ORGANOMETALLICS
Communication

Organometallics **2010,** *29,* 5773–5775 5773
DOI: 10.1021/om1009186

A Chiral Iron Complex Containing a Bis(oxazolinyl)phenyl Ligand: Preparation and Asymmetric Hydrosilylation of Ketones

Satomi Hosokawa, Jun-ichi Ito, and Hisao Nishiyama*

Department of Applied Chemistry, Graduate School of Engineering, Nagoya University, Chikusa, Nagoya 464-8603, Japan

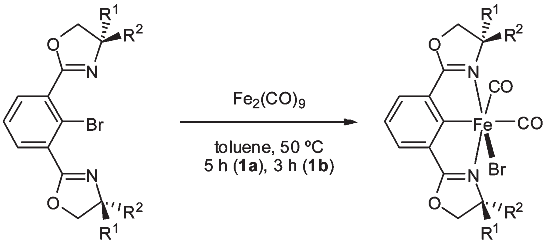
Received September 24, 2010

Summary: New chiral pincer iron complexes having bis(oxazolinyl)phenyl ligands have been synthesized by oxidative addition of $Fe_2(CO)_9$ to 2-bromo-substituted ligands. This chiral pincer iron complex can catalyze the asymmetric hydrosilylation of simple aromatic ketones to give the corresponding alcohols.

Anionic meridional ECE ligands (E = P, N) have been utilized for the stabilization of transition-metal complexes that exhibit several types of transformations of organic molecules.[1] Although Ru, Rh, Ir, and Pd complexes with PCP- and NCN-type ligands have been developed for catalytic reactions,[1] iron complexes with ECE-type meridional ligands have been limited to 1,3-bis(dimethylphosphinomethyl)phenyl and 1,3-bis(dimethylaminomethyl)phenyl ligands, reported by Kaska and van Koten, respectively.[2] In contrast, neutral NNN-type meridional ligands, which have skeletons similar to those of anionic ECE ligands, have attracted much attention for use in iron complexes.[3−5] In this context, 2,6-bis(imino)pyridine ligands have the potential to generate highly reactive iron complexes for catalytic reactions, such as polymerization,[3] cycloaddition,[4] and hydrogenation.[5] Other neutral meridional ligands based on pyridine and two-electron-donor moieties, such as phosphine,[6] NHC,[7] and oxazoline groups,[8] have also been reported as supporting ligands for iron atoms. Bis(oxazoline)pyridine (pybox) ligands, which are a prominent class of chiral ligands for a range of transition metals, have been utilized in the generation of chiral iron alkyl complexes and asymmetric hydrosilylation.[8b]

Recently, we reported chiral transition-metal complexes having chiral meridional NCN-type ligands, namely bis(oxazolinyl)phenyl (phebox) ligands, for asymmetric catalytic reactions.[9] The Rh and Ru complexes displayed high catalytic activity and enantioselectivity toward several asymmetric reactions, including reductive aldol coupling, conjugate reduction with hydrosilanes, hydrogenation, and cyclopropanation. We now turn our attention to the construction of iron complexes having the phebox ligand. Here we report the first synthesis of both achiral and chiral Phebox−Fe complexes and their utilization in the asymmetric hydrosilylation of ketones.

Oxidative addition of Fe(0) complexes with alkyl halides leads to the formation of the corresponding alkyl Fe(II) complexes.[10] In this reaction, $Fe_2(CO)_9$ is thought to be a suitable iron source because it generates the unsaturated iron species "$Fe(CO)_4$".[11] The initial experiment was carried out using an achiral bromide ligand precursor, (phebox-*dm*)Br (**1a**).[12] The reaction of **1a** with $Fe_2(CO)_9$ in toluene at 50 °C for 5 h resulted in the formation of a new phebox−Fe(II) complex, (phebox-*dm*)FeBr$(CO)_2$ (**2a**) (eq 1). Purification by column chromatography on silica gel afforded **2a** in 52% yield. In contrast, the reaction of **1a** with $Fe_3(CO)_{12}$ in toluene at 50 °C significantly decreased the yield of **2a** (5%) and the reaction of **1a** with $Fe(CO)_5$ failed.



(1)

1a: $R^1 = R^2 =$ Me
1b: $R^1 =$ *i*-Pr, $R^2 =$ H

2a: $R^1 = R^2 =$ Me (52%)
2b: $R^1 =$ *i*-Pr, $R^2 =$ H (69%)

---

*To whom correspondence should be addressed. E-mail: hnishi@apchem.nagoya-u.ac.jp.

[1] (a) Albrecht, M.; van Koten, G. *Angew. Chem., Int. Ed.* **2001**, *40*, 3750. (b) van der Boom, M. E.; Milstein, D. *Chem. Rev.* **2003**, *103*, 1759. (c) *The Chemistry of Pincer Compounds*; Morales-Morales, D., Jensen, C. M., Eds.; Elsevier: Oxford, U.K., 2007.

[2] (a) de Koster, A.; Kanters, J. A.; Spek, A. L.; van der Zeijden, A. A. H.; van Koten, G.; Vrieze, K. *Acta Crystallogr.* **1985**, *C41*, 893. (b) Contel, M.; Stol, M.; Casado, M. A.; van Klink, G. P. M.; Ellis, D. D.; Spek, A. L.; van Koten, G. *Organometallics* **2002**, *21*, 4556. (c) Kaska, W. C. *Inorg. Chim. Acta* **1978**, *30*, L325.

[3] (a) Britovsek, G. J. P.; Bruce, M.; Gibson, V. C.; Kimberley, B. S.; Maddox, P. J.; Mastroianni, S.; McTavish, S. J.; Redshaw, C.; Solan, G. A.; Strömberg, S.; White, A. J. P.; Williams, D. J. *J. Am. Chem. Soc.* **1999**, *121*, 8728. (b) Givson, V. V. *Chem. Commun* **1998**, 849. (c) Small, B. L.; Brookhart, M.; Bennett, A. M. A. *J. Am. Chem. Soc.* **1998**, *120*, 4049. (d) Takeuchi, D.; Matsuura, R.; Park, S.; Osakada, K. *J. Am. Chem. Soc.* **2007**, *129*, 7002.

[4] Bouwkamp, M. W.; Bowman, A. C.; Lobkovsky, E.; Chirik, P. J. *J. Am. Chem. Soc.* **2006**, *128*, 13340.

[5] (a) Bart, S. C.; Lobkovsky, E.; Chirik, P. J. *J. Am. Chem. Soc.* **2004**, *126*, 13794. (b) Enthaler, S.; Hagemann, B.; Erre, G.; Junge, K.; Beller, M. *Chem. Asian J.* **2006**, *1*, 598.

[6] Benito-Garagorri, D.; Wiedermann, J.; Pollak, M.; Mereiter, K.; Kirchner, K. *Organometallics* **2007**, *26*, 217.

[7] (a) Danopoulos, A. A.; Tsoureas, N.; Wright, J. A.; Light, M. E. *Organometallics* **2004**, *23*, 166. (b) Danopoulos, A. A.; Wright, J. A.; Motherwell, W. B. *Chem. Commun.* **2005**, 784.

[8] (a) Redlich, M.; Hossain, M. M. *Tetrahedron Lett.* **2004**, *45*, 8987. (b) Tondreau, A. M.; Darmon, J. M.; Wile, B. M.; Floyd, S. K.; Lobkovsky, E.; Chirik, P. J. *Organometallics* **2009**, *28*, 3928.

[9] (a) Nishiyama, H. *Chem. Soc. Rev.* **2007**, *36*, 1133–1141. (b) Nishiyama, H.; Ito, J. *Chem. Rec.* **2007**, *7*, 159. (c) Nishiyama, H.; Ito, J. *Chem. Commun.* **2010**, 203.

[10] (a) Cardaci, G.; Bellachioma, G.; Zanazzi, P. *Organometallics* **1998**, *7*, 172. (b) Pankowski, M.; Bigorgne, M. *J. Organomet. Chem.* **1971**, *30*, 227. (c) Murdoch, H. D.; Weiss, E. *Helv. Chim. Acta* **1962**, *45*, 1927.

[11] Braterman, P. S.; Wallace, W. J. *J. Organomet. Chem.* **1971**, *30*, C17.

The phebox−Fe complex **2a** is diamagnetic. The ^{1}H NMR spectrum of **2a** exhibited two singlet signals at δ 1.42 (6H) and 1.25 (6H), which were assigned to the methyl groups on the oxazoline rings. Likewise, the AB doublet signals for the oxazoline CH_2 groups were observed at δ 4.43 (2H) and 4.39 (2H). These spectral features indicated that **2a** has a C_s-symmetric structure. In the IR spectrum of **2a**, strong absorptions were observed at 2020 and 1969 cm^{-1}, which were assigned to the symmetric and asymmetric CO stretching vibrations, respectively. The intensity ratio of these peaks implied a cis arrangement of the CO ligands. The wavenumbers of these peaks are close to those of the related phebox−Ru analogue (phebox)Ru(CO)$_2$Br, (2037, 1959 cm^{-1}).[13]

Reaction of the chiral isopropyl phebox precursor [(*S*,*S*)-phebox-*ip*]Br (**1b**) with $Fe_2(CO)_9$ at 50 °C for 3 h also produced the chiral phebox−Fe complex **2b** in 69% yield (eq 1). In the ^{1}H NMR spectrum of **2b**, there are four doublet signals for methyl protons of the isopropyl group at δ 0.43, 0.45, 0.49, and 0.83, due to the lack of symmetry elements in the molecule.

The molecular structure of **2a** was determined by X-ray analysis using crystals obtained from a CH_3CN/CH_2Cl_2 solution.[14] The ORTEP diagram shows pseudo-octahedral geometry with the meridionally coordinated phebox ligand (Figure 1). The Fe−C1 bond length of 1.930(2) Å is comparable to that of $[C_6H_3(CH_2NMe_2)_2]FeCl_2$ (1.937(2) Å).[2a] This bond length of the phebox−Fe complex **2a** is slightly shorter than that of the phebox−Ru complexes (1.96−2.00 Å).[13] Similarly, the Fe−N bond lengths (2.0122(17) and 2.0060(18) Å) are also shorter than those of the phebox−Ru complexes (2.10−2.13 Å). The Br ligand is coordinated to the position vertical to the phebox plane, and the two CO ligands are oriented in a cis arrangement. This CO configuration is similar to that of (PCP)RuCl(CO)$_2$.[15] The Fe(1)−C(18) bond length of 1.839(2) Å is longer than the Fe(1)−C(17) bond length of 1.792(2) Å, probably due to the trans influence of a phenyl fragment.

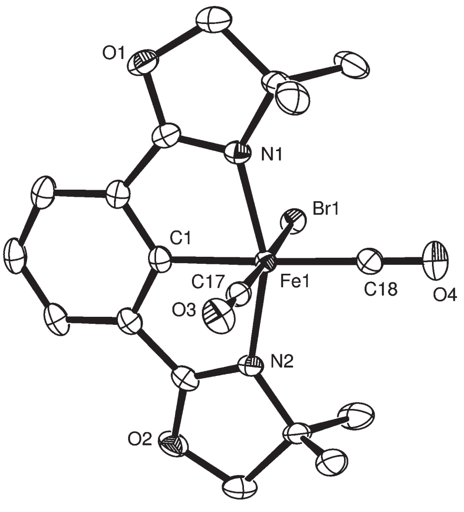


Figure 1. ORTEP diagram of **2a** at the 50% probability level. Hydrogen atoms have been omitted for clarity. Selected bond lengths (Å): Fe(1)−C(1) = 1.930(2), Fe(1)−C(17) = 1.792(2), Fe(1)−C(18) = 1.839(2), Fe(1)−N(1) = 2.0122(17), Fe(1)−N(2) = 2.0060(18), Fe(1)−Br(1) = 2.4924(5), C(17)−O(3) = 1.086(3), C(18)−O(4) = 1.134(3). Selected angles (deg): N(1)−Fe(1)−N(2) = 157.42(7), Br(1)−Fe(1)−C(17) = 177.48(7), C(1)−Fe(1)−C(18) = 175.82(9).

Asymmetric reduction of ketone is one of the most versatile methods for preparation of optically active secondary alcohols.[16] In this context, the iron-catalyzed asymmetric reduction of carbonyl compounds is thought to be a environmentally benign method.[17,18] Next, we examined the catalytic activity of the phebox−Fe complex in the hydrosilylation of simple aromatic ketones. Initially, the phebox−Fe complex **2b** was subjected to hydrosilylation of 4-phenylacetophenone (**3a**) using HSi(OEt)$_2$Me as a hydrogen source (Table 1). The reduction of **3a** with 1.2 equiv of HSi(OEt)$_2$Me in the presence of 5 mol % of **2b** in toluene at 50 °C yielded the corresponding (*R*)-alcohol **4a** in 12% yield with 24% ee (entry 1). The use of 1.5 equiv of HSi(OEt)$_2$Me increased the yield and enantioselectivity (entry 2). In contrast, other hydrosilanes, $HSiPh_2Me$, $HSiCl_3$, and H_2SiPh_2 were not effective as hydrogen sources (entries 3−5). When the reaction using HSi(OEt)$_2$Me was performed at 80 °C, the yield was improved to 91% without a decrease in enantioselectivity (entry 6). It was found that the reaction rate and enantioselectivity were significantly influenced by additives. Use of a strong base (2 mol %), namely NaO-*t*-Bu and NaOMe, increased the reaction rate but decreased the enantioselectivity of **4a** (entries 7 and 8). On the other hand, the reaction in the presence of Na(acac) (2 mol %) was completed within 1 h to give **4a** in 99% yield with 49% ee (entry 9). The catalytic reaction in the presence of Na(acac) also proceeded at 50 °C to give **4a** in 86% yield with the same enantioselectivity (entry 10). Furthermore, the reaction solvent affected the enantioselectivity. The reaction in THF gave a result similar to that in toluene (entry 11). On the other hand, reduction of **3a** in hexane quantitatively provided the (*R*)-alcohol **4a** with 66% ee (entry 12).

Several ketones, e.g., 2-acetylanthracene (**3b**) and 2-acetylnaphthalene (**3c**), were found to give the corresponding secondary alcohols **4b** (49% ee) and **4c** (53% ee). In contrast, 4-methoxyphenyl methyl ketone (**3d**) and 4-tolyl methyl ketone (**3e**) resulted in low enantioselectivities (21−38% ee).

---

(12) Motoyama, Y.; Okano, M.; Narusawa, H.; Makihara, N.; Aoki, K.; Nishiyama, H. *Organometallics* **2001**, *20*, 1580.

(13) Ito, J.; Ujiie, S.; Nishiyama, H. *Organometallics* **2009**, *28*, 630.

(14) Crystallographic data for **2a**: $C_{19}H_{21}BrCl_2FeN_2O_4$, M_r = 548.04, temperature 143 K, triclinic, $P\bar{1}$, a = 8.555(2) Å, b = 11.224(3) Å, c = 12.970(3) Å, α = 69.062(5)°, β = 82.751(5)°, γ = 69.821(5)°, V = 1091.8(5) Å^3, Z = 2; ρ_{calcd} = 1.667 Mg/m^3, μ = 2.793 mm^{-1}, 7847 reflections collected, 4993 independent reflections (R(int) = 0.0251), 4993/0/266 data/restraints/parameters, goodness of fit on F^2 1.060, final R indices ($I > 2\sigma(I)$) R1 = 0.0333 and wR2 = 0.0881, R indices (all data) R1 = 0.0370 and wR2 = 0.0901, largest difference peak/hole 0.0901 and −0.379 Å^{-3}.

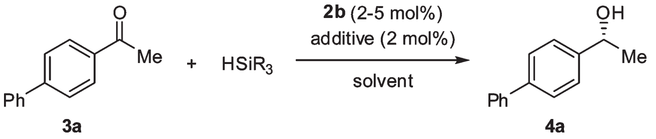
(15) (a) Amoroso, D.; Jabri, A.; Yap, G. P. A.; Gusev, D. G.; dos Santos, E. N.; Fogg, D. E. *Organometallics* **2004**, *23*, 4047. (b) Jia, G.; Lee, H. M.; Williams, I. D. *J. Organomet. Chem.* **1997**, *534*, 173.

(16) For examples of reviews, see: (a) Noyori, R.; Ohkuma, T. *Angew. Chem., Int. Ed.* **2001**, *40*, 40. (b) *Transition Metals for Organic Synthesis*, 2nd ed.; Beller, M., Bolm, C., Eds.; Wiley-VCH: Weinheim, Germany, 2004. (c) Tang, W.; Zhang, X. *Chem. Rev.* **2003**, *103*, 3029. (d) Ikariya, T.; Blacker, A. J. *Acc. Chem. Rev.* **2007**, *40*, 1300. (e) Nishiyama, H.; Itoh, K. Asymmetric Hydrosilylation and Related Reactions. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; Wiley-VCH: New York, 2000; Chapter 2.

(17) (a) Nishiyama, H.; Furuta, A. *Chem. Commun.* **2007**, 760. (b) Inagaki, T.; Le, T. P.; Furuta, A.; Ito, J.; Nishiyama, H. *Chem. Eur. J.* **2010**, *16*, 3090.

(18) (a) Shaikh, N. S.; Enthaler, S.; Junge, K.; Beller, M. *Angew. Chem., Int. Ed.* **2008**, *47*, 2497. (b) Addis, D.; Shaikh, N.; Zhou, S.; Das, S.; Junge, K.; Beller, M. *Chem. Asian J.* **2010**, *5*, 1687. (c) Sui-Seng, C.; Feutel, F.; Lough, A. J.; Morris, R. H. *Angew. Chem., Int. Ed.* **2008**, *47*, 940. (d) Mikhailine, A.; Lough, A. J.; Morris, R. H. *J. Am. Chem. Soc.* **2009**, *131*, 1394. (e) Meyer, N.; Lough, A. J.; Morris, R. H. *Chem. Eur. J.* **2009**, *15*, 5605. (f) Morris, R. H. *Chem. Soc. Rev.* **2009**, *38*, 2282. (g) Langlotz, B. K.; Wadepohl, H.; Gade, L. H. *Angew. Chem., Int. Ed.* **2008**, *47*, 4670. (h) Naik, A.; Maji, T.; Reiser, O. *Chem. Commun.* **2010**, 4475.

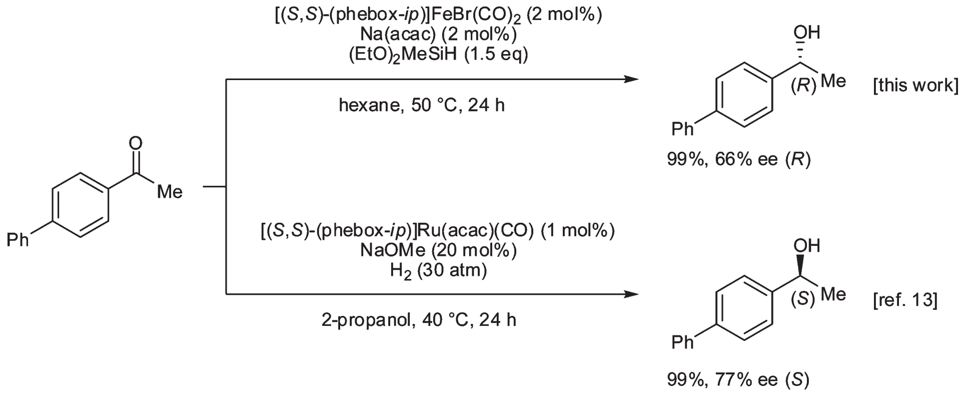
Table 1. Enantioselective Hydrosilylation of 3a Catalyzed by 2b



entry	silane (amt (equiv))	amt of **2b** (mol %)	additive	solvent	temp (°C)/time (h)	yield[a] (%)	ee[b] (%)
1	$HSi(OEt)_2Me$ (1.2)	5		toluene	50/24	12	24
2	$HSi(OEt)_2Me$ (1.5)	5		toluene	50/24	40	48
3	$HSiPh_2Me$ (1.5)	5		toluene	50/24	trace	
4	$HSiCl_3$ (1.5)	5		toluene	50/24	trace	
5	H_2SiPh_2 (1.5)	5		toluene	50/24	2	6
6	$HSi(OEt)_2Me$ (1.5)	2		toluene	80/24	91	49
7	$HSi(OEt)_2Me$ (1.5)	2	NaO-*t*-Bu	toluene	80/1	70	36
8	$HSi(OEt)_2Me$ (1.5)	2	NaOMe	toluene	80/1	85	32
9	$HSi(OEt)_2Me$ (1.5)	2	Na(acac)	toluene	80/1	99	49
10	$HSi(OEt)_2Me$ (1.5)	2	Na(acac)	toluene	50/24	86	49
11	$HSi(OEt)_2Me$ (1.5)	2	Na(acac)	THF	50/24	89	48
12	$HSi(OEt)_2Me$ (1.5)	2	Na(acac)	hexane	50/24	99	66

[a] Isolated yield. [b] Determined by HPLC.

Scheme 1. Asymmetric Reduction of Ketone Catalyzed by Fe and Ru Complexes Containing (*S*,*S*)-phebox-*ip* Ligands



Hydrosilylation with the (*S*,*S*)-phebox-*ip*−Fe catalysts afforded the alcohol with the *R* absolute configuration in toluene and hexane. On the other hand, we previously reported that asymmetric hydrogenation catalyzed by (*S*,*S*)-phebox-*ip*−Ru catalysts afforded alcohols with the *S* absolute configuration (Scheme 1).[13] These results illustrate that both enantiomers of a secondary alcohol in the asymmetric reduction of ketones can be obtained by using a single chiral source.[19] Such a reversal of absolute configuration of the products upon changing from an Rh atom to Ir was reported in the asymmetric hydrosilylation of ketones.[20] Recently, Chirik et al. reported that hydrosilylation of acetophenone derivatives using $[(S,S)\text{-pybox-}ip]Fe(CH_2SiMe_3)_2$ gave the *R* alcohol.[8b] Thus, the (*S*,*S*)-phebox−Fe and (*S*,*S*)-pybox−Fe systems have similar prochiral face discrimination properties for ketones. As several types of Fe silyl hydride complexes have been synthesized by the reaction with hydrosilane,[21] we assumed that such an active Fe−H intermediate can be generated by the initial reaction of **2b** with Na(acac) and hydrosilane.

In summary, we have described the synthesis and structural characterization of the first chiral iron complexes with bis(oxazolinyl)phenyl ligands resulting from the oxidative addition of phebox−Br to $Fe_2(CO)_9$. The phebox−Fe complex was utilized in the enantioselective hydrosilylation of ketones with $HSi(OEt)_2Me$ with asymmetric induction. Further investigation of this chiral phebox Fe complex is ongoing.

Acknowledgment. This research was partially supported by a Grant-in-Aid for Scientific Research from the Japan Society for the Promotion of Science (Nos. 22245014, 20750073) and the G-COE in chemistry (Nagoya).

Supporting Information Available: Text, figures, and a CIF file giving preparation details and spectral data for **2a**,**b**, crystal data for **2a**, and data of catalytic hydrosilylation. This material is available free of charge via the Internet at http://pubs.acs.org.

---

(19) (a) Tanaka, T.; Hayashi, M. *Synthesis* **2008**, 3361. (b) Bartók, M. *Chem. Rev.* **2010**, *110*, 1663.

(20) (a) Faller, J. W.; Chase, K. J. *Organometallics* **1994**, *13*, 989. (b) Nishibayashi, Y.; Segawa, K.; Ohe, K.; Uemura, S. *Organometallics* **1995**, *14*, 5486. (c) Frölander, A.; Moberg, C. *Org. Lett.* **2007**, *9*, 1371.

(21) Examples of Fe silyl hydride complexes: (a) Trovitch, R. J.; Lobkovsky, E.; Chirik, P. J. *Inorg. Chem.* **2006**, *45*, 7252. (b) Brunner, H.; Fisch, K. *J. Organomet. Chem.* **1991**, *412*, C11. (c) Gutsulyak, D. V.; Kuzmina, L. G.; Howard, J. A. K.; Vyboishchikov, S. F.; Nikonov, G. I. *J. Am. Chem. Soc.* **2008**, *130*, 3732.