

Rhodium-Catalyzed Asymmetric Phenylation of *N*-Phosphinoylarylimines with Triphenylborane.^a

Xinyu Hao,^b Qian Chen,^c Masami Kuriyama,^b Ken-ichi Yamada,^b Yasutomo Yamamoto^d and Kiyoshi Tomioka^{*d}

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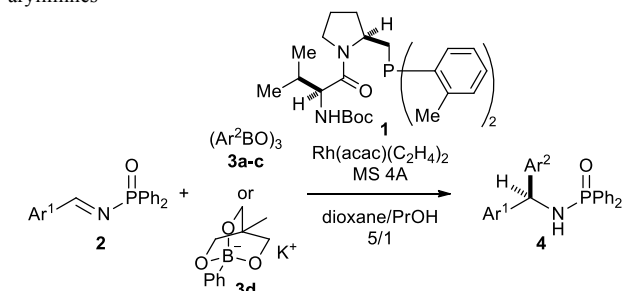
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Triphenylborane asymmetrically transfers its phenyl group to *N*-diphenylphosphinoylarylimines to give diarylmethylamines with high ee in high yield without imine hydrolysis under the catalysis of a chiral amidomonophosphate–rhodium(I) complex.

The success in the chiral amidomonophosphate–rhodium-catalyzed asymmetric arylation of *N*-diphenylphosphinoyl (Dpp) imines with arylboroxines^{1,2} relied on the use of molecular sieves 4A (MS 4A) as a dehydrating agent to realize almost water-free conditions, giving the corresponding diarylmethylamines with extremely high enantioselectivity in satisfactory high yield.^{3,4} For example, the arylation of benzaldehyde *N*-Dpp-imine **2a** with 4-methylphenyl- and 4-methoxyphenylboroxines **3b** and **3c** in a 5:1 mixture of dioxane and propanol in the presence of the 1–Rh(I) catalyst and MS 4A at 80 °C for 12 h gave the corresponding arylated amines (*S*)-**4b** and (*S*)-**4c** with 98% ee each in 96% and 92% yields, respectively (Table 1, entries 1 and 2).⁴ Continuing scope and limitation studies, however, revealed that the reaction of less reactive 4-methyl- and 4-methoxybenzaldehyde *N*-Dpp-imines **2b** and **2c** with phenylboroxine **3a** gave the products (*R*)-**4b** and (*R*)-**4c** with lower 84% and 83% ee in decreased 79% and 10% yields, respectively, probably due to competitive hydrolysis of the imines (entries 3 and 4). Then, our problem solving research was focused on the survey of arylation conditions that give shorter reaction time to avoid the hydrolysis.

Table 1 Scope and Limitation of Asymmetric Arylation of *N*-Dpp-arylimines^a



entry	2	Ar ¹	3	Ar ²	temp (°C)	time (h)	4	yield (%)	ee (%) ^b
1 ^c	2a	Ph	3b	4-MeC ₆ H ₄	80	12	(<i>S</i>)- 4b	96	98
2 ^c	2a	Ph	3c	4-MeOC ₆ H ₄	80	12	(<i>S</i>)- 4c	92	98
3	2b	4-MeC ₆ H ₄	3a	Ph	80	1	(<i>R</i>)- 4b	79	84
4	2c	4-MeOC ₆ H ₄	3a	Ph	80	12	(<i>R</i>)- 4c	10	83
5 ^d	2c	4-MeOC ₆ H ₄	3a	Ph	220	0.15	(<i>R</i>)- 4c	45	68
6 ^{e,f}	2b	4-MeC ₆ H ₄	3d	Ph	80	20	(<i>R</i>)- 4b	0 ^g	-

^a The reaction was conducted with 1.67 equiv of (Ar²BO)₃ in the presence of 6.6 mol % of **1**, and 6.0 mol % of the Rh(I) excepting entry 6. ^b The ee was determined by chiral stationary phase HPLC analysis. ^c See ref 4. ^d Microwave irradiation. ^e 5 equiv of triolborate **3d** was used. ^f Without MS 4A. ^g Racemic phenyl(4-tolyl)methanol, aldehyde adduct, was obtained in 76% yield.

Microwave irradiation of a mixture of **2c** and phenylboroxine **3a** at 220 °C for 10 min was apparently beneficial but not satisfactory to give (*R*)-**4c** with 68% ee in improved 45% yield (entry 5). A cyclic triolborate **3d** failed to give an imine adduct (*R*)-**4b** but gave the corresponding racemic aldehyde adduct, phenyl(4-tolyl)methanol, in 76% yield (entry 6).

Finally, we found triphenylborane as a reactive phenylation reagent to give phenylated amines (*R*)-**4b** and (*R*)-**4c** with 93% ee each in 92% and 91% yields, respectively, without imine hydrolysis. Herein, we report a catalytic asymmetric phenylation of *N*-Dpp-arylimines **2** with triphenylborane. In contrast to the widely used boronic reagents, triarylboranes have not been utilized as an aryl source in asymmetric catalysis,⁶ although a mixture of triphenylborane and diethylzinc has been employed for in situ generation of diphenylzinc.⁷

When a mixture of 4-tolylaldehyde *N*-Dpp-imine **2b** and triphenylborane (1.67 equiv) was heated in propan-1-ol at 100 °C for 12 h in the presence of a catalytic amount of **1** (6.6 mol %) and acetylacetonatobis(ethylene)rhodium(I) (6.0 mol %), the phenylated product (*R*)-**4b** with 81% ee was obtained in 63% yield (Table 2, entry 1). The reaction was then performed in the presence of KF because promotion of a transmetalation process of organoboron reagents by fluoride was described.⁸ The reactions with anhydrous KF and KF on alumina resulted in less satisfactory 39% and 44% yields, and 60% and 81% enantioselectivity, respectively (entries 2 and 3). When the reaction was conducted in the presence of KF on Celite, the reaction more smoothly proceeded to give (*R*)-**4b** with 89% ee in increased 72% yield (entry 4). A mixture of dioxane and propanol⁴ was not suitable solvent for the reaction with triphenylborane, and only a trace amount of the product was produced (entry 5). Finally, *tert*-butanol was found to be the choice to complete the reaction in only 1 h at 100 °C, giving (*R*)-**4b** with 93% ee in 92% yield (entry 6).

Table 2 Survey of Reaction Conditions^a

entry	Solvent	KF source	time (h)	yield (%)	ee (%) ^b
1	PrOH	-	12	63	81
2	PrOH	KF	6	39	60
3	PrOH	KF/Al ₂ O ₃	6	44	81
4	PrOH	KF/Celite	6	72	89
5	dioxane/PrOH (1:1)	KF/Celite	6	<5	-
6	<i>t</i> -BuOH	KF/Celite	1	92	93

^a The reaction was conducted with 1.67 equiv of Ph₃B in the presence of 2.0 equiv of the indicated KF source, 6.6 mol % of **1**, and 6.0 mol % of Rh(acac)(C₂H₄)₂. ^b The ee was determined by chiral stationary phase HPLC analysis.

This asymmetric phenylation with triphenylborane was applicable to other *N*-Dpp-arylimines **2** (Table 3). Phenylation of 3-tolylimine **2d** gave the corresponding **4d** with high 96% ee in high 92% yield (entry 2). Electron-deficient 4-chlorobenzaldimine **2f** bearing a chlorine atom was converted to **4f** with 92% ee in 91% yield (entry 4). Although the reaction of sterically demanding *ortho*-substituted arylimines **2e** and **2g** was slower, the reaction proceeded in highly enantioselective manner to give **4e** and **4g** with 90% ee and 93% ee in 86% and 84% yield, respectively (entries 3 and 5). It is noteworthy that the reaction of 4-methoxybenzaldimine **2c**, miserable results of which were the starting point for this study (Table 1, entry 4), also successfully proceeded for 12 h to give **4c** with 93% ee in 91% yield (entry 6). Polyaromatic 2-naphthaldimine **2h** and heteroaromatic 2-furancarboaldimine **2i** were also good substrates to give **4h** and **4i** with 90% and 91% ee in 94% and 86% yield, respectively (entries 7 and 8).

Table 3 Catalytic Asymmetric Phenylation of *N*-Dpp-arylimines **2** with Triphenylborane^a

entry	2	Ar	time (h)	4	yield (%)	ee (%) ^b
1 ^d	2b	4-MeC ₆ H ₄	1	4b	92	93
2	2d	3-MeC ₆ H ₄	1	4d	92	96
3	2e	2-MeC ₆ H ₄	10	4e	86	90
4	2f	4-ClC ₆ H ₄	1	4f	91	92
5	2g	2-ClC ₆ H ₄	10	4g	84	93
6	2c	4-MeOC ₆ H ₄	12	4c	91	93
7	2h	2-naphthyl	1	4h	94	90
8	2i	2-furyl	1	4i	86	91

^a The reaction was conducted with 1.67 equiv of Ph₃B in the presence of 2.0 equiv of KF/Celite, 6.6 mol % of **1**, and 6.0 mol % of the Rh(I).

^b The ee was determined by chiral stationary phase HPLC analysis. ^d Entry 6 of Table 2 is presented for comparison.

In conclusion, we have developed a widely applicable chiral amidomonophosphane–rhodium-catalyzed enantioselective phenylation of aryl-*N*-Dpp-imines with triphenylborane. The results clearly indicate the utility of triarylborane in avoiding in situ water generation. Because a Dpp group is cleaved under milder acidic conditions than a Boc group,⁹ this reaction provides a versatile methodology to access a variety type of optically active diarylmethylamines.

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Notes and references

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^b Graduate School of Pharmaceutical Sciences, Kyoto University, Yoshida, Sakyo-ku, Kyoto 606-8501, Japan. Fax: 81 75 753 4604; Tel: 81 75 753 4573; E-mail: yamak@pharm.kyoto-u.ac.jp

⁴⁵ ^c The Academy of Fundamental and Interdisciplinary Science, Harbin Institute of Technology, Harbin, Heilongjiang, 150080, P. R. China. E-mail: chenqianlj@yahoocoo.jp

^d Faculty of Pharmaceutical Sciences, Doshisha Women's College of Liberal Arts, Kodo, Kyotanabe 610-0395, Japan. Fax: 81 774 65 8658;

⁵⁰ Tel: 81 774 65 8676; E-mail: tomioka@pharm.kyoto-u.ac.jp

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‡ General procedure of the catalytic asymmetric phenylation: Under argon atmosphere, a round-bottom flask was charged with Rh(acac)(C₂H₄)₂ (3.1 mg, 0.012 mmol), **1** (6.5 mg, 0.013 mmol), **2** (0.200 mmol), triphenylborane (0.334 mmol), and 50% KF on celite (40 mg). To the flask was added *t*-BuOH (0.5 mL), and the mixture was stirred at 100 °C. After the indicated reaction time, the mixture was diluted with AcOEt, washed with brine, dried over Na₂SO₄, and then concentrated. The resulting residue was purified through silica gel column chromatography.

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