3 4		1 1	98 99
3	2-CN	3		1	99
4	4-Ac	3	$\sim$	2	95
5	4-NO <sub>2</sub>	3	0 <sub>2</sub> N-	2	96
6	4-COOMe	3	MeO	2	99
7	4-CF <sub>3</sub>	3	F <sub>3</sub> C-	2	94
8	Н	3	н-	12	97
9 10	4-Me	3 4	Me	20 20	91 90
11 12	3-OMe	3 4	MeO	20 20	96 92
13	2,6-Me	3		20	5

<sup>*a*</sup> Reaction conditions: ArCl (1.0 mmol), PhB(OH)<sub>2</sub> (1.2 mmol), K<sub>2</sub>CO<sub>3</sub> (3 mmol), toluene (2 mL), **2** (0.002 mmol), and **3** (0.002 mmol) or **4** (0.002 mmol), 80 °C, substrate : Pd =  $500 : 1.^{b}$  Isolated yield.

biphenyl (<1%) resulting from the homo-coupling of phenylboronic acid were detected. Additional reactions involving different L/Pd ratios were carried out to gain further insight into the nature of the active species. No difference in the catalytic activity was observed using one or two equivalents of ligand when the reaction was performed at 80 °C. In contrast,

Table 3Further studies<sup>a</sup>



Entry	R	Cat. (%)	L/Pd	$T/^{\circ}\mathrm{C}$	t/h	Yield $(\%)^b$
1	4-CN	0.2	1:1	80	1	>99
2	4-CN	0.2	2:1	80	1	>99
3	4-CN	0.2	10:1	80	1	37
4	4-CN	1.0	1:1	25	12	99
5	4-CN	1.0	2:1	25	12	5
6	4-CN	$1.0^{c}$	0	25	12	Trace
7	$4-NO_2$	1.0	1:1	25	16	91
8	4-COOMe	1.0	1:1	25	24	89

<sup>*a*</sup> Reaction conditions: ArCl (1.0 mmol), PhB(OH)<sub>2</sub> (1.2 mmol), K<sub>2</sub>CO<sub>3</sub> (3 mmol), toluene (2 mL). <sup>*b*</sup> GC yield. <sup>*c*</sup> 0.5% [Pd(allyl)Cl]<sub>2</sub>.

the use of a ten-fold amount of ligand led to a significant decrease in the catalytic activity (see Table 3).

Finally, the catalytic activity of **3** at room temperature was also evaluated. Excellent yields were obtained after 12–24 h at room temperature when operating at a L/Pd ratio of 1 : 1 for activated aryl chlorides (Table 3, entries 4, 7 and 8). In contrast to other catalytic systems that allow the use of aryl chlorides at room temperature, catalyst **3** shows an important activity with potassium carbonate as a base, meaning that there is no need for expensive fluoride or caesium salts, or strong alkoxide bases.<sup>15</sup> Importantly, when using L/Pd ratios of 2 : 1 or higher, the catalytic activity decreased significantly (Table 3, entry 5), suggesting that a 12 VE complex may act as the active species.<sup>16</sup> Note also that in the absence of ligand, only trace amounts of the desired biphenyl product were formed (Table 3, entry 6).

Interestingly, ligand **2** showed the best performance with a low L/Pd ratio, in contrast to several other bulky phosphine ligands, where the best performances are obtained when reactions are performed at higher L/Pd ratios of 2-6:1. Both catalytic precursors **3** and **4** utilized herein efficiently catalyze the Suzuki–Miyaura cross-coupling of aryl chlorides at relatively low catalyst loadings (0.2%), with a good tolerance for functional groups such as methoxy, ester, keto, fluoro, cyano and nitro.

In conclusion, we have synthesized a new bulky phosphine ligand from a phosphinine derivative *via* a [4 + 2] Diels–Alder reaction with benzyne. This method easily allows modification of the bulkiness of the ligands *via* 2,6-disubstitution of the starting phosphinine derivative. A relatively rare example of a PdL<sub>2</sub> (L = phosphine) complex, **4** has been synthesized and structurally characterized. Additionally, an air-stable catalyst precursor, **3**, which has been shown to generate a room temperature catalytic active species, has been synthesized. As such, complex **3** ranks among the very best systems for this cross-coupling reaction.

Therefore, 1-phosphabarrelenes should be regarded as a promising class of ligands in catalyzed cross-coupling reactions, due to the modular synthetic approach that allows fine tuning of their steric properties.

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## Notes and references

‡ Crystal data for 2: C<sub>19</sub>H<sub>29</sub>PSi<sub>2</sub>, M = 344.57, orthorhombic, space group *Pnma*, a = 15.043(1), b = 16.246(1), c = 8.401(1) Å, V = 2053.1(3) Å<sup>3</sup>, T = 150.0(1) K, Z = 4, 12956 reflections measured, 3085 unique ( $R_{int} = 0.0412$ ), which were used in all calculations. The final *R*1 and w*R*2 were 0.0707 and 0.1174 (all data). CCDC 699913.†

**Crystal data for 3**:  $C_{22}H_{34}$ CIPPdSi<sub>2</sub>, M = 527.49, triclinic, space group *P*-1, a = 10.056(1), b = 15.490(1), c = 16.211(1) Å,  $\alpha = 86.602(1)$ ,  $\beta = 83.472(1)$ ,  $\gamma = 89.719(1)^{\circ}$ , V = 2504.4(3) Å<sup>3</sup>, T = 150.0(1) K, Z = 4, 22441 reflections measured, 11 297 unique ( $R_{int} = 0.0598$ ), which were used in all calculations. The final *R*1 and w*R*2 were 0.0723 and 0.1479 (all data). CCDC 699914.†

**Crystal data for 4**:  $C_{38}H_{58}P_2PdSi_4$ , M = 795.54, orthorhombic, space group *Pbca*, a = 10.310(1), b = 18.846(1), c = 43.610(1) Å, V = 8473.5(10) Å<sup>3</sup>, T = 150.0(1) K, Z = 8, 44281 reflections measured, 10810 unique ( $R_{int} = 0.0872$ ), which were used in all

calculations. The final R1 and wR2 were 0.0918 and 0.2271 (all data). CCDC 699915.<sup>†</sup>

§ General procedure for the Suzuki-Miyaura cross-coupling: An ovendried Schlenk tube equipped with a magnetic stirrer bar was charged with potassium carbonate (3 mmol, 414.6 mg) and phenylboronic acid (1.2 mmol, 146.3 mg). The Schlenk tube was sealed, and then evacuated and backfilled with nitrogen (this sequence was repeated three times). Freshly distilled toluene (1.9 mL) was added via a rubber septum and a 0.02 M solution of 3 (0.002 mmol, 100 µL) in toluene was added via a microsyringe. Aryl chlorides (1 mmol) were added in a single portion and the Schlenk tube was sealed and placed into an oil bath at 80 °C. Upon complete consumption of the starting material, as judged by GC analysis, the reaction mixture was allowed to cool to room temperature, diluted with diethyl ether (10 mL), filtered through a thin pad of silica gel (eluting with diethyl ether) and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel when necessary. All of the biphenyl products reported in Table 1, Table 2 and Table 3 are known compounds, and were characterized by favorable comparison of their <sup>1</sup>H and <sup>13</sup>C NMR spectra with previously reported data in the literature (see the ESI<sup>+</sup>).

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