

# Synthesis of 2,5-Bis(binaphthyl)phospholes and Phosphametallocene Derivatives and Their Application in Palladium-Catalyzed Asymmetric Hydrosilylation

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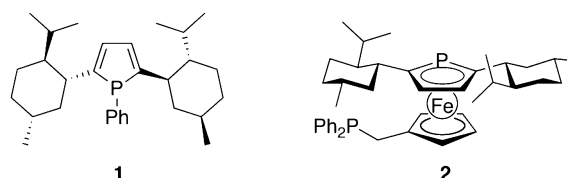
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**Summary:** Novel chiral and enantiomerically pure phospholes, which have axially chiral biaryl substituents at the 2- and 5-positions of the phosphole rings, have been prepared and converted into a variety of phosphametallocenes with retention of the chiral substituents. The phospholes and the phosphametallocenes have been applied to palladium-catalyzed asymmetric hydrosilylation of 5,5-dimethyl-1-hexen-3-yne to give an axially chiral allenylsilane with high enantioselectivity of up to 92% ee.

Recently, we reported enantiomerically pure chiral phosphole **1**. The compound **1** was the first example of phospholes having chiral substituents on the carbon atoms of the phosphole ring<sup>1a</sup> and could be transformed into the corresponding phospholyl anion with retention of the chiral substituents, (–)-menthyl groups. Thus, **1** could be an excellent precursor to a variety of novel chiral phosphametallocene derivatives.<sup>1</sup> Among the phosphametallocene derivatives, phosphinophosphaferrocene **2** was applied to palladium-catalyzed asymmetric allylic alkylation as a chiral ligand and showed excellent enantioselectivity of up to 99% ee.<sup>1b</sup>

Another strategy for preparing chiral phosphametallocenes is the use of unsymmetrically substituted  $\eta^5$ -phospholides, which induces planar chirality in phosphametallocenes. Indeed, several enantiomerically pure planar chiral phosphoferrocenes were reported.<sup>2–4</sup> Some of them were applied to transition-metal-catalyzed asymmetric reactions and displayed high potential as chiral ligands.<sup>3,4</sup> Because these planar chiral phosphoferrocenes

were obtained as racemates or diastereomeric mixtures, appropriate optical resolution was inevitable prior to their application in the asymmetric reactions. On the other hand, the chiral phosphametallocenes derived from our chiral phosphole **1** were obtained in enantiomerically pure form without optical resolution.<sup>1</sup>



**Figure 1.** Chiral phosphole **1** and phosphinophosphaferrocene **2**.

Here we report the preparation of additional examples of chiral phospholes of which the design concept is analogous to that of **1**. The phospholes **3a** and **3b** possess axially chiral atropisomeric biaryl substituents at the 2- and 5-carbons of the phosphole rings, and the latter was converted to a variety of phosphametallocene derivatives in enantiomerically pure forms. Application of these chiral compounds in Pd-catalyzed asymmetric hydrosilylation of 5,5-dimethyl-1-hexen-3-yne<sup>5a</sup> was examined, and the phosphametallocenes showed excellent enantioselectivity.

Preparation of **3** is illustrated in Scheme 1. Enantiomerically pure (*R*)-carboxylic acid **7a**, which was derived from commercially available (*R*)-binaphthol (**4a**) in three steps via binaphthyl triflate **5a** and methyl ester **6a**, was treated with 2 equiv of MeLi in THF at 0 °C, followed by aqueous workup, to give methyl ketone **8a** in 80% yield.<sup>6</sup> The methyl ketone **8a** was converted to the corresponding terminal alkyne **9a** in 90% yield according to Negishi's protocol.<sup>7</sup> Copper-catalyzed oxidative homocoupling of **9a** afforded conjugate diyne **10a** in 98% yield.<sup>8</sup> The diyne **10a** was reacted with excess PhPHLi, which was generated in situ from PhPH<sub>2</sub> and <sup>*n*</sup>BuLi, to give the chiral phosphole **3a** in 46% yield as a bright yellow crystalline solid.<sup>9</sup> Preparation of the chiral phosphole **3b**, which has 2-(5,5',6,6',7,7',8,8'-H<sub>8</sub>-2'-MeO-binaphthyl)yl substituents, was achieved by the analogous multistep route from (*R*)-H<sub>8</sub>-binaphthol (**4b**).

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(1) (a) Ogasawara, M.; Yoshida, K.; Hayashi, T. *Organometallics* **2001**, *20*, 1014. (b) Ogasawara, M.; Yoshida, K.; Hayashi, T. *Organometallics* **2001**, *20*, 3917. (c) Ogasawara, M.; Nagano, T.; Yoshida, K.; Hayashi, T. *Organometallics* **2002**, *21*, 3062. (d) Ogasawara, M.; Yoshida, K.; Hayashi, T. *Organometallics* **2003**, *22*, 1783.

(2) (a) Ganter, C.; Brassat, L.; Ganter, B. *Tetrahedron: Asymmetry* **1997**, *8*, 2607. (b) Qiao, S.; Hoic, D. A.; Fu, G. C. *Organometallics* **1998**, *17*, 773. (c) Klys, A.; Zakrzewski, J.; Rybarczyk-Pirek, A.; Olszak, T. A. *Tetrahedron: Asymmetry* **2001**, *12*, 533. (d) Agustsson, S. O.; Hu, C.; Englert, U.; Marx, T.; Wesemann, L.; Ganter, C. *Organometallics* **2002**, *21*, 2993.

(3) (a) Qiao, S.; Fu, G. C. *J. Org. Chem.* **1998**, *63*, 4168. (b) Shintani, R.; Lo, M. M.-C.; Fu, G. C. *Org. Lett.* **2000**, *2*, 3695. (c) Tanaka, K.; Qiao, S.; Tobisu, M.; Lo, M. M.-C.; Fu, G. C. *J. Am. Chem. Soc.* **2000**, *122*, 9870. (d) Tanaka, K.; Fu, G. C. *J. Org. Chem.* **2001**, *66*, 8177. (e) Shintani, R.; Fu, G. C. *Org. Lett.* **2002**, *4*, 3699. (f) Shintani, R.; Fu, G. C. *Angew. Chem., Int. Ed.* **2003**, *42*, 4082. (g) Shintani, R.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 19778. (h) Suárez, A.; Downey, W.; Fu, G. C. *J. Am. Chem. Soc.* **2005**, *127*, 11244.

(4) (a) Ganter, C.; Glinsböckel, C.; Ganter, B. *Eur. J. Inorg. Chem.* **1998**, 1163. (b) Ganter, C.; Kaulen, C.; Englert, U. *Organometallics* **1999**, *18*, 5444.

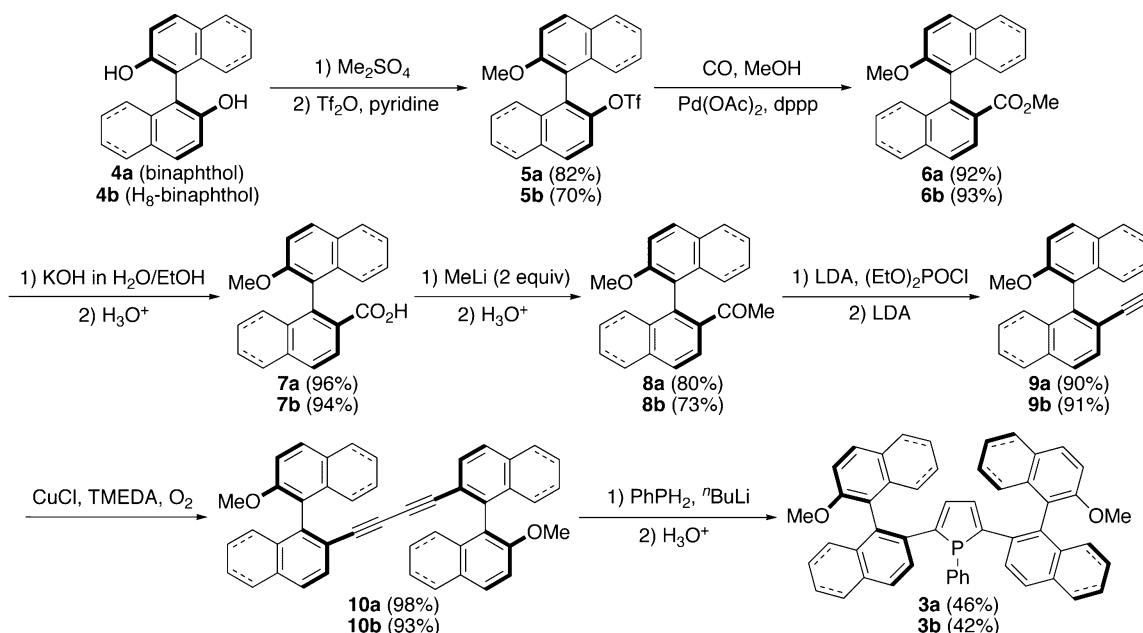
(5) (a) Han, J. W.; Tokunaga, N.; Hayashi, T. *J. Am. Chem. Soc.* **2001**, *123*, 12915. (b) Han, J. W.; Tokunaga, N.; Hayashi, T. *Helv. Chim. Acta* **2002**, *85*, 3848.

(6) Jorgenson, M. J. *Org. React.* **1970**, *18*, 2.

(7) (a) Negishi, E.; King, A. O.; Klima, W. L.; Patterson, W.; Silveira, A., Jr. *J. Org. Chem.* **1980**, *45*, 2526. (b) Negishi, E.; King, A. O.; Tour, J. M. *Organic Syntheses*; Wiley: New York, 1990; Collect. Vol. VII, p 63.

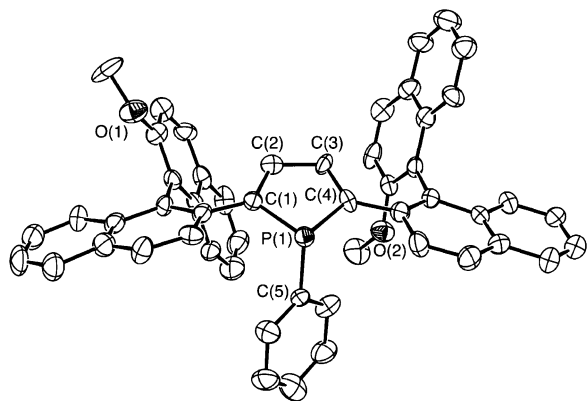
(8) Siemsen, P.; Livingston, R. C.; Diederich, F. *Angew. Chem., Int. Ed.* **2000**, *39*, 2632.

(9) Märkl, G.; Potthast, R. *Angew. Chem.* **1967**, *79*, 58.

Scheme 1. Preparation of 2,5-Bis(binaphthyl)phospholes **3a** and **3b**

Preparation of **9a** in a shorter sequence by utilizing Pd-catalyzed Sonogashira coupling was unsuccessful. Reactions of the triflate **5a** with trimethylsilyl- or triphenylsilylacetylene were examined under various conditions in the presence of the Pd-(PPh<sub>3</sub>)<sub>4</sub> catalyst; however, no alkynylated products were obtained in any cases.

Crystals of **3a** were grown from dichloromethane/ethanol, and the solid-state structure was clarified by X-ray crystallography (Figure 2). The crystal structure of the phosphole was asymmetric with the envelope-like bent phosphole ring; the dihedral angle between the C(1)–P(1)–C(4) plane and the C(1)–C(2)–C(3)–C(4) plane is 6.15°. The C<sub>α</sub>–C<sub>β</sub> distance is 1.35 Å (mean value), and the C<sub>β</sub>–C<sub>β</sub> distance is 1.47 Å. The difference between the two values, 0.12 Å, is quite large compared to those of the other structurally characterized phospholes,<sup>1a,10</sup> indicating weaker electronic delocalization (less aromatic) in **3a**. In accordance with these observations, the phosphorus atom in **3a** shows clear pyramidal geometry (more sp<sup>3</sup>-like): the sum of the angles at the phosphorus<sup>11</sup> is only 304°. In a phosphole with



**Figure 2.** ORTEP drawing of **3a** with 30% thermal ellipsoids. All hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and angles (deg): P(1)–C(1) = 1.83(1), P(1)–C(4) = 1.85(1), C(1)–C(2) = 1.35(2), C(2)–C(3) = 1.47(2), C(3)–C(4) = 1.36(2); C(1)–P(1)–C(4) = 91.6(6), P(1)–C(1)–C(2) = 107.7(1), C(1)–C(2)–C(3) = 117.4(1), C(2)–C(3)–C(4) = 113.3(1), P(1)–C(4)–C(3) = 109.5(9), C(1)–P(1)–C(5) = 106.1(5), C(4)–P(1)–C(5) = 106.3(5).

a bulky aryl substituent (–C<sub>6</sub>H<sub>2</sub>–2,4,6-*t*Bu<sub>3</sub>) at the phosphorus, which shows strong aromatic character, the sum of the angles is as large as 331.7°.<sup>12</sup>

Conversion of the chiral phospholes **3a** and **3b** into the corresponding phospholide anions was examined. Unfortunately, however, the phosphole **3a** was found to be robust to reductive cleavage of the P–Ph bond by a reaction with lithium metal or sodium naphthalenide.<sup>13</sup> Treatment of a THF solution of **3a** with lithium metal afforded an NMR-inactive dark green solution, which indicated formation of a phosphole anion radical by a single-electron transfer from the reductant.<sup>14</sup> The anion radical showed thermal stability and did not decompose into the corresponding phospholide anion. The anion radical was generated in dioxane or xylene in a similar manner and heated to reflux for several hours. Formation of the corresponding phospholide anion, however, was not detected under these conditions. The unusual thermal stability of the anion radical could be ascribed to delocalization of anionic charge over the binaphthyl substituents. Since α,α′-diarylphospholides, such as 2,5-Ph<sub>2</sub>-phospholide or 2,3,4,5-Ph<sub>4</sub>-phospholide,<sup>13,15</sup> could be prepared from the corresponding P–Ph phospholes by the reactions with alkaline metals, it was expected that breaking the extended conjugation of the binaphthyl substituents in **3a** might reduce the thermal stability of the anion radical. As expected, the phosphole **3b**, which has partially hydrogenated binaphthyl (H<sub>8</sub>-binaphthyl) groups, was cleanly converted to sodium phospholide **11** (<sup>31</sup>P NMR analysis in THF: δ +92)<sup>16</sup> by treatment with sodium naphthalenide. It should be mentioned that generation of an

(10) (a) Coggon, P.; Engel, J. F.; McPhail, A. T.; Quin, L. D. *J. Am. Chem. Soc.* **1970**, *92*, 5773. (b) Ozbirn, W. P.; Jacobson, R. A.; Clardy, J. C. *Chem. Commun.* **1971**, 1062.

(11) Jochem, G.; Nöth, H.; Schmidpeter, A. *Chem. Ber.* **1996**, *129*, 1083.

(12) Keglevich, G.; Böcskei, Z.; Keserü, G. M.; Ujszászy, K.; Quin, L. D. *J. Am. Chem. Soc.* **1997**, *119*, 5095.

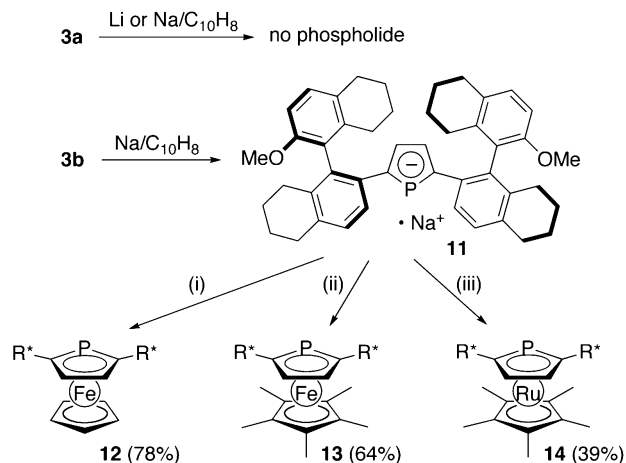
(13) Braye, E. H.; Caplier, I.; Saussez, R. *Tetrahedron* **1971**, *27*, 5523.

(14) (a) Thomson, C.; Kilcast, D. *Angew. Chem., Int. Ed. Engl.* **1970**, *9*, 310. (b) Kilcast, D.; Thomson, C. *Tetrahedron* **1971**, *27*, 5705. (c) Thomson, C.; Kilcast, D. *J. Chem. Soc., Chem. Commun.* **1971**, 214.

(15) Charrier, C.; Bonnard, H.; de Lauzon, G.; Mathey, F. *J. Am. Chem. Soc.* **1983**, *105*, 6871.

(16) Quin, L. D.; Orton, W. L. *J. Chem. Soc., Chem. Commun.* **1979**, 401.

**Scheme 2. Generation of Phospholide 11 and Preparation of Chiral Phosphametalloenes 12–14**

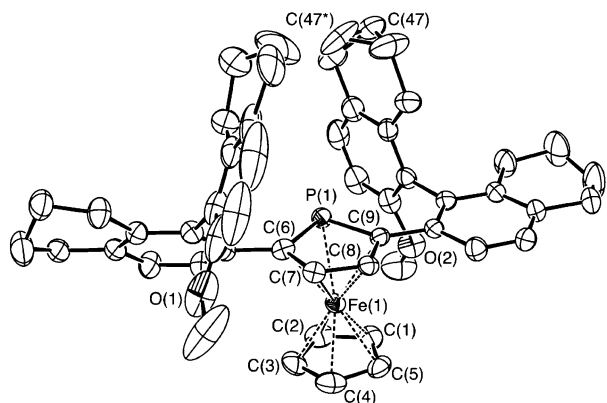


$\alpha$ -naphthyl phospholide was achieved recently by a [1,5]-sigmatropic aryl shift in a *P*-naphthylphosphole.<sup>17</sup>

Whereas the chiral H<sub>8</sub>-binaphthyl substituents were retained in **11**, the phospholide **11** served as a versatile precursor to a variety of chiral phosphametalloenes. Monophosphaferrocenes **12**<sup>18</sup> and **13**<sup>19</sup> were prepared in 78% and 64% yields, respectively, as bright red crystalline solids. Monophospharuthenocene **14**<sup>20</sup> was obtained in 39% yield (Scheme 2).

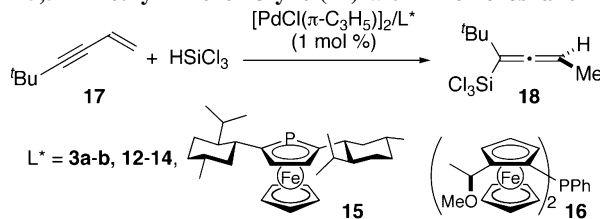
The solid-state structure of the monophosphaferrocene **12** was determined by an X-ray diffraction study. As shown in Figure 3, two sterically demanding H<sub>8</sub>-binaphthyl groups construct a unique chiral pocket around the phosphorus atom. The two 2-MeO-H<sub>4</sub>-naphthyl groups occupy the side opposite the FeCp moiety with respect to the phospholyl plane, avoiding steric interaction with the Cp ligand. The phospholyl ligand and the Cp ligand are nearly parallel, with a dihedral angle of 3.07°. The Fe–Cp (1.644 Å) and Fe–phospholyl (1.648 Å) distances are nearly the same.

The potential of the newly prepared compounds as chiral ligands in asymmetric synthesis was explored for the palladium-catalyzed enantioselective hydrosilylation of 5,5-dimethyl-1-hexen-3-yne (**17**) with trichlorosilane, forming the axially chiral allenylsilane **18**,<sup>5a</sup> and the results are summarized in Table 1. In the precedent report,<sup>5a</sup> the highest enantioselectivity of 90%



**Figure 3.** ORTEP drawing of **12** with 30% thermal ellipsoids. All hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and angles (deg): P(1)–C(6) = 1.79(6), P(1)–C(9) = 1.80(6), C(6)–C(7) = 1.41(8), C(7)–C(8) = 1.40(8), C(8)–C(9) = 1.42(8), Fe(1)–phospholyl = 1.644, Fe(1)–Cp = 1.648; C(6)–P(1)–C(9) = 90.0(3), P(1)–C(6)–C(7) = 112.2(5), C(6)–C(7)–C(8) = 112.6(5), C(7)–C(8)–C(9) = 115.1(6), P(1)–C(9)–C(8) = 110.0(5).

**Table 1. Pd-Catalyzed Asymmetric Hydrosilylation of 5,5-Dimethyl-1-hexen-3-yne (**17**) with Trichlorosilane<sup>a</sup>**



entry	L*	temp/°C	time/h	yield/% <sup>b</sup>	% ee <sup>c</sup> (config) <sup>d</sup>
1	3a	20	120	<10	
2	3b	20	72	39	16 (R)
3	12	20	72	57	41 (R)
4	13	20	72	79	84 (R)
5	13	0	72	82	92 (R)
6	14	20	72	59	75 (R)
7	15	20	72	trace	
8 <sup>e,f</sup>	16	0	160	37	90 (S)

<sup>a</sup> The asymmetric hydrosilylation was carried out with **17** (1.0 mmol) and HSiCl<sub>3</sub> (1.1 mmol) in the presence of 1 mol % of the catalyst generated from [PdCl(π-allyl)]<sub>2</sub> and L\* (Pd/P = 1/2.2). <sup>b</sup> Isolated yield by bulb-to-bulb distillation under vacuum. <sup>c</sup> Determined by HPLC analysis of homopropargyl alcohol, <sup>t</sup>BuC≡CCHMeCH(OH)Ph, obtained from **18** and PhCHO with complete chirality transfer (see ref 5). <sup>d</sup> Determined by correlation with the product of known configuration (see ref 5a). <sup>e</sup> Taken from ref 5. <sup>f</sup> With **17** (2.0 mmol) and HSiCl<sub>3</sub> (4.4 mmol).

ee (at 0 °C) was reported for the asymmetric reaction using monodentate ferrocenylphosphine **16**<sup>5</sup> (Table 1, entry 8). For the success of Pd-catalyzed asymmetric hydrosilylations, use of a monodentate chiral phosphine is crucial.<sup>21</sup>

The reaction was sluggish with a palladium catalyst (1 mol %) generated from [PdCl(π-C<sub>3</sub>H<sub>5</sub>)]<sub>2</sub> and **3a**, giving less than 10% of **18**. With **3b**, the yield of **18** was improved to 39%; however, the enantioselectivity was only 16% (entry 2). It was found that the phosphametalloenes showed much better performance, giving **18** in higher yields with better enantioselectivity. The allenylsilane **18** of 41% ee was obtained in 57% yield by the Pd/**12** catalyst (entry 3). With the phosphoferrocene **13**, which has a sterically demanding η<sup>5</sup>-C<sub>5</sub>Me<sub>5</sub> ligand, the yield and the enantioselectivity were greatly improved to 79% and 84% ee (at 20 °C), respectively (entry 4). At 0 °C, the Pd/**13** catalyst outperformed the Pd/**16** species with 92% ee in 82% yield in a shorter reaction time (entry 5 vs entry 8). This enantioselectivity is the highest value reported to date for the reaction. The phospharuthenocene **14**, which is isostructural with **13** (entry 6). The chiral phospholyl moiety was away from the η<sup>5</sup>-C<sub>5</sub>Me<sub>5</sub> ligand in **14** with the larger central metal, and thus the positive effects from η<sup>5</sup>-C<sub>5</sub>Me<sub>5</sub> were somewhat diminished. Note that phosphoferrocene **15**,<sup>1a</sup> which was prepared from the (–)-menthyl phosphole **1**, did not appreciably afford **18** in the present hydrosilylation (entry 7).

In summary, two novel phospholes with chiral biaryl substituents were prepared, and one of them was converted to the

(17) Carmichael, D.; Ricard, L.; Seeboth, N.; Brown, J. M.; Claridge, T. D. W.; Odell, B. *Dalton Trans.* **2005**, 2173.

(18) Roberts, R. M. G.; Wells, A. S. *Inorg. Chim. Acta* **1986**, *112*, 171.

(19) Roman, E.; Leiva, A. M.; Casasemper, M. A.; Charrier, C.; Mathey, F.; Garland, M. T.; Le Maroille, J. Y. *J. Organomet. Chem.* **1986**, *309*, 323.

(20) Carmichael, D.; Ricard, L.; Mathey, F. *J. Chem. Soc., Chem. Commun.* **1994**, 1167.

(21) (a) Hayashi, T. *Acta Chem. Scand.* **1996**, *50*, 259. (b) Hayashi, T. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Berlin, 1999; Vol. 1, Chapter 7, p 319. (c) Hayashi, T. *Acc. Chem. Res.* **2000**, *33*, 354. (d) Nishiyama, H.; Itoh, K. In *Catalytic Asymmetric Synthesis*, 2nd ed.; Ojima, I., Ed.; Wiley-VCH: New York, 2000; p 111.

corresponding phosphametalloenes with retention of the chiral substituents. These compounds were applied to the Pd-catalyzed asymmetric hydrosilylation of 5,5-dimethyl-1-hexen-3-yne, and the axially chiral allenylsilane was obtained with high enantioselectivity of up to 92% ee.

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**Supporting Information Available:** Detailed experimental procedures, compound characterization data, and crystallographic data for **3a** and **12**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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