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A new class of C_2-symmetric diphosphine ligands derived from valine: remarkably diverse behavior in catalytic asymmetric transformations

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Abstract

A new C_2-symmetric diphosphine ligand **8a** was readily prepared in one step by treatment of the synthetic precursor of VALAP, **7**, with phthaloyl chloride. Remarkably high levels of asymmetric induction, over 99% ee, were achieved using **8a** in palladium-catalyzed asymmetric allylic transformations of sterically less demanding cyclohexenyl substrates **9**. The ligand system was easily extended to the development of analogous chiral auxiliaries **8b**,**c** by the identical procedure but using isophthaloyl chloride and succinyl chloride. However, the ligands **8b**,**c** exhibited much lower catalytic activity. In contrast to the asymmetric allylic substitutions, **8c** demonstrated significant improvement of enantioselectivity, up to 64% ee, in rhodium-catalyzed asymmetric hydrosilylations of acetophenone **11a** compared to 35% ee using **8a**. In this way, the versatility of the present ligand system played an important role in variations of substrates and reaction types.

1. Introduction

Transition metal-catalyzed asymmetric reactions have been recognized as the most fruitful and efficient methodology in terms of the selective generation of desirable chiral compounds.[1] In the course of our work in the field of asymmetric synthesis, we have developed the novel versatile ligand system based on the amidine–phosphine hybrid ligand VALAP **1** which could be readily derived from L-valine.[2] Chiral P–N hybrid ligands **2**[2c] consisting of a diphenylphosphino group and phenyl imino groups with different substituents at the *para* position could be derived via only one step from the synthetic precursor of VALAP, **7**.

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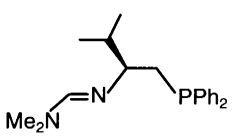
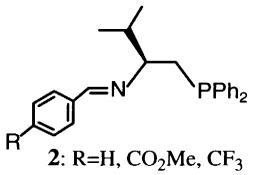


1: VALAP

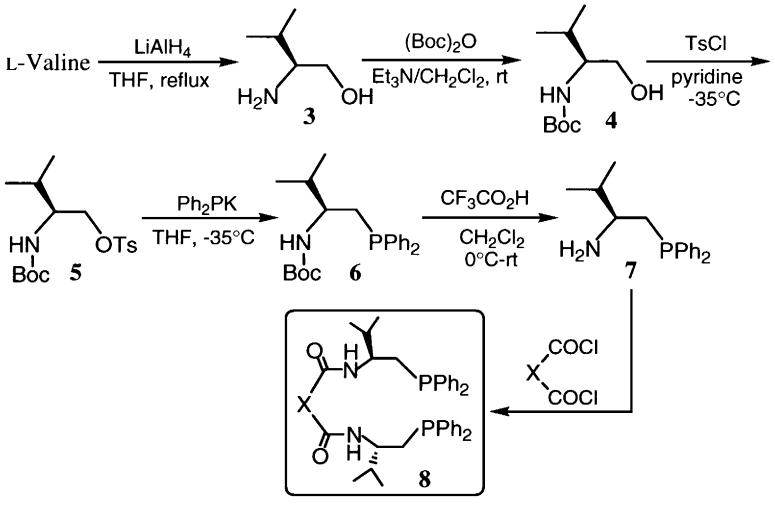


2: R=H, CO_2Me, CF_3, Me, OMe, NMe_2

It was envisaged that the facile parallel synthesis of ligands with electronically and sterically different chiral arrangements would realize efficient asymmetric induction for a number of reaction types and substrates. In the initial stage of the present work, VALAP was applied to palladium-catalyzed asymmetric allylic transformations where high levels of asymmetric induction for 1,3-diphenylallyl substrate were achieved.[2a–c] The electronic influence of ligands on the asymmetric allylations using **2** clearly demonstrated that the use of a chiral ligand having a more electron-donating dimethylamino group at the *p*-position on the phenyl group exhibited a dramatic improvement of catalytic activity together with an excellent level of asymmetric induction.[2c] Moderate enantiomeric excess up to 69% ee was obtained in the asymmetric allylic substitution of a sterically less demanding cyclohexenyl substrate by employing **2** with the dimethylamino group.[2c] Based on this result, our recent effort was focused on further extension of the present ligand system to new C_2-symmetric diphosphine ligands. This paper reports the preparation of a new series of C_2-symmetric diphosphine ligands **8** and their application to transition metal-catalyzed asymmetric transformations.

2. Results and discussion

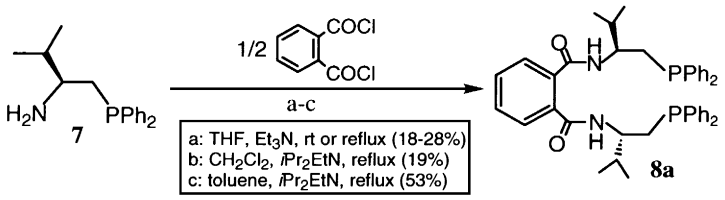
Optically active diphosphine ligands with C_2-symmetry have been recognized as being able to create effective chiral environments for substrates and nucleophiles by which this class of ligands are used for a variety of transition metal-catalyzed reactions.[3] Hence, the preparation of chiral diphosphine ligands **8** in one step from the precursor of VALAP, **7**,[2a] was planned (Scheme 1).[2d] The present ligand system has potential to afford a number of analogs by employing different acid chlorides. Other choices for the starting amino acids would produce further variations.



Scheme 1.

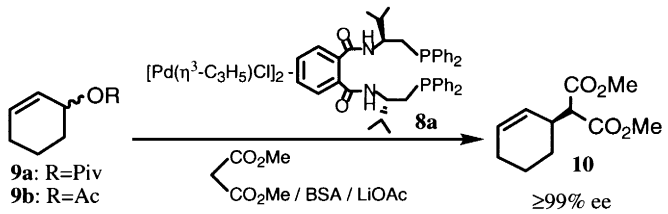
The phosphinobutanamine **7** was easily accessible in four steps from L-valinol **3** prepared by the reduction of a commercially available α-amino acid, L-valine (Scheme 1). L-Valinol **3** was converted quantitatively into **4** by protection with di-*tert*-butyl dicarbonate. The treatment of **4** with *p*-toluenesulfonyl chloride in pyridine afforded the sulfonyloxybutane **5**. A diphenylphosphino group was introduced by the reaction of **5** with potassium diphenylphosphide in THF, giving the diphenylphosphinobutane **6**, which was converted into **7** by deprotection of the amino moiety using trifluoroacetic acid.

In the initial attempts at the preparation of **8a**, two equivalents of **7** were treated with phthaloyl chloride in THF in the presence of triethylamine (Scheme 2). The desired product was successfully obtained, however the yields were low (18–28%). Therefore, the optimization of reaction conditions was examined. The use of CH_2Cl_2 and diisopropylethylamine led to almost the same result (19%). Furthermore, the treatment in the presence of diisopropylethylamine in toluene at reflux was carried out, demonstrating the preferable production of **8a** in 53% yield.



Scheme 2.

Chiral diphosphine ligands with C_2-symmetry elements possessing a large bite angle induced remarkably high enantioselectivity for sterically less demanding cycloalkenyl substrates.[4] Thus, the new diphosphine ligand **8a** was examined in palladium-catalyzed asymmetric allylic replacements of sterically less demanding cyclohexen-2-yl pivalate **9a** with an anionic soft nucleophile derived from dimethyl malonate/*N*,*O*-bis(trimethylsilyl)acetamide(BSA)/AcOLi. Surprisingly, **8a** exhibited a high level of asymmetric induction to give (*S*)-**10** in over 99% ee and 64% yield (Scheme 3, Table 1, entry 1). Thus, the utility of our versatile ligand system for the variation of reaction types and substrates was successfully demonstrated. Like the transformation of the acyclic substrates by VALAP, better results were obtained by the use of dichloromethane as a solvent compared with the use of THF. In the latter case, a decrease in catalytic activity (99% ee, 11% yield) was observed (entry 3).



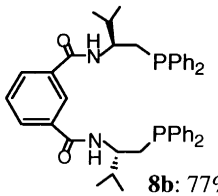
Scheme 3.

The analogous ligands **8b**,**c** with different backbones to connect the two amide groups were synthesized in order to understand the origin of the high asymmetric induction by **8a**. Based on the procedure for **8a**, the ligands **8b**,**c** were readily prepared using isophthaloyl chloride and succinyl chloride as white solids in 77% and 44%, respectively. Thus, the ligands were applied to the palladium-catalyzed asymmetric allylic substitutions of **9a**, however both **8b** and **8c** exhibited much lower catalytic activity (entries 4 and 5, **8a**≫**8b**, **8c**) so that no peak assignable to **10** was observed by gas chromatography.

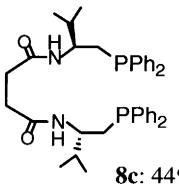
Table 1
Asymmetric allylic alkylations of **9** catalyzed by palladium–**8** complexes[a]

entry	ligand	substrate	solvent	yield[b] (%)	ee[c] (%)
1	**8a**	**9a**	CH_2Cl_2	64	≥ 99(*S*)[d]
2	**8a**	**9a**	THF	11	≥ 99(*S*)
3	**8a**	**9b**	CH_2Cl_2	65	≥ 99(*S*)
4	**8b**	**9a,b**	CH_2Cl_2	-	-
5	**8c**	**9a,b**	CH_2Cl_2	-	-

a. Molar ratio: $[Pd(h^3\text{-}C_3H_5)Cl]_2$/ligand/**9**/dimethyl malonate/BSA/AcOLi =2.5/6/100/300/300/5. b. Isolated yield. c. Enantiomeric excess for **10** was determined by gas chromatography with a CP-Chirasil-DEX CB column [25 m x 0.25 mm(ID), 0.25 mm film thickness]. As a reference sample, rac-**10** was prepared using a Pd-dppp catalyst. d. $[a]_D^{23}$ -43.2 (*c* 1.75, $CHCl_3$).



8b: 77%



8c: 44%

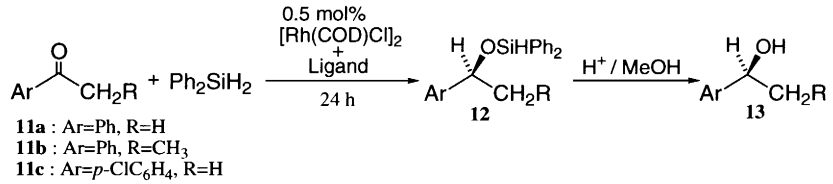
Furthermore, cyclohexene-2-yl acetate **9b** with a smaller leaving group as a substrate was subjected to the reactions using **8**. The experiments were conducted under the identical conditions as those for **9a**. However, the lower catalytic activity was again observed in the runs using **8b**,**c** (entries 4, 5). The ligand **8a** also demonstrated the same level of asymmetric induction as that of **9a** (entry 3).

It is of interest that small differences in the bridging part far from the reactive site give a drastic change in the asymmetric catalysis. Unfavorable complexation of the ligands[5] and/or the obstruction in the oxidative addition of the palladium(0) complex or a nucleophilic attack to the π-allyl complex by steric effects of the ligands are suggested as possible causes of the present behavior.

Since the unique catalytic performance was demonstrated in the asymmetric allylations, the ligands were further applied to another type of asymmetric catalysis, rhodium-catalyzed asymmetric hydrosilylations. Enantioselective reduction of carbonyl compounds using the transition metal–chiral ligand complexes and hydrosilanes is a useful synthetic tool for the production of optically active alcohols.[6] Chiral ligands consisting of an oxazoline skeleton such as pyridinyloxazolines, bisoxazolines and phosphorous-containing oxazolines have been proven to be useful in rhodium-catalyzed asymmetric hydrosilylations of ketones.[7] In pioneering work on asymmetric hydrosilylations, chiral diphosphine ligands such as DIOP were found to be less effective where a high level of asymmetric induction was not attained in a reaction condition using $[Rh(COD)Cl]_2$/acetophenone/Ph_2SiH_2.[8] However, several reports using recently developed diphosphine ligands demonstrated high levels of enantioselectivity.[9]

Using **8a**–**c**, rhodium-catalyzed asymmetric hydrosilylation of acetophenone **11a** with diphenylsilane, which is frequently employed, was examined in toluene (Scheme 4).

The catalyst solution was prepared in situ by mixing 0.5 mol% of $[Rh(COD)Cl]_2$ and the ligand in a solvent at room temperature. To the solution was added diphenylsilane at the corresponding temperatures, followed by treating with ketones **11**. The resulting silyl ether **12** was hydrolyzed with



Scheme 4.

aqueous HCl in methanol to afford chiral *sec*-alcohols **13**. The enantiomeric excess was determined by gas chromatography with a capillary chiral column. The results are summarized in Table 2.

Table 2
Rhodium-catalyzed asymmetric hydrosilylations of acetophenone **11a**[a]

entry	ligand	solvent	ligand/Rh	reaction temp. (°C)	yield[b] (%)	*ee*[c] (%)
1	**8a**	toluene	1.2	rt	31	35 (*S*)
2	**8b**	toluene	1.2	rt	54	33 (*S*)
3	**8c**	toluene	1.2	rt	48	60 (*S*)
4	**8c**	toluene	1.2	0	46	64 (*S*)
5	**8c**	THF	1.2	rt	53	51 (*S*)
6	**8c**	toluene	3	0	64	62 (*S*)[d]

a. $[Rh(COD)Cl]_2$/**11a**/Ph_2SiH_2=1/200/250. Reaction time for all entries: 24h
b. Isolated yield by a preparative TLC on silica-gel (toluene : AcOEt=20 : 1).
c. The enantiomeric excess was obtained using glc with a chiral column, CP-Chiralsil-DEX CB. The absolute configuration was determined by comparing specific rotation data with the literature value.
d. $[\alpha]_D^{24}$=-34.7 (*c* 1, $CHCl_3$)

Moderate yields were attained, whereas a small amount of $[Rh(COD)Cl]_2$ (0.5 mol%) was employed as a standard condition. The first examined compound, **8a**, showed unsatisfactory asymmetric induction (entry 1). Essentially the same asymmetric induction was obtained in the run using **8b**. Interestingly, the ligand **3c** derived from succinyl chloride clearly demonstrated a significant improvement of the ee (entry 3), whereas much lower catalytic activity was observed in palladium-catalyzed asymmetric allylic substitutions of **9**.

Using the ligand **8c**, the reaction conditions were optimized. Although the use of THF enhanced the yield of (*S*)-*sec*-phenethyl alcohol **13a**, a drop of enantioselectivity was observed (entry 5). The reduction of reaction temperature to 0°C exhibited a moderate effect to improve the enantioselectivity while keeping the yield of **13a** (entry 4). Further lowering of the reaction temperature to −20°C caused precipitation of a part of the catalyst and slowdown of the reaction rate without any improvement in ee. N–N bidentate ligands such as pyridinyloxazolines and bisoxazolines usually requires large excess amounts of ligand to induce high levels of enantioselectivity[7b,c,f,h] so that the ratio of ligand with respect to rhodium metal was increased up to 3 (entry 6). With the ligand **8c**, the reaction proceeded smoothly compared with entry 4, however no significant increase in the enantioselectivity was observed.

Next, other prochiral ketones related to acetophenone were examined based on the preferred reaction conditions thus obtained. As listed in Table 3, the clear trend in the degree of asymmetric induction was observed by variation of ligands **8c**>**8b**>**8a**. The ligand **8c** was also effective in the asymmetric reduction of **11b**,**c** prior to **8a** and **8b**.

Table 3
Application to other ketones

entry	ketone	ligand	yield[b] (%)	*ee*[c] (%)
1	**11b**	**8a**	11	8 (*S*)
2	**11b**	**8b**	12	14 (*S*)
3	**11b**	**8c**	30	48 (*S*)[d]
4	**11c**	**8a**	54	6 (*S*)
5	**11c**	**8b**	61	30 (*S*)
6	**11c**	**8c**	74	53 (*S*)[e]

a. $[Rh(COD)Cl]_2$/ligand/**11b,c**/Ph_2SiH_2=1/2.4/200/250. Reaction time, temperature for all entries: 24h, 0°C
b. Isolated yield by a preparative TLC on silica-gel (toluene : AcOEt=20 : 1).
c. The enantiomeric excess was obtained using glc with a chiral column, CP-Chiralsil-DEX CB. The absolute configuration was determined by comparing specific rotation data with the literature value.
d. $[\alpha]_D^{24}$=-21.4 (*c* 0.7, $CHCl_3$). e. $[\alpha]_D^{23}$=-24.6 (*c* 1.5, $CHCl_3$).

Since the mechanism of asymmetric hydrosilylations is still not fully understood, the explanation for the present phenomenon is limited within a range of speculation.[7c,k,10] From the point of view of the steric effect of ligands,[11] the positioning array of four phenyl rings on phosphorus atoms, which could be varied by the different bite angles, would give the unexpected behavior in the catalytic asymmetric reactions. It was previously demonstrated that DIOP analogs consisting of various carbocyclic backbones, which afford different bite angles, have an effect on the enantioselectivity in rhodium-catalyzed asymmetric hydrogenations of *N*-acyldehydroamino acids.[12]

In summary, a new series of chiral diphosphine ligands **8** was successfully prepared in one step from the synthetic precursor of VALAP, **7**. Among the ligands, **8a** derived from phthaloyl chloride exhibited excellent levels of enantioselectivity over 99% ee in palladium-catalyzed asymmetric allylic substitutions of cyclohexenyl substrates. In contrast to the high catalytic performance, the analogous ligands **8b** and **8c** demonstrated much lower catalytic activity. Thus, it was found that relatively minor differences in backbones to connect the two amide groups of the present diphosphine ligands resulted in a remarkable change in the degree of asymmetric induction. The trends of these effects was totally different between rhodium-catalyzed asymmetric hydrosilylations and palladium-catalyzed allylic substitutions. In this way, the versatility of the current ligand system also played an important role in variations of reaction types. Further studies regarding ligand structure–enantioselectivity relationships are being progressed for various types of substrates and reactions.

3. Experimental

3.1. General methods and materials

^1H NMR and ^{13}C NMR spectra were recorded on a JEOL JNM-GX270 spectrometer in $CDCl_3$ solution at 270 and 67.8 MHz, respectively. ^{31}P NMR spectra were measured by a JEOL JNM-A400

in $CDCl_3$ solution at 161.7 MHz. Chemical shift values are expressed in ppm based on tetramethylsilane for ^1H, $CDCl_3$ for ^{13}C and phosphoric acid for ^{31}P. IR spectra were measured using JASCO FT/IR-3000. Mass spectra were obtained by a JEOL JMS-SX-102 (FAB-MS) and a JEOL JMS-300 and 700 (HRMS). Gas chromatographic analysis was performed by using a Shimadzu GC-14A fitted with a 0.25 mm×50 m, SE-30 capillary column for a general analysis and a 0.25 mm×50 m, Chirasil-DEX CB for determining the enantiomeric excess of optically active products. Specific rotatory power was measured using a JASCO DIP-140. Melting points were determined by a Yazawa BY-1 and are uncorrected. Column chromatographic isolation was conducted using silica gel 60 (70–230 mesh, Merck). Silica gel 60 F254 (0.5 and 2 mm, Merck) was used for preparative TLC.

All reagents for the preparation of **7**, phthaloyl chloride, isophthaloyl chloride and succinyl chloride, were used as purchased. *N*,*N*-Diisopropylethylamine was dried over molecular sieves 4A before use. Dehydrated toluene stored over molecular sieves 4A was used for the preparation of ligands. THF was distilled over sodium metal/benzophenone ketyl. Dichloromethane and toluene were dried over molecular sieves 4A.

Acetophenone **11a**, propiophenone **11b**, 4′-chloroacetophenone **11c**, diphenylsilane and dimethyl malonate were purified by distillation before use. Cyclohexen-2-yl pivalate **9a** was derived from the reaction of 2-cyclohexenol with pivaloyl chloride in pyridine and a catalytic amount of 4-dimethylaminopyridine. Cyclohexen-2-yl acetate **9b** was prepared by treatment of 2-cyclohexenol with acetic anhydride in dichloromethane in the presence of triethylamine and 4-dimethylaminopyridine. BSA and AcOLi were used as purchased. For the asymmetric catalysis, dehydrated toluene and dichloromethane were purchased and degassed before exposing to the reaction. THF was distilled over sodium benzophenone ketyl and used as a peroxide-free solvent. Chloro(1,5-cyclooctadiene)rhodium(I) dimer and allyl palladium(II) chloride dimer were used as purchased.

*3.2. (1S)-[1-(Hydroxymethyl)-2-methylpropyl]carbamic acid 1,1-dimethylethyl ester **4***

To a stirred solution of L-valinol **3** (1.5 g, 14.5 mmol) and Et_3N (1.53 g, 15.1 mmol) in CH_2Cl_2 (45 mL) was added di-*tert*-butyl dicarbonate (3.3 g, 15.1 mmol) on an ice-cold water bath at 0°C. The reaction flask was maintained at 0°C for 2 h and then allowed to proceed at room temperature for 8 h. The reaction mixture was washed with brine and dried over $MgSO_4$. Removal of volatile fractions under vacuum afforded **4** as a viscous liquid quantitatively. $[\alpha]_D^{30}=-13.6$ (*c* 1, MeOH); ^1H NMR (270 MHz, $CDCl_3$) δ 0.94 (d, 3H, *J*=6.6 Hz), 0.96 (d, 3H, *J*=6.6 Hz), 1.45 (s, 9H), 1.80–1.85 (m, 1H), 2.38 (brs, 1H), 3.38–3.45 (m, 1H), 3.60 (1H, J_{BX}=6.3 Hz, J_{AB}=11.2 Hz), 3.70 (1H, J_{AX}=3.6 Hz, J_{AB}=11.2 Hz), 4.66 (brs, 1H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 18.4, 19.4, 28.3, 31.0, 57.0, 63.6, 79.2, 156.7; IR (neat) 3355, 1694, 1512 cm^{-1}; FAB-MS: *m/z* 204 (MH^+).

*3.3. (1S)-[2-Methyl-1-[[[(4-methylphenyl)sulfonyl]oxy]methyl]propyl]carbamic acid 1,1-dimethylethyl ester **5***

p-Toluenesulfonyl chloride (7.96 g, 41.7 mmol) dissolved in pyridine (30 mL) was added dropwise to **4** (7.89 g, 38.8 mmol) in pyridine (70 mL) at −35°C under argon. The resulting solution was stirred at the low temperature for 18 h and on an ice-water bath for 3 h. The excess pyridine was carefully quenched by adding aqueous 10% HCl and the product was extracted with AcOEt. The organic extract was successively washed with saturated aqueous $NaHCO_3$ and brine. Removal of the solvent followed by purification using silica gel column chromatography eluted by a 20:1 mixture of toluene and AcOEt afforded **5** as a white solid in 77% yield. $[\alpha]_D^{27}=-17.5$ (*c* 1, MeOH); mp 75–76°C; ^1H NMR (270 MHz,

$CDCl_3$) δ 0.86 (d, 3H, *J*=6.9 Hz), 0.90 (d, 3H, *J*=6.9 Hz), 1.41 (s, 9H), 1.75–1.87 (m, 1H), 2.45 (s, 3H), 3.45–3.54 (1H, m), 3.99–4.11 (m, 2H), 4.58 (brd, 1H, *J*=9.6 Hz), 7.35 (d, 2H, *J*=8.2 Hz), 7.78 (d, 2H, *J*=8.2 Hz); ^{13}C NMR (68 MHz, $CDCl_3$) δ 18.5, 19.2, 21.5, 28.2, 28.9, 54.7, 70.0, 79.4, 127.9, 129.8, 132.5, 144.9, 155.4; IR (KBr) 3306, 1672, 1535, 1356, 1169 cm^{-1}; FAB-MS: *m/z* 358 (MH^+).

3.4. (1S)-[1-[(Diphenylphosphino)methyl]-2-methylpropyl]carbamic acid 1,1-demethylethyl ester ***6***

Potassium diphenylphosphide 0.5 M THF solution, (27 mL, 13.5 mmol), was added dropwise to **5** (2.28 g, 6.40 mmol) in THF (30 mL) at −35°C under argon. After stirring while cooling was continued overnight, the solution was allowed to warm to an ambient temperature and filtered through Celite. The reaction mixture was concentrated under reduced pressure, and then **6** was isolated as a viscous liquid in 70% yield by silica gel column chromatography using toluene containing 0.5 vol.% of Et_3N as the eluent. $[\alpha]_D^{27}$=+2.7 (*c* 1, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.85 (d, 3H, *J*=6.6 Hz), 0.87 (d, 3H, *J*=6.6 Hz), 1.40 (s, 9H), 1.86–1.94 (m, 1H), 2.05–2.25 (m, 2H), 3.52–3.68 (m, 1H), 4.40 (brd, 1H, *J*=10.8 Hz), 7.26–7.44 (m, 10H); IR (neat) 3341, 1701, 1501 cm^{-1}; MS (EI) *m/z*: 371 (M^+), 314, 298, 199; FAB-MS: *m/z* 372 (MH^+).

3.5. (2S)-1-(Diphenylphosphino)-3-methyl-2-butanamine ***7***

To a stirred solution of **6** (6 g, 16.2 mmol) in CH_2Cl_2 (350 mL) was added trifluoroacetic acid (60 mL, 0.779 mol) on an ice-water bath under argon. The solution was stirred at the low temperature for 1 h and at room temperature overnight. The resulting solution was quenched with water and the organic layer was separated. The aqueous layer was neutralized with aqueous NaOH and extracted with CH_2Cl_2. The combined organic layers were successively washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated under vacuum to give **7** as a viscous liquid in 89% yield. $[\alpha]_D^{28}$=+88.7 (*c* 1, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.88 (d, 3H, *J*=6.6 Hz), 0.90 (d, 3H, *J*=6.6 Hz), 1.65–1.80 (m, 1H), 1.89–1.99 (m, 1H), 2.29–2.36 (m, 1H), 2.58–2.68 (m, 1H), 7.30–7.49 (m, 10H); IR (neat) 3366, 1586 cm^{-1}; MS (EI) *m/z*: 271(M^+), 255, 228, 199, 185; FAB-MS: *m/z* 272 (MH^+).

*3.6. (1S),(1′S)-*N,N′*-Bis[1-(diphenylphosphinomethyl)-2-methylpropyl]phthalamide* ***8a***

To a solution of **7** (400 mg, 1.48 mmol) and *N*,*N*-diisopropylethylamine (286 mg, 2.21 mmol) in toluene (10 mL) was added phthaloyl dichloride (150 mg, 0.738 mmol) in toluene (3 mL) on an ice-cold water bath, followed by stirring at the low temperature for 1 h. The reaction mixture was heated at the reflux temperature overnight and then left to cool. To work up the reaction, saturated aqueous $NaHCO_3$ was added. The organic phase was separated and the remaining aqueous layer was treated with AcOEt. Then, the combined organic phase was successively washed with saturated aqueous $NaHCO_3$ and brine. The solvent was evaporated from the solution, dried over $MgSO_4$ and the residue was purified by silica gel column chromatography eluted by toluene:AcOEt (20:1), giving **8a** as a white solid in 58% yield. $[\alpha]_D^{24}$=+21.3 (*c* 0.5, $CHCl_3$); mp 57–59°C; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.90 (d, 6H, *J*=6.6 Hz), 0.92 (d, 6H, *J*=6.6 Hz), 2.00–2.12 (m, 2H), 2.26–2.41 (m, 4H), 4.03–4.17 (m, 2H), 6.78 (d, 2H, *J*=8.9 Hz), 7.26–7.47 (m, 24H); ^{31}P{^{1}H} NMR (161.7 MHz, $CDCl_3$, H_3PO_4) δ −22.74; IR (KBr): 3256, 1643, 1530 cm^{-1}; FAB-MS: *m/z* 673 (MH^+); HRMS (EI) calcd for $C_{42}H_{46}O_2N_2P_2$ 672.3038, found 672.3063.

3.7. (1S),(1′S)-N,N′-Bis[1-(diphenylphosphinomethyl)-2-methylpropyl]isophthalamide **8b**

To a solution of **7** (400 mg, 1.48 mmol) and *N*,*N*-diisopropylethylamine (286 mg, 2.21 mmol) in toluene (10 mL) was added isophthaloyl dichloride (150 mg, 0.738 mmol) in toluene (3 mL) at 0°C. The solution was stirred at the low temperature for 1 h and heated at the reflux temperature overnight. The resulting solution was worked up by adding saturated aqueous $NaHCO_3$. The aqueous layer separated from the organic solution was treated with AcOEt, and then the combined organic layer was washed with saturated aqueous $NaHCO_3$ and brine. After removal of the solvent under vacuum, the product was isolated by silica gel column chromatography eluted by toluene:AcOEt (20:1) as a white solid in 77% yield. $[\alpha]_D^{24}$=+57.9 (*c* 0.5, $CHCl_3$); mp 165–166°C; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.96 (d, 12H, *J*=6.9 Hz), 2.03–2.14 (m, 2H), 2.28–2.48 (m, 4H), 4.12–4.26 (m, 2H), 5.99 (d, 2H, *J*=9.2 Hz), 7.29–7.49 (m, 21H), 7.61 (d, 2H, *J*=7.6 Hz), 7.90 (s, 1H); ^{31}P{^{1}H} NMR (161.7 MHz, $CDCl_3$, H_3PO_4) δ: −22.63; IR (KBr): 3291, 1644, 1532 cm^{-1}; FAB-MS: *m/z* 673 (MH^+); HRMS (EI) calcd for $C_{42}H_{46}O_2N_2P_2$ 672.3038, found 672.3004.

3.8. (1S),(1′S)-N,N′-Bis[1-(diphenylphosphinomethyl)-2-methylpropyl]succinylamide **8c**

A solution of succinyl chloride (114 mg, 0.738 mmol) in toluene (3 mL) was added to a stirred solution of **7** (400 mg, 1.48 mmol) and *N*,*N*-diisopropylethylamine (286 mg, 2.21 mmol) in toluene (10 mL) on an ice-water bath. The reaction flask was maintained at 0°C for 1 h, and then heated at reflux temperature overnight. The mixture was quenched with saturated aqueous $NaHCO_3$. The water layer separated from the organic phase was treated with AcOEt, and then the combined organic phase was washed with saturated aqueous $NaHCO_3$ and brine. After removal of the solvent, the adduct **8c** was isolated by silica gel column chromatography eluted by toluene:AcOEt (10:1) as a white solid in 44% yield. $[\alpha]_D^{23}$=−5.0 (*c* 0.5, $CHCl_3$); mp 123–124°C; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.85 (d, 12H, *J*=6.6 Hz), 1.85–1.97 (m, 2H), 2.12–2.32 (m, 8H), 3.86–3.98 (m, 2H), 5.79 (d, 2H, *J*=9.6 Hz), 7.30–7.45 (m, 20H); ^{31}P{^{1}H} NMR (161.7 MHz, $CDCl_3$, H_3PO_4) δ: −22.24; IR (KBr): 3274, 1640, 1545 cm^{-1}; FAB-MS: *m/z* 625 (MH^+); HRMS (EI) calcd for $C_{38}H_{46}O_2N_2P_2$ 624.3038, found 624.3046.

3.9. General procedure for asymmetric allylic transformations of **9**

A mixture of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (4 mg, 0.0109 mmol) and **8a** (17.6 mg, 0.0262 mmol) in CH_2Cl_2 (1 mL) was stirred at room temperature under argon, followed by adding **9a** (79.4 mg, 0.436 mmol) in CH_2Cl_2 (1 mL). To the solution was added a nucleophile solution prepared in another flask by treating dimethyl malonate (173 mg, 1.31 mmol) and BSA (266 mg, 1.31 mmol) in the presence of lithium acetate (1.4 mg, 0.0218 mmol) in the solvent (1 mL). The reactions were monitored by gas chromatography. The mixture was stirred at an ambient temperature for 24 h, and then the volatile fractions were removed in vacuo. The product **10** was isolated by preparative TLC (toluene:AcOEt (20:1)).

3.10. General procedure typified by entry 4 in Table 1 for asymmetric hydrosilylations

A solution of $[Rh(COD)Cl]_2$ (4 mg, 8.11×10^{-3} mmol) and **8c** (12.2 mg, 0.0195 mmol) in toluene (1 mL) was stirred at room temperature under argon for 30 min. To the catalyst solution on an ice-water bath was added diphenylsilane(374 mg, 2.03 mmol) in the solvent (0.5 mL), followed by adding acetophenone (194 mg, 1.62 mmol) in toluene (0.5 mL). The reaction was monitored by TLC. The reaction mixture was maintained at 0°C for 24 h and quenched with 10% aqueous HCl in methanol. After treatment

of the solution at 0°C for 30 min, the product was extracted with AcOEt, followed by washing the organic extract with saturated aqueous $NaHCO_3$ and brine. The residue after evaporation separated using preparative TLC (toluene:AcOEt (20:1)).

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