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Synthesis of a new type of chiral amino phosphine ligands for asymmetric catalysis

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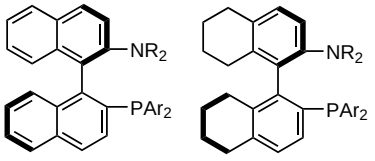
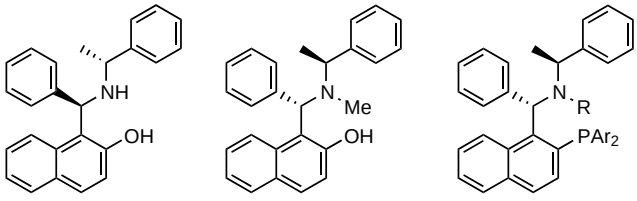
Abstract—This article describes the synthesis of a new type of chiral amino phosphine ligands from an amino naphthol starting material derived by asymmetric 1-aminoalkylation of 2-naphthol with (*R*)-1-phenylethylamine and benzaldehyde. The asymmetric induction properties of the ligands in the Pd(0)-catalyzed allylic substitution of 1,3-diphenylprop-2-en-1-yl acetate with dimethyl malonate has also been investigated, with near-quantitative yields and ee of up to 72.2% of the product being obtained under the optimized reaction conditions.

1. Introduction

The development of novel chiral ligands remains the most attractive area in the field of transition metal-catalyzed asymmetric reactions. Chiral *N*,*P* ligands represent one important type of chirality transfer agent for asymmetric catalysis.[1] Recently, a new type of amino phosphine ligands (**MAP** and **H_8-MAP**) have been synthesized and applied to Pd-catalyzed asymmetric allylation and Suzuki coupling reactions with moderate to good asymmetric induction.[2]



(*R*)-**MAP** (*R*)-**H_8-MAP**



1 **2** **3**

Palmieri et al.[3] and Wang et al.[4] developed a practical condensation reaction for the stereoselective synthesis of optically pure amino naphthol **1** from 2-naphthol, benzaldehyde, and commercially available (*R*)-1-phenylethylamine. This ligand exhibited fairly good enantioselectivity in the asymmetric addition of diethylzinc to aromatic aldehydes.[5] Ligand **2**, an *N*-methylated analogue of **1**, showed even higher enantioselectivity than **1** under the same reaction conditions, with ee of up to 99.8% of secondary alcohol being obtained.[4] As part of a continuous effort to develop *N*,*P*-ligands for enantioselective catalysis, we report in the work presented herein the synthesis of a new type of amino phosphine ligands **3** (based on **1**), and the application of ligands **3** in Pd-catalyzed asymmetric allylic alkylation.

2. Results and discussions

2.1. Synthesis of the chiral amino phosphine ligands

Diastereomerically pure amino naphthol (*R*,*R*)-**1** was prepared according to the literature method.[3] The reductive methylation of (*R*,*R*)-**1** with $(CH_2O)_n$ and $NaBH_4$ in the presence of trifluoroacetic acid gave the oxazine derivative (*R*,*R*)-**4**, rather than the expected *N*-methylated product (*R*,*R*)-**2** (Scheme 1). Obviously, the hydroxy group was very prone to reaction with the active methylene imine intermediate. Fortunately, the C–O bond of oxazine (*R*,*R*)-**4** could be reduced with $LiAlH_4$ at 0°C to give *N*-methylated amino naphthol in good yield. Treatment of (*R*,*R*)-**2** with trifluoro-

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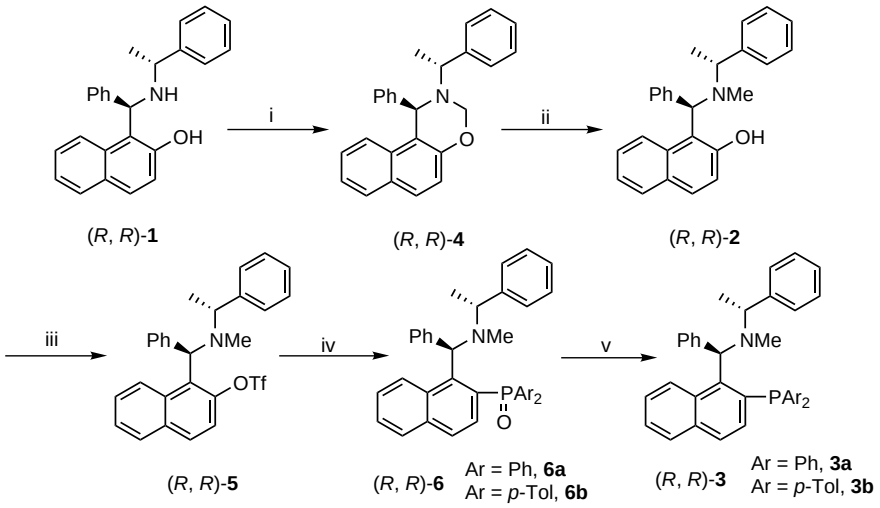
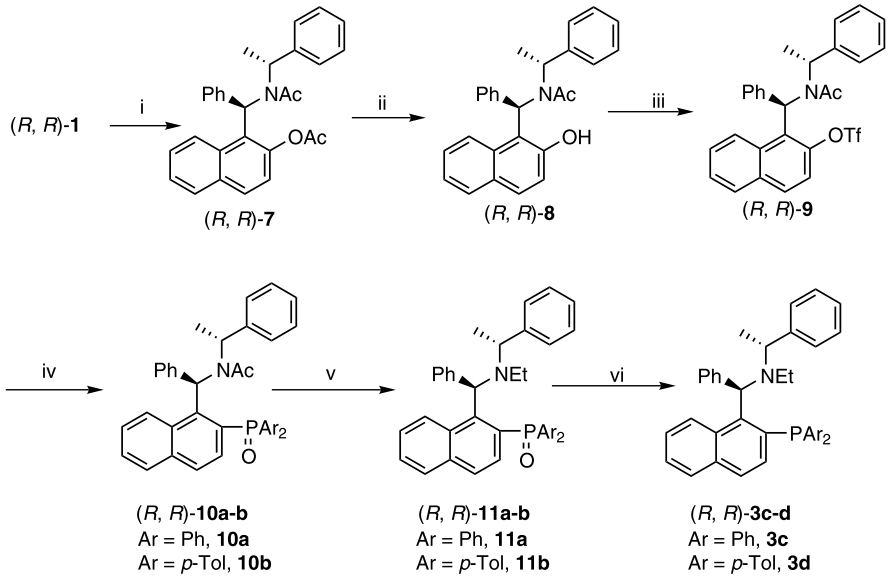


Scheme 1. *Reagents and conditions*: (i) 40% aq. HCHO, TFA, THF, 4 h, 90%; (ii) $LiAlH_4$, THF, 0°C, 5 h, 81%; (iii) Tf_2O, Et_3N, CH_2Cl_2, −78°C, 1 h, 99%; (iv) $Pd(OAc)_2$, dppp, $HP(O)Ar_2$, $(i\text{-}Pr)_2NEt$, DMSO, 100°C, 12 h, 23–41%; (v) $HSiCl_3$, Et_3N, toluene, 100°C, 17 h, 30–36%.

methanesulfonic anhydride in the presence of Et_3N gave its triflate derivative (*R*,*R*)-**5** in 99% yield. The coupling reaction of (*R*,*R*)-**5** with $Ar_2P(O)H$ catalyzed by $Pd(OAc)_2$/dppp (dppp = 1,3-bis(diphenylphosphino)propane) yielded (*R*,*R*)-**6a**,**b** in 23–41% yields. Reduction of (*R*,*R*)-**6a**,**b** with $HSiCl_3$ in the presence of Et_3N gave the desired amino phosphine ligands (*R*,*R*)-**3a**,**b** in 30–36% yields.

In order to develop the *N*-ethylated analogues of (*R*,*R*)-**3a**,**b**, we tried an alternative approach. As shown in Scheme 2, amino naphthol (*R*,*R*)-**1** was firstly treated with acetyl chloride in pyridine, and then hydrolyzed in the presence of NaOH to remove the acetyl group attached to hydroxy group, affording (*R*,*R*)-**8** in 80% total yield. Treatment of (*R*,*R*)-**8** with trifluoromethanesulfonic anhydride in the presence of Et_3N gave its triflate derivative (*R*,*R*)-**9** in 93% yield. It was found that triflate **9** underwent a coupling reaction with $Ar_2P(O)H$ catalyzed by $Pd(OAc)_2$/dppp to give (*R*,*R*)-**10a**,**b** in moderate yields. Noyori et al. reported that both an acetamide group and a phosphinyl group could be reduced by $BH_3{\cdot}Me_2S$ to afford the corresponding amino and phosphino groups, respectively.[6] However, under these reaction conditions, only the acetamide groups of (*R*,*R*)-**10a**,**b** were reduced to give (*R*,*R*)-**11a**,**b**



Scheme 2. *Reagents and conditions*: (i) AcCl, pyridine, 0°C–rt, 12 h, 85%; (ii) NaOH, CH_3OH, H_2O, rt, 1 h, 94%; (iii) Tf_2O, CH_2Cl_2, Et_3N, −78°C, 4 h, 93%; (iv) $Pd(OAc)_2$, dppp, $HP(O)Ar_2$, $(i\text{-}Pr)_2NEt$, DMSO, 100°C, 12–17 h, 61–64% yield; (v) $BH_3{\cdot}Me_2S$, THF, 0°C–reflux, 18 h, 70–95%; (vi) $HSiCl_3$, Et_3N, toluene, 100°C, 12 h, 51–56%.

in 70–95% yield. Thus, the target amino phosphine ligands (*R*,*R*)-**3c**,**d** were obtained by reduction of **11a**,**b** with $HSiCl_3/Et_3N$ in moderate yields.

2.2. Asymmetric induction of chiral amino phosphine ligands 3a–d in Pd(0)-catalyzed enantioselective allylic alkylation

Chiral *N*,*P*-ligands have been proved to be an efficient type of ligands for asymmetric allylic alkylation reactions.[7,8] In order to investigate the efficiency of the newly developed amino phosphine ligands **3a**–**d** in asymmetric catalysis, the Pd(0)-catalyzed allylic substitution of racemic 1,3-diphenylprop-2-en-1-yl acetate **12** with dimethyl malonate was taken as a model reaction.

Table 1 shows the details of our results. The reaction carried out in CH_2Cl_2 at 25°C with $[Pd(C_3H_5)Cl]_2$ as catalyst precursor, **3c** as chiral ligand, and Cs_2CO_3 as base yielded (*S*)-**13** in 96% yield and 66.5% ee (entry 1). Increasing the ratio of chiral ligand to palladium precursor led to a slight improvement in the enantioselectivity of the reaction, but the yield of the product dropped significantly (entry 2 versus 1). Examination of solvent effects showed that the reaction proceeded in $ClCH_2CH_2Cl$ with higher enantioselectivity, but the yield of product was only moderate (entries 3–6 versus 2). It should be noted that the absolute configuration of the product obtained in CH_3CN was switched to *R* (entry 5). Therefore, the asymmetric induction properties of other *N*,*P*-ligands **3a**, **3b** and **3d** were examined for the same reaction in CH_2Cl_2, the best result of 99% yield and 71.2% ee was obtained with the $[Pd(C_3H_5)Cl]_2$/**3a** catalytic complex (entries 7–9). Substitution of the reaction solvent with $ClCH_2CH_2Cl$ also gave comparable results, with 99% yield and ee of 72.2% (entry 10 versus 8).

3. Conclusion

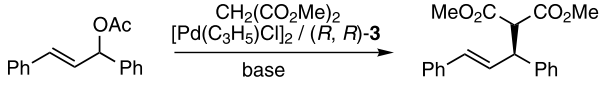
In summary, a series of novel chiral amino phosphine ligands have been prepared from an amino phenol which was derived through 1-aminoalkylation of 2-naphthol with (*R*)-1-phenylethylamine and benzaldehyde. The asymmetric induction properties of these ligands in the Pd(0)-catalyzed allylic substitution of 1,3-diphenylprop-2-en-1-yl acetate with dimethyl malonate was also investigated, with near-quantitative yield and 72.2% ee of the product being obtained under the optimized reaction conditions.

4. Experimental

4.1. General considerations

^1H NMR spectra were recorded in $CDCl_3$ on a Bruker AM300 spectrometers at 25°C, Chemical shifts are reported in ppm with TMS as an internal standard ($\delta = 0$ ppm). ^{31}P NMR spectra were recorded on a Bruker AM300 instrument in $CDCl_3$ with 85% H_3PO_4 as an external reference. Optical rotation was measured with a PE-341 automatic polarimeter. Liquid chromatographic analyses were conducted on a JASCO 1580 system. IR spectra were measured on a Bio-Rad FTS-185 spectrometer in KBr pellets. EI Mass and ESI spectra were obtained on HP5989A and Mariner LC-TOF spectrometers, respectively. HRMS were obtained on a Kratos Concept 1H instrument. Elemental analyses were performed using an Elemental VARIO EL apparatus. All experiments 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, 1,2-

Table 1. Asymmetric Pd(0)-catalyzed substitution of (±)-**12** with malonate[a]



rac-**12** (*S*)-**13**

Entry	Ligand	Solvent	Time (h)	Yield[b] (%)	Ee[c] (%)
1	**3c**	CH_2Cl_2	24	96	66.5
2	**3c**[d]	CH_2Cl_2	24	42	69.5
3	**3c**	THF	24	58	41.5
4	**3c**	Toluene	24	45	50.7
5	**3c**	CH_3CN	24	41	11.6[e]
6	**3c**	$ClCH_2CH_2Cl$	24	67	70.2
7	**3d**	CH_2Cl_2	24	83	59.7
8	**3a**	CH_2Cl_2	24	99	71.2
9	**3b**	CH_2Cl_2	24	96	61.5
10	**3a**	$ClCH_2CH_2Cl$	24	99	72.2

[a] $[Pd(C_3H_5)Cl]_2$:ligand:(±)-**12**:Cs_2CO_3:malonate = 2.5:6:100:200:200; all the reactions were carried out at 25°C.
[b] Isolated yield.
[c] Determined by HPLC on Chiralpak AD column, the absolute configuration of the product was assigned (by comparing the retention time with the reported value as *S*).[2k,2f]
[d] $[Pd(C_3H_5)Cl]_2$:ligand:(±)-**12** = 2.5:11:100.
[e] The absolute configuration of the product is *R*.

dichlorethane, CH_3CN were freshly distilled from calcium hydride and THF, toluene from sodium benzophenone ketyl. Enantiomerically pure amino naphthol (*R*,*R*)-**1** was prepared according to the reported procedure.[3]

4.2. (1*R*)-1-Phenyl-2-((1′*R*)-1′-phenylethyl)-2,3-dihydro-1*H*-naphtho[1,2-*e*][1,3]oxazine, (*R*,*R*)-4[3]

To a solution of (*R*,*R*)-**1** (2.824 g, 8 mmol) in THF (12 mL), were added 40% aqueous formaldehyde (0.6 mL) and TFA (1 mL). The reaction mixture was stirred at room temperature for 4 h, and then diluted and extracted with ethyl acetate. The extracts were washed with water, saturated aqueous $NaHCO_3$, and brine, respectively, dried over Na_2SO_4, and then concentrated under reduced pressure. The residue was submitted to chromatographic separation on silica gel with hexane/EtOAc (20:1) as eluent to give a white amorphous solid (2.641 g, 90%): $[\alpha]_D^{20}=-171.3$ (*c* 2.785, $CHCl_3$) (lit.:[2] −132.5 (*c* 3.2, $CHCl_3$)); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.55 (d, $J=6.2$ Hz, 3H), 3.98 (q, $J=6.6$ Hz, 1H), 4.94 (d, $J=11.0$ Hz, 1H), 5.14 (dd, $J=1.8$, 10.6 Hz, 1H), 5.20 (s, 1H), 7.03–7.06 (m, 3H), 7.14–7.41 (m, 11H), 7.74–7.78 (m, 2H); EIMS (*m*/*z*): 367 ([M]$^+$, 0.3%).

4.3. 1-{(*R*)-[Methyl((1′*R*)-1′-phenylethyl)amino]phenylmethyl}naphthalen-2-ol, (*R*,*R*)-2[4]

To a Schlenk tube containing $LiAlH_4$ (320 mg, 8.4 mmol) and dried THF (12 mL), was added (*R*,*R*)-**3** (2.558 g, 7.0 mmol) in THF (12 mL) at 0°C. After the mixture was stirred for 5 h, the reaction was quenched with water. Then the reaction mixture was extracted with ethyl acetate for three times, the combined organic layer was washed with water, brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was recrystallized from CH_2Cl_2/hexane, furnishing white crystal (2.089 g, 81%): $[\alpha]_D^{20}=-265.7$ (*c* 0.49, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.52 (m, 3H), 2.16 (m, 3H), 4.21 (brm, 1H), 5.33 (s, 1H), 7.17–7.43 (m, 11H), 7.61–7.85 (m, 5H), 14.02 (brs, 1H); IR (KBr pellet): *v* 3060 (w), 3022 (w), 2995 (w), 2968 (w), 1621 (s), 1599 (s), 1452 (vs), 1267 (s), 1237 (vs), 1151 (m), 1122 (m), 1043 (m), 1027 (m), 821 (s), 751 (vs), 701 (vs); EIMS (*m*/*z*): 367 ([M]$^+$, 5%).

4.4. 1-{(*R*)-[Methyl((1′*R*)-1′-phenylethyl)amino]-phenylmethyl}naphthalen-2-yl trifluoromethanesulfonate, (*R*,*R*)-5

Trifluoromethanesulfonic anhydride (1 mL, 5.5 mmol) was slowly added to a solution of (*R*,*R*)-**2** (1.835 g, 5 mmol) and Et_3N (3.5 mL, 25 mmol) in dried CH_2Cl_2 (16.3 mL) at −78°C, the reaction mixture was stirred for 1 h, then warmed to room temperature. After removal of the solvent under reduced pressure, the resulting residue was submitted to chromatographic separation on silica gel with hexane/EtOAc (20:1) as eluent to give (*R*,*R*)-**5** as a light yellow solid (2.481 g, 99%): mp 71–73°C; $[\alpha]_D^{20}=-48.1$ (*c* 0.57, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.45 (d, $J=6.7$ Hz, 3H), 2.06 (s, 3H), 4.29 (q, $J=6.7$ Hz, 1H), 5.86 (s, 1H), 7.13–7.16 (m, 1H), 7.21–7.43 (m, 6H), 7.52–7.65 (m, 3H), 7.69–7.81 (m, 5H), 9.87 (d, $J=9.2$ Hz, 1H); IR (KBr pellet): *v* 3088 (w), 2978 (m), 1598 (m), 1510 (m), 1494 (m), 1450 (m), 1419 (s), 1249 (s), 1216 (vs), 1141 (vs), 1051 (m), 941 (s), 883 (s), 841 (s), 809 (s); EIMS (*m*/*z*): 484 ([M−15]$^+$, 56%). Anal. calcd for $C_{27}H_{24}F_3NO_3S$: C, 64.92; H, 4.84; N, 2.80. Found: C, 64.98; H, 5.03; N, 2.55%.

4.5. {(*R*)-[2-(Diphenylphosphinoyl)naphthalen-1-yl]phenylmethyl}methyl((1′*R*)-1′-phenylethyl)amine, (*R*,*R*)-6a

To a mixture of (*R*,*R*)-**5** (998 mg, 2 mmol), diphenylphosphine oxide (808 mg, 4 mmol), $Pd(OAc)_2$ (45 mg, 0.2 mmol), and dppp (124 mg, 0.3 mmol) were added DMSO (10 mL) and diisopropylethylamine (1.8 mL, 10 mmol), and the mixture was stirred at 100°C for 12 h. After cooling to room temperature, the reaction mixture was diluted with ethyl acetate, washed with water twice, washed with brine, dried over Na_2SO_4, and then concentrated under reduced pressure. The resulting residue was submitted to chromatographic separation on silica gel with hexane/EtOAc (10:1–4:1) as eluent to give (*R*,*R*)-**6a** as a white solid (449 mg, 41%): $[\alpha]_D^{20}=+132.9$ (*c* 0.525, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.41 (d, $J=6.7$ Hz, 3H), 1.86 (s, 3H), 4.37 (q, $J=6.7$ Hz. 1H), 6.93–6.98 (m, 3H), 7.00–7.62 (m, 16H), 7.65–7.81 (m, 7H), 9.93 (d, $J=8.6$ Hz, 1H); ^{31}P NMR (121.46 MHz, $CDCl_3$): δ 35.0; IR (KBr pellet): *v* 3053 (w), 2966 (w), 1598 (w), 1492 (m), 1436 (s), 1187 (s), 1115 (s), 1029 (m), 702 (vs), 694 (vs); EIMS (*m*/*z*): 446 ([M−105]$^+$, 100%). Anal. calcd for $C_{38}H_{34}NOP$: C, 82.37; H, 6.21; N, 2.54. Found: C, 82.25; H, 6.54; N, 2.47%.

4.6. {(*R*)-[2-(Di-*p*-tolylphosphinoyl)naphthalen-1-yl]phenylmethyl}methyl((1′*R*)-1′-phenylethyl)amine, (*R*,*R*)-6b

Following the same procedure for the preparation of (*R*,*R*)-**6a**, reaction of (*R*,*R*)-**5** with di(4-toly)phosphine oxide afforded (*R*,*R*)-**6b** as an amorphous white solid (yield, 23%): $[\alpha]_D^{20}=+139.5$ (*c* 0.555, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.42 (d, $J=6.7$ Hz, 3H), 1.78 (s, 3H), 2.39 (s, 3H), 2.44 (s, 3H), 4.37 (q, $J=6.7$ Hz, 1H), 6.93–7.04 (m, 3H), 7.13–7.71 (m, 21H), 9.90 (d, $J=8.6$ Hz, 1H); ^{31}P NMR (121.46 MHz, $CDCl_3$): δ 35.1; IR (KBr pellet): *v* 1600 (m), 1499 (m), 1455 (m), 1114 (s), 809 (s), 751 (s), 700 (s), 659 (s); EIMS (*m*/*z*): 474 ([M−105]$^+$, 53%). Anal. calcd for $C_{40}H_{38}NOP$: C, 82.87; H, 6.61; N, 2.42. Found: C, 82.53; H, 6.80; N, 2.30%.

4.7. {(*R*)-[2-(Diphenylphosphanyl)naphthalen-1-yl]phenylmethyl}methyl((1′*R*)-1′-phenylethyl)amine, (*R*,*R*)-3a

To a solution of (*R*,*R*)-**6a** (416 mg, 0.76 mmol) and dried Et_3N (1.5 mL, 10.6 mmol) in dried toluene (5 mL), was added $HSiCl_3$ (1.2 mL, 10.6 mmol) at 0°C, the reaction mixture was stirred for 0.5 h, and then heated to 120°C under stirring for additional 17 h. The

reaction was quenched at room temperature, with 1N aqueous NaOH. The mixture was filtered through Celite, and the filtrate was extracted with ethyl acetate, washed with water, brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was submitted to chromatographic separation on silica gel with hexane/EtOAc (10:1) as eluent to give a white amorphous solid (147 mg, 36%): $[\alpha]_D^{20}=+135$ (*c* 0.285, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 1.42 (d, $J=6.9$ Hz, 3H), 1.92 (s, 3H), 4.41 (q, $J=6.6$ Hz, 1H), 7.00–7.09 (m, 4H), 7.12–7.53 (m, 16H), 7.59–7.73 (m, 6H), 9.69 (d, $J=8.6$ Hz, 1H); ^{31}P NMR (121.46 MHz, $CDCl_3$): δ −14.5; IR (KBr pellet): *v* 3055 (w), 2966 (w), 1598 (w), 1585 (w), 1491 (m), 1432 (s), 1050 (m), 1028 (s), 818 (s), 739 (vs), 697 (vs); EIMS (*m*/*z*): 535 ([M]$^+$, 0.4%). Anal. calcd for $C_{38}H_{34}NP$: C, 85.21; H, 6.40; N, 2.61. Found: C, 84.90; H, 6.51; N, 2.49%.

4.8. {(*R*)-[2-(Di-*p*-tolylphosphanyl)naphthalen-1-yl]phenylmethyl}methyl((1′*R*)-1′-phenylethyl)amine, (*R*,*R*)-3b

Following the same procedure for the preparation of (*R*,*R*)-**3a**, reduction of (*R*,*R*)-**6b** afforded (*R*,*R*)-**3b** as amorphous white solids (yield, 30%): $[\alpha]_D^{20}=+161$ (*c* 0.19, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 1.42 (d, $J=6.9$ Hz, 3H), 1.89 (s, 3H), 2.34 (s, 3H), 2.36 (s, 3H), 4.41 (q, $J=6.6$ Hz, 1H), 6.99–7.29 (m, 14H), 7.36–7.70 (m, 10H), 9.22 (d, $J=8.6$ Hz, 1H); ^{31}P NMR (121.46 MHz, $CDCl_3$): δ −16.2; IR (KBr pellet): *v* 2970 (w), 1599 (m), 1495 (s), 1448 (m), 1186 (m), 1028 (m), 806 (vs), 746 (m), 699 (vs); EIMS (*m*/*z*): 563 ([M]$^+$, 2%); ESIMS (*m*/*z*): 564.3 ([M+1]$^+$, 100%); HRMS (EI) calcd for $C_{40}H_{38}NP$: 563.2742. Found: 563.2728.

4.9. 1-{(*R*)-[Acetyl((1′*R*)-1′-phenylethyl)amino]-phenylmethyl}naphthalen-2-yl acetate, (*R*,*R*)-7

Acetyl chloride (1.8 mL, 25.05 mmol) was slowly added to a solution of amino naphthol (*R*,*R*)-**1** (2.949 g, 8.35 mmol) in dry pyridine (42 mL) at 0°C, and the mixture was stirred at room temperature for 12 h. Then reaction was quenched with water. The solvent was removed under reduced pressure, and the resulting residue was diluted with ethyl acetate, washed with water, 1N aqueous HCl, saturated aqueous $NaHCO_3$, and brine. The organic phase was dried over Na_2SO_4, and concentrated again under reduced pressure. The resulting residue was submitted to chromatographic separation on silica gel with hexane/EtOAc (2:1) as eluent to give (*R*,*R*)-**7** as a white solid (3.091 g, 85%): mp 133–135°C; $[\alpha]_D^{20}=+73.4$ (*c* 0.42, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 1.60–1.68 (m, 3H), 1.93–2.04 (m, 5H), 2.28 (brs, 1H), 4.58 (brs, 1H), 5.04 (m, 1H), 6.71–6.91 (m, 5H), 7.17–7.78 (m, 10H), 8.30 (brs, 1H); IR (KBr pellet): *v* 3055 (w), 1766 (vs), 1622 (vs), 1496 (m), 1428 (m), 1366 (m), 1312 (m), 1274 (m), 1191 (vs), 1016 (s), 809 (s), 737 (s), 699 (s); EIMS (*m*/*z*): 437 ([M]$^+$, 0.5%). Anal. calcd for $C_{29}H_{27}NO_3$: C, 79.61; H, 6.22; N, 3.20. Found: C, 79.17; H, 6.44; N, 3.09%.

4.10. *N*-[(*R*)-(2-Hydroxynaphthalen-1-yl)phenylmethyl]-*N*-((1′*R*)-1′-phenylethyl)acetamide, (*R*,*R*)-8

To a solution of (*R*,*R*)-**4** (3.019 g, 6.9 mmol) in water (12 mL) and CH_3OH (180 mL) was added NaOH (1.2 g, 30 mmol). The mixture was stirred at room temperature for 1 h. The solvent was removed under reduced pressure and the resulting residue was neutralized with saturated aqueous NH_4Cl and extracted three times with ethyl acetate. The combined organic layers were washed with saturated aqueous $NaHCO_3$, water, brine, dried over Na_2SO_4, and then concentrated under reduced pressure. The residue was recrystallized from a mixed solvent of THF/hexane, affording (*R*,*R*)-**8** as a white crystal (2.577 g, 94%): mp 164°C dec.; $[\alpha]_D^{20}=-509.2$ (*c* 0.515, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 2.02 (d, $J=6.7$ Hz, 3H), 2.36 (s, 3H), 5.25 (q, $J=6.1$ Hz, 1H), 6.35 (s, 1H), 6.58–6.61 (m, 3H), 6.95–7.31 (m, 11H), 7.50–7.54 (m, 2H), 9.84 (brs, 1H); IR (KBr pellet): *v* 1629 (m), 1596 (vs), 1576 (vs), 1516 (s), 1495 (m), 1436 (s), 1374 (s), 1273 (vs), 1160 (m), 1032 (m), 815 (s), 742 (s), 697 (vs); EIMS (*m*/*z*): 395 ([M]$^+$, 4%). Anal. calcd for $C_{27}H_{25}NO_2$: C, 82.00; H, 6.37; N, 3.54. Found: C, 81.61; H, 6.44; N, 3.48%.

4.11. 1-{(*R*)-[Acetyl((1′*R*)-1′-phenylethyl)amino]-phenylmethyl}naphthalen-2-yl trifluoromethanesulfonate, (*R*,*R*)-9

Following the same procedure for the preparation of (*R*,*R*)-**5**, the reaction of (*R*,*R*)-**8** and Tf_2O afforded (*R*,*R*)-**9** (yield, 93%): mp 148–150°C; $[\alpha]_D^{20}=+81.7$ (*c* 0.61, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 1.98 (d, $J=7.3$ Hz, 3H), 1.99–2.22 (m, 3H), 4.43 (brs, 1H), 6.63 (brs, 2H), 6.90–7.47 (m, 13H), 7.77–7.80 (m, 2H); IR (KBr pellet): *v* 3061 (w), 3022 (w), 1658 (vs), 1601 (w), 1512 (m), 1493 (m), 1447 (m), 1423 (vs), 1415 (vs), 1303 (s), 1214 (vs), 1140 (s), 952 (vs), 763 (s), 612 (s); EIMS (*m*/*z*): 422 ([M−105]$^+$, 43%). Anal. calcd for $C_{28}H_{24}F_3NO_4S$: C, 63.75; H, 4.59; N, 2.66. Found: C, 63.61; H, 4.45; N, 2.66%.

4.12. *N*-{(*R*)-[2-(Diphenylphosphinoyl)naphthalen-1-yl]phenylmethyl}-*N*-((1′*R*)-1′-phenylethyl)acetamide, (*R*,*R*)-10a

Following the same procedure for the preparation of (*R*,*R*)-**6a**, the coupling reaction of (*R*,*R*)-**9** with $H(O)PPh_2$ afforded (*R*,*R*)-**10a** (yield, 64%): mp 274.5–275.5°C; $[\alpha]_D^{20}=+233.5$ (*c* 0.56, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 2.02 (d, $J=6.1$ Hz, 3H), 2.29 (s, 3H), 4.60–4.62 (m, 1H), 6.14 (s, 1H), 6.85–6.87 (m, 1H), 7.02–7.22 (m, 8H), 7.25–7.78 (m, 16H), 8.23–8.24 (m, 1H); ^{31}P NMR (121.46 MHz, $CDCl_3$): δ 34.1; IR (KBr pellet): *v* 3053 (w), 2975 (w), 1646 (vs), 1438 (s), 1413 (s), 1292 (vs), 1187 (vs), 1115 (s), 761 (s), 736 (m), 724 (m), 696 (vs); EIMS (*m*/*z*): 474 ([M−105]$^+$, 46%). Anal. calcd for $C_{39}H_{34}NO_2P$: C, 80.81; H, 5.91; N, 2.42. Found: C, 80.48; H, 5.96; N, 2.36%.

4.13. *N*-{(*R*)-[2-(Di-*p*-tolylphosphinoyl)naphthalen-1-yl]phenylmethyl}-*N*-((1′*R*)-1′-phenylethyl)acetamide, (*R*,*R*)-10b

Following the same procedure for the preparation of (*R*,*R*)-**6b**, the coupling reaction of (*R*,*R*)-**9** with di(4-toly)phosphine oxide afforded (*R*,*R*)-**10b** (yield, 61%): mp 244–245°C; $[\alpha]_D^{20}=+203.2$ (*c* 0.57, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 2.02 (d, $J=6.1$ Hz, 3H), 2.30 (s, 3H), 2.39 (s, 3H), 2.44 (s, 3H), 4.58–4.60 (m, 1H), 6.15 (s, 1H), 6.85 (m, 1H), 7.04–7.28 (m, 12H), 7.38–7.43 (m, 2H), 7.52–7.58 (m, 4H), 7.70–7.77 (m, 4H), 8.25–8.26 (m, 1H); ^{31}P NMR (121.46 MHz, $CDCl_3$): δ 34.2; IR (KBr pellet): *v* 1658 (vs), 1600 (s), 1492 (m), 1420 (m), 1296 (s), 1181 (s), 1114 (s), 1098 (m), 809 (s), 758 (s), 698 (s), 663 (vs); EIMS (*m*/*z*): 502 ([M−105]$^+$, 18%). Anal. calcd for $C_{41}H_{38}NO_2P\cdot 0.5H_2O$: C, 79.85; H, 6.37; N, 2.27. Found: C, 80.23; H, 6.45; N, 2.32%.

4.14. {(*R*)-[2-(Diphenylphosphinoyl)naphthalen-1-yl]phenylmethyl}ethyl((1′*R*)-1′-phenylethyl)amine, (*R*,*R*)-11a

To a solution of (*R*,*R*)-**10a** (552 mg, 0.953 mmol) in dried THF (25 mL), was added $BH_3\cdot Me_2S$ (0.33 mL, 3.43 mmol) at 0°C. The reaction mixture was heated to reflux, and stirred for additional 18 h. After cooling to room temperature, the reaction was carefully quenched with saturated aqueous NH_4Cl and the mixture was extracted with ethyl acetate. The organic phase was washed with water, brine, dried over Na_2SO_4, and then concentrated under reduced pressure. The residue was submitted to chromatographic separation on silica gel with hexane/EtOAc (4:1) as eluent to give a white amorphous solid (509 mg, 95%): $[\alpha]_D^{20}=+57.9$ (*c* 0.535, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 0.39 (t, $J=7.0$ Hz, 3H), 1.48 (d, $J=6.8$ Hz, 3H), 2.46–2.62 (m, 2H), 4.39 (q, $J=6.2$ Hz, 1H), 6.90–7.00 (m, 4H), 7.08–7.73 (m, 22H), 10.23 (d, $J=8.8$ Hz, 1H); ^{31}P NMR (121.46 MHz, $CDCl_3$): δ 35.5; IR (KBr pellet): *v* 3057 (w), 1598 (w), 1494 (m), 1437 (s), 1182 (s), 1115 (s), 818 (m), 750 (s), 721 (s), 698 (vs); EIMS (*m*/*z*): 460 ([M−105]$^+$, 79%). Anal. calcd for $C_{39}H_{36}NOP$: C, 82.81; H, 6.41; N, 2.48. Found: C, 82.39; H, 6.71; N, 2.48%.

4.15. {(*R*)-[2-(Di-*p*-tolylphosphinoyl)naphthalen-1-yl]phenylmethyl}ethyl((1′*R*)-1′-phenylethyl)amine, (*R*,*R*)-11b

Following the same procedure for the preparation of (*R*,*R*)-**11a**, the reduction of (*R*,*R*)-**10b** afforded (*R*,*R*)-**11b** (yield, 70%): $[\alpha]_D^{20}=+66.9$ (*c* 0.495, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 0.38 (t, $J=7.3$ Hz, 3H), 1.49 (d, $J=6.7$ Hz, 3H), 2.39 (s, 3H), 2.41 (s, 3H), 2.49–2.64 (m, 2H), 4.39 (q, $J=6.1$ Hz, 1H), 6.93–6.99 (m, 3H), 7.09–7.36 (m, 8H), 7.45–7.64 (m, 8H), 7.67–7.72 (m, 5H), 10.21 (d, $J=8.6$ Hz, 1H); ^{31}P NMR (121.46 MHz, $CDCl_3$): δ 35.5; IR (KBr pellet): *v* 1600 (m), 1494 (m), 1449 (m), 1398 (w), 1182 (vs), 1113 (vs), 1098 (s), 809 (s), 700 (s), 657 (s); EIMS (*m*/*z*): 488 ([M−105]$^+$, 100%). Anal. calcd for $C_{41}H_{40}NOP$: C, 82.94; H, 6.79; N, 2.36. Found: C, 82.46; H, 7.28; N, 2.37%.

4.16. {(*R*)-[2-(Diphenylphosphanyl)naphthalen-1-yl]phenylmethyl}ethyl((1′*R*)-1′-phenylethyl)amine, (*R*,*R*)-3c

Following the same procedure for the preparation of (*R*,*R*)-**3a**, the reduction of (*R*,*R*)-**11a** afforded (*R*,*R*)-**3c** (yield, 51%): $[\alpha]_D^{20}=-25.9$ (*c* 0.525, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 0.57 (t, $J=7.3$ Hz, 3H), 1.49 (d, $J=6.7$ Hz, 3H), 2.51–2.60 (m, 1H), 2.66–2.75 (m, 1H), 4.39 (q, $J=6.7$ Hz, 1H), 6.93–6.97 (m, 3H), 7.07–7.39 (m, 14H), 7.45–7.62 (m, 8H), 7.71 (d, $J=8.6$ Hz, 1H), 10.05 (d, $J=9.2$ Hz, 1H); ^{31}P NMR (121.46 MHz, $CDCl_3$): δ −14.4; IR (KBr pellet): *v* 3053 (w), 2967 (w), 1598 (w), 1584 (m), 1493 (m), 1450 (m), 1433 (s), 1180 (m), 1027 (m), 818 (s), 742 (vs), 696 (vs); EIMS (*m*/*z*): 549 ([M]$^+$, 0.3%); ESIMS (*m*/*z*): 550.3 ([M+1]$^+$, 100%); HRMS (EI) calcd for $C_{39}H_{36}NP$: 549.2585. Found: 549.2583.

4.17. {(*R*)-[2-(Di-*p*-tolylphosphanyl)naphthalen-1-yl]phenylmethyl}ethyl((1′*R*)-1′-phenylethyl)amine, (*R*,*R*)-3b

Following the same procedure for the preparation of (*R*,*R*)-**3a**, the reduction of (*R*,*R*)-**11b** afforded (*R*,*R*)-**3d** (yield, 56%): $[\alpha]_D^{20}=+8.4$ (*c* 0.515, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 0.55 (t, $J=7.2$ Hz, 3H), 1.50 (d, $J=6.9$ Hz, 3H), 2.32 (s, 3H), 2.36 (s, 3H), 2.51–2.58 (m, 1H), 2.67–2.74 (m, 1H), 4.41 (q, $J=6.9$ Hz, 1H), 6.95–7.01 (m, 7H), 7.02–7.36 (m, 9H), 7.44–7.63 (m, 7H), 7.70–7.72 (m, 1H), 10.02 (d, $J=8.6$ Hz, 1H); ^{31}P NMR (121.46 MHz, $CDCl_3$): δ −16.2; IR (KBr pellet): *v* 3057 (w), 3027 (w), 2968 (m), 2920 (m), 1598 (m), 1495 (vs), 1449 (s), 1395 (m), 1375 (m), 1185 (m), 1089 (m), 1029 (m), 805 (vs), 699 (vs); EIMS (*m*/*z*): 577 ([M]$^+$, 0.9%); ESIMS (*m*/*z*): 578.3 ([M+1]$^+$, 100%); HRMS (EI) calcd for $C_{41}H_{40}NP$: 577.2898. Found: 577.2891.

4.18. Typical procedure for Pd(0)-catalyzed asymmetric allylic alkylation reaction

In a Schlenk tube containing 1,3-dipheylprop-2-en-1-yl acetate (±)-**12** (57 mg, 0.227 mmol), $[Pd(C_3H_5)Cl]_2$ (2.1 mg, 0.0568 mmol, 2.5 mol%), (*R*,*R*)-**3a** (7.3 mg, 0.136 mmol, 6 mmol%), Cs_2CO_3 (148 mg, 0.45 mmol) was added $ClCH_2CH_2Cl$ (2 mL). The mixture was stirred at room temperature for 20 min, and dimethyl malonate (59.4 mg, 0.45 mmol) was then added. The reaction mixture was allowed to stir at room temperature for 24 h. The reaction was quenched with saturated aqueous NH_4Cl, extracted with EtOAc (3×20 mL). The organic phase was washed with saturated aqueous $NaHCO_3$, water, and brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel with hexane/EtOAc (4:1) as eluent to produce (*S*)-**13** (73 mg, 99%) as a colorless oil with 72.2% ee. ^1H 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 (Chiralpak AD, flow rate = 1 mL/min, hexane:*iso*-propanol = 90:10, $t_R=12.6$ min, $t_S=18.9$ min).

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