

SYNLETT Spotlight 164

Biphenyl-Based Phosphine Ligands

Compiled by Padmaja Gunda



This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Padmaja Gunda was born in Mancheril, India in 1977 and received her BSc degree in 1997 from Osmania University (India). She completed her MSc degree (Chemical Sciences) and MPhil (Chemistry) in 1999 and 2000, respectively, at the University of Hyderabad (India). She is currently working towards her PhD with Prof. Mahesh K. Lakshman at the City University of New York in the area of palladium-catalyzed C–C and C–N bond formation reactions of nucleoside derivatives. Her research interests include the development of new transition-metal-mediated reactions with an emphasis on the elucidation of reaction mechanisms. She thanks Prof. Mahesh K. Lakshman for valuable suggestions and constant encouragement.

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Introduction

A family of biphenyl ligands for transition-metal-catalyzed cross-coupling reactions is becoming well documented in the literature.^{1–5} Buchwald and colleagues invented and developed ligands **1** and **2**, which have found utility in C–C,² C–N^{2a,3a,3c} and C–O^{3b} bond formation.

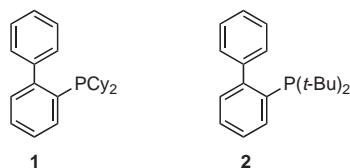


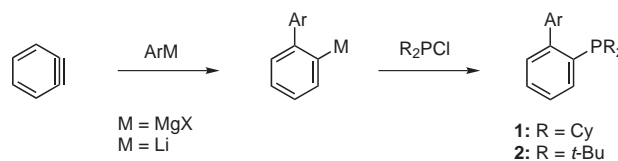
Figure 1 Biphenyl-based phosphine ligands

Palladium complexes supported by ligands **1** and **2** are efficient catalysts for C–C, and C–heteroatom (C–N and C–O) bond formation of aryl halides,^{2,3} triflates^{3a} and sulfonates.⁴ Catalysts supported by the ligands shown in Figure 1 are reactive, efficient and operationally simple to generate. Ligand **1** is effective for hindered substrates at very low catalyst loadings (0.000001 mol%)² compared with ligand **2**. The efficiency of catalysts derived from

ligands **1** and **2** is most likely due to a combination of several factors such as steric and electronic properties, basicity of the phosphorus and their abilities to form palladacycles.²

Preparation of the ligands **1** and **2**

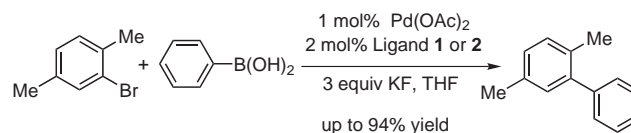
Ligands **1** and **2** were prepared in high yields in a one-pot transformation (Scheme 1) and are also now commercially available.^{2b} They are generally air-stable, white, crystalline solids that require no special handling. These ligands interact in unusual and interesting manners with the metal and thereby modulate the reactivity of the metal for various transformations. There is also a balance between steric and electronic properties among these compounds.^{2b}



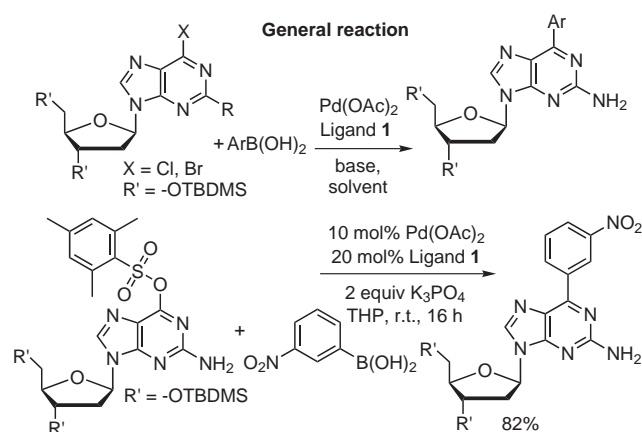
Scheme 1

Abstracts

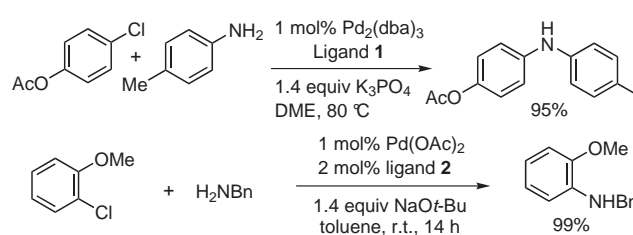
(A) Buchwald and co-workers have used biphenyl ligands **1** and **2** for palladium-catalyzed Suzuki reactions of arylhalides at room temperature.^{2b}



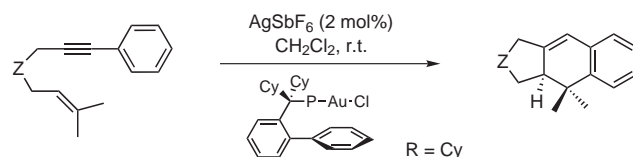
(B) Lakshman et al. extended the utility of these phosphine ligands to the class of nucleosides.⁴ Use of ligand **1** for palladium-catalyzed Suzuki–Miyaura cross-coupling reactions of nucleosides resulted in the C-6 aryl derivatives and yielded 80–90%. Ligand **2** was less effective.



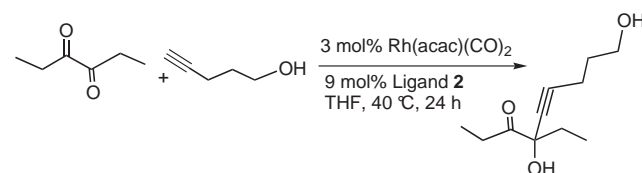
(C) Ligands **1** and **2** yield efficient catalytic systems for palladium-mediated amination of aryl chlorides, bromides and triflates.^{3a}



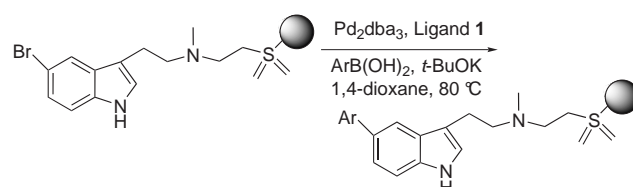
(D) Recently it was reported by Echavarren and co-workers that ligand **1** in a complex with Au(I) acts as an efficient catalyst to give a variety of cycloisomerization and addition derivatives. 1,3-Enynes or arylalkynes react at room temperature with alkenyl or an aryl groups in intramolecular [4+2] cycloaddition of to give hydridanes or linearly fused tricyclic systems.⁵



(E) Ligand **2** was also utilized in rhodium-catalyzed additions of alkynes to activated 1,2-diketones and aldehydes.⁶



(F) Ligand **1** was used in Pd-mediated Suzuki coupling reaction of resin-bound monomethylated tryptamine and arylboronic acid.⁷



References and Notes

- (1) (a) Tomori, H.; Fox, J. M.; Buchwald, S. L. *J. Org. Chem.* **2000**, *65*, 5334. (b) Huang, X.; Anderson, K. W.; Zim, D.; Jiang, L.; Klapars, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2003**, *125*, 6653.
- (2) (a) Wolfe, J. P.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **1999**, *38*, 2413. (b) Wolfe, J. P.; Singer, R. A.; Yang, B. H.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 9550.
- (3) (a) Wolfe, J. P.; Tomori, H.; Sadighi, J. P.; Yin, J.; Buchwald, S. L. *J. Org. Chem.* **2000**, *65*, 1158. (b) Aranyos, A.; Old, D. W.; Kiyomori, A.; Wolfe, J. P.; Sadighi, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 4369. (c) Strieter, E. R.; Blackmond, D. G.; Buchwald, S. L. *J. Am. Chem. Soc.* **2003**, *125*, 13978.
- (4) (a) Lakshman, M. K.; Hilmer, J. H.; Martin, J. Q.; Keeler, J. C.; Dinh, Y. Q. V.; Ngassa, F. N.; Russon, L. M. *J. Am. Chem. Soc.* **2001**, *123*, 7779. (b) Lakshman, M. K.; Thomson, P. F.; Nuqui, M. A.; Hilmer, J. H.; Sevova, N.; Boggess, B. *Org. Lett.* **2002**, *4*, 1479. (c) Gunda, P.; Russon, L. M.; Lakshman, M. K. *Angew. Chem. Int. Ed.* **2004**, *43*, 6372. (d) Lakshman, M. K.; Gunda, P.; Pradhan, P. *J. Org. Chem.* **2005**, *70*, 10329.
- (5) Nieto-Oberhuber, C.; López, S.; Echavarren, A. M. *J. Am. Chem. Soc.* **2005**, *127*, 6178.
- (6) Dhondi, P. K.; Chisholm, J. D. *Org. Lett.* **2006**, *8*, 67.
- (7) Wu, T. Y. H.; Schultz, P. G. *Org. Lett.* **2002**, *4*, 4033.