Tetrahedron: *Asymmetry* 23 (2012) 284–293

Contents lists available at SciVerse ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

# (*S*)-Phenylalanine-derived chiral phosphorus–olefin ligands in rhodium-catalyzed asymmetric 1,4-addition reactions

Rintaro Narui [a], Sayuri Hayashi [a], Haruka Otomo [a], Ryo Shintani [a,*], Tamio Hayashi [a,b,*]

[a] *Department of Chemistry, Graduate School of Science, Kyoto University, Sakyo, Kyoto 606-8502, Japan*
[b] *Chemistry Department, Faculty of Science, King Abdulaziz University, PO Box 80203, Jeddah 21589, Saudi Arabia*

ARTICLE INFO

*Article history:*
Received 29 January 2012
Accepted 10 February 2012
Available online 13 March 2012

ABSTRACT

Chiral phosphorus–olefins (*S*)-**1**, (*S*)-**4**, and (*S*)-**5** have been designed and synthesized. These ligands were all synthesized from (*S*)-phenylalanine derivatives and act as phosphorus–olefin bidentate ligands to rhodium. The coordination face of the olefin can be effectively controlled by the original chirality of (*S*)-phenylalanine in all cases; the rhodium complexes coordinated with these ligands have been employed as catalysts for the asymmetric 1,4-addition of arylboronic acids to α,β-unsaturated ketones, to give 1,4-adducts with high enantioselectivities for cyclic enones and moderate enantioselectivities for acyclic enones.



## 1. Introduction

Since the first report on the development of effective chiral diene ligands for asymmetric catalysis,[1] a structurally diverse range of chiral dienes have been synthesized and utilized as ligands for various transition metal-catalyzed enantioselective processes.[2] The success of this new class of chiral ligand prompted many researchers to design and synthesize chiral olefin ligands bearing another coordinating group based on a phosphorus,[3,4] nitrogen,[5] or sulfoxide group.[6] Our group also introduced chiral phosphine–olefins **A** as early examples of this type of hybrid chiral olefin ligands (Fig. 1, left).[4] Ligands **A** have a bicyclo[2.2.1]heptene backbone with high rigidity, and provide highly active and stereoselective catalysts for the rhodium-catalyzed asymmetric 1,4-addition of arylboronic acids to electron-deficient olefins.[4a,c] However, these ligands require a long synthetic scheme involving a resolution of the two enantiomers using chiral HPLC. In order to solve this synthetic problem while maintaining the good chiral environment around the olefin, we recently developed a new class of phosphorus–olefin ligand **B** based on 1-(diphenylphosphino)-2,5-dihydro-1*H*-pyrrole, whose chirality is derived from natural (*S*)-phenylalanine (Fig. 1, right), and have demonstrated that these ligands are highly effective for the rhodium-catalyzed asymmetric addition of arylboroxines to *N*-sulfonyl imines.[7] Herein, we introduce new members of this family of phosphorus–olefin ligand and describe the use of these ligands in the rhodium-catalyzed asymmetric 1,4-addition of arylboronic acids to α,β-unsaturated ketones.[8]

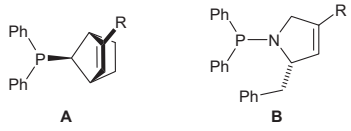



**Figure 1.** Previously developed chiral phosphine–olefin ligand **A** (left) and newly prepared chiral phosphorus–olefin ligand **B** (right).

## 2. Results and discussion

### 2.1. The design and synthesis of chiral phosphorus–olefins B and their analogues

A new class of phosphorus–olefins **B**, the configuration of which can be derived from natural (*S*)-phenylalanine, were designed to coordinate with a transition-metal by the phosphorus atom and the olefin, as was the case for ligands **A**. The coordination face of the olefin should be controlled by the stereogenic carbon center with a benzyl group on the dihydropyrrole ring. Thus, in order to avoid the unfavorable steric interaction of the benzyl group, the β*re*-face of the olefin should preferentially coordinate with a metal **M** and thereby the substituent on the olefin (R) effectively dictates the chiral environment around the metal (Fig. 2). As an initial member of this class of ligand **B**, we prepared compound (*S*)-**1a** from the readily available allylamine derivative (*S*)-**2** (Scheme 1), which is known to be easily synthesized from (*S*)-phenylalanine.[9] N-Alkylation of (*S*)-**2** with 2-methyl-2-propenyl bromide, followed

* Corresponding authors.
*E-mail addresses:* shintani@kuchem.kyoto-u.ac.jp (R. Shintani), thayashi@kuchem.kyoto-u.ac.jp (T. Hayashi).

0957-4166/$ - see front matter © 2012 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2012.02.007

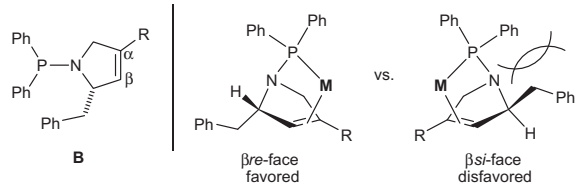
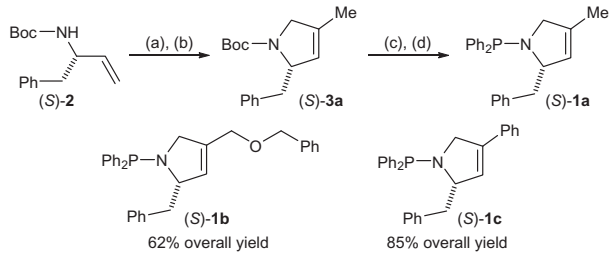


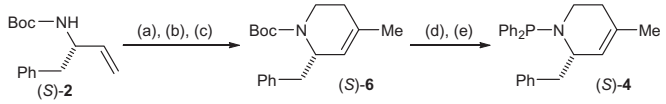

**Figure 2.** Structure of phosphorus–olefin **B** and its coordination modes to a transition metal.



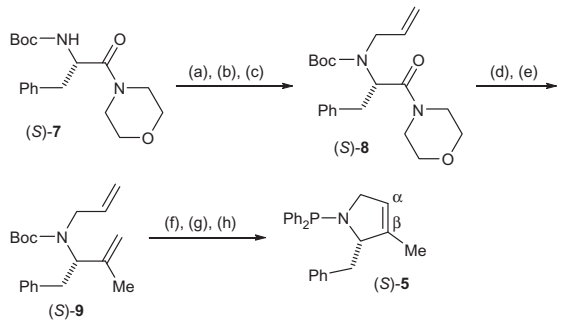

**Scheme 1.** Synthesis of chiral phosphorus–olefins (*S*)-**1**. Reagents and conditions: (a) NaH, 2-methyl-2-propenyl bromide, DMF, rt; 95%; (b) cat. Grubbs 2nd generation, $C_6H_6$, 60 °C; 98%; (c) $CF_3CO_2H$, $CH_2Cl_2$, rt; 95%; (d) (i) NaOH (aq) then $Et_2O$ extraction, (ii) $Ph_2PCl$, $Et_3N$, THF, 0 °C to rt; 83%.

by ruthenium-catalyzed ring-closing metathesis,[10] gave (*S*)-**3a** in a 93% yield over two steps. Removal of the *tert*-butoxycarbonyl group and subsequent N-phosphination with chlorodiphenylphosphine completed the synthesis of (*S*)-**1a** in a 79% yield from (*S*)-**3a**. Chiral phosphorus–olefins (*S*)-**1b** and (*S*)-**1c** with a benzyloxymethyl group and a phenyl group on the olefin, respectively, were also prepared from (*S*)-**2** in good overall yield by following the same synthetic scheme for (*S*)-**1a**.

In addition to these ligands (*S*)-**1a**–**1c**, we also synthesized analogous phosphorus–olefins (*S*)-**4** with a tetrahydropyridine framework instead of dihydropyrrole (Scheme 2) and (*S*)-**5** with a methyl group at the β-carbon instead of at the α-carbon (Scheme 3), starting from (*S*)-phenylalanine derivatives in both




**Scheme 2.** Synthesis of chiral phosphorus–olefin (*S*)-**4**. Conditions: (a) $CF_3CO_2H$, $CH_2Cl_2$, rt; 87%; (b) (i) $NaHCO_3$ (aq) then $CH_2Cl_2$ extraction, (ii) 3-methyl-3-butenyl methanesulfonate, $K_2CO_3$, MeCN, rt, (iii) $(Boc)_2O$, $Et_3N$, THF, rt; 55%; (c) cat. Grubbs 2nd generation, $C_6H_6$, 60 °C; 96%; (d) $CF_3CO_2H$, $CH_2Cl_2$, rt; 99%; (e) (i) NaOH (aq) then $Et_2O$ extraction, (ii) $Ph_2PCl$, $Et_3N$, THF, rt; 83%.




**Scheme 3.** Synthesis of chiral phosphorus–olefin (*S*)-**5**. Reagents and conditions: (a) $CF_3CO_2H$, $CH_2Cl_2$, rt; 99%; (b) allyl bromide, $Na_2CO_3$, MeCN, rt; 62%; (c) $(Boc)_2O$, $Et_3N$, THF, rt; 95%; (d) MeMgCl, THF, −20 °C to rt; 81%; (e) (i) $MePPh_3Br$, $NaN(SiMe_3)_2$, $Et_2O$/THF, rt, (ii) recrystallization from hexane; 74%; (f) cat. Grubbs 2nd generation, $C_6H_6$, 60 °C; 99%; (g) $CF_3CO_2H$, $CH_2Cl_2$, rt; 86%; (h) (i) NaOH (aq) then $Et_2O$ extraction, (ii) $Ph_2PCl$, $Et_3N$, THF, rt; 77%.

cases. For the synthesis of (*S*)-**4**, a 3-methyl-3-butenyl group was installed on the nitrogen atom of (*S*)-**2** by sequential N-deprotection, alkylation, and reprotection,[11] and the resulting 1,7-diene was subjected to the ruthenium-catalyzed ring-closing metathesis to give (*S*)-**6** in a 46% overall yield. Removal of the *tert*-butoxycarbonyl group and subsequent N-phosphination with chlorodiphenylphosphine gave (*S*)-**4** in an 82% yield from (*S*)-**6**. The synthesis of (*S*)-**5** was initiated by the installation of an allyl group on the nitrogen atom of (*S*)-**7**[12] through a similar sequence of N-deprotection, allylation, and reprotection to give (*S*)-**8** in a 58% yield. Treatment of (*S*)-**8** with methylmagnesium chloride provided the methyl ketone, which was then reacted with a phosphonium ylide to give (*S*)-**9** with 98% ee. Recrystallization of this material from hexane gave (*S*)-**9** with >99% ee in a 60% overall yield from (*S*)-**8**. The ruthenium-catalyzed ring-closing metathesis of (*S*)-**9**, followed by removal of the *tert*-butoxycarbonyl group and the subsequent N-phosphination with chlorodiphenylphosphine, completed the synthesis of (*S*)-**5** in a 66% yield from (*S*)-**9**.

## 2.2. Structures of rhodium complexes coordinated with phosphorus–olefins (*S*)-1a, (*S*)-4 and (*S*)-5

A ligand exchange reaction of $Rh(acac)(C_2H_4)_2$ with (*S*)-**1a** ($^{31}P$ NMR: 43.5 ppm; $^1H$ NMR: 5.24 ppm for the olefin H in benzene-$d_6$) in benzene cleanly produced Rh(acac)((*S*)-**1a**) [**10**; $^{31}P$ NMR: 127.9 ppm ($J$ = 202 Hz); $^1H$ NMR: 3.75 ppm for the olefin H in benzene-$d_6$] in an 85% yield (eq 1). Recrystallization of this complex from benzene/pentane afforded single crystals suitable for X-ray crystallographic analysis (Fig. 3 and Table 1).[13] As shown in Figure 3, (*S*)-**1a** acts as a phosphorus–olefin bidentate ligand to rhodium while the olefin coordinates with its β*re*-face to keep the benzyl group on the dihydropyrrole ring away from rhodium, successfully satisfying the initial design of this ligand. In addition, it shows that two phenyl groups on the phosphorus atom are symmetrically projected, and the chiral environment around the rhodium is effectively constructed by the steric difference between the two substituents (Me and H) on the olefin. Similarly, Rh(acac)((*S*)-**4**) [**11**; $^{31}P$ NMR: 105.5 ppm ($J$ = 202 Hz); $^1H$ NMR: 4.14 ppm for the olefin H in benzene-$d_6$] and Rh(acac)((*S*)-**5**) [**12**; $^{31}P$ NMR: 128.2 ppm ($J$ = 204 Hz); $^1H$ NMR: 3.87 ppm for the olefin H in benzene-$d_6$] were also isolated in good yields as single isomers (eq 1), indicating that the coordination face of the olefins is effectively controlled in both cases by the stereogenic carbon center having the benzyl group. Single crystals suitable for X-ray analysis were obtained for complex **11** by recrystallization from $Et_2O$/pentane and its X-ray crystal structure is illustrated in Figure 4 (see

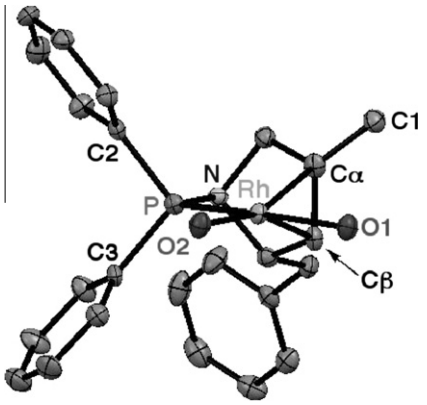



**Figure 3.** X-ray crystal structure of complex **10** with thermal ellipsoids drawn at the 50% probability level (carbon atoms of the acac moiety and hydrogen atoms are omitted for clarity).

**Table 1**
Selected bond lengths (Å) and angles (deg) for complexes **10**–**12**

| | Complex **10** | Complex **11** | Complex **12** |
|---|---|---|---|
| *Bond distances* | | | |
| Rh–P | 2.1683(9) | 2.1748(11) | 2.187(6) |
| Rh–Cα | 2.138(4) | 2.149(5) | 2.11(3) |
| Rh–Cβ | 2.075(4) | 2.120(5) | 2.14(3) |
| Rh–O1 | 2.085(2) | 2.109(3) | 2.080(15) |
| Rh–O2 | 2.046(3) | 2.065(3) | 2.08(2) |
| P–N | 1.746(3) | 1.717(4) | 1.79(2) |
| P–C2 | 1.820(4) | 1.828(4) | 1.811(18) |
| P–C3 | 1.816(4) | 1.818(5) | 1.76(2) |
| Cα–Cβ | 1.409(6) | 1.405(6) | 1.45(3) |
| C1–Cα (or C1–Cβ) | 1.516(6) | 1.537(6) | 1.48(3) |
| *Bond angles* | | | |
| ∠O1–Rh–O2 | 89.66(12) | 89.08(15) | 89.5(7) |
| ∠P–Rh–Cα | 82.08(11) | 88.41(13) | 82.4(7) |
| ∠P–Rh–Cβ | 82.62(11) | 81.91(12) | 82.8(6) |
| ∠Cα–Rh–Cβ | 39.04(16) | 38.43(16) | 39.7(8) |
| ∠Rh–Cα–C1 (or ∠Rh–Cβ–C1) | 114.3(2) | 110.4(3) | 113.4(19) |
| ∠C1–Cα–Cβ (or ∠C1–Cβ–Cα) | 127.1(3) | 121.4(4) | 122(2) |

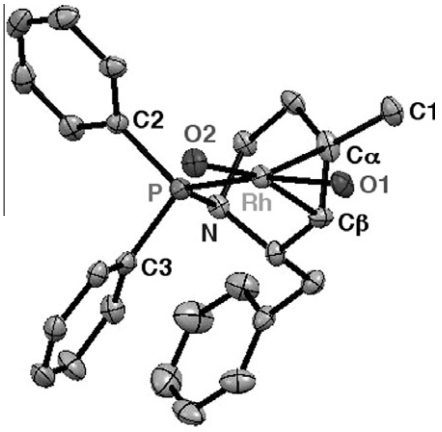



**Figure 4.** X-ray crystal structure of complex **11** with thermal ellipsoids drawn at the 50% probability level (carbon atoms of the acac moiety and hydrogen atoms are omitted for clarity).

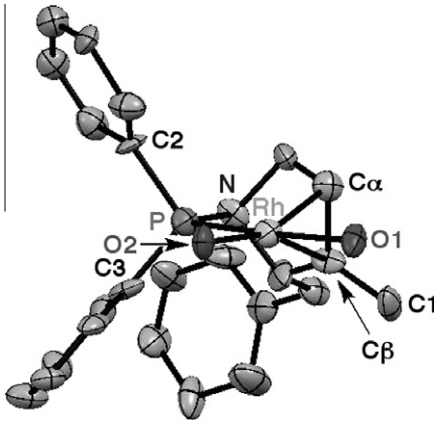
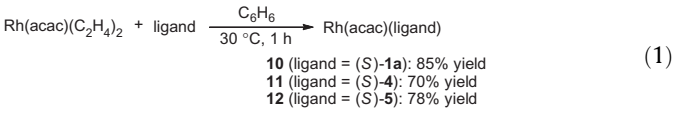



**Figure 5.** X-ray crystal structure of complex **12** with thermal ellipsoids drawn at the 30% probability level (carbon atoms of the acac moiety and hydrogen atoms are omitted for clarity).

also Table 1).[13] This structure confirms the β*re*-face coordination of the olefin to rhodium; the overall structure is a somewhat distorted square planar around the rhodium (distance of Rh from P–O1–O2 plane = 0.181 Å) compared to complex **10** (distance of Rh from P–O1–O2 plane = 0.000 Å), presumably due to the less compact tetrahydropyridine ring. With regards to the X-ray analysis for complex **12**, only single crystals of moderate quality have been obtained to date by recrystallization from 1,2-dichloroethane/pentane; the structure is shown in Figure 5 (see also Table 1).[13] This also confirms the β*re*-face coordination of the olefin to rhodium as expected, and the overall structure is almost identical to the structure of complex **10** (Fig. 3), except that the position of the methyl group on the olefin is switched from Cα to Cβ. This positional change of the methyl group makes complex **12** a pseudo-enantiomer of complex **10**, although the configuration of both complexes **10** and **12** is derived from naturally occurring (*S*)-phenylalanine.

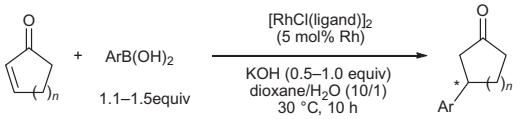



(1)

## 2.3. Asymmetric 1,4-addition reactions catalyzed by rhodium complexes coordinated with (*S*)-1, (*S*)-4, and (*S*)-5

Table 2 summarizes the results of asymmetric 1,4-addition of arylboronic acids to several α,β-unsaturated cyclic ketones in the presence of rhodium/phosphorus–olefin catalysts. In the reaction of 2-cyclohexenone with phenylboronic acid, ligands (*S*)-**1a**–**1c** exhibited good catalytic activity to give (*S*)-3-phenylcyclohexanone with high enantioselectivity (91–94% ee; entries 1–3). In contrast, ligand (*S*)-**4** with a tetrahydropyridine ring instead of a dihydropyrrole ring displayed much lower activity, giving the 1,4-adduct in only a 28% yield (entry 4). As expected from the ligand design and the X-ray structures in Figures 3 and 4, the sense of chiral induction is the same as (*S*)-**1a** (entry 1), but the enantioselectivity of the product was significantly lower with ligand (*S*)-**4** [77% ee (*S*)]. On the other hand, the use of ligand (*S*)-**5** led to the formation of (*R*)-3-phenylcyclohexanone in a 98% yield with high enantiomeric excess (entry 5), confirming the pseudo-enan-

**Table 2**
Rhodium-catalyzed asymmetric 1,4-addition of arylboronic acids to α,β-unsaturated cyclic ketones




| Entry | Substrate | Ar | Ligand | Yield[a] (%) | ee[b] (%) | Config. |
|---|---|---|---|---|---|---|
| 1 | *n* = 2 | Ph | (*S*)-**1a** | 89 | 94 | (*S*) |
| 2 | | | (*S*)-**1b** | 91 | 93 | (*S*) |
| 3 | | | (*S*)-**1c** | 81 | 91 | (*S*) |
| 4 | | | (*S*)-**4** | 28 | 77 | (*S*) |
| 5 | | | (*S*)-**5** | 98 | 97 | (*R*) |
| 6 | | 4-$MeOC_6H_4$ | (*S*)-**1a** | 86 | 96 | (*S*) |
| 7 | | | (*S*)-**5** | 93 | 97 | (*R*) |
| 8 | | 4-$CF_3C_6H_4$ | (*S*)-**1a** | 87 | 94 | (*S*) |
| 9 | | | (*S*)-**5** | 84 | 97 | (*R*) |
| 10 | | 2-$MeC_6H_4$ | (*S*)-**1a** | 92 | 95 | (*S*) |
| 11 | | | (*S*)-**5** | 99 | 98 | (*R*) |
| 12 | *n* = 1 | Ph | (*S*)-**1a** | 92 | 93 | (*S*) |
| 13 | | | (*S*)-**5** | 93 | 95 | (*R*) |
| 14 | *n* = 3 | Ph | (*S*)-**1a** | 90 | 87 | (*S*) |
| 15 | | | (*S*)-**5** | 87 | 95 | (*R*) |

[a] Isolated yield.
[b] Determined by chiral HPLC.

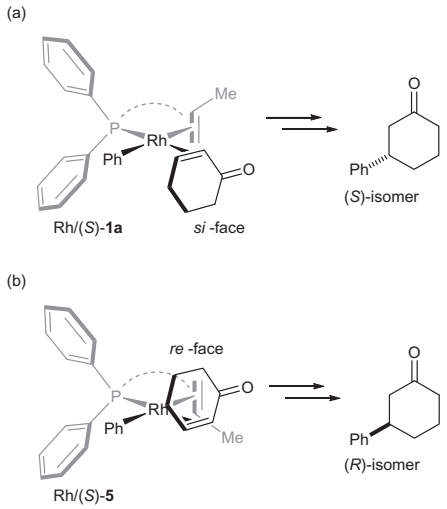
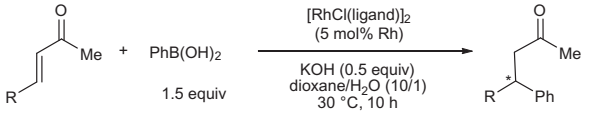



**Figure 6.** Proposed stereochemical pathways for the asymmetric 1,4-addition of phenylboronic acid to 2-cyclohexenone catalyzed by Rh/(*S*)-**1a** (a) and Rh/(*S*)-**5** (b).

**Table 3**
Rhodium-catalyzed asymmetric 1,4-addition of phenylboronic acid to α,β-unsaturated acyclic ketones




| Entry | Substrate | Ligand | Yield[a] (%) | ee[b] (%) | Config. |
|---|---|---|---|---|---|
| 1 | R = Me | (*S*)-**1a** | 89 | 85 | (*R*) |
| 2 | | (*S*)-**5** | 79 | 50 | (*S*) |
| 3 | R = *n*-$C_5H_{11}$ | (*S*)-**1a** | 91 | 83 | (*R*) |
| 4 | | (*S*)-**5** | 73 | 58 | (*S*) |
| 5 | R = *i*-Pr | (*S*)-**1a** | 93 | 81 | (*S*) |
| 6 | | (*S*)-**5** | 79 | 65 | (*R*) |

[a] Isolated yield.
[b] Determined by chiral HPLC.

tiomeric nature of this ligand compared to (*S*)-**1a** as discussed above (see Figs. 3 and 5). This relationship was also observed in the addition of other arylboronic acids to 2-cyclohexenone, giving (*S*)-products in the presence of ligand (*S*)-**1a** and (*R*)-products in the presence of ligand (*S*)-**5** with high enantioselectivity (94–98% ee; entries 6–11). Other cyclic enones effectively undergo the 1,4-addition of phenylboronic acid as well to give (*S*)-3-phenylcycloalkanones with ligand (*S*)-**1a** and their (*R*)-isomers with ligand (*S*)-**5** (entries 12–15).

Based on the results of these 1,4-additions and the X-ray structure of the Rh/(*S*)-**1a** complex (Fig. 3), the stereochemical pathway for the 1,4-addition of phenylboronic acid to 2-cyclohexenone catalyzed by Rh/(*S*)-**1a** can be explained as shown in Figure 6a.[8,14] Thus, the phenylrhodium species has a *trans*-relationship between the phenyl group and the olefin ligand and 2-cyclohexenone binds to rhodium with its *si*-face at the *cis*-position of the olefin ligand, leading to the 1,4-adduct with an (*S*)-configuration. The formation of the (*R*)-product using Rh/(*S*)-**5** can be similarly rationalized by the *re*-face coordination of 2-cyclohexenone to rhodium as illustrated in Figure 6b.

We also applied these phosphorus–olefin ligands to the reactions of several acyclic enones with phenylboronic acid (Table 3). In contrast to the use of cyclic enone substrates (Table 2), both ligands (*S*)-**1a** and (*S*)-**5** showed significantly lower efficiency to give 1,4-adducts with 81–85% ee using (*S*)-**1a** and with 50–65% ee using (*S*)-**5** (entries 1–6). In these reactions, the sense of chiral induction with ligand (*S*)-**5** is opposite in comparison with ligand (*S*)-**1a**.

## 3. Conclusion

We have designed and synthesized chiral phosphorus–olefin ligands (*S*)-**1**, (*S*)-**4**, and (*S*)-**5**, and analyzed the structures of their rhodium complexes. All of these ligands can be synthesized from (*S*)-phenylalanine derivatives and they act as phosphorus–olefin bidentate ligands to rhodium. The coordination face of the olefin can be effectively controlled by the original configuration of (*S*)-phenylalanine in all cases. The rhodium complexes coordinated with these ligands were employed as catalysts for the asymmetric 1,4-addition of arylboronic acids to α,β-unsaturated ketones. Herein, it has been shown that ligands (*S*)-**1a** and (*S*)-**5** produce the opposite enantiomers of the 1,4-adducts with high enantioselectivities for cyclic enones and moderate enantioselectivities for acyclic enones.

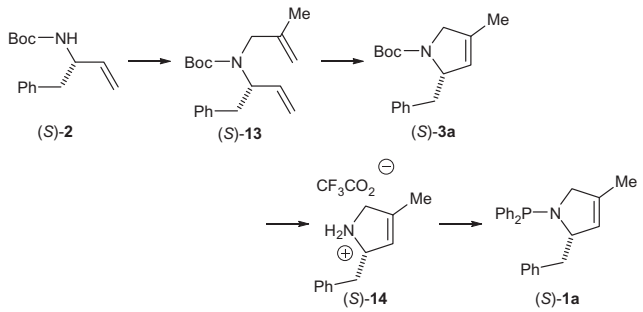
## 4. Experimental

### 4.1. General

All air- and moisture-sensitive manipulations were carried out with standard Schlenk techniques under nitrogen or in a glove box under argon. THF, $Et_2O$, and dioxane were purified by passing through neutral alumina columns under nitrogen. $C_6H_6$ and hexane were distilled over benzophenone ketyl under nitrogen. Pentane was distilled over benzophenone ketyl in the presence of triglyme under nitrogen. DMF was distilled over $CaH_2$ under vacuum. $CH_2Cl_2$ and 1,2-dichloroethane were distilled over $CaH_2$ under nitrogen. $Et_3N$ was distilled over KOH under nitrogen. Rh(acac)$(C_2H_4)_2$[15] and $[RhCl(C_2H_4)_2]_2$[16] were synthesized following literature procedures.

### 4.2. Preparation of chiral phosphorus–olefin ligands

#### 4.2.1. (*S*)-1a




2-Methyl-2-propenyl bromide (726 mg, 5.38 mmol) and NaH (256 mg, 6.40 mmol; 60 wt% in mineral oil) were successively added to a solution of (*S*)-**2**[9] (1.01 g, 4.08 mmol) in DMF (9.0 mL) at 0 °C and the mixture was stirred for 1.5 h at room temperature. The reaction was quenched with $H_2O$ at 0 °C and this was extracted with EtOAc/hexane (1/10). The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was chromatographed on silica gel with EtOAc/hexane = 1/20 to

afford compound (*S*)-**13** as a colorless oil (1.17 g, 3.88 mmol; 95% yield). $[\alpha]_D^{25} = -55.4$ (*c* 1.02, $CHCl_3$). $^1H$ NMR ($CDCl_3$, 50 °C): $\delta$ 7.25 (t, $^3J_{HH}$ = 7.5 Hz, 2H), 7.19–7.15 (m, 3H), 6.00 (ddd, $^3J_{HH}$ = 17.0, 10.2, and 6.8 Hz, 1H), 5.06 (d, $^3J_{HH}$ = 10.8 Hz, 1H), 5.04 (d, $^3J_{HH}$ = 18.4 Hz, 1H), 4.77 (s, 1H), 4.73 (s, 1H), 4.34 (br s, 1H), 3.75–3.56 (m, 1H), 3.46 (d, $^2J_{HH}$ = 16.3 Hz, 1H), 3.16–3.04 (m, 1H), 2.91 (dd, $^2J_{HH}$ = 13.6 Hz and $^3J_{HH}$ = 6.8 Hz, 1H), 1.60 (s, 3H), 1.42 (s, 9H). $^{13}C$ NMR ($CDCl_3$, 50 °C): $\delta$ 155.4, 142.8, 139.0, 137.5, 129.5, 128.4, 126.4, 116.2, 111.6, 79.7, 61.5, 52.2, 39.2, 28.6, 20.1. HRMS (ESI-TOF) calcd for $C_{19}H_{27}NO_2Na$ (M+Na$^+$) 324.1934, found 324.1930.

Grubbs catalyst (66.3 mg, 78.1 μmol; 2nd generation) was added to a solution of (*S*)-**13** (1.16 g, 3.85 mmol) in $C_6H_6$ (38 mL) and the mixture was stirred for 6 h at 60 °C. The solvent was removed under vacuum, and the residue was chromatographed on silica gel with EtOAc/hexane = 1/20 to afford compound (*S*)-**3a** as a colorless oil (1.03 g, 3.77 mmol; 98% yield, ~6/4 mixture of rotamers). $[\alpha]_D^{25} = +177$ (*c* 1.10, $CHCl_3$). $^1H$ NMR ($CDCl_3$): $\delta$ 7.28–7.22 (m, 2H), 7.22–7.17 (m, 1H), 7.15 (d, $^3J_{HH}$ = 7.5 Hz, 0.8H), 7.12 (d, $^3J_{HH}$ = 7.5 Hz, 1.2H), 5.26 (s, 0.4H), 5.23 (s, 0.6H), 4.73–4.67 (m, 0.4H), 4.61–4.55 (m, 0.6H), 4.02 (d, $^2J_{HH}$ = 15.0 Hz, 0.6H), 3.89 (d, $^2J_{HH}$ = 14.9 Hz, 0.4H), 3.70 (dd, $^2J_{HH}$ = 14.9 Hz and $^4J_{HH}$ = 4.0 Hz, 0.6H), 3.56 (dd, $^2J_{HH}$ = 15.0 Hz and $^4J_{HH}$ = 4.8 Hz, 0.4H), 3.17 (dd, $^2J_{HH}$ = 12.9 Hz and $^3J_{HH}$ = 3.4 Hz, 0.4H), 3.13 (dd, $^2J_{HH}$ = 13.0 Hz and $^3J_{HH}$ = 3.4 Hz, 0.6H), 2.84 (dd, $^2J_{HH}$ = 13.0 Hz and $^3J_{HH}$ = 8.2 Hz, 0.4H), 2.69 (dd, $^2J_{HH}$ = 12.9 Hz and $^3J_{HH}$ = 8.1 Hz, 0.6H), 1.66 (s, 1.8H), 1.63 (s, 1.2H), 1.55 (s, 5.4H), 1.50 (s, 3.6H). $^{13}C$ NMR ($CDCl_3$): $\delta$ 154.2, 154.0, 138.2, 135.2, 135.1, 129.9, 129.6, 128.2, 127.9, 126.2, 126.0, 123.5, 123.3, 79.5, 79.1, 65.9, 65.6, 56.9, 56.6, 41.3, 39.8, 28.70, 28.66, 14.2, 14.1. HRMS (ESI-TOF) calcd for $C_{17}H_{23}NO_2Na$ (M+Na$^+$) 296.1621, found 296.1617.

Trifluoroacetic acid (7.5 mL) was added to a solution of (*S*)-**3a** (1.03 g, 3.77 mmol) in $CH_2Cl_2$ (37 mL) and the mixture was stirred for 1.5 h at room temperature. The solvent was removed under vacuum, and the remaining trifluoroacetic acid was further removed by dissolving the residue in $C_6H_6$ and concentrated under vacuum three times, followed by the same sequence with hexane three times. The residue thus obtained was chromatographed on silica gel with MeOH/$CH_2Cl_2$ = 1/10 to afford compound (*S*)-**14** as a purple solid (1.03 g, 3.59 mmol; 95% yield). $[\alpha]_D^{25} = +54.5$ (*c* 0.32, $CHCl_3$). $^1H$ NMR ($CDCl_3$): $\delta$ 10.30 (br s, 1H), 9.23 (br s, 1H), 7.31 (t, $^3J_{HH}$ = 7.5 Hz, 2H), 7.25 (t, $^3J_{HH}$ = 8.1 Hz, 1H), 7.20 (d, $^3J_{HH}$ = 6.8 Hz, 2H), 5.34 (s, 1H), 4.70–4.62 (m, 1H), 3.84 (d, $^2J_{HH}$ = 15.0 Hz, 1H), 3.80 (d, $^2J_{HH}$ = 15.0 Hz, 1H), 3.15 (dd, $^2J_{HH}$ = 13.6 Hz and $^3J_{HH}$ = 6.1 Hz, 1H), 2.95 (dd, $^2J_{HH}$ = 13.6 Hz and $^3J_{HH}$ = 8.9 Hz, 1H), 1.78 (s, 3H). $^{13}C$ NMR ($CDCl_3$): $\delta$ 162.8 (q, $^2J_{CF}$ = 35.9 Hz), 135.8, 135.3, 129.2, 128.8, 127.2, 122.4, 117.0 (q, $^1J_{CF}$ = 293 Hz), 66.9, 53.9, 39.3, 13.6. HRMS (ESI-TOF) calcd for $C_{12}H_{16}N$ (M–$CF_3CO_2^-$) 174.1277, found 174.1278.

Next, 1 M NaOH (aq) (15 mL) was added to a solution of (*S*)-**14** (1.03 g, 3.59 mmol) in $Et_2O$ (5.0 mL) and the mixture was extracted with $Et_2O$. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was dissolved in THF (9.0 mL), and $Et_3N$ (2.20 mL, 15.8 mmol) and chlorodiphenylphosphine (710 μL, 3.95 mmol) were successively added to it with additional THF (2.0 mL). The mixture was stirred for 9 h at room temperature, and the volatiles were removed under vacuum. This was chromatographed on silica gel with degassed $Et_3N$/hexane = 1/2 to afford compound (*S*)-**1a** as a yellow oil (1.06 g, 2.97 mmol; 83% yield). $[\alpha]_D^{25} = +235$ (*c* 1.03, THF). $^1H$ NMR ($C_6D_6$): $\delta$ 7.58 (t, $^3J$ = 7.2 Hz, 2H), 7.48 (t, $^3J$ = 7.4 Hz, 2H), 7.23–7.19 (m, 2H), 7.18–7.05 (m, 9H), 5.27–5.21 (m, 1H), 4.77–4.68 (m, 1H), 3.60 (br s, 2H), 3.44 (ddd, $^2J_{HH}$ = 12.8 Hz, $^3J_{HH}$ = 3.9 Hz, and $^4J_{HH}$ = 2.8 Hz, 1H), 2.75 (dd, $^2J_{HH}$ = 12.8 Hz and $^3J_{HH}$ = 9.5 Hz, 1H), 1.28 (s, 3H). $^{13}C$ NMR ($C_6D_6$): $\delta$ 140.2 (d, $J_{CP}$ = 7.7 Hz), 139.5 (d, $J_{CP}$ = 18.1 Hz), 139.4, 137.1, 132.7 (d, $J_{CP}$ = 19.6 Hz), 132.6 (d, $J_{CP}$ = 19.6 Hz), 130.0, 128.62 (d, $J_{CP}$ = 3.6 Hz), 128.59, 128.57, 128.53, 128.49, 126.3, 125.2 (d, $J_{CP}$ = 6.7 Hz), 73.1 (d, $J_{CP}$ = 30.5 Hz), 57.6 (d, $J_{CP}$ = 9.3 Hz), 45.2 (d, $J_{CP}$ = 5.7 Hz), 14.0. $^{31}P\{^1H\}$ NMR ($C_6D_6$): $\delta$ 43.5 (s). HRMS (ESI-TOF) calcd for $C_{24}H_{25}NP$ (M+H$^+$) 358.1719, found 358.1717.

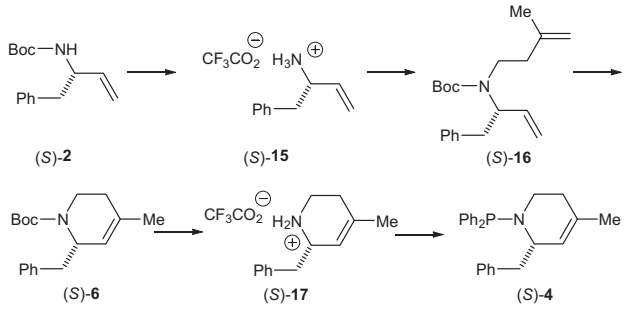
#### 4.2.2. (*S*)-1b

This was synthesized from (*S*)-**2** and 2-(benzyloxymethyl)-2-propenyl methanesulfonate, following the procedure for (*S*)-**1a**. Brown oil. 62% overall yield. $[\alpha]_D^{25} = +187$ (*c* 0.56, THF). $^1H$ NMR ($C_6D_6$): $\delta$ 7.57 (t, $^3J$ = 7.1 Hz, 2H), 7.46 (t, $^3J$ = 7.6 Hz, 2H), 7.21–7.11 (m, 13H), 7.09–7.04 (m, 3H), 5.56–5.53 (m, 1H), 4.80–4.73 (m, 1H), 4.15 (d, $^2J_{HH}$ = 12.2 Hz, 1H), 4.11 (d, $^2J_{HH}$ = 12.1 Hz, 1H), 3.86–3.76 (m, 2H), 3.68–3.61 (m, 2H), 3.38 (ddd, $^2J_{HH}$ = 12.7 Hz, $^3J_{HH}$ = 4.2 Hz, and $^4J_{HH}$ = 2.8 Hz, 1H), 2.80 (ddd, $^2J_{HH}$ = 12.8 Hz, $^3J_{HH}$ = 9.3 Hz, and $^4J_{HH}$ = 0.6 Hz, 1H). $^{13}C$ NMR ($C_6D_6$): $\delta$ 139.8 (d, $J_{CP}$ = 7.2 Hz), 139.3 (d, $J_{CP}$ = 18.1 Hz), 139.2, 139.0, 138.9, 132.7 (d, $J_{CP}$ = 20.2 Hz), 132.6 (d, $J_{CP}$ = 19.1 Hz), 130.0, 128.7, 128.62, 128.56, 128.55, 128.5, 127.9, 127.7, 127.3 (d, $J_{CP}$ = 6.7 Hz), 126.4, 72.9 (d, $J_{CP}$ = 31.5 Hz), 72.0, 66.9, 54.6 (d, $J_{CP}$ = 9.3 Hz), 44.7 (d, $J_{CP}$ = 5.2 Hz). $^{31}P\{^1H\}$ NMR ($C_6D_6$): $\delta$ 44.8 (s). HRMS (ESI-TOF) calcd for $C_{31}H_{31}NOP$ (M+H$^+$) 464.2138, found 464.2130.

#### 4.2.3. (*S*)-1c

This was synthesized from (*S*)-**2** and 2-phenyl-2-propenyl bromide, following the procedure for (*S*)-**1a**. Pink solid. 85% overall yield. $[\alpha]_D^{25} = +224$ (*c* 0.53, THF). $^1H$ NMR ($C_6D_6$): $\delta$ 7.65–7.61 (m, 2H), 7.54–7.50 (m, 2H), 7.25–7.21 (m, 2H), 7.17–7.05 (m, 9H), 6.99–6.95 (m, 5H), 6.00 (dt, $^3J_{HH}$ = 4.9 Hz and $^4J_{HH}$ = 2.2 Hz, 1H), 4.92–4.85 (m, 1H), 4.24–4.15 (m, 2H), 3.52 (ddd, $^2J_{HH}$ = 12.8 Hz, $^3J_{HH}$ = 4.2 Hz, and $^4J$ = 2.8 Hz, 1H), 2.80 (dd, $^2J_{HH}$ = 12.8 Hz and $^3J_{HH}$ = 9.5 Hz, 1H). $^{13}C$ NMR ($C_6D_6$): $\delta$ 139.9 (d, $J_{CP}$ = 8.3 Hz), 139.6, 139.14 (d, $J_{CP}$ = 17.6 Hz), 139.09, 134.2, 132.7 (d, $J_{CP}$ = 20.2 Hz), 132.5 (d, $J_{CP}$ = 19.6 Hz), 130.0, 128.73 (d, $J_{CP}$ = 3.6 Hz), 128.69, 128.68, 128.64, 128.63, 128.62, 127.8, 126.4, 125.9, 125.5 (d, $J_{CP}$ = 6.7 Hz), 73.6 (d, $J_{CP}$ = 31.0 Hz), 54.5 (d, $J_{CP}$ = 9.3 Hz), 45.1 (d, $J_{CP}$ = 6.2 Hz). $^{31}P\{^1H\}$ NMR ($C_6D_6$): $\delta$ 44.2 (s). HRMS (ESI-TOF) calcd for $C_{29}H_{27}NP$ (M+H$^+$) 420.1876, found 420.1864.

#### 4.2.4. (*S*)-4




Trifluoroacetic acid (20 mL) was added to a solution of (*S*)-**2** (1.09 g, 4.40 mmol) in $CH_2Cl_2$ (20 mL) and the mixture was stirred for 1 h at room temperature. After removal of the solvent under vacuum, the residue was washed with hexane and dried under vacuum to afford compound (*S*)-**15** as a pink solid (1.00 g, 3.84 mmol; 87% yield). $[\alpha]_D^{30} = +5.2$ (c 0.64, $CHCl_3$). $^1H$ NMR ($CDCl_3$): δ 8.13 (br s, 3H), 7.30 (t, $^3J_{HH}$ = 7.2 Hz, 2H), 7.24 (t, $^3J_{HH}$ = 7.3 Hz, 1H), 7.16 (d, $^3J_{HH}$ = 7.0 Hz, 2H), 5.79 (ddd, $^3J_{HH}$ = 17.6, 10.5, and 7.7 Hz, 1H), 5.27 (d, $^3J_{HH}$ = 10.5 Hz, 1H), 5.23 (d, $^3J_{HH}$ = 17.2 Hz, 1H), 3.90–3.81 (m, 1H), 3.11 (dd, $^2J_{HH}$ = 13.5 Hz and $^3J_{HH}$ = 5.8 Hz, 1H), 2.90 (dd,

$^2J_{HH}$ = 13.5 Hz and $^3J_{HH}$ = 8.9 Hz, 1H). $^{13}$C NMR ($CDCl_3$): δ 162.7 (q, $^2$JCF = 35.1 Hz), 135.3, 132.8, 129.5, 128.9, 127.4, 121.1, 116.7 (q, $^1$JCF = 286 Hz), 55.9, 39.6. HRMS (ESI-TOF) calcd for $C_{10}H_{14}N$ (M–CF3CO2$^-$) 148.1121, found 148.1120.

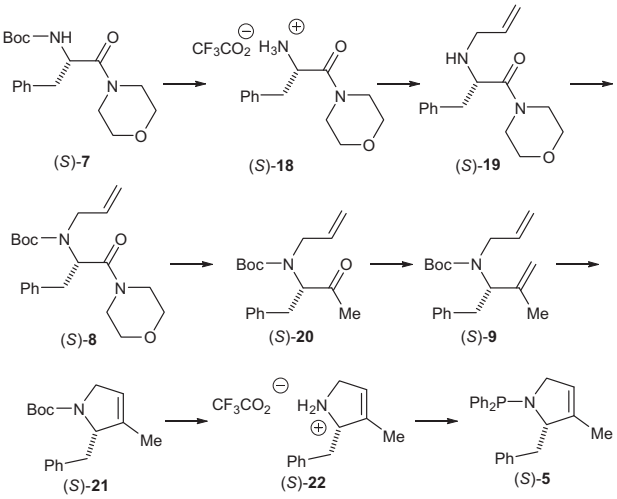
Saturated $NaHCO_3$ (aq) (10 mL) was added to a solution of (*S*)-**15** in $CH_2Cl_2$ (10 mL) and the mixture was extracted with $CH_2Cl_2$. The organic layer was dried over $K_2CO_3$, filtered, and concentrated under vacuum. The residue was dissolved in MeCN (28 mL) and $K_2CO_3$ (514 mg, 3.71 mmol) was added to it. The mixture was stirred for 1 h at room temperature, and 3-methyl-3-butenyl methanesulfonate was added to it. This mixture was stirred for 24 h at 90 °C and the precipitate was filtered off with $CH_2Cl_2$ at room temperature. After removal of the solvent under vacuum, the residue was extracted with $CH_2Cl_2$ and saturated $NaHCO_3$ (aq). The organic layer was dried over $K_2CO_3$, filtered, and concentrated under vacuum. This was then dissolved in THF (12 mL) and a solution of $(Boc)_2O$ (996 mg, 4.56 mmol) in THF (7.0 mL) was added to it at 0 °C. The mixture was stirred for 21 h at room temperature, and the solvent was removed under vacuum. The residue was extracted with $Et_2O$ and 1 M HCl (aq), and the organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. This was chromatographed on silica gel with EtOAc/hexane = 1/10 to afford compound (*S*)-**16** as a colorless oil (658 mg, 2.08 mmol; 55% yield). $[\alpha]_D^{30} = -67.9$ (*c* 1.11, $CHCl_3$). $^1$H NMR ($CDCl_3$, 50 °C): δ 7.28–7.23 (m, 2H), 7.20–7.15 (m, 3H), 6.01–5.93 (m, 1H), 5.15–5.08 (m, 2H), 4.72–4.70 (m, 1H), 4.65–4.62 (m, 1H), 4.51 (br s, 1H), 3.17–2.96 (m, 3H), 2.91 (dd, $^2J_{HH}$ = 13.7 Hz and $^3J_{HH}$ = 6.7 Hz, 1H), 2.22–2.00 (m, 2H), 1.70 (s, 3H), 1.40 (s, 9H). $^{13}$C NMR ($CDCl_3$, 50 °C): δ 155.0, 143.3, 138.7, 137.7, 129.2, 128.2, 126.2, 115.9, 111.2, 79.3, 60.8, 44.9, 38.6, 37.7, 28.4, 22.5. HRMS (ESI-TOF) calcd for $C_{20}H_{29}NO_2Na$ (M+Na$^+$) 338.2091, found 338.2082.

Grubbs catalyst (36.4 mg, 42.8 μmol; 2nd generation) was added to a solution of (*S*)-**16** (647 mg, 2.05 mmol) in $C_6H_6$ (20 mL) and the mixture was stirred for 5 h at 60 °C. The solvent was removed under vacuum, and the residue was chromatographed on silica gel with EtOAc/hexane = 1/5 to afford compound (*S*)-**6** as a colorless oil (568 mg, 1.97 mmol; 96% yield). $[\alpha]_D^{30} = +172$ (*c* 1.07, $CHCl_3$). $^1$H NMR ($CDCl_3$, 60 °C): δ 7.25 (t, $^3J_{HH}$ = 7.3 Hz, 2H), 7.21–7.14 (m, 3H), 5.29–5.24 (m, 1H), 4.51 (br s, 1H), 4.11 (br s, 1H), 2.85 (dd, $^2J_{HH}$ = 12.9 Hz and $^3J_{HH}$ = 6.3 Hz, 1H), 2.77 (ddd, $^2J_{HH}$ = 13.1 Hz and $^3J_{HH}$ = 11.8 and 3.9 Hz, 1H), 2.73 (dd, $^2J_{HH}$ = 12.8 Hz and $^3J_{HH}$ = 7.7 Hz, 1H), 2.19–2.08 (m, 1H), 1.75 (dd, $^2J_{HH}$ = 16.6 Hz and $^3J_{HH}$ = 2.5 Hz, 1H), 1.68 (d, $^4J_{HH}$ = 1.1 Hz, 3H), 1.38 (s, 9H). $^{13}$C NMR ($CDCl_3$, 60 °C): δ 154.6, 138.8, 133.3, 129.6, 128.3, 126.2, 122.0, 79.4, 53.7, 40.7, 36.9, 29.9, 28.5, 23.3. HRMS (ESI-TOF) calcd for $C_{18}H_{25}NO_2Na$ (M+Na$^+$) 310.1778, found 310.1775.

Trifluoroacetic acid (3.9 mL) was added to a solution of (*S*)-**6** (563 mg, 1.96 mmol) in $CH_2Cl_2$ (3.9 mL) and the mixture was stirred for 1 h at room temperature. The solvent was removed under vacuum, and the remaining trifluoroacetic acid was further removed by dissolving the residue in $CH_2Cl_2$ and concentrated under vacuum twice, followed by the same sequence with hexane twice, to afford compound (*S*)-**17** as a colorless oil (590 mg, 1.95 mmol; 99% yield). $[\alpha]_D^{30} = +29.8$ (*c* 1.05, $CHCl_3$). $^1$H NMR ($CDCl_3$): δ 9.84 (br s, 1H), 9.06 (br s, 1H), 7.30 (t, $^3J_{HH}$ = 7.3 Hz, 2H), 7.27–7.19 (m, 3H), 5.27 (s, 1H), 3.98 (br s, 1H), 3.42–3.30 (m, 1H), 3.14 (dd, $^2J_{HH}$ = 13.3 Hz and $^3J_{HH}$ = 5.9 Hz, 1H), 3.10–3.00 (m, 1H), 2.81 (dd, $^2J_{HH}$ = 13.3 Hz and $^3J_{HH}$ = 9.4 Hz, 1H), 2.51–2.40 (m, 1H), 2.09 (d, $^2J_{HH}$ = 18.2 Hz, 1H), 1.74 (s, 3H). $^{13}$C NMR ($CDCl_3$): δ 162.4 (q, $^2J_{CF}$ = 35.1 Hz), 135.3, 134.3, 129.5, 128.9, 127.4, 117.9, 116.8 (q, $^2J_{HH}$ = 293 Hz), 54.5, 40.6, 39.4, 26.5, 23.1. HRMS (ESI-TOF) calcd for $C_{13}H_{18}N$ (M–$CF_3CO_2^-$) 188.1434, found 188.1433.

NaOH (aq, 1 M) (10 mL) was added to a solution of (*S*)-**17** (586 mg, 1.94 mmol) in $Et_2O$ (10 mL) and the mixture was extracted with $Et_2O$. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was dissolved in THF (5.0 mL), and $Et_3N$ (1.20 mL, 8.68 mmol) and chlorodiphenylphosphine (410 μL, 2.28 mmol) were successively added to it with additional THF (1.0 mL). The mixture was stirred for 24 h at room temperature, and the volatiles were removed under vacuum. This was chromatographed on silica gel with degassed $Et_3N$/hexane = 1/2 to afford compound (*S*)-**4** as a brown oil (598 mg, 1.60 mmol; 83% yield). $[\alpha]_D^{30} = -41.3$ (*c* 1.00, THF). $^1$H NMR ($C_6D_6$): δ 7.61–7.55 (m, 2H), 7.46 (t, $^3J$ = 7.6 Hz, 2H), 7.26–7.06 (m, 10H), 7.04 (t, $^3J_{HH}$ = 7.3 Hz, 1H), 5.38 (br s, 1H), 4.22 (br s, 1H), 3.25–3.17 (m, 1H), 3.17–3.07 (m, 1H), 2.90 (dd, $^2J_{HH}$ = 12.6 Hz and $^3J_{HH}$ = 5.2 Hz, 1H), 2.74 (dd, $^2J_{HH}$ = 12.7 Hz and $^3J_{HH}$ = 9.4 Hz, 1H), 1.68–1.55 (m, 1H), 1.43 (s, 3H), 1.34 (d, $^2J_{HH}$ = 17.1 Hz, 1H). $^{13}$C NMR ($C_6D_6$): δ 141.1 (d, $J_{CP}$ = 15.5 Hz), 140.9 (d, $J_{CP}$ = 15.5 Hz), 139.6, 133.3 (d, $J_{CP}$ = 21.2 Hz), 133.1, 131.7 (d, $J_{CP}$ = 19.6 Hz), 129.8, 129.0, 128.6, 128.5 (d, $J_{CP}$ = 2.6 Hz), 128.4 (d, $J_{CP}$ = .1 Hz), 128.2, 126.3, 124.4 (d, $J_{CP}$ = 5.2 Hz), 60.5 (d, $J_{CP}$ = 25.8 Hz), 42.9 (d, $J_{CP}$ = 4.7 Hz), 42.5 (d, $J_{CP}$ = 4.7 Hz), 30.8 (d, $J_{CP}$ = 1.0 Hz), 23.6. $^{31}$P{$^1$H} NMR ($C_6D_6$): δ 62.2 (s). HRMS (ESI-TOF) calcd for $C_{25}H_{27}NP$ (M+H$^+$) 372.1876, found 372.1873.

#### 4.2.5. (*S*)-5




Trifluroacetic acid (46 mL) was added to a solution of (*S*)-**7**[12] (4.08 g, 12.1 mmol) in $CH_2Cl_2$ (46 mL) and the mixture was stirred for 1 h at room temperature. The solvent was removed under vacuum, and the remaining trifluoroacetic acid was further removed by dissolving the residue in $CH_2Cl_2$ and concentrated under vacuum twice, followed by the same sequence with hexane twice, to afford compound (*S*)-**18** as a white solid (4.21 g, 12.0 mmol; 99% yield). $[\alpha]_D^{30} = +51.2$ (*c* 0.55, THF). $^1$H NMR ($CD_3OD$): δ 7.37 (t, $^3J_{HH}$ = 7.2 Hz, 2H), 7.33 (t, $^3J_{HH}$ = 7.3 Hz, 1H), 7.27 (d, $^3J_{HH}$ = 7.5 Hz, 2H), 4.84 (br s, 3H), 4.66 (dd, $^3J_{HH}$ = 9.4 and 5.8 Hz, 1H), 3.60–3.54 (m, 1H), 3.54–3.44 (m, 2H), 3.44–3.34 (m, 2H), 3.29–3.22 (m, 1H), 3.19 (dd, $^2J_{HH}$ = 13.2 Hz and $^3J_{HH}$ = 5.7 Hz, 1H), 3.05 (dd, $^2J_{HH}$ = 13.2 Hz and $^3J_{HH}$ = 9.5 Hz, 1H), 2.88–2.77 (m, 2H). $^{13}$C NMR ($CD_3OD$): δ 168.4, 163.1 (q, $^2J_{CF}$ = 32.6 Hz), 135.4, 130.8, 130.1, 129.0, 118.4 (q, $^1J_{CF}$ = 284 Hz), 67.1, 66.9, 51.6, 47.1, 43.6, 38.7. HRMS (ESI-TOF) calcd for $C_{13}H_{19}N_2O_2$ (M–$CF_3CO_2^-$) 235.1441, found 235.1443.

$Na_2CO_3$ (4.08 g, 81.0 mmol) and allyl bromide (1.52 g, 12.6 mmol) were successively added to a solution of (*S*)-**18** (4.03 g, 11.5 mmol) in MeCN (39 mL) at 0 °C, and the mixture was stirred for 24 h at room temperature. The reaction was

quenched with $H_2O$ at 0 °C and this was extracted with EtOAc. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was chromatographed on silica gel with MeOH/$CH_2Cl_2$ = 1/10 to afford compound (*S*)-**19** as a yellow oil (1.98 g, 7.24 mmol; 62% yield). $[\alpha]_D^{25} = +50.4$ (*c* 1.01, $CHCl_3$). $^1H$ NMR ($CDCl_3$): $\delta$ 7.28 (t, $^3J_{HH}$ = 7.2 Hz, 2H), 7.23 (tt, $^3J_{HH}$ = 7.3 Hz and $^4J_{HH}$ = 1.3 Hz, 1H), 7.21–7.17 (m, 2H), 5.87 (ddt, $^3J_{HH}$ = 17.0, 10.3, and 5.9 Hz, 1H), 5.16 (dd, $^3J_{HH}$ = 17.2 Hz and $^4J_{HH}$ = 1.6 Hz, 1H), 5.10 (d, $^3J_{HH}$ = 10.3 Hz, 1H), 3.77 (dd, $^3J_{HH}$ = 10.0 and 5.1 Hz, 1H), 3.65 (ddd, $^2J_{HH}$ = 13.3 Hz and $^3J_{HH}$ = 5.8 and 2.4 Hz, 1H), 3.58 (ddd, $^2J_{HH}$ = 10.7 Hz and $^3J_{HH}$ = 5.5 and 2.4 Hz, 1H), 3.47–3.30 (m, 3H), 3.27 (dd, $^2J_{HH}$ = 13.7 Hz and $^3J_{HH}$ = 5.5 Hz, 1H), 3.13 (ddd, $^2J_{HH}$ = 13.3 Hz and $^3J_{HH}$ = 7.6 and 3.2 Hz, 1H), 3.07 (dd, $^2J_{HH}$ = 13.8 Hz and $^3J_{HH}$ = 6.6 Hz, 1H), 3.05 (dd, $^2J_{HH}$ = 13.2 Hz and $^3J_{HH}$ = 5.2 Hz, 1H), 2.82 (dd, $^2J_{HH}$ = 12.8 Hz and $^3J_{HH}$ = 10.0 Hz, 1H), 2.77 (ddd, $^2J_{HH}$ = 13.3 Hz and $^3J_{HH}$ = 5.5 and 3.0 Hz, 1H), 2.69 (ddd, $^2J_{HH}$ = 11.6 Hz and $^3J_{HH}$ = 7.5 and 2.9 Hz, 1H), 1.96 (br s, 1H). $^{13}C$ NMR ($CDCl_3$): $\delta$ 173.0, 137.5, 136.8, 129.4, 128.5, 126.8, 116.4, 66.6, 66.0, 57.7, 50.5, 45.5, 42.1, 40.8. HRMS (ESI-TOF) calcd for $C_{16}H_{23}N_2O_2$ (M+H$^+$) 275.1754, found 275.1752.

$Et_3N$ (3.50 mL, 25.1 mmol) and $(Boc)_2O$ (2.05 g, 9.40 mmol) were added to a solution of (*S*)-**19** (1.96 g, 7.17 mmol) in THF (53 mL) at 0 °C, and the mixture was stirred for 24 h at room temperature. The reaction was quenched with saturated $NH_4Cl$ (aq) at 0 °C and this was extracted with EtOAc. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was chromatographed on silica gel with EtOAc/hexane = 1/3→1/2 to afford compound (*S*)-**8** as a colorless oil (2.55 g, 6.81 mmol; 95% yield). $[\alpha]_D^{30} = -106$ (*c* 1.07, $CHCl_3$). $^1H$ NMR ($CDCl_3$, 60 °C): $\delta$ 7.28–7.14 (m, 5H), 5.79 (br s, 1H), 5.28 (br s, 1H), 5.13 (d, $^3J_{HH}$ = 17.2 Hz, 1H), 5.07 (d, $^3J_{HH}$ = 10.1 Hz, 1H), 4.02–3.86 (m, 1H), 3.78 (dd, $^2J_{HH}$ = 15.7 Hz and $^3J_{HH}$ = 6.5 Hz, 1H), 3.70–3.28 (m, 8H), 3.25–3.08 (m, 1H), 2.96 (dd, $^2J_{HH}$ = 13.2 Hz and $^3J_{HH}$ = 6.9 Hz, 1H), 1.34 (br s, 9H). $^{13}C$ NMR ($CDCl_3$, 60 °C): $\delta$ 168.8, 154.9, 137.6, 135.0, 129.5, 128.2, 126.3, 116.4, 80.2, 66.5, 54.7, 45.8, 42.3, 36.3, 28.1. HRMS (ESI-TOF) calcd for $C_{21}H_{30}N_2O_4Na$ (M+Na$^+$) 397.2098, found 397.2090.

Methylmagnesium chloride (11.0 mL, 10.2 mmol; 0.93 M solution in THF) was added dropwise over 1 h to a solution of (*S*)-**8** in THF (26 mL) at –20 °C, and the mixture was stirred for 2 h at –20 °C and for 20 min at room temperature. The reaction was quenched with 1 M HCl (aq) (14 mL) at 0 °C and this was extracted with EtOAc. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was chromatographed on silica gel with EtOAc/hexane = 1/5 to afford compound (*S*)-**20** as a colorless oil (1.66 g, 5.46 mmol; 81% yield, ~6/4 mixture of rotamers). $[\alpha]_D^{25} = -245$ (*c* 1.11, $CHCl_3$). $^1H$ NMR ($CDCl_3$): $\delta$ 7.31–7.25 (m, 2H), 7.22 (d, $^3J_{HH}$ = 7.1 Hz, 1H), 7.17 (d, $^3J_{HH}$ = 7.4 Hz, 0.8H), 7.13 (d, $^3J_{HH}$ = 7.4 Hz, 1.2H), 5.72–5.57 (m, 1H), 5.09 (d, $^3J_{HH}$ = 10.1 Hz, 0.6H), 5.04 (d, $^3J_{HH}$ = 10.2 Hz, 0.4H), 4.98 (d, $^3J_{HH}$ = 17.1 Hz, 1H), 4.14 (dd, $^3J_{HH}$ = 8.9 and 5.2 Hz, 0.4H), 4.07 (dd, $^2J_{HH}$ = 14.6 Hz and $^3J_{HH}$ = 4.9 Hz, 0.6H), 3.85–3.68 (m, 1H), 3.39–3.23 (m, 1 H), 3.08 (dd, $^2J_{HH}$ = 15.2 Hz and $^3J_{HH}$ = 7.2 Hz, 0.4H), 3.03 (dd, $^2J_{HH}$ = 13.9 Hz and $^3J_{HH}$ = 9.5 Hz, 0.4H), 2.93 (dd, $^2J_{HH}$ = 14.0 Hz and $^3J_{HH}$ = 10.0 Hz, 0.6H), 2.82 (dd, $^2J_{HH}$ = 15.0 Hz and $^3J_{HH}$ = 8.3 Hz, 0.6H), 2.14 (s, 3H), 1.46 (s, 9H). $^{13}C$ NMR ($CDCl_3$): $\delta$ 205.8, 205.3, 155.0, 154.3, 138.7, 138.6, 134.0, 133.6, 129.4, 128.6, 128.4, 126.5, 126.4, 119.1, 117.8, 81.5, 80.6, 67.8, 67.1, 51.3, 50.8, 34.9, 34.0, 28.3, 27.2, 26.7. HRMS (ESI-TOF) calcd for $C_{18}H_{25}NO_3Na$ (M+Na$^+$) 326.1727, found 326.1722.

Sodium hexamethyldisilazide (5.60 mL, 10.6 mmol; 1.9 M solution in THF) was added to a solution of methyltriphenylphosphonium bromide (4.06 g, 11.4 mmol) in $Et_2O$ (300 mL) at 0 °C, and the mixture was stirred for 1 h at 0 °C. A solution of (*S*)-**20** (1.64 g, 5.39 mmol) in $Et_2O$ (37 mL) was added to it dropwise over 1 h, and this mixture was stirred for 1.5 h at room temperature. The reaction was quenched with 1 M HCl (aq) (150 mL) at 0 °C and this was extracted with EtOAc. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was chromatographed on silica gel with EtOAc/hexane = 1/10, followed by recrystallization from hexane, to afford compound (*S*)-**9** as a white solid (1.20 g, 3.97 mmol; 74% yield). $[\alpha]_D^{30} = -187$ (*c* 1.03, $CHCl_3$). $^1H$ NMR ($CDCl_3$, 50 °C): $\delta$ 7.24 (t, $^3J_{HH}$ = 7.3 Hz, 2H), 7.21–7.14 (m, 3H), 5.72 (br s, 1H), 5.04 (d, $^3J_{HH}$ = 17.1 Hz, 1H), 5.02–4.95 (m, 3H), 4.74 (br s, 1H), 3.72–3.59 (m, 1H), 3.54 (dd, $^2J_{HH}$ = 15.5 Hz and $^3J_{HH}$ = 6.5 Hz, 1H), 3.01 (dd, $^2J_{HH}$ = 14.0 Hz and $^3J_{HH}$ = 5.6 Hz, 1H), 2.94 (dd, $^2J_{HH}$ = 14.0 Hz and $^3J_{HH}$ = 9.4 Hz, 1H), 1.73 (s, 3H), 1.32 (s, 9H). $^{13}C$ NMR ($CDCl_3$): $\delta$ 155.5, 144.3, 138.9, 135.7, 129.2, 128.1, 126.1, 116.0, 112.7, 79.4, 61.4, 59.9, 46.2, 36.6, 28.2, 21.8. HRMS (ESI-TOF) calcd for $C_{19}H_{27}NO_2Na$ (M+Na$^+$) 324.1934, found 324.1931.

Grubbs catalyst (61.2 mg, 72.0 μmol; 2nd generation) was added to a solution of (*S*)-**9** (1.08 g, 3.60 mmol) in $C_6H_6$ (36 mL) and the mixture was stirred for 5 h at 60 °C. The solvent was removed under vacuum, and the residue was chromatographed on silica gel with EtOAc/hexane = 1/5 to afford compound (*S*)-**21** as a colorless oil (981 mg, 3.58 mmol; 99% yield, ~5/5 mixture of rotamers). $[\alpha]_D^{20} = +145$ (*c* 0.56, $CHCl_3$). $^1H$ NMR ($CDCl_3$): $\delta$ 7.25–7.15 (m, 3H), 7.10 (d, $^3J_{HH}$ = 7.4 Hz, 2H), 5.26 (s, 0.5H), 5.20 (s, 0.5H), 4.62 (br s, 0.5H), 4.55 (br s, 0.5H), 3.97 (d, $^2J_{HH}$ = 14.7 Hz, 0.5H), 3.83 (d, $^2J_{HH}$ = 15.2 Hz, 0.5H), 3.46–3.31 (m, 1H), 3.30–3.15 (m, 1H), 2.88–2.80 (m, 1H), 1.76 (s, 1.5H), 1.72 (s, 1.5H), 1.54 (s, 4.5H), 1.50 (s, 4.5H). $^{13}C$ NMR ($CDCl_3$): $\delta$ 154.0, 153.9, 137.5, 137.4, 137.2, 137.0, 129.9, 129.7, 128.0, 127.7, 126.3, 126.1, 120.9, 120.8, 79.6, 79.0, 67.1, 66.9, 53.2, 52.8, 37.4, 35.7, 28.74, 28.66, 14.4, 14.3. HRMS (ESI-TOF) calcd for $C_{17}H_{23}NO_2Na$ (M+Na$^+$) 296.1621, found 296.1624.

Trifluoroacetic acid (7.0 mL) was added to a solution of (*S*)-**21** (950 mg, 3.47 mmol) in $CH_2Cl_2$ (34 mL) and the mixture was stirred for 1 h at room temperature. The solvent was removed under vacuum, and the remaining trifluoroacetic acid was further removed by dissolving the residue in $CH_2Cl_2$ and concentrated under vacuum twice, followed by the same sequence with hexane twice. The residue was chromatographed on silica gel with MeOH/$CH_2Cl_2$ = 1/10 to afford compound (*S*)-**22** as a purple solid (857 mg, 2.98 mmol; 86% yield). $[\alpha]_D^{20} = -10.6$ (*c* 0.54, $CHCl_3$). $^1H$ NMR ($CDCl_3$): $\delta$ 10.42 (br s, 1H), 9.05 (br s, 1H), 7.31–7.19 (m, 5H), 5.41 (s, 1H), 4.52 (br s, 1H), 3.61 (br s, 2H), 3.15 (dd, $^2J_{HH}$ = 14.8 Hz and $^3J_{HH}$ = 5.1 Hz, 1H), 2.95 (dd, $^2J_{HH}$ = 14.8 Hz and $^3J_{HH}$ = 8.5 Hz, 1H), 1.72 (s, 3H). $^{13}C$ NMR ($CDCl_3$): $\delta$ 162.0 (q, $^2J_{CF}$ = 34.8 Hz), 138.0, 135.4, 129.1, 128.8, 127.2, 119.3, 116.7 (q, $^1J_{CF}$ = 293 Hz), 67.5, 50.2, 37.0, 13.6. HRMS (ESI-TOF) calcd for $C_{12}H_{16}N$ (M–$CF_3CO_2^-$) 174.1277, found 174.1276.

NaOH (aq, 1 M) (10 mL) was added to a solution of (*S*)-**22** (258 mg, 0.898 mmol) in $Et_2O$ (8 mL) and the mixture was extracted with $Et_2O$. The organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was dissolved in THF (1.5 mL), and $Et_3N$ (570 μL, 4.08 mmol) and chlorodiphenylphosphine (190 μL, 1.05 mmol) were successively added to it with additional THF (1.0 mL) at 0 °C. The mixture was stirred for 20 h at room temperature, and the volatiles were removed under vacuum. This was chromatographed on silica gel with degassed $Et_3N$/hexane = 1/2, followed by passing through a pad of alumina with $Et_3N$/hexane = 1/10 under $N_2$, to afford (*S*)-**5** as an orange solid (247 mg, 0.691 mmol; 77% yield). $[\alpha]_D^{20} = +209$ (*c* 0.52, THF). $^1H$ NMR ($C_6D_6$): $\delta$ 7.53–7.48 (m, 2H), 7.43–7.37 (m, 2H), 7.20–7.03 (m, 11H), 5.02 (d, $J_{HH}$ = 1.4 Hz, 1H), 4.62–4.54 (m, 1H), 3.65–3.58 (m, 1H), 3.45–3.38 (m, 1H), 3.07 (ddd, $^2J_{HH}$ = 13.7 Hz, $^3J_{HH}$ = 6.3 Hz, and $^4J_{HP}$ = 0.5 Hz, 1H), 2.99 (ddd, $^2J_{HH}$ = 13.8 Hz, $^3J_{HH}$ = 3.8 Hz, and $^4J_{HP}$ = 1.5 Hz, 1H), 1.45 (br s, 3H). $^{13}C$ NMR ($C_6D_6$): $\delta$ 140.1 (d, $J_{CP}$ = 19.6 Hz), 139.9 (d, $J_{CP}$ = 7.2 Hz), 139.4 (d, $J_{CP}$ = 5.7 Hz), 138.9, 133.1 (d, $J_{CP}$ = 21.1 Hz), 132.2 (d, $J_{CP}$ = 19.1 Hz), 130.4, 128.7,

128.6 (d, $J_{CP}$ = 5.2 Hz), 128.42 (d, $J_{CP}$ = 6.7 Hz), 128.39, 128.1, 126.2, 123.2, 74.3 (d, $J_{CP}$ = 30.0 Hz), 53.8 (d, $J_{CP}$ = 8.8 Hz), 41.7 (d, $J_{CP}$ = 4.1 Hz), 14.6. $^{31}P\{^1H\}$ NMR ($C_6D_6$): $\delta$ 46.7 (s). HRMS (ESI-TOF) calcd for $C_{24}H_{25}NP$ ($M+H^+$) 358.1719, found 358.1715.

### 4.3. Preparation of rhodium/chiral phosphorus–olefin complexes

#### 4.3.1. Rh(acac)((*S*)-1a) 10

A solution of (*S*)-**1a** (318 mg, 0.890 mmol) in $C_6H_6$ (4.0 mL) was added slowly over 25 min to a solution of Rh(acac)$(C_2H_4)_2$ (214 mg, 0.829 mmol) in $C_6H_6$ (1.0 mL) at 30 °C, and the mixture was stirred for 1 h at 30 °C. The reaction mixture was filtered through a PTFE membrane with $C_6H_6$ and the solvent was removed under vacuum. The solid thus obtained was washed with hexane and dried under vacuum to afford complex **10** as a yellow solid (396 mg, 0.708 mmol; 85% yield). $[\alpha]_D^{25} = -20.5$ (*c* 0.52, THF). Recrystallization of this complex from $C_6H_6$/pentane afforded single crystals suitable for X-ray crystallographic analysis. $^1H$ NMR ($C_6D_6$): $\delta$ 8.25–8.18 (m, 2H), 7.98–7.92 (m, 2H), 7.17–7.07 (m, 3H), 7.06–6.94 (m, 8H), 5.36 (s, 1H), 3.75 (s, 1H), 3.52–3.45 (m, 1H), 2.84 (t, $J_{HH}$ = 14.0 Hz, 1H), 2.63 (dd, $^2J_{HH}$ = 12.8 Hz and $^3J_{HP}$ = 8.8 Hz, 1H), 2.44–2.29 (m, 2H), 1.97 (s, 3H), 1.93 (s, 3H), 1.89 (s, 3H). $^{31}P\{^1H\}$ NMR ($C_6D_6$): $\delta$ 127.9 (d, $^1J_{PRh}$ = 202 Hz). Anal. Calcd for $C_{29}H_{31}NO_2PRh$: C, 62.26; H, 5.59. Found: C, 62.27; H, 5.52.

#### 4.3.2. Rh(acac)((*S*)-4) 11

A solution of (*S*)-**4** (93.2 mg, 0.250 mmol) in $C_6H_6$ (6.0 mL) was added slowly over 2 h to a solution of Rh(acac)$(C_2H_4)_2$ (76.7 mg, 0.297 mmol) in $C_6H_6$ (2.5 mL) at 30 °C, and the mixture was stirred for 1 h at 30 °C. The reaction mixture was filtered through a PTFE membrane with $C_6H_6$ and the solvent was removed under vacuum. The solid thus obtained was washed with hexane, recrystallized from $Et_2O$, and dried under vacuum to afford complex **11** as an orange solid (101 mg, 0.176 mmol; 70% yield). $[\alpha]_D^{20} = +69.6$ (*c* 0.58, THF). Recrystallization of this complex from $Et_2O$/pentane afforded single crystals suitable for X-ray crystallographic analysis. $^1H$ NMR ($C_6D_6$): $\delta$ 8.14 (t, $^3J$ = 8.4 Hz, 2H), 8.00 (t, $^3J$ = 8.7 Hz, 2H), 7.22–7.08 (m, 5H), 7.08–7.01 (m, 3H), 7.01–6.92 (m, 3H), 5.33 (s, 1H), 4.14 (s, 1H), 3.79–3.67 (m, 1H), 3.16–2.99 (m, 1H), 2.90 (dd, $^2J_{HH}$ = 13.8 Hz and $^3J_{HH}$ = 9.1 Hz, 1H), 2.69 (dd, $^2J_{HH}$ = 14.1 Hz and $^3J_{HH}$ = 5.6 Hz, 1H), 2.65–2.45 (m, 2H), 1.91 (s, 3H), 1.86 (s, 6H), 1.48–1.39 (m, 1H). $^{31}P\{^1H\}$ NMR ($C_6D_6$): $\delta$ 105.5 (d, $^1J_{PRh}$ = 202 Hz). Anal. Calcd for $C_{30}H_{33}NO_2PRh$: C, 62.83; H, 5.80. Found: C, 62.98; H, 5.85.

#### 4.3.3. Rh(acac)((*S*)-5) 12

A solution of (*S*)-**5** (75.8 mg, 0.212 mmol) in $C_6H_6$ (4.5 mL) was added slowly over 1 h to a solution of of Rh(acac)$(C_2H_4)_2$ (60.4 mg, 0.233 mmol) in $C_6H_6$ (2.5 mL) at 30 °C, and the mixture was stirred for 1 h at 30 °C. The reaction mixture was filtered through PTFE membrane with $C_6H_6$ and the solvent was removed under vacuum. The solid thus obtained was washed with hexane and dried under vacuum to afford complex **12** as a yellow solid (92.2 mg, 0.164 mmol; 78% yield). $[\alpha]_D^{25} = +91.6$ (*c* 0.58, THF). Recrystallization of this complex from 1,2-dichloroethane/pentane afforded single crystals suitable for X-ray crystallographic analysis. $^1H$ NMR ($C_6D_6$): $\delta$ 8.15–8.06 (m, 2H), 7.88–7.80 (m, 2H), 7.25–7.11 (m, 3H), 7.06–6.89 (m, 8H), 5.38 (s, 1H), 3.87 (s, 1H), 3.44–3.34 (m, 1H), 2.85 t, $J_{HH}$ = 13.6 Hz, 1H), 2.66 (dd, $^2J_{HH}$ = 13.5 Hz and $^3J_{HH}$ = 3.3 Hz, 1H), 2.43 (dd, $^3J_{HP}$ = 46.8 Hz and $^2J_{HH}$ = 13.6 Hz, 1H), 2.24 (t, *J* = 12.1 Hz, 1H), 1.96 (s, 3H), 1.94 (s, 3H), 1.92 (s, 3H). $^{31}P\{^1H\}$ NMR ($C_6D_6$): $\delta$ 128.2 (d, $^1J_{PRh}$ = 204 Hz). Anal. Calcd for $C_{29}H_{31}NO_2PRh$: C, 62.26; H, 5.59. Found: C, 62.03; H, 5.64.

#### 4.3.4. General procedure for [RhCl(ligand)]$_2$

A solution of ligand (1.0 equiv) in $C_6H_6$ (5.0–15 mL for 1.0 mmol of ligand) was added slowly over 20 min to a solution of $[RhCl(C_2H_4)_2]_2$ (1.1–1.4 equiv Rh) in $C_6H_6$ (2.5 mL for 1.0 mmol of ligand) at 30 °C, and the mixture was stirred for 1 h at 30 °C. The reaction mixture was filtered through PTFE membrane with $C_6H_6$ and the solvent was removed under vacuum. The solid thus obtained was washed with hexane and dried under vacuum to afford complex $[RhCl(ligand)]_2$, which was directly used as a catalyst for the 1,4-addition reaction.

### 4.4. Rhodium-catalyzed asymmetric 1,4-addition reactions

#### 4.4.1. General procedure for the rhodium-catalyzed asymmetric 1,4-addition (Tables 2 and 3)

At first, KOH (50 μL, 0.10–0.20 mmol; 2.0–4.0 M aqueous) was added to a solution of $[RhCl(ligand)]_2$ (10 μmol Rh), α,β-unsaturated ketone (0.20 mmol), and arylboronic acid (0.22–0.30 mmol) in dioxane (0.50 mL), and the resulting mixture was stirred for 10 h at 30 °C. This was directly passed through a pad of silica gel with EtOAc and the solvent was removed under vacuum. The residue was purified by silica gel preparative TLC with EtOAc/hexane to afford the 1,4-adduct.

#### 4.4.2. (*S*)-3-Phenylcyclohexanone (Table 2, entry 1)

(CAS 57344–86–2) The reaction was conducted with 1.1 equiv of phenylboronic acid and 0.5 equiv. of KOH. Yellow oil. 89% yield. The ee was determined on a Daicel Chiralpak AD-H column with hexane/2-propanol = 100/1, flow = 0.5 mL/min. Retention times: 25.3 min [major enantiomer], 31.2 min [minor enantiomer]. 94% ee. $[\alpha]_D^{30} = -20.2$ (*c* 1.02, $CHCl_3$). $^1H$ NMR ($CDCl_3$): $\delta$ 7.33 (t, $^3J_{HH}$ = 7.5 Hz, 2H), 7.27–7.20 (m, 3H), 3.01 (tt, $^3J_{HH}$ = 11.8 and 3.9 Hz, 1H), 2.60 (ddt, $^2J_{HH}$ = 14.0 Hz, $^3J_{HH}$ = 4.4 Hz, and $^4J_{HH}$ = 1.9 Hz, 1H), 2.53 (ddd, $^2J_{HH}$ = 14.0 Hz, $^3J_{HH}$ = 12.3 Hz, and $^4J_{HH}$ = 1.0 Hz, 1H), 2.50–2.43 (m, 1H), 2.38 (dddd, $^2J_{HH}$ = 14.3 Hz, $^3J_{HH}$ = 12.4 and 6.1 Hz, and $^4J_{HH}$ = 0.9 Hz, 1H), 2.19–2.12 (m, 1H), 2.12–2.06 (m, 1H), 1.91–1.73 (m, 2H).

#### 4.4.3. (*R*)-3-Phenylcyclohexanone (Table 2, entry 5)

(CAS 34993–51–6) The reaction was conducted with 1.1 equiv of phenylboronic acid and 0.5 equiv of KOH. Colorless oil. 98% yield. The ee was determined on a Daicel Chiralpak AD-H column with hexane/2-propanol = 100/1, flow = 0.5 mL/min. Retention times: 28.9 min [minor enantiomer], 33.7 min [major enantiomer]. 97% ee. $[\alpha]_D^{30} = +20.0$ (*c* 1.03, $CHCl_3$).

#### 4.4.4. (*S*)-3-(4-Methoxyphenyl)cyclohexanone (Table 2, entry 6)

(CAS 250782–40–2) The reaction was conducted with 1.1 equiv of 4-methoxyphenylboronic acid and 0.5 equiv of KOH. Colorless oil. 86% yield. The ee was determined on a Daicel Chiralpak AD-H column with hexane/ethanol = 70/30, flow = 1.0 mL/min. Retention times: 10.8 min [minor enantiomer], 13.4 min [major enantiomer]. 96% ee. $[\alpha]_D^{20} = -17.3$ (*c* 1.01, $CHCl_3$). $^1H$ NMR ($CDCl_3$): $\delta$ 7.14 (d, $^3J_{HH}$ = 8.5 Hz, 2H), 6.87 (d, $^3J_{HH}$ = 8.7 Hz, 2H), 3.80 (s, 3H), 2.97 (tt, $^3J_{HH}$ = 11.8 and 4.0 Hz, 1H), 2.57 (ddt, $^2J_{HH}$ = 13.9 Hz, $^3J_{HH}$ = 4.3 Hz, and $^4J_{HH}$ = 2.2 Hz, 1H), 2.49 (ddd, $^2J_{HH}$ = 13.9 Hz, $^3J_{HH}$ = 12.4 Hz, and $^4J_{HH}$ = 1.1 Hz, 1H), 2.48–2.41 (m, 1H), 2.36 (dddd, $^2J_{HH}$ = 14.3 Hz, $^3J_{HH}$ = 12.4 and 6.1 Hz, and $^4J_{HH}$ = 0.9 Hz, 1H), 2.17–2.10 (m, 1H), 2.10–2.02 (m, 2H), 1.86–1.71 (m, 2H).

#### 4.4.5. (*R*)-3-(4-Methoxyphenyl)cyclohexanone (Table 2, entry 7)

(CAS 479586–33–9) The reaction was conducted with 1.1 equiv of 4-methoxyphenylboronic acid and 0.5 equiv of KOH. Colorless oil. 93% yield. The ee was determined on a Daicel Chiralpak AD-H column with hexane/ethanol = 70/30, flow = 1.0 mL/min. Retention

times: 9.6 min [major enantiomer], 11.9 min [minor enantiomer]. 97% ee. $[\alpha]_D^{20} = +18.7$ (*c* 1.02, $CHCl_3$).

#### 4.4.6. (*S*)-3-(4-Trifluoromethylphenyl)cyclohexanone (Table 2, entry 8)

(CAS 658711–11–6) The reaction was conducted with 1.1 equiv of 4-trifluoromethylphenylboronic acid and 0.5 equiv of KOH. White solid. 87% yield. The ee was determined on a Daicel Chiralpak AS-H column with hexane/2-propanol = 90/10, flow = 0.5 mL/min. Retention times: 22.7 min [minor enantiomer], 24.7 min [major enantiomer]. 94% ee. $[\alpha]_D^{15} = -11.8$ (*c* 1.02, $CHCl_3$). $^1$H NMR ($CDCl_3$): $\delta$ 7.59 (d, $^3J_{HH}$ = 8.0 Hz, 2H), 7.34 (d, $^3J_{HH}$ = 8.1 Hz, 2H), 3.08 (tt, $^3J_{HH}$ = 11.9 and 3.9 Hz, 1H), 2.60 (ddt, $^2J_{HH}$ = 13.9 Hz, $^3J_{HH}$ = 4.4 Hz, and $^4J_{HH}$ = 2.1 Hz, 1H), 2.52 (ddd, $^2J_{HH}$ = 14.0 Hz, $^3J_{HH}$ = 12.4 Hz, and $^4J_{HH}$ = 0.9 Hz, 1H), 2.52–2.45 (m, 1H), 2.39 (dddd, $^2J_{HH}$ = 14.4 Hz, $^3J_{HH}$ = 12.6 and 6.2 Hz, and $^4J_{HH}$ = 1.0 Hz, 1H), 2.22–2.14 (m, 1H), 2.14–2.06 (m, 1H), 1.93–1.75 (m, 2H).

#### 4.4.7. (*R*)-3-(4-Trifluoromethylphenyl)cyclohexanone (Table 2, entry 9)

(CAS 610273–87–5) The reaction was conducted with 1.5 equiv of 4-trifluoromethylphenylboronic acid and 0.5 equiv of KOH. White solid. 84% yield. The ee was determined on two Daicel Chiralpak AS-H columns with hexane/2-propanol = 90/10, flow = 0.5 mL/min. Retention times: 41.9 min [major enantiomer], 46.0 min [minor enantiomer]. 97% ee. $[\alpha]_D^{20} = +12.0$ (*c* 1.01, $CHCl_3$).

#### 4.4.8. (*S*)-3-(2-Methylphenyl)cyclohexanone (Table 2, entry 10)

(CAS 475599–60–1) The reaction was conducted with 1.1 equiv of 2-methylphenylboronic acid and 0.5 equiv of KOH. Colorless oil. 92% yield. The ee was determined on a Daicel Chiralpak AD-H column with hexane/2-propanol = 100/1, flow = 0.5 mL/min. Retention times: 22.4 min [major enantiomer], 28.9 min [minor enantiomer]. 95% ee. $[\alpha]_D^{25} = -44.5$ (*c* 1.01, $CHCl_3$). $^1$H NMR ($CDCl_3$): $\delta$ 7.25–7.19 (m, 2H), 7.18–7.11 (m, 2H), 3.27–3.16 (m, 1H), 2.55–2.46 (m, 3H), 245–2.37 (m, 1H), 2.33 (s, 3H), 2.21–2.12 (m, 1H), 2.04–1.97 (m, 1H), 1.90–1.74 (m, 2H).

#### 4.4.9. (*R*)-3-(2-Methylphenyl)cyclohexanone (Table 2, entry 11)

(CAS 91663–37–5) The reaction was conducted with 1.5 equiv of 2-methylphenylboronic acid and 0.5 equiv of KOH. Colorless oil. 99% yield. The ee was determined on a Daicel Chiralpak AD-H column with hexane/2-propanol = 100/1, flow = 0.5 mL/min. Retention times: 22.7 min [minor enantiomer], 29.0 min [major enantiomer]. 98% ee. $[\alpha]_D^{20} = +44.4$ (*c* 1.00, $CHCl_3$).

#### 4.4.10. (*S*)-3-Phenylcyclopentanone (Table 2, entry 12)

(CAS 86505–50–2) The reaction was conducted with 1.5 equiv of phenylboronic acid and 0.5 equiv of KOH. Colorless oil. 92% yield. The ee was determined on three Daicel Chiralpak AD-H columns with hexane/ethanol = 98/2, flow = 0.5 mL/min. Retention times: 88.0 min [minor enantiomer], 92.4 min [major enantiomer]. 93% ee. $[\alpha]_D^{20} = -91.1$ (*c* 1.14, $CHCl_3$). $^1$H NMR ($CDCl_3$): $\delta$ 7.37–7.32 (m, 2H), 7.28–7.23 (m, 3H), 3.47–3.38 (m, 1H), 2.67 (dd, $^2J_{HH}$ = 18.2 Hz and $^3J_{HH}$ = 7.3 Hz, 1H), 2.52–2.40 (m, 2H), 2.35 (ddd, $^2J_{HH}$ = 18.0 Hz, $^3J_{HH}$ = 11.2 Hz, and $^4J_{HH}$ = 1.3 Hz, 1H), 2.34–2.26 (m, 1H), 2.05–1.94 (m, 1H).

#### 4.4.11. (*R*)-3-Phenylcyclopentanone (Table 2, entry 13)

(CAS 86505–44–4) The reaction was conducted with 1.5 equiv of phenylboronic acid and 0.5 equiv of KOH. Colorless oil. 93% yield. The ee was determined on two Daicel Chiralcel OB-H columns with hexane/2-propanol = 98/2, flow = 0.3 mL/min. Retention times: 141.7 min [minor enantiomer], 147.2 min [major enantiomer]. 95% ee. $[\alpha]_D^{25} = +92.9$ (*c* 1.07, $CHCl_3$).

#### 4.4.12. (*S*)-3-Phenylcycloheptanone (Table 2, entry 14)

(CAS 435269–65–1) The reaction was conducted with 1.5 equiv of phenylboronic acid and 1.0 equiv of KOH. Colorless oil. 90% yield. The ee was determined on two Daicel Chiralcel OD-H columns with hexane/2-propanol = 98/2, flow = 0.5 mL/min. Retention times: 54.3 min [major enantiomer], 60.8 min [minor enantiomer]. 87% ee. $[\alpha]_D^{20} = -54.0$ (*c* 0.88, $CHCl_3$). $^1$H NMR ($CDCl_3$): $\delta$ 7.30 (t, $^3J_{HH}$ = 7.5 Hz, 2H), 7.22–7.16 (m, 3H), 2.97–2.86 (m, 2H), 2.70–2.54 (m, 3H), 2.13–1.95 (m, 3H), 1.80–1.67 (m, 2H), 1.55–1.45 (m, 1H).

#### 4.4.13. (*R*)-3-Phenylcycloheptanone (Table 2, entry 15)

(CAS 501919–44–4) The reaction was conducted with 1.5 equiv of phenylboronic acid and 0.5 equiv of KOH. Colorless oil. 87% yield. The ee was determined on a Daicel Chiralcel OD-H column with hexane/2-propanol = 98/2, flow = 0.5 mL/min. Retention times: 21.8 min [minor enantiomer], 24.2 min [major enantiomer]. 95% ee. $[\alpha]_D^{25} = +54.2$ (*c* 0.85, $CHCl_3$).

#### 4.4.14. (*R*)-4-Phenyl-2-pentanone (Table 3, entry 1)

(CAS 67110–72–9) Colorless oil. 89% yield. The ee was determined on two Daicel Chiralcel OJ-H columns with hexane/2-propanol = 98/2, flow = 0.7 mL/min. Retention times: 35.1 min [minor enantiomer], 36.8 min [major enantiomer]. 85% ee. $[\alpha]_D^{30} = -39.9$ (*c* 0.50, $CHCl_3$). $^1$H NMR ($CDCl_3$): $\delta$ 7.31–7.27 (m, 2H), 7.23–7.17 (m, 3H), 3.30 (sext, $^3J_{HH}$ = 7.1 Hz, 1H), 2.75 (dd, $^2J_{HH}$ = 16.2 Hz and $^3J_{HH}$ = 6.5 Hz, 1H), 2.65 (dd, $^2J_{HH}$ = 16.3 Hz and $^3J_{HH}$ = 7.8 Hz, 1H), 2.06 (s, 3H), 1.27 (d, $^3J_{HH}$ = 6.9 Hz, 3H).

#### 4.4.15. (*S*)-4-Phenyl-2-pentanone (Table 3, entry 2)

(CAS 32587–80–7) Colorless oil. 79% yield. The ee was determined on two Daicel Chiralcel OJ-H columns with hexane/2-propanol = 98/2, flow = 0.7 mL/min. Retention times: 34.9 min [major enantiomer], 37.0 min [minor enantiomer]. 50% ee. $[\alpha]_D^{25} = +23.5$ (*c* 1.02, $CHCl_3$).

#### 4.4.16. (*R*)-4-Phenyl-2-nonanone (Table 3, entry 3)

(CAS 435269–67–3) Colorless oil. 91% yield. The ee was determined on two Daicel Chiralcel OJ-H columns with hexane/2-propanol = 98/2, flow = 0.5 mL/min. Retention times: 23.7 min [minor enantiomer], 25.1 min [major enantiomer]. 83% ee. $[\alpha]_D^{25} = -17.0$ (*c* 1.03, $CHCl_3$). $^1$H NMR ($CDCl_3$): $\delta$ 7.28 (t, $^3J_{HH}$ = 7.4 Hz, 2H), 7.20–7.15 (m, 3H), 3.14–3.06 (m, 1H), 2.72 (dd, $^2J_{HH}$ = 16.0 Hz and $^3J_{HH}$ = 7.3 Hz, 1H), 2.68 (dd, $^2J_{HH}$ = 16.0 Hz and $^3J_{HH}$ = 7.1 Hz, 1H), 2.00 (s, 3H), 1.65–1.50 (m, 2H), 1.28–1.05 (m, 6H), 0.82 (t, $^3J_{HH}$ = 6.9 Hz, 3H).

#### 4.4.17. (*S*)-4-Phenyl-2-nonanone (Table 3, entry 4)

(CAS 501919–45–5) Colorless oil. 73% yield. The ee was determined on two Daicel Chiralcel OJ-H columns with hexane/2-propanol = 100/1, flow = 0.5 mL/min. Retention times: 33.8 min [major enantiomer], 37.3 min [minor enantiomer]. 58% ee. $[\alpha]_D^{25} = +12.6$ (*c* 1.01, $CHCl_3$).

#### 4.4.18. (*S*)-5-Methyl-4-phenyl-2-hexanone (Table 3, entry 5)

(CAS 435269–66–2) Yellow oil. 93% yield. The ee was determined on three Daicel Chiralcel OD-H columns with hexane/2-propanol = 98/2, flow = 0.5 mL/min. Retention times: 38.7 min [minor enantiomer], 43.0 min [major enantiomer]. 81% ee. $[\alpha]_D^{25} = -31.1$ (*c* 0.99, $CHCl_3$). $^1$H NMR ($CDCl_3$): $\delta$ 7.27 (t, $^3J_{HH}$ = 7.4 Hz, 2H), 7.18 (tt, $^3J_{HH}$ = 7.3 Hz and $^4J_{HH}$ = 1.2 Hz, 1H), 7.15–7.14 (m, 2H), 2.91 (ddd, $^3J_{HH}$ = 8.8, 7.6, and 5.8 Hz, 1H), 2.81 (dd, $^2J_{HH}$ = 15.8 Hz and $^3J_{HH}$ = 5.6 Hz, 1H), 2.77 (dd, $^2J_{HH}$ = 15.9 Hz and $^3J_{HH}$ = 9.0 Hz, 1H), 1.97 (s, 3H), 1.83 (sext, $^3J_{HH}$ = 6.9 Hz, 1H), 0.93 (d, $^3J_{HH}$ = 6.7 Hz, 3H), 0.74 (d, $^3J_{HH}$ = 6.7 Hz, 3H).

#### 4.4.19. (*R*)-5-Methyl-4-phenyl-2-hexanone (Table 3, entry 6)

(CAS 162239–77–2) Yellow oil. 79% yield. The ee was determined on three Daicel Chiralcel OD-H columns with hexane/2-propanol = 98/2, flow = 0.5 mL/min. Retention times: 38.4 min [major enantiomer], 42.6 min [minor enantiomer]. 65% ee. $[\alpha]_D^{25} = +11.6$ (*c* 0.28, $CHCl_3$).

## Acknowledgments

Support has been provided in part by a Grant-in-Aid for Scientific Research (S) (19105002), the Ministry of Education, Culture, Sports, Science and Technology, Japan.

## References

1. (a) Hayashi, T.; Ueyama, K.; Tokunaga, N.; Yoshida, K. *J. Am. Chem. Soc.* **2003**, *125*, 11508; (b) Fischer, C.; Defieber, C.; Suzuki, T.; Carreira, E. M. *J. Am. Chem. Soc.* **2004**, *126*, 1628.
2. For reviews, see: (a) Feng, C.-G.; Xu, M.-H.; Lin, G.-Q. *Synlett* **2011**, 1345; (b) Shintani, R.; Hayashi, T. *Aldrichimica Acta* **2009**, *42*, 31; (c) Defieber, C.; Grützmacher, H.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2008**, *47*, 4482; (d) Johnson, J. B.; Rovis, T. *Angew. Chem., Int. Ed.* **2008**, *47*, 840.
3. (a) Maire, P.; Deblon, S.; Breher, F.; Geier, J.; Böhler, C.; Rüegger, H.; Schönberg, H.; Grützmacher, H. *Chem. Eur. J.* **2004**, *10*, 4198; (b) Piras, E.; Läng, F.; Rüegger, H.; Stein, D.; Wörle, M.; Grützmacher, H. *Chem. Eur. J.* **2006**, *12*, 5849; (c) Kasák, P.; Arion, V. B.; Widhalm, M. *Tetrahedron: Asymmetry* **2006**, *17*, 3084; (d) Stemmler, R. T.; Bolm, C. *Synlett* **2007**, 1365; (e) Defieber, C.; Ariger, M. A.; Moriel, P.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2007**, *46*, 3139; (f) Roggen, M.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2011**, *50*, 5568; (g) Stepnicka, P.; Lamac, M.; Císarová, I. J. *Organomet. Chem.* **2008**, *693*, 446; (h) Mariz, R.; Briceño, A.; Dorta, R.; Dorta, R. *Organometallics* **2008**, *27*, 6605; (i) Drinkel, E.; Briceño, A.; Dorta, R.; Dorta, R. *Organometallics* **2010**, *29*, 2503; (j) Minuth, T.; Boysen, M. M. K. *Org. Lett.* **2009**, *11*, 4212; (k) Grugel, H.; Minuth, T.; Boysen, M. M. K. *Synthesis* **2010**, 3248; (l) Liu, Z.; Du, H. *Org. Lett.* **2010**, *12*, 3054; (m) Cao, Z.; Liu, Y.; Liu, Z.; Feng, X.; Zhuang, M.; Du, H. *Org. Lett.* **2011**, *13*, 2164; (n) Liu, Z.; Cao, Z.; Du, H. *Org. Biomol. Chem.* **2011**, *9*, 5369; (o) Cao, Z.; Liu, Z.; Liu, Y.; Du, H. *J. Org. Chem.* **2011**, *76*, 6401. See also; (p) Pregosin, P. S. *Chem. Commun.* **2008**, 4875.
4. (a) Shintani, R.; Duan, W.-L.; Nagano, T.; Okada, A.; Hayashi, T. *Angew. Chem., Int. Ed.* **2005**, *44*, 4611; (b) Shintani, R.; Duan, W.-L.; Okamoto, K.; Hayashi, T. *Tetrahedron: Asymmetry* **2005**, *16*, 3400; (c) Duan, W.-L.; Iwamura, H.; Shintani, R.; Hayashi, T. *J. Am. Chem. Soc.* **2007**, *129*, 2130.
5. (a) Hahn, B. T.; Tewes, F.; Fröhlich, R.; Glorius, F. *Angew. Chem., Int. Ed.* **2010**, *49*, 1143; (b) Kuuloja, N.; Tois, J.; Franzén, R. *Tetrahedron: Asymmetry* **2011**, *22*, 468.
6. (a) Thaler, T.; Guo, L.-N.; Steib, A. K.; Raducan, M.; Karaghiosoff, K.; Mayer, P.; Knochel, P. *Org. Lett.* **2011**, *13*, 3182; (b) Feng, X.; Wang, Y.; Wei, B.; Yang, J.; Du, H. *Org. Lett.* **2011**, *13*, 3300; (c) Qi, W.-Y.; Zhu, T.-S.; Xu, M.-H. *Org. Lett.* **2011**, *13*, 3410; (d) Jin, S.-S.; Wang, H.; Xu, M.-H. *Chem. Commun.* **2011**, *47*, 7230; (e) Chen, G.; Gui, J.; Li, L.; Liao, J. *Angew. Chem., Int. Ed.* **2011**, *50*, 7681.
7. Shintani, R.; Narui, R.; Tsutsumi, Y.; Hayashi, S.; Hayashi, T. *Chem. Commun.* **2011**, *47*, 6213.
8. (a) Takaya, Y.; Ogasawara, M.; Hayashi, T.; Sakai, M.; Miyaura, N. *J. Am. Chem. Soc.* **1998**, *120*, 5579; (b) Hayashi, T.; Takahashi, M.; Takaya, Y.; Ogasawara, M. *J. Am. Chem. Soc.* **2002**, *124*, 5052. For reviews of 1,4-addition reactions, see:; (c) Tian, P.; Dong, H.-Q.; Lin, G.-Q. *ACS Catal.* **2012**, *2*, 95; (d) Edwards, H. J.; Hargrave, J. D.; Penrose, S. D.; Frost, C. G. *Chem. Soc. Rev.* **2010**, *39*, 2093; (e) Jerphagnon, T.; Pizzuti, M. G.; Minnaard, A. J.; Feringa, B. L. *Chem. Soc. Rev.* **2009**, *38*, 1039; (f) Alexakis, A.; Bäckvall, J. E.; Krause, N.; Pàmies, O.; Diéguez, M. *Chem. Rev.* **2008**, *108*, 2796; (g) Christoffers, J.; Koripelly, G.; Rosiak, A.; Rössle, M. *Synthesis* **2007**, 1279; (h) Hayashi, T. *Bull. Chem. Soc. Jpn.* **2004**, *77*, 13.
9. Luly, J. R.; Dellaria, J. F.; Plattner, J. J.; Soderquist, J. L.; Yi, N. *J. Org. Chem.* **1987**, *52*, 1487.
10. (a) Fu, G. C.; Nguyen, S. T.; Grubbs, R. H. *J. Am. Chem. Soc.* **1993**, *115*, 9856; (b) Grubbs, R. H.; Miller, S. J.; Fu, G. C. *Acc. Chem. Res.* **1995**, *28*, 446; (c) Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953; (d) Bujard, M.; Briot, A.; Gouverneur, V.; Mioskowski, C. *Tetrahedron Lett.* **1999**, *40*, 8785; (e) Cren, S.; Wilson, C.; Thomas, N. R. *Org. Lett.* **2005**, *7*, 3521.
11. Direct installation of 3-methyl-3-butenyl group to (S)-2 was unsuccessful. See: Banba, Y.; Abe, C.; Nemoto, H.; Kato, A.; Adachi, I.; Takahata, H. *Tetrahedron: Asymmetry* **2001**, *12*, 817.
12. Pradhan, T. K.; Krishnan, K. S.; Vasse, J.-L.; Szymoniak, J. *Org. Lett.* **2011**, *13*, 1793.
13. CCDC-819417, CCDC-862089, and CCDC-862097 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
14. For DFT studies on the origin of enantioselectivity for the rhodium/chiral diene-catalyzed 1,4-addition reactions, see: (a) Kantchev, E. A. B. *Chem. Commun.* **2011**, *47*, 10969; (b) Gosiewska, S.; Raskatov, J. A.; Shintani, R.; Hayashi, T.; Brown, J. M. *Chem. Eur. J.* **2012**, *18*, 80. For relevant empirical explanations, see reference 4c.
15. Cramer, R. *Inorg. Synth.* **1974**, *15*, 16.
16. Cramer, R. *Inorg. Synth.* **1974**, *15*, 14.