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Synthesis of novel N,P chiral ligands for palladium-catalyzed asymmetric allylations: the effect of binaphthyl backbone on the enantioselectivity

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Abstract

A series of novel chiral aminophosphine ligands with a 5,5,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl backbone (H_8-MAPs) have been synthesized. The application of these ligands in asymmetric allylic substitutions was examined and higher enantioselectivity was observed than that by using the parent ligand (MAP). Under the optimized conditions, the allylation product can be obtained in up to 90.9% ee with H_8-MAP having 3,5-xylyls as chiral inducer. The dramatic effect of the binaphthyl backbone on the enantioselectivity of the reaction can be attributed to the change of the bite angle in H_8-MAPs/Pd complexes.

1. Introduction

The ligands derived from 2-amino-2′-hydroxy-1,1′-binaphthyl **1** (NOBIN) have been found to be excellent chiral inducers for asymmetric catalysis of some reactions.[1] Very recently, a new type of aminophosphine, MAP **3** (Ar = Ph), which can be regarded as a nitrogen analogue of Hayashi's MOP,[2] was first reported by Kocovsky et al., Ding and Mikami et al., respectively.[3] The MAP ligand exhibited a dramatic acceleration of the Hartwig–Buchwald amination and Suzuki reaction of acryl halides[4] and showed moderate asymmetric induction in Pd(0)-catalyzed allylic substitution.[3a] Very recent research showed that the chiral catalysts derived from 5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl ligands exhibited higher efficiency and enantioselectivity for asymmetric reactions than those prepared from their parent ligands, due to the steric and electronic modulation in the binaphthyl backbone.[5] We have recently developed a convenient protocol for the preparation of H_8-binaphthyls through the partial reduction of the corresponding binaphthyls with Ni–Al alloy in dilute aqueous alkaline solution. Enantiopure

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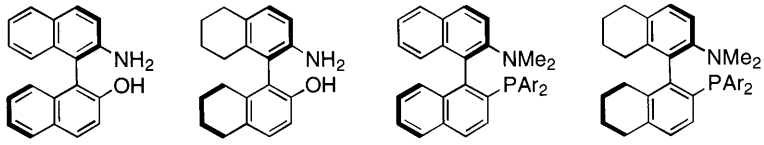
H_8-NOBIN **2** could be prepared in reasonably good yield by the reduction of enantiopure **1**.[6] In the present work, we report the synthesis of a series of novel N,P ligands, H_8-MAPs **4**, by direct transformation of H_8-NOBIN **2**, their application to palladium-catalyzed asymmetric allylation, and the dramatic effect of the binaphthyl backbone on the enantioselectivity of the reaction.

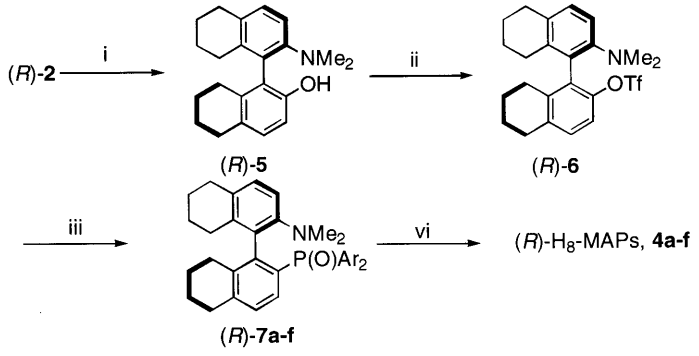


(*R*)-**NOBIN, 1** (*R*)-H_8-**NOBIN, 2** (*R*)-**MAPs, 3** (*R*)-H_8-**MAPs, 4**

2. Results and discussion

2.1. Synthesis of H_8-MAPs 4

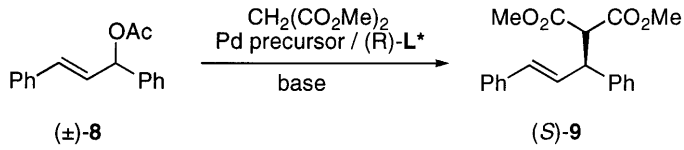
Both enantiomers of NOBIN **1** can be easily achieved by a highly efficient and practical resolution procedure developed in our group through molecular complexation with *N*-benzylcinchonidium chloride.[3b] Partial reduction of **1** with Ni–Al alloy in dilute aqueous alkaline solution yielded **2** in good yield without racemization.[6] With enantiopure **2** in hand, we extended its application to the synthesis of a new series of aminophosphine chiral ligands. As shown in Scheme 1, the enantiopure *N*,*N*-dimethyl derivative **5** can be obtained by reductive methylation of **2** with $NaBH_4$–CH_2O–H_2SO_4 in THF–H_2O in 89% yield according to Kocovsky's procedure.[7] Treatment of **5** with trifluoromethanesulfonic anhydride in the presence of Et_3N gives its triflate derivative **6** in 96% yield. It was found that triflate **6** underwent a coupling reaction with $Ar_2P(O)H$ efficiently in the presence of $Pd(OAc)_2$/dppp (dppp = 1,3-bis(diphenylphosphino)propane) and diisopropylethylamine to give **7a–f** in 54–94% yield. The target chiral ligands **4a–f** could be easily obtained in 73–93% yield by the reduction of their oxides with $LiAlH_4$–$CeCl_3$[8] (in the molar ratio of 4:3) under mild reaction conditions.



Scheme 1. Synthesis of (*R*)-H_8-MAPs (**4a–f**). (i) 40% aqueous CH_2O, 20% H_2SO_4, $NaBH_4$, THF, rt, 89%; (ii) $(TfO)_2O$, Et_3N, CH_2Cl_2, −50°C, 96%; (iii) $Pd(OAc)_2$, dppp, $(^iPr)_2NEt$, $HP(O)Ar_2$, DMSO, 100°C, 54–94%; (iv) $CeCl_3$–$LiAlH_4$, THF, 40°C, 73–93%. Ar = C_6H_5, **4a**; Ar = 4-MeC_6H_5, **4b**; Ar = 3-MeC_6H_5, **4c**; Ar = 4-$MeOC_6H_5$, **4d**; Ar = 4-$^tBuC_6H_5$, **4e**; Ar = 3,5-$(Me)_2C_6H_3$, **4f**

2.2. Asymmetric induction of H_8-MAPs in palladium-catalyzed enantioselective allylation

Asymmetric allylation catalyzed by palladium complexes is a useful approach to asymmetric carbon–carbon bond formation.[9] Several types of N,P chiral ligands have been successfully applied to the asymmetric catalysis of such type of reaction.[10] With the novel chiral ligands **4** in hand, we set out to examine their application in Pd(0)-catalyzed allylic substitution of dimethyl malonate with racemic 1,3-diphenylprop-2-en-l-yl acetate (±)-**8** (Scheme 2). The effects of Pd precursors, solvents, bases, and reaction temperatures were also investigated and the results are summarized in Table 1. Thus with $Pd_2dba_3{\cdot}CHCl_3$ as catalyst precursor, **4a** as chiral ligand and Cs_2CO_3 as base, the reaction in CH_2Cl_2 at 13°C offered (*S*)-**9** in 82.5% ee, which was significantly higher than the result obtained with MAP (entry 2 versus 1).[11] Alternating the solvents and bases had no good effect on the enantioselectivity and the activity of the reaction (entries 3, 4 and 6). Raising the reaction temperature to 25°C could highly increase the reaction



(±)-**8** (*S*)-**9**

Scheme 2. Asymmetric allylic substitution

Table 1
Asymmetric Pd(0)-catalyzed substitution of racemic allylic substrate **8** with malonate nucleophiles[a]

Entry	Catalyst precursor	Ligand	Solvent	Base	Temp. (°C)	Time (h)	Yield[c] (%)	ee[d] (%)
1	$Pd_2dba_3{\cdot}CHCl_3$	(*R*)-**3**	CH_2Cl_2	Cs_2CO_3	13	48	55	67.5
2	$Pd_2dba_3{\cdot}CHCl_3$	(*R*)-**4a**	CH_2Cl_2	Cs_2CO_3	13	48	51	82.5
3	$Pd_2dba_3{\cdot}CHCl_3$	(*R*)-**4a**	CH_2Cl_2	BSA	13	96	55	71.2
4	$Pd_2dba_3{\cdot}CHCl_3$	(*R*)-**4a**	Toluene/CH_2Cl_2[b]	BSA	13	72	36	74.0
5	$Pd_2dba_3{\cdot}CHCl_3$	(*R*)-**4a**	CH_2Cl_2	Cs_2CO_3	25	36	90	79.0
6	$Pd_2dba_3{\cdot}CHCl_3$	(*R*)-**4a**	Toluene	KO^{t}Bu	13	60	54	71.5
7	$[Pd(C_3H_5)Cl]_2$	(*R*)-**4a**	CH_2Cl_2	BSA	20	12	99	81.0
8	$[Pd(C_3H_5)Cl]_2$	(*R*)-**4a**	CH_2Cl_2	Cs_2CO_3	20	12	99	82.5
9	$[Pd(C_3H_5)Cl]_2$	(*R*)-**4b**	CH_2Cl_2	Cs_2CO_3	20	12	99	75.0
10	$[Pd(C_3H_5)Cl]_2$	(*R*)-**4c**	CH_2Cl_2	Cs_2CO_3	20	12	99	80.4
11	$[Pd(C_3H_5)Cl]_2$	(*R*)-**4d**	CH_2Cl_2	Cs_2CO_3	20	12	96	78.8
12	$[Pd(C_3H_5)Cl]_2$	(*R*)-**4e**	CH_2Cl_2	Cs_2CO_3	20	12	89	73.0
13	$[Pd(C_3H_5)Cl]_2$	(*R*)-**4f**	CH_2Cl_2	Cs_2CO_3	20	12	98	84.4
14	$[Pd(C_3H_5)Cl]_2$	(*R*)-**4a**	Toluene	BSA	0	36	73	86.4
15	$[Pd(C_3H_5)Cl]_2$	(*R*)-**4f**	Toluene	BSA	0	24	99	87.2
16	$[Pd(C_3H_5)Cl]_2$	(*R*)-**4f**	Toluene	BSA	−20	24	62	90.9

[a] Reactions were carried out under standard Schlenk technique; the catalysts were generated in situ from Pd precursors and the N,P ligands; Pd/ligand/base/malonate/**8** = 0.05:0.075:2:2:1.

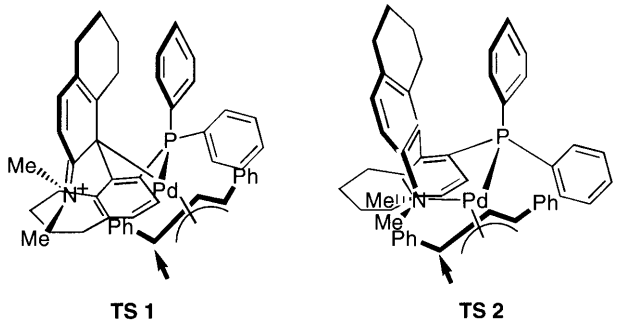
[b] Toluene/CH_2Cl_2 = 2:1.

[c] Isolated yield.

[d] Determined by HPLC on Chiralcel OD column; the absolute configuration of the product was assigned to be *S* by comparison of chiroptical values with those of the literature.[3a]

rate, but decrease the ee value to some extent (entry 5). Exciting results were obtained when the palladium $[Pd(C_3H_5)Cl]_2$ was used as catalyst precursor: excellent yields and good asymmetric induction were obtained at 20°C in CH_2Cl_2 after 12 hours. Both *N*,*O*-bis(trimethylsilyl)acetamide (BSA) and Cs_2CO_3 were found to be suitable bases for the reaction (entries 7 and 8).

The H_8-MAPs ligands with different substituents on the phenyl groups, namely (*R*)-**4b–f**, were screened for the present asymmetric reaction in order to examine the substituent effect on the enantioselectivity of the reaction. It was found that **4b–f** exhibited similar asymmetric induction to the unsubstituted one (entries 9–13 versus entry 8) with the maximum of 84.4% ee attained in the case of a more sterically hindered ligand (*R*)-**4f**. The high reaction activity achieved when $[Pd(C_3H_5)Cl]_2$ was used as catalyst precursor (entries 7 and 8) prompted us to try less polar solvent and a lower reaction temperature (entries 14, 15 and 16). The best asymmetric induction as high as 90.9% ee was obtained by using toluene as solvent and in the presence of BSA–KOAc at −20°C (entry 16).



Scheme 3. Proposed transition states for asymmetric induction

Although the X-ray crystal structure studied by Kocovsky assumed a P,C_σ-Pd complex to be the catalyst of Pd(0)-MAP promoted asymmetric allylation,[4b–c] it is hard to identify which transition state (**TS 1** or **TS 2**) operates in the present catalytic system (Scheme 3). However, the higher energy level of the intermediate involved in **TS 1** compared with **TS 2** (1,3-butadiene versus benzene structure) perhaps provides support that the asymmetric induction observed in the above Pd(0)-catalyzed allylic substitution is consistent with **TS 2**. The nucleophilic attack occurs preferentially at the carbon *trans*-related (via Pd) to the phosphorus acceptor. The enhanced ee value (H_8-MAP versus MAP) may be caused by the larger dihedral angle of biphenyl moiety after partial reduction of the naphthyl backbone, which may influence the bite angle of the Pd catalysts.

In conclusion, a series of novel chiral aminophosphine ligands with 5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl backbone (H_8-MAPs) have been synthesized, which exhibited higher enantioselectivity for asymmetric allylation than their parent ligand (MAP). The dramatic effect of the binaphthyl backbone on the enantioselectivity of the reaction may be attributed to the change of the bite angle in H_8-MAPs/Pd complexes. Further studies on the detailed mechanism and new application of H_8-MAPs in other asymmetric reactions are actively pursuing in our group.

3. Experimental

3.1. General considerations

^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker AM300 and Bruker DRX400 spectrometers at 25°C, respectively. Chemical shifts were expressed in ppm with TMS as an internal standard ($\delta = 0$ ppm) for ^{1}H NMR and with residual signal of $CDCl_3$ as an internal standard ($\delta = 77.0$ ppm) for ^{13}C NMR. The ^{31}P NMR spectra were recorded on a Bruker DRX400 instrument in $CDCl_3$ with 85% H_3PO_4 as an external reference. Optical rotations were measured with a PE-341 automatic polarimeter. Liquid chromatographic analyses were conducted on a JASCO 1580 system. EI mass spectra were obtained on a HP5989A spectrometer. HRMS was carried out on a MAT-95 or Kratos Concept 1H instrument. IR spectra were measured on a PE 983G spectrometer in KBr pellets. Elemental analysis was performed with an Elemental VARIO EL apparatus. All the experiments which are sensitive to moisture or air were carried out under an argon atmosphere using standard Schlenk techniques. Commercial reagents were used as received without further purification unless otherwise noted. Dichloromethane and dimethyl sulfoxide were freshly distilled from calcium hydride and THF from sodium benzophenone ketyl. Enantiomerically pure H_8-NOBIN was prepared according to the reported procedure[6] and its transformation to *N*,*N*-dimethyl derivative **5** was carried out following the literature method.[7] Diarylphosphine oxides were synthesized according to the literature procedure.[12]

3.2. Synthesis of (R)-2-(dimethylamino)-2′-(trifluoromethylsulfonyloxy)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl, (R)-6

Trifluoromethanesulfonic anhydride (0.187 mL, 2.2 mmol) was slowly added to a solution of (*R*)-**5** (321.0 mg, 1 mmol) in dichloromethane (4.5 mL) and triethylamine (0.3 mL, 2.2 mmol) at −50°C, and the mixture was stirred for 2 h. The reaction mixture was then warmed to room temperature. After the removal of the solvent under reduced pressure, the resulting residue was submitted to chromatographic separation on silica gel with hexane/EtOAc (10:1) as eluent to give (*R*)-**6** as a white solid (435.3 mg, 96%): $[\alpha]_D^{25} = -20.4$ ($c = 0.9$, THF). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.56–1.82 (m, 8H), 2.10–2.29 (m, 2H), 2.34–2.38 (m, 2H), 2.41 (s, 6H), 2.75–2.79 (m, 2H), 2.82–2.86 (m, 2H), 6.97 (d, $J = 8.2$ Hz, 1H), 7.08–7.12 (m, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 22.58, 22.64, 22.96, 23.11, 27.47, 27.80, 29.45, 29.47, 44.23, 117.19, 117.96, 128.97, 129.09, 129.87, 132.25, 132.56, 136.45, 137.44, 139.00, 145.16, 150.05. IR (KBr pellet): ν 2953 (m), 2851 (m), 1592 (w), 1481 (m), 1417 (vs), 1219 (s), 936 (s), 850 (s). EIMS (m/z): 453 ([M]$^+$, 77%). Anal. calcd for $C_{23}H_{26}F_3NO_3S$: C, 60.91; H, 5.78; N, 3.09%. Found C, 60.93; H, 5.79; N, 3.08%.

3.3. Synthesis of (R)-2-(dimethylamino)-2′-(diphenylphosphinyl)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl, (R)-7a

To a mixture of (*R*)-**6** (453.0 mg, 1 mmol), diphenylphosphine oxide (404.0 mg, 2 mmol), palladium acetate (22.4 mg, 0.1 mmol), and 1,3-bis(diphenylphosphino)propane (dppp, 61.8 mg, 0.15 mmol) were added dimethyl sulfoxide (5 mL) and diisopropylethylamine (0.87 mL, 5 mmol), and the mixture was stirred at 100°C for 66 h. The reaction mixture was concentrated under reduced pressure to give a red residue. The residue was dissolved in 50 mL of EtOAc,

washed with water and saturated brine, dried over anhydrous $MgSO_4$, and concentrated again under reduced pressure. Chromatography of the crude product on silica gel (elution with a 2:1:0.09 hexane/EtOAc/Et_3N mixture) gave (*R*)-**7a** as a white solid (473.3 mg, 94%): $[\alpha]_D^{25}=+55.8$ ($c=0.5$, THF). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.53–1.76 (m, 10H), 1.90–1.94 (m, 2H), 2.16 (s, 6H), 2.57–2.60 (m, 2H), 2.84–2.88 (m, 2H), 6.72 (d, $J=8.2$ Hz, 1H), 6.88 (d, $J=8.3$ Hz, 1H), 7.11 (d, $J=5.4$ Hz, 1H), 7.27–7.50 (m, 11H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 22.58, 22.77, 22.99, 23.01, 27.49, 27.84, 29.35, 30.24, 43.62, 116.78, 127.36, 127.76, 127.92, 129.28, 130.72, 130.86, 130.89, 131.91, 131.95, 132.04, 132.07, 133.16, 137.63, 141.78. ^{31}P NMR (161.9 MHz) δ 29.9. IR (KBr pellet): ν 2931 (s), 1592 (w), 1482 (s), 1434 (vs), 1207 (vs), 751 (s), 719 (s), 703 (s). EIMS (m/z): 505 ([M]$^+$, 100%). Anal. calcd for $C_{34}H_{36}NOP$: C, 80.76; H, 7.18; N, 2.77%. Found C, 81.01; H, 6.81; N, 2.86%.

*3.3.1. (*R*)-2-(Dimethylamino)-2′-(di(4-tolyl)phenylphosphinyl)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl, (*R*)-**7b***

Following the same procedure for the preparation of (*R*)-**7a**, (*R*)-**7b** was obtained as a white solid (yield, 88%): $[\alpha]_D^{25}=+52.3$ ($c=0.5$, THF). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.55–1.75 (m, 10H), 1.88–1.90 (m, 2H), 2.19 (s, 6H), 2.33 (s, 3H), 2.34 (s, 3H), 2.53–2.60 (m, 2H), 2.83–2.87 (m, 2H), 6.70 (d, $J=8.2$ Hz, 1H), 6.87 (d, $J=8.2$ Hz, 1H), 7.05–7.13 (m, 5H), 7.26–7.48 (m, 5H). ^{31}P NMR (161.9 MHz): δ 30.0. IR (KBr pellet): ν 2956 (s), 1599 (s), 1449 (s), 1312 (m), 811 (s), 662 (vs). EIMS (m/z): 533 ([M]$^+$, 100%). HRMS (EI) calcd for $C_{36}H_{40}NOP$: 533.2848. Found: 533.2849.

*3.3.2. (*R*)-2-(Dimethylamino)-2′-(di(3-tolyl)phenylphosphinyl)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl, (*R*)-**7c***

Following the same procedure for the preparation of (*R*)-**7a**, (*R*)-**7c** was obtained as a white solid (yield, 82%): $[\alpha]_D^{25}=+57.2$ ($c=0.5$, THF). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.46–1.75 (m, 10H), 1.91–1.93 (m, 2H), 2.21 (s, 6H), 2.27 (s, 3H), 2.29 (s, 3H), 2.51–2.60 (m, 2H), 2.84–2.88 (m, 2H), 6.71 (d, $J=8.2$ Hz, 1H), 6.86 (d, $J=8.2$ Hz, 1H), 7.11–7.51 (m, 10H). ^{31}P NMR (161.9 MHz): δ 30.1. IR (KBr pellet): ν 2926 (s), 1592 (m), 1449 (s), 1313 (m), 813 (m), 785 (vs). EIMS m/z (%) 533 ([M]$^{\bullet+}$, 100%). HRMS (EI) calcd for $C_{36}H_{40}NOP$: 533.2848. Found: 533.2820.

*3.3.3. (*R*)-2-(Dimethylamino)-2′-(di(4-anisyl)phenylphosphinyl)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl, (*R*)-**7d***

Following the same procedure for the preparation of (*R*)-**7a**, (*R*)-**7d** was obtained as a white solid (yield, 84%): $[\alpha]_D^{25}=+53.2$ ($c=0.5$, THF). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.59–1.77 (m, 10H), 1.89–1.92 (m, 2H), 2.21 (s, 6H), 2.51–2.62 (m, 2H), 2.83–2.87 (m, 2H), 3.80 (s, 6H), 6.70–6.78 (m, 3H), 6.82–6.88 (m, 3H), 7.12 (d, $J=8.0$ Hz, 1H), 7.27–7.55 (m, 5H). ^{31}P NMR (161.9 MHz): δ 29.6. IR (KBr pellet): ν 2929 (s), 1595 (vs), 1457 (m), 1255 (s), 1118 (s), 831 (m), 679 (s). EIMS (m/z): 565 ([M]$^+$, 16%). HRMS (EI) calcd for $C_{36}H_{40}NO_3P$: 565.2746. Found: 565.2764.

*3.3.4. (*R*)-2-(Dimethylamino)-2′-(di(4-tert-butylphenyl)phosphinyl)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl, (*R*)-**7e***

Following the same procedure for the preparation of (*R*)-**7a**, (*R*)-**7e** was obtained as a white solid (yield, 54%): $[\alpha]_D^{25}=+42.1$ ($c=0.5$, THF). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.29 (s, 18H), 1.50–1.79 (m, 10H), 1.86–1.90 (m, 2H), 2.22 (s, 6H), 2.56–2.70 (m, 2H), 2.84–2.86 (m, 2H), 6.69

(d, $J=8.2$ Hz, 1H), 6.83 (d, $J=8.2$ Hz, 1H), 7.12 (d, $J=7.0$ Hz, 1H), 7.29–7.45 (m, 9H). ^{31}P NMR (161.9 MHz): δ 29.5. IR (KBr pellet) ν 2930 (vs), 1597 (m), 1479 (s), 1313 (m), 1136 (s), 831 (m), 673 (m) 617 (s). EIMS (m/z): 617 ([M]$^+$, 100%). HRMS (EI) calcd for $C_{42}H_{52}NOP$: 617.3787. Found: 617.3836.

*3.3.5. (*R*)-2-(Dimethylamino)-2′-(di(3,5-xylyl)phosphinyl)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl, (*R*)-**7f***

Following the same procedure for the preparation of (*R*)-**7a**, (*R*)-**7f** was obtained as a white solid (yield, 87%): $[\alpha]_D^{25}=+72.7$ ($c=0.5$, THF). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.52–1.78 (m, 10H), 1.90–1.95 (m, 2H), 2.23 (s, 6H), 2.25 (s, 6H), 2.51–2.57 (m, 2H), 2.84–2.88 (m, 2H), 6.71 (d, $J=8.2$ Hz, 1H), 6.85 (d, $J=8.2$ Hz, 1H), 6.98–7.26 (m, 7H), 7.49–7.56 (m, 1H). ^{31}P NMR (161.9 MHz): δ 30.5. IR (KBr pellet): ν 2926 (vs), 1597 (m), 1481 (s), 1449 (s), 1313 (m), 1204 (s), 1132 (s), 855 (s), 697 (s). EIMS (m/z): 561 ([M]$^+$, 100%). HRMS (EI) calcd for $C_{38}H_{44}NOP$: 561.3161. Found: 561.3160.

*3.4. Synthesis of (*R*)-2-(dimethylamino)-2′-(diphenylphosphino)-5,5′,6,6′,7,7′8,8′-octahydro-1,1′-binaphthyl, (*R*)-**4a***

THF (10 mL) was added to anhydrous $CeCl_3$ (739.8 mg, 3 mmol) in a Schlenk tube and the mixture was stirred at room temperature for 2 h. Then $LiAlH_4$ (113.9 mg, 4 mmol) and (*R*)-**7a** (505.0 mg, 1 mmol) were added, and the mixture was stirred for an additional 1.5 h at 40°C. After cooling to room temperature, the reaction was quenched with water, diluted with 50 ml of diethyl ether, and filtered through Celite. The filtrate was washed with water and saturated brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The residue was chromatographed on silica gel (elution with 10:1 hexane/EtOAc mixture) to afford (*R*)-**4a** as a white solid (452.8 mg, 93%): $[\alpha]_D^{25}=+62.6$ ($c=0.6$, THF). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.59–1.84 (m, 8H), 2.00–2.10 (m, 2H), 2.23 (s, 6H), 2.32–2.36 (m, 2H), 2.72–2.76 (m, 2H), 2.80–2.84 (m, 2H), 6.89 (d, $J=8.2$ Hz, 1H), 7.01–7.11 (m, 3H), 7.17–7.24 (m, 11H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 22.91, 23.00, 23.10, 23.20, 27.87, 28.09, 29.52, 30.00, 43.32, 116.49, 127.09, 127.71, 127.78, 127.99, 128.08, 128.94, 131.26, 132.54, 132.78, 133.65, 133.93, 135.78, 135.87, 138.66, 150.80. ^{31}P NMR (161.9 MHz) δ –14.3. IR (KBr pellet): ν 3051 (m), 2922 (s), 1585 (m), 1480 (s), 1432 (s), 812 (m), 741 (vs), 695 (vs). EIMS (m/z): 489 ([M]$^+$, 12%). HRMS (EI) calcd for $C_{34}H_{36}NP$: 489.2585. Found: 489.2538.

*3.4.1. (*R*)-2-(Dimethylamino)-2′-(di(4-tolyl)phosphino)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl, (*R*)-**4b***

Following the same procedure for the preparation of (*R*)-**4a**, (*R*)-**4b** was obtained as a white solid (yield, 82%): $[\alpha]_D^{25}=+20.6$ ($c=0.5$, THF). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.48–1.74 (m, 8H), 2.01–2.07 (m, 2H), 2.25 (s, 6H), 2.27 (s, 3H), 2.31 (s, 3H), 2.44–2.51 (m, 2H), 2.74–2.81 (m, 4H), 6.89 (d, $J=8.0$ Hz, 1H), 7.04–7.25 (m, 11H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 21.23, 22.95, 23.02, 23.10, 23.25, 27.84, 28.07, 29.58, 30.02, 43.48, 116.57, 128.04, 128.52, 128.60, 128.81, 128.91, 129.08, 131.27, 132.53, 132.76, 133.76, 133.97, 135.75, 135.98, 138.45, 149.46. ^{31}P NMR (161.9 MHz): δ –15.9. IR (KBr pellet): ν 3010 (w), 2929 (s), 1593 (m), 1480 (s), 1449 (m), 1311 (m), 805 (vs). EIMS (m/z): 517 ([M]$^+$, 8%). HRMS (EI) calcd for $C_{36}H_{40}NP$: 517.2898. Found: 517.2911.

*3.4.2. (*R*)-2-(Dimethylamino)-2′-(di(3-tolyl)phosphino)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl, (*R*)-**4c***

Following the same procedure for the preparation of (*R*)-**4a**, (*R*)-**4c** was obtained as a white solid (yield, 82%): $[\alpha]_D^{25}=+42.7$ ($c=0.5$, THF). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.49–1.81 (m, 8H), 1.99–2.07 (m, 2H), 2.23–2.27 (m, 12H), 2.33–2.43 (m, 2H), 2.71–2.76 (m, 2H), 2.80–2.82 (m, 2H), 6.90 (d, $J=8.2$ Hz, 1H), 6.98–7.25 (m, 11H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 21.40, 21.52, 22.95, 23.02, 23.10, 23.25, 27.84, 28.08, 29.57, 30.02, 43.49, 116.57, 127.39, 127.54, 127.85, 127.94, 128.07, 128.88, 131.26, 132.61, 132.64, 133.20, 133.45, 135.74, 136.00, 139.17, 149.45. ^{31}P NMR (161.9 MHz): δ −13.8. IR (KBr pellet): ν 3040 (m), 2929 (s), 1590 (m), 1480 (s), 1449 (m), 1313 (m), 778 (s), 698 (vs). EIMS (m/z): 517 ([M]$^+$, 9%). HRMS (EI) calcd for $C_{36}H_{40}NP$: 517.2898. Found: 517.2878.

*3.4.3. (*R*)-2-(Dimethylamino)-2′-(di(4-anisyl)phosphino)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl, (*R*)-**4d***

Following the same procedure for the preparation of (*R*)-**4a**, (*R*)-**4d** was obtained as a white solid (yield, 81%): $[\alpha]_D^{25}=+15.2$ ($c=0.5$, THF). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.45–1.78 (m, 8H), 1.97–1.99 (m, 1H), 2.01–2.05 (m, 1H), 2.27 (s, 6H), 2.32–2.34 (m, 2H), 2.71–2.75 (m, 2H), 2.79–2.81 (m, 2H), 3.76 (s, 3H), 3.78 (s, 3H), 6.76–6.82 (m, 4H), 6.90 (d, $J=8.2$ Hz, 1H), 7.02 (d, $J=7.8$, 1H), 7.07–7.25 (m, 6H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 22.97, 23.04, 23.13, 23.26, 27.86, 28.02, 29.59, 30.03, 43.60, 55.25, 113.51, 113.74, 116.63, 128.02, 128.90, 131.30, 132.21, 133.87, 134.12, 135.19, 135.49, 135.70, 136.00, 138.39, 149.48, 159.06. ^{31}P NMR (161.9 MHz): δ −17.6. IR (KBr pellet): ν 2934 (m), 1595 (s), 1495 (s), 1458 (m), 1285 (m), 1247 (vs), 826 (s), 539 (m). EIMS (m/z): 549 ([M]$^+$, 7%). HRMS (EI) calcd for $C_{36}H_{40}NO_2P$: 549.2797. Found: 549.2807.

*3.4.4. (*R*)-2-(Dimethylamino)-2′-(di(4-*tert*-butylphenyl)phosphino)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl, (*R*)-**4e***

Following the same procedure for the preparation of (*R*)-**4a**, (*R*)-**4e** was obtained as a white solid (yield, 84%): $[\alpha]_D^{25}=+12.3$ ($c=0.5$, THF). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.26 (s, 9H), 1.29 (s, 9H), 1.55–1.74 (m, 8H), 1.80–2.04 (m, 2H), 2.30 (br, 8H), 2.69–2.73 (m, 2H), 2.79–2.82 (m, 2H), 6.91 (d, $J=8.2$ Hz, 1H), 7.01–7.15 (m, 7H), 7.22–7.28 (m, 4H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 22.95, 22.97, 23.01, 23.26, 27.69, 27.98, 29.58, 30.02, 31.14, 31.26, 31.32, 34.48, 34.53, 43.60, 116.70, 124.71, 124.78, 124.99, 125.08, 127.90, 128.84, 131.28, 132.32, 132.55, 133.85, 134.13, 135.72, 136.07, 138.28, 149.43. ^{31}P NMR (161.9 MHz): δ −16.6. IR (KBr pellet): ν 3080 (w), 2934 (vs), 1598 (m), 1480 (m), 1392 (m), 1268 (m), 1092 (s), 826 (s). EIMS (m/z): 601 ([M]$^+$, 8%). HRMS (EI) calcd for $C_{42}H_{52}NP$: 601.3837. Found: 601.3825.

*3.4.5. (*R*)-2-(Dimethylamino)-2′-(3,5-xylyl)phosphino)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl, (*R*)-**4f***

Following the same procedure for the preparation of (*R*)-**4a**, (*R*)-**4f** was obtained as a white solid (yield, 74%): $[\alpha]_D^{25}=+43.5$ ($c=0.5$, THF). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.40–1.76 (m, 8H), 1.89–2.00 (s, 6H), 2.13 (s, 6H), 2.14 (s, 6H), 2.21–2.23 (m, 8H), 2.67–2.70 (m, 2H), 2.73–2.75 (m, 2H), 6.73–7.18 (m, 10H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 20.25, 20.36, 21.78, 21.93, 21.99, 22.23, 26.80, 27.02, 28.58, 28.98, 42.59, 115.60, 127.08, 127.73, 127.81, 128.96, 129.22, 129.46, 130.23, 130.41, 130.75, 131.05, 131.50, 135.83, 136.20, 137.28, 148.00. ^{31}P NMR (161.9 MHz): δ −13.4. IR (KBr pellet): ν 2930 (s), 1581 (m), 1481 (s), 1450 (m), 1313 (m), 846

(s), 694 (s). EIMS (m/z): 545 ([M]$^+$, 10%). HRMS (EI) calcd for $C_{38}H_{44}NP$: 545.3211, Found: 545.3202.

3.5. A typical procedure for the Pd(0)-catalyzed asymmetric allylic substitution

In a Schlenk tube containing 2 mg of newly fused KOAc, $[Pd(C_3H_5)Cl]_2$ (1.8 mg, 0.005 mmol, 2.5 mol%) and the ligand (*R*)-**4f** (8.1 mg, 0.0147 mmol, 7.5 mmol%) were dissolved in 2 mL of toluene and the mixture was stirred at room temperature for 10 min. BSA (76 mg, 0.392 mmol) and dimethyl malonate (51.7 mg, 0.392 mmol) were then added, and the mixture was stirred for an additional 10 min. After cooling to −20°C, 1,3-diphenylprop-2-en-l-yl acetate (±)-**8** (49.4 mg, 0.196 mmol) was added. The reaction mixture was allowed to stir at −20°C for 24 h. The reaction was quenched with 5% aqueous HCl and extracted with EtOAc (3×20 mL). The organic phase was washed with saturated aqueous $NaHCO_3$, water, and brine, dried over anhydrous $MgSO_4$, then concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel with hexane/EtOAc (4:1) as eluent to produce (*S*)-**9** (39.6 mg, 62%) as a colorless oil with 90.9% ee. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.52 (s, 3H), 3.69 (s, 3H), 3.97 (d, J=10.9 Hz, 1H), 4.27 (dd, J=10.9, 8.7 Hz, 1H), 6.34 (dd, J=15.4, 8.4 Hz, 1H), 6.48 (d, J=15.8 Hz, 1H), 7.17–7.24 (m, 10H). The enantiomeric excess was determined by HPLC (Chiralcel OD, flow rate=0.5 mL/min, hexane:isopropanol=99:1, t_R=23.42 min, t_S=24.99 min).

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