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4-Substituted-Phenyl(bisoxazoline)-Rhodium Complexes: Efficiency in the Catalytic Asymmetric Reductive Aldol Reaction

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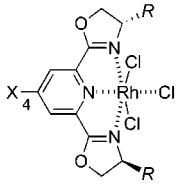
Electronic effects of the substituents on the phenyl ring of the phenyl(bisoxazoline) ligand skeleton of rhodium catalysts was examined in the asymmetric reductive aldol reactions of acrylates and aldehydes. The electron-withdrawing NO_2 group of Rh(4-NO_2-Phebox-R)$(OAc)_2$ showed an increase in the enantioselectivity of the products in the reductive reaction of methyl acrylate but not in the reactions of *tert*-butyl- and trimethylsilyl acrylates. Theoretical calculations of the corresponding model rhodium-Phebox complexes indicate that the remote electron-withdrawing substituent slightly shortens the Rh–C_{phebox} bond. Also, the Rh–C bonds of Rh(4-NO_2-Phebox-*i*Pr)$(OAc)_2$ and the corresponding Rh(4-H-Phebox-*i*Pr)$(OAc)_2$ were compared on the basis of X-ray analysis.

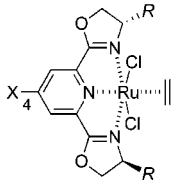
Introduction

In asymmetric catalysis, chiral ligands are inevitable counterparts to metal atoms and aid to control the catalytic activity and stereochemical interaction between substrates and reagents. We have demonstrated *remote electronic control in asymmetric catalysis* and shown that the substituents on the ligands that are situated far from the active metal center can significantly influence the enantioselectivity and the rate of the reaction.[1,2] We have shown that electron-withdrawing groups enhance the reaction rate and induce higher levels of enantioselectivity in the asymmetric hydrosilylation of simple ketones catalyzed by Rh–Pyridine(bisoxazoline) (abbreviated Pybox) and the asymmetric cyclopropanation of olefins with Ru–Pybox. Similar remote electronic effects of ligand–substituents has been observed in both asymmetric and nonasymmetric catalysis.[3–8]

Recently, we reported that chiral Rh–Phebox complexes exhibited high performance in the asymmetric reductive aldol reaction of acrylates and aldehydes with hydrosilanes to give high *anti*-selectivity and high enantioselectivity.[9] The complexes also act as efficient catalysts for the asymmetric conjugate reduction of unsaturated ketones and esters.[10,11] We report here a remote substituent effect in the asymmetric reductive aldol reaction with chiral Rh–Phebox catalysts by using 4-substituted-phenyl(bisoxazoline) ligands.[12–14]



(4-X-Pybox)$RhCl_3$



(4-X-Pybox)$RuCl_2(C_2H_4)$

Results and Discussion

Synthesis of Ligands and Complexes

4-Substituted (X)-Phebox–*i*Pr/H ligands **1a** (X = NO_2), **1c** (X = Me), and **1d** (X = MeO) were readily synthesized in three steps by acid chloride formation of the corresponding 4-substituted isophthalic acids in thionyl chloride, condensation with the appropriate β-amino alcohol, and oxazoline formation with methanesulfonyl chloride and triethylamine, according to the same procedure used for the preparation of prototype **1b** (X = H) (Scheme 1). Heating of a mixture of ligand **1** and $RhCl_3(H_2O)_3$ in a methanol solution gave corresponding chloro complexes **3**. The chloro complexes could in turn be converted into acetato complexes **5** in high yields by treatment with an excess amount of silver acetate. 4-NO_2-Phebox benzyl complex **6** was prepared in the same sequence from ligand **2** and chloro complex **4**.

Structure Analysis

The molecular structure of **5a** was analyzed by X-ray crystallography and showed the C_2 symmetric form (Figure 1). The 4-NO_2-Phebox skeleton meridionally binds to

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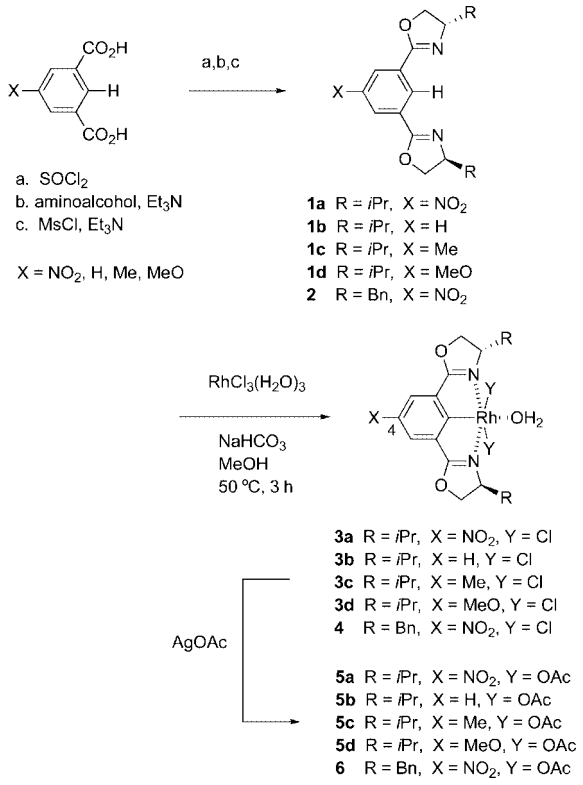


Scheme 1.

the rhodium atom with a Rh–C bond length of 1.914(3) Å compared with 1.923 Å for that of **5b**, whose structure was previously reported.[10a] Thus, 4-NO_2-Phebox rhodium complex **5a** has a slightly shorter Rh–C bond length, and it has a wider N,N bite angle [159.00(10)°] compared with that of **5b** [158.36(7)°].

Theoretical Calculations

Calculations were performed for model isocyanides **7a**–**c** and model aldehyde complexes **9a**–**c** to compare bond lengths, bond angles, and natural charges to those of synthesized compounds **8** and **10**, respectively (Tables 1 and 2).[15–19] Isocyanide complex **8** previously reported by us has a Rh–C_{phebox} bond length of 1.941 Å, whereas the calculation gave a little longer length of 1.97 Å for that of model **7b**.[11d,11f] However, the Rh–$C^2_{isonitrile}$ (2.10 Å) and the C^2–N^2 (1.150–1.168 Å) bond lengths of **7** are in good accordance with those of real complex **8** (2.106 and 1.145 Å, respectively). The NO_2 electron-withdrawing group slightly shortens the Rh–C_{phebox} bond (1.963 Å for **7a**) so that the bite angle N–Rh–N becomes wider when compared with those of **7b** and **7c** (1.970 and 1.971 Å, respectively). This inclination was also found for formaldehyde model complexes **9a**–**c**, 1.923 Å for **9a** versus 1.932 Å for **9c** compared with 1.93 Å for acetone complex **10** previously reported by us.[11d]

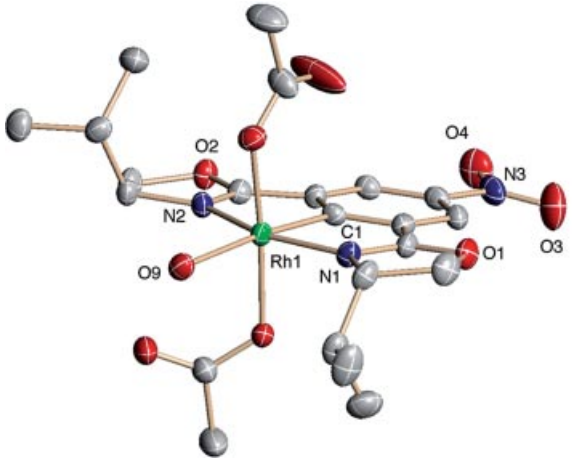


Figure 1. Molecular structure of complex **5a**. Selected bond lengths [Å] and angles [°]: Rh1–C1 1.914(3), Rh1–N1 2.055(3), Rh1–N2 2.057(3), Rh1–O9 2.195(2); C1–Rh1–O9 174.38(12), N1–Rh1–N2 159.00(10), C1–Rh1–N1 79.72(12), C1–Rh1–N2 79.29(12).

As for the natural charges, the electron-withdrawing group influences the charges on C^1 and N^2 for the isocyanide complexes and the charges on C^1 and C^2 for the formaldehyde complexes. As a consequence, the NO_2 group decreases the electron density on the nitrogen atom of the iso-

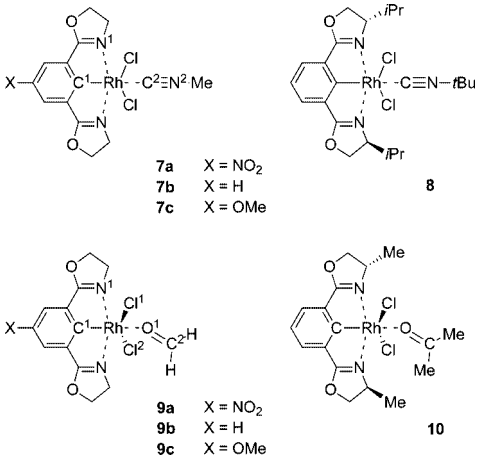
Table 1. Selected bond lengths, bond angle, and natural charges for complexes **7a**–**c**.

Complex		Bond length [Å]					Bond angle [°]	Natural charge			
	X	Rh–C^1	Rh–N^1	Rh–Cl	Rh–C^2	C^2–N^2	N–Rh–N	Rh	C^1	C^2	N^2
7a	NO_2	1.963	2.100	2.410	2.100	1.150	156.5	0.615	0.032	0.333	–0.417
7b	H	1.970	2.090	2.420	2.110	1.168	156.3	0.615	0.023	0.332	–0.424
7c	OMe	1.971	2.100	2.420	2.100	1.150	155.9	0.616	–0.001	0.333	–0.425

Table 2. Selected bond lengths, bond angle, and natural charges for complexes **9a**–**c**.

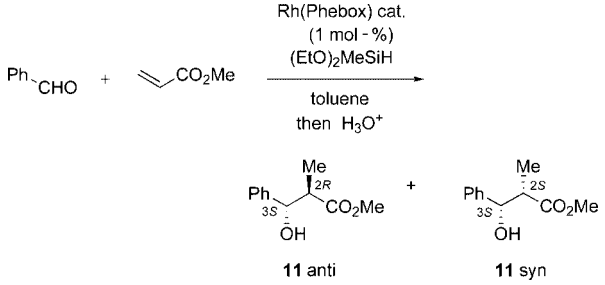
Complex		Bond length [Å]						Bond angle [°]	Natural charge			
	X	Rh–C^1	Rh–N^1	Rh–Cl^1	Rh–Cl^2	Rh–O^1	C^2–O^1	N–Rh–N	Rh	C^1	C^2	O^1
9a	NO_2	1.923	2.090	2.390	2.410	2.350	1.210	158.7	0.721	0.098	0.269	–0.528
9b	H	1.931	2.090	2.390	2.420	2.370	1.210	158.5	0.719	0.090	0.265	–0.526
9c	OMe	1.932	2.090	2.390	2.420	2.370	1.210	158.0	0.719	0.066	0.264	–0.525

cyanide skeleton and the carbon atom of the formaldehyde functionality. In conclusion, it can be thought that the remote substituents on the Phebox skeleton control the electronic state of the equatorial ligand through the rhodium atom to influence the catalytic reactions to some extent.



Asymmetric Reductive Aldol Reactions

The asymmetric reductive coupling reaction of benzaldehyde and methyl acrylate was first examined with 4-substituted/isopropyl catalysts **5a**–**d**, 4-nitro/benzyl catalyst **6** (1 mol-%), and $(EtO)_2MeSiH$ (1.6 equiv.) in a toluene solution heated at 50 °C (Scheme 2; Table 3). The reactions were complete within 0.5 h in all cases to give the aldol products in high yields (93–97%) with not much variance in the *anti*/*syn* product ratios of **11**. 4-Nitro/isopropyl catalyst **5a** and benzyl catalyst **6** gave higher *ee*'s, 87% and 86%, respectively, compared with an *ee* of 77% for both 4-methyl catalyst **5c** and 4-methoxy catalyst **5d**. Thus, a weak electronic effect of the substituent at the 4-position of the phenyl ring was observed.



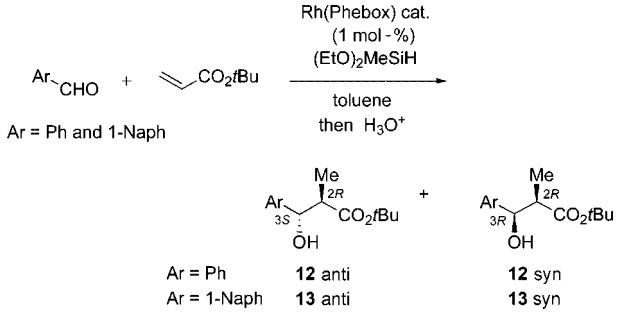
Scheme 2.

Next, when the reaction of *tert*-butyl acrylate as a substrate and benzaldehyde as an acceptor was employed, all of the catalysts exhibited high efficiency and the catalysis proceeded at 50 °C within 0.5 h to again give almost the same *anti*/*syn* ratio of 94:6–96:4 and 92–94% *ee* for aldol products **12** (Scheme 3; Table 4). In the case of 1-naphthaldehyde, not significant, but a slight increase in the ratio and *ee*, 98:2 and 98%, respectively, for aldol product **13** were observed as the highest limit with 4-nitro/benzyl catalyst **6**. Therefore, the differences among the substituents at the 4-position is diminished.

Table 3. Reductive aldol reaction of methyl acrylate and benzaldehyde with Rh(Phebox) catalysts **5** and **6**.[a]

Entry	Catalyst	Yield of **11** [%]	*anti*/*syn*	% *ee anti*	% *ee syn*
1	**5a**	93	88:12	87	1
2	**5b**	97	87:13	83	1
3	**5c**	95	85:15	77	32
4	**5d**	95	85:15	77	28
5	**6**	95	87:13	86	1

[a] Aldehyde (1.0 mmol), catalyst (0.01 mmol), methyl acrylate (1.5 mmol), silane (1.6 mmol), toluene (2 mL), 50 °C, 0.5 h. Absolute configuration, (2*R*,3*S*) for *anti* and (2*S*,3*S*) for *syn*.



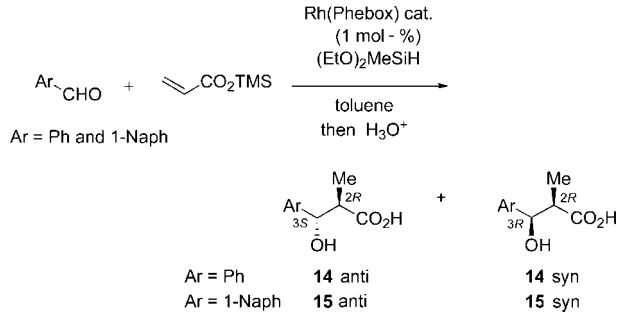
Scheme 3.

Table 4. Reductive aldol reaction of *tert*-butyl acrylate, benzaldehyde, and 1-naphthaldehyde with Rh(Phebox) catalysts **5** and **6**.[a]

Entry	Catalyst	Aldehyde	Yield of **12**,**13** [%]	*anti*/*syn* ratio	% *ee anti*	% *ee syn*
1	**5a**	PhCHO	82	96:4	93	10
2	**5b**	PhCHO	93	95:5	92	10
3	**5c**	PhCHO	94	95:5	92	12
4	**5d**	PhCHO	90	94:6	92	17
5	**6**	PhCHO	90	94:6	94	17
6	**5a**	1-NpCHO	92	98:2	95	31
7	**5b**	1-NpCHO	97	97:3	95	20
8	**5c**	1-NpCHO	99	97:3	95	24
9	**5d**	1-NpCHO	94	96:4	95	14
10	**6**	1-NpCHO	99	98:2	98	8

[a] Aldehyde (1.0 mmol), catalyst (0.01 mmol), *tert*-butyl acrylate (1.5 mmol), silane (1.6 mmol), toluene (2 mL), 50 °C, 0.5 h. Absolute configuration for **12** (2*R*,3*S*) for *anti* and (2*R*,3*R*) for *syn*; for **13** not determined.

Trimethylsilyl acrylate was in turn employed because it may be synthetically important to directly produce the corresponding aldol-carboxylic acid after facile hydrolysis under acidic conditions. The reaction with benzaldehyde in the presence of 4-nitro catalyst **5a** afforded **14** with a slightly lower *anti*/*syn* ratio of 82:18 and 81% *ee* (Scheme 4; Table 5, Entry 1) compared with an *anti*/*syn* ratio of 86:14 and 86% *ee with* catalyst **5b** (Entry 2). However, the reaction of 1-naphthaldehyde with **5a** afforded **15** with good stereoselectivity: *anti*/*syn* ratio 87:13 and 96% *ee* (Entry 4). The electronic effect of the nitro group is not clear from these examples, and it is probably slightly dependent on the substrates. Benzyl catalyst **6** also gave higher *anti*/*syn* ratios (Entries 3, 6).



Scheme 4.

Table 5. Reductive aldol reaction of trimethylsilyl acrylate, benzaldehyde, and 1-naphthaldehyde with Rh(Phebox) catalysts **5** and **6**.[a]

Entry	Catalyst	Aldehyde	Yield of **14**,**15** [%]	*anti*/*syn*	% *ee anti*	% *ee syn*
1	**5a**	PhCHO	87	82:18	81	2
2	**5b**	PhCHO	98	86:14	86	3
3	**6**	PhCHO	93	91:9	88	37
4	**5a**	1-NpCHO	85	87:13	96	23
5	**5b**	1-NpCHO	92	88:12	91	59
6	**6**	1-NpCHO	94	91:9	92	55

[a] Aldehyde (1.0 mmol), catalyst (0.01 mmol), trimethylsilyl acrylate (1.5 mmol), silane (1.6 mmol), toluene (3 mL), 50 °C, 0.5 h. Absolute configuration for **14** (2*R*,3*S*) for *anti* and (2*R*,3*R*) for *syn*; for **15** not determined.

Conclusions

We have demonstrated the synthesis of 4-substituted-phenyl(bisoxazoline) ligands and their rhodium complexes and have examined the catalytic asymmetric reductive aldol reactions with acrylates and aldehydes. We have found that 4-nitro-substituted catalysts show a slight increase in the *anti*/*syn* selectivity and enantioselectivity of the reaction and they also provide the highest limits compared with those of the prototype catalyst. These catalysts also clearly gave higher efficiencies compared with those of the electron-donating group catalysts. Although we cannot clarify whether the electron-withdrawing group enhances the aldol reaction of the rhodium-enolate or the coordination of the aldehyde, we think that the slightly shorter Rh–C_{phebox} bond length, at least in some cases, may influence the transition state of the enantio-determining step of the reaction to cause the increase in the enantioselectivity.

Experimental Section

General: ^{1}H- and ^{13}C NMR spectra were obtained at 25 °C with a Varian Mercury 300 spectrometer. ^{1}H NMR chemical shifts are reported relative to the singlet at δ = 7.26 ppm for chloroform. ^{13}C NMR spectra are reported relative to the triplet at δ = 77.0 ppm for $CDCl_3$ as an internal standard. Infrared spectra were recorded with a JASCO FTIR-230 spectrometer. Absolute toluene and $(EtO)_2MeSiH$ were purchased from TCI. Column chromatography was performed with a silica gel column (Merck Silica gel 60). 5-Nitroisophthalic acid, 5-methylisophthalic acid, and 5-methoxyisophthalic acid were purchased from Aldrich. For preparation of **1b**, **3b**, and **5b**, see ref.[10a]

Synthesis of [(*S*,*S*)-4-NO_2-Phebox-*i*Pr]H (1a): A mixture of 5-nitroisophthalic acid (1.05 g, 5.00 mmol) and thionyl chloride (11 mL) was heated at reflux for 48 h, and the excess thionyl chloride was then removed under reduced pressure to give 5-nitroisophthaloyl chloride, which was used in the next step without further purification. A solution of the acid chloride in CH_2Cl_2 (20 mL) was slowly added to a solution of L-valinol (1.03 g, 10.0 mmol) and triethylamine (10.5 mL) in CH_2Cl_2 (20 mL) at 0 °C. The mixture was stirred at room temp. for 1 h. Methanesulfonyl chloride (0.85 mL, 11 mmol) was added at 0 °C, and the mixture was then stirred at room temp. for 5 h. Formation of product **1a** was monitored by TLC examination. At 0 °C, aqueous potassium carbonate (1 N, ca 30 mL) was added, and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine, dried with magnesium sulfate, and concentrated. The crude product was purified by column chromatography on silica gel (ethyl acetate/hexane, 1:3) to give **1a** as a colorless solid. Yield: 1.05 g (3.05 mmol), 61%. R_f = 0.7 (ethyl acetate/hexane, 2:1. M.p. 66–68 °C. $[\alpha]_D^{28}$ = –97.9 (c 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.95 (d, *J* = 6.6 Hz, 6 H), 1.04 (d, *J* = 6.9 Hz, 6 H), 1.87 (m, 2 H), 4.17 (m, 4 H), 4.48 (m, 2 H), 8.82 (t, *J* = 1.5 Hz, 1 H), 8.86 (d, *J* = 1.5 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.29, 18.91, 32.88, 70.83, 72.98, 125.1, 129.9, 133.1, 148.0, 160.7 ppm. IR (KBr disk): $\tilde{\nu}$ = 1653, 1348, 975 cm^{-1}. $C_{18}H_{23}N_3O_4$ (345.39): calcd. C 62.59, H 6.71, N 12.17; found C 62.61, H 6.67, N 12.18.

[(*S*,*S*)-4-Me-Phebox-*i*Pr]H (1c): Starting from 5-methylisophthalic acid (900 mg, 5.00 mmol). Colorless oil. Yield: 1.28 g, 81%. $[\alpha]_D^{25}$ = –98.5 (c 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.93 (d, *J* = 6.6 Hz, 6 H), 1.03 (d, *J* = 6.9 Hz, 6 H), 1.86 (m, 2 H), 2.41 (s, 3 H), 4.12 (m, 4 H), 4.41 (m, 2 H), 7.90 (d, *J* = 0.9 Hz, 2 H), 8.27 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.13, 19.02, 21.15, 70.11, 72.63, 125.2, 127.9, 131.4, 138.2, 162.8 ppm. IR (KBr disk): $\tilde{\nu}$ = 1652, 1234, 978 cm^{-1}. $C_{19}H_{26}N_2O_2$ (314.42): calcd. C 72.58, H 8.33, N 8.91; found C 72.54, H 8.48, N 8.81.

[(*S*,*S*)-4-MeO-Phebox-*i*Pr]H (1d): Starting from 5-methoxyisophthalic acid (785 mg, 4.00 mmol). Colorless solid. Yield: 1.08 g, 81%. M.p. 75–76 °C. $[\alpha]_D^{27}$ = –105.7 (c 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.92 (d, *J* = 6.6 Hz, 6 H), 1.03 (d, *J* = 6.9 Hz, 6 H), 1.86 (m, 2 H), 3.87 (s, 3 H), 4.12 (m, 4 H), 4.40 (m, 2 H), 7.60 (d, *J* = 1.2 Hz, 2 H), 8.10 (t, *J* = 1.2 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.15, 19.01, 55.74, 70.19, 72.68, 116.3, 120.5, 129.3, 159.2, 162.5 ppm. IR (KBr disk): $\tilde{\nu}$ = 1650, 1595, 1375, 978 cm^{-1}. $C_{19}H_{26}N_2O_3$ (330.42): calcd. C 69.06, H 7.93, N 8.48; found C 68.98, H 8.06, N 8.43.

[(*S*,*S*)-4-NO_2-Phebox-Bn]H (2): Starting from 5-nitroisophthalic acid (1.05 g, 5.00 mmol) and L-phenylalaninol (1.51 g, 10.0 mmol). Colorless oil. Yield: 1.25 g, 56%. $[\alpha]_D^{28}$ = +6.1 (c 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.80 (dd, *J* = 5.7, 13.8 Hz, 2 H), 3.24 (dd, *J* = 5.1, 13.8 Hz, 2 H), 4.21 (dd, *J* = 7.8, 8.7 Hz, 2 H), 4.44 (dd, *J* = 8.7, 9.3 Hz, 2 H), 4.66 (m, 2 H), 7.22–7.35 (m, 10 H), 8.82 (t, *J* = 1.5 Hz, 1 H), 8.87 (d, *J* = 1.5 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 41.60, 68.15, 72.46, 125.3, 126.6, 128.5, 129.1, 129.8, 133.2, 137.3, 148.1, 161.3 ppm. IR (KBr disk): $\tilde{\nu}$ = 1654, 1539, 1346, 974 cm^{-1}. $C_{26}H_{23}N_3O_4$ (441.48): calcd. C 70.73, H 5.25, N 9.52; found C 70.67, H 5.28, N 9.55.

Synthesis of [Rh{(*S*,*S*)-4-NO_2-Phebox-*i*Pr}$(OAc)_2$]·H_2O (5a): $RhCl_3$·$3H_2O$ (579 mg, 2.20 mmol), **1a** (691 mg, 2.00 mmol), and sodium hydrogencarbonate (168 mg, 2.00 mmol) were placed in a 50-mL flask. After addition of methanol (20 mL) and H_2O (1 mL), the mixture was stirred at 60 °C for 5 h. The concentrated residue

was passed through a silica gel column with ethyl acetate/hexane (2:1) as eluent to give **3a** as a brown solid. Yield: 326 mg (0.61 mmol), 30%. M.p. 208 °C (dec). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.94 (d, J = 6.6 Hz, 6 H), 0.99 (d, J = 7.2 Hz, 6 H), 2.41 (m, 2 H), 4.22 (m, 2 H), 4.74–4.88 (m, 4 H), 8.47 (s, 2 H) ppm. Complex **3a** (268 mg, 0.50 mmol) and silver acetate (334 mg, 2.00 mmol) were placed in a 50-mL flask. After addition of CH_2Cl_2 (15 mL), the mixture was stirred at room temp. for 12 h. After filtration and removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel with ethyl acetate/methanol (10:1) to give **5a** as a yellow solid. Yield: 220 mg (0.38 mmol), 76%. M.p. 135 °C (dec). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.71 (d, J = 6.6 Hz, 6 H), 0.98 (d, J = 6.9 Hz, 6 H), 1.66 (s, 6 H), 2.27 (br., 2 H), 2.52 (m, 2 H), 4.45 (m, 2 H), 4.73–4.86 (m, 4 H), 8.48 (s, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.35, 19.15, 23.78, 29.30, 68.09, 71.65, 121.9, 132.1, 145.0, 171.0, 182.2, 200.8 (d, J_{Rh-C} = 24.5 Hz) ppm. $C_{22}H_{30}N_3O_9Rh\cdot$(0.5EtOAc) (627.45): calcd. C 45.94, H 5.46, N 6.70; found C 45.80, H 5.29, N 6.63.

[Rh{(*S*,*S*)-4-Me-Phebox-*i*Pr}(OAc)$_2$]·H$_2$O (5c): The preparation procedure of **3c** was similar to that of **3a** with **1c** (628 mg, 2.00 mmol). Brown solid. Yield: 760 mg (1.50 mmol), 75%. M.p. 157 °C (dec). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.92 (d, J = 6.6 Hz, 6 H), 0.97 (d, J = 7.2 Hz, 6 H), 2.40 (m, 2 H), 3.49 (s, 3 H), 4.26 (m, 2 H), 4.65–4.79 (m, 4 H), 7.44 (s, 2 H) ppm. The preparation procedure of **5c** was similar to that of **5a** with **3c** (253 mg, 0.5 mmol) and silver acetate (334 mg, 2 mmol). Yellow solid. Yield: 186 mg (0.34 mmol), 67%. M.p. 241 °C (dec). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.69 (d, J = 6.6 Hz, 6 H), 0.95 (d, J = 7.2 Hz, 6 H), 1.66 (s, 6 H), 2.51 (m, 2 H), 2.51 (s, 3 H), 3.54 (br., 2 H), 4.38 (m, 2 H), 4.62–4.74 (m, 4 H), 7.44 (d, J = 3.0 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.19, 19.23, 21.55, 24.00, 29.16, 67.65, 70.89, 128.2, 131.3, 133.0, 171.6, 182.1, 184.4 (d, J_{Rh-C} = 23.9 Hz) ppm. $C_{23}H_{33}N_2O_3Rh$ (552.42): calcd. C 50.01, H 6.02, N 5.07; found C 49.85, H 5.82, N 4.84.

[Rh{(*S*,*S*)-4-MeO-Phebox-*i*Pr}(OAc)$_2$]·H$_2$O (5d): The preparation procedure of **3d** was similar to that of **3a** with **1d** (660 mg, 2.00 mmol). Brown solid. Yield: 729 mg (1.40 mmol), 70%. M.p. 156 °C (dec). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.93 (d, J = 6.9 Hz, 6 H), 0.98 (d, J = 7.2 Hz, 6 H), 2.40 (m, 2 H), 3.87 (s, 3 H), 4.28 (m, 2 H), 4.65–4.80 (m, 4 H), 7.24 (s, 2 H) ppm. The preparation procedure of **5d** was similar to that of **5a** with **3d** (261 mg, 0.5 mmol) and silver acetate (334 mg, 2 mmol). Yellow solid. Yield: 212 mg (0.37 mmol), 75%. M.p. 85 °C (dec). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.69 (d, J = 6.6 Hz, 6 H), 0.95 (d, J = 7.2 Hz, 6 H), 1.66 (s, 6 H), 2.51 (m, 2 H), 3.90 (s, 3 H), 4.39 (m, 2 H), 4.62–4.75 (m, 4 H), 7.25 (s, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.49, 19.20, 23.78, 29.34, 56.24, 71.11, 114.4, 131.3, 157.0, 171.5, 176.7 (d, J_{Rh-C} = 24.3 Hz), 182.2 ppm. $C_{23}H_{33}N_2O_8Rh\cdot$(0.2EtOAc) (586.04): calcd. C 48.78, H 5.95, N 4.78; found C 48.66, H 6.01, N 4.71.

[Rh{(*S*,*S*)-4-NO$_2$-Phebox-Bn}(OAc)$_2$]·H$_2$O (6): The preparation procedure of **4** was similar to that of **3a** with **2** (691 mg, 2.00 mmol). Brown solid. Yield: 566 mg (0.90 mmol), 45%. M.p. 162 °C (dec). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.82 (dd, J = 9.6, 14.4 Hz, 2 H), 3.58 (dd, J = 4.80, 15.0 Hz, 2 H), 4.63 (m, 2 H), 4.67 (m, 2 H), 4.83 (m, 2 H), 7.22–7.38 (m, 10 H), 8.50 (s, 2 H) ppm. The preparation procedure of **6** was similar to that of **5a** with **4** (316 mg, 0.5 mmol) and silver acetate (334 mg, 2 mmol). Yellow solid. Yield: 199 mg (0.29 mmol), 59%. M.p. 141 °C (dec). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.73 (s, 6 H), 2.66 (dd, J = 9.6, 14.1 Hz, 2 H), 3.68 (dd, J = 3.3, 13.8 Hz, 2 H), 4.68 (m, 2 H), 4.75 (m, 2 H), 4.79 (m, 2 H), 7.23–7.38 (m, 10 H), 8.51 (s, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 23.81, 39.81, 64.29, 75.85, 122.1, 127.0, 128.8, 129.2, 132.3, 136.1, 145.1, 171.5, 182.4, 200.8 (d, J_{Rh-C} = 24.5 Hz) ppm. $C_{30}H_{30}N_3O_9Rh$ (586.04): calcd. C 53.03, H 4.45, N 6.18; found C 53.03, H 4.27, N 6.36.

X-ray Crystallographic Determination: Single-crystals suitable for X-ray analysis were obtained by recrystallization from hexane/dichloromethane/ethyl acetate at room temp. A crystal was mounted on a CryoLoop with Paratone-N, and diffraction data were collected in θ ranges with graphite-monochromated Mo-K_α radiation (λ = 0.71073 Å). An empirical absorption correction was applied by using SADABS. The structure was solved by direct methods and refined by full-matrix least-squares on F^2 by using SHELXTL. All non-hydrogen atoms except ethyl acetate were refined with anisotropic displacement parameters. Refinement details: Empirical formula. $C_{22}H_{30}N_3O_9Rh\cdot0.3(C_4H_8O_2)$; Mr = 612.77; crystal system: hexagonal; space group: $P6_1$ (#169); a = 17.291(3), b = 17.291, c = 17.575(7) Å; V = 4551(2) Å^3; Z = 6; $\rho_{calcd.}$ = 1.342 Mg m^{-3}; μ = 0.613 mm^{-1}; F(000) = 1896; crystal size = 0.50 × 0.50 × 0.20 mm; θ range = 2.69–27.60°; index ranges: –22 ≤ h ≤ 15, –21 ≤ k ≤ 22, –22 ≤ l ≤ 18; reflections collected: 31924; independent reflections: 6540 [R_{int} = 0.0627]; completeness to θ = 27.60°, 99.2%; max/min transmission: 1.000000/0.702050; data/restraints/parameters: 6540/1/382; goodness-of-fit on F^2: 1.065; Final R indices [$I > 2\sigma(I)$]; $R1$ = 0.0315, $wR2$ = 0.0801; R indices (all data): $R1$ = 0.0364, $wR2$ = 0.0838; absolute structure parameter –0.02(2); largest diff. peak/hole 0.724/–0.462 e Å^{-3}. CCDC-611476 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Computational Methods: Geometry optimizations and atomic charge calculations for the optimized geometries were carried out with the Gaussian 03 program package.[15] The geometries of complexes **7a**–**c**, **9a**–**c** were fully optimized by means of the Becke's three-parameter hybrid density functional method (B3LYP)[16] with the basis set, which uses a double-ζ basis set with the relativistic effective core potential of Hay and Wadt (LanL2 ECP)[17] for Rh and the 6-31G(d)[18] basis sets for other elements. Natural charges were computed at the same level by using the natural population analysis method as implemented in Gaussian 03.[19]

Typical Reactions, 11-*antilsyn* (Table 3, Entry 1)**:** To a mixture of rhodium complex **5a** (5.8 mg, 0.010 mmol) and benzaldehyde (106 mg, 1.00 mmol) in toluene (2.0 mL), methyl acrylate (129 mg, 135 μL, 1.50 mmol) was added at 50 °C. Diethoxymethylsilane (215 mg, 1.60 mmol) was then slowly added by a syringe. The mixture was stirred at 50 °C for 0.5 h. At 0 °C, ethanol (1 mL) was added and the solvent was removed under reduced pressure. THF (1 mL), MeOH (1 mL), and aq HCl (4 N, 1 mL) were added and the mixture was stirred for 30 min. A saturated aqueous solution of sodium hydrogencarbonate (15 mL) was added and the mixture was extracted with ethyl acetate (3 × 5 mL). The combined organic layers were dried with $MgSO_4$. After concentration, the residue was purified by silica gel column chromatography with hexane/ethyl acetate as an eluent to give the mixture of desired products **11**-*anti* and **11**-*syn* in 93% (182 mg, 0.93 mmol). The *antilsyn* ratio was determined by ^{1}H NMR and found to be 88:12. The optical purity was determined by HPLC analysis with DAICEL-CHIRALCEL OD (eluent: hexane/*i*PrOH = 97:3, flow rate: 1.0 mL/min) and found to be 87% *ee* (2*R*,3*S*) for *anti*; retention time: 13.1 (*syn*, 2*R*,3*R*), 15.8 (*syn*, 2*S*,3*S*), 20.2 (*anti*, 2*R*,3*S*), 37.1 min (*anti*, 2*S*,3*R*); for HPLC analysis, see ref.[20] **11**-*anti*: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.02 (d, J = 7.2 Hz, 3 H), 2.82 (m, 1 H), 2.90 (d, J =

4.5 Hz, 1 H, O*H*), 3.73 (s, 3 H), 4.75 (dd, *J* = 8.4, 4.5 Hz, 1 H), 7.26–7.41 (m, 5 H) ppm. **11**-*syn*: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.13 (d, *J* = 6.9 Hz, 3 H), 3.68 (s, 3 H), 5.12 (d, *J* = 3.6 Hz, 1 H), 7.26–7.41 (m, 5 H) ppm. NMR spectra were consistent with the authentic data previously reported in ref.[14a]

12-*antilsyn* (Table 4, Entry 1)**:** The reaction procedure was the same as that of Entry 1, Table 1: *tert*-butyl acrylate (192 mg, 1.50 mmol). A mixture of products **12**-*anti* and **12**-*syn* (96:4, determined by ^{1}H NMR) was obtained as a colorless oil. Yield: 195 mg (0.82 mmol), 82%. The optical purity was determined by HPLC analysis with DAICEL-CHIRALPAK AS-H (eluent: hexane/*i*PrOH = 99:1, flow rate: 1.0 mL/min) to be 93% *ee* (2*R*,3*S*) for *anti* and 10% *ee* (2*R*,3*R*) for *syn*. Retention time: 8.9 (*syn*, 2*R*,3*R*), 11.4 (*anti*, 2*S*,3*R*), 13.4 (*syn*, 2*S*,3*S*), 15.1 min. (*anti*, 2*R*,3*S*). **12**-*anti*: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.02 (d, *J* = 6.9 Hz, 3 H), 1.44 (s, 9 H), 2.67 (m, 1 H), 3.11 (br., 1 H), 4.70 (dd, *J* = 8.1, 4.8 Hz, 1 H), 6.91–7.38 (m, 5 H) ppm. **12**-*syn*: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.10 (d, *J* = 7.2 Hz, 3 H), 1.40 (s, 9 H), 2.67 (m, 1 H), 3.11 (br., 1 H), 5.03 (dd, *J* = 4.2, 3.0 Hz, 1 H), 6.91–7.38 (m, 5 H) ppm. NMR spectra were consistent with the authentic data previously reported in ref.[9]

13-*antilsyn* (Table 4, Entry 6)**:** The reaction procedure was the same as that of Entry 1, Table 1: *tert*-butyl acrylate (192 mg, 1.50 mmol) and 1-naphthaldehyde (156 mg, 1.00 mmol). A mixture of products **13**-*anti* and **13**-*syn* (98:2, determined by ^{1}H NMR) was obtained as a colorless oil. Yield: 263 mg (0.92 mmol), 92%. The optical purity was determined by HPLC analysis with DAICEL-CHIRALPAK AD (eluent: hexane/*i*PrOH = 99:1, flow rate: 2.0 mL/min) to be 95% *ee* (2*R*,3*S*) for *anti* and 31% *ee* for *syn*. Retention time: 11.9 (*syn*, major), 15.1 (*syn*, minor), 17.6 (*anti*, 2*R*,3*S*), 24.3 min. (*anti*, 2*S*,3*R*). **13**-*anti*: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.12 (d, *J* = 7.5 Hz, 3 H), 1.52 (s, 9 H), 3.09 (dq, *J* = 7.5 × 3 and 6.9 Hz, 1 H), 3.67 (d, *J* = 4.8 Hz, 1 H), 5.55 (dd, *J* = 7.8, 4.8 Hz, 1 H), 7.50–7.65 (m, 4 H), 7.70–7.93 (m, 2 H), 8.27 (d, *J* = 8.1 Hz, 1 H) ppm. **13**-*syn*: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.14 (d, *J* = 7.2 Hz, 3 H), 1.50 (s, 9 H), 2.99 (dq, *J* = 7.2 × 3 and 3.0 Hz, 1 H), 3.28 (br., 1 H), 5.97 (br. s, 1 H), 7.50–7.65 (m, 4 H), 7.70–7.93 (m, 2 H), 8.27 (d, *J* = 8.2 Hz, 1 H) ppm. NMR spectra were consistent with the authentic data previously reported in ref.[9]

14-*antilsyn* (Table 5, Entry 3)**:** The reaction procedure was the same as that of Entry 1, Table 1: trimethylsilyl acrylate (216 mg, 1.50 mmol) and **6** (6.8 mg, 0.010 mmol). After work up, the crude product was purified by chromatography with ethyl acetate as an eluent to give a mixture of desired products **14**-*anti* and **14**-*syn* (91:9, determined by ^{1}H NMR) as a colorless solid. Yield: 168 mg (0.93 mmol), 93%. Some of the product was converted into methyl ester **11** with trimethylsilyl diazomethane for determination of the optical purity (HPLC): 88% *ee* (2*R*,3*S*) for *anti* and 37% *ee* (2*R*,3*R*) for *syn*. ^{1}H NMR (300 MHz, $CDCl_3$): **14**-*anti*: δ = 1.03 (d, *J* = 7.5 Hz, 3 H), 2.86 (dq, *J* = 7.5 × 3 and 9.0 Hz, 1 H), 4.77 (d, *J* = 9.0 Hz, 1 H), 7.30–7.40 (m, 5 H) ppm. **14**-*syn*: δ = 1.15 (d, *J* = 7.2 Hz, 3 H, CH_3), 5.19 (d, *J* = 3.9 Hz, 1 H, C*H*OH) ppm. Mixture of **14**: $C_{10}H_{12}O_3$ (180.20): calcd. C 66.65, H 6.77; found C 66.43, H 6.76.

15-*antilsyn* (Table 5, Entry 4)**:** The reaction procedure was the same as that of Entry 1, Table 1: trimethylsilyl acrylate (216 mg, 1.50 mmol) and 1-naphthaldehyde (156 mg, 1.00 mmol). After work up, the crude product was purified by chromatography with ethyl acetate as an eluent to give a mixture of desired products **15**-*anti* and **15**-*syn* (91:9 determined by ^{1}H NMR) as a colorless solid. Yield: 196 mg (0.85 mmol), 85%. Some of the product was converted into the corresponding methyl ester with trimethylsilyl diazomethane for determination of the optical purity (HPLC)(eluent: hexane/*i*PrOH, 97:3, flow rate: 1.0 mL/min): 96% *ee* for *anti* and 23% *ee* for *syn*. Retention time: 33.4 (*syn*, minor), 36.7 (*syn*, major), 43.5 (*anti*, minor), 49.5 min. (*anti*, major). The absolute configuration was not determined. ^{1}H NMR (300 MHz, $CDCl_3$): **15**-*anti*: δ = 1.06 (d, *J* = 7.2 Hz, 3 H), 3.24 (dq, *J* = 7.2 × 3 and 9.0 Hz, 1 H), 5.56 (d, *J* = 9.0 Hz, 1 H), 7.46–7.60 (m, 4 H), 7.84–7.89 (m, 2 H), 8.27 (m, 1 H) ppm; **15**-*syn*: δ = 1.11 (d, *J* = 7.2 Hz, 3 H, CH_3), 6.10 (d, *J* = 2.1 Hz, 1 H, C*H*OH) ppm; Recrystallization of the acid mixture from ether–hexane gave almost-pure acid **15**-*anti*. M.p. 109–110 °C. IR (KBr disk): $\tilde{\nu}$ = 3500–2600 (br), 1720, 1402, 1265 cm^{-1}. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.95, 46.90, 73.52, 123.4, 124.8, 125.6, 126.2, 128.7, 128.8, 130.9, 133.8, 136.5, 181.1 ppm. $[\alpha]_D^{23}$ = –13.1 (c 1.56, EtOH). $C_{14}H_{14}O_3$ (230.26): calcd. C 73.03, H 6.13; found C 72.93, H 6.12.

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