

## Silver Salt Effects on an Asymmetric Heck Reaction. Catalytic Asymmetric Total Synthesis of (+)-Xestoquinone.

Futoshi Miyazaki, Koichiro Uotsu, and Masakatsu Shibasaki\*

Graduate School of Pharmaceutical Sciences, The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113-0033, Japan

Received 16 July 1998; accepted 18 August 1998

**Abstract:** An enantioselective total synthesis of (+)-xestoquinone has been achieved using a cascade-type asymmetric Heck reaction (in up to 63% ee and 39% chemical yield (66% conversion yield)) of the aryl bromide derivative (**4**). The use of a larger amount of silver exchanged zeolite resulted in a decrease in ee and yield. This is the first example of an effect of the amount of a silver salt on the ee and yield of a product. © 1998 Elsevier Science Ltd. All rights reserved.

**Keywords:** Asymmetric reactions, Heck reactions, Natural products, Palladium and compounds

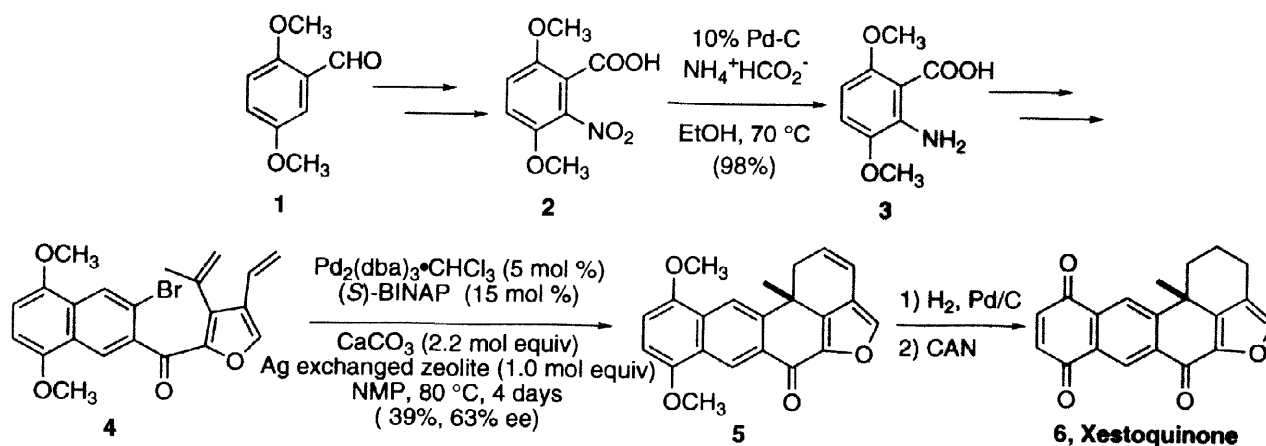
### INTRODUCTION

Asymmetric Heck reactions are one of the most important C-C bond-forming reactions known to date.<sup>1</sup> The first examples of asymmetric Heck reactions were reported in 1989, concurrently and independently by ourselves<sup>2</sup> and Overman.<sup>3</sup> Since then we<sup>1,4</sup> have demonstrated, along with others,<sup>5</sup> that this type of catalytic asymmetric C-C bond forming reaction is useful for the synthesis of various optically active compounds.

In 1996, Keay and co-workers reported an elegant catalytic asymmetric total synthesis of (+)-xestoquinone (**6**), in which a highly efficient cascade-type asymmetric Heck reaction was developed.<sup>6</sup> In that synthesis, high chemical yield and modest to good enantioselectivity (up to 68% ee) were achieved when aryl triflates were used as substrates. However, the use of the corresponding aryl halides resulted in only poor enantioselectivities (5–13% ee). Therefore, there remained room for improvement for reactions starting from aryl halides, which are obtained more readily than the corresponding aryl triflates. Recently we have developed 2,2'-bis(diphenylarsino)-1,1'-binaphthyl (BINAs), and have found that BINAs is more useful than BINAP in the catalytic asymmetric synthesis of *cis*-decalin derivatives from alkenyl iodides.<sup>7</sup> Thus, investigations were carried out in an attempt to enhance the cascade-type asymmetric Heck reaction with aryl halides. In this note, we report a much improved cascade-type asymmetric Heck reaction of aryl halides, in which highly interesting and useful silver salt effects are discussed.

### RESULTS AND DISCUSSION

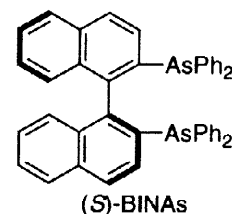
The starting aryl bromide **4** was first prepared according to the procedure developed by Keay<sup>6, 8a, 8b</sup> and Wallace<sup>8c, 8d</sup>, in which the one step (**2**→**3**) reaction conditions were improved for the large-scale synthesis of **4** (Scheme 1). The cascade-type asymmetric Heck reaction of **4** was then examined using BINAs and/or BINAP. It has been well established that the addition of a silver salt is essential to form cationic palladium intermediates with 16-electron configurations, leading to products with high enantiomeric excesses.<sup>9</sup> Among the many silver salts available, the use of silver phosphate or silver exchanged zeolite has been found to give the best results.<sup>1, 4</sup>



Scheme 1

Table 1. Asymmetric Heck Reaction of **4** using (*S*)-BINAs

4	Pd <sub>2</sub> (dba) <sub>3</sub> ·CHCl <sub>3</sub> (5 mol %) ( <i>S</i> )-BINAs (15 mol %)	5	entry	temperature (°C)	yield (%)	ee (%)	recovery of <b>4</b> (%)
	CaCO <sub>3</sub> (2.2 mol equiv) Ag <sub>3</sub> PO <sub>4</sub> (2.0 mol equiv) NMP, 4 days		1	60	trace	-	69
			2	80	11	50	38
			3	100	7	37	5

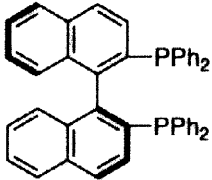


As shown in Table 1, a cascade-type asymmetric Heck reaction of **4** was initially carried out under the well established conditions of [Pd<sub>2</sub>(dba)<sub>3</sub>·CHCl<sub>3</sub> (5 mol %), (*S*)-BINAs (15 mol %), Ag<sub>3</sub>PO<sub>4</sub> (2.0 mol equiv), CaCO<sub>3</sub> (2.2 mol equiv) and 1-methyl-2-pyrrolidinone (NMP)]. However, at 60 °C only a trace amount of the desired product **5** was obtained and 69% of starting material **4** was recovered<sup>10</sup> (entry 1, Table 1). This was the best temperature previously reported by ourselves for alkenyl halide systems.<sup>1,4</sup> When the temperature was increased to 80 °C, we succeeded in obtaining **5** in 11% yield and 50% ee, with a 38% recovery of starting material **4**. When the reaction was carried out at 100 °C, however, the yield and ee of the product was lower compared to the values obtained at 80 °C. These results suggest that **4** and **5** might be decomposed by silver phosphate at 100 °C. The absolute configuration of **5** was determined by comparison with an authentic sample,<sup>6</sup> and the ee of **5** was determined by HPLC analysis using a DAICEL CHIRALCEL OJ column. Although the chemical yield of **5** was poor, our ee was much better than Keay's reported result using **4** as a substrate,<sup>6</sup> encouraging us to further improve the cascade-type asymmetric Heck reaction of the aryl bromide **4**.

Due to the possible decomposition of **4** and **5** by an excess amount of silver phosphate, even at 80 °C, we next investigated the amount of silver phosphate required for this reaction (entries 1-3, Table 2). As a result (entry 3, Table 2), using BINAs as a ligand, we were pleased to find that the chemical yield and enantioselectivity were improved by decreasing the amount of silver phosphate. The highest yield (16%) and enantioselectivity (63%) were obtained using 0.33 mol equiv of silver phosphate (corresponding to *ca.* 1.0 equiv of Ag<sup>+</sup>). We also examined the use of BINAP as an asymmetric ligand and tried to optimize the amount of silver phosphate (entries 4-7, Table 2). The best chemical yield (35%) was obtained when 4.0 mol equiv of silver phosphate (entry 4, Table 2) was used and the best enantioselectivity (49%) was obtained when 2.0 mol equiv of Ag<sub>3</sub>PO<sub>4</sub> was used (entry 5, Table 2). These results might be reasonably explained by considering that, in the presence of Ag<sub>3</sub>PO<sub>4</sub>, the chemical stability of the BINAs-Pd complex is slightly lower than that of the BINAP-Pd complex.<sup>11</sup> In other words, it is likely that the transfer of BINAs from Pd<sup>0</sup> to silver phosphate occurs more readily than with BINAP. Furthermore, the unexpected observation that BINAP is more effective than BINAs might be understood by the fact that the present cascade type asymmetric Heck reaction requires a higher temperature (80 °C) than generally required (60 °C).<sup>7a</sup> At 80 °C, a small amount of undesired ligand transfer of BINAs from Pd<sup>0</sup>

to silver phosphate appears to happen. Interestingly, the amount of silver phosphate that produces the best result depends upon the type of asymmetric ligand employed.

**Table 2.** Asymmetric Heck Reaction of **4** under Various Reaction Conditions

$\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$ (5 mol %) $(S)$ -ligand (15 mol %)		$\text{CaCO}_3$ (2.2 mol equiv) Ag reagent NMP, 80 °C, 4 days		 $(S)$ -BINAP		
entry	Ag reagent (mol equiv)	ligand	yield (%)	ee (%)	recovery of <b>4</b> (%)	conversion (%)
1	$\text{Ag}_3\text{PO}_4$ (2.0)	$(S)$ -BINAs	11	50	38	18
2	$\text{Ag}_3\text{PO}_4$ (0.67)	$(S)$ -BINAs	12	59	65	34
3	$\text{Ag}_3\text{PO}_4$ (0.33)	$(S)$ -BINAs	16	63	55	36
4	$\text{Ag}_3\text{PO}_4$ (4.0)	$(S)$ -BINAP	35	44	32	51
5	$\text{Ag}_3\text{PO}_4$ (2.0)	$(S)$ -BINAP	29	49	23	38
6	$\text{Ag}_3\text{PO}_4$ (0.67)	$(S)$ -BINAP	25	47	45	45
7	$\text{Ag}_3\text{PO}_4$ (0.33)	$(S)$ -BINAP	21	46	33	31
8	Ag exchanged zeolite (6.0) <sup>a</sup>	$(S)$ -BINAs	trace	39	45	trace
9	Ag exchanged zeolite (2.0) <sup>a</sup>	$(S)$ -BINAs	24	52	31	35
10	Ag exchanged zeolite (1.0) <sup>a</sup>	$(S)$ -BINAs	21	53	54	46
11	Ag exchanged zeolite (6.0) <sup>a</sup>	$(S)$ -BINAP	9	11	trace	9
12	Ag exchanged zeolite (2.0) <sup>a</sup>	$(S)$ -BINAP	28	47	33	42
13	Ag exchanged zeolite (1.0) <sup>a</sup>	$(S)$ -BINAP	39	63	41	66

<sup>a</sup> Ald 36,660-9, Ag content; typically 20-25%, 100 mesh powder.

In an attempt to further improve the cascade-type asymmetric Heck reaction of **4**, we next examined the effect of silver exchanged zeolite on this reaction. This effect is known to accelerate the asymmetric Heck reaction of alkenyl iodides.<sup>1, 4g</sup> When BINAs was employed as an asymmetric ligand, in the presence of 1.0 equivalent of silver exchanged zeolite, the desired product **5** was formed in 21% chemical yield (46% conversion yield) and 53% ee (entry 10, Table 2). As expected, the use of larger amounts of silver exchanged zeolite produced only a trace amount of **5** (entry 8, Table 2). Quite surprisingly, even when BINAP was used as an asymmetric ligand, 1.0 equivalent of silver exchanged zeolite gave the best result, affording **5** in 39% chemical yield (66% conversion yield) and in 63% ee (entry 13, Table 2). When 2.0 or 6.0 equivalents of silver exchanged zeolite were used, less satisfactory results were obtained (entries 11 and 12, Table 2). This suggests that excess amounts of silver exchanged zeolite might lead to the undesired ligand transfer, even in the case of BINAP as a ligand. These observations are in accordance with the fact that silver exchanged zeolite accelerates asymmetric Heck reactions of alkenyl iodides,<sup>1, 4g</sup> by working as a more naked and reactive  $\text{Ag}^+$  than silver phosphate. The above mentioned result is quite useful for determining the best reaction conditions for asymmetric Heck reactions employing aryl halides and/or alkenyl halides.

The results discussed herein appear to suggest the following possibilities. Firstly, undesired asymmetric ligand exchange might take place between  $\text{Pd}^0$  and  $\text{Ag}^+$ ,<sup>12</sup> which suggests that the amount of a silver salt employed is very important. Secondly, considering the electronegativities of both metals ( $\text{Pd}$ ; 1.35,  $\text{Ag}$ ; 1.42), undesired electron transfer might occur from  $\text{Pd}^0$  to  $\text{Ag}^+$  at relatively high temperature, causing the decomposition of an asymmetric catalyst. Finally an excess amount of a silver salt might decompose **4** and **5**. The cascade-type asymmetric Heck reaction product **5** was finally converted to (+)-xestoquinone (**6**) according to the procedure developed by Keay and co-workers (Scheme 1).<sup>6</sup>

## SUMMARY

Although aryl bromide **4** was reported to be an ineffective substrate for cascade-type asymmetric Heck reactions,<sup>6</sup> we have succeeded in greatly improving the reaction of **4** by modifying the reaction conditions.

Desired product **5** has been isolated in up to 63% ee albeit in modest chemical yield. Moreover, these studies have revealed for the first time that the amount of silver salt is quite important for an asymmetric Heck reaction using aryl halides. The amount of a silver salt required depends not only on the type of silver salt, but also on the type of asymmetric ligand. These results would be useful for further development of an asymmetric Heck reaction. Further studies along this line are currently under investigation.

## EXPERIMENTAL SECTION

**General Methods.**  $\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$ , (*S*)-BINAP,  $\text{Ag}_3\text{PO}_4$ , silver exchanged zeolite (Ald 36,660-9), 10% Pd-C, ammonium formate, EtOH (99.9% pure) and  $\text{Et}_2\text{O}$  (99.8% pure) used are available from commercially sources. These reagents and solvents were used without further purification, except for  $\text{CaCO}_3$  which was dried with heating under vacuum at 80 °C before use. Toluene, 1,2-dichloroethane, hexane, ethyl acetate, dichloromethane and 1-methyl-2-pyrrolidinone were distilled before use. Preparative TLC (Merck 60 F<sub>254</sub> precoated silica gel plates (0.25 mm thickness)) and silica gel (Merck silica gel 60 (230-400 mesh)) for chromatography was washed with dichloromethane before use. BINAs was prepared according to the reported procedure.<sup>7a</sup> Synthesis of (+)-xestoquinone (**6**) was carried out according to the procedure reported by Keay<sup>6, 8a, 8b</sup> and Wallace<sup>8c, 8d</sup> except for **2**→**3** and **4**→**5**. All experiments were performed under an argon atmosphere, unless otherwise mentioned, and monitored with analytical TLC (Merck Art. 5715, silica gel 60 F<sub>254</sub> plates). All products were previously known, and their <sup>1</sup>H NMR, <sup>13</sup>C NMR, IR spectra and Mass spectra were consistent with literature spectral data.<sup>6</sup> <sup>1</sup>H NMR and <sup>13</sup>C NMR were taken in  $\text{CDCl}_3$  or  $\text{DMSO-d}_6$  at 500 and 125 Mhz, respectively.

**2-Amino-3,6-dimethoxybenzoic acid (3).** To a solution of **2**<sup>8c</sup> (20 g, 88 mmol) in ethanol (99.9% pure, 500 mL) was added 10% Pd-C (9.4 g, 8.8 mmol) and this mixture was stirred at 0 °C. To this mixture was then added ammonium formate (22 g, 350 mmol) and the suspension was stirred at 70 °C for 7 h. The catalyst was removed by filtration and washed with ethanol (100 mL), and the filtrate was evaporated under reduced pressure to give the crude amino acid, which was separated from a trace amount of the 4-amino isomer by silica gel chromatography (ether) to give the title compound **3** (17 g, 98%). The spectral data of **3** thus obtained were superimposable with those of an authentic sample.<sup>8c</sup> <sup>1</sup>H NMR (500 MHz,  $\text{DMSO-d}_6$ )  $\delta$  6.83 (1H, d, *J* = 8.9 Hz), 6.15 (1H, d, *J* = 8.9 Hz), 3.74 (3H, s), 3.72 (3H, s); <sup>13</sup>C NMR (125 MHz)  $\delta$  168.6, 152.8, 141.4, 140.5, 112.9, 103.9, 97.2, 56.2, 56.1; MS (EI) *m/z* 197 (*M*<sup>+</sup>, 66), (*M*<sup>+</sup>-33, 100), (*M*<sup>+</sup>-63, 51); IR (KBr,  $\text{cm}^{-1}$ ) 3496, 3363, 1692.

**5-((3-Bromo-5,8-dimethoxynaphth-2-yl)carbonyl)-3-ethenyl-4-(propen-2-yl)furan (4).** <sup>1</sup>H NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.44 (s, 1H), 8.24 (s, 1H), 7.64 (s, 1H), 6.79 (d, 1H, *J* = 8.3 Hz), 6.74 (d, 1H, *J* = 8.4 Hz), 6.38 (dd, 1H, *J* = 11, 18 Hz), 5.61 (dd, 1H, *J* = 1.3, 18 Hz), 5.25 (dd, 1H, *J* = 1.3, 11.2 Hz), 5.09 (d, 1H, *J* = 1.5 Hz), 4.97 (d, 1H, *J* = 1.7 Hz), 3.96 (s, 3H), 3.92 (s, 3H), 1.94 (s, 3H); <sup>13</sup>C NMR (125 MHz)  $\delta$  184.1, 150.1, 148.6, 147.8, 143.2, 137.2, 136.4, 135.9, 127.9, 126.6, 126.5, 125.5, 124.4, 124.0, 118.6, 117.4, 116.6, 106.1, 104.6, 56.1, 56.0, 23.0; MS (EI, *m/z*) 428, 426 (*M*<sup>+</sup>, 13), 18 ( $\text{H}_2\text{O}$ , 100); IR (KBr,  $\text{cm}^{-1}$ ) 1637, 1463, 1264, 1108. The spectral data of **4** thus obtained were superimposable with those of an authentic sample.<sup>6</sup>

**(12*bS*)-8,11-Dimethoxy-12*b*-methyl-1*H*-benzo[6,7]phenanthro-[10,1-*bc*]furan-6(12*bH*)-one ((+)-**5**).**

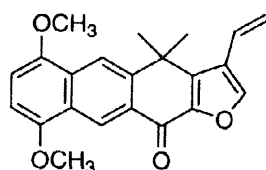
**1. Representative procedure using BINAP.**  $\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$  (4.8 mg, 5.0 mol %), (*S*)-BINAP (8.8 mg, 15 mol %),  $\text{CaCO}_3$  (21 mg, 2.2 mol eq), a silver salt and substrate **4** (40 mg, 0.094 mmol) were placed in a reaction flask. To this mixture was added distilled NMP (1.3 mL). The mixture (0.072 *M*) was degassed by freeze-pump-thaw cycles, and stirred at 80 °C for 4 days. The crude reaction mixture was filtered through a pad of silica gel (dichloromethane) to afford a yellow solid which was purified by preparative TLC (first, hexane : ethyl acetate = 3:1 and then toluene : 1,2-dichloroethane = 1:1).

**2. Using BINAs.** Pd<sub>2</sub>(dba)<sub>3</sub>•CHCl<sub>3</sub> (4.8 mg, 5.0 mol %), (S)-BINAs (10 mg, 15 mol %), CaCO<sub>3</sub> (21 mg, 2.2 mol eq) and a silver salt were placed in a reaction flask. To this mixture was added degassed NMP (0.50 mL). The mixture was degassed by freeze-pump-thaw cycles, and stirred at 60 °C for 30 min. To this mixture was added a solution of the substrate **4** (40 mg, 0.094 mmol) in degassed NMP (0.80 mL). The mixture was degassed by freeze-pump-thaw cycles, and stirred at 80 °C for 4 days. The crude reaction mixture was filtered through a pad of silica gel (dichloromethane) to afford a yellow solid which was purified by preparative TLC (first, hexane : ethyl acetate = 3:1 and then toluene : 1,2-dichloroethane = 1:1). The enantiopurity was assessed by dissolving the sample in CH<sub>2</sub>Cl<sub>2</sub> and separating the enantiomers by a Daicel CHIRALCEL OJ column (hexane : ethanol = 85 : 15; λ = 350 nm, flow rate = 1.3 mL/min). The relative peak areas (12.0 and 15.5 min) indicated an ee of 5. The spectral data of **5** thus obtained were superimposable with those of an authentic sample.<sup>6</sup> <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 9.30 (s, 1H), 8.26 (s, 1H), 7.57 (s, 1H), 6.82 (d, 1H, J = 8.4 Hz), 6.71 (d, 1H, J = 8.4 Hz), 6.62 (dd, 1H, J = 3.1, 9.8 Hz), 6.11 (ddd, 1H, J = 2.5, 6.1, 9.8 Hz), 4.00 (s, 3H), 3.99 (s, 3H), 3.15 (dd, 1H, J = 6.1, 17 Hz), 2.67 (br d, 1H, J = 17 Hz), 1.53 (s, 1H); <sup>13</sup>C NMR (125 MHz) δ 173.0, 151.1, 149.0, 146.0, 144.6, 144.5, 141.7, 131.6, 129.0, 127.8, 125.1, 124.5, 121.3, 118.5, 117.8, 106.4, 103.7, 56.0, 56.0, 35.7, 35.7, 32.4; MS (EI, m/z) 346 (M<sup>+</sup>, 86), 331 (M<sup>+</sup>-15, 100); IR (KBr, cm<sup>-1</sup>) 1667, 1623, 1595.

## REFERENCES

1. (a) Shibasaki, M.; Boden, C. D.J.; Kojima, A. *Tetrahedron* **1997**, *53*, 7371. (b) Cabri, W.; Candiani, I. *Acc. Chem. Res.* **1995**, *28*, 2.
2. Sato, Y.; Sodeoka, M.; Shibasaki, M. *J. Org. Chem.* **1989**, *54*, 4738.
3. Carpenter, N. E.; Kucera, D. J.; Overman, L. E. *J. Org. Chem.* **1989**, *54*, 5846.
4. (a) Sato, Y.; Sodeoka, M.; Shibasaki, M. *Chem. Lett.* **1990**, 1953. (b) Kagechika, K.; Shibasaki, M. *J. Org. Chem.* **1991**, *56*, 4093. (c) Sato, Y.; Watanabe, S.; Shibasaki, M. *Tetrahedron Lett.* **1992**, *33*, 2589. (d) Sato, Y.; Honda, T.; Shibasaki, M. *Tetrahedron Lett.* **1992**, *33*, 2593. (e) Shibasaki, M.; Sato, Y.; Kagechika, K. *J. Synth. Org. Chem., Jpn.* **1992**, *50*, 826. (f) Takemoto, T.; Sodeoka, M.; Sasai, H.; Shibasaki, M. *J. Am. Chem. Soc.* **1993**, *115*, 8477. (g) Nukui, S.; Sodeoka, M.; Shibasaki, M. *Tetrahedron Lett.* **1993**, *34*, 4965. (h) Kondo, K.; Sodeoka, M.; Mori, M.; Shibasaki, M. *Synthesis* **1993**, 920. (i) Kagechika, K.; Ohshima, T.; Shibasaki, M. *Tetrahedron* **1993**, *49*, 1773. (j) Kondo, K.; Sodeoka, M.; Mori, M.; Shibasaki, M. *Tetrahedron Lett.* **1993**, *34*, 4219. (k) Sato, Y.; Nukui, S.; Sodeoka, M.; Shibasaki, M. *Tetrahedron* **1994**, *50*, 371. (l) Shibasaki, M.; Sodeoka, M. *J. Synth. Org. Chem., Jpn.* **1994**, *52*, 956. (m) Koga, Y.; Sodeoka, M.; Shibasaki, M.; *Tetrahedron Lett.* **1994**, *35*, 1227. (n) Ohrai, K.; Kondo, K.; Sodeoka, M.; Shibasaki, M. *J. Am. Chem. Soc.* **1994**, *116*, 11737. (o) Kondo, K.; Sodeoka, M.; Shibasaki, M. *Tetrahedron: Asymmetry* **1995**, *6*, 2453. (p) Nukui, S.; Sodeoka, M.; Sasai, H.; Shibasaki, M. *J. Org. Chem.* **1995**, *60*, 398. (q) Kondo, K.; Sodeoka, M.; Shibasaki, M. *J. Org. Chem.* **1995**, *60*, 4322. (r) Sato, Y.; Mori, M.; Shibasaki, M. *Tetrahedron: Asymmetry* **1995**, *6*, 757. (s) Kojima, A.; Takemoto, T.; Sodeoka, M.; Shibasaki, M. *J. Org. Chem.* **1996**, *61*, 4876. (t) Ohshima, T.; Kagechika, K.; Adachi, M.; Sodeoka, M.; Shibasaki, M. *J. Am. Chem. Soc.* **1996**, *118*, 7108. (u) Kojima, A.; Takemoto, T.; Sodeoka, M.; Shibasaki, M. *Synthesis* **1998**, 581.
5. (a) Brunner, H.; Kramler, K. *Synthesis* **1991**, 1121. (b) Ozawa, F.; Kubo, A.; Hayashi, T. *J. Am. Chem. Soc.* **1991**, *113*, 1417. (c) Hayashi, T.; Kubo, A.; Ozawa, F. *Pure Appl. Chem.* **1992**, *64*, 421. (d) Ozawa, F.; Kubo, A.; Hayashi, T. *Tetrahedron Lett.* **1992**, *33*, 1485. (e) Ozawa, F.; Hayashi, T. *J. Organomet. Chem.* **1992**, *428*, 267. (f) Sakamoto, T.; Kondo, Y.; Yamanaka, H. *Tetrahedron Lett.* **1992**, *33*, 6845. (g) Ashimori, A.; Overman, L. E. *J. Org. Chem.* **1992**, *57*, 4571. (h) Ozawa, F.; Kobatake, Y.; Hayashi, T. *Tetrahedron Lett.* **1993**, *34*, 2505. (i) Ozawa, F.; Kubo, A.; Matsumoto, Y.; Hayashi, T. *Organometallics* **1993**, *12*, 4188. (j) Ashimori, A.; Matsuura, T.; Overman, L. E.; Poon, D. *J. Org. Chem.* **1993**, *58*, 6949. (k) Tietze, L. F.; Schimpf, R. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1089. (l) Sakuraba, S.; Awano, K.; Achiwa, K. *Synlett* **1994**, 291. (m) Ozawa, F.; Kobatake, Y.; Kubo, A.; Hayashi, T. *J. Chem. Soc., Chem. Commun.* **1994**, 1323. (n) Moinet, C.; Fiaud, J.-C. *Tetrahedron Lett.*

- 1995, 36, 2051. (o) Overman, L. E.; Poon, D. J. *Angew. Chem., Int. Ed. Engl.* **1997**, 36, 518. (p) Cheng, C.-Y.; Liou, J.-P.; Lee, M.-J. *Tetrahedron Lett.* **1997**, 38, 4571. (q) Wipf, P.; Yokokama, F. *Tetrahedron Lett.* **1998**, 39, 2223. (r) Diaz, P.; Gendre, F.; Stella, L.; Charpenter, B. *Tetrahedron* **1998**, 54, 4579.
6. (a) Maddaford, S. P.; Andersen, N. G.; Cristofoli, W. A.; Keay, B. A. *J. Am. Chem. Soc.* **1996**, 118, 10766. For another total synthesis of (+)-6, see: (b) Harada, N.; Sugioka, T.; Uda, H.; Kuriki, T. *J. Org. Chem.* **1990**, 55, 3158. For a total synthesis of (±)-6, see: (c) Kanematsu, K.; Soejima, S.; Wang, G. *Tetrahedron Lett.* **1991**, 32, 4761. (d) Carlini, R.; Higgs, K.; Older, C.; Randhawa, S.; Rodrigo, R. *J. Org. Chem.* **1997**, 115, 8477.
7. BINAs, triphenylarsine, BINAP toxicity data: oral; rat; 30 mg/kg; no toxic effect noted; [Kyorin Pharma. Co., LTD.] (a) Kojima, A.; Boden, C. D.J.; Shibasaki, M. *Tetrahedron Lett.* **1997**, 38, 3459. (b) Cho, S. Y.; Shibasaki, M. *Tetrahedron Lett.* **1998**, 39, 1773.
8. (a) Keay, B. A.; Bontront, J.-L. *J. Can. J. Chem.* **1991**, 69, 1326. (b) Andersen, N. G.; Maddaford, S. P.; Keay, B. A. *J. Org. Chem.* **1996**, 61, 2885. (c) Azadi-Ardakani, M.; Wallace, T. W. *Tetrahedron* **1988**, 44, 5939. (d) Azadi-Ardakani, M.; Hayes, R.; Wallace, T. W. *Tetrahedron* **1990**, 46, 6851.
9. Overman and coworkers proposed a different possibility to obtain products with high ees in some cases. See ref 5o.
10. We could also isolate a trace amount of the following compound in entry 1 of Table 1.



11. (a) Nagase, S. *The Chemistry of Organic Arsenic, Antimony and Bismuth Compounds*; Patai, S., Ed; John Wiley & Sons, Ltd.: Chichester, 1994, pp 1-24. (b) Farina, V. *Pure & Appl. Chem.*, **1996**, 68, 73.
12. For a Ag<sup>+</sup>-phosphine complex, see: (a) Yanagisawa, A.; Matsumoto, Y.; Nakashima, H.; Asakawa, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1997**, 119, 9319. (b) Ohkouchi, M.; Yamaguchi, M.; Yamagishi, T. 44th Symposium on Organometallic Chemistry, Tokyo, 1997, Abstract p 294.