Regio- and Enantioselective Allylic Substitution with Less Active *N*- or *O*-Nucleophiles Catalyzed by Iridium-Complex of Bis(oxazolinyl)pyridine

Hideto Miyabe,*[a,b] Katsuhiko Moriyama,[a] and Yoshiji Takemoto*[a]

[a] *Graduate School of Pharmaceutical Sciences, Kyoto University; Yoshida, Sakyo-ku, Kyoto 606–8501, Japan: and* [b] *School of Pharmacy, Hyogo University of Health Sciences; Minatojima, Chuo-ku, Kobe 650–8530, Japan.*

Received January 27, 2011; accepted February 28, 2011

The utility of hydroxylamines as nitrogen nucleophiles was investigated in the iridium-catalyzed regio- and enantioselective allylic substitution. Allylic substitution with hydroxylamines proceeded with good enantioselectivities by using the iridium-complex of bis(oxazolinyl)pyridine ligand. The good regio- and enantioselectivities were also achieved in the reaction with alkylamines, *p*-anisidine, and 4-methoxyphenol.

Key words allylic substitution; catalytic; enantioselective; iridium

Enantioselective transition metal-catalyzed allylic substitutions have been developed as fundamentally important cross-coupling reactions.[1—8] In general, the heteroatom nucleophiles in these reactions have been largely limited to alkylamines, anilines, carboxylates and phenols. Our laboratory is interested in searching the synthetically useful heteroatom nucleophiles for the synthesis of functionalized allylic compounds (Fig. 1).[9] As our successful examples, we have recently reported the utility of oximes **1** and guanidines **5** and **6** as nucleophiles in the transition metal-catalyzed allylic substitution.[10—14]

Hydroxylamines are also attractive synthetic reagents for allylic substitution, since they have nitrogen and oxygen atoms as nucleophiles. However, the allylic substitution with hydroxylamines has not been studied well and is limited to a simple palladium-catalyzed amination[15,16]; thus, there are no reports on asymmetric reactions. We have recently reported that hydroxylamines **2** and **3** having an *N*-electron-withdrawing substituent, also known as hydroxamic acids, act as reactive oxygen nucleophiles in the enantioselective allylic substitution (Fig. 1).[17,18] As a part of our program directed toward searching the synthetically useful heteroatom nucleophiles, we describe in detail the study of hydroxylamines **4** as nitrogen nucleophiles in the regio- and enantioselective iridium-catalyzed allylic substitutions.[19] In this study, we also expected that comparison with alkylamines, *p*-anisidine, and 4-methoxyphenol would lead to informative suggestions regarding the asymmetric reaction using the iridium complex of pybox (bis(oxazolinyl)pyridine) ligand.

Results and Discussion

Controlling both regio- and enantioselectivities has been of great importance in the allylic substitution of unsymmetrical substrates with heteroatom nucleophiles.[20—24] The regioselectivities in reactions using rhodium,[25—33] iridium,[34—38] and ruthenium[39—41] complexes are quite different from those of palladium-catalyzed reaction. Therefore, chiral iridium complexes controlling regio- and enantioselectivities have been a subject of current interest.[42—84] Recently, we reported that the iridium-complex of pybox catalyzed allylic substitution of unsymmetrical substrates to form branched products with good enantioselectivities.[13,14,17,19]

Prior to exploring the enantioselective reaction, we first investigated the viability of hydroxylamine **4A** having *N*-benzoyl and *O*-benzyl groups (Chart 1). Although the reaction of **4A** with carbonate **7** was less effective in the absence of a base, the reaction of **4A** with acetate **8** proceeded smoothly by employing Et_2Zn as a base to give the branched product **9Aa** in 60% yield without formation of the linear product.

Based on these results, we next investigated iridium-catalyzed asymmetric allylic substitution with hydroxylamine **4A** under basic conditions (Chart 2). In this study, phosphate **10a** was employed as an unsymmetrical substrate to prove the efficiency of iridium complex of pybox ligand **12**. In our preliminary communication,[19] we reported that the base drama tically influenced the regio- and enantioselectivities. Here

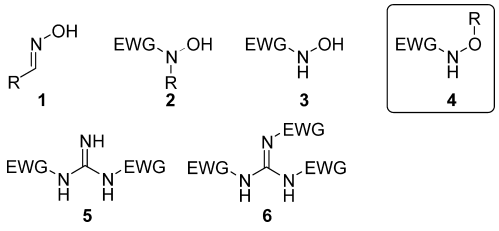

Fig. 1. Heteroatom Nucleophiles in Transition Metal-Catalyzed Allylic Substitution

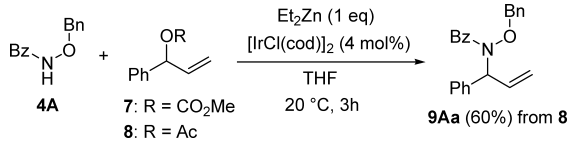

Chart 1. Iridium-Catalyzed Allylic Substitution of Hydroxylamine **4A**

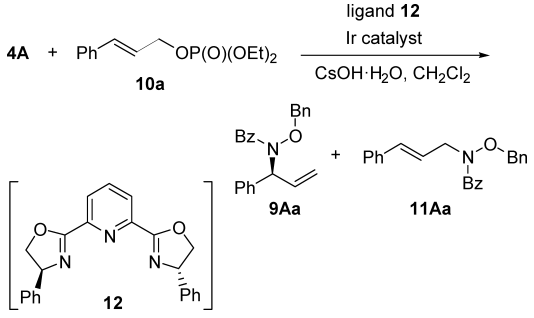

Chart 2. Regio- and Enantioselective Iridium-Catalyzed Allylic Substitution

* To whom correspondence should be addressed. e-mail: miyabe@huhs.ac.jp; takemoto@pharm.kyoto-u.ac.jp

Table 1. Enantioselective Reaction of Hydroxylamine **4A** with **10a**[a)]

Entry	Catalyst	$CsOH \cdot H_2O$	T (°C)	Time (h)	% Yield[b)] (Ratio)[c)]	Ee (%)[d)]
1	$[IrCl(cod)]_2$	1.0 eq	+20	1	94 (76 : 24)	79
2	$[IrCl(cod)]_2$	1.0 eq	−20	8	89 (86 : 14)	92
3	$[IrCl(cod)]_2$	1.0 eq	−40	17	86 (90 : 10)	92
4	$[IrCl(cod)]_2$	1.0 eq	−60	40	45 (87 : 13)	87
5	$[IrCl(cod)]_2$	0.5 eq	−20	18	45 (76 : 24)	79
6	$[IrCl(cod)]_2$	none	−20	50	NR	
7	$[IrOMe(cod)]_2$	1.0 eq	−20	3	94 (86 : 14)	95
8	$[IrOMe(cod)]_2$	none	−20	50	NR	
9	$[IrCl(coe)]_2$	1.0 eq	−20	50	trace	

a) Reactions were carried out with **4A** and **10a** in CH_2Cl_2 in the presence of catalyst (4 mol%) and pybox **12** (8 mol%). *b*) Combined yields. *c*) Ratio for **9Aa** : **11Aa**. *d*) Enantioselectivities were determined by HPLC analysis.

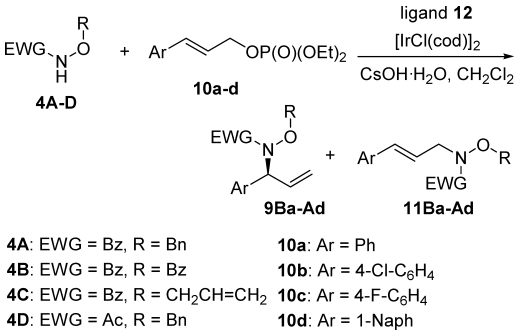

Chart 3. Regio- and Enantioselective Amination Using **4A**—**D**

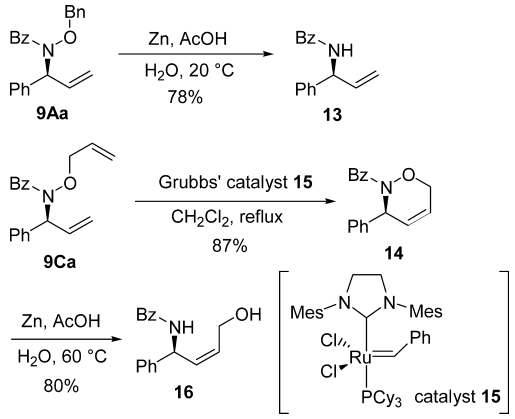

Chart 4. Conversion into Functionalized Compounds

too, good yields of **9Aa** were obtained with reasonable regio- and enantioselectivities by employing $CsOH \cdot H_2O$ or $Ba(OH)_2 \cdot H_2O$ as a base. The results using $Ba(OH)_2 \cdot H_2O$ have been described in our report[19]; thus, Table 1 outlines the optimization of reaction conditions using $CsOH \cdot H_2O$. To a solution of hydroxylamine **4A** and $CsOH \cdot H_2O$ in CH_2Cl_2 was added a solution of the phosphate **10a**, $[IrCl(cod)]_2$ (4 mol%) and ligand **12** (8 mol%) in CH_2Cl_2, and then the reaction mixture was stirred at 20 °C for 1 h (entry 1). The reaction proceeded smoothly to give the branched product **9Aa** and the linear product **11Aa** in 94% combined yield although low regioselectivity was observed. Enantiomeric excess of **9Aa** was determined to be 79% by high performance liquid chromatography analysis using Chiralcel OD-H. The degree of regio- and enantioselectivities was shown to be dependent on the reaction temperature (entries 2—4). Thus, changing the temperature from 20 to −20 °C led to an increase in regioselectivity to 86 : 14 and enantioselectivity to 92% ee (entry 2). The branched product **9Aa** was also obtained with 92% ee, after being stirred at −40 °C for 17 h (entry 3). In the absence of ligand **12**, the iridium-catalyzed reaction of **4A** with phosphate **10a** did not occur. This result indicates the remarkable background reaction did not proceed under the present mild conditions using $CsOH \cdot H_2O$. The reaction proceeded slowly at −60 °C to afford **9Aa** with 87% ee in 87 : 13 ratio (entry 4). The reaction did not proceed effectively when 0.5 eq of $CsOH \cdot H_2O$ was employed (entry 5). In the absence of $CsOH \cdot H_2O$, practically no reaction occurred (entry 6). The use of $[IrOMe(cod)]_2$ led to an increase in enantioselectivity to 95% ee (entry 7). However, in the absence of base, the reaction using $[IrOMe(cod)]_2$ did not proceed (entry 8). In contrast to $[IrCl(cod)]_2$ and $[IrOMe(cod)]_2$, the reaction did not proceed effectively when $[IrCl(coe)]_2$ was employed (entry 9).

To gain further insight into the reactivity of hydroxylamines, several hydroxylamines **4A**—**D** and allylic substrates **10a**—**d** were tested under the reaction conditions using $[IrCl(cod)]_2$ (Chart 3). The nitrogen atom of hydroxylamine **4B** having two electron-withdrawing substituents acted as a reactive nucleophile in allylic substitution (Table 2, entries 1 and 2). The reaction at −20 °C gave the branched product **9Ba** with 87% ee in a 73 : 23 regioselectivity (entry 1). When the reaction was carried out at −40 °C, the product **9Ba** was obtained with 85% ee (entry 2). The hydroxylamine **4C** having *N*-benzoyl and *O*-allyl groups worked well as a nitrogen nucleophile (entries 3 and 4). Changing the temperature from −20 to −40 °C led to a decrease in regio- and enantioselectivity (entry 4). In contrast, moderate enantioselectivities were observed in the reaction with hydroxylamine **4D** having *N*-acetyl and *O*-benzyl groups (entries 5 and 6). Phosphates **10b**—**d** worked well, allowing facile incorporation of structural variety (entries 7—11). The use of phosphate **10d** having 1-naphthyl group led to an increase in regioselectivity to >95 : 5 and enantioselectivity to 96% ee (entries 10 and 11).

The branched products can be converted into functionalized allylic compounds (Chart 4). The branched product **9Aa** was easily converted into **13**. The absolute configuration of product **13** was determined to be *S* upon comparison with authentic compound (*R*)-**13**.[85] The combination of intermolecular allylic substitution with metathesis is a useful method for the synthesis of heterocycles as demonstrated by Evans.[25,26,86]

Table 2. Reaction of Hydroxylamines **4A**—**D** with **10a**—**d**[a]

Entry	Hydroxyl-amine	Phosphate	T (°C)	Time (h)	% Yield[b] (ratio)	Ee (%)[c]
1	**4B**	**10a**	−20	12	73 (**9Ba** : **11Ba** = 73 : 27)	87
2	**4B**	**10a**	−40	12	44 (**9Ba** : **11Ba** = 72 : 28)	85
3	**4C**	**10a**	−20	8	88 (**9Ca** : **11Ca** = 89 : 11)	94
4	**4C**	**10a**	−40	50	47 (**9Ca** : **11Ca** = 87 : 13)	89
5	**4D**	**10a**	+20	12	84 (**9Da** : **11Da** = 89 : 11)	33
6	**4D**	**10a**	−20	65	69 (**9Da** : **11Da** = 90 : 10)	65
7	**4A**	**10b**	−20	20	75 (**9Ab** : **11Ab** = 70 : 30)	87
8	**4A**	**10c**	−20	30	67 (**9Ac** : **11Ac** = 71 : 29)	83
9	**4A**	**10c**	−40	65	45 (**9Ac** : **11Ac** = 80 : 20)	82
10	**4A**	**10d**	−20	30	95 (**9Ad** : **11Ad** = >95 : 5)	96
11	**4A**	**10d**	−40	65	56 (**9Ad** : **11Ad** = >95 : 5)	96

a) Reactions were carried out with **4A**—**D** and **10a**—**d** in CH_2Cl_2 in the presence of $[IrCl(cod)]_2$ (4 mol%) and pybox **12** (8 mol%). *b*) Combined yields. *c*) Enantioselectivities were determined by HPLC analysis.

Table 3. Reaction of Amines **17A**—**C** with **10a**[a]

Entry	Amine	Base	T (°C)	Time (h)	% Yield[b] (ratio)[c]	Ee (%)[d]
1	**17A**	$CsOH \cdot H_2O$	−20	1	91 (71 : 29)	95
2	**17A**	$CsOH \cdot H_2O$	−40	2	86 (70 : 30)	87
3	**17A**	none	−20	24	53 (67 : 33)	76
4	**17B**	$CsOH \cdot H_2O$	−20	20	66 (78 : 22)[e]	94
5	**17C**	$CsOH \cdot H_2O$	+20	5	87 (71 : 29)	56
6	**17C**	$CsOH \cdot H_2O$	−20	65	67 (68 : 32)	71

a) Reactions were carried out with **17A**—**C** and phosphate **10a** in CH_2Cl_2 in the presence of $[IrCl(cod)]_2$ (4 mol%) and pybox **12** (8 mol%). *b*) Combined yields. *c*) Ratio for **18A**—**C** : **19A**—**C**. *d*) Enantioselectivities were determined by HPLC analysis. *e*) A small amount of dicinnamylated product was obtained.

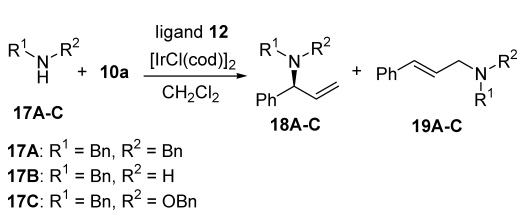

Chart 5. Regio- and Enantioselective Amination Using Other Amines

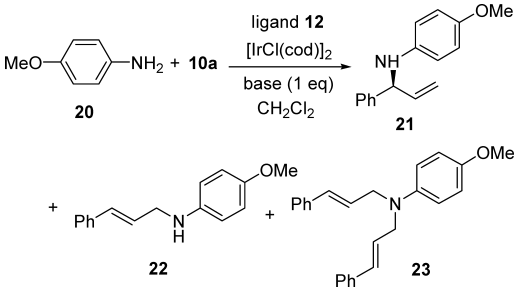

Chart 6. Regio- and Enantioselective Amination Using **20**

Cyclic compound **14** was obtained by ring-closing metathesis (RCM) reaction of **9Ca** using Grubbs' 2nd gen. catalyst **15**. The cleavage of N–O bond of **14** was achieved by reduction using Zn and AcOH to give the aminoalcohol **16** in 80% yield.

We next studied the asymmetric reaction with alkylamines as compared with hydroxylamines (Chart 5). Although *N*,*N*-dibenzylamine **17A** has nucleophilic property even in the absence of a base, excellent enantioselectivity and chemical efficiency were obtained when $CsOH \cdot H_2O$ was employed (Table 3, entries 1—3). In the presence of $CsOH \cdot H_2O$, the reaction proceeded smoothly at −20 °C to give the branched product **18A** with 95% ee within 1 h (entry 1). The reaction at −40 °C afforded the product **18A** with 87% ee (entry 2). In the absence of $CsOH \cdot H_2O$, the reaction with **17A** was less effective (entry 3). Similar trend was observed in the reaction with *N*-benzylamine **17B**. The product **18B** was obtained with 94% ee under the reaction conditions using $CsOH \cdot H_2O$ (entry 4). *N*,*O*-Dibenzylhydroxylamine **17C** worked well (entries 5 and 6). Treatment of phosphate **10a** with **17C** at −20 °C gave the branched product **18C** with 71% ee (entry 6).

Table 4. Reaction of **20** with **10a**[a]

Entry	Base	T (°C)	Time (h)	% Yield[b] (ratio)[c]	Ee (%)[d]
1	$CsOH \cdot H_2O$	−20	3	95 (81 : 9 : 10)	88
2	$CsOH \cdot H_2O$	−40	24	86 (80 : 10 : 10)	87
3	none	−40	24	55 (71 : 15 : 14)	72

a) Reactions were carried out with **20** and phospate **10a** in CH_2Cl_2 in the presence of $[IrCl(cod)]_2$ (4 mol%) and pybox **12** (8 mol%). *b*) Combined yields. *c*) Ratio for **21** : **22** : **22**. *d*) Enantioselectivities were determined by HPLC analysis.

Next, the asymmetric reaction with less reactive aniline derivative was investigated (Chart 6). Although *p*-anisidine **20** participated in the present reaction, formation of branched product **21**, linear product **22** and diallylated product **23** were observed. The use of $CsOH \cdot H_2O$ as a base led to an increase in regioselectivity and enantioselectivity (Table 4). *p*-Anisidine **20** worked well at −20 °C to give the branched product **21** with 88% ee in 81 : 9 : 10 ratio (entry 1). The product **21** was also obtained with 87% ee after being stirred at

Table 5. Reaction of **24** with **10a**[a)]

Entry	Base	T (°C)	Time (h)	% Yield[b)] (ratio)[c)]	ee (%)[d)]
1	$CsOH \cdot H_2O$	+20	48	61 (78 : 22)	24
2	$Ba(OH)_2 \cdot H_2O$	+20	1	84 (87 : 13)	45
3	$Ba(OH)_2 \cdot H_2O$	−20	48	65 (98 : 2)	51
4	K_2CO_3	+20	3	86 (83 : 17)	58
5	K_2CO_3	−20	48	88 (92 : 8)	72

a) Reactions were carried out with **24** and phosphate **10a** in CH_2Cl_2 in the presence of $[IrCl(cod)]_2$ (4 mol%) and pybox **12** (8 mol%). *b*) Combined yields. *c*) Ratio for **25** : **26**. *d*) Enantioselectivities were determined by HPLC analysis.

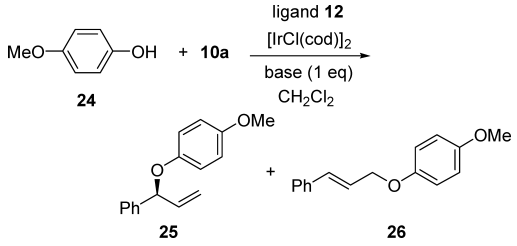

Chart 7. Regio- and Enantioselective Amination Using **24**

−40 °C for 24 h (entry 2). In the absence of $CsOH \cdot H_2O$, treatment of phosphate **10a** with **20** gave **21** with 72% ee (entry 3). Although the effect of base on these enantioselectivities was questioned, we assume that one role would involve the activation of catalyst.

We finally investigated the asymmetric reaction with 4-methoxyphenol **24** (Chart 7). In the presence of $CsOH \cdot H_2O$, the reaction of **10a** with 4-methoxyphenol **24** proceeded slowly to afford the branched product **25** with poor enantioselectivity (Table 5, entry 1). To improve the reactivity and selectivities, the effect of bases was next studied (entries 2—5). Although $Ba(OH)_2 \cdot H_2O$ was less effective for the present reaction, improved selectivities and chemical efficiencies were observed when K_2CO_3 was employed. The reaction using K_2CO_3 at −20 °C gave the 72% ee of the branched product **25** with a 92 : 8 regioselectivity (entry 5). Results from this study show that the iridium complex of pybox ligand is able to catalyze the allylic substitution with less reactive *O*-nucleophiles such as phenols.

In conclusion, we have demonstrated that the iridium-complex of pybox catalyzed the allylic substitution with hydroxylamines in good enantioselectivities. Good regio- and enantioselectivities were also achieved in allylic substitution with alkylamines, *p*-anisidine, and 4-methoxyphenol.

Experimental

General Melting points are uncorrected. ^{1}H- and ^{13}C-NMR spectra were recorded at 500 MHz, and at 125 MHz, respectively. IR spectra were recorded using Fourier transform (FT)-IR apparatus. Mass spectra were obtained by EI or FAB methods. Preparative TLC separations were carried out on precoated silica gel plates (E. Merck $60F_{254}$). Flash column chromatography was performed using E. Merck Kieselgel 60 (230—400 mesh). $[\alpha]_D$ values are measured in 10^{-1} deg cm^2 g^{-1}. The ratios of products were determined by ^{1}H-NMR analysis. Enantiomeric excess was determined by high performance liquid chromatography (HPLC) analysis. Products **19A**,[87] **19B**,[88] **22**,[89] **23**,[89] and **26**[90] are the known compounds.

General Procedure for Enantioselective Allylic Substitution of Amines A mixture of amine **4A**—**D** or **17A**—**C** (1.0 mmol) and $CsOH \cdot H_2O$ (168 mg, 1.0 mmol) in CH_2Cl_2 (4.0 ml) was stirred under argon atmosphere at 20 °C for 10 min. To the reaction mixture was added a solution of allylic phosphate **10a**—**d** (1.5 mmol), pybox **12** (29.6 mg, 0.080 mmol) and $[IrCl(cod)]_2$ (26.9 mg, 0.040 mmol) in CH_2Cl_2 (2.0 ml) at temperature indicated in Tables 2—4. After the reaction was completed, the reaction mixture was diluted with saturated NH_4Cl and then extracted with AcOEt. The organic phase was dried over $MgSO_4$ and concentrated at reduced pressure. The ratio of products was determined by ^{1}H-NMR analysis of crude products. Purification of the residue by preparative TLC (hexane : AcOEt = 5 : 1—25 : 1, 2-fold development) afforded the products **9Aa**—**Ad**, **11Aa**—**Ad**, **18A**—**C**, and **19A**—**C**.

***N*-(Benzyloxy)-*N*-((*S*)-1-phenylallyl)benzamide (9Aa)** As a colorless oil: IR ($CHCl_3$) cm^{-1}: 1635, 1495, 1451. ^{1}H-NMR ($CDCl_3$) δ: 7.70 (2H, d, J=7.0 Hz), 7.60—7.15 (11H, m), 6.83 (2H, d, J=7.0 Hz), 6.32 (1H, ddd, J=17.7, 11.0, 6.1 Hz), 6.15 (1H, d, J=6.1 Hz), 5.39 (1H, d, J=17.7 Hz), 5.38 (1H, d, J=11.0 Hz), 4.48 (1H, d, J=8.5 Hz), 4.11 (1H, d, J=8.5 Hz). ^{13}C-NMR ($CDCl_3$) δ: 170.6, 138.1, 134.9, 134.2, 134.1, 130.6, 129.5, 128.8, 128.6 (2C), 128.3, 128.3, 128.1, 118.6, 78.5, 64.1. One carbon peak was missing due to overlapping. MS (EI$^+$) m/z: 343 (M$^+$, 11), 115 (100). HR-MS m/z: 343.1570 (Calcd for $C_{23}H_{21}NO_2$: 343.1572). HPLC (Chiralcel OD-H, hexane/2-propanol=95/5, 0.5 ml/min, 254 nm) t_R (*S*)=15.8 min, t_R (*R*)=18.1 min. A sample of 92% ee (*S*) by HPLC analysis gave $[\alpha]_D^{29}$ −33.8 (c=1.02, $CHCl_3$).

***N*-(Benzoyloxy)-*N*-((*S*)-1-phenylallyl)benzamide (9Ba)** As a colorless oil: IR ($CHCl_3$) cm^{-1}: 1767, 1665, 1495, 1451. ^{1}H-NMR ($CDCl_3$) δ: 7.84 (2H, d, J=7.6 Hz), 7.68 (2H, d, J=7.3 Hz), 7.55 (1H, t, J=7.6 Hz), 7.45—7.22 (10H, m), 6.22 (1H, ddd, J=17.1, 8.9, 6.1 Hz), 6.11 (1H, d, J=6.1 Hz), 5.40 (1H, d, J=8.9 Hz), 5.37 (1H, d, J=17.1 Hz). ^{13}C-NMR ($CDCl_3$) δ: 170.6, 164.0, 134.0, 133.9, 133.8, 131.1, 129.8, 128.6, 128.4, 128.1, 127.8, 127.2, 119.4, 66.1. Two carbon peaks were missing due to overlapping. MS (EI$^+$) m/z: 357 (M$^+$, 7), 116 (100). HR-MS m/z: 357.1371 (Calcd for $C_{23}H_{19}NO_3$: 357.1365). HPLC (Chiralcel AD-H, hexane/2-propanol=90/10, 1.0 ml/min, 254 nm) t_R (*S*)=19.7 min, t_R (*R*)=15.1 min. A sample of 87% ee (*S*) by HPLC analysis gave $[\alpha]_D^{31}$ +2.6 (c=0.96, $CHCl_3$).

***N*-(Allyloxy)-*N*-((*S*)-1-phenylallyl)benzamide (9Ca)** As a colorless oil: IR ($CHCl_3$) cm^{-1}: 1767, 1665, 1495, 1451. ^{1}H-NMR ($CDCl_3$) δ: 7.68 (2H, d, J=7.0 Hz), 7.46—7.30 (8H, m), 6.30 (1H, ddd, J=17.2, 10.4, 6.4 Hz), 6.03 (1H, d, J=6.4 Hz), 5.51 (1H, m), 5.39 (1H, d, J=10.4 Hz), 5.38 (1H, d, J=17.2 Hz), 5.06 (1H, d, J=10.4 Hz), 4.98 (1H, d, J=17.2 Hz), 4.03 (1H, m), 3.75 (1H, m). ^{13}C-NMR ($CDCl_3$) δ: 170.5, 138.1, 134.8, 134.3, 131.2, 130.6, 128.6, 128.5, 128.1, 128.0 (2C), 119.9, 118.6, 77.6, 64.4. MS (EI$^+$) m/z: 293 (M$^+$, 3), 77 (100). HR-MS m/z: 293.1412 (Calcd for $C_{19}H_{19}NO_2$: 293.1416). HPLC (Chiralcel AD-H, hexane/2-propanol=90/10, 0.5 ml/min, 254 nm) t_R (*S*)=19.2 min, t_R (*R*)=14.2 min. A sample of 94% ee (*S*) by HPLC analysis gave $[\alpha]_D^{25}$ +50.1 (c=1.3, $CHCl_3$).

***N*-(Benzoyloxy)-*N*-((*S*)-1-phenylallyl)acetamide (9Da)** As a colorless oil: IR ($CHCl_3$) cm^{-1}: 1767, 1665, 1495, 1451. ^{1}H-NMR ($CDCl_3$) δ: 7.46 (2H, d, J=7.0 Hz), 7.42—7.30 (6H, m), 7.19—7.13 (2H, m), 6.26 (1H, ddd, J=17.1, 10.4, 5.5 Hz), 6.12 (1H, d, J=5.5 Hz), 5.35 (1H, d, J=10.4 Hz), 5.31 (1H, d, J=17.1 Hz), 4.67 (1H, d, J=9.8 Hz), 4.27 (1H, d, J=9.8 Hz), 2.22 (3H, s). ^{13}C-NMR ($CDCl_3$) δ: 173.6, 138.2, 134.4, 134.0, 129.0, 128.8 (2C), 128.5 (2C), 128.0, 118.5, 78.7, 63.2, 21.0. MS (EI$^+$) m/z: 281 (M$^+$, 15), 91 (100). HR-MS m/z: 281.1410 (Calcd for $C_{18}H_{19}NO_2$: 281.1416). HPLC (Chiralcel OD-H, hexane/2-propanol=95/5, 0.5 ml/min, 254 nm) t_R (*S*)=18.9 min, t_R (*R*)=20.5 min. A sample of 65% ee (*S*) by HPLC analysis gave $[\alpha]_D^{29}$ −13.1 (c=1.03, $CHCl_3$).

***N*-(Benzyloxy)-*N*-((*S*)-1-(4-chlorophenyl)allyl)benzamide (9Ab)** As a colorless oil: IR ($CHCl_3$) cm^{-1}: 1639, 1492, 1449. ^{1}H-NMR ($CDCl_3$) δ: 7.67 (2H, d, J=7.0 Hz), 7.52—7.19 (10H, m), 6.87 (2H, d, J=7.3 Hz), 6.29 (1H, ddd, J=15.9, 9.5, 6.7 Hz), 6.09 (1H, d, J=6.7 Hz), 5.40 (1H, d, J=9.5 Hz), 5.37 (1H, d, J=15.9 Hz), 4.54 (1H, br d, J=8.9 Hz), 4.22 (1H, br d, J=8.9 Hz). ^{13}C-NMR ($CDCl_3$) δ: 170.7, 136.8, 134.7, 133.9 (2C), 130.7, 130.0, 129.4, 128.8, 128.4, 128.2, 128.1, 119.2, 78.7, 63.7. Two carbon peaks were missing due to overlapping. MS (EI$^+$) m/z: 377 (M$^+$, 2), 91 (100). HR-MS m/z: 377.1187 (Calcd for $C_{23}H_{20}ClNO_2$: 377.1188). HPLC (Chiralcel AD-H, hexane/2-propanol=90/10, 0.5 ml/min, 254 nm) t_R (*S*)=28.0 min, t_R (*R*)=21.9 min. A sample of 87% ee (*S*) by HPLC analysis gave $[\alpha]_D^{26}$ −3.7 (c=1.15, $CHCl_3$).

***N*-(Benzyloxy)-*N*-((*S*)-1-(4-fluorophenyl)allyl)benzamide (9Ac)** As a colorless oil: IR ($CHCl_3$) cm^{-1}: 1637, 1510, 1449. ^{1}H-NMR ($CDCl_3$) δ: 7.68 (2H, d, J=7.0 Hz), 7.52—7.38 (5H, m), 7.30—7.20 (3H, m), 7.07 (2H, t, J=8.5 Hz), 6.86 (2H, d, J=7.3 Hz), 6.29 (1H, ddd, J=17.1, 10.4, 6.4 Hz), 6.11 (1H, d, J=6.4 Hz), 5.39 (1H, d, J=10.4 Hz), 5.37 (1H, d, J=17.1 Hz), 4.52 (1H, br d, J=8.9 Hz), 4.16 (1H, br d, J=8.9 Hz). ^{13}C-NMR ($CDCl_3$) δ: 170.7, 162.6 (d, J=247 Hz), 134.8, 134.2, 134.0, 130.7, 130.5, 130.4, 129.4, 128.7, 128.3, 128.2, 128.1, 118.9, 115.5 (d, J=21 Hz), 78.6, 63.5. Two carbon peaks were missing due to overlapping. MS (EI$^+$) m/z: 361 (M$^+$, 3), 91

(100). HR-MS *m/z*: 361.1476 (Calcd for $C_{23}H_{20}FNO_2$: 361.1478). HPLC (Chiralcel AD-H, hexane/2-propanol=90/10, 0.5 ml/min, 254 nm) t_R (*S*)= 23.9 min, t_R (*R*)=20.6 min. A sample of 83% ee (*S*) by HPLC analysis gave $[\alpha]_D^{26}$ −22.7 (*c*=1.30, $CHCl_3$).

***N*-(Benzyloxy)-*N*-((*S*)-1-(naphthalen-1-yl)allyl)benzamide (9Ad)** As a colorless oil: IR ($CHCl_3$) cm^{-1}: 1632, 1511, 1495, 1449. ^{1}H-NMR ($CDCl_3$) δ: 8.37 (1H, d, *J*=8.5 Hz), 7.90 (2H, d, *J*=8.2 Hz), 7.76 (3H, d, *J*=7.9 Hz), 7.65 (1H, t, *J*=7.0 Hz), 7.57—7.35 (5H, m), 7.20—7.05 (4H, m), 6.50—6.40 (3H, m), 5.59 (1H, d, *J*=17.1 Hz), 5.48 (1H, d, *J*=10.7 Hz), 3.94 (1H, br s), 3.36 (1H, br s). ^{13}C-NMR ($CDCl_3$) δ: 170.1, 134.8, 134.1, 133.7, 133.6, 133.4, 132.0, 130.5, 129.5, 129.3, 128.9, 128.5, 128.3, 128.1, 128.0, 127.8, 127.1, 126.1, 125.1, 123.5, 117.8, 78.4, 58.7. MS (EI^+) *m/z*: 393 (M^+, 6), 167 (100). HR-MS *m/z*: 393.1727 (Calcd for $C_{27}H_{23}NO_2$: 393.1729). HPLC (Chiralcel AD-H, hexane/2-propanol=90/10, 0.5 ml/min, 254 nm) t_R (*S*)=17.4 min, t_R (*R*)=14.9 min. A sample of 96% ee (*S*) by HPLC analysis gave $[\alpha]_D^{28}$ −20.6 (*c*=1.07, $CHCl_3$).

***N*-(Benzyloxy)-*N*-cinnamylbenzamide (11Aa)** As a colorless oil: IR ($CHCl_3$) cm^{-1}: 1635, 1496, 1450. ^{1}H-NMR ($CDCl_3$) δ: 7.67 (2H, d, *J*= 7.3 Hz), 7.49—7.22 (11H, m), 7.07 (2H, d, *J*=6.7 Hz), 6.61 (1H, d, *J*= 15.9 Hz), 6.31 (1H, dt, *J*=15.9, 6.1 Hz), 4.72 (2H, s), 4.49 (2H, d, *J*=6.1 Hz). ^{13}C-NMR ($CDCl_3$) δ: 170.3, 136.5, 134.5, 134.3, 134.0, 130.6, 129.5, 128.8, 128.6, 128.5, 128.3, 128.1, 127.9, 126.6, 123.4, 77.1, 50.5. One carbon peak was missing due to overlapping. MS (FAB^+) *m/z*: 344 ($M+H^+$, 64), 117 (100). HR-MS *m/z*: 344.1656 (Calcd for $C_{23}H_{22}NO_2$: 344.1651).

***N*-(Benzoyloxy)-*N*-cinnamylbenzamide (11Ba)** As a colorless oil: IR ($CHCl_3$) cm^{-1}: 1764, 1663, 1495, 1449. ^{1}H-NMR ($CDCl_3$) δ: 7.91 (2H, d, *J*=7.6 Hz), 7.65 (2H, d, *J*=7.0 Hz), 7.56 (1H, d, *J*=7.3 Hz), 7.44—7.21 (10H, m), 6.61 (1H, d, *J*=15.9 Hz), 6.31 (1H, dt, *J*=15.9, 6.4 Hz), 4.67 (2H, d, *J*=6.4 Hz). ^{13}C-NMR ($CDCl_3$) δ: 170.8, 164.6, 136.3, 134.4, 134.1, 133.5, 131.1, 129.9, 128.7, 128.6, 128.3, 128.0, 127.9, 127.0, 126.6, 122.6, 52.3. MS (EI^+) *m/z*: 357 (M^+, 3), 116 (100). HR-MS *m/z*: 357.1369 (Calcd for $C_{23}H_{19}NO_3$: 357.1365).

***N*-(Allyloxy)-*N*-cinnamylbenzamide (11Ca)** As a colorless oil: IR ($CHCl_3$) cm^{-1}: 1634, 1495, 1449, 1427. ^{1}H-NMR ($CDCl_3$) δ: 7.70 (2H, d, *J*=7.0 Hz), 7.46—7.23 (8H, m), 6.63 (1H, d, *J*=15.9 Hz), 6.34 (1H, dt, *J*=15.9, 6.4 Hz), 5.71 (1H, m), 5.19 (1H, d, *J*=16.2 Hz), 5.18 (1H, d, *J*=11.0 Hz), 4.50 (2H, d, *J*=6.4 Hz), 4.26 (2H, d, *J*=6.4 Hz). ^{13}C-NMR ($CDCl_3$) δ: 170.1, 136.5, 134.4, 133.8, 131.5, 130.6, 128.6, 128.3, 128.0, 127.9, 126.5, 123.4, 120.5, 76.0, 50.6. MS (EI^+) *m/z*: 293 (M^+, 2), 77 (100). HR-MS *m/z*: 293.1419 (Calcd for $C_{19}H_{19}NO_2$: 293.1416).

***N*-(Benzyloxy)-*N*-cinnamylacetamide (11Da)** As a colorless oil: IR ($CHCl_3$) cm^{-1}: 1655, 1496, 1434. ^{1}H-NMR ($CDCl_3$) δ: 7.40—7.21 (10H, m), 6.55 (1H, d, *J*=15.9 Hz), 6.25 (1H, dt, *J*=15.9, 5.8 Hz), 4.87 (2H, s), 4.39 (2H, d, *J*=5.8 Hz), 2.13 (3H, s). ^{13}C-NMR ($CDCl_3$) δ: 172.6, 136.5, 134.6, 133.7, 129.2, 129.0, 128.7, 128.6, 127.8, 126.5, 123.5, 77.0, 48.7, 20.5. MS (EI^+) *m/z*: 281 (M^+, 7), 91 (100). HR-MS *m/z*: 281.1417 (Calcd for $C_{18}H_{19}NO_2$: 281.1416).

***N*-(4-Chlorocinnamyl)-*N*-(benzyloxy)benzamide (11Ab)** As a colorless oil: IR ($CHCl_3$) cm^{-1}: 1637, 1492, 1450. ^{1}H-NMR ($CDCl_3$) δ: 7.67 (2H, d, *J*=7.0 Hz), 7.48 (1H, t, *J*=7.3 Hz), 7.44—7.20 (9H, m), 7.07 (2H, d, *J*=6.7 Hz), 6.54 (1H, d, *J*=15.9 Hz), 6.28 (1H, dt, *J*=15.9, 6.1 Hz), 4.71 (2H, s), 4.48 (2H, d, *J*=6.1 Hz). ^{13}C-NMR ($CDCl_3$) δ: 170.2, 134.9, 134.3, 134.2, 133.5, 132.6, 130.6, 129.5, 128.8, 128.7, 128.5, 128.3, 128.1, 127.7, 124.1, 76.9, 50.3. MS (EI^+) *m/z*: 377 (M^+, 0.5), 105 (100). HR-MS *m/z*: 377.1184 (Calcd for $C_{23}H_{20}ClNO_2$: 377.1188).

***N*-(4-Fluorocinnamyl)-*N*-(benzyloxy)benzamide (11Ac)** As a colorless oil: IR ($CHCl_3$) cm^{-1}: 1636, 1508, 1450. ^{1}H-NMR ($CDCl_3$) δ: 7.67 (2H, d, *J*=7.0 Hz), 7.50—7.22 (8H, m), 7.11—6.97 (4H, m), 6.56 (1H, d, *J*=15.9 Hz), 6.21 (1H, dt, *J*=15.9, 6.1 Hz), 4.71 (2H, s), 4.47 (2H, d, *J*=6.1 Hz). ^{13}C-NMR ($CDCl_3$) δ: 170.3, 162.5 (d, *J*=247 Hz), 134.4, 134.2, 132.7, 132.6, 130.6, 129.5, 128.8, 128.5, 128.3, 128.1 (2C), 123.1, 115.5 (d, *J*=22 Hz), 77.0, 50.3. MS (EI^+) *m/z*: 361 (M^+, 0.5), 105 (100). HR-MS *m/z*: 361.1477 (Calcd for $C_{23}H_{20}FNO_2$: 361.1478).

***N*-(Benzyloxy)-*N*-((*E*)-3-(naphthalen-1-yl)allyl)benzamide (11Ad)** As a colorless oil: IR ($CHCl_3$) cm^{-1}: 1637, 1496, 1450. ^{1}H-NMR ($CDCl_3$) δ: 8.06 (1H, d, *J*=8.9 Hz), 7.84 (1H, d, *J*=9.2 Hz), 7.78 (1H, d, *J*=7.9 Hz), 7.70 (2H, d, *J*=7.0 Hz), 7.58 (1H, d, *J*=7.0 Hz), 7.53—7.32 (7H, m), 7.30—7.20 (3H, m), 7.10 (2H, d, *J*=7.0 Hz), 6.34 (1H, dt, *J*=15.6, 6.1 Hz), 4.76 (2H, s), 4.61 (2H, d, *J*=6.1 Hz). ^{13}C-NMR ($CDCl_3$) δ: 170.3, 134.5, 134.3, 134.2, 133.6, 131.3, 131.1, 130.6, 129.4, 128.8, 128.5 (2C), 128.3, 128.2, 128.1, 126.6, 126.1, 125.8, 125.6, 124.1, 123.7, 77.1, 50.7. MS (EI^+) *m/z*: 393 (M^+, 0.7), 105 (100). HR-MS *m/z*: 393.1734 (Calcd for $C_{27}H_{23}NO_2$: 393.1729).

***(S)*-*N*,*N*-Dibenzyl-1-phenylprop-2-en-1-amine (18A)** A colorless oil: IR ($CHCl_3$) cm^{-1}: 1493, 1451. ^{1}H-NMR ($CDCl_3$) δ: 7.48 (2H, d, *J*=7.6 Hz), 7.40 (4H, d, *J*=7.3 Hz), 7.35—7.15 (9H, m), 6.08 (1H, ddd, *J*=17.1, 10.1, 8.5 Hz), 5.44 (1H, d, *J*=10.1 Hz), 5.20 (1H, d, *J*=17.1 Hz), 4.27 (1H, d, *J*=8.5 Hz), 3.66 (2H, d, *J*=14.0 Hz), 3.53 (2H, d, *J*=14.0 Hz). ^{13}C-NMR ($CDCl_3$) δ: 141.5, 140.1, 135.4, 128.7, 128.3, 128.2 (2C), 127.0, 126.8, 119.4, 65.2, 53.6. MS (EI^+) *m/z*: 313 (M^+, 22), 117 (100). HR-MS *m/z*: 313.1824 (Calcd for $C_{23}H_{23}N$: 313.1830). HPLC (Chiralcel OJ-H, hexane/2-propanol=95/5, 0.5 ml/min 254 nm) t_R (*S*)=10.8 min, t_R (*R*)=14.0 min. A sample of 95% ee (*S*) by HPLC analysis gave $[\alpha]_D^{31}$ −111.0 (*c*=1.06, $CHCl_3$).

***(S)*-*N*-Benzyl-1-phenylprop-2-en-1-amine (18B)**[42] A colorless oil: IR ($CHCl_3$) cm^{-1}: 3330, 1493, 1453. ^{1}H-NMR ($CDCl_3$) δ: 7.38—7.22 (10H, m), 5.95 (1H, ddd, *J*=17.4, 10.1, 7.0 Hz), 5.22 (1H, d, *J*=17.4 Hz), 5.12 (1H, d, *J*=10.1 Hz), 4.22 (1H, d, *J*=7.0 Hz), 3.74 (1H, d, *J*=13.1 Hz), 3.71 (1H, d, *J*=13.1 Hz), 1.66 (1H, br s). ^{13}C-NMR ($CDCl_3$) δ: 142.8, 141.0, 140.4, 128.6, 128.4, 128.2, 127.4, 127.2, 126.9, 115.2, 65.1, 51.2. MS (FAB^+) *m/z*: 224 ($M+H^+$, 81), 117 (100). HR-MS *m/z*: 224.1443 (Calcd for $C_{16}H_{18}N$: 224.1439). HPLC (Chiralcel OD-H, hexane/2-propanol=99/1, 0.3 ml/min 254 nm) t_R (*S*)=25.5 min, t_R (*R*)=21.7 min. A sample of 94% ee (*S*) by HPLC analysis gave $[\alpha]_D^{29}$ +5.0 (*c*= 1.0, $CHCl_3$).

***(S)*-*N*-Benzyl-*N*-(benzyloxy)-1-phenylprop-2-en-1-amine (18C)** A colorless oil: IR ($CHCl_3$) cm^{-1}: 1494, 1454. ^{1}H-NMR ($CDCl_3$) δ: 7.48 (2H, d, *J*=7.3 Hz), 7.43—7.13 (11H, m), 6.79 (2H, br m), 6.27 (1H, m), 5.26 (1H, d, *J*=17.4 Hz), 5.23 (1H, d, *J*=10.1 Hz), 4.29 (1H, d, *J*=8.5 Hz), 4.15 (1H, br m), 4.00 (1H, br d, *J*=9.2 Hz), 3.89 (1H, br m), 3.77 (1H, br d, *J*=12.5 Hz). ^{13}C-NMR ($CDCl_3$) δ: 141.4, 138.3, 138.0, 136.7, 130.1, 129.2, 128.5, 128.4, 128.1, 127.8, 127.4, 127.2, 117.6, 76.8, 75.5, 60.8. One carbon peak was missing due to overlapping. MS (EI^+) *m/z*: 329 (M^+, 3), 117 (100). HR-MS *m/z*: 329.1782 (Calcd for $C_{23}H_{23}NO$: 329.1780). HPLC (Chiralcel AD-H, hexane/2-propanol=95/5, 0.5 ml/min, 254 nm) t_R (*S*)=7.1 min, t_R (*R*)=7.6 min. A sample of 71% ee (*S*) by HPLC analysis gave $[\alpha]_D^{28}$ +15.2 (*c*=0.82, $CHCl_3$).

***(E)*-*N*-Benzyl-*N*-(benzyloxy)-3-phenylprop-2-en-1-amine (19C)** A colorless oil: IR ($CHCl_3$) cm^{-1}: 1495, 1452. ^{1}H-NMR ($CDCl_3$) δ: 7.43—7.08 (15H, m), 6.56 (1H, d, *J*=16.2 Hz), 6.36 (1H, dt, *J*=16.2, 7.0 Hz), 4.44 (2H, br s), 3.89 (2H. s), 3.56 (2H, d, *J*=7.0 Hz). ^{13}C-NMR ($CDCl_3$) δ: 137.7, 137.1 (2C), 133.6, 129.9, 129.1, 128.6, 128.2 (2C), 127.8, 127.5, 127.3, 126.4, 125.8, 76.0, 62.8, 60.9. MS (EI^+) *m/z*: 329 (M^+, 5), 117 (100). HR-MS *m/z*: 329.1773 (Calcd for $C_{23}H_{23}NO$: 329.1780).

Enantioselective Allylic Substitution with *p*-Anisidine A mixture of **20** (40.0 mg, 0.325 mmol) and $CsOH \cdot H_2O$ (54.5 mg, 0.325 mmol) in CH_2Cl_2 (1.0 ml) was stirred under argon atmosphere at 20 °C for 10 min. To the reaction mixture was added a solution of allylic phosphate **10a** (132 mg, 0.487 mmol), pybox **12** (9.60 mg, 0.0260 mmol) and $[IrCl(cod)]_2$ (8.73 mg, 0.0130 mmol) in CH_2Cl_2 (1.0 ml) at −20 °C. After the reaction was completed, the reaction mixture was diluted with water and then extracted with AcOEt. The organic phase was dried over $MgSO_4$ and concentrated at reduced pressure. The ratio of products was determined by ^{1}H-NMR analysis of crude products. Purification of the residue by preparative TLC (hexane : AcOEt=10 : 1, 2-fold development) afforded the products **21** (64.8 mg, 84%), **22**[89] (7.3 mg, 9%) and **23**[89] (8.1 mg, 10%).

4-Methoxy-*N*-((*S*)-1-phenylallyl)benzenamine (21)[91] A colorless oil: IR ($CHCl_3$) cm^{-1}: 1512, 1457. ^{1}H-NMR ($CDCl_3$) δ: 7.42—7.21 (5H, m), 6.72 (2H, d, *J*=8.9 Hz), 6.55 (2H, d, *J*=8.9 Hz), 6.02 (1H, ddd, *J*=17.1, 10.1, 5.8 Hz), 5.25 (1H, d, *J*=17.1 Hz), 5.19 (1H, d, *J*=10.1 Hz), 4.85 (1H, d, *J*=5.8 Hz), 3.70 (3H, s). ^{13}C-NMR ($CDCl_3$) δ: 152.3, 142.1, 141.3, 139.5, 128.7, 127.4, 127.2, 115.9, 115.0, 114.7, 61.8, 55.6. MS (EI^+) *m/z*: 239 (M^+, 58), 115 (100). HR-MS *m/z*: 239.1303 (Calcd for $C_{16}H_{17}NO$: 239.1310). HPLC (Chiralcel AD-H, hexane/2-propanol=90/10, 0.5 ml/min 254 nm) t_R (*S*)=15.8 min, t_R (*R*)=13.8 min. A sample of 88% ee (*S*) by HPLC analysis gave $[\alpha]_D^{28}$ −12.1 (*c*=0.95, $CHCl_3$).

Enantioselective Allylic Substitution with 4-Methoxyphenol A mixture of **24** (40.0 mg, 0.322 mmol) and K_2CO_3 (44.5 mg, 0.322 mmol) in CH_2Cl_2 (1.0 ml) was stirred under argon atmosphere at 20 °C for 10 min. To the reaction mixture was added a solution of allylic phosphate **10a** (131 mg, 0.483 mmol), pybox **12** (9.52 mg, 0.0258 mmol) and $[IrCl(cod)]_2$ (8.66 mg, 0.0129 mmol) in CH_2Cl_2 (1.0 ml) at −20 °C. After the reaction was completed, the reaction mixture was diluted with water and then extracted with AcOEt. The organic phase was dried over $MgSO_4$ and concentrated at reduced pressure. The ratio of products was determined by ^{1}H-NMR analysis of crude products. Purification of the residue by preparative TLC (hexane : AcOEt=15 : 1, 2-fold development) afforded the products **25** (62.4 mg, 81%) and **26**[90] (5.5 mg, 7%).

(*S*)-1-Phenyl-1-(4-methoxyphenoxy)-2-propene (25)[43] A colorless oil: IR ($CHCl_3$) cm^{-1}: 1505, 1458. ^{1}H-NMR ($CDCl_3$) δ: 7.42—7.25 (5H, m), 6.86 (2H, d, J=9.2 Hz), 6.76 (2H, d, J=9.2 Hz), 6.09 (1H, ddd, J=17.1, 10.4, 5.8 Hz), 5.52 (1H, d, J=5.8 Hz), 5.32 (1H, d, J=17.1 Hz), 5.24 (1H, d, J=10.4 Hz), 3.73 (3H, s). ^{13}C-NMR ($CDCl_3$) δ: 154.1, 152.1, 140.3, 138.2, 128.6, 127.8, 126.7, 117.5, 116.5, 114.5, 81.9, 55.6. MS (EI^+) m/z: 240 (M^+, 87), 136 (100). HR-MS m/z: 240.1154 (Calcd for $C_{16}H_{16}O_2$: 240.1150). HPLC (Chiralcel OD-H, hexane/2-propanol=95/5, 0.5 ml/min 254 nm) t_R (*S*)=21.6 min, t_R (*R*)=19.2 min. A sample of 72% ee (*S*) by HPLC analysis gave $[\alpha]_D^{31}$ −5.8 (c=1.4, $CHCl_3$).

Reduction of 9Aa into 13 To a solution of **9Aa** (40.0 mg, 0.116 mmol) in AcOH–H_2O (1.0 ml, 1 : 1, v/v) was added Zn powder (305 mg, 4.66 mmol) at 20 °C. After being stirred at 60 °C for 20 h, the reaction mixture was diluted with saturated $NaHCO_3$ and then extracted with $CHCl_3$. The organic phase was dried over $MgSO_4$ and concentrated at reduced pressure. Purification of the residue by preparative TLC (hexane : AcOEt=8 : 1) afforded the product **13**[85] (21.6 mg, 78%) as a white solid. IR ($CHCl_3$) cm^{-1}: 3445, 1662, 1510, 1482. ^{1}H-NMR ($CDCl_3$) δ: 7.79 (2H, d, J=7.0 Hz), 7.51—7.27 (8H, m), 6.44 (1H, br d, J=6.7 Hz), 6.11 (1H, ddd, J=17.4, 10.2, 5.5 Hz), 5.85 (1H, br m), 5.32 (1H, d, J=10.2 Hz), 5.29 (1H, d, J=17.4 Hz). ^{13}C-NMR ($CDCl_3$) δ: 166.6, 140.6, 137.2, 134.4, 131.6, 128.9, 128.6, 127.8, 127.3, 127.0, 116.2, 55.5. MS (EI^+) m/z: 237 (M^+, 35), 105 (100). HR-MS m/z: 237.1160 (Calcd for $C_{16}H_{15}NO$: 237.1154). $[\alpha]_D^{29}$ −70.6 (c=1.0, $CHCl_3$).

Conversion of 9Ca into 14 A mixture of **9Ca** (40.0 mg, 0.136 mmol) and 2nd Grubbs' Ru-catalyst **15** (11.6 mg, 0.0136 mmol) in CH_2Cl_2 (8 ml) was stirred under argon atmosphere at reflux for 12 h. After the reaction was completed, the reaction mixture was diluted with water and then extracted with CH_2Cl_2. The organic phase was dried over $MgSO_4$ and concentrated at reduced pressure. Purification of the residue by preparative TLC (hexane : AcOEt=7 : 1) afforded the product **14** (31.2 mg, 87%) as colorless oil. IR ($CHCl_3$) cm^{-1}: 1634, 1494, 1449, 1410. ^{1}H-NMR ($CDCl_3$) δ: 7.67 (2H, d, J=7.3 Hz), 7.51 (2H, d, J=7.3 Hz), 7.45—7.30 (6H, m), 6.07—6.01 (3H, m), 4.52 (1H, br d, J=15.6 Hz), 4.29 (1H, dd, J=15.6, 3.0 Hz). ^{13}C-NMR ($CDCl_3$) δ: 168.8, 138.5, 133.8, 130.8, 128.6, 128.5, 128.0, 127.9, 125.7, 123.6, 69.6, 55.1. One carbon peak was missing due to overlapping. MS (EI^+) m/z: 265 (M^+, 2), 105 (100). HR-MS m/z: 265.1095 (Calcd for $C_{17}H_{15}NO_2$: 265.1103). $[\alpha]_D^{30}$ +405 (c=1.08, $CHCl_3$).

Reduction of 14 into 16 To a solution of **14** (47.0 mg, 0.177 mmol) in AcOH–H_2O (1.6 ml, 1 : 1, v/v) was added Zn powder (463 mg, 7.09 mmol) at 20 °C. After being stirred at 60 °C for 20 h, the reaction mixture was diluted with saturated $NaHCO_3$ and then extracted with $CHCl_3$. The organic phase was dried over $MgSO_4$ and concentrated at reduced pressure. Purification of the residue by preparative TLC (hexane : AcOEt=2 : 1) afforded the product **16** (37.7 mg, 80%) as colorless crystal. mp 128—130 °C (AcOEt/hexane). IR ($CHCl_3$) cm^{-1}: 3438, 1652, 1512, 1481. ^{1}H-NMR ($CDCl_3$) δ: 7.77 (2H, d, J=7.3 Hz), 7.50 (1H, t, J=7.3 Hz), 7.45—7.31 (7H, m), 6.73 (1H, br s), 6.15 (1H, br t, J=8.6 Hz), 5.99 (1H, br m), 5.74 (1H, t, J=10.4 Hz), 4.55 (1H, dd, J=13.0, 8.1 Hz), 4.05 (1H, dd, J=13.0, 6.0 Hz), 3.82 (1H, br s). ^{13}C-NMR ($CDCl_3$) δ: 167.2, 140.1, 134.0, 131.9, 131.6, 130.6, 129.0, 128.6, 128.0, 127.0, 126.7, 57.9, 50.5. MS (FAB^+) 268 ($M+H^+$, 94), 105 (100). HR-MS m/z: 268.1332 (Calcd for $C_{17}H_{18}NO_2$: 268.1337). $[\alpha]_D^{23}$ +3.7 (c=0.7, $CHCl_3$). *Anal.* Calcd for $C_{17}H_{18}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.30; H, 6.60; N, 5.14.

Acknowledgements This work was supported in part by a Grant-in-Aid for Scientific Research (C) (H.M.) from the Ministry of Education, Culture, Sports, Science and Technology of Japan.

References

1) Johannsen M., Jorgensen K. A., *Chem. Rev.*, **98**, 1689—1708 (1998).
2) Helmchen G., *J. Organomet. Chem.*, **576**, 203—214 (1999).
3) Trost B. M., Crawley M. L., *Chem. Rev.*, **103**, 2921—2944 (2003).
4) Graening T., Schmalz H.-G., *Angew. Chem. Int. Ed.*, **42**, 2580—2584 (2003).
5) Trost B. M., *J. Org. Chem.*, **69**, 5813—5837 (2004).
6) Takemoto Y., Miyabe H., "Comprehensive Organometallic Chemistry," 3rd ed., Vol. 10.15, ed. by Crabtree R. H., Mingos D. M. P., Elsevier, Oxford, 2006, pp. 695—724.
7) Lu Z., Ma S., *Angew. Chem. Int. Ed.*, **47**, 258—297 (2008).
8) Takemoto Y., Miyabe H., "Catalytic Asymmetric Synthesis," 3rd ed., ed. by Ojima I., John Wiley & Sons, U.K., 2010, pp. 227—267.
9) Miyabe H., Takemoto Y., *Synlett*, **2005**, 1641—1655 (2005).
10) Miyabe H., Matsumura A., Yoshida K., Yamauchi M., Takemoto Y., *Synlett*, **2004**, 2123—2126 (2004).
11) Miyabe H., Yoshida K., Reddy V. K., Matsumura A., Takemoto Y., *J. Org. Chem.*, **70**, 5630—5635 (2005).
12) Reddy V. K., Miyabe H., Yamauchi M., Takemoto Y., *Tetrahedron*, **64**, 1040—1048 (2008).
13) Miyabe H., Yoshida K., Reddy V. K., Takemoto Y., *J. Org. Chem.*, **74**, 305—311 (2009).
14) Miyabe H., Matsumura A., Yoshida K., Takemoto Y., *Tetrahedron*, **65**, 4464—4470 (2009).
15) Murahashi S., Imada Y., Taniguchi Y., Kodera Y., *Tetrahedron Lett.*, **29**, 2973—2976 (1988).
16) Genet J.-P., Thorimbert S., Touzin A.-M., *Tetrahedron Lett.*, **34**, 1159—1162 (1993).
17) Miyabe H., Yoshida K., Yamauchi M., Takemoto Y., *J. Org. Chem.*, **70**, 2148—2153 (2005).
18) Miyabe H., Yoshida K., Matsumura A., Yamauchi M., Takemoto Y., *Synlett*, **2003**, 567—569 (2003).
19) Preliminary communication, see: Miyabe H., Matsumura A., Moriyama K., Takemoto Y., *Org. Lett.*, **6**, 4631—4634 (2004).
20) Hayashi T., Kishi K., Yamamoto A., Ito Y., *Tetrahedron Lett.*, **31**, 1743—1746 (1990).
21) Trost B. M., Krische M. J., Radinov R., Zanoni G., *J. Am. Chem. Soc.*, **118**, 6297—6298 (1996).
22) Trost B. M., Toste F. D., *J. Am. Chem. Soc.*, **121**, 4545—4554 (1999).
23) You S.-L., Zhu X.-Z., Luo Y.-M., Hou X.-L., Dai L.-X., *J. Am. Chem. Soc.*, **123**, 7471—7472 (2001).
24) Lüssem, B. J., Gais, H.-J., *J. Am. Chem. Soc.*, **125**, 6066—6067 (2003).
25) Leahy D. K., Evans P. A., "Modern Rhodium-Catalyzed Organic Reactions," Chap. 10, ed. by Evans P. A., Wiley-VCH, Weinheim, 2005, pp. 191—214.
26) Evans P. A., Robinson J. E., Nelson J. P., *J. Am. Chem. Soc.*, **121**, 6761—6762 (1999).
27) Evans P. A., Leahy D. K., *J. Am. Chem. Soc.*, **122**, 5012—5013 (2000).
28) Evans P. A., Robinson J. E., Moffett K. K., *Org. Lett.*, **3**, 3269—3271 (2001).
29) Evans P. A., Leahy D. K., *J. Am. Chem. Soc.*, **124**, 7882—7883 (2002).
30) Evans P. A., Leahy D. K., Andrews W. J., Uraguchi D., *Angew. Chem. Int. Ed.*, **43**, 4788—4791 (2004).
31) Evans P. A., Lai K. W., Zhang H.-R., Huffman J. C., *Chem. Commun.*, **2006**, 844—846 (2006).
32) Evans P. A., Clizbe E. A., *J. Am. Chem. Soc.*, **131**, 8722—8723 (2009).
33) Vrieze D. C., Hoge G. S., Hoerter P. Z., Haitsma J. T. V., Samas B. M., *Org. Lett.*, **11**, 3140—3142 (2009).
34) Takeuchi R., *Synlett*, **2002**, 1954—1965 (2002).
35) Takeuchi R., Ue N., Tanabe K., Yamashita K., Shiga N., *J. Am. Chem. Soc.*, **123**, 9525—9534 (2001).
36) Takeuchi R., Shiga N., *Org. Lett.*, **1**, 265—268 (1999).
37) Takeuchi R., Kezuka S., *Synthesis*, **2006**, 3349—3366 (2006).
38) Helmchen G., Dahnz A., Dübon P., Schelwies M., Weihofen R., *Chem. Commun.*, **2007**, 675—691 (2007).
39) Mbaye M. D., Renaud J.-L., Demerseman B., Bruneau C., *Chem. Commun.*, **2004**, 1870—1871 (2004).
40) Onitsuka K., Okuda H., Sasai H., *Angew. Chem. Int. Ed.*, **47**, 1454—1457 (2008).
41) Austeri M., Linder D., Lacour J., *Chem. Eur. J.*, **14**, 5737—5741 (2008).
42) Ohmura T., Hartwig J. F., *J. Am. Chem. Soc.*, **124**, 15164—15165 (2002).
43) López F., Ohmura T., Hartwig J. F., *J. Am. Chem. Soc.*, **125**, 3426—3427 (2003).
44) Kiener C. A., Shu C., Incarvito C., Hartwig J. F., *J. Am. Chem. Soc.*, **125**, 14272—14273 (2003).
45) Shu C., Hartwig J. F., *Angew. Chem. Int. Ed.*, **43**, 4794—4797 (2004).
46) Shu C., Leitner A., Hartwig J. F., *Angew. Chem. Int. Ed.*, **43**, 4797—4800 (2004).
47) Leitner A., Shekhar S., Pouy M. J., Hartwig J. F., *J. Am. Chem. Soc.*, **127**, 15506—15514 (2005).
48) Leitner A., Shu C., Hartwig J. F., *Org. Lett.*, **7**, 1093—1096 (2005).
49) Shekhar S., Trantow B., Leitner A., Hartwig J. F., *J. Am. Chem. Soc.*, **128**, 11770—11771 (2006).
50) Pouy M. J., Leitner A., Weix D. J., Ueno S., Hartwig J. F., *Org. Lett.*, **9**, 3949—3952 (2007).
51) Yamashita Y., Gopalarathnam A., Hartwig J. F., *J. Am. Chem. Soc.*,

129, 7508—7509 (2007).
52) Marković D., Hartwig J. F., *J. Am. Chem. Soc.*, **129**, 11680—11681 (2007).
53) Ueno S., Hartwig J. F., *Angew. Chem. Int. Ed.*, **47**, 1928—1931 (2008).
54) Stanley L. M., Hartwig J. F., *J. Am. Chem. Soc.*, **131**, 8971—8983 (2009).
55) Pouy M. J., Stanley L. M., Hartwig J. F., *J. Am. Chem. Soc.*, **131**, 11312—11313 (2009).
56) Ueda M., Hartwig J. F., *Org. Lett.*, **12**, 92—94 (2010).
57) Stanley L. M., Bai C., Ueda M., Hartwig J. F., *J. Am. Chem. Soc.*, **132**, 8918—8920 (2010).
58) Lipowsky G., Helmchen G., *Chem. Commun.*, **2004**, 116—117 (2004).
59) Welter C., Koch O., Lipowsky G., Helmchen G., *Chem. Commun.*, **2004**, 896—897 (2004).
60) Welter C., Dahnz A., Brunner B., Streiff S., Duebon P., Helmchen G., *Org. Lett.*, **7**, 1239—1242 (2005).
61) Weihofen R., Dahnz A., Tverskoy O., Helmchen G., *Chem. Commun.*, **2005**, 3541—3543 (2005).
62) Welter C., Moreno R. M., Streiff S., Helmchen G., *Org. Biomol. Chem.*, **3**, 3266—3268 (2005).
63) Weihofen R., Tverskoy O., Helmchen G., *Angew. Chem. Int. Ed.*, **45**, 5546—5549 (2006).
64) Spiess S., Berthold C., Weihofen R., Helmchen G., *Org. Biomol. Chem.*, **5**, 2357—2360 (2007).
65) Gnamm C., Franck G., Miller N., Stork T., Brödner K., Helmchen G., *Synthesis*, **2008**, 3331—3350 (2008).
66) Gnamm C., Krauter C. M., Brödner K., Helmchen G., *Chem. Eur. J.*, **15**, 2050—2054 (2009).
67) Gnamm C., Brödner K., Krauter C. M., Helmchen G., *Chem. Eur. J.*, **15**, 10514—10532 (2009).
68) Farwick A., Helmchen G., *Org. Lett.*, **12**, 1108—1111 (2010).
69) Raskatov J. A., Spiess S., Gnamm C., Brödner K., Rominger F., Helmchen G., *Chem. Eur. J.*, **16**, 6601—6615 (2010).
70) Tissot-Croset K., Polet D., Alexakis A., *Angew. Chem. Int. Ed.*, **43**, 2426—2428 (2004).
71) Polet D., Alexakis A., *Org. Lett.*, **7**, 1621—1624 (2005).
72) Polet D., Alexakis A., Tissot-Croset K., Corminboeuf C., Ditrich K., *Chem. Eur. J.*, **12**, 3596—3609 (2006).
73) Fischer C., Defieber C., Suzuki T., Carreira E. M., *J. Am. Chem. Soc.*, **126**, 1628—1629 (2004).
74) Lyothier I., Defieber C., Carreira E. M., *Angew. Chem. Int. Ed.*, **45**, 6204—6207 (2006).
75) Defieber C., Ariger M. A., Moriel P., Carreira E. M., *Angew. Chem. Int. Ed.*, **46**, 3139—3143 (2007).
76) Singh O. V., Han H., *J. Am. Chem. Soc.*, **129**, 774—775 (2007).
77) Singh O. V., Han H., *Org. Lett.*, **9**, 4801—4804 (2007).
78) Singh O. V., Han H., *Tetrahedron Lett.*, **48**, 7094—7098 (2007).
79) Nemoto T., Sakamoto T., Matsumoto T., Hamada Y., *Tetrahedron Lett.*, **47**, 8737—8740 (2006).
80) Kimura M., Uozumi Y., *J. Org. Chem.*, **72**, 707—714 (2007).
81) Bondzic B. P., Farwick A., Liebich J., Eilbracht P., *Org. Biomol. Chem.*, **6**, 3723—3731 (2008).
82) Xu Q.-L., Dai L.-X., You S.-L., *Org. Lett.*, **12**, 800—803 (2010).
83) He H., Liu W.-B., Dai L.-X., You S.-L., *Angew. Chem. Int. Ed.*, **49**, 1496—1499 (2010).
84) Xia J.-B., Liu W.-B., Wang T.-M., You S.-L., *Chem. Eur. J.*, **16**, 6442—6446 (2010).
85) Castagnolo D., Armaroli S., Corelli F., Botta M., *Tetrahedron: Asymmetry*, **15**, 941—949 (2004).
86) Yoshioka E., Kohtani S., Miyabe H., *Trend. Heterocyclic Chem.*, **14**, 1—16 (2009).
87) Kadota I., Shibuya A., Lutete L. M., Yamamoto Y., *J. Org. Chem*., **64**, 4570—4571 (1999).
88) Rehn S., Ofial A. R., Mayr H., *Synthesis*, **12**, 1790—1796 (2003).
89) Yang S.-C., Hsu Y.-C., Gan K.-H., *Tetrahedron*, **62**, 3949—3958 (2006).
90) Yatsumonji Y., Ishida Y., Tsubouchi A., Takeda T., *Org. Lett.*, **9**, 4603—4606 (2007).
91) Weiss M. E., Fischer D. F., Xin Z., Jautze S., Schweizer W. B., Peters R., *Angew. Chem. Int. Ed.*, **45**, 5694—5698 (2006).