Organometallics **2002,** *21,* 2599−2600

Platinum Catalysts for Suzuki Biaryl Coupling Reactions

Robin B. Bedford* and Samantha L. Hazelwood†

School of Chemistry, University of Exeter, Exeter EX4 4QD, U.K.

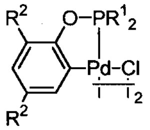
David A. Albisson

Department of Chemistry, Trinity College Dublin, Dublin 2, Ireland

Received April 1, 2002

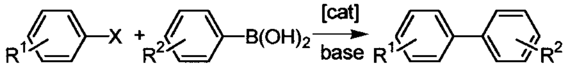
Summary: Platinum complexes with π-acidic, ortho-metalated triaryl phosphite and phosphinite ligands show unexpectedly good activity in Suzuki biaryl coupling reactions with aryl bromide substrates.

The coupling of aryl halides with arylboronic acids, the Suzuki reaction (Scheme 1), is one of the most powerful methods for the synthesis of biaryls.[1] While palladium complexes have enjoyed enormous success as catalysts, the application of platinum complexes to biaryl coupling reactions has received almost no attention.[2] To the best of our knowledge, the only reported use of a platinum complex in such a reaction was the [Pt(PPh$_3$)$_4$]-catalyzed Stille coupling of aryl triflates with vinyltributylstannane.[3] In this case the catalyst showed very poor activity, giving yields of only 30−37% after 2 days at 5 mol % Pt catalyst loading. It is probable that the slow rate of reductive elimination of the biaryl group from platinum(II) complexes compared with the rate for the analogous palladium(II) complexes accounts for the lack of activity displayed by platinum.[2] If this is the case, then the introduction of more π-acidic ligands should increase the rate of reductive elimination and thus open up the possibility of using platinum complexes in coupling reactions.[4] We recently found that the ortho-palladated complexes **1** and **2**, with π-acidic triaryl phosphite and phosphinite ligands, act as highly active catalysts in biaryl coupling reactions[5,6] and were interested to see whether such ligands would be sufficiently electron withdrawing to enable the use of analogous platinum complexes as catalysts in these reactions. The initial findings of this study are reported below.

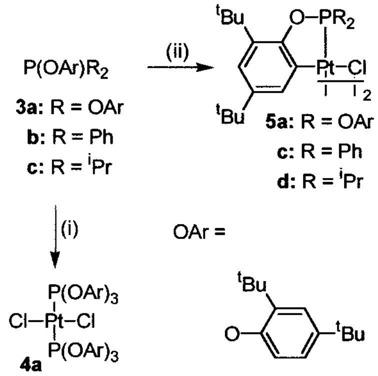


1: $R^1 = OC_6H_3\text{-}2,4\text{-}{}^tBu_2$; $R^2 = {}^tBu$
2: $R^1 = Ph, {}^iPr$; $R^2 = H, {}^tBu$

Scheme 1. Suzuki Biaryl Coupling Reaction



Scheme 2[a]



[a] Conditions: (i) (for **3a**) [PtCl$_2$(NCPh)$_2$], CH$_2$Cl$_2$, 17 h; (ii) 2-methoxyethanol or *o*-xylene, Δ, 14−17 h.

The reaction of 2 equiv of the bulky phosphite ligand tris(2,4-di-*tert*-butylphenyl) phosphite (**3a**) with [PtCl$_2$(NCPh)$_2$] in dichloromethane gives the bis(phosphite) complex *trans*-[PtCl$_2$(**3a**)$_2$] (**4a**) in 71% yield (Scheme 2). The assignment of stereochemistry was supported by a comparison of the IR and NMR spectroscopic data[7] with those reported for the trans and cis isomers of [PtCl$_2${P(OC$_6$H$_4$-2-Me)$_3$}$_2$].[8] Presumably the high steric profile of the phosphite ligands in **4a** overrides the electronic advantages associated with the cis arrangement, in which the π-acidic triaryl phosphite ligands would be trans to the π-basic chlorides. For comparison purposes we also prepared [PtCl$_2${P(OC$_6$H$_5$)$_3$}$_2$] (**4b**) according to a literature method.[8]

Heating a mixture of K$_2$[PtCl$_4$] and 1 equiv of the ligand **3a** in 2-methoxyethanol at reflux temperature led to the formation of the ortho-platinated dimer [{Pt(μ-Cl){κ^2-*P*,*C*-P(OC$_6$H$_2$-2,4-^{t}Bu$_2$)(OC$_6$H$_3$-2,4-^{t}Bu$_2$)$_2$}}$_2$] (**5a**) as a mixture of cis and trans isomers in 83% yield. The ^{31}P NMR spectrum of **5a** shows a singlet with platinum satellites at 81.2 ppm (J = 7750 Hz) corresponding to the major isomer and a second singlet with platinum satellites at 79.9 ppm (J = 7875 Hz) corresponding to the minor isomer. These data are consistent with those reported previously for the related complex [{Pt(μ-Cl){κ^2-*P*,*C*-P(OC$_6$H$_4$)(OC$_6$H$_5$)$_2$}}$_2$] (**5b**).[9] The syntheses of the related ortho-platinated phosphinite complexes **5c**,**d** by reaction of K$_2$[PtCl$_4$] with 1 equiv of the ligands **3b**,**c**, respectively, were somewhat low yielding (30% and 4% for **5c**,**d**, respectively).

---

* To whom correspondence should be addressed. Fax: +44 (0) 1392 263434. E-mail: r.bedford@ex.ac.uk.

† Née Welch.

(1) For recent reviews see: (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457. (b) Stanforth, S. P. *Tetrahedron* **1998**, *54*, 263. (c) Suzuki, A. *J. Organomet. Chem.* **1999**, *576*, 147.

(2) Clarke, M. L. *Polyhedron* **2001**, *20*, 151.

(3) Mateo, C.; Fernández-Rivas, C.; Cárdenas, D. J.; Echavarren, A. M. *Organometallics* **1998**, *17*, 3661.

(4) Merwin, R. K.; Schnabel, R. C.; Koola, J. D.; Roddick, D. M. *Organometallics* **1992**, *11*, 2972.

(5) Albisson, D. A.; Bedford, R. B.; Scully, P. N. *Chem. Commun.* **1998**, 2095.

(6) Bedford, R. B.; Welch, S. L. *Chem. Commun.* **2001**, 129.

(7) See the Supporting Information.

(8) Ahmad, N.; Ainscough, E. W.; James, T. A.; Robinson, S. D. *J. Chem. Soc., Dalton Trans.* **1973**, 1148.

(9) Albinati, A.; Affolter, S.; Pregosin, P. S. *Organometallics* **1990**, *9*, 379.

10.1021/om0202524 CCC: $22.00

Table 1. Suzuki Coupling of Aryl Bromides and Chlorides with Phenylboronic Acid[a]

entry	aryl halide	cat. ([Pt], mol % Pt)	conversn (%)[b]	TON (mol of product/mol of Pt)
1	$\mathrm{BrC_6H_4C(O)Me}$-4	**4a** (0.1)	63	630
2	$\mathrm{BrC_6H_4C(O)Me}$-4	**5a** (0.1)	100	1 000
3	$\mathrm{BrC_6H_4}$-4-C(O)Me	**5c** (0.1)	100	1 000
4	$\mathrm{BrC_6H_4}$-4-C(O)Me	**5d** (0.1)	100	1 000
5	$\mathrm{BrC_6H_4}$-4-C(O)Me	**4a** (0.001)	9.5	9 500
6	$\mathrm{BrC_6H_4}$-4-C(O)Me	**4b** (0.001)	6	6 000
7	$\mathrm{BrC_6H_4}$-4-C(O)Me	**5a** (0.001)	26	26 000
8	$\mathrm{BrC_6H_4}$-4-C(O)Me	**5a** (0.001)[c]	26	26 000
9	$\mathrm{BrC_6H_4}$-4-C(O)Me	**5b** (0.001)	16	16 000
10	$\mathrm{BrC_6H_4}$-4-C(O)Me	**5c** (0.001)	100	100 000
11	$\mathrm{BrC_6H_4}$-4-C(O)Me	**5d** (0.001)	74	74 000
12	$\mathrm{BrC_6H_4}$-4-C(O)Me	**5c** (0.0001)	100	1 000 000
13	$\mathrm{BrC_6H_4}$-4-C(O)Me	**5c** (0.0001)[d]	100	1 000 000
14	$\mathrm{BrC_6H_4}$-4-C(O)Me	**5c** (0.00001)	24	2 400 000
15	$\mathrm{BrC_6H_4}$-4-C(O)Me	**5c** (0.00001)[d]	25	2 500 000
16	$\mathrm{BrC_6H_4}$-4-C(O)Me	$\mathrm{[Pd(PPh_3)_4]}$ (0.001)	35	35 000
17	$\mathrm{BrC_6H_5}$	**5a** (0.1)	98	980
18	$\mathrm{BrC_6H_5}$	**5a** (0.001)	39	39 000
19	$\mathrm{BrC_6H_5}$	**5c** (0.001)	48	48 000
20	$\mathrm{BrC_6H_4}$-4-OMe	**5c** (1.0)	72	72
21	$\mathrm{BrC_6H_4}$-4-OMe	**5c** (0.1)	13	130
22	$\mathrm{BrC_6H_4}$-4-Me	**5c** (0.5)	72	144
23	$\mathrm{BrC_6H_4}$-4-Me	**5c** (0.5)	88	176
24	$\mathrm{BrC_6H_4}$-2-Me	**5c** (0.5)[c]	87	174
25	$\mathrm{BrC_6H_4}$-2-OMe	**5c** (0.5)	51	102
26	$\mathrm{ClC_6H_4}$-4-C(O)Me	**5c** (0.5)	29	58

[a] Reaction conditions: 10 mmol of aryl halide, 15 mmol of $\mathrm{PhB(OH)_2}$, 20 mmol of $\mathrm{K_3PO_4}$, 30 mL of 1,4-dioxane, 100 °C, 18 h (not optimized). [b] Conversion to product determined by GC, based on aryl bromide, with hexadecane internal standard. [c] Reaction time 2 h. [d] In air.

For the catalytic studies we initially performed a brief solvent/base optimization for the coupling of 4-bromoacetophenone with phenylboronic acid and found that potassium phosphate in 1,4-dioxane gave the best results.[7] These conditions were used throughout the Suzuki test reactions with the catalysts **4a**,**b** and **5a**−**d**.[10] The results of these catalytic studies are summarized in Table 1.

From a comparison of the activities of the ortho-metalated phosphite complexes **5a**,**b** with those of the nonmetalated complexes **4a**,**b** (entries 1, 2, and 5−9) in the coupling of 4-bromoacetophenone, two conclusions can be drawn. First, it can be seen that ortho-metalation leads to greatly enhanced activity, and second, increasing the size of the OAr function leads to higher activity. We have previously observed similar patterns of activity with palladium complexes.[6] In the palladium case we reasoned that reductive elimination of the ortho-metalated ring and an aryl substituent introduced by the boronic acid leads to the formation of a catalytically active, low-coordinate Pd(0) species. It is possible that similar reductive processes occur with the platinum complexes; however, at this stage we are not able to rule out the possibility of a Pt(II)/Pt(IV) cycle, although the use of strongly π-acidic ligands tends to mitigate against this. Preliminary investigations to determine whether the catalysts enter a Pt(0)/Pt(II) or a Pt(II)/Pt(IV) manifold have been inconclusive, and we are currently exploring this area further.

When the activities of the complexes **5a**,**c**,**d** in the couplings with 4-bromoacetophenone are compared, it can be seen that the order of activity is **5c** > **5d** > **5a**. The fact that **5a** shows the lowest activity indicates that, if anything, the phosphite ligand is *too* π-acidic and that the oxidative-addition step is being retarded with respect to that seen when **5c** is used. Since the platinum center in **5d** is more electron rich than that in **5c**, it would be expected that the rate of oxidative addition would be higher, but the increased electron density at the platinum appears to be deleterious. This suggests that in this case the rate-determining step is probably not oxidative addition but rather either nucleophilic attack of the base-activated boronate[11] or reductive elimination of the biaryl product. Catalyst **5c** seems to have about the best balance of electronic properties for the coupling of 4-bromoacetophenone and respectably high activity results. The maximum TON of 2,500,000 is well in excess of that shown by classical catalysts such as $\mathrm{[Pd(PPh_3)_4]}$ under the same conditions (entry 16) and is comparable with or better than the activity reported for most palladacyclic catalysts.[5,12] This activity is maintained even under air. When the performances of the catalysts **5a**,**c** in the coupling of the nonactivated substrate bromobenzene are compared, it can again be seen that **5c** shows better activity. Catalyst **5c** also shows reasonable activity with electronically deactivated and sterically hindered aryl bromide substrates (entries 20−25). Gratifyingly, **5c** also shows activity in the coupling of an activated aryl chloride substrate. It is only recently that palladium catalysts have made inroads into the activation of this technically interesting class of substrates in Suzuki coupling reactions.[13]

In summary, we have shown not only that, by judicious choice of ligand sets, the use of platinum complexes in Suzuki coupling reactions becomes viable but also that these catalysts can show activity far in excess of "classical" palladium catalysts such as $\mathrm{[Pd(PPh_3)_4]}$ and comparable with many of the new high-activity palladacyclic-based catalysts. This unexpected activity, coupled with the fact that platinum has catalytic properties that are distinct from those of palladium,[2] makes the whole area of platinum-catalyzed coupling reactions ripe for further investigation.

Acknowledgment. We thank the EPSRC for funding and Johnson Matthey Chemicals for funding and the loan of platinum salts.

Supporting Information Available: Text giving details of the synthesis and characterization of the new complexes and catalytic data. This material is available free of charge via the Internet at http://pubs.acs.org.

OM0202524

---

(10) In most cases a nonoptimized standard reaction time of 18 h was used; however, it can be seen from a comparison of entry 7 with 8 and entry 23 with 24 that the reactions are probably over in a much shorter space of time. Indeed, a plot of conversion against time for the former reaction (see the Supporting Information) showed it to be essentially over by 80 min.

(11) This process is often referred to as "transmetalation".

(12) (a) Gibson, S.; Foster, D. F.; Eastham, G. R.; Tooze, R. P.; Cole-Hamilton, D. J. *Chem. Commun.* **2001**, 779. (b) Zim, D.; Gruber, A. S.; Ebling, G.; Dupont, J.; Monteiro, A. L. *Org. Lett.* **2000**, *2*, 2881. (c) Bedford, R. B.; Draper, S. M.; Scully, P. N.; Welch, S. L. *New J. Chem.* **2000**, *24*, 745. (d) Weissman, H.; Milstein, D. *Chem. Commun.* **1999**, 1901. (e) Beller, M.; Fischer, H.; Herrmann, W. A.; Öfele, K.; Brossmer, C. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1848.

(13) For recent examples of palladium-catalyzed Suzuki coupling reactions with aryl chloride substrates see: (a) Botella, L.; Nájera, C. *Angew. Chem., Int. Ed.* **2002**, *41*, 179. (b) Liu, S.-Y.; Choi, M. J.; Fu, G. C. *Chem. Commun.* **2001**, 2408. (c) Bedford, R. B.; Cazin, C. S. J. *Chem. Commun.* **2001**, 1540. (d) Zapf, A.; Ehrentraut, A.; Beller, M. *Angew. Chem., Int. Ed.* **2000**, *39*, 4153. (e) Andreu, M. G.; Zapf, A.; Beller, M. *Chem. Commun.* **2000**, 2475. (f) Old, D. W.; Wolfe, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1998**, *121*, 9722. (g) Wolfe, J. P.; Singer, R. A.; Yang, B. H.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 9550. (h) Bei, X.; Turner, H. W.; Weinberg, W. H.; Guram, A. S. *J. Org. Chem.* **1999**, *64*, 6797. (i) Zhang, C.; Huang, J.; Trudell, M. L.; Nolan, S. P. *J. Org. Chem.* **1999**, *64*, 3804. (j) Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **1998**, *37*, 3387.