CHEMISTRY
A EUROPEAN JOURNAL

DOI: 10.1002/chem.200903118

# Iron- and Cobalt-Catalyzed Asymmetric Hydrosilylation of Ketones and Enones with Bis(oxazolinylphenyl)amine Ligands

**Tomohiko Inagaki, Le Thanh Phong, Akihiro Furuta, Jun-ichi Ito, and Hisao Nishiyama*[a]**

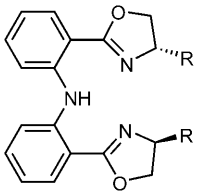
*Dedicated to Professor Kenji Itoh on the occasion of his 70th birthday*

**Abstract:** Chiral bis(oxazolinylphenyl)amines proved to be efficient auxiliary ligands for iron and cobalt catalysts with high activity for asymmetric hydrosilylation of ketones and asymmetric conjugate hydrosilylation of enones.

**Keywords:** asymmetric catalysis · bisoxazoline ligands · cobalt · hydrosilylation · iron

## Introduction

The creation of new chiral ligands that can control the chiral environment around active metal centers is of importance for asymmetric catalysis in organic synthesis. Much attention has focused on multi-nitrogen ligands such as tridentate *N*,*N*,*N*-type ligands bearing a chiral oxazoline skeleton to attain asymmetric catalysis.[1] Among them, tridentate *N*,*N*,*N*-bis(oxazolinylphenyl)amine (Bopa) ligands **1** have been used in asymmetric catalytic reactions such as Nozaki–Hiyama allylation by Guiry and co-workers,[2] and in the Henry reaction, Friedel–Crafts reaction, and nitroalkane Michael addition by Du, Xu et al.[3] Bopa can efficiently act as a chiral tridentate bisoxazoline/amine or bisoxazoline/amide ligand with $C_2$ symmetry in combination with Zn, Cu, and Cr atoms. We are interested in the potential of Bopa as a chiral ligand, and we have reported preliminary data on asymmetric Fe-catalyzed hydrosilylation of ketones with Bopa ligands.[4] Here we present the scope and limitations of asymmetric hydrosilylation of ketones with chiral Bopa ligands in combination with first-row transition metals such as Fe and Co. In addition, we have performed efficient conjugate reduction of enones with a Co–Bopa catalyst and hydrosilane.



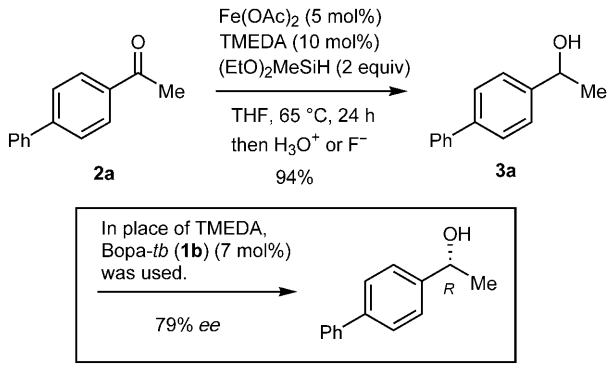

**1a** R = *i*Pr Bopa-*ip*
**1b** R = *t*Bu Bopa-*tb*
**1c** R = $CHPh_2$ Bopa-*dpm*
**1d** R = Ph Bopa-*ph*

Beller et al. reported asymmetric hydrosilylation of ketones with Fe catalysts in combination with several chiral phosphine ligands, and achieved 99% *ee* for hindered aromatic ketones.[5] Recently, Gade et al. applied new chiral bis(pyridylimino)isoindoles and their Fe complexes to asymmetric hydrosilylation to attain high enantioselectivity.[6] Chirik et al. also found that iron bis(imino)pyridine and bis(oxazolinyl)pyridine catalysts exhibit high catalytic activity for hydrosilylation of ketones.[7] The use of ubiquitous iron among the first-row transition metals is very important in terms of environmentally benign processes that avoid precious metals. With regard to Fe-catalyzed reduction of ketones, new asymmetric catalyst systems for transfer hydrogenation and hydrogenation of ketones were reported recently by Beller et al., Morris et al., and Casey et al.[8–11]

We found that $Fe(OAc)_2$-catalyzed hydrosilylation of ketones with several hydrosilanes can be readily promoted in the presence of *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA, Scheme 1).[4a] When we adopted Bopa-*tb* (**1b**, 7 mol%) as a chiral ligand in place of TMEDA, we observed

[a] T. Inagaki, L. T. Phong, A. Furuta, Assist. Prof. Dr. J.-i. Ito, Prof. Dr. H. Nishiyama
Department of Applied Chemistry
Graduate School of Engineering, Nagoya University
Chikusa, Nagoya, 464–8603 (Japan)
Fax: (+81) 52-789-3209
E-mail: hnishi@apchem.nagoya-u.ac.jp

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.200903118.

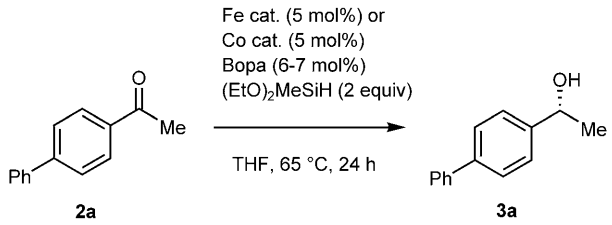



Scheme 1. Previously reported iron-catalyzed hydrosilylation reactions.

the highest enantioselectivity of 79%. We used this as a starting point to study the scope and limitations of iron catalysts in combination with chiral Bopa ligands.

## Results and Discussion

**Asymmetric hydrosilylation of ketones with Fe and Co Bopa catalysts**: We previously reported asymmetric hydrosilylation of methyl 4-phenylphenyl ketone (**2a**) catalyzed by iron(II) acetate (5 mol%) and Bopa-*ip* (**1a**) or Bopa-*tb* (**1b**) (7 mol%) with $(EtO)_2MeSiH$ (2.0 equiv) in THF at 65°C for about 24 h with 75–85% yield and 57–79% *ee*.[4] As bulky substituents on the oxazoline rings resulted in higher enantioselectivity, we examined the substrate scope with Bopa-*tb* (**1b**), new ligand Bopa-*dpm* (**1c**), and Bopa-*ph* (**1d**; Scheme 2 and Table 1, entries 1–6). The catalyst was pre-




Scheme 2. Asymmetric hydrosilylation of methyl-4-phenylphenyl ketone (**2a**).

pared by heating a mixture of $Fe(OAc)_2$ (5.0 mol%) and Bopa (7.0 mol%) in THF at 65°C in the presence of the ketone. Then the hydrosilane was added and the mixture was stirred for 24 h. After hydrolytic workup, the product secondary alcohol **3a** was isolated by column chromatography. Compared to 61% *ee* with Bopa-*ip*, Bopa-*tb* and Bopa-*dpm* gave slightly higher enantioselectivities of 68 and 73%, respectively (Table 1, entries 2–5). A lower catalyst loading of 0.5 mol% with Bopa-*dpm* resulted in almost the same result as with 5 mol% (Table 1, entry 5). Two equivalents of the hydrosilane are required to obtain satisfactory yields. Use of 1.2 equivalents of the silane decreased the yield to

Table 1. Asymmetric hydrosilylation of methyl-4-phenylphenyl ketone (**2a**) with $Fe(OAc)_2$/Bopa and $Co(OAc)_2$/Bopa catalysts.[a]

| Entry | Cat. precursor | Ligand | Yield [%] | *ee* [%] |
|---|---|---|---|---|
| 1 | $Fe(OAc)_2$ | **1a** | 99 | 61 |
| 2 | $Fe(OAc)_2$ | **1b** | 90 | 68[b] |
| 3 | $Fe(OAc)_2$ | **1c** | 99 | 72 |
| 4[c] | $Fe(OAc)_2$ | **1c** | 99 | 73 |
| 5[d] | $Fe(OAc)_2$ | **1c** | 99 | 72 |
| 6 | $Fe(OAc)_2$ | **1d** | 92 | 20 |
| 7 | $Co(OAc)_2$ | none | 19 | – |
| 8 | $Co(OAc)_2$ | **1a** | 99 | 70 |
| 9 | $Co(OAc)_2$ | **1b** | 99 | 69 |
| 10 | $Co(OAc)_2$ | **1c** | 99 | 54 |
| 11 | $Co(OAc)_2$ | **1d** | 99 | 94 |
| 12[e] | $Co(acac)_2$ | **1d** | 10 | 94 |
| 13[f] | $Co(OAc)_2$ | **1d** | 42 | 67 |

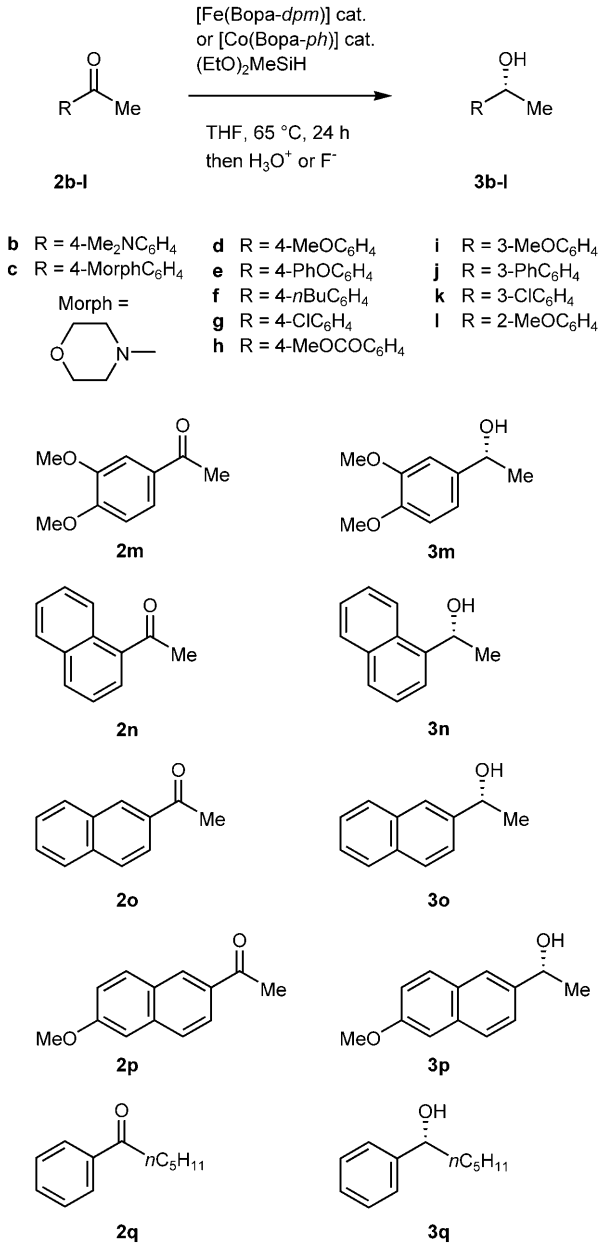
[a] For Fe cat.: Ketone **2a** (1.0 mmol), $Fe(OAc)_2$ (5.0 mol%), Bopa (7.0 mol%), $(EtO)_2MeSiH$ (2.0 mmol), THF (3.0 mL), 65°C, 24 h, workup with $H_3O^+$. For Co cat.: Ketone **2a** (1.0 mmol), $Co(OAc)_2$ (5.0 mol%), Bopa (6.0 mol%), $(EtO)_2MeSiH$ (2.0 mmol), THF (3.0 mL), 65°C, 24 h, workup with KF, tetra-*n*-butylammonium fluoride (TBAF). All products have *R* absolute configuration. [b] 48 h. Previously, 75% yield and 79% *ee* at 65°C and 48 h were reported.[4a] [c] $Fe(OAc)_2$ (2.0 mol%), Bopa-*dpm* (3.0 mol%). [d] $Fe(OAc)_2$ (0.5 mol%), Bopa-*dpm* (0.6 mol%). [e] In place of $Co(OAc)_2$, $Co(acac)_2$ (5.0 mol%) was used. [f] In place of $(EtO)_2MeSiH$, $NaBH_4$ (2.0 mmol) was used.

57%. Other hydrosilanes such as $PhMe_2SiH$, $Ph_2MeSiH$, and $Ph_2SiH_2$ did not promote hydrosilylation.

Next we extended the metal catalyst candidates for catalytic hydrosilylation to other commercially available first-row transition-metal salts such as cobalt acetate, nickel acetate, and copper acetate. Although nickel and copper salts did not show the expected catalytic activity, cobalt(II) acetate strongly promoted hydrosilylation of ketone **2a** in combination with $(EtO)_2MeSiH$. The catalyst prepared by heating cobalt acetate (5.0 mol%) and a Bopa ligand (6.0 mol%) was subjected to hydrosilylation of the ketone **2a** at 65°C for 24 h (Table 1, entries 7–11). Without the ligand, the reaction did not take place (Table 1, entry 7). Addition of the ligands activated the cobalt salt to promote the reaction to give the desired secondary alcohol in almost quantitative yield. Surprisingly, Bopa-*ph* (**1d**) attained the highest enantioselectivity of 94% (Table 1, entry 11) compared to 54–70% with the others (Table 1, entries 8–10). Use of $[Co(acac)_2]$ (acac = acetylacetonato) decreased the yield (Table 1, entry 12). Use of sodium borohydride gave **3a** in both lower yield and lower enantioselectivity (Table 1, entry 13). In short, we obtained higher enantioselectivities of up to 73% *ee* with the iron–Bopa-*dpm* catalyst and 94% *ee* with cobalt–Bopa-*ph* catalyst along with high product yields.

Next, we examined other aromatic ketones to establish the substrate scope under the optimized conditions with iron–Bopa-*dpm* and cobalt–Bopa-*ph* catalysts (Scheme 3, Table 2). Among the *para*-substituted phenyl ketones **2b**–**2h**, the dimethylamino (**2b**) and morpholino (**2c**) derivatives gave the highest *ee* values of over 80% (Table 2, entries 1 and 3). At 40°C, reduction of **2b** and **2c** gave 85 and




Scheme 3. Asymmetric hydrosilylation of other ketones.

88% *ee*, respectively (Table 2, entries 2 and 4). Ketones **2i**–**2m** bearing *meta* and *ortho* substituents gave lower *ee* values in the range of 50–73% (Table 2, entries 11–16). Furthermore, α-naphthalene derivative **2n** gave the reverse absolute configuration (Table 2, entry 17). Ketones **2o**, **2p**, and **2q** resulted in only 58–73% (Table 2, entries 18–20). Thus, the highest enantioselectivity achieved with the iron Bopa-*dpm* catalyst was 88%. With Beller and co-workers' Fe Duphos catalyst[5] and Gade and co-workers' Fe bis(pyridylimino)isoindole catalyst,[6] the hydrosilylation of the bulky 2,4,6-trimethylphenyl methyl ketone resulted in 99 and 93% *ee*, respectively. However, the iron–Bopa-*ip* catalyst slowly promoted reduction of the bulky ketone to give 22% yield and 5% ee; about 60% of the ketone was recovered.

Table 2. Asymmetric hydrosilylation of other ketones with $Fe(OAc)_2$/Bopa-*dpm* (**1c**) and $Co(OAc)_2$/Bopa-*ph* (**1d**) catalysts.[a]

| Entry | Ketone | $Fe(OAc)_2$/**1c** Yield [%] of **3** (*ee* [%]) | $Co(OAc)_2$/**1d** Yield [%] of **3** (*ee* [%]) |
|---|---|---|---|
| 1 | **2b** | 96 (80) | 98 (87) |
| 2 | **2b** | 97 (85)[b] | 99 (38)[c] |
| 3 | **2c** | 99 (83) | 99 (93) |
| 4 | **2c** | 93 (88)[b] | 99 (54)[c] |
| 5 | **2d** | 98 (78) | 99 (91) |
| 6 | **2e** | 99 (72) | 99 (94) |
| 7 | **2f** | 98 (70) | 99 (96) |
| 8 | **2f** | – | 99 (98)[d] |
| 9 | **2g** | 99 (68) | 99 (91) |
| 10 | **2h** | 93 (64) | 96 (93) |
| 11 | **2i** | 99 (54) | 98 (96) |
| 12 | **2i** | – | 98 (96)[d] |
| 13 | **2j** | 99 (58) | 99 (95) |
| 14 | **2k** | 99 (56) | 98 (94) |
| 15 | **2l** | 95 (50) | 95 (93) |
| 16 | **2m** | 99 (73) | 99 (93) |
| 17 | **2n** | 93 (22) | 95 (60) |
| 18 | **2o** | 99 (65) | 99 (92) |
| 19 | **2p** | 99 (71) | 99 (91) |
| 20 | **2q** | 88 (58) | 99 (95) |

[a] For Fe cat.: Ketone **2a** (1.0 mmol), $Fe(OAc)_2$ (2.0 mol%), Bopa-*dpm* (3.0 mol%), $(EtO)_2MeSiH$ (2.0 mmol), THF (3.0 mL), 65°C, 24 h, workup with $H_3O^+$. For Co cat.: Ketone (1.0 mmol), $Co(OAc)_2$ (5.0 mol%), Bopa-*ph* (6.0 mol%), $(EtO)_2MeSiH$ (2.0 mmol), THF (3.0 mL), 65°C, 24 h, workup with KF, TBAF. All products have *R* absolute configuration. [b] 40°C, 96 h. [c] Bopa-*ip* was used. [d] 40°C, 48 h.

On the other hand, the cobalt–Bopa-*ph* catalyst largely improved the enantioselectivities (Table 2, column 4). The dimethylamino (**2b**) and morpholino (**2c**) derivatives gave higher *ee* values of 87 and 93%, respectively (Table 2, entries 1 and 3). However, as expected, using Bopa-*ip* decreased the enantioselectivities to 38 and 54% (Table 2, entries 2 and 4). Substituted phenyl ketones **2d**–**2m** were reduced with an average *ee* value of about 94% (Table 2, entries 5–16). *para*-*n*-Butylphenyl ketone (**2f**) and *ortho*-methoxyphenyl ketone (**2i**) were subjected the hydrosilylation at 40°C (Table 2, entries 8 and 12). The reaction proceeded for 48 h to give the corresponding alcohols **3f** and **3i** with 98 and 96% *ee*, respectively. With the exception of α-naphthalene derivative **2n**, other ketones **2o**–**2q** gave higher enantioselectivities of up to 91–95% (Table 2, entries 18–20). Reduction of 2-phenylethyl methyl ketone as a linear aliphatic ketone was examined under the same conditions and resulted in a low *ee* of 15% and quantitative yield.

In summary, the cobalt–Bopa-*ph* catalyst attained high enantioselectivities of up to 98% and higher mean *ee* values of over 90%. In the context of asymmetric reduction of ketones using chiral cobalt complexes, Yamada et al. reported efficient methods for catalytic hydroboration with $NaBH_4$/alcohols or modified borohydrides.[12] With regard to enantioselective hydrosilylation catalyzed by cobalt complex, Brunner et al reported 56% *ee* for the reduction of acetophenone with 0.5 mol% of cobalt pyridine complex and chiral mono-oxazolinylpyridine ligand in the presence of

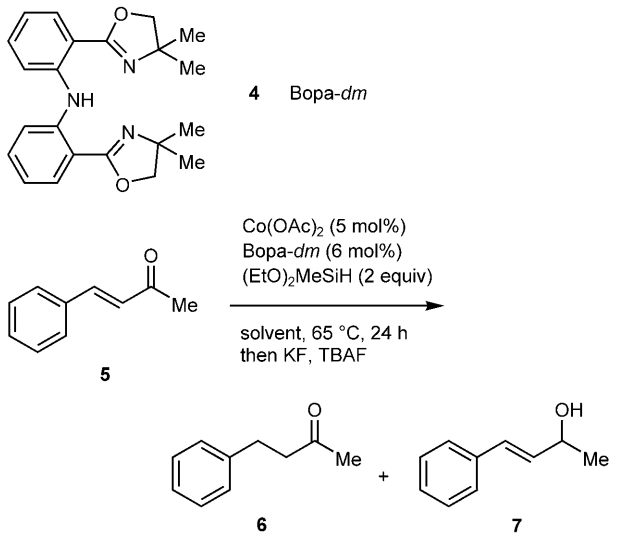
  

$Ph_2SiH_2$ in 1991,[13] but since then no other asymmetric hydrosilylation with cobalt catalysts has been reported.

**Asymmetric conjugate hydrosilylation of enones with Co–Bopa catalysts**: Asymmetric conjugate reduction of α,β-unsaturated carbonyl compounds with chiral Co catalysts has been intensively studied in combination with boron hydrides as reducing agents. Pfaltz et al.[14] reported the first asymmetric conjugate reduction with a chiral Co semicorrin catalyst and $NaBH_4$, followed by Yamada et al.[15] using a Co oxoaldiminato catalyst with $NaBH_4$, and Reiser et al.[16] with $CoCl_2$ and chiral bisoxazoline ligands. For non-asymmetric reductions, a stoichiometric $[Co_2(CO)_8]/H_2O$ system, which can promote the conjugate reduction of α,β-unsaturated ketones, was reported by Lee et al.[17]

We examined the suitability of Co–Bopa catalysts for conjugate reduction of enones in combination with $(EtO)_2MeSiH$. First, we carried out the reaction with benzalacetone (**5**) as substrate enone and Bopa-*dm* (**4**) as achiral ligand (Scheme 4, Table 3). Even without the ligand, the reduction proceeded smoothly to give a mixture of 1,4-reduction product **6** and 1,2-reduction product **7** in 39:61 ratio (Table 3, entry 1). However, addition of ligand **4** dramatically improved the 1,4-reduction in THF and toluene (Table 3, entries 2–4). $CoCl_2$ was not effective even with the ligand (Table 3, entry 5).

We next examined the asymmetric reaction with several β,β-disubstituted enones (**8a–e**) as substrates (Scheme 5, Table 4). β-Methylbenzalacetone (**8a**) resulted in 71% *ee* with Bopa-*dpm* (**1c**; Table 4, entry 3). The *ee* values depend on the substituents of the ligands (Table 4, entries 1–4). Moderate *ee* values of 65–75%, were obtained for the other enones **8b–8e** (Table 4, entries 5–8).

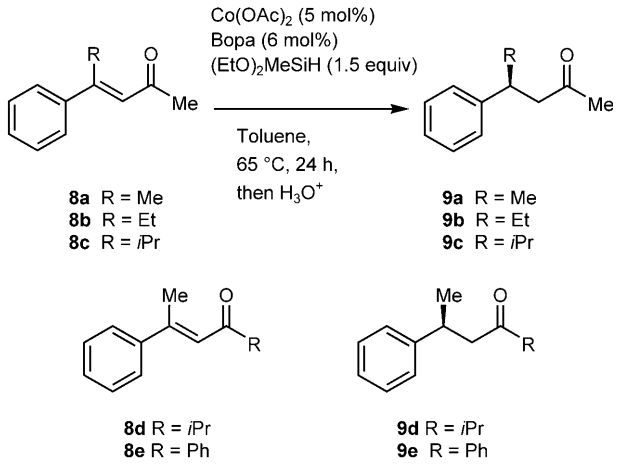



Scheme 4. Hydrosilylation of benzalacetone.

Table 3. Hydrosilylation of benzalacetone (**5**) with $Co(OAc)_2$/Bopa-*dm* (**4**) catalyst.[a]

| Entry | Solvent | Yield of **6** [%] | Yield of **7** [%] |
|---|---|---|---|
| 1[b] | THF | 39 | 61 |
| 2 | THF | 96 | 0 |
| 3 | toluene | 99 | 0 |
| 4[c] | toluene | 99 | 0 |
| 5[d] | toluene | no reaction | – |

[a] Ketone **5** (1.0 mmol), $Co(OAc)_2$ (5.0 mol%), Bopa-*dm* (6.0 mol%), $(EtO)_2MeSiH$ (2.0 mmol), solvent (3.0 mL), 65 °C, 24 h. [b] No ligand. [c] $(EtO)_2MeSiH$ (1.5 mmol). [d] In place of $Co(OAc)_2$, $CoCl_2$ (5.0 mol%) was used.




Scheme 5. Asymmetric cobalt-catalyzed conjugate reduction of some enones.

Table 4. Asymmetric conjugate hydrosilylation of enones with $Co(OAc)_2$/Bopa catalysts.[a]

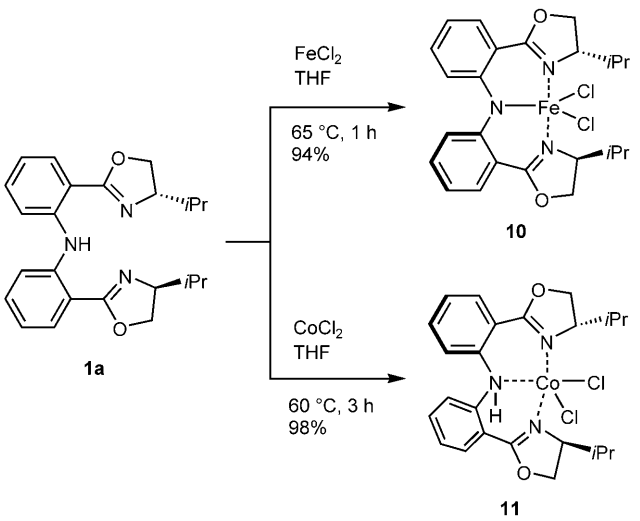
| Entry | Bopa | Enone | Yield of **9** [%] | *ee* of **9** [%] |
|---|---|---|---|---|
| 1 | **1a** | **8a** | 87 | 42 |
| 2 | **1b** | **8a** | 85 | 15 |
| 3 | **1c** | **8a** | 90 | 71 |
| 4 | **1d** | **8a** | 89 | 8 |
| 5 | **1c** | **8b** | 92 | 75 |
| 6 | **1c** | **8c** | 90 | 70 |
| 7 | **1c** | **8d** | 91 | 65 |
| 8 | **1c** | **8e** | 93 | 72 |

[a] Enone (0.5 mmol), $Co(OAc)_2$ (5.0 mol%), Bopa-*ip* (6.0 mol%), $(EtO)_2MeSiH$ (1.5 mmol), toluene (1.0 mL), 65 °C, 24 h.

We previously reported that the Fe–Bopa catalyst reduces benzalacetone in 1,2 fashion to give mainly **7** in 80% yield along with **6** in 4% yield.[4a]

**Structural analysis of Fe–Bopa and Co–Bopa complexes**: It is important to characterize an active catalyst and its stereochemistry. Therefore, we attempted to isolate the complex of iron(II) acetate and Bopa-*ip*, but the mixture did not give the corresponding complex. However, the reaction of bis(oxazolinylphenyl)amine **1a** (Bopa-*ip*) with iron(II) chloride at 65 °C did result in the formation of iron(III) bis(oxazolinylphenyl)amide complex **10** as a green solid in 94% yield (Scheme 6). Under air, the iron(II) atom was oxidized to an




Scheme 6. Preparation of iron chloro and cobalt chloro complexes.

iron(III) species bearing the *N*,*N*,*N*-tridentate amide ligand. The structure of complex **10** was confirmed by X-ray analysis to be a trigonal-bipyramidal coordination complex with $C_2$ symmetry (Figure 1). The two oxazoline rings are situated at apical positions relative to each other.

The reaction of cobalt(II) chloride and Bopa-*ip* **1a** was carried out in THF solution. Concentration of the solvent afforded amine complex **11** as a blue solid. The structure of **11** was determined by X-ray analysis to show trigonal-bipyramidal coordination with divalent cobalt atom and two chloride ligands at apical and equatorial positions. The oxazoline rings occupy two equatorial positions. One isopropyl group showed a disordered configuration.

The catalytic activities of iron and cobalt complexes **10** and **11** were examined for hydrosilylation of the ketone **2** under the same condition as described above. Unfortunately, neither chloro complex showed catalytic activity, and the ketone was recovered.

## Conclusion

We have found that the readily prepared chiral bis(oxazolinylphenyl)amines (Bopa) are efficient auxiliaries for iron and cobalt catalysts which exhibit high activity for asymmetric hydrosilylation of ketones and conjugate hydrosilylation of enones. Iron and cobalt, first-row elements, are convenient and environmentally friendly metals for asymmetric catalysis. Additionally, hydrosilanes are a safe alternative to hydrogen gas in organic synthesis. Theoretical studies are now underway to elucidate the catalytic mechanism by considering certain metal hydride species.

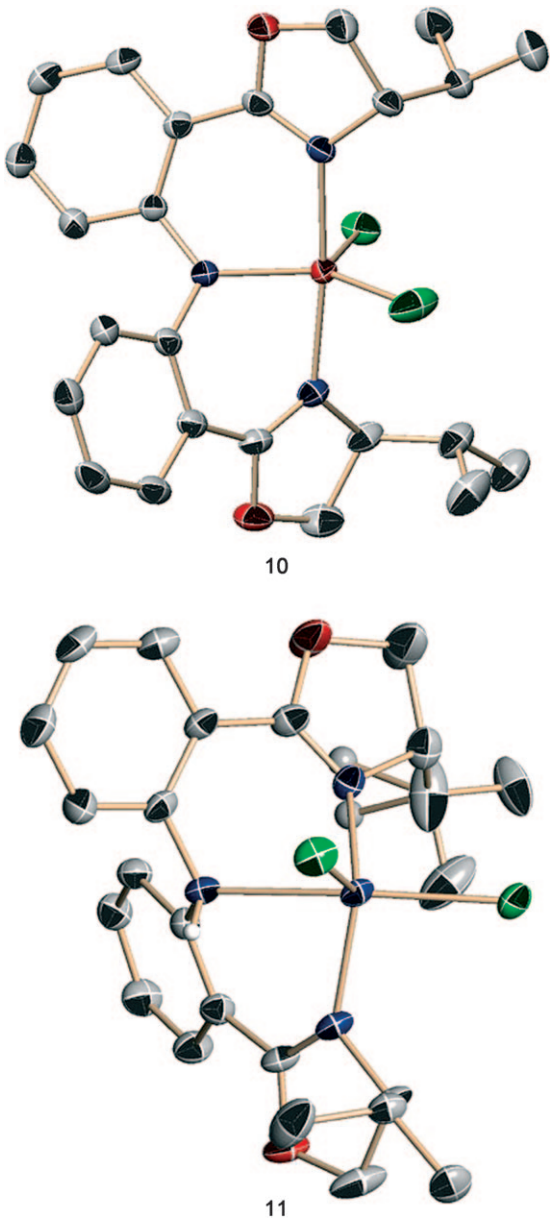



Figure 1. Molecular structures of $Fe^{III}$ [$Fe^{III}$(Bopa-*ip*)$Cl_2$]bis(oxazolinylphenyl)amide complex **10** (top) and [$Co^{II}$(Bopa-*ip*)$Cl_2$] **11** (bottom).

## Experimental Section

**General procedures**: $^1H$ and $^{13}C$ NMR spectra were recorded on a Varian Mercury 300 spectrometer. $^1H$ and $^{13}C$ chemical shifts $\delta$ are reported in ppm relative to the singlet at $\delta = 7.26$ ppm and the triplet at $\delta = 77.0$ ppm for $CDCl_3$, respectively. Infrared spectra were recorded on a Jasco FR/IR-230 spectrometer. Optical rotation was measured on a Jasco P-1020NS polarimeter. Bopa ligands **1a**, **1b**, and **1d** were prepared according to the method reported by Du, Xu et al..[3a] $Fe(OAc)_2$ was purchased from Wako Pure Chemical Industries, Ltd., and $Co(OAc)_2$ from Kishida Chemicals Co. Ltd. HRMS (FAB and EI) was measured on Jeol JMS-700 at Chemical Instrumentation Facility of Nagoya University. Characterization data, NMR spectra, and LC charts of the products are listed in the Supporting Information.

**Iron-catalyzed hydrosilylation, typical procedure (Table 2, entries 3 and 4)**: 4′-Morpholinoacetophenone (**2c**; 205 mg, 1.0 mmol), Bopa-*dpm* (19.2 mg, 0.030 mmol), and $Fe(OAc)_2$ (3.5 mg, 0.020 mmol) were placed in a flask. Under argon atmosphere, THF (3.0 mL) was added, and the mixture was stirred for 1 h at 65 °C. Then, $(EtO)_2MeSiH$ (320 μL, 2.0 mmol) was added, and the mixture was stirred for 24 h at 65 °C. The reaction was monitored by TLC (ethyl acetate/hexane = 1:3, $R_f$ = 0.35 for the ketone, $R_f$ = 0.70 for the silylated product). TBAF (THF solution, 1 M, 1.0 mL), KF (112 mg), MeOH (1.0 mL), and $H_2O$ (1.0 mL) were added at 0 °C. The mixture was extracted with ethyl acetate (5 × 2.0 mL) and washed with water (5.0 mL) and brine (5.0 mL). The combined organic layer was dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with ethyl acetate/hexane as eluent to give the desired alcohol **3c** (205 mg, 0.99 mmol) in 99% yield (Table 2, entry 3). The same reaction was carried out at 40 °C for 96 h to give the desired alcohol **3c** (193 mg, 0.93 mmol) in 93% yield (Table 2, entry 4). White solid; m.p. 93.3–95.3 °C; $[\alpha]_D^{25}$ = 45.5 ($c$ = 1.0, $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 1.48 (d, $J$ = 6.3 Hz, 3H), 1.82 (br s, 1H), 3.15 (dd, $J$ = 4.5, 6.3 Hz, 4H), 3.86 (dd, $J$ = 4.5, 6.3 Hz, 4H), 4.84 (q, $J$ = 6.0 Hz, 1H), 6.90 (m, 2H), 7.29 ppm (m, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 25.0, 49.5, 66.9, 70.0, 115.5, 126.2, 137.0, 150.4 ppm; IR (film): $\tilde{\nu}$ = 3423 (br), 2966, 1610, 1514, 1231, 1116 $cm^{-1}$; chromatography: Daicel Chiralcel OB-H, hexane/2-propanol (90/10, 1.0 mL $min^{-1}$), retention time: 21.5 min (major), 25.0 min (minor), 88% *ee*; HRMS (FAB): [$M^+$] $m/z$ found: 207.1254; calcd ($C_{12}H_{17}NO_2$): 207.1259.

**Cobalt-catalyzed hydrosilylation, typical procedure (Table 2, entries 7 and 8)**: 4′-*n*-Butylacetophenone (**2f**; 176 mg, 1.0 mmol), Bopa-*ph* (27.6 mg, 0.06 mmol), and $Co(OAc)_2$ (8.9 mg, 0.05 mmol) were placed in a flask. Under argon atmosphere, THF (3.0 mL) was added, and the mixture was stirred for 1 h at 65 °C. Then $(EtO)_2MeSiH$ (320 μL, 2.0 mmol) was added, and the mixture was stirred for 24 h at 65 °C. The reaction was monitored by TLC (ethyl acetate/hexane 1/3, $R_f$ = 0.7 for the ketone, $R_f$ = 0.9 for the silylated product). TBAF (THF solution, 1 M, 1.0 mL), KF (112 mg), MeOH (1.0 mL), and $H_2O$ (1.0 mL) were added at 0 °C. The mixture was extracted with ethyl acetate (5 × 2.0 mL) and washed with water (5.0 mL) and brine (5.0 mL). The combined organic layer was dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with ethyl acetate/hexane as eluent to give the desired alcohol **3f** (176 mg, 0.99 mmol) in 99% yield (Table 2, entry 7). The same reaction was carried out at 40 °C for 48 h to give the desired alcohol **3f** (176 mg, 0.99 mmol) in 99% yield. Colorless oil; $[\alpha]_D^{25}$ = 38.4 ($c$ = 1.0, $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 0.99 (t, $J$ = 7.2 Hz, 3H), 1.40 (m, 2H), 1.48 (d, $J$ = 6.3 Hz, 3H), 1.63 (m, 2H), 2.63 (t, $J$ = 7.5 Hz, 2H), 4.83 (q, $J$ = 6.3 Hz, 1H), 7.16 (d, $J$ = 7.8 Hz, 2H), 7.27 ppm (d, $J$ = 7.8 Hz, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 14.1, 22.5, 25.1, 33.8, 35.4, 70.1, 125.1, 128.2, 141.8, 142.7 ppm; IR (film): $\tilde{\nu}$ = 3352 (br), 2961, 2927, 1082 $cm^{-1}$; Chromatography: Daicel Chiralcel OD-H, hexane/2-propanol (95/5, 0.5 mL $min^{-1}$), retention time: 11.6 min (major), 12.6 min (minor), 98% *ee*; HRMS (FAB): [$M^+$] $m/z$ found: 178.1361; calcd ($C_{12}H_{18}O$): 178.1358.

**Cobalt-catalyzed conjugate reduction of benzalacetone**: Benzalacetone (**5**; 146 mg, 1.0 mmol), Bopa-*dm* (21.8 mg, 0.06 mmol), and $Co(OAc)_2$ (8.9 mg, 0.05 mmol) were placed in a flask. Under argon atmosphere, toluene (3.0 mL) was added, and the mixture was stirred for 1 h at 65 °C. Then, $(EtO)_2MeSiH$ (240 μL, 1.5 mmol) was added, and the mixture was stirred for 24 h at 65 °C. TBAF (THF solution, 1 M, 1.0 mL), KF (112 mg), MeOH (1.0 mL), and $H_2O$ (1.0 mL) were added at 0 °C. The mixture was extracted with ethyl acetate (5 × 2.0 mL) and washed with water (5.0 mL) and brine (5.0 mL). The combined organic layer was dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with ethyl acetate/hexane as eluent to give the desired ketone **6** (146 mg, 0.99 mmol) in 99% yield (Table 3, entry 3). Colorless oil; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 2.16 (s, 3H), 2.73–2.85 (m, 2H), 2.87–2.97 (m, 2H), 7.15–7.27 (m, 3H), 7.28–7.36 ppm (m, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 29.8, 30.2, 45.2, 1125.8, 128.0, 128.2, 140.7, 207.4 ppm; IR (film): $\tilde{\nu}$ = 1714, 1149, 752, 701 $cm^{-1}$; HRMS (EI): [$M^+$] $m/z$ found: 148.0891; calcd ($C_{10}H_{12}O$): 148.0888.

**Cobalt-catalyzed asymmetric conjugate reduction of 8b**: Enone **8b** (87 mg, 0.50 mmol), Bopa-*dpm* (19.2 mg, 0.030 mmol), and $Co(OAc)_2$ (4.4 mg, 0.025 mmol) were placed in a flask. Under argon atmosphere, toluene (1.0 mL) was added, and the mixture was stirred for 1 h at 65 °C. Then, $(EtO)_2MeSiH$ (120 μL, 0.75 mmol) was added, and the mixture was stirred for 24 h at 65 °C. After concentration, aqueous HCl (2 N, 2 mL), THF (1 mL), and MeOH (1 mL) were added at 0 °C. The mixture was extracted with ethyl acetate (5 × 2.0 mL) and washed with water (5.0 mL) and brine (5.0 mL). The combined organic layer was dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with ethyl acetate/hexane as eluent to give the desired ketone **9b** (80.8 mg, 0.46 mmol) in 92% yield (Table 4, entry 5). Colorless oil; $[\alpha]_D^{25}$ = 26.2 ($c$ = 1.0, $CHCl_3$); $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 0.79 (t, $J$ = 7.2 Hz, 3H), 1.50–1.78 (m, 2H), 2.03 (s, 3H), 2.72–2.80 (m, 2H), 3.02 (m, 1H), 7.18–7.23 (m, 3H), 7.25–7.30 ppm (m, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 12.2, 29.5, 30.8, 43.1, 50.6, 126.1, 127.3, 128.2, 144.0, 207.6 ppm; IR (film): $\tilde{\nu}$ = 1713, 1360, 754, 701 $cm^{-1}$; chromatography: Daicel Chiralcel OJ-H, hexane/2-propanol (99/1, 0.5 mL $min^{-1}$), retention time: 28.6 min (major), 36.0 min (minor), 75% *ee*; HRMS (EI): [$M^+$] $m/z$ found: 176.1204; calcd ($C_{12}H_{16}O$): 176.1201.

**Preparation of [$FeCl_2$(Bopa-*ip*)] (10)**: $FeCl_2$ (25.4 mg, 0.20 mmol) and Bopa-*ip* (78.4 mg, 0.20 mmol) were placed in a flask under argon atmosphere. THF (1.0 mL) was added, and the mixture was stirred at 65 °C for 1 h to give a green solution. The solution was filtered and concentrated to give a green solid, which was recrystalized from dichloromethane and hexane to give **10** as a green solid (93.8 mg, 0.187 mmol, 94% yield); m.p. 245–246 °C; IR (KBr disk): $\tilde{\nu}$ = 3067, 2957, 2871 $cm^{-1}$; elemental analysis calcd (%) for $C_{24}H_{28}Cl_2N_3O_2Fe$: C 55.73, H 5.46, N 8.12; found: C 55.51, H 5.44, N 7.87; $^1$H NMR could not be measured.

**Preparation of [$CoCl_2$(Bopa-*ip*)] (11)**: $CoCl_2$ (64.9 mg, 0.50 mmol) and Bopa-*ip* (196 mg, 0.50 mmol) were placed in a flask. THF (3.0 mL) was added, and the mixture stirred at 60 °C for 3 h. The solvent was removed under reduced pressure, and the residue dissolved in dichloromethane. The solution was filtered through filter paper and was concentrated to 1 mL. Then hexane was slowly added to precipitate a dark green solid, which was recrystallized from ethyl acetate and a small amount of dichloromethane to give an ultramarine solid (258 mg, 0.49 mmol) in 98% yield; m.p. 244–246 °C (decomp); IR (KBr disk): $\tilde{\nu}$ = 3437 (br), 3214, 2961, 1626, 1489, 1375, 1246 $cm^{-1}$; elemental analysis calcd (%) for $C_{24}H_{29}Cl_2N_3O_2Co \cdot 0.25\,CH_2Cl_2$: C 53.78, H 5.30, N 7.76; found: C 54.14, H 5.50, N 7.51; HRMS (FAB): [$M^+$] $m/z$ found: 520.0978; calcd ($C_{24}H_{29}Cl_2N_3O_2Co$): 520.0969; $^1$H NMR could not be measured.

**X-ray diffraction study**: The diffraction data were collected on a Bruker SMART APEX CCD diffractometer with graphite-monochromated $Mo_{K\alpha}$ radiation ($\lambda$ = 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 techniques on $F^2$ by using SHELXTL. One of the *i*Pr groups in **11** is disordered over two positions, which were refined in the ratio of 58:42. All non-hydrogen atoms were refined with anisotropic displacement parameters except the *i*Pr group in **11**. All hydrogen atoms were located on calculated positions and refined as rigid groups. Refinement details for **10**: $C_{24}H_{28}Cl_2FeN_3O_2$; $M_r$ = 517.24; $T$ = 153(2) K; crystal system monoclinic; space group $P2_1$; $a$ = 10.6822(6), $b$ = 8.7164(5), $c$ = 13.2058(7) Å, $\beta$ = 95.6620(10)°, $V$ = 1223.60(12) Å$^3$, $Z$ = 2, $\rho_{calcd}$ = 1.404 Mg m$^{-3}$, $\mu$ = 0.860 mm$^{-1}$, $F(000)$ = 538, crystal size = 0.60 × 0.50 × 0.50 mm, $\theta$ range = 1.55 to 28.23°; index ranges: $-14 \le h \le 14$, $-7 \le k \le 11$, $-17 \le l$ 17; reflections collected 9217, independent reflections 4258 [$R$(int) = 0.0184], completeness to $\theta$ = 28.23°, 99.7%; max./min. transmission 1.000000/0.731983; data/restraints/parameters 4258/1/293; goodness of fit on $F^2$ 1.075; final $R$ indices [$I > 2\sigma(I)$]: $R1$ = 0.0249, $wR2$ = 0.0641; $R$ indices (all data): $R1$ = 0.0256, $wR2$ = 0.0644; largest diff. peak/hole 0.434/−0.234 e Å$^{-3}$. Refinement details for **11**: $C_{24}H_{28}Cl_2CoN_3O_2$; $M_r$ = 520.32; $T$ = 153(2) K; crystal system: monoclinic; space group: $P2_1$; $a$ = 10.875(3), $b$ = 9.230(3), $c$ = 12.263(3) Å, $\beta$ = 101.019(5)°, $V$ = 1208.1(6) Å$^3$, $Z$ = 2, $\rho_{calcd}$ = 1.430 Mg m$^{-3}$, $\mu$ = 0.957 mm$^{-1}$, $F(000)$ = 540, crystal size = 0.40 × 0.20 × 0.20 mm, $\theta$ range = 1.69 to 28.36°; index ranges: $-6 \le h \le 14$, $-12 \le k \le 12$, $-16 \le l \le 14$; reflections collected 8832, inde-

pendent reflections 5788 [$R$(int) = 0.0221], completeness to $\theta = 28.36°$, 99.4 %; max./min. transmission 1.000000/0.775499; data/restraints/parameters 5788/1/304; goodness of fit on $F^2$ 1.022; final $R$ indices [$I > 2\sigma(I)$]: $R1 = 0.0381$, $wR2 = 0.0902$; $R$ indices (all data): $R1 = 0.0457$, $wR2 = 0.0937$; largest diff. peak/hole 0.644 and $-0.242$ e Å$^{-3}$. CCDC-752895 (**10**) and CCDC-752896(**11**) contain 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.

**Synthesis of Bopa-*dpm* (1c)**: According to the literature method,[3a] the starting amino alcohol (*S*)-2-amino-3,3-diphenylpropan-1-ol was prepared from (1*R*,2*R*)-(−)-2-amino-1-phenyl-1,3-propanediol. A solution of commercially available 2,2′-iminodibenozic acid (771 mg, 3.0 mmol; Aldrich 30895-25G) in thionyl chloride (4.5 mL) was heated at 80 °C for 1 h. Excess thionyl chloride was removed under reduced pressure and azeotropically with $CH_2Cl_2$ (3 × 10 mL) to give the bis(acid chloride) as a crude solid, a solution of which in $CH_2Cl_2$ (10 mL) was added to a solution of the amino alcohol (1.47 g, 6.6 mmol) and $Et_3N$ (2.1 mL) in $CH_2Cl_2$ (25 mL) at 0 °C. The mixture was stirred for 4 h at room temperature to form the corresponding bis(amide alcohol), and the mixture was again cooled to 0 °C. Then, $Et_3N$ (4.2 mL) and methanesulfonyl chloride (1.2 mL, 15 mmol) were added, and the mixture was stirred for 12 h at room temperature. For workup, aqueous $K_2CO_3$ (1 M, 3 mL) was added at 0 °C, and the mixture extracted with $CH_2Cl_2$ (3 × 20 mL). The combined organic layer was dried over $Na_2SO_4$ and concentrated under reduced pressure. The residual solid was purified by column chromatography with hexane/ethyl acetate as eluent to give the desired compound **1c** (1.39 g, 2.17 mmol) in 72 % yield; white solid, m.p. 105–106 °C; $[\alpha]_D^{20} = -184$ ($c$ = 1.0, $CHCl_3$); IR (KBr): $\tilde{\nu} = 1641$, 1581, 1455, 738, 697 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 3.80$ (t, $J = 9.0$ Hz, 2H), 3.85 (d, $J = 9.0$ Hz, 2H), 4.20 (t, $J = 9.0$ Hz, 2H), 4.60 (q, $J = 9.0$ Hz, 2H), 6.88 (m, 2H), 7.01–7.30 (m, 22H), 7.40 (m, 2H), 7.78 (m, 2H), 11.0 ppm (s, 1H, NH); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 56.9$, 70.1, 70.9, 115.1, 117.7, 119.2, 125.8, 126.4, 127.5, 128.3, 128.6, 128.9, 130.2, 131.1, 142.0, 142.1, 143.2, 162.2 ppm; elemental analysis calcd $C_{44}H_{37}N_3O_2$: C 82.60, H 5.83, N 6.57; found: C 82.61, H 5.85, N 6.38.

## Acknowledgements

This work was partly supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology of Japan (Concerto Catalysts, 460:18065011) and the Japan Society for the Promotion of Science (18350049).

[1] Reviews on nitrogen-based ligands for asymmetric catalysis": a) M. Gómez, G. Muller, M. Rocamora, *Coord. Chem. Rev.* **1999**, *193–195*, 769–835; b) F. Fache, E. Schulz, M. L. Tommasino, M. Lemaire, *Chem. Rev.* **2000**, *100*, 2159–2231; c) A. K. Ghosh, P. Mathivanan, J. Cappiello, *Tetrahedron: Asymmetry* **1998**, *9*, 1–45; d) G. Desimoni, G. Faita, P. Quadreil, *Chem. Rev.* **2003**, *103*, 3119–3154; e) G. Desimoni, G. Faita, K. A. Jørgensen, *Chem. Rev.* **2006**, *106*, 3561–3651; f) H. A. McManus, P. J. Guiry, *Chem. Rev.* **2004**, *104*, 4151–4202.

[2] a) H. A. McManus, P. J. Guiry, *J. Org. Chem.* **2002**, *67*, 8566–8573; b) H. A. McManus, P. G. Cozzi, P. J. Guiry, *Adv. Synth. Catal.* **2006**, *348*, 551–558; c) V. Coeffard, M. Aylward, P. J. Guiry, *Angew. Chem.* **2009**, *121*, 9316–9319; *Angew. Chem. Int. Ed.* **2009**, *48*, 9152–9155.

[3] a) S.-F. Lu, D.-M. Du, S.-W. Zhang, J. Xu, *Tetrahedron: Asymmetry* **2004**, *15*, 3433–3441; b) D.-M. Du, S.-F. Lu, T. Fang, J. Xu, *J. Org. Chem.* **2005**, *70*, 3712–3715; c) S.-F. Lu, D.-M. Du, J. Xu, *Org. Lett.* **2006**, *8*, 2115–2118; d) S.-F. Lu, D.-M. Du, J. Xu, S.-W. Zhang, *J. Am. Chem. Soc.* **2006**, *128*, 7418–7419; e) H. Liu, J. Xu, D.-M. Du, *Org. Lett.* **2007**, *9*, 4725–4728; f) H. Liu, S.-F. Lu, J. Xu, D.-M. Du, *Chem. Asian J.* **2008**, *3*, 1111–1121.

[4] a) H. Nishiyama, A. Furuta, *Chem. Commun.* **2007**, 760–762. Related catalytic hydrosilylation: b) A. Furuta, H. Nishiyama, *Tetrahedron Lett.* **2008**, *49*, 110–113; c) T. Inagaki, Y. Yamada, L. T. Phong, A. Furuta, J. Ito, H. Nishiyama, *Synlett* **2009**, 253–256.

[5] a) N. S. Shaikh, S. Enthaler, K. Junge, M. Beller, *Angew. Chem.* **2008**, *120*, 2531–2535; *Angew. Chem. Int. Ed.* **2008**, *47*, 2497–2501; b) N. S. Shaikh, K. Junge, M. Beller, *Org. Lett.* **2007**, *9*, 5429–5432.

[6] B. K. Langlotz, H. Wadepohl, L. H. Gade, *Angew. Chem.* **2008**, *120*, 4748–4752; *Angew. Chem. Int. Ed.* **2008**, *47*, 4670–4674.

[7] a) A. M. Tondreau, E. Lobkovsky, P. J. Chirik, *Org. Lett.* **2008**, *10*, 2789–2792; b) A. M. Tondreau, J. M. Darmon, B. M. Wile, S. K. Floyd, E. Lobkovsky, P. J. Chirik, *Organometallics* **2009**, *28*, 3928–3940.

[8] S. Enthaler, B. Hagemann, G. Erre, K. Junge, M. Beller, *Chem. Asian J.* **2006**, *1*, 598–604.

[9] a) C. Sui-Seng, F. Freutel, A. J. Lough, R. H. Morris, *Angew. Chem.* **2008**, *120*, 954–957; *Angew. Chem. Int. Ed.* **2008**, *47*, 940–943; b) A. Mikhailine, A. J. Lough, R. H. Morris, *J. Am. Chem. Soc.* **2009**, *131*, 1394–1395; c) N. Meyer, A. J. Lough, R. H. Morris, *Chem. Eur. J.* **2009**, *15*, 5605–5610.

[10] a) C. P. Casey, H. Guan, *J. Am. Chem. Soc.* **2007**, *129*, 5816–5817; b) C. P. Casey, H. Guan, *J. Am. Chem. Soc.* **2009**, *131*, 2499–2507.

[11] Review: R. H. Morris, *Chem. Soc. Rev.* **2009**, *38*, 2282–2291.

[12] a) H. Sato, H. Watanabe, Y. Ohtsuka, T. Ikeno, S. Fukuzawa, T. Yamada, *Org. Lett.* **2002**, *4*, 3313–3316; b) T. Yamada, T. Nagata, K. D. Sugi, K. Yorozu, T. Ikeno, Y. Ohtsuka, D. Miyazaki, T. Mukaiyama, *Chem. Eur. J.* **2003**, *9*, 4485–4509; c) A. Kokura, S. Tanaka, T. Ikeno, T. Yamada, *Org. Lett.* **2006**, *8*, 3025–3027.

[13] H. Brunner, K. Amberger, *J. Organomet. Chem.* **1991**, *417*, C63–C65.

[14] a) U. Leutenegger, A. Madin, A. Pfaltz, *Angew. Chem.* **1989**, *101*, 61–62; *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 60–61; b) M. Misun, A. Pfaltz, *Helv. Chim. Acta* **1996**, *79*, 961–972; c) P. von Matt, A. Pfaltz, *Tetrahedron: Asymmetry* **1991**, *2*, 691–700.

[15] a) T. Nagata, K. Yorozu, T. Yamada, T. Mukaiyama, *Angew. Chem.* **1995**, *107*, 2309–2311; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2145–2147. Related reduction: b) Y. Ohtsuka, T. Ikeno, T. Yamada, *Tetrahedron: Asymmetry* **2003**, *14*, 967–970.

[16] C. Geiger, P. Kreitmeier, O. Reiser, *Adv. Synth. Catal.* **2005**, *347*, 249–254.

[17] H.-Y. Lee, M. An, *Tetrahedron Lett.* **2003**, *44*, 2775–2778.

[18] D. A. Klumpp, S. L. Aquirre, G. V. Sanchez, Jr., S. J. de Leon, *Org. Lett.* **2001**, *3*, 2781–2784.

Received: November 13, 2009
Published online: January 29, 2010