A Widely Applicable Chiral Auxiliary, *cis*-2-Amino-3,3-dimethyl-1-indanol: Conversion to a Novel Phosphorus-Containing Oxazoline and Its Application as a Highly Efficient Ligand for the Palladium-Catalyzed Enantioselective Allylic Amination Reaction

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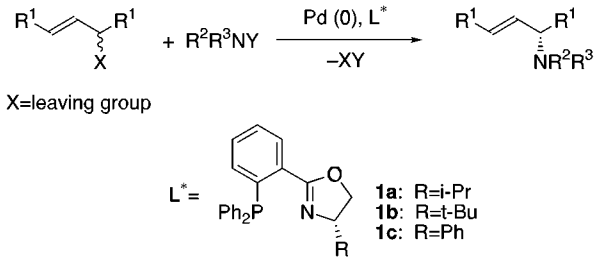
A chiral amino alcohol, *cis*-2-amino-3,3-dimethyl-1-indanol (**2**), was converted into the corresponding enantiomerically pure phosphorus-containing oxazoline **4**. Oxazoline **4** was found to be an efficient ligand for palladium-catalyzed enantioselective allylic amination reactions: In the amination reaction of (*E*)-1,3-diphenyl-2-propen-1-yl acetate (**7a**), **4** was found to be more efficient than the similar ligands **1a**−**c**, derived from valinol, *tert*-leucinol, etc. Other 1,3-bis(*p*-substituted aryl)-2-propen-1-yl acetates were also converted to the corresponding amines in a similar manner and with excellent enantioselectivity. In the amination reaction of 1-alkyl-3,3-diphenyl-2-propen-1-yl acetates **11**, the correponding amines **12** were obtained with excellent enantioselectivity when acetic acid was added to the reaction system.

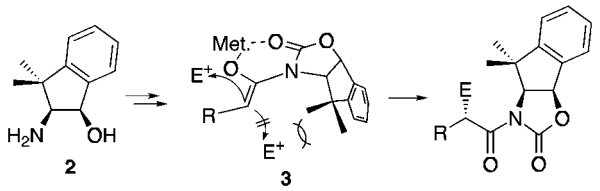
Introduction

The palladium-catalyzed allylic amination reaction is a useful synthetic transformation as the resulting amines can be converted into various kinds of chiral compounds including α-amino acid derivatives.[1] Recently, phosphorus-containing oxazolines, 2-[2-(diphenylphosphino)phenyl]-oxazolines **1**,[2−4] which are at present widely used for various kinds of transition metal-catalyzed enantioselective reactions, have been reported also to be applicable to palladium-catalyzed allylic amination reactions (Scheme 1).[5] These studies showed that the efficiency of chiral induction by **1** depends greatly on the substituent at the 4-position of the oxazoline moiety. Therefore, it is important to develop amino alcohols allowing the construction of oxazolines having suitable substituents in this position in order to achieve higher selectivity in the palladium-catalyzed allylic amination reaction.

Scheme 1



Scheme 2



In the course of our continuing investigations on the consecutive design, synthesis, and resolution of non-natural chiral auxiliaries,[6] we have recently developed a chiral amino alcohol, *cis*-2-amino-3,3-dimethyl-1-indanol (**2**),[7] and found that a chiral oxazolidinone derived from **2** is an efficient auxiliary for various kinds of diastereoselective reaction of the corresponding imide enolates **3** with electrophiles (Scheme 2).[7a] The success of these reactions is thought to arise from the structural characteristics of **2**; the two conformationally-fixed methyl substituents shield one side of the diastereofaces of **3** very effectively. These observations prompted us to

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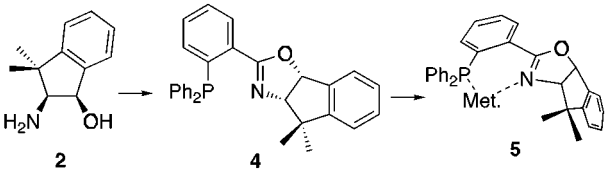
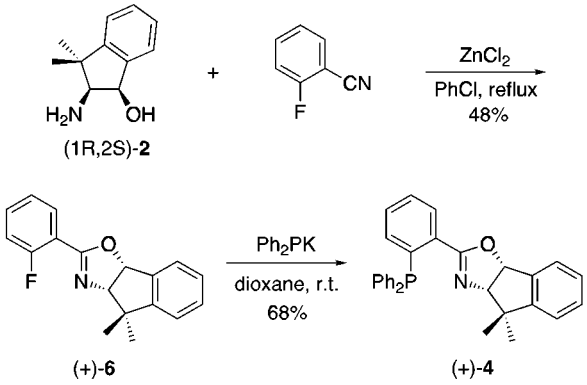
Scheme 3



Scheme 4



convert **2** to 2-[2-(diphenylphosphino)phenyl]oxazoline **4** in the expectation that this would be an efficient enantiomerically-pure ligand for transition metal-catalyzed reactions, since the two methyl substituents should strongly influence the chiral environment around the stereogenic center adjacent to the nitrogen atom of the corresponding transition metal complex **5** (Scheme 3). Amino alcohol **2** has the great advantage as a chiral auxiliary that both its enantiomers can be obtained easily via resolution. Consequently, both enantiomers of **4** are available, with use of the appropriate one leading to the synthesis of target compounds of the desired absolute configuration.

In this paper, we describe the synthesis of the new phosphorus-containing oxazoline **4** and its application as a ligand for the enantioselective palladium-catalyzed allylic amination reaction.

Results and Discussion

The enantiomerically pure ligand (+)-**4** was synthesized from (1*R*,2*S*)-**2** in two steps according to the procedure reported for the preparation of **1** (Scheme 4).[2] Condensation of (1*R*,2*S*)-**2** with 2-fluorobenzonitrile in the presence of a catalytic amount of $ZnCl_2$ gave 2-(2-fluorophenyl)oxazoline (+)-**6**, which was treated with Ph_2PK to give (+)-**4**. The enantiomer, (−)-**4**, was similarly synthesized from (1*S*,2*R*)-**2**.

The palladium-catalyzed allylic amination reaction was carried out in THF using a catalyst prepared *in situ* by mixing 1.5 mol % of $[Pd(allyl)Cl]_2$ and 3.6 mol % of (+)-**4** (Scheme 5, Table 1). As nitrogen nucleophiles, benzylamine and potassium phthalimide (2 equiv to the substrate) were selected.

The reactions of (*E*)-1,3-diphenyl-2-propen-1-yl acetate (**7a**) with benzylamine and with potassium phthalimide using (+)-**4** as a ligand gave the corresponding aminated products (*R*)-**8a** and (*R*)-**9a**, respectively, with excellent selectivities (Table 1, entries 1 and 3), superior to the results obtained by using **1** as a ligand;[5] the reaction of **7a** with benzylamine using **1b** and that with potassium phthalimide using **1a** gave **8a** of 89% ee and **9a** of 96% ee, respectively. The reaction of **7a** with benzylamine

Scheme 5

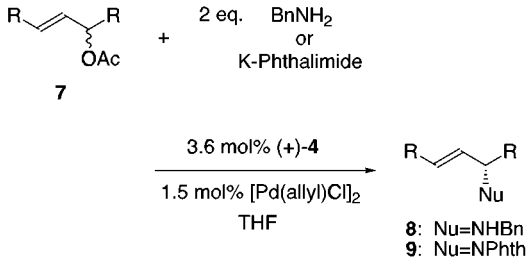


Table 1. Asymmetric Amination of 7[a]

entry	7	R	Nu	*T* (°C)	reaction time/h	product	yield/ %	% ee[b]
1	**7a**	Ph	NHBn	rt	24	(*R*)-**8a**	89	97
2[c]						(*S*)-**8a**	92	96
3			NPhth	50	11	(*R*)-**9a**	88	99
4	**7b**	*p*-Cl-C_6H_4	NHBn	rt	21	(*R*)-**8b**	94	95
5			NPhth	50	13	(*R*)-**9b**	81	98
6	**7c**	*p*-Br-C_6H_4	NHBn	rt	24	(*R*)-**8c**	66[d]	99
7			NPhth	50	10	(*R*)-**9c**	36[e]	97
8[f]	**7d**	Me	NHBn	reflux	8	(*S*)-**8d**	80[g]	20[h]

[a] (+)-**4**, 3.6 mol %; $[Pd(allyl)Cl]_2$, 1.5 mol %; $BnNH_2$ or K-phthalimide, 2 equiv; solvent, THF. [b] Determined by chiral HPLC analysis (Daicel Chiralcel OD). [c] (−)-**4** was used instead of (+)-**4**. [d] **7c** was recovered in 22% yield. [e] **7c** was recovered in 54% yield. [f] 5 mol % $[Pd(allyl)Cl]_2$ and 12 mol % (+)-**4** were used. [g] *E*:*Z* ratio of the product was determined to be 96:4 by 270 MHz ^{1}H-NMR analysis. [h] Ee of the (*E*)-isomer was determined by 270 MHz ^{1}H-NMR analysis of the corresponding MTPA amide.

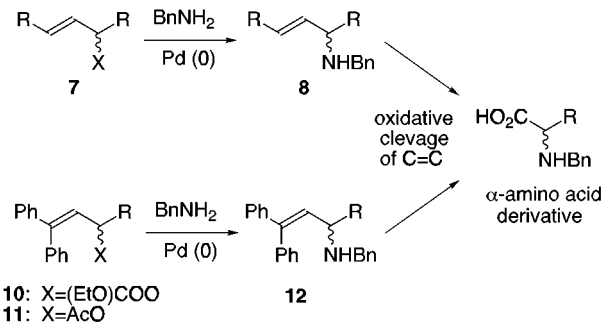
using (−)-**4** as a ligand gave (*S*)-**8a** with excellent selectivity (Table 1, entry 2). Excellent selectivities were also observed in the amination reactions of **7b** and **7c**, which contain *para*-substituted phenyl groups (Table 1, entries 4−7). These results indicate that enantiomerically pure **4** is an excellent ligand for the palladium-catalyzed asymmetric allylic amination.

However, the reactions of **7c** to give (*R*)-**8c** and (*R*)-**9c** were incomplete; the reason for this unsatisfactory result is not clear at present, since no significant byproducts, for example, such as might be formed via oxidative addition of the palladium complex to the C−Br bond of the substrate, were detected. Moreover, the reaction of 3-penten-2-yl acetate (**7d**) with benzylamine required a higher temperature and a larger amount of the catalyst and resulted in disappointingly low enantioselectivity, presumably due to the high reaction temperature (Table 1, entry 8).

The absolute configurations of **8a** and **8d** were confirmed to be *R* and *S*, respectively, by comparison of the signs of their optical rotations with those in the literature.[1,5] The absolute configurations of the other products were also deduced to be *R* by correlation of the signs of their optical rotations (the signs of all the products are minus) and of their the elution orders in HPLC analyses with those of **8a**.

As was observed in the reaction of **7d**, with a few exceptions[1b,e,f] achievement of excellent enantioselectivity in the allylic substitution of 1,3-dialkyl-2-propen-1-ol derivatives is known to be difficult. Thus, we chose the 3,3-diphenyl-2-propen-1-ol derivatives **10** and **11**, which can be regarded as synthetic equivalents of **7**, as substrates, because the product **12** gives the same amino acid derivative on oxidative cleavage of the C=C bond as does **8** (Scheme 6), and carried out the reactions of carbonate **10** and acetate **11** with benzylamine in the presence of the (+)-**4**−palladium complex as a catalyst.

Scheme 6



Scheme 7

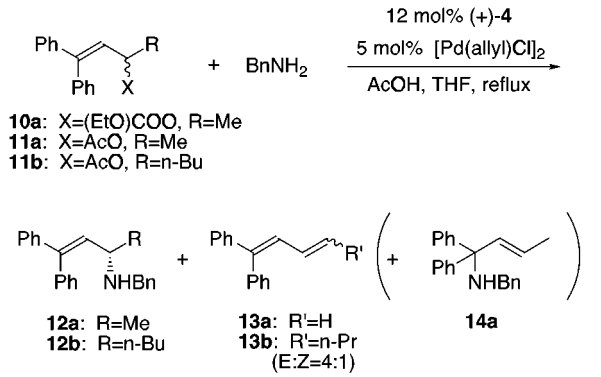


Table 2. Effect of Addition of Acetic Acid in Asymmetric Amination of 11[a]

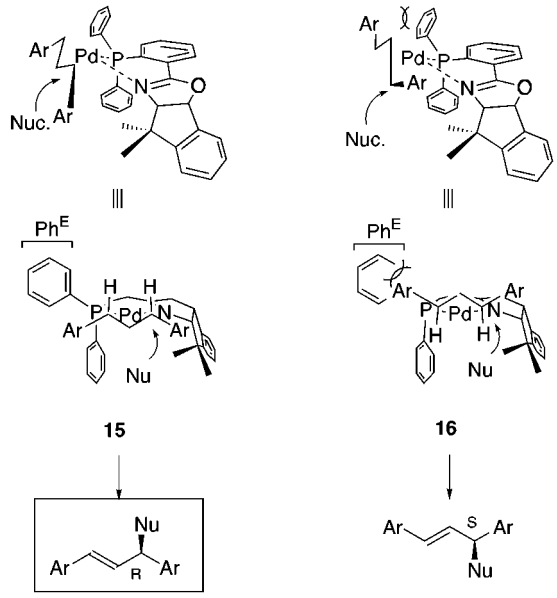
entry	substrate	amt of $BnNH_2$	amt of AcOH	reaction time/h	yield of **12**/%	yield of **13**/%	% ee of **12**[b]
1	**10a**	2	0	6	14[c]	71	85
2	**11a**			8	38	54	92
3			2	4	48	49	98
4			5	5	43	36[d]	>99
5		5		2	79	20	98
6[e]		10	10	3	82	13	98
7	**11b**			10	30[f]	58	94[g]

[a] (+)-**4**, 12 mol %; $[Pd(allyl)Cl]_2$, 5 mol %; solvent, THF; reflux. [b] Determined by chiral HPLC analysis (Daicel Chiralcel OJ). [c] A trace amount of **14a** was obtained. [d] **11a** was recovered in 21% yield. [e] The reaction was carried out at 60 °C. [f] **11b** was recovered in 12% yield. [g] Determined by chiral HPLC analysis (Daicel Chiralcel OD).

The reaction of the carbonate **10a** with benzylamine gave the corresponding amine **12a** with good enantioselectivity (Scheme 7, Table 2, entry 1). However, the chemical yield of **12a** was low, and a significant amount of 1,1-diphenyl-1,3-butadiene (**13a**) and a trace amount of *N*-benzyl-[(*E*)-1,1-diphenyl-2-butenyl]amine (**14a**) were obtained. Utilization of acetate **11a** as a substrate slightly improved both the chemical yield and the enantiomeric excess of **12a**, although **13a** was also obtained as a major product (Table 2, entry 2). These results indicate that elimination reactions must be depressed if the yield of the desired product is to be improved. To this end, we examined addition of acetic acid to the reaction of **11a** with benzylamine.

When acetic acid (2 equiv versus **11a**) was added, the reaction proceeded faster than in the absence of acid, and not only the chemical yield, as expected, but also the enantiomeric excess of **12a** were improved (Table 2, entries 2 vs. 3). However, addition of 5 equiv of acetic acid inhibited complete conversion of **11a**, probably due to decomposition of the ligand under the acidic conditions (Table 2, entry 4). In order to control the acidity of the reaction system, the amount of benzylamine was also increased from 2 to 5 equiv, and this led to great improvement in the chemical yield with no deterioration in the enantiomeric excess of the product (Table 2, entry 5). Further increasing the amounts of benzylamine and acetic acid allowed lowering of the reaction temperature (Table 2, entry 6).

Scheme 8



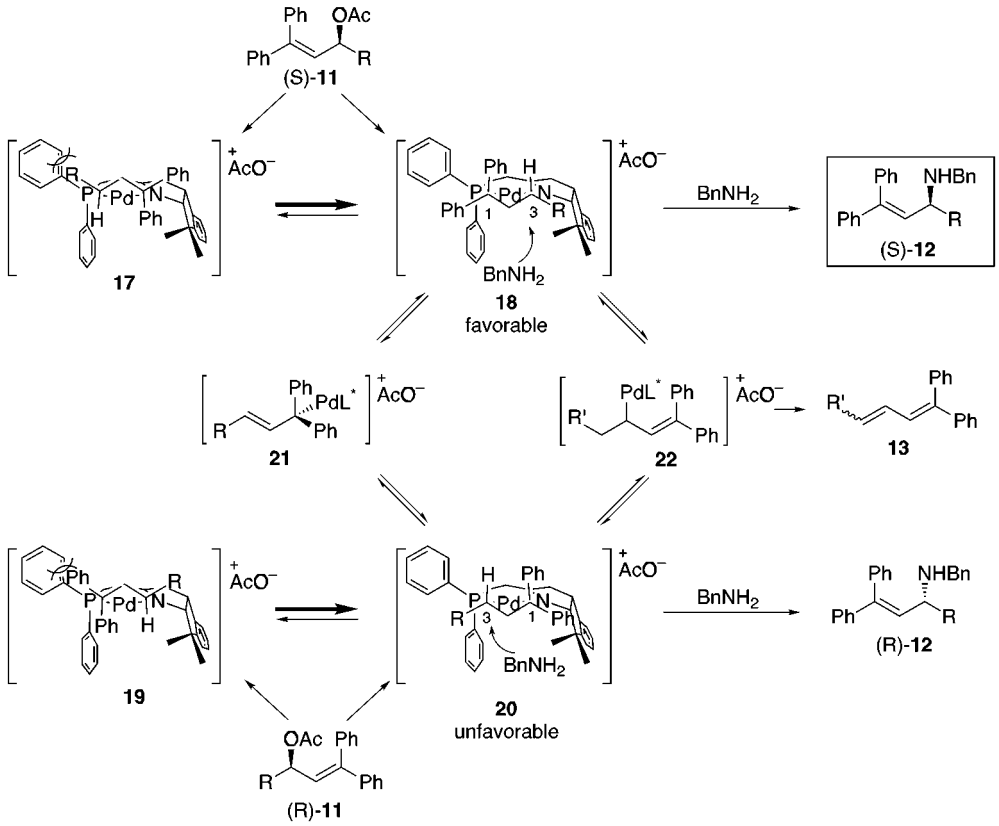
Under the conditions used in entry 6 of Table 2, the amination reaction of 1,1-diphenyl-1-hepten-3-yl acetate (**11b**) was also carried out (Table 2, entry 7). Unfortunately, the reaction did not go to completion even after 10 h, and 12% of acetate **11b** was recovered. Furthermore, the yield of the product **12b** was low (30%), and a significant amount of the corresponding diene **13b** was obtained (58%), due to the high tendency of **11b** to eliminate. However, the enantiomeric excess of amine **12b** obtained was excellent (94% ee). These results clearly demonstrate that (+)-**4** is a highly effective ligand for the palladium-catalyzed asymmetric allylic amination; Bosnich *et al.* reported that the reaction of the acetate **11a** with benzylamine was catalyzed by a complex of palladium with a chiral diphosphine to give the corresponding amine regioselectively with moderate enantioselectivity (up to 76% ee using NORPHOS as a ligand),[8] while Williams *et al.* reported that the reactions of 1-substituted 3,3-diphenyl-2-propen-1-yl acetates with potassium phthalimide using the **1a**−palladium complex as a catalyst did not proceed at all.[9]

Amine **12a** was converted to methyl (*S*)-2-(*N*-benzyl-*N*-mesylamino)propionate according to the reported procedure,[8] showing that the absolute configuration of **12a** is *S*. The absolute configuration of **12b** is considered to be *S* from correlation of the sign of its optical rotation with that of **12a**.

The excellent *R* selectivity in the reactions of **7** using (+)-**4** can be explained as follows. On the basis of detailed NMR and X-ray crystallographic studies concerning the structure of a π-allylpalladium complex with **1a**,[10a] (+)-**4** is considered to coordinate with palladium

(8) Auburn, P. R.; Mackenzie, P. B.; Bosnich, B. *J. Am. Chem. Soc.* **1985**, *107*, 2033.
(9) Dowson, G. J. ; Williams, J. M. J.; Coote, S. J. *Tetrahedron: Asymmetry* **1995**, *6*, 2535.

Scheme 9



using both phosphorus and nitrogen atoms, and the conformation of the diphenylphosphino group of (+)-**4** is presumed to be as shown in **15** and **16** (Scheme 8). Since the nucleophilic attack of benzylamine on a π-allylpalladium intermediate occurs regioselectively at the carbon atom *trans* to phosphorus,[1d,10] the enantioselectivity of the product is strongly affected by the ratio of these two intermediates. Of the two, **15** should be preferred to **16**, since the steric repulsion between the Ar of the π-allyl moiety and the equatorial phenyl group (Ph^E) on the phosphorus atom in **16** is serious. Here, the conformationally-fixed methyl substituents of the ligand (+)-**4** are considered to have more effective bulk than the *tert*-butyl substituent of **1b**, and hence, in the (+)-**4**−palladium complex, the π-allyl moiety is positioned closer to the Ph^E in order to avoid steric repulsion between the two methyl substituents of (+)-**4** and the π-allyl moiety. This causes the steric repulsion between the allylic substituent and Ph^E in **16** to become more serious, and consequently, its formation is strongly disfavored. Benzylamine selectively reacts with **15** at the carbon atom *trans* to the phosphorus of favored intermediate **15** to give the product with excellent selectivity.

In the reaction of **11**, there are four possible π-allylpalladium intermediates **17**−**20** as shown in Scheme 9.[9,11] Of these, **18** and **20** would be more favorable than **17** and **19**, respectively, as discussed above. Complex **18** reacts with benzylamine at the carbon *trans* to phosphorus to afford the product with the observed regio- and stereoselectivities. In contrast, in the case of **20** the formation of (*R*)-**12** requires reaction at the carbon atom *trans* to the nitrogen; the reaction is unfavorable, even though it is not negligible when the concentration of **20** is high. Since **18** and **20** are formed from (*S*)-**11** and (*R*)-**11**, respectively, a rapid interconversion between **18** and **20** is essential for the selective conversion of the both enantiomers of **11** into (*S*)-**12** (Scheme 9). The σ-allylpalladiums **21** and **22** would be the intermediates in such an interconversion. Diene **13** is thought to be formed by the β-elimination of palladium hydride from **22**. Therefore, the formation of a sufficient amount of **21** and **22**, along with the suppression of the β-elimination of palladium hydride from **22**, is necessary to obtain (*S*)-**12** in high yield with excellent selectivity.

Such desirable reaction conditions can be achieved by adding acetic acid to the reaction system; the role of this is thought to be as follows. Since acetate anions are able to strongly coordinate[12] and fulfill the vacant sites of palladium(II), the σ-allylpalladiums would be considerably stabilized. Furthermore, the migration of β-hydride to palladium(II) can be prevented by such coordination. The explanation is strongly supported by the fact that addition of 1-adamantylcarboxylic acid, which is unable to coordinate to palladium because of its bulkiness, in the place of acetic acid resulted in no improvement in the chemical yield of the product (16% yield, 90% ee). It might also be possible that the diene **13** is converted to **12** by palladium-catalyzed addition of benzylamine.

(10) For detailed structural investigations of the π-allypalladium complex of a phosphorus-containing oxazoline, see: (a) Sprinz, J.; Kiefer, M.; Helmchen, G.; Reggelin, M.; Huttner, G.; Walter, O.; Zsolnai, L. *Tetrahedron Lett.* **1994**, *35*, 1523. For detailed structural investigations of the π-allypalladium complexes of other P,N ligands, see: (b) Broun, J. M.; Hulues, D. I.; Guiry, P. J. *Tetrahedron* **1994**, *50*, 4493. (c) Blöchl, P. E.; Togni, A. *Organometallics* **1996**, *15*, 4125.

(11) Mackenzie, P. B.; Whelan, J.; Bosnich, B. *J. Am. Chem. Soc.* **1985**, *107*, 2046.

(12) A significant effect of the counteranion of palladium in an allylic amination has recently been reported: Burckhardt, U.; Baumann, M.; Togni, A. *Tetrahedron: Asymmetry* **1997**, *8*, 155.

(13) Armbruster, R. W.; Morgan, M. M.; Schmidt, J. L.; Lau, C. M.; Riley, R. M.; Zabrowski, D. L.; Dieck, H. A. *Organometallics* **1986**, *5*, 234.

However, this mechanism can be excluded, since **13** was inert under the reaction conditions used in entry 5 of Table 2.

Conclusions

A chiral amino alcohol, *cis*-2-amino-3,3-dimethyl-1-indanol (**2**), of which both enantiomers can be easily obtained via its resolution, was converted into the corresponding enantiomerically pure phosphorus-containing oxazoline **4**. Oxazoline **4** was found to be an efficient ligand for palladium-catalyzed enantioselective allylic amination reactions: In the amination reaction of (*E*)-1,3-diphenyl-2-propen-1-yl acetate (**7a**), **4** was found to be more efficient than the similar ligands **1**, which were derived from valinol, *tert*-leucinol, etc. Other 1,3-bis(*p*-substituted aryl)-2-propen-1-yl acetates were also converted to the corresponding amines with excellent enantioselectivity. In the amination reaction of 1-alkyl-3,3-diphenyl-2-propen-1-yl acetates **11**, the corresponding amines **12** were obtained with excellent enantioselectivity when acetic acid was added to the reaction system.

Experimental Section

General. The starting materials and reagents, purchased from commercial suppliers, were used after standard purification. *cis*-2-Amino-3,3-dimethyl-1-indanol was synthesized and resolved according to the procedure previously reported by us.[6] (*E*)-1,3-Bis(2-chlorophenyl)-1-oxo-2-propene,[14] (*E*)-1,3-bis(2-bromophenyl)-1-oxo-2-propene,[15] and 3,3-diphenylpropenal[16] were synthesized according to the reported procedures. All of the solvents were dried over sodium wire or molecular sieves and were distilled before use. Reaction flasks were flame-dried under a stream of Ar. All moisture- and oxygen-sensitive reactions were conducted under an Ar atomosphere. Flash chromatography was carried out using silica gel 60 (70−230 mesh). Preparative TLC (PTLC) was carried out with Wakogel B-5F. "Usual workup" represents the sequence of drying the combined extracts over Na_2SO_4, filtering off Na_2SO_4, and concentrating the filtrate under reduced pressure.

The melting points are uncorrected. HPLC analysis was performed with detection by UV light. ^{1}H-NMR (270 MHz) spectra were measured with Me_4Si as an internal standard; the δ and J values are given in ppm and Hz, respectively. IR spectral data are recorded in units of cm^{-1}.

(3a*R*,8b*S*)-2-(2-Fluorophenyl)-3a,8b-dihydro-4,4-dimethyl-4*H*-indeno[1,2-*d*]oxazole ((+)-6). To a suspension of $ZnCl_2$ (30 mg) and (1*R*,2*S*)-2-amino-3,3-dimethyl-1-indanol ((1*R*,2*S*)-**2**) (556 mg, 3.14 mmol) in chlorobenzene (7 mL) was added 2-fluorobenzonitrile (0.38 g, 3.2 mmol), and the mixture was stirred for 48 h under reflux. After the mixture was concentrated under reduced pressure, purification by column chromatography (hexane/ethyl acetate (20/1)) gave (+)-**6** as a greenish amorphous mass (420 mg, 1.49 mmol, 48%), which was used for the following reaction without further purification.

An analytical sample was recrystallized from hexane to give colorless prisms: mp 115−160 °C; $[\alpha]^{22}_D$ = +120 (*c* 1.71, $CHCl_3$); IR (KBr) 1640, 1495, 1150; ^{1}H-NMR ($CDCl_3$) δ 1.06 (3H, s), 1.21 (3H, s), 4.41 (1H, d, J = 7.6), 5.74 (1H, d, J = 7.6), 7.0−7.9 (8H, m). Anal. Calcd for $C_{18}H_{16}FNO$: C, 76.85; H, 5.73; N, 4.98. Found: C, 76.63; H, 5.70; N, 4.94.

(3a*S*,8b*R*)-2-(2-Fluorophenyl)-3a,8b-dihydro-4,4-dimethyl-4*H*-indeno[1,2-*d*]oxazole ((−)-6). According to the procedure given for the preparation of (+)-**6**, (−)-**6** was obtained from (1*S*,2*R*)-**2** (1.85 g, 10.4 mmol) as a greenish amorphous mass (881 mg, 3.13 mmol, 30%), which was used for the following reaction without further purification.

An analytical sample was recrystallized from hexane to give colorless prisms: $[\alpha]^{22}_D$ = −118 (*c* 0.875, $CHCl_3$). Other physical data were identical with those of (+)-**6**.

(3a*R*,8b*S*)-2-[2-(Diphenylphosphino)phenyl]-3a,8b-dihydro-4,4-dimethyl-4*H*-indeno[1,2-*d*]oxazole ((+)-4). To potassium diphenylphosphide[17] (34 mL, 9.2 mmol; 0.27 M solution in THF/dioxane (4/6)) was added a solution of (+)-**6** (1.30 g, 4.62 mmol) in THF (5 mL) at 0 °C, and the resulting solution was stirred for 1 h at rt. The reaction was quenched by adding water (30 mL), and the mixture was extracted with ether (3 × 20 mL). After usual workup, purification by column chromatography (hexane/ethyl acetate (19/1)) gave (+)-**4** as a colorless amorphous mass (1.43 g, 3.19 mmol, 65%): $[\alpha]^{22}_D$ = +95 (*c* 2.99, $CHCl_3$); IR (KBr) 1642; ^{1}H-NMR ($CDCl_3$) δ 1.08 (3H, s), 1.21 (3H, s), 4.50 (1H, d, J = 7.6), 5.84 (1H, d, J = 7.6), 6.8−6.9 (1H, m), 7.1−7.4 (16H, m), 7.8−7.9 (1H, m); HRMS(EI) calcd for $C_{30}H_{26}NOP$ 447.1752, found 447.1737.

(3a*S*,8b*R*)-2-[2-(Diphenylphosphino)phenyl]-3a,8b-dihydro-4,4-dimethyl-4*H*-indeno[1,2-*d*]oxazole ((−)-4). According to the procedure given for the preparation of (+)-**4**, (−)-**4** was obtained from (−)-**6** (800 mg, 2.84 mmol) as a colorless amorphous mass (364 mg, 0.812 mmol, 29%): $[\alpha]^{22}_D$ = −96 (*c* 2.82, $CHCl_3$). Other physical data were identical with those of (+)-**4**.

(*E*)-1,3-Bis(2-chlorophenyl)-2-propenyl Acetate (7b). Sodium borohydride (0.10 g, 2.9 mmol) was added in several portions to a suspension of (*E*)-1,3-bis(2-chlorophenyl)-1-oxo-2-propene (0.80 g, 2.9 mmol) and cerium chloride heptahydrate (1.1 g, 2.9 mmol) in methanol (20 mL) at 0 °C. After the reaction mixture had been stirred at the same temperature for 10 min, the reaction was quenched by adding water (20 mL), and the mixture was extracted with ether (3 × 30 mL). Usual workup gave a viscous oil ((*E*)-1,3-bis(2-chlorophenyl)-2-propen-1-ol), which was used for the following reaction without further purification. To an ethereal solution (4 mL) of this alcohol, pyridine (1 mL), and a catalytic amount of 4-(dimethylamino)pyridine was added acetyl chloride (0.50 mL, 7.0 mmol) dropwise at 0 °C. After the mixture had been stirred for 12 h, the reaction was quenched by adding water (10 mL), and the mixture was extracted with ether (3 × 20 mL). The combined extracts were successively washed with 10% HCl (aq) (3 × 20 mL), saturated aqueous $NaHCO_3$ (30 mL), and brine (30 mL). After usual workup, purification by column chromatography (hexane/ethyl acetate (9/1)) gave **7b** as a colorless oil (0.93 g, 2.9 mmol, quant): IR (NaCl) 1740, 1230; ^{1}H-NMR ($CDCl_3$) δ 2.13 (3H, s), 6.27 (1H, dd, J = 6.6, 16), 6.38 (1H, d, J = 6.6), 6.56 (1H, d, J = 16), 7.2−7.4 (8H, m); HRMS(EI) calcd for $C_{17}H_{14}Cl_2O_2$ 320.0371, found 320.0360.

(*E*)-1,3-Bis(2-bromophenyl)-2-propenyl Acetate (7c). According to the procedure given for the preparation of **7b**, **7c** (2.6 g, 6.3 mmol, 93%) was obtained from (*E*)-1,3-bis(2-bromophenyl)-1-oxo-2-propene (2.50 g, 6.8 mmol) as a colorless oil: IR (NaCl) 1740, 1230; ^{1}H-NMR ($CDCl_3$) δ 2.13 (3H, s), 6.30 (1H, d, J = 22), 6.30 (1H, dd, J = 16, 22), 6.54 (1H, dd, J = 16), 7.22 (2H, d, J = 8.6), 7.27 (2H, d, J = 8.6), 7.42 (2H, d, J = 8.6), 7.50 (2H, d, J = 8.6); HRMS(EI) calcd for $C_{17}H_{14}Br_2O_2$ 407.9360, found 407.9374.

1,1-Diphenyl-1-hepten-3-yl Acetate (11b). To a solution of 3,3-diphenylpropenal (1.00 g, 4.80 mmol) in THF (20 mL) was added butyllithium (3.2 mL, 5.2 mmol; 1.63 M solution in hexane) at −78 °C, and the mixture was stirred for 1 h at 0 °C. The reaction was quenched by adding saturated NH_4Cl (aq) (15 mL), and was extracted with ether (3 × 20 mL). Usual workup gave a viscous oil, 1,1-diphenyl-1-hepten-3-ol, which was used for the following reaction without further purification. To an ethereal solution (15 mL) of this alcohol, pyridine (1 mL), and a catalytic amount of 4-(dimethylamino)pyridine was added acetyl chloride (1.0 mL, 14 mmol) dropwise at 0 °C, and this mixture was stirred for 12 h. The reaction was quenched by adding water (10 mL), and the mixture was extracted with ether (3 × 20 mL). The combined extracts were

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successively washed with 10% HCl (aq) (3 × 10 mL), saturated aqueous $NaHCO_3$ (10 mL), and brine (10 mL). After usual workup, purification by column chromatography (hexane/ethyl acetate (19/1)) gave **11b** as a colorless oil (1.16 g, 3.76 mmol, 78%): IR (NaCl) 1738, 1240; ^{1}H-NMR ($CDCl_3$) δ 0.8−0.9 (3H, br t), 1.1−1.3 (4H, br m), 1.5−1.8 (2H, m), 2.00 (3H, s), 5.34 (1H, dt, J = 6.6, 9.2), 6.00 (1H, d, J = 9.2), 7.2−7.4 (10H, m); HRMS(EI) calcd for $C_{21}H_{24}O_2$ 308.1776, found 308.1772.

General Procedure for Amination of 7 with Benzylamine. To a solution of $[Pd(allyl)Cl]_2$ (3.5 mg, 0.0096 mmol) and ligand (+)-**4** (10.6 mg, 0.0237 mmol) in THF (1.0 mL), which had been prestirred for 20 min, were added in succession a solution of allylic acetate **7** (0.634 mmol) in THF (1.0 mL) and a solution of benzylamine (175 mg, 1.63 mmol) in THF (1.0 mL), and the resulting mixture was stirred for 19−24 h at rt. After the mixture had been concentrated under reduced pressure, the resulting residue was purified by PTLC (hexane/ethyl acetate (9/1−19/1)) to give the corresponding amine as colorless oil. Chiral HPLC analysis of the product was performed in order to determine the enantioselectivity (an authentic sample was prepared by the reaction of **7** with benzylamine in the presence of $Pd_2(dba)_3$·$CHCl_3$/dppf (1/1)).

(*R*)-*N*-Benzyl-[(*E*)-1,3-diphenyl-2-propenyl]amine ((*R*)-8a).[1,5a] The ee was determined to be 97% by chiral HPLC analysis (Daicel Chiralcel OD, hexane/*i*-PrOH (199/1), α 1.13, shorter retention time for the *R* isomer): $[\alpha]^{26}_D$ = −26 (*c* 1.68, $CHCl_3$) (lit. $[\alpha]^{20}_D$ −25 (*c* 1.4, $CHCl_3$) for the *R* isomer).[1a]

(*S*)-*N*-Benzyl-[(*E*)-1,3-diphenyl-2-propenyl]amine ((*S*)-8a). The ee was determined to be 96% by chiral HPLC analysis (Daicel Chiralcel OD, hexane/*i*-PrOH (199/1)): $[\alpha]^{26}_D$ = +25 (*c* 1.76, $CHCl_3$).

(*R*)-*N*-Benzyl-[(*E*)-1,3-bis(2-chlorophenyl)-2-propenyl]amine ((*R*)-8b). The ee was determined to be 95% by chiral HPLC analysis (Daicel Chiralcel OD, hexane/*i*-PrOH (99/1), α 1.50, shorter retention time for the *R* isomer): $[\alpha]^{21}_D$ = −7.3 (*c* 1.31, $CHCl_3$); IR (NaCl) 1490, 1190; ^{1}H-NMR ($CDCl_3$) δ 1.72 (1H, s), 3.74 (2H, s), 4.36 (1H, d, J = 7.3), 6.22 (1H, dd, J = 7.3, 16), 6.50 (1H, d, J = 16), 7.2−7.4 (13H, m); HRMS(EI) calcd for $C_{22}H_{19}Cl_2N$ 367.0895, found 367.0885.

(*R*)-*N*-Benzyl-[(*E*)-1,3-bis(2-bromophenyl)-2-propenyl]amine ((*R*)-8c). The ee was determined to be 97% by chiral HPLC analysis (Daicel Chiralcel OD, hexane/*i*-PrOH (99/1), α 1.40, shorter retention time for the *R* isomer): $[\alpha]^{26}_D$ = −1.5 (*c* 8.44, $CHCl_3$); IR (NaCl) 1490; ^{1}H-NMR ($CDCl_3$) δ 1.65 (1H, br s), 3.74 (2H, s), 4.34 (1H, d, J = 7.3), 6.23 (1H, dd, J = 7.3, 16), 6.49 (1H, d, J = 16), 7.2−7.6 (13H, m); HRMS(EI) calcd for $C_{22}H_{19}Br_2N$ 456.9863, found 456.9847.

General Procedure for Amination of 7 with Potassium Phthalimide. To a suspension of $[Pd(allyl)Cl]_2$ (3.5 mg, 0.0096 mmol), ligand (+)-**4** (10.6 mg, 0.0237 mmol), and potassium phthalimide (0.35 g, 1.9 mmol) in THF (2.0 mL), which had been prestirred for 20 min, was added a solution of allylic acetate **7** (0.636 mmol) in THF (1.0 mL), and the mixture was stirred for 12 h at 50 °C. After being allowed to cool to rt, the reaction was quenched by adding water (3 mL), and this mixture was extracted with ether (3 × 10 mL). After usual workup and removal of the highly polar byproducts by short column chromatography (hexane/ethyl acetate (1/1)), the mixture was purified by PTLC (hexane/ethyl acetate (9/1−19/1) to give the corresponding *N*-allylphthalimide as colorless crystals. Chiral HPLC analysis of the product was performed in order to determine the enantioselectivity (an authentic sample was prepared by the reaction of **7** with potassium phthalimide in the presence of $Pd_2(dba)_3$·$CHCl_3$/dppf (1/1)).

(*R*)-*N*-[(*E*)-1,3-Diphenyl-2-propenyl]phthalimide ((*R*)-9a). The ee was determined to be 99% by chiral HPLC analysis (Daicel Chiralcel OD, hexane/*i*-PrOH (99/1), α 1.29, longer retention time for the *R* isomer): mp 119−120 °C; $[\alpha]^{26}_D$ = −17 (*c* 1.70, $CHCl_3$); IR (KBr) 1710, 1385; ^{1}H-NMR ($CDCl_3$) δ 6.17 (1H, d, J = 8.3), 6.73 (1H, d, J = 16), 7.07 (1H, dd, J = 8.3, 16), 7.2−7.5 (10H, m), 7.6−7.9 (4H, m); HRMS(EI) calcd for $C_{23}H_{17}NO_2$ 339.1259, found 339.1261. Anal. Calcd for $C_{23}H_{17}NO_2$: C, 81.40; H, 5.05; N, 4.13. Found: C, 81.05; H, 5.21; N, 4.26.

(*R*)-*N*-[(*E*)-1,3-Bis(2-cholorophenyl)-2-propenyl]phthalimide ((*R*)-9b). The ee was determined to be 95% by chiral HPLC analysis (Daicel Chiralcel OD, hexane/*i*-PrOH (599/1), α 1.48, longer retention time for the *R* isomer): mp 144−145 °C; $[\alpha]^{26}_D$ = −14 (*c* 2.07, $CHCl_3$); IR (KBr) 1710, 1490, 1380; ^{1}H-NMR ($CDCl_3$) δ 6.07 (1H, d, J = 8.6), 6.64 (1H, d, J = 16), 6.97 (1H, dd, J = 8.6, 16), 7.3−7.5 (8H, m), 7.7−7.9 (4H, m); HRMS(EI) calcd for $C_{23}H_{15}Cl_2NO_2$ 407.0479, found 407.0486. Anal. Calcd for $C_{23}H_{15}Cl_2NO_2$: C, 67.66; H, 3.70; N, 3.43. Found: C, 67.43; H, 3.77; N, 3.40.

(*R*)-*N*-[(*E*)-1,3-Bis(2-bromophenyl)-2-propenyl]phthalimide ((*R*)-9c). The ee was determined to be 97% by chiral HPLC analysis (Daicel Chiralcel OD, hexane/*i*-PrOH (199/1), α 1.19, longer retention time for the *R* isomer): mp 89−90 °C; $[\alpha]^{26}_D$ = −11 (*c* 1.20, $CHCl_3$); IR (KBr) 1710, 1490, 1380; ^{1}H-NMR ($CDCl_3$) δ 6.05 (1H, d, J = 8.3), 6.63 (1H, d, J = 16), 6.98 (1H, dd, J = 8.3, 16), 7.2−7.5 (8H, m), 7.7−7.9 (4H, m); HRMS(EI) calcd for $C_{23}H_{15}Br_2NO_2$ 496.9419, found 496.9411.

(*S*)-*N*-Benzyl-(3,3-diphenyl-1-methyl-2-propenyl)-amine (12a).[8] To a solution of $[Pd(allyl)Cl]_2$ (5.8 mg, 0.0159 mmol) and ligand (+)-**2** (17.8 mg, 0.0398 mmol) in THF (0.75 mL), which had been prestirred for 20 min, was added a solution of acetate **11a** (83.6 mg, 0.314 mmol) and benzylamine (0.35 g, 3.3 mmol) in THF (1.0 mL), and then AcOH (0.19 g, 3.2 mmol) was added. The mixture was stirred for 3 h at 60 °C. After being cooled to 0 °C, the reaction mixture was treated with 1 M NaOH (aq) (5 mL), and this mixture was extracted with CH_2Cl_2 (3 × 10 mL). After usual workup and removal of the highly polar byproducts by short column chromatography (hexane/ethyl acetate (1/1)), the mixture was purified by PTLC (hexane/ethyl acetate (3/1)) to give 1,1-diphenyl-1,3-butadiene (**13a**) (8.6 mg, 0.042 mmol, 13%) and **12a** (80.3 mg, 0.256 mmol, 82%) as colorless oils. **12a**: $[\alpha]^{22}_D$ = −92 (*c* 4.02, $CHCl_3$).

The ee of **12a** was determined to be 98% by chiral HPLC analysis (Daicel Chiralcel OJ, hexane/*i*-PrOH = 9:1), α 1.56, shorter retention time for the *S* isomer) (an authentic sample was prepared similarly by the reaction of **11a** using racemic **2** instead of (+)-**2**).

(*S*)-*N*-Benzyl-(3,3-diphenyl-1-butyl-2-propenyl)amine (12b). A similar reaction of **11b** (96.4 mg, 0.313 mmol), followed by purification by PTLC (hexane/ethyl acetate (5/1)), gave unreacted **11b** (9.4 mg, 0.030 mmol, 9.8%), 1,1-diphenyl-1,3-heptadiene (**13b**) (43.3 mg, 0.178 nnol, 56%), and **12b** (36.7 mg, 0.103 mmol, 33%) as colorless oils. **12b**: $[\alpha]^{22}_D$ = −33 (*c* 1.84, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ 0.8−0.9 (3H, br t), 1.2−1.7 (7H, m), 3.28 (1H, dt, J = 7.3, 9.9), 3.54 (1H, d, J = 13), 3.82 (1H, d, J = 13), 5.95 (1H, d, J = 9.9), 7.1−7.4 (15H, m); HRMS(EI) calcd for $C_{26}H_{29}N$ 355.2300, found 355.2316.

The ee of **12b** was determined to be 94% by chiral HPLC analysis (Daicel Chiralcel OD, hexane/*i*-PrOH = 199:1), α 1.20, shorter retention time for the *S* isomer) (an authentic sample was prepared similarly by the reaction of **11b** using racemic **4** instead of (+)-**4**).

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Supporting Information Available: ^{1}H-NMR spectra of all new compounds (10 pages). This material is contained in libraries on microfiche, immediately follows the article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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