

# Palladium bis(phosphinite) 'PCP'-pincer complexes and their application as catalysts in the Suzuki reaction

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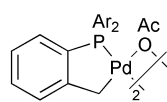
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Received (in Montpellier, France) 14th June 2000, Accepted 4th August 2000

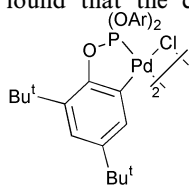
First published as an Advance Article on the web 15th September 2000

**Palladium complexes of inexpensive, easily synthesised bis(phosphinite) 'PCP'-pincer ligands show good activity in the Suzuki coupling of deactivated and sterically hindered aryl bromides.**

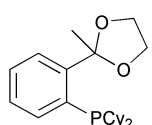
Palladium catalysed Suzuki coupling reactions (Scheme 1) generally require fairly high catalyst concentrations, limiting their attractiveness to large-scale commercial applications. This is due to technical problems and costs associated with removal of the spent palladium from the products. Consequently, there has recently been an interest in developing high-activity catalysts that can be used in very low concentrations. Beller and co-workers reported the use of the palladacyclic complex **1**,<sup>1</sup> formed by the metallation of tri(2-tolyl) phosphine, as an efficient catalyst for the Suzuki reaction.<sup>2</sup> We recently investigated the possibility of using related palladated triarylphosphite complexes and found that the complex **2**



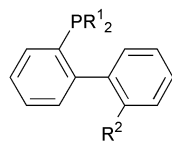
**1:** Ar = 2-MeC<sub>6</sub>H<sub>4</sub>



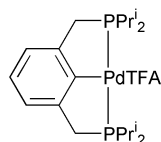
**2:** Ar = 2,4-Bu<sup>t</sup><sub>2</sub>C<sub>6</sub>H<sub>3</sub>



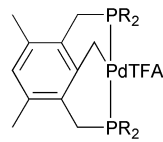
**3**



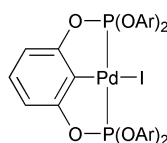
**4:** R<sup>1</sup> = Cy, Bu<sup>t</sup>;  
R<sup>2</sup> = H, Me, Pr<sup>i</sup>, NMe<sub>2</sub>



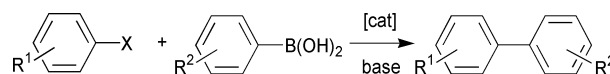
**5a**



**5b:** R = Pr<sup>i</sup>, Bu<sup>t</sup>



**6:** Ar = 4-MeOC<sub>6</sub>H<sub>4</sub>



Scheme 1 The Suzuki biaryl coupling reaction

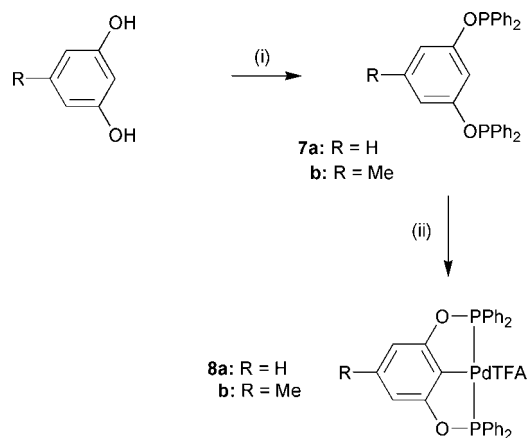
shows extremely high activity with both electronically activated and deactivated aryl bromides—considerably higher than the activity reported for **1**.<sup>3</sup>

Since then Fu and coworkers,<sup>4</sup> as well as Guram *et al.*,<sup>5</sup> have reported good, and Buchwald *et al.*<sup>6</sup> excellent, activity in the Suzuki reaction using palladium catalysts with the phosphine ligands PBu<sub>3</sub>, **3** and **4**, respectively. However, the major drawbacks of these catalyst systems is that the phosphine ligands are comparatively difficult to make or are rather expensive—considerably more expensive than the palladium precursors.<sup>7</sup> We were therefore interested in continuing our studies on high activity catalysts derived from inexpensive, easily synthesised ligand sets. Inspired by the observations of Milstein *et al.*<sup>8</sup> and Shibasaki *et al.*<sup>9</sup> that palladated bis(phosphine) 'PCP'-complexes of type **5** and bis(phosphite) 'PCP'-complexes of type **6** show very high activity in the Heck reaction, we wished to see whether related bis(phosphinite) 'PCP'-pincer complexes would show high activity in the Suzuki reaction.

The ligands **7a** and **7b** are easily synthesised in good yields by the reaction of the appropriate aromatic diol with chlorodiphenylphosphine in toluene in the presence of triethylamine (Scheme 2). The reactions of these ligands with palladium trifluoroacetate in THF at room temperature gives the 'PCP'-pincer complexes **8a** and **8b** in good yields. The complexes show excellent air and moisture stability; for instance **8a** shows no sign of decomposition in aerobic solution in the presence of water after 10 days.

The crystal structure of one of the catalysts (**8a**) has been determined<sup>10</sup> and the molecular structure and relevant data are given in Fig. 1. The geometry of the palladium centre is distorted square planar and is grossly similar to that of the complex **6**.<sup>9</sup> The X-ray analysis confirms that palladation of the pincer ligand has occurred and that the two P-donor groups are in a distorted *trans* configuration. The trifluoroacetate ligand coordinates in a unidentate, non-symmetrical fashion, giving greater steric repulsion between the non-coordinated oxygen and the phenyl residues on P1 than those on P2. This is reflected in the considerably larger angle between O3–Pd1–P1 than between O3–Pd1–P2.

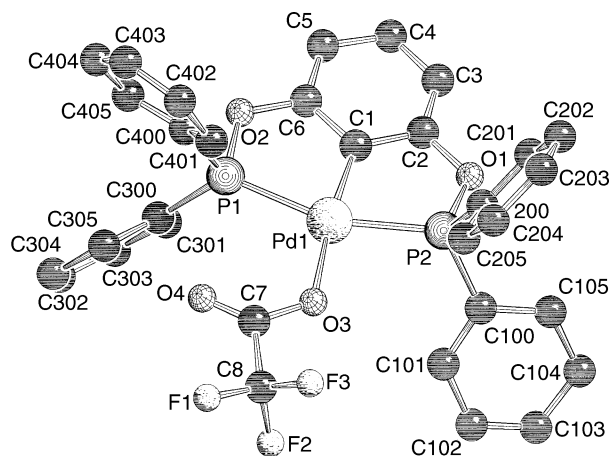
To the best of our knowledge no one has reported the application of palladium 'PCP'-pincer complexes as catalysts in the Suzuki reaction. Initially, the complexes were tested for activity in the coupling of phenylboronic acid with the 'easy-



**Scheme 2** (i) 2 CIPPh<sub>2</sub>, 2.2 Et<sub>3</sub>N, toluene, reflux. (ii) Pd(TFA)<sub>2</sub>, THF.

to-couple' substrate 4-bromoacetophenone. The results were encouraging with the catalysts showing good activity at 130 °C (Table 1), although not as high as obtained previously with **2**.<sup>3</sup>

Next we examined the activity of the complexes with the



**Fig. 1** The molecular structure of **8a**. All H atoms are omitted for clarity. Selected distances (Å) and angles (°): Pd1–C1 1.99(2), Pd1–P1 2.287(6), Pd1–P2 2.281(6), Pd1–O3 2.093(18); C1–Pd1–P1 81.5(6), C1–Pd1–P2 79.3(6), O3–Pd1–P1 104.8(5), O3–Pd1–P2 94.5(5), P1–Pd1–P2 160.2(2), C1–Pd1–O3 173.7(8).

electronically deactivated substrate 4-bromoanisole. In both cases good conversions were observed at one ten-thousandth catalyst concentration and very high turnover numbers (TONs) were observed at one hundred-thousandth catalyst concentration (Table 1). In contrast to the results obtained with 4-bromoacetophenone, catalyst **8a** shows >6 times higher activity with the more challenging substrate 4-bromoanisole than the previously reported catalyst **2** under identical conditions.<sup>3</sup> We believe this activity to be the highest yet reported for this substrate. Particularly interesting is the fact that catalysts **8a** and **8b** couple 4-bromoanisole with nearly the same activity as they show in the coupling of 4-bromoacetophenone. This may imply that the oxidative addition of the aryl bromide is not the rate-limiting step in the catalytic cycle. The catalysts show moderate to good activity at low concentrations in the coupling of the sterically hindered, electronically deactivated substrates 2-bromotoluene, 2-bromo-*p*-xylene and even 2-bromo-*m*-xylene. By comparison, palladium complexes of the ligands **4** and PBu<sub>3</sub> show TONs in the range 82–94 for these substrates, albeit run at lower temperatures.<sup>4b,6</sup>

The catalysts also show moderate activity in the coupling of activated aryl chlorides (Table 1); however, little or no activity was observed with deactivated chlorides. Comparing entries 14 and 17 to 20 it can be seen that the nature of the base plays a major role in the efficiency of coupling of the chlorides; this is an area we will investigate further. Particularly interesting was the fact that KF proved to be a very poor choice of base, even when the toluene was replaced with THF. This is in direct contrast with the finding by Buchwald *et al.* that this base–solvent mixture can give very high activity with palladium phosphine systems.<sup>6</sup>

Whilst it is difficult to establish any clear trends in catalyst activity on these preliminary data, on average **8b** shows slightly higher activity than **8a** in reactions at 0.01 to 0.001 mol% catalyst concentration, possibly due to the fact that **8b** has the more electron-rich Pd centre. At 0.0001 mol% catalyst concentration, **8a** seems more effective; this may be due to slightly higher stability and thus longevity of the catalyst.

In summary, we have demonstrated for the first time that palladium 'PCP'-pincer complexes can be used as high activity catalysts in the Suzuki reaction and that bis(phosphinite) 'PCP'-pincer complexes are ideal catalysts for the coupling of deactivated and sterically hindered aryl bromides as they are inexpensive and very easily synthesised. We are currently

**Table 1** Suzuki coupling of aryl halides with phenylboronic acid catalysed by palladium 'PCP'-pincer complexes<sup>a</sup>

Entry	Aryl halide	Catalyst (mol%)	Base	Conv. (%) <sup>b</sup>	TON <sup>c</sup>
1	4-bromoacetophenone	<b>8a</b> (0.001)	K <sub>2</sub> CO <sub>3</sub>	59	59 000
2	4-bromoacetophenone	<b>8b</b> (0.001)	K <sub>2</sub> CO <sub>3</sub>	92	92 000
3	4-bromoacetophenone	<b>8a</b> (0.0001)	K <sub>2</sub> CO <sub>3</sub>	19	190 000
4	4-bromoacetophenone	<b>8b</b> (0.0001)	K <sub>2</sub> CO <sub>3</sub>	18	180 000
5	4-bromoanisole	<b>8a</b> (0.01)	K <sub>2</sub> CO <sub>3</sub>	61	6100
6	4-bromoanisole	<b>8b</b> (0.01)	K <sub>2</sub> CO <sub>3</sub>	72	7200
7	4-bromoanisole	<b>8a</b> (0.0001)	K <sub>2</sub> CO <sub>3</sub>	19	190 000
8	4-bromoanisole	<b>8b</b> (0.0001)	K <sub>2</sub> CO <sub>3</sub>	15	150 000
9	2-bromotoluene	<b>8a</b> (0.01)	K <sub>2</sub> CO <sub>3</sub>	87	8700
10	2-bromo- <i>p</i> -xylene	<b>8a</b> (0.01)	K <sub>2</sub> CO <sub>3</sub>	67	6700
11	2-bromo- <i>p</i> -xylene	<b>8b</b> (0.01)	K <sub>2</sub> CO <sub>3</sub>	63	6300
12	2-bromo- <i>m</i> -xylene	<b>8a</b> (0.01)	K <sub>2</sub> CO <sub>3</sub>	29	2900
13	2-bromo- <i>m</i> -xylene	<b>8b</b> (0.01)	K <sub>2</sub> CO <sub>3</sub>	30	3000
14	4-chloronitrobenzene	<b>8a</b> (0.01)	K <sub>2</sub> CO <sub>3</sub>	43	4300
15	4-chloronitrobenzene	<b>8b</b> (0.01)	K <sub>2</sub> CO <sub>3</sub>	40	4000
16	4-chloronitrobenzene	<b>8b</b> (0.1)	K <sub>2</sub> CO <sub>3</sub>	67	670
17	4-chloronitrobenzene	<b>8a</b> (0.01)	K <sub>3</sub> PO <sub>4</sub>	25	2500
18	4-chloronitrobenzene	<b>8a</b> (0.01)	NaOBu <sup>t</sup>	0	0
19	4-chloronitrobenzene	<b>8a</b> (0.01)	KF	5	500
20	4-chloronitrobenzene	<b>8a</b> (0.01)	KF <sup>d</sup>	3	300

<sup>a</sup> Reaction conditions: 1.0 mmol aryl halide, 1.5 mmol PhB(OH)<sub>2</sub>, 2.0 mmol base, 5 ml toluene, catalyst added in THF solution (0.1 ml), 130 °C, 18 h. <sup>b</sup> Determined by GC, based on aryl halide. <sup>c</sup> Defined as mol product per mol catalyst. <sup>d</sup> Solvent: 5 ml THF, 75 °C.

investigating the use of a range of palladium 'PCP'-pincer complexes with phosphinite, phosphite and phosphine residues in order to elucidate which will make the optimum catalyst for a given substrate in the Suzuki and related reactions.

## Experimental

### Syntheses

**Resorcinolbis(diphenyl)phosphinite, 7a.** To a solution of resorcinol (2.5 g, 23.0 mmol) and chlorodiphenylphosphine (8.4 ml, 46.0 mmol) in toluene (40 ml) was added triethylamine (7.0 ml, 50.0 mmol) dropwise. The resultant mixture was then heated at reflux for 18 h. After cooling, the volatiles were removed *in vacuo*, the residue was extracted with THF (20 ml) and the resultant solution was filtered through celite. The celite was washed with THF (2 × 20 ml), the extracts were combined and the solvent was removed *in vacuo* to yield the title product as a yellow–orange solid that was not purified further (8.2 g, 75%). NMR (CDCl<sub>3</sub>): <sup>31</sup>P: δ 114.0; <sup>1</sup>H: δ 6.84 (d, 2H, <sup>3</sup>J<sub>HH</sub> = 8.0 Hz, 3,5-Hs of resorcinol ring); 7.02 (s, 1H, 1-H of resorcinol ring); 7.14 (t, 1H, <sup>3</sup>J<sub>HH</sub> = 8.0 Hz, 4-H of resorcinol ring); 7.44 (m, 12H, PPh<sub>2</sub>); 7.63 (m, 8H, PPh<sub>2</sub>).

**Orcinolbis(diphenyl)phosphinite, 7b.** The ligand was obtained as a yellow oil using a method analogous to that for **7a** with 3,5-dihydroxytoluene (orcinol; 2.18 g, 17.6 mmol), chlorodiphenylphosphine (7.2 ml, 39.4 mmol) and triethylamine (7.0 ml, 50 mmol) in toluene (40 ml). Yield 8.5 g, 98%. NMR (CDCl<sub>3</sub>): <sup>31</sup>P: δ 111.3; <sup>1</sup>H: δ 2.29 (s, 3H, CH<sub>3</sub>); 6.71 (s, 2H, 4,6-H of orcinol ring); 6.84 (s, 1H, 2-H of orcinol ring); 7.41 (m, 12H, PPh<sub>2</sub>); 7.60 (m, 8H, PPh<sub>2</sub>).

**Complexes 8a and 8b.** A solution of palladium trifluoroacetate (0.100 g, 0.302 mmol) and the appropriate bis(diphenyl)phosphinite (0.302 mmol) in THF (5.0 ml) was stirred under nitrogen at room temperature for 2 h. The solvent was then removed *in vacuo*. The residue was washed with ethanol and then recrystallised from dichloromethane–ethanol. Complex **8a** was obtained as a colourless solid (0.175 g, 85%). Crystals suitable for single crystal X-ray analysis were obtained by layering a solution of **8a** in dichloromethane with

hexane. Anal. calc. for C<sub>32</sub>H<sub>23</sub>F<sub>3</sub>O<sub>4</sub>P<sub>2</sub>Pd: C 55.15; H 3.3. Found: C 54.85; H 3.55%. NMR (CDCl<sub>3</sub>): <sup>31</sup>P: δ 146.2; <sup>1</sup>H: δ 6.74 (d, 2H, <sup>2</sup>J<sub>HH</sub> = 8.0 Hz, 3,5-Hs of resorcinol ring); 7.12 (t, 1H, <sup>3</sup>J<sub>HH</sub> = 8.0 Hz, 4-H of resorcinol ring); 7.57 (m, 12H, PPh<sub>2</sub>); 7.90 (m, 8H, PPh<sub>2</sub>).

Complex **8b** was obtained as a colourless solid (0.166 g, 78%). Anal. calc. for C<sub>33</sub>H<sub>25</sub>F<sub>3</sub>O<sub>4</sub>P<sub>2</sub>Pd: C 55.75; H 3.5. Found: C 55.1; H 3.3%. NMR (CDCl<sub>3</sub>): <sup>31</sup>P: δ 145.6; <sup>1</sup>H: δ 2.28 (s, 3H, CH<sub>3</sub>); 6.57 (s, 2H, 4,6-Hs of orcinol ring); 7.49 (m, 12H, PPh<sub>2</sub>); 7.86 (m, 8H, PPh<sub>2</sub>).

### Acknowledgements

This work was supported by Forbairt (now Enterprise, Ireland; studentship for P. N. S), EPSRC and Johnson Matthey (studentship for S. L. W) and the Trinity Trust Foundation. We thank Johnson Matthey for the loan of precious metals and for access to their rapid catalyst-screening programme.

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- Crystal data for **8a**: C<sub>32</sub>H<sub>23</sub>F<sub>3</sub>O<sub>4</sub>P<sub>2</sub>Pd, *M* = 696.84, orthorhombic, space group *P*<sub>2</sub><sub>1</sub><sup>2</sup><sub>1</sub>, *Z* = 4, *a* = 10.469(2), *b* = 15.8692(9), *c* = 17.2811(14) Å, *U* = 2871.0(6) Å<sup>3</sup>, *T* = 293(2) K, μ(Mo-Kα) = 0.815 mm<sup>-1</sup>, 2729 independent reflections measured, the final *R* factor was 0.0863 for 2189 reflections with *I* > 2σ(*I*). CCDC reference number 440/207. See <http://www.rsc.org/suppdata/nj/b0/b004793g/> for crystallographic files in .cif format.