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Asymmetric Synthesis of *P*-Stereogenic Diarylphosphinites by Palladium-Catalyzed Enantioselective Addition of Diarylphosphines to Benzoquinones

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Supporting Information

ABSTRACT: The reaction of phenyl(2,4,6-trimethylphenyl)phosphine with a substituted benzoquinone in the presence of a chiral phosphapalladacycle complex as a catalyst and triethylamine in chloroform at −45 °C proceeded in a new type of addition manner to give a high yield of a 4-hydroxyphenyl phenyl(2,4,6-trimethylphenyl)phosphinite with 98% enantioselectivity, which is a versatile intermediate readily convertible into various phosphines and their derivatives with high enantiomeric purity.

It has been well documented that chiral phosphorus compounds with high enantiomeric purities are a very important class of compounds, typically as chiral ligands for metal-catalyzed asymmetric reactions.[1] Of the chiral phosphorus compounds, *P*-stereogenic ones have attracted considerable attention owing to their excellent enantioselectivities observed in the catalytic asymmetric reactions.[1] Asymmetric synthesis of *P*-stereogenic compounds is one of the most challenging subjects in synthetic organic chemistry as well as in organophosphorus chemistry,[2,3] and their synthesis by asymmetric catalysis has been extensively studied because of its high efficiency.[4] The dynamic kinetic resolution of racemic secondary phosphines HPR^1R^2 upon P−C bond formation with alkyl or aryl halides $X-R^3$ giving *P*-stereogenic chiral phosphines $P^*R^1R^2R^3$ has been studied with chiral palladium,[5] platinum,[6] and ruthenium[7] complexes as catalysts (Scheme 1a). Catalytic asymmetric conjugate addition of racemic secondary phosphines to electron-deficient olefins has been also reported to produce *P*-stereogenic phosphines by the dynamic kinetic resolution.[8] In this Communication, we report a new type of catalytic asymmetric reaction where the P−H bond in diarylphosphines HPR^1R^2 is converted into a P−O bond by the Pd-catalyzed reaction with a benzoquinone to give diarylphosphinites with high enantiomeric purity (Scheme 1b). The resulting chiral diarylphosphinites are readily convertible into chiral tertiary phosphines and so on.

During our studies on the Pd-catalyzed asymmetric hydrophosphination of electron-deficient olefins,[9,10] it was found that the addition of a racemic diarylphosphine, where one of the two aryl groups is sterically demanding, to quinones in the presence of a palladium catalyst proceeds in a 1,6-addition manner to give a high yield of *O*-phosphination product with high enantioselectivity. Thus, phenyl(2,4,6-trimethylphenyl)phosphine (*rac*-**1a**) was allowed to react with 2,5-diphenylbenzoquinone (**2m**) (1.05 equiv to **1a**) in the presence of a phosphapalladacycle complex **PdL1***[9b,11] (5 mol%), which is one of the most catalytically active and enantioselective catalysts for asymmetric hydrophosphination of α,β-unsaturated ketones,[9] and triethylamine in chloroform at −45 °C for 12 h (entry 1 in Table 1). The $^{31}P\{^1H\}$ NMR analysis of the reaction mixture showed that all of the phosphine **1a** (δ −75.9 ppm in $CHCl_3$) was selectively converted into a new compound which has a new ^{31}P resonance at 115.7 ppm. It turned out that the reaction product is 2,5-diphenyl-4-hydroxyphenyl phenyl(2,4,6-trimethylphenyl)phosphinite (**3am**).[12] Isolation of the phosphinite **3am** in a chemically pure form is difficult due to its oxidation during the workup, and hence the reaction mixture was treated with sulfur to allow us to isolate the reaction product as sulfide **4am** in 96% yield. The enantioselectivity of the reaction is very high, the sulfide being obtained with 98% ee. The reaction product, phosphinite **3am**, can be also isolated pure as phosphinate **5am** by oxidation with H_2O_2. The absolute configuration of phosphinite **3am** was determined to be (*S*) by X-ray crystal structure analysis of

Scheme 1. Catalytic Asymmetric Synthesis of *P*-Stereogenic Phosphines

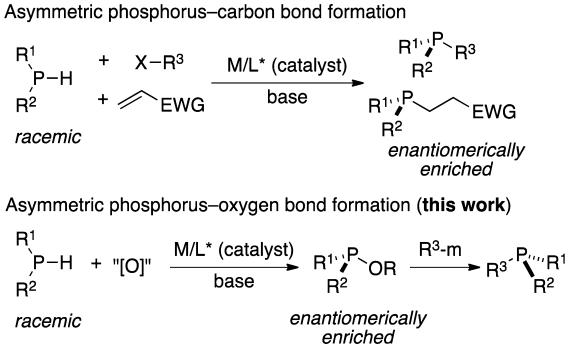

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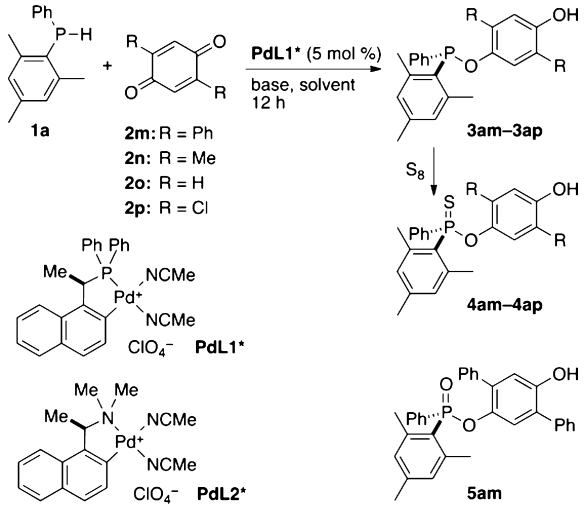
Table 1. Palladium-Catalyzed Asymmetric Addition of Diarylphosphine 1a to Benzoquinones 2[a]



entry	quinone 2	base	solvent	temp (°C)	product	% yield[b] (% ee)[c]
1	**2m**	Et_3N	$CHCl_3$	−45	**3am**	96 (98)
2	**2n**	Et_3N	$CHCl_3$	−45	**3an**	43 (87)
3	**2o**	Et_3N	$CHCl_3$	−45	**3ao**	95 (68)
4	**2p**	Et_3N	$CHCl_3$	−45	**3ap**	92 (7)
5	**2m**	—	$CHCl_3$	−45	**3am**	<3 (—)
6	**2m**	*i*-Pr_2NEt	$CHCl_3$	−45	**3am**	95 (97)
7	**2m**	Proton Sponge	$CHCl_3$	−45	**3am**	47 (78)
8	**2m**	K_2CO_3	$CHCl_3$	−45	**3am**	95 (97)
9	**2m**	Et_3N	CH_2Cl_2	−45	**3am**	96 (89)
10	**2m**	Et_3N	THF	−45	**3am**	74 (78)
11	**2m**	Et_3N	MeCN	−45	**3am**	96 (89)
12	**2m**	Et_3N	$CHCl_3$	−60	**3am**	96 (98)
13	**2m**	Et_3N	$CHCl_3$	−30	**3am**	96 (95)
14[d]	**2m**	Et_3N	$CHCl_3$	−45	**3am**	40 (2)

[a]Reaction conditions: **1a** (0.30 mmol), **2** (0.32 mmol), Pd catalyst **PdL1*** (5 mol%), base (0.30 mmol), solvent (7.5 mL) for 12 h. [b]Isolated yield of sulfide **4** after treatment of the reaction mixture with sulfur. [c]Determined by chiral HPLC analysis of sulfide **4**. [d]Reaction with **PdL2*** (5 mol%) as a catalyst.

palladium complex **7** formed by addition of enantiomerically pure palladacycle chloro-bridge dimer **6**[13] to the reaction mixture (Figure 1).

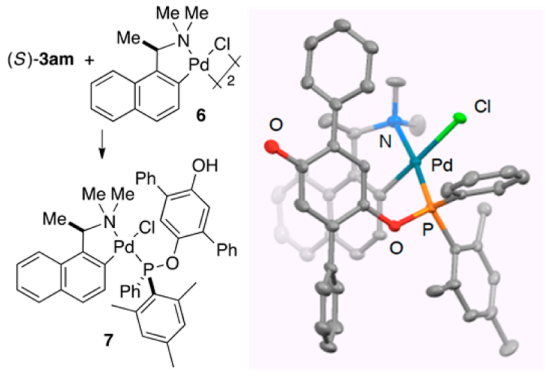
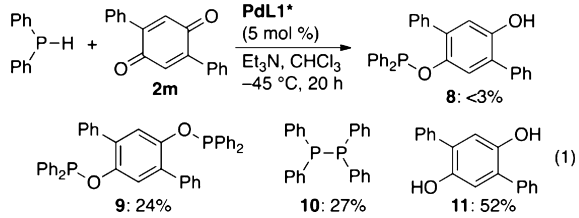


Figure 1. X-ray structure of palladacycle–phosphinite complex **7**.

The phosphorus–oxygen bond formation producing phosphinite was also observed in the Pd-catalyzed reaction of phosphine **1a** with other quinones, but the reaction was slower with 2,5-dimethylbenzoquinone (**2n**) at −45 °C (Table 1, entry 2). The enantioselectivity was lower with unsubstituted benzoquinone **2o** and dichloro-substituted **2p**, although they gave high yields of the corresponding phosphinites (entries 3 and 4). Screening of reaction conditions in the reaction of phosphine **1a** with 2,5-diphenylbenzoquinone (**2m**) showed that the presence of base is essential for the reaction to proceed (entries 5–8).[14] Diisopropylethylamine and potassium carbonate can be used as well as triethylamine. Chloroform is a solvent of choice. The yield and/or enantioselectivity was lower in the reactions in dichloromethane, THF, and acetonitrile (entries 9–11). The enantioselectivity was not strongly dependent on the reaction temperature between −30 and −60 °C (entries 1, 12, and 13). Use of azapalladacycle **PdL2*** [9a,15] in place of phosphapalladacycle **PdL1*** gave poor results, with low conversion and almost no enantioselectivity (entry 14).[16]

The selective formation of 2,5-diphenyl-4-hydroxyphenyl phosphinite in the present Pd-catalyzed oxidation with quinone **2m** was observed only with diarylphosphines where one of the aryl groups is a sterically demanding aryl group. The reaction of diphenylphosphine with **2m** under the conditions used in entry 1 of Table 1 gave a mixture consisting mainly of diphosphinite **9** (24%), diphosphine (Ph_2P-PPh_2, **10**; 27%), and hydroquinone **11** (52%), together with a trace amount of 4-hydroxyphenyl phosphinite **8** (eq 1).[17] Thus, quinone **2m**



oxidized the secondary phosphine into diphosphinite and diphosphine rather than into the expected phosphinite in the reaction of diphenylphosphine. The Pd-catalyzed oxidation with quinone derivatives did not proceed for *tert*-butyl(phenyl)-phosphine, the starting phosphine being recovered unreacted.

The results obtained for the reaction of diarylphosphines **1**, which gave the corresponding diarylphosphinites **3** in high yields, are summarized in Table 2. The enantioselectivity is high (≥95% ee) in the reaction of phenyl(aryl)phosphines **1a–1e**, where the aryl group is 2,6-disubstituted phenyl or a 2-substituted 1-naphthyl group (entries 1–5). The enantioselectivity was much lower for those substituted with ortho-monosubstituted aryl groups, although the yields giving the phosphinites are high (entries 6 and 7). The reaction of aryl(2,4,6-trimethylphenyl)phosphines **1h** and **1i** also proceeded with high selectivity to give high yields of the corresponding diarylphosphinites with 81–91% ee (entries 8 and 9).

The present catalytic asymmetric transformation, where the racemic starting compound forms the nonracemic product, should involve a kinetic resolution or dynamic kinetic resolution mechanism. The reaction of **1a** with **2m** giving **3am** was quenched before completion by addition of mCPBA to the reaction mixture to see the enantiomeric purity of unreacted diarylphosphine **1a** (eq 2). The diarylphosphine

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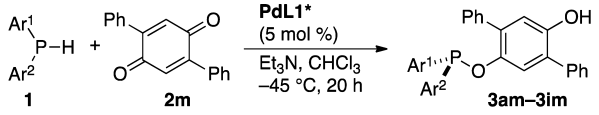
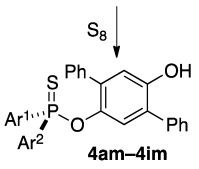
Table 2. Palladium-Catalyzed Asymmetric Addition of Diarylphosphines 1 to 2,5-Diphenylbenzoquinone 2m[a]

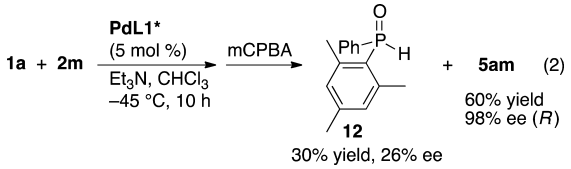


1a: Ar^1 = Ph, Ar^2 = 2,4,6-$Me_3C_6H_2$
1b: Ar^1 = Ph, Ar^2 = 2,6-$Me_2C_6H_3$
1c: Ar^1 = Ph, Ar^2 = 2,3,5,6-Me_4C_6H
1d: Ar^1 = Ph, Ar^2 = 2,3,4,5,6-Me_5C_6
1e: Ar^1 = Ph, Ar^2 = 2-Me-1-naphthyl
1f: Ar^1 = Ph, Ar^2 = 2-MeC_6H_4
1g: Ar^1 = Ph, Ar^2 = 1-naphthyl
1h: Ar^1 = 4-MeC_6H_4, Ar^2 = 2,4,6-$Me_3C_6H_2$
1i: Ar^1 = 2-thienyl, Ar^2 = 2,4,6-$Me_3C_6H_2$



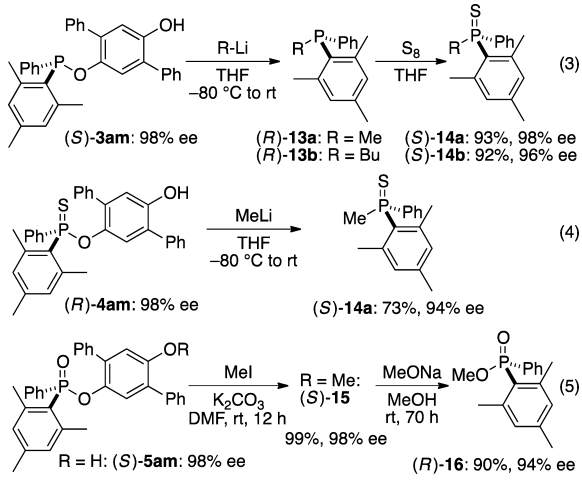
entry	phosphine **1**	product **3**	yield (%)[b] of **4**	ee (%)[c] of **4**
1	**1a**	**3am**	96	98 (*S*)
2	**1b**	**3bm**	95	98
3	**1c**	**3cm**	95	97
4	**1d**	**3dm**	95	97
5	**1e**	**3em**	94	95
6	**1f**	**3fm**	96	43
7	**1g**	**3gm**	95	24
8[d]	**1h**	**3hm**	93	91
9	**1i**	**3im**	94	81

[a]Reaction conditions: **1** (0.30 mmol), **2m** (0.32 mmol), **PdL1*** (5 mol %), Et_3N (0.30 mmol), $CHCl_3$ (7.5 mL) at −45 °C for 20 h. [b]Isolated yield of sulfide **4** after treatment of the reaction mixture with sulfur. [c]Determined by chiral HPLC analysis of sulfide **4**. [d]At 0 °C.



oxide **12** and phosphinate **5am** obtained by stopping the reaction at 63% conversion[18] of **1a** were 26% ee and 98% ee, respectively. The low ee of **12** and the same ee of **5am** as that at full conversion demonstrate that the present reaction is classified as a dynamic kinetic resolution. Although the catalytic reaction pathway remains to be clarified, the *P*-stereogenic center of diarylphosphine undergoes racemization on the palladium catalyst under the present conditions.[19]

The phenyl(2,4,6-trimethylphenyl)phosphinite (*S*)-**3am** obtained with high enantiomeric purity (98% ee) by the present catalytic asymmetric reaction was subjected to reaction with alkyllithiums to demonstrate its synthetic utility (eq 3). The reaction with methyllithium proceeded with perfect inversion of configuration[20] to give a high yield of (*R*)-methyl(phenyl)-(2,4,6-trimethylphenyl)phosphine (*R*)-**13a** with 98% ee, whose absolute configuration was determined by X-ray analysis of the sulfide (*S*)-**14a**.[21] The reaction with butyllithium also took place with high stereospecificity. The inversion of stereochemistry was also observed in the methylation of thiophosphinate (*R*)-**4am** with methyllithium to give (*S*)-**14a** of 94% ee (eq 4).[22] Ester exchange proceeded successfully with high stereospecificity in the reaction of phosphinate (*S*)-**15**, which was obtained by methylation of the phenol oxygen in **5am**, to give methyl phosphinate **16** with 94% ee (eq 5). The high stereospecificity may be ascribed to the phenoxide being a good leaving group, which promotes the reaction under mild



conditions and prevents the product from being racemized by further ester exchange reaction.[23]

In summary, we have developed a new type of catalytic asymmetric transformation where diarylphosphines are converted into enantiomerically enriched diarylphosphinites in the reaction with 2,5-diphenylbenzoquinone catalyzed by a chiral phosphapalladacycle complex.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedures, compound characterization data, and crystallographic data (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

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■ REFERENCES

(1) Selected recent reviews: (a) Lühr, S.; Holz, L.; Börner, A. *ChemCatChem* **2011**, *3*, 1708. (b) *Privileged Chiral Ligands and Catalysts*;Zhou, Q.-L., Ed.; Wiley-VCH: Weinheim, 2011. (c) *Catalytic Asymmetric Synthesis*, 3rd ed.; Ojima, I., Ed.; Wiley: Hoboken, NJ, 2010. (d) *Phosphorus Ligands in Asymmetric Catalysis*; Börner, A., Ed.; Wiley-VCH: Weinheim, 2008; Vols. *I*–*III*. (e) Guiry, P. J.; Saunders, C. P. *Adv. Synth. Catal.* **2004**, *346*, 497. (f) Tang, W.; Zhang, X. *Chem. Rev.* **2003**, *103*, 3029.

(2) Reviews on *P*-stereogenic phosphorus compounds: (a) Kolodiazhnyi, O. I. *Tetrahedron: Asymmetry* **2012**, *23*, 1. (b) Jugé, S. *Phosphorus, Sulfur Silicon* **2008**, *183*, 233. (c) Grabulosa, A.; Granell, J.; Muller, G. *Coord. Chem. Rev.* **2007**, *251*, 25. (d) Wozniak, L. A.; Okruszek, A. *Chem. Soc. Rev.* **2003**, *32*, 158. (e) Kolodiazhnyi, O. I. *Tetrahedron: Asymmetry* **1998**, *9*, 1279. (f) Pietrusiewicz, K. M.; Zablocka, M. *Chem. Rev.* **1994**, *94*, 1375.

(3) Recent examples of stoichiometric asymmetric synthesis of *P*-stereogenic compounds: (a) Han, Z. S.; Goyal, N.; Herbage, M. A.; Sieber, J. D.; Qu, B.; Xu, Y.; Li, Z.; Reeves, J. T.; Desrosiers, J.-N.; Ma, S.; Grinberg, N.; Lee, H.; Mangunuru, H. P. R.; Zhang, Y.; Krishnamurthy, D.; Lu, B. Z.; Song, J. J.; Wang, G.; Senanayake, C. H. *J. Am. Chem. Soc.* **2013**, *135*, 2474. (b) Berger, O.; Montchamp, J.-

L. *Angew. Chem., Int. Ed.* **2013**, *52*, 11377. (c) Adam, H.; Collins, R. C.; Jones, S.; Warner, C. J. A. *Org. Lett.* **2011**, *13*, 6576. (d) Gatineau, D.; Giordano, L.; Buono, G. *J. Am. Chem. Soc.* **2011**, *133*, 10728. (e) Gammon, J. J.; Gessner, V. H.; Barker, G. R.; Granander, J.; Whitwood, A. C.; Strohmann, C.; O'Brien, P.; Kelly, B. *J. Am. Chem. Soc.* **2010**, *132*, 13922. (f) Bauduin, C.; Moulin, D.; Kaloun, E. B.; Darcel, C.; Jugé, S. *J. Org. Chem.* **2003**, *68*, 4293. (g) Ohashi, A.; Kikuchi, S.-I.; Yasutake, M.; Imamoto, T. *Eur. J. Org. Chem.* **2002**, 2535. (h) Moulin, D.; Bago, S.; Bauduin, C.; Darcel, C.; Jugé, S. *Tetrahedron: Asymmetry* **2000**, *11*, 3939.

(4) Reviews on catalytic asymmetric synthesis of *P*-stereogenic compounds: (a) Harvey, J. S.; Gouverneur, V. *Chem. Commun.* **2010**, *46*, 7477. (b) Glueck, D. S. *Chem.—Eur. J.* **2008**, *14*, 7108. (c) Glueck, D. S. *Synlett* **2007**, 2627.

(5) (a) Moncarz, J. R.; Laritcheva, N. F.; Glueck, D. S. *J. Am. Chem. Soc.* **2002**, *124*, 13356. (b) Brunker, T. J.; Anderson, B. J.; Blank, N. F.; Glueck, D. S.; Rheingold, A. L. *Org. Lett.* **2007**, *9*, 1109. (c) 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. (d) Korff, C.; Helmchen, G. *Chem. Commun.* **2004**, 530.

(6) (a) Scriban, C.; Glueck, D. S. *J. Am. Chem. Soc.* **2006**, *128*, 2788. (b) Scriban, C.; Glueck, D. S.; Golen, J. A.; Rheingold, A. L. *Organometallics* **2007**, *26*, 1788. (c) Anderson, B. J.; Glueck, D. S.; DiPasquale, A. G.; Rheingold, A. L. *Organometallics* **2008**, *27*, 4992. (d) Chapp, T. W.; Glueck, D. S.; Golen, J. A.; Moore, C. E.; Rheingold, A. L. *Organometallics* **2010**, *29*, 378.

(7) (a) Chan, V. S.; Stewart, I. C.; Bergman, R. G.; Toste, F. D. *J. Am. Chem. Soc.* **2006**, *128*, 2786. (b) Chan, V. S.; Chiu, M.; Bergman, R. G.; Toste, F. D. *J. Am. Chem. Soc.* **2009**, *131*, 6021.

(8) (a) Kovacik, I.; Wicht, D. K.; Grewal, N. S.; Glueck, D. S. *Organometallics* **2000**, *19*, 950. (b) Scriban, C.; Kovacik, I.; Glueck, D. S. *Organometallics* **2005**, *24*, 4871.

(9) (a) Huang, Y.; Pullarkat, S. A.; Li, Y.; Leung, P. H. *Chem. Commun.* **2010**, *46*, 6950. (b) Huang, Y.; Chew, R. J.; Li, Y.; Pullarkat, S. A.; Leung, P. H. *Org. Lett.* **2011**, *13*, 5862. (c) Huang, Y.; Pullarkat, S. A.; Li, Y.; Leung, P. H. *Inorg. Chem.* **2012**, *51*, 2533. (d) Xu, C.; Kennard, G. J. H.; Hennersdorf, F.; Li, Y.; Pullarkat, S. A.; Leung, P. H. *Organometallics* **2012**, *31*, 3022. (e) Huang, Y.; Pullarkat, S. A.; Teong, S.; Chew, R. J.; Li, Y.; Leung, P. H. *Organometallics* **2012**, *31*, 4871. (f) Huang, Y.; Chew, R. J.; Pullarkat, S. A.; Li, Y.; Leung, P. H. *J. Org. Chem.* **2012**, *77*, 6849. (g) Chew, R. J.; Huang, Y.; Li, Y.; Pullarkat, S. A.; Leung, P. H. *Adv. Synth. Catal.* **2013**, *355*, 1403.

(10) Examples of transition-metal-catalyzed asymmetric hydrophosphination reported by other groups: (a) Feng, J.-J.; Chen, X.-F.; Shi, M.; Duan, W.-L. *J. Am. Chem. Soc.* **2010**, *132*, 5562. (b) Du, D.; Duan, W.-L. *Chem. Commun.* **2011**, *47*, 11101. (c) Lu, J.; Ye, J.; Duan, W.-L. *Chem. Commun.* **2014**, *50*, 698 and their previous reports cited therein. (d) Yang, M.-J.; Liu, Y.-J.; Gong, J.-F.; Song, M.-P. *Organometallics* **2011**, *30*, 3793. (e) Sadow, A. D.; Togni, A. *J. Am. Chem. Soc.* **2005**, *127*, 17012. (f) Sadow, A. D.; Haller, I.; Fadini, L.; Togni, A. *J. Am. Chem. Soc.* **2004**, *126*, 14704.

(11) Ng, J. K. P.; Tan, G. K.; Vittal, J. J.; Leung, P. H. *Inorg. Chem.* **2003**, *42*, 7674.

(12) The reaction of P(O)−H compounds, typically $(EtO)_2P(O)H$, with quinones has been reported to give *O*-phosphoryl hydroquinone derivatives in the presence of triethylamine: Xiong, B.; Shen, R.; Goto, M.; Yin, S.-F.; Han, L.-B. *Chem.—Eur. J.* **2012**, *18*, 16902.

(13) (a) Dupont, J.; Consorti, C. S.; Spencer, J. *Chem. Rev.* **2005**, *105*, 2527. (b) Allen, D. G.; McLaughlin, G. M.; Robertson, G. B.; Steffen, W. L.; Salem, G.; Wild, S. B. *Inorg. Chem.* **1982**, *21*, 1007.

(14) It has been proposed that the base deprotonates the Pd-coordinated $HPAr_2$ to generate a reactive phosphide species. See ref 9.

(15) Chooi, S. Y. M.; Leung, P. H.; Lim, C. C.; Mok, K. F.; Quek, G. H.; Sim, K. Y.; Tan, M. K. *Tetrahedron: Asymmetry* **1992**, *3*, 529.

(16) Under the reaction conditions shown in entry 14, $Pd(PPh_3)_4$ gave 90% yield of **4am**, while the yield of **4am** was low (<10%), with a Pd(0)(binap) complex (generated from $Pd(dba)_2$ and binap) and cationic Pd(II) complexes generated from $Pd(MeCN)_4(ClO_4)_2/2PPh_3$ and $Pd(MeCN)_4(ClO_4)_2$/binap.

(17) The products **9** and **10** were isolated and characterized as their sulfides after treatment of the reaction mixture with sulfur.

(18) The conversion was determined by $^{31}P\{^1H\}$ NMR of the reaction mixture. At 97% conversion, recovered phosphine **1a** (isolated as oxide **12**) was 84% ee. The racemization of secondary phosphines has been discussed: (a) Bader, A.; Pabel, M.; Willis, A. C.; Wild, S. B. *Inorg. Chem.* **1996**, *35*, 3874. (b) Albert, J.; Cadena, J. M.; Granell, J.; Muller, G.; Panyella, D.; Sañudo, C. *Eur. J. Inorg. Chem.* **2000**, 1283.

(19) Mechanisms involving the kinetic resolution steps have been discussed in detail in the catalytic asymmetric P−C bond-forming reactions of secondary phosphines. See ref 4.

(20) The inversion of stereochemistry has been reported in the reaction of menthyl phosphinites with alkyllithiums. Some examples: (a) Omelanczuk, J.; Perlikowska, W.; Mikolajczyk, M. *J. Chem. Soc., Chem. Commun.* **1980**, 24. (b) Chodkiewicz, W.; Jore, D.; Pierrat, A.; Wodzki, W. *J. Organomet. Chem.* **1979**, *174*, C21. See also review articles shown in ref 2.

(21) See Supporting Information.

(22) While the inversion of configuration on phosphorus has been well established in the reaction of phosphinates ($R^1R^2P(O)OR$) with organometallic reagents,[2] only scattered examples have been studied on the stereochemistry in the reaction of thiophosphinates ($R^1R^2P(S)OR$). An example: Corey, E. J.; Chen, Z.; Tanoury, G. J. *J. Am. Chem. Soc.* **1993**, *115*, 11000.

(23) The non-methylated phosphinate **5am** did not undergo the ester exchange reaction under the same conditions.