

# Catalytic activity of $\eta^2$ -(olefin)palladium(0) complexes with iminophosphine ligands in the Suzuki–Miyaura reaction. Role of the olefin in the catalyst stabilization

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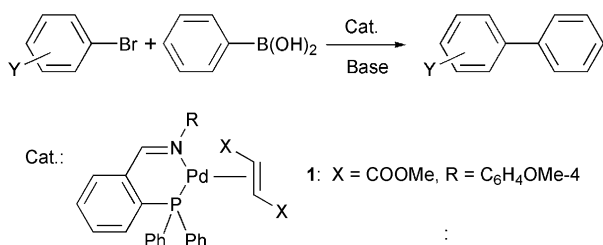
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**Abstract**—The catalytic activity of  $\eta^2$ -(olefin)palladium(0)(iminophosphine) complexes in the Suzuki–Miyaura coupling is strongly dependent on the reaction conditions and on the nature of the ligands. The reaction is at the best carried out in aromatic solvents in the presence of  $K_2CO_3$  at 90–110 °C. Higher reaction rates are obtained when the R substituent on the *N*-imino group is an aromatic group of low steric hindrance and the olefin is a moderate  $\pi$ -accepting ligand such as dimethyl fumarate. At temperatures lower than 90 °C, a self-catalyzed process leading to catalyst deactivation becomes predominant. Preliminary mechanistic investigations indicate that the oxidative addition of the aryl bromide to a Pd(0) species is the rate determining step in the catalytic cycle and that the olefin plays a key role in catalyst stabilization. Systems in situ prepared by mixing  $Pd(OAc)_2$  or  $Pd(dba)_2$  with 1 equiv of iminophosphine appear substantially less active than the preformed catalysts.

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## 1. Introduction

The Suzuki–Miyaura reaction (Scheme 1) is one of the most powerful and versatile synthetic methods for the formation of carbon–carbon bonds.<sup>1</sup> In particular, this reaction is finding increasing application in the synthesis of biaryls,<sup>1,2</sup> which are key intermediates in fine chemistry (pharmaceuticals, agrochemicals) as well as in advanced material chemistry (dendrimers, polymers and nanostructured materials).



Scheme 1.

**Keywords:** Suzuki–Miyaura reaction; Iminophosphine complexes; Palladium; Arylboronic acids; Biaryls; Cross-coupling.

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Recently, we have reported that iminophosphine–palladium(0) complexes of type **1** (Scheme 1) catalyze the coupling of aryl bromides with boronic acids with high efficiency allowing to obtain turnover numbers of up to  $10^5 h^{-1}$  (turnover number: mol of substrate converted/mol of catalyst).<sup>3</sup> Among the most interesting features of these catalysts, is to mention: (i) the relative insensitivity to the presence of deactivating groups on the aryl bromide, (ii) the almost complete conversion attainable with a wide variety of substrates upon a suitable choice of the reaction conditions and (iii) the good stability under aerobic conditions.<sup>3</sup>

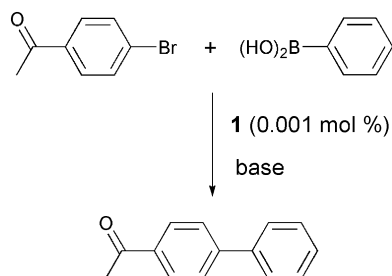
These results prompted us to investigate more deeply the catalytic activity of complexes of type **1** in order to optimize the reaction conditions and understand the factors, which control the catalytic activity. In particular, we thought it interesting to study the effects brought about by the nature of the imino substituent and of the olefin. Furthermore, we have checked if a comparable catalytic efficiency can be obtained using catalysts prepared in situ by reacting some palladium(0) catalyst precursors with an iminophosphine.

## 2. Results and discussion

A wide variety of solvents and bases are commonly used in

the Suzuki coupling. Inspection of the literature reveals that there is not a set rule and that each catalyst needs a specific solvent and a certain base to attain the highest efficiency.

The coupling of 4-bromoacetophenone with phenylboronic acid (Scheme 2) was used as the model reaction in order to highlight the influence of the solvent and of the base on the catalytic activity. The relevant results are reported in Tables 1 and 2, respectively. The reaction appears to be quite sensitive to the nature of the solvent. In general, in solvents of moderate or low polarity such as aromatic hydrocarbons or even alkanes (entries 1–4) the reaction proceeds faster, the highest rate being observed in toluene at 110 °C.



Scheme 2.

Table 1. Influence of the solvent<sup>a</sup>

Entry	Solvent	T (°C)	Yield (%) <sup>b</sup>	TON <sup>c</sup> (×10 <sup>-3</sup> )
1	Toluene	110	82	164
2	<i>n</i> -Dodecane	110	30	60
3	<i>n</i> -Tetradecane	110	25	50
4	1,3,5-Trimethylbenzene	110	20	11
5	<i>N</i> -Methylpiperidone	110	0	0
6	<i>N,N</i> -Dimethylformamide	110	10	20
7	Dimethyl sulfoxide	110	0	0
8	<i>N,N</i> -Dimethylacetamide	110	30	60
9	<i>o</i> -Xylene	140	70	140
10	<i>m</i> -Xylene	140	56	112
11	<i>p</i> -Xylene	140	45	90
12	<i>o</i> -Dichlorobenzene	140	56	112
13	1,2-Dimethoxyethane	140	9	18

<sup>a</sup> Reaction conditions. Solvent: 12 mL; *t*: 2 h; catalyst: complex **1** (2 × 10<sup>-5</sup> mmol); 4-bromoacetophenone: 4.0 mmol; phenylboronic acid: 6.0 mmol; base: K<sub>2</sub>CO<sub>3</sub> (8.0 mmol); [ArBr]/[**1**] = 200,000; [acid]/[ArBr] = 1.5; base/ArBr = 2.0 (mol/mol).

<sup>b</sup> GLC with *n*-undecane as internal standard.

<sup>c</sup> Mol of substrate converted/mol of catalyst.

Table 2. Influence of the base<sup>a</sup>

Entry	Base	pK <sub>a</sub> <sup>b</sup>	Yield (%) <sup>c</sup>
1	CH <sub>3</sub> COONa	4.76	3
2	Piperidine	11.1	0
3	Na <sub>2</sub> CO <sub>3</sub>	10.3	26
4	K <sub>2</sub> CO <sub>3</sub>	10.3	30
5	Cs <sub>2</sub> CO <sub>3</sub>	10.3	17
6	K <sub>3</sub> PO <sub>4</sub>	12.3	12

<sup>a</sup> Reaction conditions. Solvent: *N,N*-dimethylacetamide (12 mL); *T*: 110 °C; *t*: 2 h; catalyst: complex **1** (2 × 10<sup>-5</sup> mmol); 4-bromoacetophenone: 4.0 mmol; phenylboronic acid: 6.0 mmol; [ArBr]/[**1**] = 200,000; [acid]/[ArBr] = 1.5; base/ArBr = 2.0 (mol/mol).

<sup>b</sup> The values refer to dilute aqueous solutions, data from Ref. 5.

<sup>c</sup> GLC with *n*-undecane as internal standard.

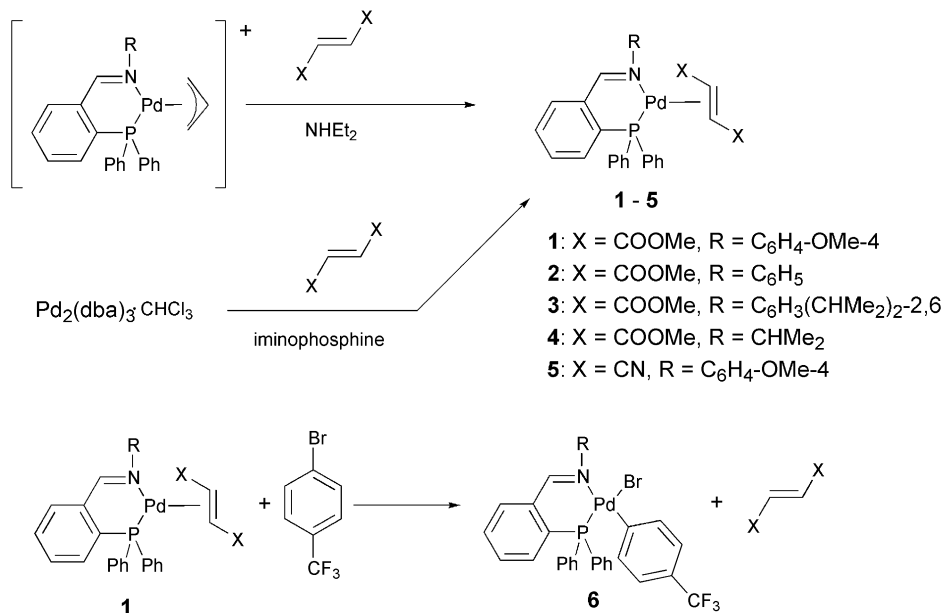
In highly polar solvents the catalytic activity is lower, possibly owing to the coordinating properties of these solvents. Toluene appears superior to other more substituted aromatics as demonstrated by the low activity of 1,3,5-trimethylbenzene (entry 4) and xylenes even at higher temperatures (entries 9–11). It is interesting to observe that since the catalyst is not able to promote the coupling of aryl chlorides with boronic acids<sup>3</sup> it is possible to carry out the reaction in *o*-dichlorobenzene at 140 °C with fairly good yields.

As far as the nature of the base is concerned, it is generally accepted that the use of stronger bases leads to higher yields in the Suzuki coupling.<sup>4</sup> The data obtained using complex **1** in *N,N*-dimethylacetamide in the presence of some different bases are reported in Table 2. The experiments do not reveal a plain connection between the catalytic activity and the strength of the base. Indeed, in the presence of organic bases such as the weak base sodium acetate or the stronger base piperidine, the reaction proceeds sluggishly. This behavior is likely due to the coordinating properties of these bases, which may compete with the substrates for the coordination to the metal center. The use of inorganic bases such as carbonates or phosphates allows to obtain much higher reaction rates, but still there is not a plain relationship between the base strength and the catalytic activity, since the best activity is achieved employing the lesser basic carbonates. In this connection, it is worth noting that the best reaction rates are obtained using the inexpensive sodium or potassium carbonates.

As a further step of our investigations we have studied the influence brought about by the R substituent on the iminophosphine and by the olefin coordinated to palladium. To this purpose, we have examined the catalytic activities of the iminophosphine–palladium complexes **1–6** (Scheme 3).

Complexes **1–5** were prepared either by reacting the corresponding cationic η<sup>3</sup>-(allyl) complexes with diethylamine in the presence of the appropriate olefin<sup>6</sup> or by reacting Pd(dba)<sub>3</sub>CHCl<sub>3</sub> (dba = dibenzylideneacetone) with the appropriate iminophosphine and olefin.<sup>7</sup> Complex **6** was synthesized by reacting **1** with 4-(trifluoromethyl)bromobenzene as described in Section 4. The coordination geometry of **6** with the aryl ligand trans to the imino nitrogen is based on trans influence considerations, the aryl group and the phosphorus atom being the strongest donors,<sup>8</sup> and X-ray structural analyzes of related complexes [PdI(Ph)(P–N)] (P–N = iminophosphine).<sup>9</sup>

The data of entries 1–5 in Table 3 show that the highest reaction rates are observed when R is an aromatic group of low steric requirements, such as C<sub>6</sub>H<sub>4</sub>OMe-4 or C<sub>6</sub>H<sub>5</sub>. The catalytic activity decreases considerably when R is the more sterically demanding C<sub>6</sub>H<sub>3</sub>(CHMe<sub>2</sub>)<sub>2</sub>-2,6 group (complex **3**, entry 3), and even more when R is an electron-donating substituent such as the isopropyl group (complex **4**, entry 4). The catalytic activity is also influenced by the π-accepting properties of the η<sup>2</sup>-bound olefin, as indicated by the significant drop in the reaction rate on going from the dimethyl fumarate complex **1** to the analogous complex **5** containing the much stronger π-accepting olefin



Scheme 3.

Table 3. Influence of the catalyst structure<sup>a</sup>

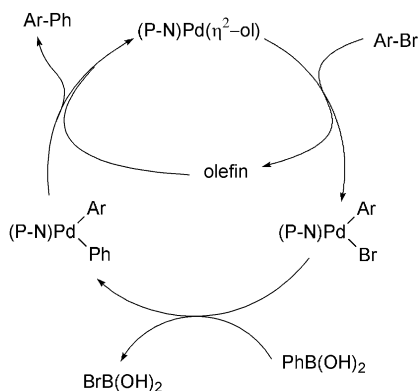
Entry	Catalyst	Yield (%) <sup>b</sup>
1	<b>1</b>	82
2	<b>2</b>	78
3	<b>3</b>	33
4	<b>4</b>	11
5	<b>5</b>	54
6	<b>6</b>	17

<sup>a</sup> Reaction conditions. Solvent: toluene (12 mL); T: 110 °C; t: 2 h; catalyst: complex **1** ( $2 \times 10^{-5}$  mmol); 4-bromoacetophenone: 4.0 mmol; phenylboronic acid: 6.0 mmol; base: K<sub>2</sub>CO<sub>3</sub> (8.0 mmol); [ArBr]/[**1**] = 200,000; [acid]/[ArBr] = 1.5; base/ArBr = 2.0 (mol/mol).

<sup>b</sup> GLC with *n*-undecane as internal standard.

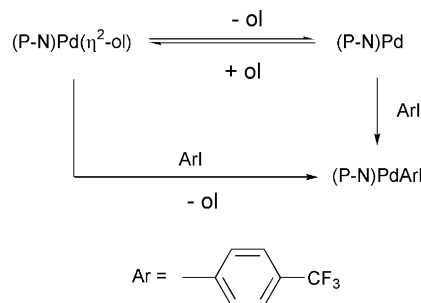
fumaronitrile. Similar effects are seen in Pd(dba)<sub>n</sub> complexes described by Fairlamb and co-workers.<sup>10</sup>

The commonly accepted mechanism for the Suzuki reaction involves the initial oxidative addition of the aryl halide to a zerovalent palladium species, followed by transmetalation and reductive elimination to give the coupling product and restore the catalytically active palladium(0) species (Scheme 4).<sup>11</sup>



Scheme 4.

A mechanistic study on the single steps of the catalytic cycle is currently in progress.<sup>12</sup> Preliminary results indicate that (i) with the complexes **1–5** the rate-determining step of the catalytic cycle is the oxidative addition of the aryl bromide and that (ii) the rate of the oxidative addition of 4-(trifluoromethyl)bromobenzene to complexes **1–5** decreases in the order **1** ≈ **2** > **3** > **4** ≫ **5**. This reactivity order closely parallels that found for the oxidative addition of 4-(trifluoromethyl)iodobenzene to complexes **1**, **4**, and **5** for which the observed reaction rates decrease in the order **1** > **4** ≫ **5**.<sup>7</sup> The two parallel pathways depicted in Scheme 5 are operative and the much lower reactivity of complex **5** is explained on the basis of the greater π-accepting properties of fumaronitrile, which (i) increase the strength of the palladium–olefin bond thus lowering the concentration of the highly reactive (P–N)Pd species and (ii) reduce the electron density on the metal making the (P–N)Pd(η<sup>2</sup>-ol) complex less susceptible of oxidative addition by the aryl halide.



Scheme 5.

However, at the light of the reactivity order **1** ≈ **2** > **3** > **4** > **5** found for the oxidative addition of 4-(trifluoromethyl)bromobenzene to complexes **1–5**, the fairly good catalytic activity of complex **5** is somewhat outstanding, as it appears from the data of Table 3, which show the catalytic activity to be decreasing in the order **1** ≈ **2** > **5** > **3** > **4**.

To further explore the role played by the olefin coordinated to the metal center we have carried out some experiments using complex **6** as the catalyst. Indeed, we deemed it interesting to evaluate the catalytic efficiency of this Pd(II) species since being the product of the oxidative addition of 4-(trifluoromethyl)bromobenzene to **1** it is one of the key intermediates of the catalytic cycle. In absence of any olefin, its catalytic activity should be that of a ‘naked’ (P–N)Pd fragment and, hence, comparable if not superior to that of **1**. Unpredictably, the experiments reveal that **6** is much less active than both **1** and **5**.

The observation that during the synthesis of complex **6** we detected the formation of significant amounts of metallic palladium helps to rationalize this result, suggesting that the low product yield observed using **6** should be attributed to a short life of the catalytic species rather than to an intrinsic low activity.

From these findings it emerges that the olefin has an important role in catalysis as its presence contributes to stabilize the catalytically active species. Accordingly, the fairly good activity of **5** is better interpreted in terms of a greater stabilization of the (P–N)Pd fragment by the strongly  $\pi$ -accepting fumaronitrile ligand. Such stabilizing effect is substantiated by the observation that when a toluene solution of **1** is heated at 90 °C in the presence of phenylboronic acid and  $K_2CO_3$  (**1**/PhB(OH)<sub>2</sub>/ $K_2CO_3$  molar ratio = 1:10:15) extensive decomposition to metallic palladium is detected. Under the same experimental conditions, a slight decomposition occurs also for complex **5**, but at a much lower rate.

Catalyst deactivation has been previously noticed in the Suzuki coupling by several authors and, in particular, Bedford has pointed out the importance of the catalyst longevity in order to achieve high substrate conversions and product yields.<sup>4,13</sup>

The occurrence of catalyst deactivation is further supported by the issues of the studies of the temperature influence on the catalysis.

The use of mild reaction conditions is essential with substrates bearing thermally unstable functional groups, and therefore the development of systems active at low temperatures is of great relevance. Accordingly, we have investigated the influence of the temperature on the catalytic activity of complex **1**. The relevant data (Table 4) show that

on lowering the temperature to 90 °C the rate of the model reaction is approximately halved so that using an aryl bromide/catalyst molar ratio of 80,000:1 only a 55% conversion is obtained after 2 h. In order to obtain an almost quantitative yield in 2 h it is necessary to double the amount of the catalyst employed.

When the reaction temperature is further decreased to 70 °C, a lower, but still good catalyst activity is observed (25% substrate conversion after 2 h, entry 4 of Table 4). However, when the reaction time is increased up to 24 h, the product yield increases only to 27% (entry 5 of Table 4), indicating that after 2 h at this temperature the catalyst loses its activity.

Catalyst deactivation is commonly accompanied by the formation of metallic palladium.<sup>4,13</sup> During our experiments we did not observe the formation of palladium black; however, this can be ascribed either to the use of a minute amount of complex **1** in the presence of a huge amount of potassium carbonate or to the formation of colloidal palladium, which may be hardly visible to the naked eye. In this connection, it is to remind that in the synthesis of complex **6** a significant amount of metallic palladium is also formed.

In order to increase the product yield, some reactions at increasing catalyst concentrations were carried out. A series of isochronous experiments at 70 °C reveals that the substrate conversion does not increase linearly with the amount of the employed catalyst (entries 4, 6–8, Table 4). On the contrary, by taking into account the turnover numbers it appears that the catalyst efficiency decreases with increasing its concentration. Summing up, the experiments at low temperature reveal that (i) under 90 °C catalyst deactivation becomes much more significant, and (ii) that its rate increases with increasing the catalyst concentration, that is, the deactivation process is self-catalyzed.

Also these findings can be explained by taking into account the stability of the coordinatively unsaturated and highly reactive (P–N)Pd fragment, which forms in the reductive elimination step at the end of the catalytic cycle. To enter a new catalytic cycle the (P–N)Pd fragment must add an aryl bromide molecule. This productive process is in competition with a second one, which leads to the formation of metallic palladium particles inactive in catalysis (Scheme 6).

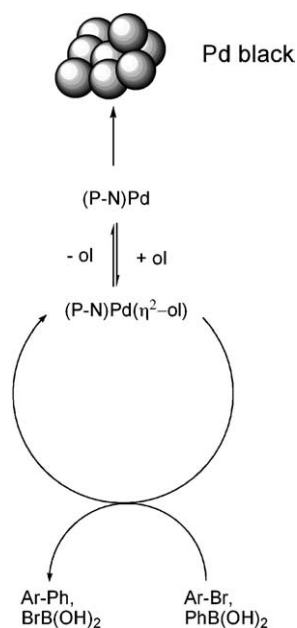
**Table 4.** Influence of the temperature and of the catalyst concentration<sup>a</sup>

Entry	<i>T</i> (°C)	<b>1</b> (mmol)	[ArBr]/[ <b>1</b> ]	<i>t</i> (h)	Yield (%) <sup>b</sup>	TON <sup>c</sup>
1	110	$5 \times 10^{-5}$	80,000	2	99	80,000
2	90	$5 \times 10^{-5}$	80,000	2	55	44,000
3	90	$1 \times 10^{-4}$	40,000	2	96	38,400
4	70	$5 \times 10^{-5}$	80,000	2	25	20,000
5	70	$5 \times 10^{-5}$	80,000	24	27	21,600
6	70	$1 \times 10^{-4}$	40,000	2	40	16,000
7	70	$2 \times 10^{-4}$	20,000	2	51	10,000
8	70	$4 \times 10^{-4}$	10,000	2	57	5,700

<sup>a</sup> Reaction conditions. Solvent: toluene (12 mL); ArBr: 4-bromoacetophenone (4.0 mmol); base:  $K_2CO_3$  (8.0 mmol); phenylboronic acid: 6.0 mmol; [acid]/[ArBr] = 1.5; base/ArBr = 2.0 (mol/mol).

<sup>b</sup> GLC with *n*-undecane as internal standard.

<sup>c</sup> Mol of substrate converted/mol of catalyst.



Scheme 6.

When the oxidative addition is too slow owing to the low reaction temperature, or when at high catalyst loadings the palladium metal forming process is very fast owing to its self-catalytic nature, the formation of metallic palladium becomes the predominant process leading to the removal of all the active species from the catalytic cycle.

During our investigation on the catalytic activity of iminophosphine palladium(0) complexes of the type **1** in the Stille reaction, we observed that the activity of these species can be further enhanced by the addition of 1 equiv of free iminophosphine.<sup>14</sup> Moreover, it was found that a comparable catalytic efficiency can be obtained by in situ combining Pd(OAc)<sub>2</sub> or Pd(dba)<sub>2</sub> (dba = dibenzylideneacetone) with 2 equiv of iminophosphine. Therefore, we have investigated if also in Suzuki reaction it is possible to employ such in situ systems instead of the preformed catalysts of the type **1**. At first, in order to determine the

optimal Pd/imino-phosphine ratio we studied the activity of the system obtained by mixing complex **1** with an equivalent of free ligand in the coupling of 4-bromoacetophenone with phenylboronic acid. The experiment shows that the addition of 1 equiv of the free P–N ligand to complex **1** has almost no effect on the reaction rate (compare entries 1 and 2 of Table 5). This result is confirmed by the observation that the oxidative addition of an excess of BrC<sub>6</sub>H<sub>4</sub>CF<sub>3</sub>-4 to the complex **1** or to an equimolar mixture **1**/iminophosphine proceeds at comparable rate in toluene at 90 °C, with a BrC<sub>6</sub>H<sub>4</sub>CF<sub>3</sub>-4/**1** molar ratio of 10:1. As indicated by the IR spectra at different times, the reaction goes to completion in about 15 min in both cases.

This result contrasts with what we found for complex **1** in the Stille reaction where the addition of 1 equiv of free iminophosphine to complex **1** leads to an approximate doubling of the reaction rate. Possibly, the different behavior is to be attributed to the quite different experimental conditions (solvent, temperature, substrate/catalyst molar ratio) employed in the two reactions. Consequently, we extended our investigation to the systems Pd(OAc)<sub>2</sub>/P–N and Pd(dba)<sub>2</sub>/P–N (P–N = 2-(PPh<sub>2</sub>)C<sub>6</sub>H<sub>4</sub>-1-CH=NC<sub>6</sub>H<sub>4</sub>OMe-4) with a Pd/P–N molar ratio of 1:1.

The activity of the catalyst prepared by combining Pd(OAc)<sub>2</sub> with 1 equiv of iminophosphine turns out to be much lower than that of complex **1** (entries 3 and 1 of Table 5). Moreover, almost the same catalytic activity is obtained when Pd(OAc)<sub>2</sub> is combined with 2 equiv of iminophosphine, thus confirming that the presence of a second P–N ligand has no effect on the catalytic system (compare entries 3 and 4 of Table 5). On the other hand, the system obtained by combining Pd(dba)<sub>2</sub> with one iminophosphine ligand appears significantly more active than the analogous one prepared using Pd(OAc)<sub>2</sub> (entries 5 and 3 of Table 5) although somewhat less efficient than complex **1**. In keeping with what found with complex **1** and Pd(OAc)<sub>2</sub>, the addition of a second iminophosphine ligand does not change the catalytic activity. It is also interesting to note that the reactivity of the system

Table 5. Comparison of the catalytic activity of **1** with some in situ catalysts<sup>a</sup>

Entry	Catalyst	Aryl bromide	Equivalents of added ligand <sup>b</sup>	Total P/Pd ratio	Yield (%) <sup>c</sup>
1	Complex <b>1</b>	4-CH <sub>3</sub> COC <sub>6</sub> H <sub>4</sub> Br	—	1:1	82
2	Complex <b>1</b>	4-CH <sub>3</sub> COC <sub>6</sub> H <sub>4</sub> Br	1	2:1	84
3	Pd(OAc) <sub>2</sub>	4-CH <sub>3</sub> COC <sub>6</sub> H <sub>4</sub> Br	1	1:1	20
4	Pd(OAc) <sub>2</sub>	4-CH <sub>3</sub> COC <sub>6</sub> H <sub>4</sub> Br	2	2:1	17
5	Pd(dba) <sub>2</sub>	4-CH <sub>3</sub> COC <sub>6</sub> H <sub>4</sub> Br	1	1:1	52
6	Pd(dba) <sub>2</sub>	4-CH <sub>3</sub> COC <sub>6</sub> H <sub>4</sub> Br	2	2:1	53
7	Complex <b>1</b>	4-CF <sub>3</sub> C <sub>6</sub> H <sub>4</sub> Br	—	1:1	95
8	Pd(OAc) <sub>2</sub>	4-CF <sub>3</sub> C <sub>6</sub> H <sub>4</sub> Br	1	1:1	42
9	Pd(dba) <sub>2</sub>	4-CF <sub>3</sub> C <sub>6</sub> H <sub>4</sub> Br	1	1:1	50
10	Complex <b>1</b>	C <sub>6</sub> H <sub>5</sub> Br	—	1:1	80
11	Pd(OAc) <sub>2</sub>	C <sub>6</sub> H <sub>5</sub> Br	1	1:1	18
12	Pd(dba) <sub>2</sub>	C <sub>6</sub> H <sub>5</sub> Br	1	1:1	27
13	Complex <b>1</b>	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> Br	—	1:1	68
14	Pd(OAc) <sub>2</sub>	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> Br	1	1:1	22
15	Pd(dba) <sub>2</sub>	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> Br	1	1:1	28

<sup>a</sup> Reaction conditions. Solvent: toluene (12 mL); *T*: 110 °C; *t*: 2 h; catalyst: complex **1** (2 × 10<sup>-5</sup> mmol); aryl bromide: 4.0 mmol; phenylboronic acid: 6.0 mmol; base: K<sub>2</sub>CO<sub>3</sub> (8.0 mmol); [ArBr]/[Pd] = 200,000; [acid]/[ArBr] = 1.5; base/ArBr = 2.0 (mol/mol).

<sup>b</sup> Ligand = 2-(PPh<sub>2</sub>)C<sub>6</sub>H<sub>4</sub>-1-CH=NC<sub>6</sub>H<sub>4</sub>OMe-4.

<sup>c</sup> GLC with *n*-undecane as internal standard.

Pd(dba)<sub>2</sub>/iminophosphine is very close to that displayed by complex **5** (compare entry 5 of Table 3 with entry 5 of Table 5).

This quite remarkable reactivity pattern is not due to the particular substrate used in these reactions as shown by the experiments carried out with other activated or deactivated aryl bromides (see Table 5).

These investigations confirm the important role played by the olefin in stabilizing the Pd(P–N) fragment, which forms in the last step of the catalytic cycle. In fact, the data of Table 5 show a catalytic activity decreasing in the order **1** > Pd(dba)<sub>2</sub>/P–N > Pd(OAc)<sub>2</sub>/P–N, which can be rationalized on the basis of the following considerations. When no olefin is present, as in the case of the system Pd(OAc)<sub>2</sub>/P–N, the lack of stabilization brings about a lower catalytic activity due to decomposition of the Pd(P–N) fragment to inactive palladium metal particles. In this connection, it is worth noting that the activity of the system Pd(OAc)<sub>2</sub>/P–N is quite close to that of complex **6** under the same experimental conditions (compare entry 3 of Table 5 with entry 6 of Table 3). The activity increases moderately for the Pd(dba)<sub>2</sub>/P–N system due to the presence of dibenzylideneacetone, which is an olefin of moderate  $\pi$ -accepting ability, and much more for the complex **1** due to the better  $\pi$ -accepting properties of dimethyl fumarate.<sup>15</sup>

### 3. Conclusive remarks

Our investigations indicate that the catalyst activity is significantly affected by its composition and the reaction conditions. In particular, it emerges that a key role is played by the olefin bound to palladium in order to assure a long life to the catalytically active species. This appears of primary importance because the Suzuki–Miyaura reaction is currently used as a key step in the synthesis of valuable fine chemicals. While the here reported catalytic and preliminary mechanistic studies suggest that the commonly accepted catalytic cycle is operative and that oxidative addition of the aryl bromide to a palladium(0) species is the rate determining step, some peculiar effects such as that of the nature of the base and of the solvent deserve further mechanistic investigations, which are currently in progress.

## 4. Experimental

### 4.1. General methods

All reactions, unless otherwise stated, were carried out under an inert atmosphere (argon). Commercial solvents (Aldrich or Fluka) were purified before the use according to standard procedures.<sup>16</sup> Bromobenzene, 4-bromoanisole, 1-bromo-4-trifluoromethylbenzene, and piperidine (Aldrich) were distilled before the use. 4-Bromoacetophenone (Aldrich) was recrystallized from methanol.<sup>16</sup> Anhydrous sodium acetate, anhydrous potassium carbonate, anhydrous sodium carbonate, and cesium carbonate (p.a.) were obtained from Aldrich. Complexes **1–5** were prepared

as described in the literature.<sup>6,7</sup> The coupling products were identified by their GC–MS and <sup>1</sup>H NMR spectra. GLC analyzes were performed on a Agilent 6850 gas chromatograph; GC–MS analyzes were performed on a HP 5890 series II gas chromatograph interfaced to a HP 5971 quadrupole mass-detector. <sup>1</sup>H and <sup>31</sup>P NMR spectra were registered on a Bruker Avance 300 NMR spectrometer operating at 300.11 and 121.49 MHz, respectively. The IR spectra were recorded on a Perkin-Elmer 983G spectrophotometer using KBr cells.

### 4.2. Catalytic experiments

The coupling reactions were carried out in a magnetically stirred glass reactor (50 mL) having an inert gas inlet and a side arm closed with a rubber septum for the withdrawing of GLC samples. In a typical experiment (entry 1 of Table 1), the reactor was charged with 4-bromoacetophenone (0.80 g, 4.0 mmol), phenylboronic acid (0.73 g, 6.0 mmol), K<sub>2</sub>CO<sub>3</sub> (1.10 g, 8.0 mmol), complex **1** (0.013 mg, 2.0 × 10<sup>−5</sup> mmol) and 12 mL of toluene (freshly distilled from sodium/benzophenone). The mixture was heated under stirring at 110 °C for 2 h and then cooled to rt. After filtration on Celite the raw reaction mixture was analyzed by GLC using *n*-undecane as internal standard.

**4.2.1. [PdBr(C<sub>6</sub>H<sub>4</sub>CF<sub>3</sub>-4)(2-(PPh<sub>2</sub>)C<sub>6</sub>H<sub>4</sub>-1-CH=NC<sub>6</sub>H<sub>4</sub>-OMe-4)] (**6**).** Complex **1** (0.646 g, 1 mmol) and 4-(trifluoromethyl)bromobenzene (2.55 g, 10 mmol) were dissolved in dry toluene (40 mL). The mixture was heated at 110 °C (5 min) under N<sub>2</sub> atmosphere. Despite the short reaction time, some decomposition to metallic palladium took place. The solvent was then removed at reduced pressure, and the solid residue was extracted with CH<sub>2</sub>Cl<sub>2</sub>. After addition of charcoal and filtration, the resulting clear solution was evaporated to ca. 3 mL and diluted with Et<sub>2</sub>O to precipitate a yellow solid. Recrystallization from CH<sub>2</sub>Cl<sub>2</sub>/Et<sub>2</sub>O afforded analytically pure complex **6** (0.480 g, 66% yield); Analytical data: found: C 52.54, H 3.96, N 2.11%. C<sub>33</sub>H<sub>26</sub>F<sub>3</sub>BrNOPPd requires C 52.74, H 3.66, N 2.20%; IR (Nujol):  $\nu$ (C=N) at 1611 cm<sup>−1</sup> *m*. <sup>1</sup>H NMR (CDCl<sub>3</sub>,  $\delta$ ): 8.21 (1H, s, N=CH), 7.80–7.26 (18H, m, aryl protons), 6.96–6.81 (4H, m, *m*-H of C<sub>6</sub>H<sub>4</sub>CF<sub>3</sub>-4 and C<sub>6</sub>H<sub>4</sub>OMe-4), 3.83 (3H, s, OCH<sub>3</sub>); <sup>31</sup>P NMR (CDCl<sub>3</sub>): 28.3 (s).

### 4.3. Studies of the oxidative addition reaction

The reactions of 4-(trifluoromethyl)bromobenzene with complexes **1–5** were carried out in dry toluene at 90 °C under a N<sub>2</sub> atmosphere. The initial complex concentration was 1 × 10<sup>−2</sup> mol/L and the aryl bromide/complex molar ratio was 10:1; in the experiments carried out in the presence of added iminophosphine, the same initial complex concentration was used and the aryl bromide/iminophosphine/complex molar ratios were 10:1:1. The course of the reaction was monitored by IR spectroscopy of the reacting mixtures either following the intensity of the  $\nu$ (C=O) band at 1725 cm<sup>−1</sup> relevant to free dimethyl fumarate (reactions of the complexes **1–4**), or the intensity of the  $\nu$ (C≡N) band at 2204 cm<sup>−1</sup> (reaction of complex **5**).

## References and notes

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