Chiral Oxazolinylferrocene–Phosphine Hybrid Ligand for the Asymmetric Hydrosilylation of Ketones

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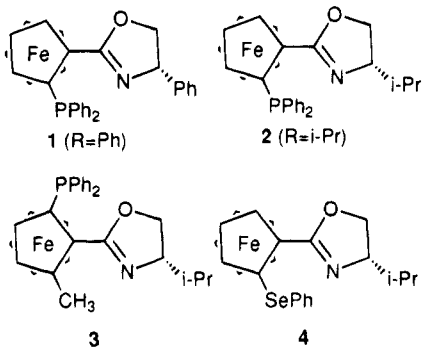
Summary: A new type of chiral oxazolinylferrocene–phosphine hybrid is a very effective ligand for Rh(I)-catalyzed asymmetric hydrosilylation of simple ketones to give the corresponding sec-alcohols (91% ee) after acid hydrolysis. Similar reactions also proceed highly selectively (96% ee) by use of Ir(I) catalyst, but the configuration of the products is completely reverse.

Molecular design of a chiral ligand is essential for obtaining highly enantiomerically pure compounds in transition-metal-catalyzed asymmetric reactions, and there has been much effort devoted to prepare efficient ligands.[1] The enantioselective reduction of prochiral ketones is an important reaction, because the optically active alcohol products are useful intermediates in synthetic organic chemistry.[2] We now envisage the preparation of newly designed chiral ligands and their use in the rhodium(I)- and iridium(I)-catalyzed asymmetric hydrosilylation of ketones. Preliminary results are reported here.

A new type of chiral ligand, an oxazolinylferrocene–phosphine hybrid ligand, was designed because the ligand could be easily prepared from reactions of either ferrocenecarboxylic acid or ferrocenecarbonitrile with chiral amino alcohols and also ferrocenes with planar chirality were known to be useful ligands for asymmetric reactions.[3] At first, the four ligands **1**,[4a,b] **2**,[4a] **3**, and **4**[4a] were prepared and applied to the hydrosilylation of acetophenone with diphenylsilane in the presence of a catalytic amount of $[Rh(COD)Cl]_2$ in Et_2O at 25 °C. The enantiomeric excesses of 1-phenylethanol obtained by acid hydrolysis of the hydrosilylation product were 60% ee (*R*), 48% ee (*R*), 37% ee (*R*), and 13% ee (*R*), respectively. Generally, in hydrosilylation, oxidative addition of hydrosilane to the rhodium(I) complex takes place first and coordination of the carbonyl group of the ketone to vacant sites of the complex follows. Therefore,



the bulkiness and the position of substituents on an oxazoline ring might affect the stereoselectivity.

With the intention of obtaining a much higher selectivity, we then designed and prepared the ligand **5**, (*S,S,S*)-[2-(4,5-*dip*henyl*o*xazolin-2-yl)*f*errocenyl]diphenylphosphine. It was abbreviated as (*S,S,S*)-DIPOF and separated from its diastereoisomer (*S,S,R*)-DIPOF (**6**) (Scheme 1). Hydrosilylation of several ketones with diphenylsilane was then investigated in the presence of a catalytic amount of $[Rh(COD)Cl]_2$ and **5** (Scheme 2).[5] As shown in Table 1, the reaction proceeded highly stereoselectively. The reactions with aryl methyl ketones gave a high enantioselectivity (runs 1–3), but those with propiophenone and α-chloroacetophenone were slow and the enantioselectivity was quite low (runs 5 and 6), in contrast to hydrosilylation using nitrogen-containing chiral ligands such as Pybox, Pythia, etc.[6] Interestingly, the ligand **5** acted effectively not only for aryl methyl ketones but also for alkyl methyl ketones (runs 7 and 8; 87–89% ee), the ee values being the highest among those obtained so far in the hydrosilylation of these alkyl methyl ketones.[7,8] Even the simple dialkyl ketone, 2-octanone, afforded moderate enantioselectivity (run 9; 60% ee).

[⊗] Abstract published in *Advance ACS Abstracts,* November 15, 1995.

(1) For reviews, see: (a) Ojima, I., Ed. *Catalytic Asymmetric Synthesis;* VCH: New York, 1993. (b) Noyori, R. *Asymmetric Catalysis in Organic Synthesis;* Wiley: New York, 1994.

(2) For examples: (a) Ohkuma, T.; Ooka, H.; Hashiguchi, S.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1995**, *117*, 2675. (b) Noyori, R.; Ohkuma, T.; Kitamura, M.; Takaya, H.; Sayo, N.; Kumobayashi, H.; Akutagawa, S. *J. Am. Chem. Soc.* **1987**, *109*, 5856. (c) Kitamura, M.; Ohkuma, T.; Inoue, S.; Sayo, N.; Kumobayashi, H.; Akutagawa, S.; Ohta, T.; Takaya, H.; Noyori, R. *J. Am. Chem. Soc.* **1988**, *110*, 629. (d) Corey, E. J.; Bakshi, R. K.; Shibata, S.; Chen, C. P.; Singh, V. K. *J. Am. Chem. Soc.* **1987**, *109*, 7925. (e) Noyori, R.; Tomino, I.; Tanimoto, Y. *J. Am. Chem. Soc.* **1979**, *101*, 3129. (f) Dumont, W.; Poulin, J. C.; Dang, T.-P.; Kagan, H. B. *J. Am. Chem. Soc.* **1973**, *95*, 8295.

(3) For example: Sawamura, M.; Ito, Y. *Chem. Rev.* **1992**, *92*, 867.

(4) (a) Nishibayashi, Y.; Uemura, S. *Synlett* **1995**, 79. (b) Richards, C. J.; Damalidis, T.; Hibbs, D. E.; Hursthouse, M. B. *Synlett* **1995**, 74. (c) Sammakia et al. have also reported the highly diastereoselective ortho-lithiation of chiral oxazolinylferrocenes: Sammakia, T.; Latham, H. A.; Schaad, D. R. *J. Org. Chem.* **1995**, *60*, 10.

(5) After $[Rh(COD)Cl]_2$ (0.0025 mmol) and the ligand **5** (0.005 mmol) were stirred in Et_2O (3 mL) at 25 °C, acetophenone (1 mmol) and then diphenylsilane (1.3 mmol) were slowly added to the mixture, the temperature being kept at 25 °C. After the mixture was stirred for suitable time at 25 °C, the addition of 1 N aqueous HCl (5 mL) and the general workup procedure afforded 1-phenylethanol quantitatively with 91% ee. The optical purity was determined by GLC or HPLC with a chiral phase. The absolute configuration was determined by an optical rotation. The ee value obtained by similar treatment with the ligand **6** was moderate.

(6) For example: (a) Brunner, H.; Becker, R.; Roepl, G. *Organometallics* **1984**, *3*, 1354. (b) Nishiyama, H.; Kondo, M.; Nakamura, T.; Itoh, K. *Organometallics* **1991**, *10*, 500. (c) Nishiyama, H.; Yamaguchi, S.; Kondo, M.; Itoh, K. *J. Org. Chem.* **1992**, *57*, 4306.

(7) With the chiral aminophosphine ligand AMPHOS, 72% ee was obtained in the hydrosilylation of *tert*-butyl methyl ketone: Payne, N. C.; Stephan, D. W. *Inorg. Chem.* **1982**, *21*, 182.

(8) With the trans-chelating diphosphine *n*-BuTRAP, 80% ee was obtained in the hydrosilylation of cyclohexyl methyl ketone: Sawamura, M.; Kuwano, R.; Ito, Y. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 111.

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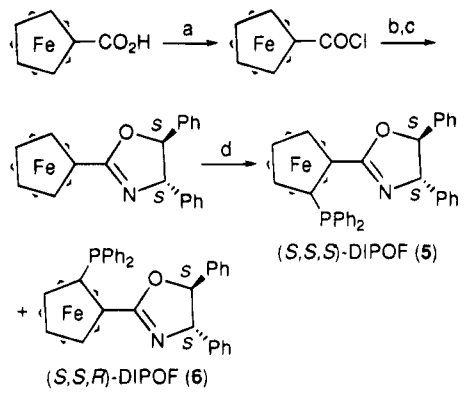
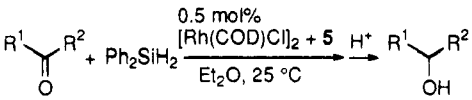
Scheme 1[a]

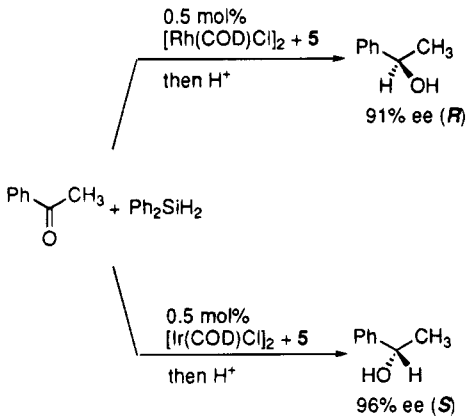


[a] Conditions: (a) $SOCl_2$, 50 °C, 54%; (b) (1*R*,2*S*)-(−)-2-amino-1,2-diphenylethanol, Et_3N, room temperature, 40%; (c) $SOCl_2$, −78 to 0 °C then 20% K_2CO_3(aq), 0 °C, 51%; (d) *s*-BuLi, −78 °C, PPh_2Cl, reflux, 68% (**5**/**6** = 35/65), **5** isolated (24%) with column chromatography (SiO_2).

Scheme 2



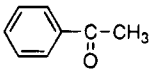
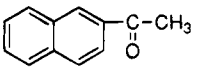
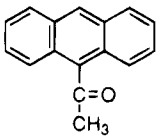
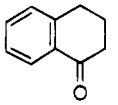
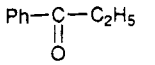
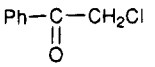
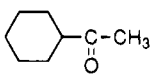
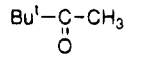
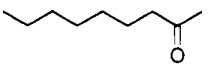
Scheme 3



Surprisingly, in the presence of $[Ir(COD)Cl]_2$ as a catalyst in place of $[Rh(COD)Cl]_2$, hydrosilylation of acetophenone with the ligand **5** at 0 °C for 20 h afforded 1-phenylethanol of the opposite configuration (*S*) with high enantioselectivity (96% ee) almost quantitatively (Scheme 3). Although similar phenomena have been observed in a few cases, only low enantioselectivity has been obtained to the best of our knowledge.[9] This is also the first example of highly enantioselective Ir-catalyzed asymmetric hydrosilylation of ketones. We are making efforts to apply this DIPOF/Ir(I) system to other ketones, the results of which will be reported in due course.[10]

In conclusion, we designed and prepared a new type of chiral oxazolinylferrocene−phosphine hybrid ligand, (*S,S,S*)-DIPOF (**5**), for the Rh(I)-catalyzed asymmetric hydrosilylation of simple ketones lacking a secondary coordinating functional group. This ligand was found to be a very effective ligand for the reduction of aryl and alkyl methyl ketones to the corresponding *sec*-alcohols with *R* configuration after acid hydrolysis. On the other hand, enantioselective hydrosilylation of acetophenone with the (*S,S,S*)-DIPOF/Ir(I) system occurred highly selectively (96% ee) to give the alcohol with an *S* configuration.

Table 1. Asymmetric Hydrosilylation of Various Ketones Catalyzed by Rh(I)−(*S,S,S*)-DIPOF (5)[a]

run	ketones	alcohols yield(%)[b]	ee(%)[c]	config.
1		100	91	*R*
2		99	88	*R*
3		100	90	*R*
4		95	57	*R*
5		12	23	*S*
6		19	8	*S*
7		45	89	*R*
8		100	87	*R*
9		92	60	*R*

[a] All the reactions were carried out in the presence of $[Rh(COD)Cl]_2$ (0.25 mol %) and (*S,S,S*)-DIPOF (**5**) (0.5 mol %) with diphenylsilane (1.5 mmol) and ketones (1.0 mmol) in Et_2O at 25 °C for 15−25 h. [b] Isolated yield. [c] The ee was determined by HPLC and GLC.

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Supporting Information Available: Text giving the preparative methods and spectral details for the ligands **1**−**5** (8 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(9) The enantioselectivity of the Ir(I)-catalyzed hydrosilylation of acetophenone was up to 32% ee: (a) Faller, J. W.; Chase, K. J. *Organometallics* **1994**, *13*, 989. (b) Kinting, A.; Kreuzfeld, H.-J.; Abicht, H.-P. *J. Organomet. Chem.* **1989**, *370*, 343.

(10) The preliminary results for several ketones are as follows: propiophenone (100%, 92% ee), phenyl *n*-propyl ketone (100%, 91% ee), and *p*-chloroacetophenone (97%, 88% ee).