J|A|C|S COMMUNICATIONS

Published on Web 04/01/2010

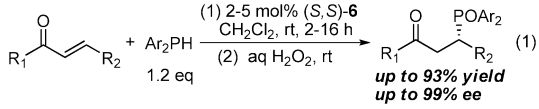
Palladium-Catalyzed Asymmetric Addition of Diarylphosphines to Enones toward the Synthesis of Chiral Phosphines

Jian-Jun Feng,[‡] Xue-Feng Chen,[†] Min Shi,[†,‡] and Wei-Liang Duan*[,†]

State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 LingLing Road, Shanghai 200032, China, and School of Chemistry and Molecular Engineering, East China University of Science and Technology, 130 Meilong Road, Shanghai 200237, China

Received January 22, 2010; E-mail: wlduan@mail.sioc.ac.cn

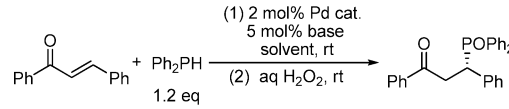
Chiral phosphines, as the most fundamental ligands coordinated to transition metals, have been extensively employed in asymmetric catalysis to convert achiral compounds into enantioenriched products with high efficiency and enantioselectivity.[1] However, the preparation of chiral phosphine ligands usually starts from stoichiometric amounts of chiral auxiliaries or involves optical resolution of racemates.[2] The synthesis of phosphorus ligands through asymmetric catalysis is rare.[3] Only recently have a few effective catalytic methods with high stereoselection (up to 99% ee) begun to appear, typical examples of which include asymmetric arylation and alkylation of secondary phosphines,[4,5] allylic phosphination,[6] and hydrophosphination of methacrylonitrile and enals.[7,8] In addition, several groups have reported the use of diaryl- or diallylphosphine oxide-containing substrates in asymmetric addition,[9] [2 + 2 + 2] cycloaddition,[10] hydrogenation,[11] and ring-closing metathesis processes[12] to provide optically active phosphine oxide compounds with high enantioselectivity, which are very useful precursors for chiral phosphines. However, to date there are no examples of catalytic asymmetric additions of diarylphosphines to β-substituted enones with stereoselection.[13] In this communication, we describe the first catalytic asymmetric addition of diarylphosphines to β-substituted enones using a pincer−palladium complex, providing chiral phosphine derivatives in good yields with excellent enantioselectivities (eq 1).[14,15]



(1)

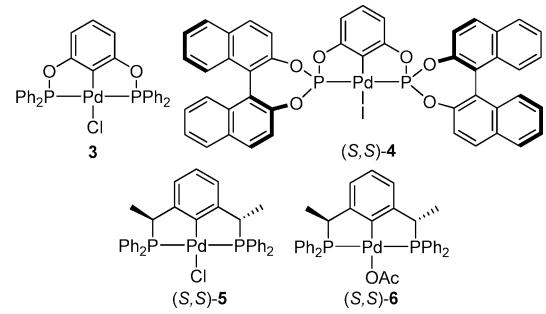
Our initial experiment began with the addition of diphenylphosphine to 1,3-diphenyl-2-propen-1-one as the model reaction to examine the effect of metal complexes as catalysts. After some investigation, because of the strong binding ability of diphenylphosphine and its adduct to transition metals, which may deactivate the catalyst by coordination or replacement of the ligand, the robust and stable pincer−palladium complex **3** was selected as the catalyst.[16] The reaction proceeded smoothly in the presence of 2 mol % **3**, furnishing the desired product in 70% yield (Table 1, entry 1). Thus, we started to screen various chiral pincer−palladium catalysts for this addition reaction. The employment of easily prepared complex (*S*,*S*)-**4**,[17] which is derived from optically active binaphthol, gave the product in moderate yield but no stereoselectivity (43% yield, 0% ee; entry 2). It was encouraging that the use of chiral pincer−palladium complex (*S*,*S*)-**5**[18] furnished the hydrophosphination product in excellent yield and ee (95% yield, 97% ee; entry 3). Changing the coordinating anion on palladium from chloride to acetate without additional base further improved the enantioselectivity to 99% (entry 4). The solvents had little influence on the product yield and ee (entries 5−8).

Table 1. Palladium-Catalyzed Addition of Diphenylphosphine to Chalcone



entry	catalyst	base	solvent	time (h)	yield (%)[a]	ee (%)[b]
1	**3**	K_2CO_3	CH_2Cl_2	24	70	−
2	(*S*,*S*)-**4**	K_2CO_3	CH_2Cl_2	24	42	0
3	(*S*,*S*)-**5**	K_2CO_3	CH_2Cl_2	2	95	97
4	(*S*,*S*)-**6**	none	CH_2Cl_2	2	93	99
5	(*S*,*S*)-**6**	none	toluene	2	88	98
6	(*S*,*S*)-**6**	none	THF	2	83	99
7	(*S*,*S*)-**6**	none	*t*-BuOH	2	93	99
8	(*S*,*S*)-**6**	none	CH_3CN	2	91	99

[a] Isolated yields. [b] Determined by HPLC with hexane/2-propanol.



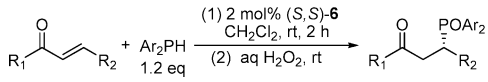
Under these optimum conditions with (*S*,*S*)-**6** as the catalyst, various enones having electron-donating or -withdrawing groups on the aromatic ring smoothly react with diphenylphosphine, providing the chiral phosphine oxides uniformly in high yields with excellent stereoselectivities (63−93% yield, 90−99% ee; Table 2, entries 1−10). In addition, this process is also effective for the enone substrate bearing a methyl moiety attached to the carbonyl group, which gives the desired adduct in 71% yield with 96% ee (entry 11).[19] Furthermore, besides diphenylphosphine, both electron-rich and -poor diarylphosphines can be used as nucleophiles toward enones under the current mild conditions, leading to the corresponding products with excellent yields and enantioselectivities (86−92% yield, 94−96% ee; entries 12 and 13).

This catalytic method was applied to the enantioselective synthesis of a chiral pincer−PdCl complex[16] with >99% ee and 71% yield in one step (eq 2); this complex proved to be an effective

[†] Shanghai Institute of Organic Chemistry.
[‡] East China University of Science and Technology.

10.1021/ja100606v

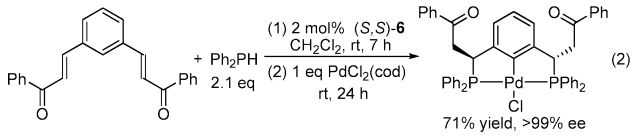
Table 2. Palladium-Catalyzed Asymmetric Addition of Diarylphosphines to Enones



entry	R_1	R_2	Ar	yield (%)[a]	ee (%)[b,c]
1	Ph	Ph	Ph	93	99
2	*p*-BrC_6H_4	Ph	Ph	89	99
3	*p*-$MeOC_6H_4$	Ph	Ph	75	98
4	*m*-BrC_6H_4	Ph	Ph	93	97
5	*p*-$O_2NC_6H_4$	Ph	Ph	78	95
6	Ph	*p*-BrC_6H_4	Ph	90	98
7	Ph	*p*-$O_2NC_6H_4$	Ph	88	99
8	Ph	*m*-BrC_6H_4	Ph	90	99
9[d]	Ph	*o*-$MeOC_6H_4$	Ph	69	90
10[d]	Ph	*p*-MeC_6H_4	Ph	63	90
11	Me	*p*-BrC_6H_4	Ph	71	96
12	Ph	Ph	*p*-$MeOC_6H_4$	86	94
13	Ph	Ph	*p*-ClC_6H_4	92	96

[a] Isolated yields. [b] Determined by HPLC with hexane/2-propanol. [c] The absolute configurations of products were determined to be *S* according to the X-ray crystal diffraction analysis of the product in entry 2; see the Supporting Information for details. [d] Using 5 mol % catalyst and 16 h reaction time.

catalyst for the addition of diphenylphosphine to chalcone under the current conditions without further optimization (80% yield, 64% ee).



A proposed catalytic cycle for this reaction is illustrated in Figure 1. On the basis of a preliminary NMR study,[20] catalyst **6** may act as a base toward the diarylphosphine instead of a Lewis acid toward the enone. Thus, the transphosphination between the diarylphosphine and the pincer−PdOAc complex affords the palladium phosphido complex. Next, addition of the diarylphosphido group on palladium to the enone provides an oxa-π-allylpalladium intermediate, which undergoes protonolysis with acetic acid in the system, leading to the formation of the phosphine product along with regeneration of the active catalyst **6**.

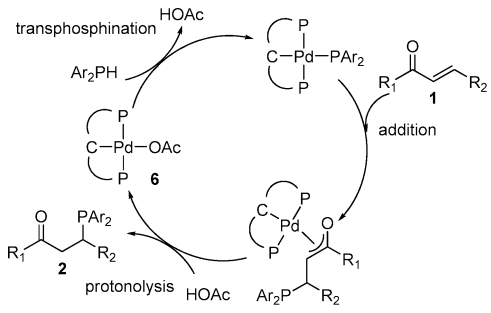


Figure 1. Proposed catalytic cycle for the palladium-catalyzed addition of diarylphosphines to enones.

In summary, we have developed a palladium-catalyzed asymmetric addition of diarylphosphines to β-substituted enones that provides the corresponding chiral phosphine derivatives in high yields with excellent enantioselectivities. The current process can tolerate various substrates under mild conditions, and the products can be used as chiral phosphine ligands for asymmetric catalysis. Further investigation of the detailed reaction mechanism and application of this pincer−palladium catalyst in other asymmetric reactions are in progress.

Acknowledgment. We thank the NSFC (20902099), the National Basic Research Program of China (973 Program 2010CB833300), and SIOC for financial support.

Supporting Information Available: Experimental procedures, product characterization data, and X-ray data (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) *Comprehensive Asymmetric Catalysis I−III*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer-Verlag: New York, 1999.
(2) *Phosphorus Ligands in Asymmetric Catalysis: Synthesis and Applications*; Börner, A., Ed.; Wiley-VCH: Weinheim, Germany, 2008; Vols. 1−3.
(3) For reviews, see: (a) Glueck, D. S. *Chem.—Eur. J.* **2008**, *14*, 7108. (b) Glueck, D. S. *Synlett* **2007**, 2627. (c) Crépy, K. V. L.; Imamoto, T. *Top. Curr. Chem.* **2003**, *229*, 1. For leading examples, see: (d) Kovacik, I.; Wicht, D. K.; Grewal, N. S.; Glueck, D. S.; Incarvito, C. D.; Guzei, I. A.; Rheingold, A. L. *Organometallics* **2000**, *19*, 950. (e) Scriban, C.; Kovacik, I.; Glueck, D. S. *Organometallics* **2005**, *24*, 4871. (f) Bartoli, G.; Bosco, M.; Carlone, A.; Locatelli, M.; Mazzanti, A.; Sambri, L.; Melchiorre, P. *Chem. Commun.* **2007**, 722.
(4) (a) Moncarz, J. R.; Laritcheva, N. F.; Glueck, D. S. *J. Am. Chem. Soc.* **2002**, *124*, 13356. (b) Blank, N. F.; Moncarz, J. R.; Brunker, T. J.; Scriban, C.; Anderson, B. J.; Amir, O.; Glueck, D. S.; Zakharov, L. N.; Golen, J. A.; Incarvito, C. D.; Rheingold, A. L. *J. Am. Chem. Soc.* **2007**, *129*, 6847. (c) Chan, V. S.; Bergman, R. G.; Toste, F. D. *J. Am. Chem. Soc.* **2007**, *129*, 15122.
(5) (a) Chan, V. S.; Stewart, I. C.; Bergman, R. G.; Toste, F. D. *J. Am. Chem. Soc.* **2006**, *128*, 2786. (b) Scriban, C.; Glueck, D. S. *J. Am. Chem. Soc.* **2006**, *128*, 2788. (c) Chan, V. S.; Chiu, M.; Bergman, R. G.; Toste, F. D. *J. Am. Chem. Soc.* **2009**, *131*, 6021.
(6) Butti, P.; Rochat, R.; Sadow, A. D.; Togni, A. *Angew. Chem., Int. Ed.* **2008**, *47*, 4878.
(7) (a) Sadow, A. D.; Haller, I.; Fadini, L.; Togni, A. *J. Am. Chem. Soc.* **2004**, *126*, 14704. (b) Sadow, A. D.; Togni, A. *J. Am. Chem. Soc.* **2005**, *127*, 17012.
(8) (a) Carlone, A.; Bartoli, G.; Bosco, M.; Sambri, L.; Melchiorre, P. *Angew. Chem., Int. Ed.* **2007**, *46*, 4504. (b) Ibrahem, I.; Rios, R.; Vesely, J.; Hammar, P.; Eriksson, L.; Himo, F.; Cordova, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 4507.
(9) (a) Nishimura, T.; Hirabayashi, S.; Yasuhara, Y.; Hayashi, T. *J. Am. Chem. Soc.* **2006**, *128*, 2556. (b) Nishimura, T.; Guo, X.-X.; Hayashi, T. *Chem.—Asian J.* **2008**, *3*, 1505. (c) Kawamoto, T.; Hirabayashi, S.; Guo, X.-X.; Nishimura, T.; Hayashi, T. *Chem. Commun.* **2009**, 3528.
(10) (a) Nishida, G.; Noguchi, K.; Hirano, M.; Tanaka, K. *Angew. Chem., Int. Ed.* **2007**, *46*, 3951. (b) Nishida, G.; Noguchi, K.; Hirano, M.; Tanaka, K. *Angew. Chem., Int. Ed.* **2008**, *47*, 3410.
(11) Cheruku, P.; Paptchikhine, A.; Church, T. L.; Andersson, P. G. *J. Am. Chem. Soc.* **2009**, *131*, 8285.
(12) Harvey, J. S.; Malcolmson, S. J.; Dunne, K. S.; Meek, S. J.; Thompson, A. L.; Schrock, R. R.; Hoveyda, A. H.; Gouverneur, V. *Angew. Chem., Int. Ed.* **2009**, *48*, 762.
(13) For a review of 1,4-addition reaction of phosphorus nucleophiles to electron-deficient olefins, see: (a) Enders, D.; Saint-Dizier, A.; Lannou, M,-I.; Lenzen, A. *Eur. J. Org. Chem.* **2006**, 29. For examples of asymmetric addition of phosphites to enones and nitroalkenes, see: (b) Zhao, D.; Yuan, Y.; Chan, A. S. C.; Wang, R. *Chem.—Eur. J.* **2009**, *15*, 2738. (c) Terada, M.; Ikehara, T.; Ube, H. *J. Am. Chem. Soc.* **2007**, *129*, 14112. (d) Zhu, Y.; Malerich, J. P.; Rawal, V. H. *Angew. Chem., Int. Ed.* **2010**, *49*, 153.
(14) For examples of nonasymmetric addition of silylphosphines to enones, see: (a) Trepohl, V. T.; Oestreich, M. *Chem. Commun.* **2007**, 3300. (b) Trepohl, V. T.; Mori, S.; Itami, K.; Oestreich, M. *Org. Lett.* **2009**, *11*, 1091. For asymmetric hydrophosphination of enones using a stoichiomeric amount of chiral palladium complex, see: (c) Liu, F.; Pullarkat, S. A.; Li, Y.; Chen, S.; Yuan, M.; Lee, Z.; Leung, P.-H. *Organometallics* **2009**, *28*, 3941.
(15) For ease of operation in the experiments, the phosphines were oxidized to the corresponding phosphine oxides for analysis.
(16) For a review of pincer−metal complexes, see: Albrecht, M.; van Koten, G. *Angew. Chem., Int. Ed.* **2001**, *40*, 3750.
(17) Wallner, O. A.; Olsson, V. J.; Eriksson, L.; Szabó, K. J. *Inorg. Chim. Acta* **2006**, *359*, 1767.
(18) For the synthesis and application of **6**, see: (a) Longmire, J. M.; Zhang, X. *Tetrahedron Lett.* **1997**, *38*, 1725. (b) Longmire, J. M.; Zhang, X.; Shang, M. *Organometallics* **1998**, *17*, 4374.
(19) Moderate stereoselectivities were observed for 2-cyclohexen-1-one (52% ee) and (*E*)-3-isopropyl-1-phenylprop-2-en-1-one (36% ee).
(20) The formation of the pincer−$PdPPh_2$ intermediate from the reaction of catalyst **6** with diphenylphosphine was observed and confirmed by ^{31}P NMR experiments (see the Supporting Information for details).

JA100606V