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## A new insight into *ortho*-(dimesitylboryl)diphenylphosphines: applications in Pd-catalyzed Suzuki–Miyaura couplings and evidence for secondary $\pi$ -interaction<sup>†</sup>

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ortho-(Dimesitylboryl)phenylphosphines 1 and 2 were applied in Pd-catalyzed Suzuki–Miyaura C–C couplings. Coordination studies were performed in order to rationalize the relationship between structure and reactivity. Full characterization of a Pd(0) complex derived from 1 has evidenced a new coordination mode for phosphine-arylboranes involving secondary  $\pi$ -interaction between one of the mesityl groups at boron and the metal centre.

Palladium catalysis has become a major tool in organic synthesis, performing a range of valuable transformations.<sup>1</sup> In particular, the last decade has witnessed spectacular progress in cross-couplings thanks to the use of biaryl-phosphines.<sup>2</sup> These readily accessible and highly modular ligands proved to be extremely versatile and were successfully applied to a range of C–C and C-heteroatom bond-forming processes.<sup>3,4</sup> Key features of biaryl-phosphines are their (i) high resistance towards oxidation<sup>5</sup> and (ii) ability to stabilize low-valent Pd(0) intermediates by secondary interactions between the remote aryl ring and the metal centre.<sup>6</sup>

Over the last few years, some of us have been investigating the coordination properties of phosphine-boranes and related ambiphilic ligands. Four different coordination modes have been evidenced, differing in the participation of the Lewis acid site that can (i) remain pendant, (ii) interact with a co-ligand, typically a halogen atom, (iii) abstract an X co-ligand to give a zwitterionic complex or (iv) coordinate to the metal as a  $\sigma$ -acceptor ligand.<sup>7,8</sup> Recent studies have pointed out some unexpected analogies between *ortho*-(dimesitylboryl)phenylphosphines and biaryl-phosphines (Fig. 1). First, no sign of oxidation of [R<sub>2</sub>P(o-C<sub>6</sub>H<sub>4</sub>)BMes<sub>2</sub>] (R = Ph for 1; R = *i*Pr for 2) was noted upon air bubbling in solution at rt.<sup>9</sup> Second, very similar catalytic behaviour was found for the phosphine-borane 1 and biaryl-phosphine [Ph<sub>2</sub>P(o-C<sub>6</sub>H<sub>4</sub>)Ar] 3 (Ar = 2,4,6-*i*Pr<sub>3</sub>C<sub>6</sub>H<sub>2</sub>) in Rh-catalyzed hydroformylation of 1-octene.<sup>10</sup> These observations prompted us to further compare these two classes of ligands, and we naturally became interested in Pd-catalyzed cross-couplings, especially in the Suzuki–Miyaura reaction.

Here we report the catalytic evaluation of ligands 1 and 2 in this type of reaction. The influence of Pd precursor, base, temperature, reaction time and ligand/palladium ratio was studied. A catalytically relevant Pd(0) complex derived from 1 was prepared and fully characterized.

We studied the coupling of phenyl boronic acid with the deactivated substrate 4-bromoanisole as a model reaction.<sup>11</sup> The catalytic species was generated *in situ* mixing the appropriate palladium precursor and phosphine ligand, starting with palladium(II) acetate and **1** (catalytic data collected in Table 1). The effect of the base, temperature and reaction time were studied (Table S1, ESI†). Anhydrous potassium phosphate was used as a base at 80 °C for 2 h using a ligand/Pd ratio of 2 (entry 1). Longer reaction time and higher temperature only slightly improved the catalytic activity (up to 86.5% of cross-coupling product, entry 2). When higher phenyl boronic acid/4-bromoanisole ratio was applied, chemoselectivity dramatically decreased, giving in particular benzene as by-product (entry 3).

A ligand 1/Pd ratio of 1 led to a more active system than that observed for 1/Pd = 2 (entry 4 vs. 1), affording up to 87% of the expected product. This suggests that the more active catalytic species probably involves only one phosphine ligand per palladium. Pd(II) organometallic precursors, [PdCl( $\eta^3$ -C<sub>3</sub>H<sub>5</sub>)]<sub>2</sub> and [PdCl<sub>2</sub>(cod)], gave similar reactivity as that observed with palladium acetate (Table S1†). However, [Pd<sub>2</sub>(dba)<sub>3</sub>] led to a less active system (47% conversion after 20 h, Table S1†), probably due to the slow formation of the active Pd species.

The presence of an Ar-BMes<sub>2</sub> moiety in the ligand raises the question of side cross-couplings.<sup>12</sup> With the aim of characterizing the formation of such undesirable products, the catalyst content was increased to 25 mol% (see ESI†). However,



Fig. 1 Phosphine-boranes 1, 2 and biaryl-phosphine 3.

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**Table 1** Suzuki cross-couplings between 4-bromoanisole and phenyl boronic acid catalyzed by Pd/L systems<sup>*a*</sup>



<sup>*a*</sup> Results from duplicate experiments. *Reaction conditions*: 1 mmol 4-bromoanisole; 2 ml toluene;  $K_3PO_4$ /boronic acid/4-bromoanisole = 2.1/1.1/1; 0.01 mmol Pd(OAc)<sub>2</sub> or **1-Pd**; the corresponding amount of **L**. <sup>*b*</sup> Determined by GC analysis; in parentheses, substrate conversion. <sup>*c*</sup> Ph–B(OH)<sub>2</sub>/substrate = 2. <sup>*d*</sup> In square brackets, data after 6 h of reaction.

no trace of the two conceivable cross-coupling products  $Ar-(4-OCH_3-C_6H_4)$  (where  $Ar = Ph_2P(o-C_6H_4)$  or Mes) was detected. Thus, the BMes<sub>2</sub> group of **1** does not compete with Ph-B(OH)<sub>2</sub> in the cross-coupling reaction, probably due to the substantial steric protection induced by the presence of the PPh<sub>2</sub>.

The Pd/1 system was sensitive to the steric hindrance of the reactants. While for the coupling between 4-bromoanisole and 2-methylphenyl boronic acid up to 75% of the corresponding cross-coupling product was achieved, less than 20% of cross-coupling product was obtained using 2,4,6-tris(isopropyl)bromobenzene. Pd/1 also activated the C–Cl bond of 4-chloroanisole, but only giving 27% yield of I (Scheme S1<sup>†</sup>).

Surprinsigly, the basicity of the phosphorus atom of the phosphine-borane ligand did not induce an important effect on the catalytic behaviour (entries 2 and 5). The Pd/PPh<sub>3</sub> catalytic system (entry 6) exhibited a notable lower activity and about similar chemoselectivity relative to Pd/1 and Pd/2. Hence, the dimesityl boron moiety enhances the catalytic activity, conversely to what was found in the Rh-catalyzed hydroformylation of 1-octene.<sup>10</sup>

With the aim to compare the catalytic behaviour of our phosphine-boranes 1 and 2 with the outstanding biarylmonophosphines described by Buchwald's group, the Pd/3 system was tested. This catalytic system was more active than Pd/1 and Pd/2, giving *ca*. 97% of cross-coupling with a nearly complete substrate conversion, and was more chemoselective (entry 7 *vs*. 2 and 5): only *ca*. 3% of by-products were obtained with negligible formation of benzene and anisole. This behaviour points to a higher robustness of Pd/3 than that exhibited by Pd/1 and Pd/2.<sup>13</sup>

To gain more insight into the behaviour of the *ortho*-(dimesitylboryl)phenylphosphines in these catalytic couplings, coordination studies were performed with the aim of characterizing some catalytically relevant Pd(0) species.<sup>14</sup> The stoichiometric reaction of **1** with  $[Pd(nbd)(ma)]^{15}$  (nbd = norborna-1,4-diene, ma = maleic anhydride) gave complex **1-Pd** as an orange powder

in 86% yield after 1 h at 65 °C in THF (Scheme 1). NMR spectroscopic data and elemental analysis are consistent with the general formula [Pd(1)(ma)]. At 298 K, two <sup>31</sup>P NMR signals in a 4:5 ratio were observed at 31.1 and 26.6 ppm, respectively. The coexistence of two isomers was corroborated by the coalescence of the two signals upon heating at 75 °C. <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy confirmed the presence of two very similar species and revealed the absence of any symmetry in both. In particular, two sets of signals were observed for the ma coligand of each isomer. In addition, mesityl groups give four sets of signals for each isomer, indicating that the two Mes rings are inequivalent and rotation around B-Cinso bonds is hindered. Most noticeably, one of the NMR signals associated to quaternary carbon atoms of the Mes ring is shifted upfield to a significant extent ( $\delta = 104.66$  and 107.67 ppm for the two isomers), while the other carbon atoms resonate at  $\delta > 125$  ppm. Such a feature is typically observed upon  $\pi$ -coordination of arene rings to transition metals.<sup>16</sup> The <sup>11</sup>B NMR signal at 69.4 ppm is close to that of the free ligand (75.0 ppm),<sup>17</sup> suggesting the retention of a tricoordinate environment around boron.

To get more insight into the precise structure of 1-Pd, an X-ray diffraction study was carried out (Scheme 1). Complex 1-Pd was found to adopt a monomeric structure with a tricoordinate Pd centre. The ma co-ligand is  $\eta^2$ -coordinated. More striking is the bidentate coordination of the phosphineborane through the phosphorus atom and one of the mesityl rings at boron. The Pd centre establishes close contacts with the  $C_{ipso}$  carbon atom [2.292 Å] and one of the  $C_{ortho}$  carbon atoms [2.590 Å], while the other carbon atoms lie at >2.9 Å. The geometry of the Mes ring is almost unchanged upon  $\pi$ -coordination: the involved C<sub>ipso</sub>-C<sub>ortho</sub> bond is not elongated and both C atoms remain in planar environments. The two isomers observed by NMR in solution most likely result from the relative orientation of the facing ma and BMes<sub>2</sub> groups. Despite the coordination of the Mes ring, the B atom does not participate in the coordination. The Pd–B distance (2.898 A) is rather long and the 2p(B) orbital does not point toward the Pd centre, precluding  $Pd \rightarrow B$  back-donation. Consistently, the B atom does not deviate from planarity. Overall, the BMes<sub>2</sub> group of 1 adopts  $\eta^2$ -C-C coordination to Pd, and thereby stabilizes the 14-electron [(phosphine)Pd(ma)] fragment. Such weak Pd-arene coordinations have been occasionally evidenced with biaryl-phosphines,<sup>18</sup> and they are likely to play a critical role in the unique behaviour of these ligands in Pd-catalvzed cross-coupling reactions.<sup>6</sup> The bonding situation observed in



Scheme 1 Synthesis and crystal structure of 1-Pd (ellipsoids drawn at 50% probability; hydrogen atoms omitted for clarity). Selected bond lengths (Å): P2–Pd1 2.2901(11), Pd1–C31 2.292(4), Pd1–C32 2.590(4), C53–C54 1.406(6).

complex **1-Pd** suggests that some structural analogy can be drawn between the phosphine-borane **1** and biaryl-phosphines. It also provides evidence for a new coordination mode of phosphine-arylboranes. Thus far, arene coordination was found to systematically support  $M \rightarrow B$  interactions (M = Rh, Pd, Pt, Cu) resulting in multi-centre  $\eta^2$ -BC or  $\eta^3$ -BCC coordinations.<sup>19</sup>

To verify that complex **1-Pd** can be involved in the catalytic process, it was evaluated in the model reaction chosen for the Suzuki–Miyaura coupling (entry 8). The cross-coupling product was obtained in 82% yield. This gives support to the contribution of weak  $\pi$ -arene coordination to stabilize catalytic species deriving from *ortho*-(dimesitylboryl)phenylphosphines, similarly to that envisioned with biaryl-phosphines.

In conclusion, ligands **1** and **2** were successfully applied in Pd-catalyzed Suzuki–Miyaura C–C couplings. The presence of the BMes<sub>2</sub> moiety in *ortho* position to phosphorus is compatible with the cross-coupling process and actually improves the catalytic activity. This activity enhancement compared to the Pd/PPh<sub>3</sub> system is likely attributed to the ability of the mesityl group linked to boron to engage into a weak  $\pi$ -coordination to the metal centre, as shown by the X-ray diffraction analysis of **1-Pd**. These results as a whole further substantiate some analogy between *o*-(dimesitylboryl)phenylphosphines and biaryl-monophosphines<sup>20</sup> and thereby open interesting perspectives for phosphine-borane ligands in catalysis.<sup>21</sup>

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