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Steric influence of *N*-phosphorus-arylimines on the rhodium-catalyzed asymmetric arylation

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ABSTRACT

Examination of the rhodium-catalyzed asymmetric arylation of benzaldehyde-imines bearing ethoxy, isopropoxy, phenyl, cyclohexyl, 3,5-xylyl, and 2,4,6-mesityl *N*-phosphorus activating/protecting groups revealed that bulky *N*-phosphorus groups retarded the arylation and at the same time prevented the competitive hydrolysis of an imine. Although the level of enantioselectivity was dependent favorably on the bulkiness ranging from 88% ee to 53% ee, the reactivity was drastically decreased along with bulkiness ranging from 95% to 3%.

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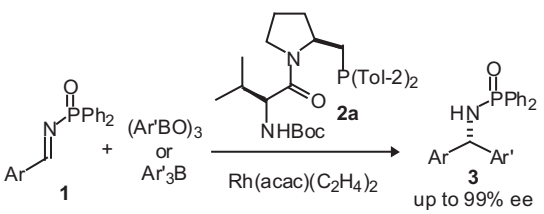
1. Introduction

Diarylmethylamines are key building blocks and potential intermediates for some biologically significant pharmaceuticals.[1] Our studies directed toward the catalytic asymmetric addition reaction of an *N*-PMP (4-methoxyphenyl)-imine were disclosed first in 1990 by using 5 mol % of chiral aminoether as a catalytic controller for the reaction of organolithium reagents.[2] This strategy[3] was successfully extended to the chiral diether[4] or aminoether[5]-controlled asymmetric Mannich-type addition of lithium ester enolate to imines. Chiral amidophosphane–copper(II) catalyst was the second generation for asymmetric alkylation of *N*-sulfonylimine with diorganozinc reagents.[6,7] The continuing studies of catalytic carbon–carbon bond forming reaction resulted in the amidophosphane–rhodium(I) complex-catalyzed asymmetric arylation of *N*-Ts (toluenesulfonyl)-arylimine with arylboronic acids as an aryl group source in 2004,[8] in which *ortho*-trimethylsilyl substituent of arylimine was the key for high enantioselectivity.[9] Then, the more general asymmetric arylation of a *N*-Dpp (diphenylphosphonyl)-arylimine **1** was developed by relying on chiral amidophosphane **2a**, tuned sterically by introducing 2-methyl substituent on diphenyl-phosphane group as one of the keys, which was anticipated by the stereochemical analysis of an imine–Rh(I)–amidophosphane complex (Scheme 1).[10] Produced *N*-Dpp-amide was easily deprotected to the corresponding free amine by mild acidic hydrolysis, being contrasting to the *N*-Ts protecting group, which requires rather harsh conditions to remove off.[9] On the contrary, the major problem in the arylation of *N*-Dpp (diphenylphosphonyl)-arylimine was the competitive imine hydrolysis that was overcome by using water-removing conditions[10a] or water-free conditions.[10b] The present purpose is the study of steric influences of phosphorus *N*-activating/protecting group on the reactivity, enantioselectivity, and competitive imine hydrolysis.



Scheme 1. Sterically tuned-up amidomonophosphane **2a**-Rh(I)-catalyzed arylation under water-removing or water-free conditions.

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In our hypothetical model the C=N double bond of *N*-Dpp-imine **1** is expected to coordinate to rhodium(I) on the *re*-face as shown in **A** to give the product with the observed *S*-configuration (Fig. 1).[10a] Coordination on the *si*-face (**B**) is unfavorable due to steric repulsion between the axial phenyl of the phosphorus (**2b**) and the phenyl group of Dpp. This analysis indicated that the bulkiness of the phenyl group on the phosphorus atom of a ligand favors **A** over **B**, and therefore increased bulkiness around this ligand part is expected to improve the enantioselectivity of the reaction.

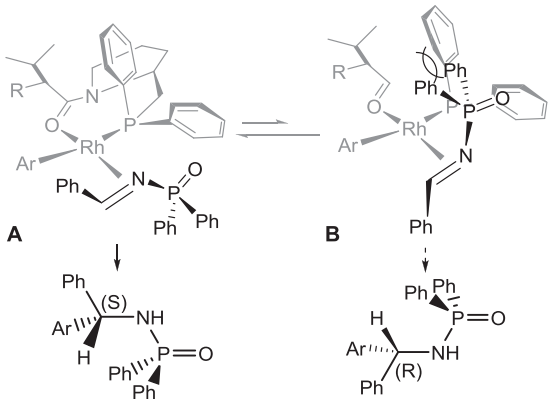


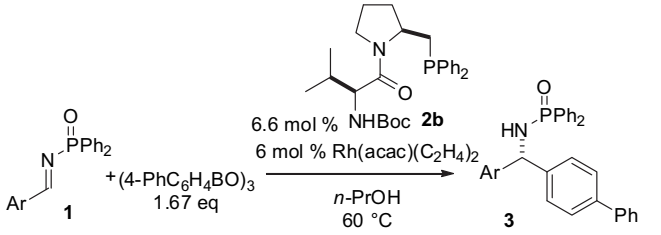
Fig. 1. Imine–Rh(I)–amidophosphane **2b** complexes **A** and **B**.

In order to experimentally confirm this hypothetical model the steric modification of phosphane ligand as shown in **2a** was found to be one certain approach, and examination of the steric influence of imine *N*-phosphorous part should be another possibility that is also another purpose of the present study. We describe the steric influence of *N*-phosphorus-arylimines on reactivity, competitive hydrolysis, and enantioselectivity.

2. Influences of aryl substituents on reactivity, competitive hydrolysis, and enantioselectivity

At first the influence of aryl substituent of the *N*-Dpp-arylimines **1** was examined on the reactivity and enantioselectivity under the established conditions[9] for *N*-Ts-imines by using 6.6 mol % of our prototype diphenylphosphino-ligand **2b**, 6 mol % of Rh(I), and 1.67 equiv of 4-phenylphenylboroxine as an aryl source in *n*-propanol at 60 °C for 2–5 h (Table 1). 4-Phenylphenylation of benzaldehyde-imine **1a** and bulkier 2-trimethylsilylbenzaldehyde-imine **1b** gave the corresponding addition product **3a** with 70% ee in good 95% yield and **3b** with higher 81% ee in 74% yield, respectively, as has been described[10a] (entries 1 and 2). The enantioselectivity was determined by chiral stationary phase HPLC (see Experimental section). 1-Naphthaldimine **1c** afforded **3c** with 78% ee in 93% yield (entry 3). 4-Methylbenzaldehyde-imine **1d** was converted to the corresponding product **3d** with 69% ee in 91% yield (entry 4).[11] Such small reactivity and moderate enantioselectivity dependencies on the bulkiness of aryl substituent indicated the usefulness of the model **A** and **B** where steric interaction may be critical at the *N*-protecting/activating site. Additional support to this hypothetical model is the fact that benzaldehyde-imine bearing a smaller *N*-Ts group was converted to the corresponding amide with somewhat poorer 66% ee in 83% yield,[9] indicating that *N*-Dpp should be a little bit bulkier than *N*-Ts group.

Table 1
Rh(I)-**2b**-catalyzed asymmetric 4-phenylphenylation of imines **1**



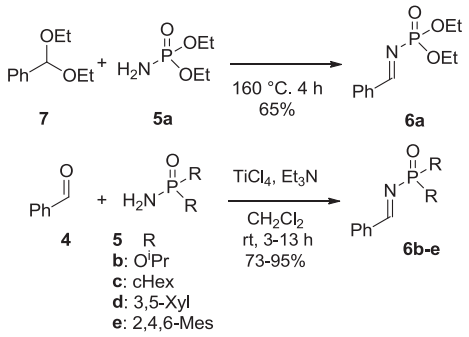
Entry	1	Ar	Time/h	3	Yield/%	ee/%
1[a]	**1a**	Ph	2	**3a**	95	70
2[a]	**1b**	2-TMSC$_6$H$_4$	3.5	**3b**	74	81
3	**1c**	1-Naph	5	**3c**	93	78
4	**1d**	4-MeC$_6$H$_4$	3.5	**3d**	91	69

[a] The data was referred from Ref. 10a.

The reaction of **1a** was further examined at lower 40 °C for prolonged 9 h to give **3a** with 59% ee in 36% yield. The reaction in a different solvent, dioxane, at 100 °C for 2 h gave **3a** with 56% ee in 65% yield, indicating *n*-propanol at 60 °C is the suitable conditions.

3. Preparation of *N*-phosphorus imines

Other benzaldehyde-imines **6** bearing ethoxy, isopropoxy, cyclohexyl, 3,5-xylyl, and 2,4,6-mesityl *N*-phosphorus groups, **6a**,[12] **6b**–**e**,[13] were prepared by the condensation of benzaldehyde **4** or its acetal **7** with the corresponding amides **5a**,[12] **5b**,[14] **5c**,[13] **5d**,[15] and **5e**[16] (Scheme 2).

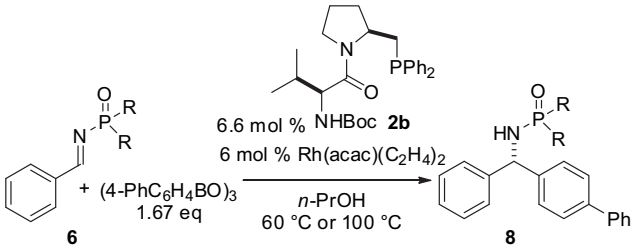


Scheme 2. Preparation of imines **6a**–**e** bearing *N*-phosphorus activating/protecting groups.

4. Asymmetric 4-phenylphenylation of *N*-phosphorus imines

Diethoxyphosphorimide **6a** and isopropoxy derivative **6b** were converted to the corresponding products **8a** with 61% ee in 74% yield and **8b** with 53% ee in 76% yield, suggesting that alkoxy substituents on the phosphorus is not bulky enough than a phenyl group in **1a** (Table 2, entries 1–3). It is important to note the formation of benzaldehyde in each 15% yields by competitive hydrolysis of imines **6a** and **6b**. Dicyclohexyl-phosphorimide **6c** was better than **1a** with regards to enantioselectivity, 78% ee versus 70% ee, however, the reactivity is rather poorer than that of **1a** to give **8c** in only 10% yield and recover **6c** in 81% yield without hydrolysis after 22 h heating at 100 °C[17] (entry 4). Although 3,5-xylyl phosphorimide **6d** was converted to **8d** in 42% yield at 60 °C for 20 h, the enantioselectivity was 67% ee and **6d** was recovered in 40% yield without substantial detection of benzaldehyde (entry 5). Imine **6e** bearing the bulkiest 2,4,6-mesitylphosphorus group was converted to **8e** with expectedly high 88% ee. However, the yield was unsatisfactorily low of only 3% after 8 h at 100 °C[17] and starting imine **6e** was recovered in 89% yield without hydrolysis (entry 6).[18]

Table 2
4-Phenylphenylation of benzaldehyde-imines **6** with various phosphorus *N*-activating/protecting groups



Entry	6	R	Temp/°C	Time/h	8	Yield/%	ee/%
1	**6a**	OEt	60	4	**8a**	74 (15[a])	61
2	**6b**	O^{i}Pr	60	6	**8b**	76 (15[a])	53
3[b]	**1a**	Ph	60	2	**3a**	95	70
4	**6c**	*c*Hex	100[c]	22	**8c**	10 (81[d])	78
5	**6d**	3,5-Xyl	60	20	**8d**	42 (40[d])	67
6	**6e**	2,4,6-Mes	100[c]	8	**8e**	3 (89[d])	88

[a] Recovery % of benzaldehyde.
[b] The data is duplicated from entry 1, Table 1 for easy comparison.
[c] No reaction took place at 60 °C.
[d] Recovery % of starting imine **6** without hydrolysis.

5. Mechanistic insight

Substituents of phenyl group in *N*-Dpp-arylimines influenced not so much on reactivity and enantioselectivity to give products with 81–69% ee in reasonably high yields, indicating the plausibility of hypothetical imine–Rh(I)–amidophosphane complex model. On the other hand, the bulkiness of *N*-phosphorus part influenced much on the reactivity negatively and enantioselectivity positively, implying also plausibility of the model. With bulky *N*-phosphorus groups the competitive hydrolysis of imine was prevented. The poor reactivity of imines bearing bulky *N*-phosphorus part may indicate the difficulty in coordination of imine to Rh(I).

6. Conclusion

Possibility in the control of reactivity, enantioselectivity, and competitive hydrolysis of *N*-phosphorus arylimine was pursued by examining the steric influences of *N*-phosphorus groups on arylation. Although the bulky cyclohexyl and 2,4,6-mesityl *N*-phosphorus groups retarded hydrolysis, but arylation was also blocked. As has been expected from imine–Rh(I)–amidophosphane complex model, the bulkiest mesityl derivative gave the highest enantioselectivity of 88% although the yield was poorest. These clearly indicated the reality and utility of imine–Rh(I)–amidophosphane complex model as the fundamental of our further approach.

7. Experimental

7.1. General

All NMR was recorded at 500 MHz (^{1}H), 125 MHz (^{13}C), and 202 MHz (^{31}P) in $CDCl_3$. Chemical shift was expressed in δ parts per million. Specific rotation was measured in $CHCl_3$.

*7.1.1. P,P-Diphenyl-N-(2-(trimethylsilyl)benzylidene)phosphinic amide (**1b**)[19].* Colorless oil. ^{1}H NMR: 0.33 (9H, s), 7.40–7.55 (8H, m), 7.64 (1H, d, *J*=6.1 Hz), 7.92 (4H, dd, *J*=7.9, 11.7 Hz), 8.33 (1H, d, *J*=7.6 Hz), 9.59 (1H, d, *J*=32.4 Hz). ^{13}C NMR: 0.7 (CH_3), 128.46 (CH), 128.51 (d, *J*=12.4 Hz, CH), 129.4 (CH), 131.7 (d, *J*=8.7 Hz, CH), 131.8 (d, *J*=2.1 Hz, CH), 132.2 (CH), 132.8 (d, *J*=126 Hz, C), 135.0 (CH), 140.9 (C), 144.8 (C), 174.7 (d, *J*=7.2 Hz, CH). IR (KBr): 1585, 1123, 702, 621 cm^{-1}. EIMS *m*/*z*: 377 (M^+). Anal. Calcd for $C_{22}H_{24}NOPSi$: C, 70.00; H, 6.41; N, 3.71. Found: C, 69.72; H, 6.65; N, 3.54.

*7.1.2. Diisopropyl benzylidenephosphoramidate (**6b**)[13].* Colorless oil. ^{1}H NMR: 1.35 (6H, d, *J*=6.1 Hz), 1.39 (6H, d, *J*=6.1 Hz), 4.70–4.85 (2H, m), 7.45–7.55 (2H, m), 7.58 (1H, m), 7.90–8.00 (2H, m), 9.08 (1H, d, *J*=32.4 Hz). ^{13}C NMR: 23.7 (CH_3), 23.9 (CH_3), 72.0 (d, *J*=6.2 Hz, CH_3), 128.9 (CH), 130.4 (CH), 133.8 (CH), 135.5 (d, *J*=29.9 Hz, C), 175.1 (d, *J*=5.2 Hz, CH). IR (KBr): 1631, 995 cm^{-1}. EIMS *m*/*z*: 269 (M^+). HRMS-EI *m*/*z*: calcd for $C_{13}H_{20}NO_3P$, 269.1181. Found: 269.1178.

*7.1.3. N-Benzylidene-P,P-dicyclohexylphosphinic amide (**6c**)[13].* Colorless solid of mp 127–128 °C. ^{1}H NMR: 1.15–1.55 (10H, m), 1.60–1.71 (2H, m), 1.72–1.88 (6H, m), 1.90–2.10 (4H, m), 7.45–7.55 (2H, m), 7.56 (1H, m), 7.91 (2H, d, *J*=7.6 Hz), 9.06 (1H, d, *J*=29.3 Hz). ^{13}C NMR: 24.8 (d, *J*=3.1 Hz, CH_2), 25.3 (d, *J*=4.1 Hz, CH_2), 25.9 (CH_2), 26.2 (CH_2), 26.3 (CH_2), 26.4 (CH_2), 34.4 (CH), 35.0 (CH), 128.9 (CH), 129.8 (CH), 133.1 (CH), 136.0 (d, *J*=22.6 Hz, C), 174.2 (d, *J*=9.2 Hz, CH). ^{31}P NMR: 47.3. IR (KBr): 1627, 1180 cm^{-1}. EIMS *m*/*z*: 317 (M^+). HRMS-EI *m*/*z*: calcd for $C_{19}H_{28}NOP$, 317.1909. Found: 317.1914.

*7.1.4. N-Benzylidene-P,P-bis(3,5-xylyl)phosphinic amide (**6d**)[13].* Colorless solid of mp 75–76 °C. ^{1}H NMR: 2.33 (12H, s), 7.12 (2H, m), 7.45–7.65 (7H, m), 7.02 (2H, d, *J*=7.3 Hz), 9.30 (1H, d, *J*=31.8 Hz). ^{13}C NMR: 21.2 (CH_3), 129.1 (d, *J*=25.7 Hz, CH), 129.2 (CH), 130.2 (CH), 132.7 (d, *J*=126 Hz, C), 133.5 (CH), 133.6 (d, *J*=3.1 Hz, CH), 136.0 (d, *J*=24.7 Hz, C), 138.1 (C), 138.2 (C), 173.3 (d, *J*=8.2 Hz, CH). IR (KBr): 1126, 694 cm^{-1}. EIMS *m*/*z*: 361 (M^+). HRMS-EI *m*/*z*: calcd for $C_{23}H_{24}NOP$, 361.1596. Found: 361.1601.

*7.1.5. N-Benzylidene-P,P-bis(2,4,6-mesityl)phosphinic amide (**6e**)[13].* Colorless solid of mp 149–150 °C. ^{1}H NMR: 2.25 (6H, s), 2.42 (12H, s), 6.82 (2H, s), 6.83 (2H, s), 7.48 (2H, m), 7.54 (1H, m), 7.93 (2H, d, *J*=7.9 Hz), 9.30 (1H, d, *J*=33.0 Hz). ^{13}C NMR: 20.9 (CH_3), 23.0 (d, *J*=3.1 Hz, CH_3), 128.9 (CH), 129.2 (d, *J*=121 Hz, C), 130.2 (CH), 130.8 (d, *J*=13.4 Hz, CH), 133.1 (CH), 136.6 (d, *J*=24.7 Hz, C), 140.9 (d, *J*=3.1 Hz, C), 142.0 (d, *J*=10.3 Hz, C), 171.4 (d, *J*=7.2 Hz, CH). IR (KBr): 1454, 1377, 825 cm^{-1}. EIMS *m*/*z*: 389 (M^+). Anal. Calcd for $C_{25}H_{28}NOP$: C, 77.10; H, 7.25; N, 3.60. Found: C, 77.37; H, 7.27; N, 3.54.

7.2. General procedure for the catalytic asymmetric 4-phenylphenylation of an imine with boroxine

Under argon atmosphere, a reaction flask was charged with $Rh(acac)(C_2H_4)_2$ (15.5 mg, 0.06 mmol), **2b** (31.0 mg, 0.066 mmol), imine **1** (**6**) (1 mmol), and (4-$PhC_6H_4BO)_3$ (902 mg, 1.67 mmol). To the flask was added *n*-PrOH (2.5 mL). The reaction mixture was put in a preheated oil bath (60 °C or 100 °C), and then stirred for 2–22 h at the same temperature. After dilution with AcOEt, the mixture was washed with brine, dried over Na_2SO_4, and then concentrated. The resulting residue was purified through silica gel column chromatography to give **3** (**8**).

*7.2.1. (−)-(S)-N-[Biphenyl-4-yl(phenyl)methyl]-P,P-diphenylphosphinic amide (**3a**).* Chromatography (hexane/acetone=5/1) gave **3a** (438 mg, 95%) as colorless solid of mp 190–191 °C. $[\alpha]_D^{25}$ −27.0 (*c* 0.56, $CHCl_3$). 70% ee (HPLC, Daicel Chiralpak AD, hexane/*i*-PrOH=4/1, 1.0 mL/min, 254 nm, major 14.2 min and minor 17.4 min). ^{1}H NMR: 3.66 (1H, dd, *J*=6.4, 9.8 Hz), 5.50 (1H, dd, *J*=9.8, 11.6 Hz), 7.24–7.35 (8H, m), 7.36–7.40 (4H, m), 7.41–7.49 (4H, m), 7.52 (2H, d, *J*=8.2 Hz), 7.57 (2H, d, *J*=8.2 Hz), 7.84–7.88 (4H, m). ^{13}C NMR: 58.3 (CH), 127.1 (CH), 127.2 (CH), 127.3 (CH), 127.6 (CH), 128.1 (CH), 128.4 (d, *J*=13.4 Hz, CH), 128.6 (CH), 128.8 (CH), 131.9 (CH), 132.3 (d, *J*=8.8 Hz, CH), 132.31 (d, *J*=129 Hz, C), 132.39 (d, *J*=8.8 Hz, CH),

132.41 (d, *J*=129 Hz, C), 140.1 (C), 140.8 (C), 142.4 (d, *J*=4.1 Hz, C), 143.3 (d, *J*=4.1 Hz, C). ^{31}P NMR: 22.3. IR (KBr): 1184, 725, 694 cm^{-1}. EIMS *m*/*z*: 459 (M^+). Anal. Calcd for $C_{31}H_{26}NOP$: C, 81.03; H, 5.70; N, 3.05. Found: C, 80.75; H, 5.87; N, 3.08.

*7.2.2. (−)-N-[Biphenyl-4-yl-(2-trimethylsilylphenyl)methyl]diphenylphosphinic amide (**3b**).* Chromatography (hexane/acetone=5/1) gave **3b** (395 mg, 74%) as colorless solid of mp 211–212 °C. $[\alpha]_D^{25}$ −27.6 (*c* 1.00, $CHCl_3$). 81% ee (HPLC, Daicel Chiralpak OD-H, hexane/*i*-PrOH=10/1, 1.0 mL/min, 254 nm, major 7.8 min and minor 14.9 min). ^{1}H NMR: −0.17 (9H, s), 3.74 (1H, dd, *J*=6.1, 9.8 Hz), 5.83 (1H, dd, *J*=9.8, 11.0 Hz), 7.25 (1H, m), 7.32–7.36 (5H, m), 7.39–7.44 (5H, m), 7.47–7.49 (4H, m), 7.53–7.57 (3H, m), 7.73–7.77 (3H, m), 7.91–7.95 (2H, m). ^{13}C NMR: 0.04 (CH_3), 56.7 (CH), 126.5 (CH), 127.0 (CH), 127.1 (CH), 127.3 (CH), 128.3 (d, *J*=12.4 Hz, CH), 128.6 (d, *J*=12.4 Hz, CH), 128.8 (CH), 129.3 (CH), 129.4 (CH), 131.7 (CH), 131.80 (CH), 131.83 (d, *J*=129 Hz, C), 131.9 (CH), 132.5 (d, *J*=129 Hz, C), 133.1 (d, *J*=10.3 Hz, CH), 134.8 (CH), 138.4 (C), 140.0 (C), 140.7 (C), 143.6 (d, *J*=3.1 Hz, C), 143.6 (d, *J*=4.1 Hz, C). ^{31}P NMR: 20.2. IR (KBr): 1126, 845 cm^{-1}. EIMS *m*/*z*: 531 (M^+). HRMS-EI *m*/*z*: calcd for $C_{34}H_{34}NOPSi$: 531.2147. Found: 531.2153.

*7.2.3. (−)-N-[Biphenyl-4-yl(naphthylmethyl)diphenylphosphinic amide (**3c**).* Chromatography (hexane/acetone=5/1) gave **3c** (473 mg, 93%) as colorless solid of mp 228–229 °C. $[\alpha]_D^{25}$ −12.5 (*c* 1.04, $CHCl_3$). 78% ee (HPLC, Daicel Chiralpak OD-H, hexane/*i*-PrOH=4/1, 1.0 mL/min, 254 nm, major 6.8 min and minor 10.4 min). ^{1}H NMR: 3.76 (1H, dd, *J*=6.8, 9.5 Hz), 6.23 (1H, dd, *J*=9.5, 12.5 Hz), 7.30–7.34 (2H, m), 7.37–7.43 (9H, m), 7.45–7.48 (3H, m), 7.50–7.55 (3H, m), 7.70 (1H, m), 7.72–7.91 (8H, m). ^{13}C NMR: 55.6 (CH), 123.9 (CH), 125.3 (CH), 125.4 (CH), 125.6 (CH), 126.2 (CH), 127.0 (CH), 127.3 (CH), 128.3 (CH), 128.4 (d, *J*=6.2 Hz, CH), 128.5 (d, *J*=12.4 Hz, CH), 128.7 (CH), 128.8 (CH), 130.5 (C), 131.82 (d, *J*=127 Hz, C), 131.84 (d, *J*=2.1 Hz, CH), 131.9 (d, *J*=2.1 Hz, CH), 132.0 (d, *J*=9.3 Hz, CH), 132.4 (d, *J*=9.5 Hz, CH), 132.7 (d, *J*=127 Hz, C), 134.0 (C), 138.4 (d, *J*=5.2 Hz, C), 140.0 (C), 140.7 (C), 142.4 (d, *J*=3.1 Hz, C). IR (KBr): 1184, 752, 698 cm^{-1}. EIMS *m*/*z*: 509 (M^+). Anal. Calcd for $C_{35}H_{28}NOP$: C, 82.49; H, 5.54; N, 2.75. Found: C, 82.23; H, 5.84; N, 2.63.

*7.2.4. (−)-N-[Biphenyl-4-yl-(4-methylphenyl)methyl]diphenylphosphinic amide (**3d**).* Chromatography (hexane/acetone=5/1) gave **3d** (429 mg, 91%) as colorless solid of mp 187–188 °C. $[\alpha]_D^{22}$ −16.3 (*c* 1.09, $CHCl_3$). 69% ee (HPLC, Daicel Chiralpak AD, hexane/*i*-PrOH=4/1, 1.0 mL/min, 254 nm, major 17.0 min and minor 19.2 min). ^{1}H NMR: 2.33 (3H, s), 3.64 (1H, dd, *J*=6.7, 10.1 Hz), 5.47 (1H, dd, *J*=10.1, 11.3 Hz), 7.12 (2H, d, *J*=7.9 Hz), 7.19 (2H, d, *J*=7.9 Hz), 7.32–7.41 (7H, m), 7.42–7.48 (4H, m), 7.49 (2H, d, *J*=7.9 Hz), 7.56 (2H, d, *J*=7.9 Hz), 7.84–7.88 (4H, m). ^{13}C NMR: 21.0 (CH_3), 58.1 (CH), 127.1 (CH), 127.2 (CH), 127.3 (CH), 127.5 (CH), 128.0 (CH), 128.4 (d, *J*=12.4 Hz, CH), 128.8 (CH), 129.3 (CH), 131.9 (CH), 132.3 (d, *J*=8.8 Hz, CH), 132.36 (d, *J*=8.8 Hz, CH), 132.39 (d, *J*=129 Hz, C), 132.5 (d, *J*=129 Hz, C), 136.9 (C), 140.0 (C), 140.4 (d, *J*=5.2 Hz, C), 140.8 (C), 142.6 (d, *J*=4.1 Hz, C). ^{31}P NMR: 22.2. IR (KBr): 1184, 725, 694 cm^{-1}. EIMS *m*/*z*: 473 (M^+). Anal. Calcd for $C_{32}H_{28}NOP$: C, 81.16; H, 5.96; N, 2.96. Found: C, 80.99; H, 5.91; N, 2.88.

*7.2.5. (−)-Diethyl [biphenyl-4-yl(phenyl)methyl]phosphoramidate (**8a**).* Chromatography (hexane/AcOEt=4/1) gave **8a** (294 mg, 74%) as colorless solid of mp 124–125 °C. $[\alpha]_D^{24}$ −13.5 (*c* 0.48, $CHCl_3$). 61% ee (HPLC, Daicel Chiralpak OD-H, hexane/*i*-PrOH=15/1, 1.0 mL/min, 254 nm, major 7.9 min and minor 10.2 min). ^{1}H NMR: 1.19 (3H, dt, *J*=0.9, 7.0 Hz), 1.20 (3H, dt, *J*=0.9, 7.0 Hz), 3.38 (1H, dd, *J*=9.8, 9.8 Hz), 3.83–3.91 (2H, m), 3.98–4.06 (2H, m), 5.47 (1H, dd, *J*=9.8, 9.8 Hz), 7.27–7.36 (8H, m), 7.43 (2H, m), 7.54–7.58 (4H, m). ^{13}C NMR: 15.9 (d, *J*=3.1 Hz, CH_3), 16.0 (d, *J*=3.1 Hz, CH_3), 59.0 (CH), 62.4 (d, *J*=3.1 Hz, CH_2), 127.1 (CH), 127.2 (CH), 127.3 (CH), 127.4 (CH), 127.6 (CH), 128.6 (CH), 128.8 (CH), 140.2 (C), 140.7 (C), 142.3 (d, *J*=5.1 Hz, C), 143.2 (d, *J*=5.1 Hz, C). ^{31}P NMR: 4.55. IR (KBr): 1223, 763, 702 cm^{-1}. EIMS *m*/*z*: 395 (M^+). Anal. Calcd for $C_{23}H_{26}NO_3P$: C, 69.86; H, 6.63; N, 3.54. Found: C, 70.02; H, 6.73; N, 3.53.

*7.2.6. (−)-Diisopropyl [biphenyl-4-yl(phenyl)methyl]phosphoramidate (**8b**).* Chromatography (hexane/AcOEt=4/1) gave **8b** (320 mg, 76%) as a white solid of mp 126–127 °C. $[\alpha]_D^{25}$ −9.8 (*c* 1.05, $CHCl_3$). 53% ee (HPLC, Daicel Chiralpak OD-H, hexane/*i*-PrOH=15/1, 1.0 mL/min, 254 nm, major 4.6 min and minor 5.5 min). ^{1}H NMR: 1.10 (3H, d, *J*=6.1 Hz), 1.11 (3H, d, *J*=6.1 Hz), 1.29 (6H, d, *J*=6.1 Hz), 3.29 (1H, dd, *J*=9.8, 9.8 Hz), 4.52–4.55 (2H, m), 5.47 (1H, dd, *J*=9.8, 9.8 Hz), 7.26 (1H, m), 7.31–7.36 (7H, m), 7.41–7.44 (2H, m), 7.53–7.58 (4H, m). ^{13}C NMR: 23.4 (d, *J*=5.1 Hz), 23.5 (d, *J*=5.1 Hz, CH_3), 23.7 (d, *J*=4.1 Hz, CH_3), 58.9 (CH), 71.0 (d, *J*=5.1 Hz, CH), 127.1 (CH), 127.2 (CH), 127.3 (CH), 127.32 (CH), 127.7 (CH), 128.5 (CH), 128.8 (CH), 140.1 (C), 140.7 (C), 142.6 (d, *J*=5.1 Hz, C), 143.4 (d, *J*=5.1 Hz, C). ^{31}P NMR: 2.64. IR (KBr): 1254, 891, 759 cm^{-1}. EIMS *m*/*z*: 423 (M^+). Anal. Calcd for $C_{25}H_{30}NO_3P$: C, 70.90; H, 7.14; N, 3.31. Found: C, 70.70; H, 7.15; N, 3.25.

*7.2.7. (−)-N-[Biphenyl-4-yl(phenyl)methyl] dicyclohexylphosphinic amide (**8c**).* Chromatography (hexane/acetone=5/1) gave **8c** (48 mg, 10%) as colorless solid of mp 245–246 °C. $[\alpha]_D^{23}$ −15.3 (*c* 0.30, $CHCl_3$). 78% ee (HPLC, Daicel Chiralpak AD, hexane/*i*-PrOH=15/1, 1.0 mL/min, 254 nm, major 46.7 min and minor 42.2 min). ^{1}H NMR: 1.10–1.16 (6H, m), 1.20–1.50 (4H, m), 1.60–1.80 (10H, m), 1.85–1.99 (2H, m), 2.69 (1H, dd, *J*=9.5, 9.5 Hz), 5.71(1H, dd, *J*=9.5, 9.5 Hz), 7.32–7.39 (8H, m), 7.43 (2H, t, *J*=7.9 Hz), 7.52–7.61 (4H, m). ^{13}C NMR: 25.38 (CH_2), 25.40 (CH_2), 25.71 (CH_2), 25.74 (CH_2), 25.77 (CH_2), 25.9 (CH_2), 26.4 (d, *J*=3.1 Hz, CH_2), 26.5 (d, *J*=4.1 Hz, CH_2), 36.3 (d, *J*=11.3 Hz, CH), 37.0 (d, *J*=12.4 Hz, CH), 127.1 (CH), 127.2 (CH), 127.3 (CH), 127.6 (CH), 128.1 (CH), 128.5 (CH), 128.8 (CH), 139.9 (C), 140.8 (C), 143.4 (d, *J*=3.1 Hz, C), 144.2 (d, *J*=3.1 Hz, C). ^{31}P NMR: 45.03. IR (KBr): 1164, 702 cm^{-1}. EIMS *m*/*z*: 471 (M^+). HRMS-EI *m*/*z*: calcd for $C_{31}H_{38}NOP$: 471.2691. Found: 471.2684.

*7.2.8. (−)-N-[Biphenyl-4-yl(phenyl)methyl] bis(3,5-xylyl)phosphinic amide (**8d**).* Chromatography (hexane/Et_2O=5/1) gave **8d** (218 mg, 42%) as colorless solid of mp 218–219 °C. $[\alpha]_D^{23}$ −17.4 (*c* 1.00, $CHCl_3$). 67% ee (HPLC, Daicel Chiralpak AD, hexane/*i*-PrOH=15/1, 1.0 mL/min, 254 nm, major 17.5 min and minor 20.2 min). ^{1}H NMR: 2.249 (6H, s), 2.254 (6H, s), 3.60 (1H, dd, *J*=6.7, 10.1 Hz), 5.49 (1H, dd, *J*=10.1, 11.9 Hz), 7.07 (2H, m), 7.25–7.35 (8H, m), 7.42–7.45 (6H, m), 7.52–7.58 (4H, m). ^{13}C NMR: 21.1 (CH_3), 58.2 (CH), 127.1 (d, *J*=10.3 Hz, CH), 127.3 (d, *J*=8.2 Hz, CH), 127.7 (CH), 128.2 (CH), 128.5 (CH), 128.8 (CH), 129.9 (d, *J*=5.1 Hz, CH), 130.0 (d, *J*=5.1 Hz, CH), 133.56 (CH), 133.59 (CH), 138.1 (d, *J*=11.3 Hz, C), 140.0 (C), 140.9 (C), 142.7 (d, *J*=3.1 Hz, C), 143.5 (d, *J*=5.1 Hz, C). ^{31}P NMR: 22.17. IR (KBr): 1195, 825, 652 cm^{-1}. EIMS *m*/*z*: 515 (M^+). HRMS-EI *m*/*z*: calcd for $C_{35}H_{34}NOP$: 515.2378. Found: 515.2374.

*7.2.9. (−)-N-[Biphenyl-4-yl(phenyl)methyl] bis(2,4,6-mesityl)-phosphinic amide (**8e**).* Chromatography (hexane/acetone=5/1) gave **8e** (14 mg, 3%) as colorless solid of mp 122–123 °C. $[\alpha]_D^{23}$ −18.1 (*c* 0.35, $CHCl_3$). 88% ee (HPLC, Daicel Chiralpak AD, hexane/*i*-PrOH=4/1, 1.0 mL/min, 254 nm, major 11.5 min and minor 27.4 min). ^{1}H NMR: 2.23 (3H, s), 2.24 (3H, s), 2.27 (6H, s), 2.28 (6H, s), 3.68 (1H, dd, *J*=5.2, 9.2 Hz), 5.34 (1H, dd, *J*=9.2, 10.4 Hz), 6.74 (2H, s), 6.75 (2H, s), 7.19–7.27 (7H, m), 7.32 (1H, t, *J*=7.6 Hz), 7.42 (2H, t, *J*=7.6 Hz), 7.46 (2H, d, *J*=8.3 Hz), 7.54 (2H, d, *J*=7.3 Hz). ^{13}C NMR: 20.9 (CH_3), 22.92 (CH_3), 22.96 (CH_3), 22.99 (CH_3), 59.9 (CH), 127.0 (CH), 127.1 (CH), 127.2 (CH), 127.5 (CH), 127.9 (CH), 128.4 (CH), 128.7 (CH), 129.9 (d, *J*=121 Hz, C), 131.0 (d, *J*=122 Hz, C), 130.9 (d, *J*=12.4 Hz, CH), 139.8 (C), 140.45 (C), 140.48 (C), 140.51 (C), 140.9 (C),141.4 (d, *J*=10.3 Hz, C), 141.6 (d, *J*=10.5 Hz, C), 143.0 (d, *J*=5.1 Hz, C), 143.8 (d, *J*=5.1 Hz, C). IR

(KBr): 1161, 721, 648 cm^{-1}. EIMS *m*/*z*: 544 (M+1). Anal. Calcd for $C_{37}H_{38}NOP$: C, 81.74; H, 7.04; N, 2.58. Found: C, 81.91; H, 7.18; N, 2.53.

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