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Synthesis of homologated binaphthyl N,P-ligands for Pd-catalyzed asymmetric allylic alkylation

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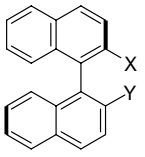
Abstract—2-Pyrrolidinylmethyl-2′-diphenylphosphino-1,1′-binaphthyl has been found to be a highly reactive and enantioselective N,P-ligand in the palladium-catalyzed asymmetric allylic alkylation of 1,3-diphenylpropen-2-yl acetate with dimethyl malonate. This axially chiral binaphthyl-based homologated N,P-ligand can be conveniently prepared from enantiomerically pure binaphthol using a five-step reaction sequence, and provides for efficient asymmetric catalysis using the chirality of the binaphthyl skeleton alone.

1. Introduction

Since the report by Trost in 1977,[1] palladium-catalyzed asymmetric allylic alkylation has been one of the most studied processes for enantioselective formation of carbon–carbon bonds.[2] Among the numerous chiral ligands designed for allylation, including the successful Trost's P,P-ligand[3] and Pfaltz's N,P-ligand,[4] binaphthyl-based ligands have attracted a great deal of attention, due to their efficient steric and electronic modulation of the chiral backbone. Two of the previously known N,P-ligands having chiral 1,1′-binaphthyl skeletons are the aminophosphine (MAP) **1**[5,6] and phosphino-oxazoline ligands **2**.[7] However, these ligands require additional chirality on the nitrogen donor moiety to improve their enantioselectivity.[6,7] In our previous reports, we synthesized the 2-dialkylaminomethyl-2′-hydroxy-1,1′-binaphthyls **3** and used them as N,O-ligands for catalytic asymmetric organozinc addition reactions.[8] These homologated ligands, having a methylene inserted between the binaphthyl and the amino group of the NOBIN (2-amino-2′-hydroxy-1,1′-binaphthyl, **4**), showed better catalytic activity and enantioselectivity than NOBIN itself in the addition reactions. This improvement is apparently related to the increased bite angle between bidentate binaphthyl N,O-ligand and the metal. There have been numerous studies on the influence of the bite angle of 1,1′-biaryl-2,2′-bisphosphines on the enantioselectivity of diverse asymmetric processes.[9] These studies mainly focused on substituent changes at the 5- and/or 6-positions of the biaryls, and only a limited number of homologated bidentate ligands having a binaphthyl backbone have been reported.[10] To investigate the effect of the homologated MAP ligand, we prepared 2-dialkylaminomethyl-2′-diphenylphosphino-1,1′-binaphthyl **5** and applied it to the Pd-catalyzed asymmetric allylic alkylation of racemic 1,3-diphenylpropen-2-yl acetate with dimethyl malonate.



1: X = NR_2, Y = PPh_2
2: X = Oxazol-2-yl, Y = PPh_2
3: X = CH_2NR_2, Y = OH
4: X = NR_2, Y = OH
5: X = CH_2NR_2, Y = PPh_2

2. Results and discussion

Aminophosphines **5a**–**5d** were conveniently prepared from ester **6**,[11] which was obtained by the selective monocarbomethoxylation of (*R*)-BINOL bistriflate, followed by the Pd(0)-catalyzed coupling of the resulting monotriflate with diphenylphosphine oxide. Ester **6** was condensed with the corresponding aluminum amides, generated in situ from the corresponding amines and trimethylaluminum, to form amides **7a**–**7d**.[12] The amide and phosphine oxide functionalities of **7a**–**7d** were simultaneously reduced to aminophosphines **5a**–**5d** with trichlorosilane (Scheme 1). Dimethylaminophosphine **5b** was previously synthesized by Hayashi et al.[11] through the reduction and methylation of the corresponding cyano-phosphine,

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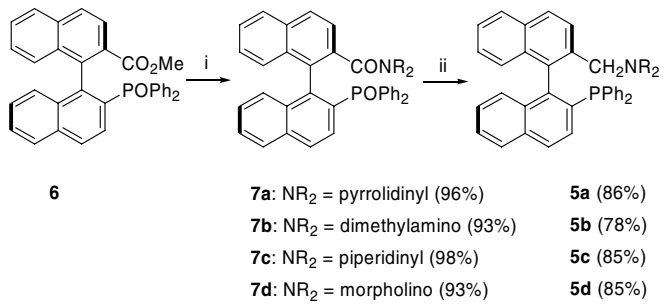


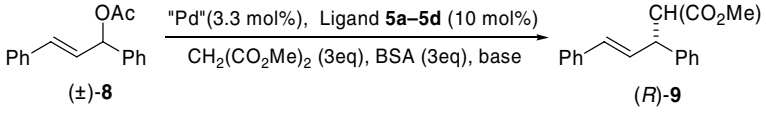
Scheme 1. Synthesis of homologated (*R*)-MAPs **5a**–**5d**. Reagents and conditions: (i) R_2NH, $AlMe_3$, toluene, 80 °C; (ii) $HSiCl_3$, Et_3N, toluene, 100 °C.

but has not previously been used as a chiral ligand for allylic alkylation.

The aminophosphines **5a**–**5d** were tested for their ability to bring about the Pd(0)-catalyzed asymmetric allylic substitution of racemic 1,3-diphenyl-2-propenyl acetate **8** with dimethyl malonate. The effects of the solvents, palladium precursors, reaction temperature, and base were studied and the results are summarized in Table 1. Initially, the catalyst generated in situ from the allyl chloride palladium dimer $[Pd(C_3H_5)Cl]_2$ (3.3 mol %) and **5a** (10 mol %) was tested for its ability to effect allylic alkylation in the presence of KOAc (30 mol %) and *N*,*O*-bis(trimethylsilyl)acetamide (BSA, 3 equiv). The catalytic conversion afforded the product (*R*)-**9** with a reasonably high yield and enantioselectivity at ambient temperature in either dichloromethane or toluene (entries 1 and 2). Though the reaction was allowed to proceed for 24 h, the conversion seemed to reach its maximum within a couple of hours and no further consumption of the starting allyl acetate was observed thereafter. The reaction was completed within an hour in more polar solvents, and the optimum result was obtained in THF solvent with 98% isolated yield and 93% ee (entry 4). When the reaction was performed at lower temperatures, with smaller amounts of the catalyst, or with the use of NaOAc instead of KOAc, the reaction proceeded slowly to provide decreased conversions without significantly affecting the enantioselectivity (entries 5–7). The use of other palladium precursors, such as $Pd_2(dba)_2$ and $Pd(OAc)_2$, provided inferior results to those afforded by $[Pd(C_3H_5)Cl]_2$ (entries 8 and 9). Other aminophosphines **5b**–**5d** were also tested under optimized conditions (entries 10–12). The dimethylamino derivative **5b** provided similar enantioselectivity to **5a** with a decreased conversion yield. Increasing the size of the amino group to piperidinyl **5c** and morpholino **5d** resulted in a deterioration in the enantioselectivity. The use of a bulkier amino group seems to counterbalance the stereoselectivity offered by the increased bite angle of the homologated MAP-Pd complex.[5,6a]

Interestingly, the absolute stereochemistry of **9** in our study was different from that resulting from the use of ligand MAP (**1**)[5a] and its octahydro derivative (H_8-MAP).[6] Both the (*R*)-MAP and (*R*)-H_8-MAP ligands have been reported to give the (*S*)-**9** product, while the (*R*)-ligands **5a**–**5d** in our study produced (*R*)-**9**. It was reported by Kocovsky et al.[5b] that the MAP-Pd catalyst is in dynamic equilibrium between the N,P-Pd and C_σ,P-Pd chelates together with the P-monocoordinated one. It was assumed that the C_σ,P-Pd complex, shown as **A** as its π-allyl complex, is an active catalyst in the allylic alkylation. Ding et al. showed that the enhancement of the enantioselectivity obtained with the use of the H_8-MAP ligand originates from the different chelating mode, N,P-Pd chelation (**B**), of the catalyst.[6c] The increase of the bite angle of the H_8-MAP N,P-donor with palladium was considered to be directly responsible for the selectivity enhancement. The further improvement

Table 1. Enantioselective allylic alkylation of racemic 1,3-diphenyl-2-propenyl acetate **8** with dimethyl malonate catalyzed by Pd/ligand **5a**–**5d**

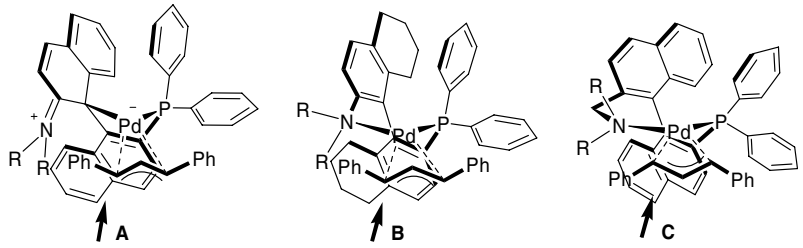


(±)-**8** (*R*)-**9**

Entry	Pd-precursor	Ligand	Solvent	Base	Temp	Time (h)	Yield[a,b] (%)	ee[c,d] (%)
1	$[Pd(C_3H_5)Cl]_2$	**5a**	CH_2Cl_2	KOAc	rt	24	85	80
2	$[Pd(C_3H_5)Cl]_2$	**5a**	Toluene	KOAc	rt	24	71	91
3	$[Pd(C_3H_5)Cl]_2$	**5a**	CH_3CN	KOAc	rt	1	96	90
4	$[Pd(C_3H_5)Cl]_2$	**5a**	THF	KOAc	rt	1	98	93
5	$[Pd(C_3H_5)Cl]_2$	**5a**	THF	KOAc	0 °C	24	77	94
6[e]	$[Pd(C_3H_5)Cl]_2$	**5a**	THF	KOAc	rt	24	74	91
7	$[Pd(C_3H_5)Cl]_2$	**5a**	THF	NaOAc	rt	24	72	93
8	$Pd_2(dba)_2$	**5a**	THF	KOAc	rt	6	96	85
9	$Pd(OAc)_2$	**5a**	THF	KOAc	rt	24	75	70
10	$[Pd(C_3H_5)Cl]_2$	**5b**	THF	KOAc	rt	2	82	92
11	$[Pd(C_3H_5)Cl]_2$	**5c**	THF	KOAc	rt	2	98	80
12	$[Pd(C_3H_5)Cl]_2$	**5d**	THF	KOAc	rt	24	82	74

[a] Isolated yields.
[b] 0.05 M substrate concentration.
[c] Determined by chiral HPLC (Chiralpak AD-H column).
[d] Absolute configuration assigned by comparison to the literature.[5a]
[e] 2 mol % of $[Pd(C_3H_5)Cl]_2$ and 4 mol % of **5a** used.

of enantioselectivity in the allylic alkylation observed in our study with **5a**, an N,P-donor, can also be explained by the increased bite angle induced by the homologation. With the changes in steric environments caused by the N,P-substituents of **5a**–**5d**, the equilibrium of the π-allyl complexation is believed to shift to the M-type, shown as **C**, to give (*R*)-**9** after the nucleophilic addition.



3. Conclusions

2-Pyrrolidinylmethyl-2′-diphenylphosphino-1,1′-binaphthyl was found to be a highly stereoselective N,P-ligand in the Pd-catalyzed asymmetric allylic alkylation of racemic 1,3-diphenylpropen-2-yl acetate using dimethyl malonate as the nucleophile. This homologated MAP can easily be prepared from the readily available optically pure BINOL using a five-step reaction sequence. This simple homologation of MAP provides for more efficient catalysis in the allylic alkylation and an opposite stereochemical result compared to that obtained with the use of the MAP ligand. Further studies to address the scope of these binaphthyl-based homologated N,P-ligands in other asymmetric catalytic reactions are currently in progress.

4. Experimental

4.1. General

IR spectra were recorded on an IlluminatIR FT-IR microspectrometer. Optical rotations were measured with a Rudolph Research Autopol III polarimeter. ^{1}H NMR spectra were recorded on a Varian Germini 300 (300 MHz) with TMS as an internal reference. ^{13}C NMR spectra were recorded on a Bruker AMX 400 (100 MHz) with TMS or $CDCl_3$ as an internal reference. High-resolution mass spectra were recorded on a JEOL JMS-AX505WA spectrometer. Elemental analyses were performed at the Korea Research Institute of Chemical Technology, Daejon. Chiral HPLC analysis was performed on a Jasco LC-1500 Series HPLC system with a UV detector. TLC was performed on Merck silica gel 60 F_{254} precoated glass backed plates. All reactions were carried out in oven-dried glassware under an argon atmosphere and the solvents were dried by distillation before use.

4.2. General procedure for the synthesis of amides 7a–7d

To a solution of amine (3.0 mmol) in 3 mL of toluene was added 2.0 M trimethylaluminum (1.5 mL in toluene, 3.0 mmol) and the reaction mixture was stirred for 30 min at 0 °C under an argon atmosphere. After the addition of ester **6** (512 mg, 1.0 mmol) in 6 mL of toluene, the resulting solution was heated at reflux for 6 h and cooled to 0 °C. Aqueous 1 M HCl (5 mL) was slowly added to the solution, followed by addition of saturated $NaHCO_3$ (50 mL). The mixture was extracted with ethyl acetate (50 mL × 3), and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel eluted with dichloromethane/methanol (30:1) to give the desired amide.

4.2.1. (*R*)-2-(Pyrrolidine-1-carbonyl)-2′-diphenylphosphinyl-1,1′-binaphthyl 7a. Yield (96%) as a white solid (mp 179–180 °C); $[\alpha]_D^{25} = +170.0$ (*c* 1.00, THF); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.86 (m, 1H), 1.57 (m, 3H), 3.27 (m, 3H), 6.94–7.85 (m, 22H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.75, 25.39, 45.35, 48.54, 123.59, 125.76, 125.88, 125.95, 126.25, 126.88, 127.06, 127.24, 127.30, 127.46, 127.58, 127.62, 127.74, 127.78, 130.86, 130.89, 130.95, 130.99, 131.40, 131.52, 131.62, 131.75, 132.79, 133.01, 133.16, 133.33, 133.50, 133.53, 133.87, 134.14, 134.30, 134.38, 134.53, 134.85, 134.91, 143.20, 143.29, 168.21; IR (solid) 3050, 2961, 2870, 1614, 1414, 1198 cm^{-1}; HRMS calcd for $C_{37}H_{30}NO_2P$ $[M]^+$: 551.2014, found: 551.2016; Anal. Calcd for $C_{37}H_{30}NO_2P$: C, 80.56; H, 5.48; N, 2.54. Found: C, 80.20; H, 5.65; N, 2.28.

4.2.2. (*R*)-2-(*N*,*N*-Dimethylcarbamoyl)-2′-diphenylphosphinyl-1,1′-binaphthyl 7b. Yield (93%) as a white solid (mp 266–267 °C); $[\alpha]_D^{25} = +192.8$ (*c* 1.00, THF); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.66 (d, 6H), 6.98–7.86 (m, 24H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.92, 39.44, 123.96, 126.05, 126.11, 126.53, 127.00, 127.40, 127.56, 127.65, 127.85, 127.91, 128.02, 128.07, 128.29, 128.71, 130.81, 131.13, 131.17, 131.23, 131.26, 131.62, 131.75, 131.84, 131.98, 132.36, 132.93, 133.15, 133.75, 133.78, 133.83, 133.93, 134.42, 134.53, 135.20, 135.46, 135.52, 170.15; IR (solid) 3054, 2928, 1629, 1178, 1112 cm^{-1}; HRMS calcd for $C_{35}H_{28}NO_2P$ $[M]^+$: 525.1858, found: 525.1848; Anal. Calcd for $C_{35}H_{28}NO_2P$: C, 79.98; H, 5.37; N, 2.67. Found: C, 79.64; H, 5.73; N, 2.66.

4.2.3. (*R*)-2-(Piperidine-1-carbonyl)-2′-diphenylphosphinyl-1,1′-binaphthyl 7c. Yield (98%) as a white solid (mp 114–115 °C); $[\alpha]_D^{25} = +203.1$ (*c* 1.00, THF); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (m, 6H), 1.71 (m, 4H), 7.25–7.87 (m, 22H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.10, 25.25, 25.65, 42.10, 48.17, 123.19, 125.58, 127.61, 127.98, 128.14, 130.73, 131.44–131.65, 132.57, 132.81, 133.03,

133.40, 168.43 (120 < peaks δ < 134 could not be resolved); IR (solid) 3049, 2930, 2850, 1625, 1433, 1200 cm^{-1}; HRMS calcd for $C_{38}H_{32}NO_2P$ $[M]^+$: 565.2171, found: 565.2169; Anal. Calcd for $C_{38}H_{32}NO_2P$: C, 80.69; H, 5.70; N, 2.48. Found: C, 80.50; H, 5.98; N, 2.34.

4.2.4. (*R*)-2-(Morpholine-4-carbonyl)-2′-diphenylphosphinyl-1,1′-binaphthyl 7d. Yield (93%) as a white solid (mp 189–190 °C); $[\alpha]_D^{25} = +179.1$ (*c* 1.00, THF); ^1H NMR (300 MHz, $CDCl_3$) δ 3.34 (m, 4H), 3.47 (m, 4H), 7.17–8.07 (m, 22H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 41.41, 46.29, 66.23, 66.46, 123.36, 126.35–127.73, 130.89–133.22, 168.77 (122 < peaks δ < 134 could not be resolved); IR (solid) 3051, 2959, 2851, 1628, 1432, 1424, 1198 cm^{-1}; HRMS calcd for $C_{37}H_{30}NO_3P$ $[M]^+$: 567.1858, found: 567.1960; Anal. Calcd for $C_{37}H_{30}NO_3P$: C, 78.29; H, 5.33; N, 2.47. Found: C, 77.87; H, 5.69; N, 2.43.

4.3. General procedure for the synthesis of aminophosphine 5a–5d

To a solution of amide **7** (0.49 mmol) and triethylamine (2.7 mL, 19.4 mmol) in 12 mL of toluene was added trichlorosilane (0.60 mL, 5.9 mmol), followed by heating at 100 °C for 6 h and cooling to 0 °C. The reaction solution was quenched by slow addition of saturated $NaHCO_3$ (1 mL), diluted with 50 mL of dichloromethane, and filtered through a Celite pad. The filtrate was added with 30 mL of brine and extracted with dichloromethane (40 mL × 2). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel eluted with dichloromethane/methanol (50:1) to give the desired aminophosphine **5**.

4.3.1. (*R*)-2-Pyrrolidinylmethyl-2′-diphenylphosphino-1,1′-binaphthyl 5a. Yield (86%) as a white solid (mp 81–82 °C); $[\alpha]_D^{25} = +62.0$ (*c* 1.00, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.56 (s, 4H), 2.17 (s, 4H), 2.98 (d, $J = 14$ Hz, 1H), 3.27 (d, $J = 14$ Hz, 1H), 6.79 (d, $J = 8$ Hz, 1H), 7.00 (dd, $J = 14$, 7 Hz, 3H), 7.13 (dd, $J = 18$, 10 Hz, 2H), 7.26 (m, 8H), 7.46 (dd, $J = 9$, 7 Hz, 2H), 7.88 (dd, $J = 15$, 7 Hz, 3H), 7.97 (d, $J = 8$ Hz, 1H); ^{31}P NMR (75 MHz, $CDCl_3$) δ −15.30 (s, 1P); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.45, 54.02, 57.30, 125.03, 125.56, 126.00, 126.33, 126.38, 127.71, 127.80, 127.83, 128.00, 128.09, 128.15, 128.25, 128.33, 130.37, 130.40, 132.27, 132.66, 132.76, 133.06, 133.10, 133.29, 133.44, 133.53, 133.56, 133.69, 134.56, 134.68, 135.54, 135.69, 136.61, 137.35, 137.53, 137.58, 137.76, 143.84, 144.30; IR (solid) 3046, 2953, 2779, 1431 cm^{-1}; HRMS calcd for $C_{37}H_{32}NP$ $[M]^+$: 521.2272, found: 521.2259; Anal. Calcd for $C_{37}H_{32}NP$: C, 85.19; H, 6.18; N, 2.69. Found: C, 85.19; H, 6.48; N 2.60.

4.3.2. (*R*)-2-Dimethylaminomethyl-2′-diphenylphosphinyl-1,1′-binaphthyl 5b.[11] Yield (78%) as a white solid (mp 68–69 °C); $[\alpha]_D^{25} = +105.7$ (*c* 1.00, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.92 (s, 6H), 2.78 (d, $J = 14$ Hz, 1H), 3.05 (d, $J = 14$ Hz, 1H), 6.79 (d, $J = 8$ Hz, 1H), 6.96–7.48 (m, 16H), 7.84–7.99 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 45.56, 61.50, 126.09, 125.61, 125.84, 126.34, 126.45, 126.84, 126.88, 127.74, 127.81, 127.88, 128.02, 128.11, 128.19, 128.26, 128.34, 132.34, 132.61, 132.71, 133.14, 133.18, 133.33, 133.46, 133.46, 133.60, 133.71, 135.07, 135.19, 135.73, 135.87, 136.44, 136.47, 137.36, 137.54, 137.60, 137.78, 143.79, 144.26; IR (solid) 3046, 2811, 2762, 1431 cm^{-1}; HRMS calcd for $C_{35}H_{30}NP$ $[M]^+$: 495.2116, found: 494.2071; Anal. Calcd for $C_{35}H_{30}NP$: C, 84.82; H, 6.10; N, 2.83. Found: C, 84.84; H, 6.47; N 2.76.

4.3.3. (*R*)-2-Piperidinomethyl-2′-diphenylphosphino-1,1′-binaphthyl 5c. Yield (85%) as a white solid (mp 86–87 °C); $[\alpha]_D^{25} = +56.3$ (*c* 1.00, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.21 (m, 2H), 1.39 (m, 4H), 1.97 (s, 4H), 2.95 (dd, $J = 18$, 10 Hz, 2H), 6.79 (d, $J = 8$ Hz, 1H), 7.00 (dd, $J = 14$, 7 Hz, 3H), 7.13 (dd, $J = 18$, 10 Hz, 2H), 7.26 (m, 8H), 7.46 (dd, $J = 8$, 7 Hz, 2H), 7.78 (m, 5H), 7.88 (dd, $J = 15$, 7 Hz, 3H); ^{31}P NMR (75 MHz, $CDCl_3$) δ −15.18 (s, 1P); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.20, 25.90, 54.48, 60.94, 124.95, 125.51, 125.96, 126.26, 126.29, 126.79, 126.93, 126.96, 127.51, 127.71, 127.74, 127.81, 128.00, 128.09, 128.17, 128.26, 128.35, 128.47, 130.40, 130.43, 132.29, 132.74, 132.84, 133.22, 133.27, 133.47, 133.54, 133.79, 135.07, 135.19, 135.28, 135.43, 136.65, 137.35, 137.52, 137.69, 137.84, 144.04, 144.50; IR (solid) 3047, 2926, 1431 cm^{-1}; HRMS calcd for $C_{38}H_{34}NP$ $[M]^+$: 535.2429, found: 535.2430; Anal. Calcd for $C_{38}H_{34}NP$: C, 85.21; H, 6.40; N, 2.61. Found: C, 84.96; H, 6.60; N, 2.44.

4.3.4. (*R*)-2-Morpholinomethyl-2′-diphenylphosphino-1,1′-binaphthyl 5d. Yield (85%) as a white solid (mp 83–84 °C); $[\alpha]_D^{25} = +45.3$ (*c* 1.00, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 2.04 (s, 4H), 2.98 (dd, $J = 19$, 14 Hz, 2H), 3.48 (m, 4H), 6.79 (d, $J = 9$ Hz, 1H), 7.18 (m, 13H), 7.46 (m, 2H), 7.91 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 53.42, 60.40, 66.84, 125.15, 125.63, 125.90, 126.29, 126.34, 126.74, 126.81, 127.68, 127.84, 127.87, 128.00, 128.09, 128.17, 128.28, 128.30, 128.38, 130.29, 130.29, 130.32, 132.36, 132.21, 133.27, 133.40, 133.49, 133.54, 133.67, 135.20, 135.35, 135.41, 135.45, 135.56, 135.6, 137.20, 137.38, 137.42, 137.60, 143.70, 144.16; IR (solid) 3047, 2849, 2803, 1290, 1113 cm^{-1}; HRMS calcd for $C_{37}H_{32}NOP$ $[M]^+$: 537.2222, found: 537.2214; Anal. Calcd for $C_{37}H_{32}NOP$: C, 82.66; H, 6.00; N, 2.61. Found: C, 82.75; H, 6.34; N, 2.54.

4.4. Procedure for Pd-catalyzed allylation of 1,3-diphenylpropenyl acetate with dimethyl malonate using ligand 5a

To a solution of $[Pd(C_3H_5)Cl]_2$ (2 mg, 0.006 mmol) in 1 mL of THF was added ligand **5a** (10 mg, 0.02 mmol) under an argon atmosphere, and the reaction mixture stirred at room temperature for 30 min. A premixed solution of 1,3-diphenylpropenyl acetate (51 mg, 0.20 mmol), KOAc (6 mg, 0.06 mmol), dimethyl malonate (0.07 mL, 0.6 mmol), and *N*,*O*-bis(trimethylsilyl)acetamide (BSA, 0.15 mL, 0.6 mmol) in 3 mL of THF was added the catalyst solution via cannula and the resulting mixture was stirred at ambient temperature. The reaction was quenched by addition of aqueous saturated NH_4Cl (3 mL) and the product extracted with CH_2Cl_2 (10 mL × 3). The combined

organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel eluted with ethyl acetate/hexanes (1:10) to give (*R*)-**9** as a colorless solid (302 mg, 98%). The enantiomeric excess (93%) was determined by HPLC with a chiral stationary phase column, Chiralcel OD [hexane/2-propanol = 90:10, flow rate: 1.0 mL/min, retention times: 11.3 min (*R*), 15.8 min (*S*)].

Acknowledgments

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