

# Orthopalladated triaryl phosphite complexes as highly active catalysts in biaryl coupling reactions

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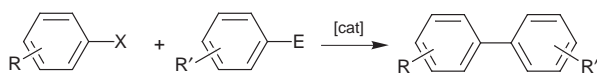
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Orthopalladation of inexpensive, commercially available tris(2,4-di-*tert*-butylphenyl) phosphite gives a dimeric complex **3** which proves to be an extremely active catalyst in biaryl coupling reactions, giving unprecedented turnover numbers of up to 1 000 000 [mol product (mol Pd)<sup>-1</sup>] and turnover frequencies of nearly 900 000 [mol product (mol Pd)<sup>-1</sup> h<sup>-1</sup>] in the Suzuki reaction and turnover numbers of up to 830 000 in the Stille reaction.

The use of triaryl phosphite complexes in catalysis has recently enjoyed a renaissance as a result of the activity they show in hydroformylation,<sup>1</sup> asymmetric hydrocyanation<sup>2</sup> and enantioselective alternating co-polymerisation of CO and propene.<sup>3</sup> Our interest lies in the synthesis and catalytic behaviour of orthometallated triaryl phosphite complexes and the role that the metallation plays in their activities.<sup>4</sup> So far the exploitation of such systems has been limited to a few catalytic reductions<sup>4b,5</sup> and only one example of catalytic C–C bond formation.<sup>6</sup>

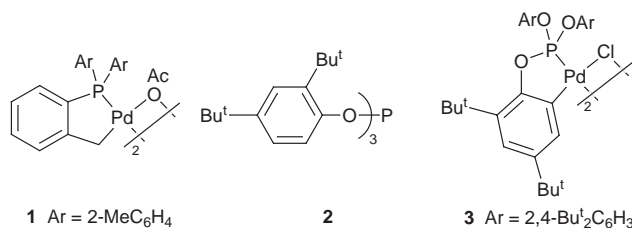
One particularly important class of C–C coupling reaction is the catalytic formation of non-symmetric biaryls (Scheme 1) by the coupling of aryl halides with either arylboronic acids (the Suzuki reaction) or aryltin reagents (the Stille reaction). In general, catalyst loadings in such reactions are high (1–10 mol%) which imposes financial constraints on scaling up reactions and problems associated with catalyst removal. Therefore the synthesis of high activity catalysts which can be used in low concentrations is a desirable goal. Recently, Beller and co-workers reported the use of the metallated tris(2-



**Scheme 1** Suzuki [E = B(OH)<sub>2</sub>] and Stille (E = SnR<sub>3</sub>) biaryl coupling reactions

methylphenyl)phosphinepalladium(II) complex **1** as an efficient catalyst for the Suzuki reaction.<sup>7</sup> The ready ability of triaryl phosphites to undergo analogous metallation reactions as well as their ease of synthesis, commercial availability and very low cost prompted us to examine the possibility of designing well-defined orthometallated Pd<sup>II</sup>–triaryl phosphite complexes capable of catalysing biaryl coupling reactions.

The reaction of bulky tris(2,4-di-*tert*-butylphenyl)phosphite **2** with PdCl<sub>2</sub> gives the orthometallated dimer **3** in 96% yield. Compound **3** has been characterised by satisfactory elemental analysis, <sup>1</sup>H and <sup>31</sup>P NMR spectroscopy and by single crystal



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

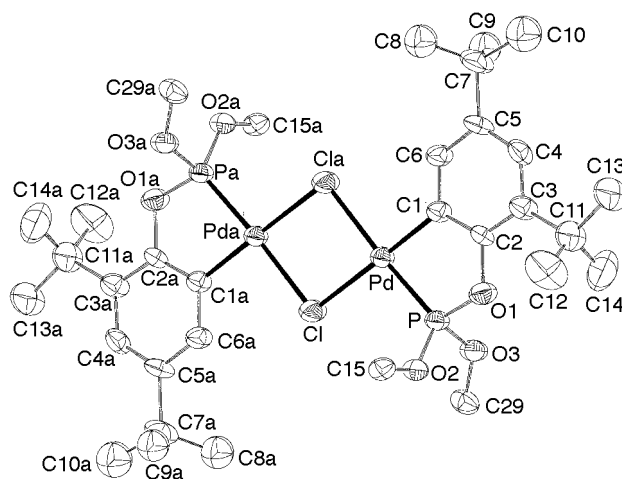
**2**

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

X-ray analysis (Fig. 1).<sup>§</sup> Compound **3** shows remarkable stability to air and moisture—in solution it shows no sign of decomposition after several weeks, whilst solid samples can be kept in air for at least six months. No decomposition is observed when **3** is heated at 130 °C in toluene for 24 h, demonstrating that the catalyst also shows good thermal stability.

The coupling of aryl halides and phenylboronic acid catalysed by **3** was investigated and representative results are summarised in Table 1. With 4-bromoacetophenone as substrate, extraordinarily high turnover numbers (TONs) of up to 1 000 000 [mol product (mol Pd)<sup>-1</sup>] and turnover frequencies (TOFs) of nearly 900 000 [mol product (mol Pd)<sup>-1</sup> h<sup>-1</sup>] were obtained at 110 °C. The previous highest activity with this substrate was achieved with complex **1** which gave a TON of 74 000 at the higher temperature of 130 °C over 16 h.<sup>7</sup> In the present reaction, lowering the temperature to 70 °C leads to a reduction in activity, but even at 20 °C high levels of activity are observed relative to previous reports of ambient temperature reactions.<sup>8</sup> The reaction is strongly influenced by a change of solvent or base, thus replacing toluene with THF at 70 °C leads to a substantial drop in rate. Similarly, with NaOAc as the base in DMA lower rates are observed.

With 4-bromobenzophenone as substrate high rates and ultimate conversions are also seen. As expected, activity decreases with increasing electron density on the aryl bromide. For instance, when 4-bromoanisole is employed TOFs are about two orders of magnitude lower than with 4-bromoacetophenone, however the ultimate TONs—up to 30 000—are, we believe, without precedent.



**Fig. 1** Molecular structure of **3**. Thermal ellipsoids set at 50% probability. All H-atoms omitted for clarity, as are all but the *ipso*-carbons of the non-metallated aryl rings. Three Bu<sup>t</sup> groups are disordered, only major orientation of C7–10 shown. Selected distances (Å) and angles (°): Pd–C1 1.998(6), Pd–Cl 2.4180(16), Pd–Cl<sub>a</sub> 2.4073(17), Pd–P 2.1668(17), P–O1 1.592(4), P–O2 1.585(4), P–O3 1.584(4), C1–Pd–P 80.7(2), P–Pd–Cl 100.35(6), Cl–Pd–Cl<sub>a</sub> 83.92(6), Cl<sub>a</sub>–Pd–C1 95.0(2), Pd–P–O1 108.3(2), Pd–P–O2 120.4(2), Pd–P–O3 120.6(2).

**Table 1** Suzuki coupling of aryl bromides with phenylboronic acid catalysed by **3**. Reaction conditions: 10 mmol aryl bromide, 15 mmol PhB(OH)<sub>2</sub>, 20 mmol base in 30 ml solvent

Aryl bromide	Solvent	[Pd]/mol%	Base	T/°C	t/h	Conversion (%) <sup>a</sup>	TON/mol product (mol Pd) <sup>-1</sup>
4-bromoacetophenone	DMA	0.1	NaOAc	130	18	66	660
4-bromoacetophenone	DMA	0.1	K <sub>2</sub> CO <sub>3</sub>	130	1	19	190
4-bromoacetophenone	DMA	0.1	K <sub>2</sub> CO <sub>3</sub>	130	15	98	980
4-bromoacetophenone	toluene	0.1	K <sub>2</sub> CO <sub>3</sub>	110	1	100	1000
4-bromoacetophenone	toluene	0.0001	K <sub>2</sub> CO <sub>3</sub>	110	1	87	870 000
4-bromoacetophenone	toluene	0.0001	K <sub>2</sub> CO <sub>3</sub>	110	2.25	100	1 000 000
4-bromobenzophenone	toluene	0.0001	K <sub>2</sub> CO <sub>3</sub>	110	1	33	330 000
4-bromobenzophenone	toluene	0.0001	K <sub>2</sub> CO <sub>3</sub>	110	15	60	600 000
4-bromoacetophenone	toluene	0.1	K <sub>2</sub> CO <sub>3</sub>	70	2	100	1000
4-bromoacetophenone	THF	0.1	K <sub>2</sub> CO <sub>3</sub>	70	2	20	200
4-bromoacetophenone	toluene	0.1	K <sub>2</sub> CO <sub>3</sub>	20	2	95	950
4-bromoanisole	toluene	0.1	K <sub>2</sub> CO <sub>3</sub>	110	1	97.5	975
4-bromoanisole	toluene	0.001	K <sub>2</sub> CO <sub>3</sub>	110	1	5	5000
4-bromoanisole	toluene	0.001	K <sub>2</sub> CO <sub>3</sub>	110	15	16	16 000
4-bromoanisole	toluene	0.001	K <sub>2</sub> CO <sub>3</sub>	130	15	30	30 000

<sup>a</sup> Determined by GC and/or <sup>1</sup>H NMR analysis of reaction mixture samples, based on aryl bromide.

**Table 2** Stille coupling of aryl bromides with PhSnBu<sub>3</sub> catalysed by **3**. Reaction conditions: 4 mmol aryl bromide, 5 mmol PhSnBu<sub>3</sub> in 20 ml toluene

Aryl bromide	[Pd]/mol%	T/°C	t/h	Conversion (%) <sup>a</sup>	TON/mol product (mol Pd) <sup>-1</sup>
4-bromoacetophenone	0.2	100	17.5	54	270
4-bromoacetophenone	0.2	120	15	100	500
4-bromoacetophenone	0.0001	120	18	83	830 000
4-bromoanisole	0.1	120	15	84	840

<sup>a</sup> Determined by GC and/or <sup>1</sup>H NMR analysis of reaction mixture samples, based on aryl halide.

In the coupling reactions with higher catalyst concentrations ( $\geq 0.1$  mol% Pd) deposition of palladium is observed in the later stages of the reaction. Similarly, reaction of **3** with 1 equiv. of PhB(OH)<sub>2</sub> and K<sub>2</sub>CO<sub>3</sub> in the absence of an aryl bromide leads to deposition. When this reaction was repeated with 1 equiv. of **2** included, decomposition was inhibited and it was possible to monitor the reaction by <sup>31</sup>P NMR spectroscopy. The spectrum after 30 min showed the mixture to be predominantly **2** and **3** but amongst other minor peaks two relatively major low field doublets were apparent.¶ We have tentatively assigned these to the two isomers of [Pd(Ph){P(OC<sub>6</sub>H<sub>2</sub>-2,4-Bu<sub>2</sub>)-(OC<sub>6</sub>H<sub>3</sub>-2,4-Bu<sub>2</sub>)<sub>2</sub>}] {P(OC<sub>6</sub>H<sub>3</sub>-2,4-Bu<sub>2</sub>)<sub>3</sub>} in which the P atoms are disposed *trans* (major) or *cis* (minor). Also apparent is a small peak at  $\delta -18.3$ . Such a high field shift is consistent with the formation of a Pd<sup>0</sup>-phosphite complex. We postulate that reductive elimination of the orthometallated phosphite aryl and a phenyl groups occurs, yielding a catalytically active zero valent palladium species. This is in accord with findings for the use of **1** in the Stille reaction.<sup>9</sup> However, a Pd<sup>II</sup>/Pd<sup>IV</sup> couple has recently been suggested to be active in the Heck arylation of alkenes catalysed by **1** and related complexes<sup>10</sup> and at this stage we cannot rule out a related pathway.

Encouraged by the results obtained in the Suzuki reaction we decided to investigate the application of **3** to the Stille reaction. Representative results for the coupling of tributylphenyltin with aryl bromides are summarised in Table 2. With 4-bromoacetophenone as substrate TONs of up to 840 000 were achieved within 18 h at 120 °C. To the best of our knowledge this is the highest reported activity to date, comparing well with that obtained with **1** which gives a TON of 1650 in the coupling of 4-bromoacetophenone with PhSnMe<sub>3</sub> at the same temperature.<sup>9</sup> The reaction is again somewhat more sluggish with 4-bromoanisole, but useful conversions are still obtained.

In summary the complex **3** is extremely active in biaryl coupling reactions under both Suzuki and Stille conditions and

consequently can be used in very low concentrations. In view of this unprecedented activity and the low cost of **2**—at least two orders of magnitude cheaper than tris(2-methylphenyl)phosphine—we believe that it will be the catalyst of choice in such reactions. We are currently investigating its application to further catalytic processes. Preliminary investigations show it to be extremely active in the Heck arylation of alkenes, showing TONs of up to 5.75 million for activated aryl bromides, and these findings will be published elsewhere.

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## Notes and References

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§ Crystal data for **3**: C<sub>84</sub>H<sub>124</sub>Cl<sub>2</sub>O<sub>6</sub>P<sub>2</sub>Pd<sub>2</sub>, *M* = 1575.47, triclinic, space group *P* $\bar{1}$ , *Z* = 1, *a* = 11.957(1), *b* = 12.911(3), *c* = 15.300(3) Å,  $\alpha$  = 81.08(2),  $\beta$  = 69.46(1),  $\gamma$  = 76.45(1)°, *V* = 2143.3(6) Å<sup>3</sup>, *T* = 293(2) K,  $\mu$  = 0.566 mm<sup>-1</sup>, the final *R*-factor was 0.057 for 4257 reflections with *I* > 2 $\sigma$ (*I*). CCDC 182/978.

¶ NMR data:  $\delta_p$  155.2 and 118.1 (<sup>2</sup>*J*<sub>PP</sub> = 29.8 Hz) (minor isomer) and 141.4 and 117.3 (<sup>2</sup>*J*<sub>PP</sub> = 868.4 Hz) (major isomer).

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