Available online at www.sciencedirect.com
SCIENCE DIRECT®
Tetrahedron Letters 46 (2005) 9017–9020
Tetrahedron Letters

Cross-coupling reactions catalyzed by P, O chelate palladium complexes at room temperature

Mengping Guo,[a,c] Fangfang Jian[b] and Ren He[a,*]

[a]*State Key Laboratory of Fine Chemicals, Dalian University of Technology, Dalian 116012, China*
[b]*New Materials & Function Coordination Chemistry Laboratory, Qingdao University of Science and Technology, Qingdao 266042, China*
[c]*Department of Chemistry, Yichun Institute, Yichun 336000, China*

Received 13 May 2005; revised 18 October 2005; accepted 21 October 2005

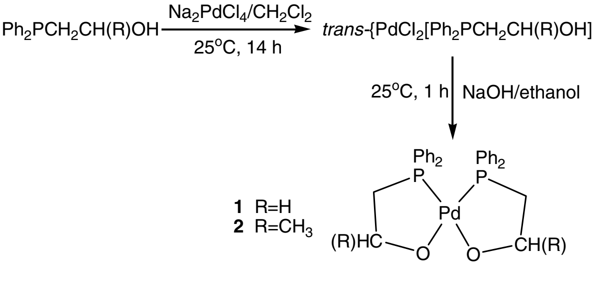
Abstract—A new catalytic system based on P, O chelate palladium complexes for cross-coupling reactions is described. These catalysts have all shown high activity and selectivity under mild reaction condition.

Palladium-catalyzed cross-coupling reaction between aryl halides and aryl boronic acids, known as Suzuki reaction, is very useful for the synthesis of symmetrical and unsymmetrical biaryls,[1–3] which can be pharmaceuticals, polymers, materials, liquid crystals and so on. Since Suzuki and co-workers reported the preparation of biaryls in 1981,[4] various catalytic systems have been described, for example, the bulky electron-rich phosphine ligands,[5] phosphites,[6] *N*-heterocyclic carbenes.[7] In the field of cross-coupling reactions, could focus their attention on (i) easier coupling of the widely available and inexpensive aryl chloride; (ii) enhance turnover numbers; (iii) milder reaction conditions; (iv) the opportunity to substitute the expensive palladium catalysts for cheaper nickel ones.[8] Consequently, the development of milder conditions (e.g., room temperature) for Suzuki couplings of aryl halides would also be a significant advance. In this letter, we describe some new efficient chelate-stabilized alkoxo-palladium(II) catalysts, which can catalyzed the Suzuki cross-coupling reactions of arylboronic acids and aryl bromides at room temperature.

The alkoxo-palladium(II) complexes are often unstable because they form easily hydrides or palladium(0) and the isolable complexes are rare.[9] Some of them are postulated intermediates of stoichiometric or catalytic reactions, which Pd complexes take part in alcoholic solvents.[10,11] However, all alkoxo-palladium(II) complexes we describe here are remarkably stable in air, water and thermal. Although they are well known in transition metal chemistry, they have not been used in cross-coupling reactions.

Alkoxo-palladium(II) complexes, $[Pd(Ph_2PCH_2CH_2O)_2]$ **1** and $[Pd(Ph_2PCH_2CH(CH_3)O)_2]$ **2**, were prepared from the corresponding alcohol containing a tertiary phosphino functional group, such as Ph_2PCH_2CHROH (R=H, CH_3). They are bidentate, chelating ligands and can form stable complexes with palladium. The coordinational reaction of ligand with natrium tetrachloropalladate in NaOH ethanol at 25 °C gives complexes **1** and **2** (Scheme 1).[12,13]

The catalysis of the complex **2** for Suzuki coupling between 4-bromoanisole and phenyl boronic acid revealed that the cross-coupling reaction took place smoothly in



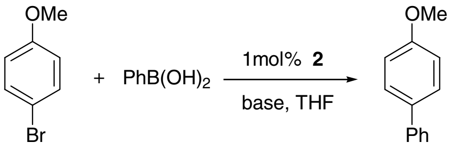
Scheme 1. Synthesis of alkoxo-palladium complexes (**1**–**2**).

---

* Corresponding author. Tel.: +86 0411 88993861; fax: +86 0411 83685859; e-mail: guomengping@yahoo.com.cn

0040-4039/$ - see front matter
doi:10.1016/j.tetlet.2005.10.104

Table 1. Base effect in Suzuki reaction[a]



Entry	Base	Reaction time (h)	Yield[b,c] (%)
1	$K_3PO_4{\cdot}3H_2O$	5	82
2	$KF{\cdot}2H_2O$	7	29
3	Na_2CO_3	5	67
4	KOH	7	44
5	NaAc	11	47
6	Et_3N	5	75

[a] 4-Bromoanisole (1.0 mmol), phenyl boronic acid (1.5 mmol), base (3.0 mmol, dissolved in 2 mL H_2O), **2** (0.01 mmol), THF(2.0 mL), the reaction was performed at room temperature.

[b] Isolated yield.

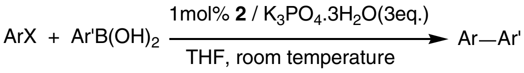
[c] Reaction time not optimized, bromoanisole was not completely consumed.

THF, K_3PO_4 as a base at room temperature (Table 1, entry 1). The catalyst **1** also showed good performance, although 4-bromoanisole is electronically deactivated and should resist oxidative addition and enter the catalytic circle with difficulty.

The base usually is important in cross-coupling reaction and different kind of bases were screened. The results are summarized in Table 1. $K_3PO_4{\cdot}3H_2O$, Na_2CO_3 and Et_3N were better among these bases in the cross-coupling reaction (Table 1, entries 1, 3, 6), and $K_3PO_4{\cdot}3H_2O$ was the best one.

The cross-coupling reactions of both electron-rich and -poor aryl bromides and arylboronic acids have been investigated and representative results are summarized in Table 2. The electron-poor aryl bromide, such as 4-bromoacetophenone, reacted with different aryl boronic acids to give excellent yield at room temperature for 6–8 h (Table 2, entries 1–3). The electron-rich aryl bromide,

Table 2. Suzuki reaction of aryl bromides catalyzed by **2**



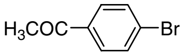
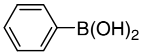
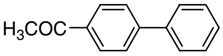
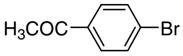
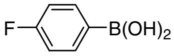
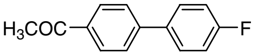
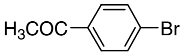
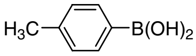
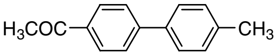
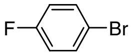
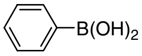
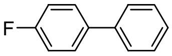
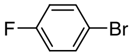
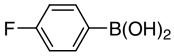
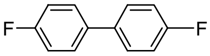
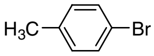
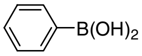
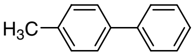
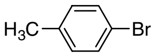
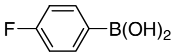
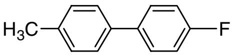
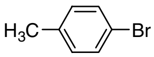
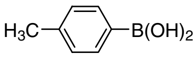
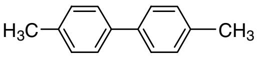
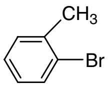
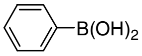
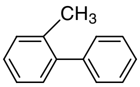
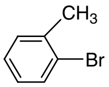
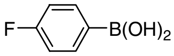
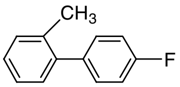
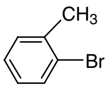
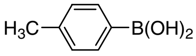
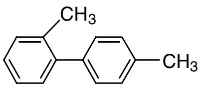
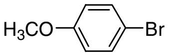
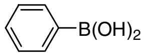
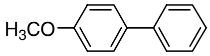
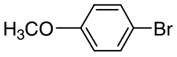
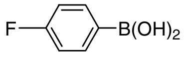
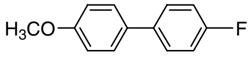
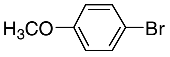
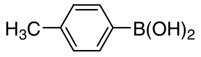
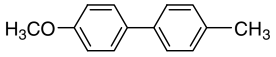
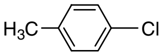
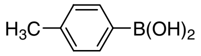
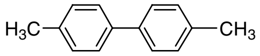
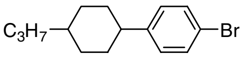
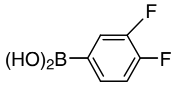
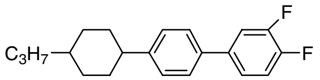
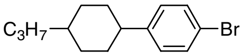
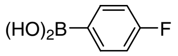
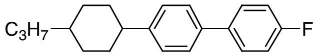
Entry	ArBr	Ar′B(OH)$_2$	Product[a]	Time[b] (h)	Yield[c] (%)
1				6	99
2				8	99
3				6	99
4				9	98
5				9	99
6				12	98
7				6	83
8				5	99
9				9	68
10				5	85
11				5	80

Table 2 (*continued*)

Entry	ArBr	Ar′B(OH)$_2$	Product[a]	Time[b]	Yield[c](%)
12				15	96
13				9	98
14				8	96
15				12.5	21[d]
16				5	96
17				5	95

[a] Reaction conditions: 1.0 mmol of aryl bromide, 1.5 mmol of aryl boronic acid, 3.0 mmol of $K_3PO_4{\cdot}3H_2O$ (dissolved in 2.0 mL H_2O), **2** (0.01 mmol), THF (2.0 mL).

[b] Reaction time not optimized.

[c] Isolated yield.

[d] The reaction was performed in DMF at 100 °C.

such as 4-bromoanisole, also gave good yield at the same temperature for 8–15 h[14] (Table 2, entries 12–14). The bromide containing *ortho* substituent also reacted effectively to prepare the desired sterically demanding biaryl products at room temperature for 5–9 h in moderate to good yields (Table 2, entries 9–11). The inconspicuousness difference was observed in yield and the reaction time, while the varying aryl boronic acids were used in the Suzuki cross-coupling reactions. In addition, liquid crystal compounds with the construction of C_{SP}^2–C_{SP}^2 bonds, for example, 4-fluoro-(4′-propylcyclohexyl) biphenyl and 3,4-difluoro-(4′-propylcyclohexyl) biphenyl, can be synthesized by this reaction to give excellent yield at room temperature for 5 h (Table 2, entries 16–17). However, if these procedures were catalyzed by triarylphosphane-based systems, it will require elevated reaction temperatures (usually 50–100 °C).[5c] Only with reactions involving aryl chloride are low conversions achieved even at higher reaction temperature, giving biaryls in 21% yield after 12.5 h in DMF at 100 °C (Table 2, entry 15).

In conclusion, we demonstrated that alkoxo-palladium(II) complexes, $[Pd(Ph_2PCH_2CH_2O)_2]$ **1** and $[Pd(Ph_2PCH_2CH(CH_3)O)_2]$ **2**, are excellent air-stable catalysts for general Suzuki cross-coupling reactions of arylboronic acids and aryl bromides. All reactions process in short times and at mild temperatures. These complexes are ideal catalysts for the coupling of deactivated and sterically hindered aryl bromides as they are comparatively inexpensive, very easily synthesized and can be used to give high conversions at low temperature. To our knowledge, there have been only a few reports on efficient Suzuki cross-coupling reactions of aryl bromides at room temperature.[5c,b,6b,15] Further investigations focusing on mechanistic aspects in related cross-coupling reactions are ongoing in our laboratories.

Acknowledgement

We gratefully acknowledge financial support of this work by the National Natural Science Foundation of China (Grants 20333060).

References and notes

1. Szmant, H. H. *Organic Building Blocks for the Chemical Industry*; John Wiley & Sons: New York, 1989.
2. (a) Nicolaou, K. C.; Boddy, C. N. C.; Brase, S.; Winssinger, N. *Angew. Chem., Int. Ed.* **1999**, *38*, 2096; (b) Wang, X.; Snieckus, V. *Tetrahedron Lett.* **1991**, *32*, 1879; (c) Siddiqui, M. A.; Snieckus, V. *Tetrahedron Lett.* **1990**, *31*, 1523; (d) Kelly, T. R.; Garcia, A.; Lang, F.; Walsh, J. J.; Bhaskar, K. V.; Boyd, M. R.; Götz, R.; Keller, P. A.; Walter, R.; Bringmann, G. *Tetrahedron Lett.* **1994**, *35*, 7621.
3. (a) Hird, M.; Gray, G. W.; Toyne, K. J. *Mol. Cryst. Liq. Cryst.* **1991**, *206*, 187; (b) Kim, Y. H.; Webster, O. W. *J. Am. Chem. Soc.* **1990**, *112*, 4592; (c) Wallow, T. I.; Novak, B. M. *J. Am. Chem. Soc.* **1991**, *113*, 7411; (d) Lamba, J. J. S.; Tour, J. M. *J. Am. Chem. Soc.* **1994**, *116*, 11723.
4. Miyaura, N.; Yanagi, T.; Suzuki, A. *Synth. Commun.* **1981**, *11*, 513.
5. (a) Littke, A. F.; Dai, C.; Fu, G. C. *J. Am. Chem. Soc.* **2000**, *122*, 4020; (b) Wolfe, J. P.; Singer, R. A.; Yang, B. H.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 9550; (c) Wolfe, J. P.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **1999**, *38*, 2413; (d) Bei, X.; Turner, H. W.; Weinberg, W. H.; Guram, A. S.; Petersen, J. L. *J. Org. Chem.* **1999**, *64*, 6797.
6. (a) Griffiths, C.; Leadbeater, N. E. *Tetrahedron Lett.* **2000**, *41*, 2487; (b) Albisson, D. A.; Bedford, R. B.; Lawrence, S. E.; Scully, P. N. *Chem. Commun.* **1998**, 2095; (c) Zapf, A.; Beller, M. *Chem. Eur. J.* **2000**, *6*, 1830.
7. (a) Grasa, G. A.; Viciu, M. S.; Huang, J.; Zhang, C.; Trudell, M. L.; Nolan, S. P. *Organometallics* **2002**, *21*, 2866; (b) Böhm, V. P. W.; Gstöttmayr, C. W. K.;

Weskamp, T.; Herrmann, W. A. *J. Organomet. Chem.* **2000**, *595*, 186; (c) Beller, M.; Fischer, H.; Herrmann, W. A.; Oefele, K.; Brossmer, C. *Angew. Chem., Int. Engl.* **1995**, *34*, 1848; (d) Zhang, C.; Huang, J.; Trudell, M. L.; Nolan, S. P. *J. Org. Chem.* **1999**, *64*, 3804.

8. Sambasivarao, K.; Kakali, L.; Dhurke, K. *Tetrahedron* **2002**, *58*, 9633.
9. Montgomery, C. D.; Payne, N. C.; Willis, C. J. *Inorg. Chim. Acta* **1986**, *117*, 103.
10. Bryndza, H. E.; Kretchmar, S. A.; Tulip, T. H. *Chem. Commun.* **1985**, 977.
11. Alper, H.; Despeyroux, B.; Woell, J. B. *Tetrahedron Lett.* **1983**, *24*, 5691.
12. Platt, A. W. G.; Pringle, P. G. *J. Chem. Soc., Dalton Trans.* **1989**, 1193.
13. Boere, R. T.; Montgomery, C. D.; Payne, N. C.; Willis, C. J. *Inorg. Chem.* **1985**, *24*, 3680.
14. The reaction was carried out in standard Schlenck technique. THF (2 mL), 4-bromoanisole (187.2 mg, 1 mmol), aryl boronic acid (182.9 mg, 1.5 mmol), $K_3PO_4 \cdot 3H_2O$ (787.9 mg, 3 mmol, dissolved in 2 mL water) and **2** (5.9 mg, 0.01 mmol) were mixed in reaction tube. The reaction mixture was stirred at room temperature (25–27 °C) for 15 h. Reaction progress was monitored by TLC and when the reaction was completed, the mixture was quenched with 5 mL of H_2O and extracted by 3 × 5 mL of ether. The organic layers were combined, dried over $MgSO_4$, filtered and concentrated in vacuo. Purification of crude product by flash chromatography on silica gel afforded 176.8 mg of 4-methoxybiphenyl (96%) as a solid. Mp = 87–89 °C; ^{1}H NMR (400 MHz. $CDCl_3$): $\delta = 7.56–7.25$ (m, 7H); 6.96–6.99 (m, 2H); 3.85 (s, 3H).
15. (a) Anderson, J. C.; Namli, H.; Roberts, C. A. *Tetrahedron* **1997**, *53*, 15123; (b) Frank, S. A.; Chen, H.; Kunz, R. K.; Schnaderbeck, M. J.; Roush, W. R. *Org. Lett.* **2000**, *2*, 2691; (c) Kataoka, N.; Shelby, Q.; Stambuli, J. P.; Hartwig, J. F. *J. Org. Chem.* **2002**, *67*, 5553; (d) Johnson, C. R.; Johns, B. A. *Synlett* **1997**, 1406; (e) Kamatani, A.; Overman, L. E. *J. Org. Chem.* **1999**, *64*, 8743; (f) Uozumi, Y.; Danjo, H.; Hayashi, T. *J. Org. Chem.* **1999**, *64*, 3384; (g) Colacot, T. J.; Gore, E. S.; Kuber, A. *Organometallics* **2002**, *21*, 3301; (h) Zim, D.; Gruber, A. S.; Ebeling, G.; Dupont, J.; Monteiro, A. L. *Org. Lett.* **2000**, *2*, 2881; (i) Campi, E. M.; Jackson, W. R.; Marcuccio, S. M.; Naeslund, C. G. M. *J. Chem. Soc., Chem. Commun.* **1994**, 2395; (j) Bumagin, N. A.; Bykov, V. V. *Tetrahedron* **1997**, *53*, 14437; (k) Bussolari, J. C.; Rehborn, D. C. *Org. Lett.* **1999**, *1*, 965; (l) Weng, Z. Q.; Teo, S.; Koh, L. L.; Hor, T. S. A. *Organometallics* **2004**, *23*, 3603.