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A new P-chiral bisphosphine, 1,1′-bis[(*t*-butyl)methylphosphino]ferrocene, as an effective ligand in catalytic asymmetric hydrosilylation of simple ketones

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Abstract

The asymmetric hydrosilylation of simple ketones was catalyzed by a rhodium complex with a P-chiral bisphosphine, 1,1′-bis[(*t*-butyl)methylphosphino]ferrocene, to give optically active alcohols with enantiomeric excesses of up to 92%.

1. Introduction

The design and synthesis of new chiral ligands for transition metal complexes have played a significant role in the development of catalytic asymmetric reactions, and there has been much effort devoted to the preparation of efficient ligands.[1] In particular, chiral diphosphine ligands with C_2-symmetry are of great importance in the development of transition metal-catalyzed asymmetric reactions. Recently, we synthesized electron-rich trialkylphosphine ligands BisP*,[2] and proved their efficient utility in rhodium-catalyzed asymmetric hydrogenation of α-(acylamino)acryl derivatives. Based on these results, we planned to develop a new ligand having higher reactivity and enantioselectivity, and thus designed a new P-chiral ligand,[3] 1,1′-bis[(*t*-butyl)methylphosphino]ferrocene **1**.[4,5] In this paper we report on the synthesis of the ligand and its use in the highly enantioselective hydrosilylation of simple ketones.

2. Results and discussion

The newly designed P-chiral ligand **1** was prepared by use of a phosphine borane as the intermediate (Scheme 1).[6] Thus, the 1,1′-dilithioferrocene–TMEDA complex was treated sequentially with *t*-butyldichlorophosphine, methylmagnesium bromide, and borane–THF complexes to afford a mixture of

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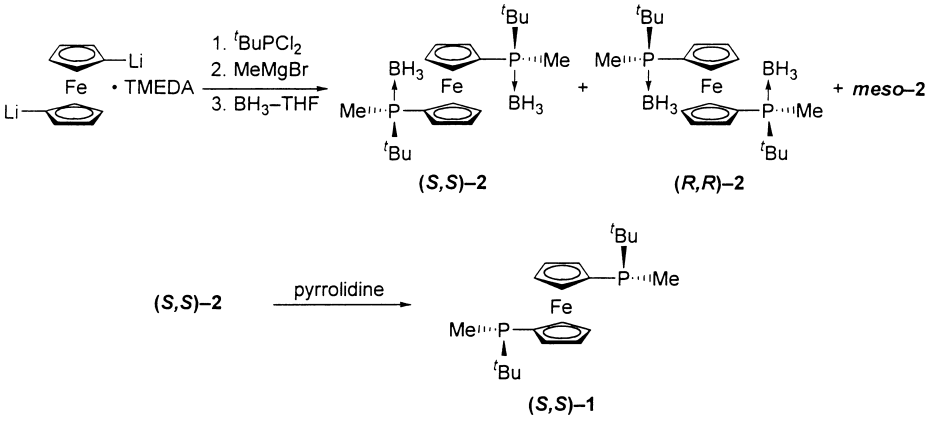
both the *dl*-form (50%) and the *meso*-form (10%). The *dl*-form was resolved by HPLC using a preparative chiral column (Daicel Chiralpak AD).



Scheme 1.

One enantiomer ($[\alpha]_D^{26}$ −249 (*c* 0.5, $CHCl_3$)) was subjected to single-crystal X-ray analysis in order to determine its absolute configuration. Fig. 1 shows its molecular structure.

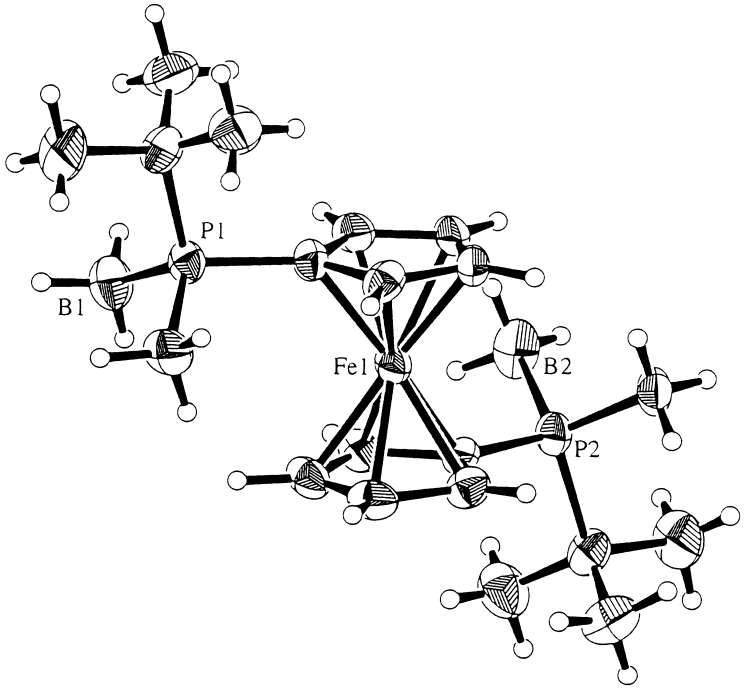


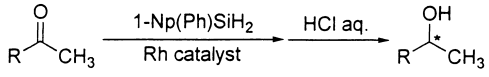
Figure 1. An ORTEP drawing of the molecular structure of (*S*,*S*)-**2**

Compound (*S*,*S*)-**2** was treated with excess pyrrolidine at 70°C for 90 min to furnish the phosphine ligand (*S*,*S*)-**1** in almost quantitative yield. Complexation of this ligand with $[Rh(nbd)_2]BF_4$ afforded the desired chiral rhodium cation complex.

First, the rhodium complex was employed for the catalytic asymmetric hydrogenation of methyl α-acetamidecinnamate and α-acetamideacrylic acid. The reaction proceeded smoothly in methanol

under ordinary conditions (2 atm, S/C=500, 50°C), but the enantiomeric excess of the products was disappointingly low (ca. 20%).

We then examined the use of the rhodium complex as a catalyst for asymmetric hydrosilylation of acetophenone (Scheme 2).[7] To our delight, the reaction proceeded in THF at −20°C using 1 mol% rhodium catalyst and 1.5 equiv. of diphenylsilane to give (*S*)-1-phenylethanol with 89% ee in 99% yield. Furthermore, the enantiomeric excess improved to 92% when a more bulky silane agent, naphthylphenylsilane, was used.



Scheme 2.

Other ketones were also subjected to hydrosilylation under the same conditions and the results are summarized in Table 1. In the tolyl methyl ketones reaction, *meta* and *para* substituted ketones were reduced with good enantioselectivity (entries 4, 5). However, reduction of the *ortho* derivative resulted in lower enantioselectivity (entry 3). Other simple ketones were reduced with good enantioselectivity (entries 7–9). The only exception was the reduction of *p*-methoxyacetophenone, which led to a racemic product (entry 6). This is probably ascribed to the so-called '*p*-methoxy effect'.[8] It is also noted that an aliphatic ketone was subjected to asymmetric hydrosilylation in good enantioselectivity (entry 10).

Table 1
Asymmetric hydrosilylation of ketone catalyzed by rhodium complex[a]

entry	R	yield (%)[b]	ee (%)[c]	config.[d]
1[e]	phenyl	99	89	*S*
2	phenyl	96	92	*S*
3	*o*-$CH_3C_6H_4$	99	44[f]	*S*
4	*m*-$CH_3C_6H_4$	96	85[g]	*S*
5	*p*-$CH_3C_6H_4$	98	84	*S*
6	*p*-$CH_3OC_6H_4$	61	*rac*[h]	
7	*p*-ClC_6H_4	79	69[i]	*S*
8	1-naphthyl	90	75	*S*
9	2-naphthyl	99	85	*S*
10	$C_6H_5CH_2CH_2$	86	68[j]	*S*

[a]All reactions were carried out at –20 °C in THF. Ketone:Rh:Silane = 100:1:150. [b]Isolated yield. [c]Determined by HPLC analysis using DAICEL CHIRALCEL OJ column (1:9 ^{i}PrOH–Hexane). [d]Determined by sign of rotation. [e]Diphenylsilane was used. [f]SHISEIDO Ceramospher Chiral RU-1 column (1:9 ^{i}PrOH–Hexane). [g]A 1:30 ^{i}PrOH–Hexane. [h]DAICEL CHIRALCEL OB column (1:9 ^{i}PrOH–Hexane). [i]DAICEL CHIRALCEL OB column (1:30 ^{i}PrOH–Hexane). [j]DAICEL CHIRALCEL OD–H column (1:19 ^{i}PrOH–Hexane).

There have been many reports dealing with rhodium-catalyzed asymmetric hydrosilylation of ketones. In general, the ligands containing oxazoline units give rise to high-to-excellent enantioselectivity,[9] while diphosphine ligands lead to low-to-moderate selectivity except in the case of *trans*-chelating diphosphine ligands (TRAP).[10] The present results are the first example of highly enantioselective hydrosilylation obtained by use of *cis*-chelating diphosphine.

3. Conclusion

We have synthesized optically active 1,1′-bis(*t*-butylmethylphosphino)ferrocene, and demonstrated its utility in rhodium-catalyzed asymmetric hydrosilylation of simple ketones.

4. Experimental

4.1. General

Optical rotations were measured with a JASCO DIP-370 polarimeter. NMR spectra were measured with a JEOL JMN-GSX-500 (500 MHz) spectrometer or a JEOL JMN-LA-400 (400 MHz) spectrometer in $CDCl_3$. Chemical shifts are reported in δ ppm. HRMS (FAB) spectra were measured with a JEOL HX-110 spectrometer at the Chemical Analysis Center, Chiba University. HPLC analyses were performed on a Hitachi L-6000 pump and L-4000 UV detector with a chiral column.

4.2. Synthesis of 1,1′-bis[boranato(t-butyl)methylphosphino]ferrocene

A hexane slurry of 1,1′-dilithioferrocene–TMEDA (20 mmol), prepared from ferrocene (3.72 g), *n*-BuLi (46 mmol), and TMEDA (25 mmol) in hexane, was added dropwise over a period of 1 h into a solution of *t*-butyldichlorophosphine (6.7 g, 42 mmol) in dry THF (60 mL) with vigorous stirring at −78°C under argon. After the addition, the cooling bath was removed, and stirring was continued for 1 h. The mixture was cooled at 0°C, then methylmagnesium bromide (70 mL, 1.0 M THF solution) added, and the mixture warmed to 50°C. After stirring for 1 h, borane−THF complex (100 mL, 1.0 M) was added at 0°C. The reaction mixture was carefully poured into a mixture of ice-water containing HCl. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The product was isolated by column chromatography (silica gel, toluene:ethyl acetate, 50:1) to afford 4.15 g of the *dl*-form (50%) and 0.84 g of the *meso*-form (10%). A small amount (ca. 200 mg) of the *dl*-form was separated to each enantiomer by HPLC using a semi-preparative chiral column [Daicel Chiralpak AD, EtOH:hexane, 5:95, (*S*,*S*) t_1=7.5 min, (*R*,*R*) t_2=13.4 min].

4.2.1. (S,S)-1,1′-Bis[boranato(t-butyl)methylphosphino]ferrocene

Orange crystals: mp 203°C (dec.); $[\alpha]_D^{26}$ −249 (*c* 0.49, $CHCl_3$); R_f=0.29 (toluene:ethyl acetate=50:1); ^{1}H NMR ($CDCl_3$) δ 1.00 (d, $^3J_{HP}$=14.1 Hz, 9H), 1.51 (d, $^2J_{HP}$=9.8 Hz, 3H), 4.24–4.25 (m, 1H), 4.67–4.68 (m, 2H), 4.72–4.73 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 5.91 (d, J_{CP}=38.0 Hz), 25.08 (d, $^2J_{CP}$=2.5 Hz), 28.80 (d, J_{CP}=34.7 Hz), 70.81 (s), 70.83 (s), 73.92 (d, $^2J_{CP}$=8.3 Hz), 73.98 (d, $^2J_{CP}$=5.0 Hz), 75.51 (d, J_{CP}=15.7 Hz); ^{11}B NMR ($CDCl_3$) δ −62.5 (d, J_{BP}=58.6 Hz); ^{31}P NMR ($CDCl_3$) δ 24.2 (m); IR (KBr) 3085, 2980, 2370, 1475, 1295, 1065, 830 cm^{-1}; HRMS calcd for $C_{20}H_{38}B_2FeKP_2$ ($M+K^+$) 457.1630, found 457.1618.

4.2.2. (R,R)-1,1′-Bis[boranato(t-butyl)methylphosphino]ferrocene

Orange crystals: mp 205°C (dec.); $[\alpha]_D^{27}$+250 (*c* 0.54, $CHCl_3$); R_f=0.29 (toluene:ethyl acetate=50:1); ^{1}H NMR ($CDCl_3$) δ 1.00 (d, $^3J_{HP}$=13.9 Hz, 9H), 1.51 (d, $^2J_{HP}$=10.0 Hz, 3H), 4.23–4.24 (m, 1H), 4.67–4.68 (m, 2H), 4.72–4.73 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 5.90 (d, J_{CP}=38.0 Hz), 25.07 (d, $^2J_{CP}$=2.5 Hz), 28.79 (d, J_{CP}=34.7 Hz), 70.82 (br s), 73.91 (d, $^2J_{CP}$=8.3 Hz), 73.98 (d, $^2J_{CP}$=5.8 Hz), 75.50 (d,

J_{CP}=15.7 Hz); ^{11}B NMR ($CDCl_3$) δ −62.5 (d, J_{BP}=58.6 Hz); ^{31}P NMR ($CDCl_3$) δ 24.2 (m); IR (KBr) 3085, 2980, 2370, 1475, 1295, 1065, 830 cm^{-1}; HRMS calcd for $C_{20}H_{38}B_2FeKP_2$ (M+K$^+$) 457.1630, found 457.1620.

4.2.3. meso-*1,1′-Bis[boranato(*t*-butyl)methylphosphino]ferrocene*

Orange crystals: mp 160–162°C; R_f=0.35 (toluene:ethyl acetate=50:1); ^{1}H NMR ($CDCl_3$) δ 1.00 (d, $^3J_{HP}$=13.9 Hz, 9H), 1.56 (d, $^2J_{HP}$=10.0 Hz, 3H), 4.37–4.39 (m, 1H), 4.61–4.63 (m, 2H), 4.65–4.68 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 5.87 (d, J_{CP}=38.9 Hz), 25.08 (d, $^2J_{CP}$=2.5 Hz), 28.78 (d, J_{CP}=34.7 Hz), 71.70 (s), 71.72 (s), 73.35 (d, $^2J_{CP}$=5.0 Hz), 73.59 (d, $^2J_{CP}$=8.3 Hz), 75.23 (d, $^2J_{CP}$=15.7 Hz); ^{11}B NMR ($CDCl_3$) δ −57.9 (d, J_{BP}=60.9 Hz); ^{31}P NMR ($CDCl_3$) δ 24.7 (m); IR (KBr) 3085, 2975, 2380, 1475, 1295, 1070, 835 cm^{-1}; HRMS calcd for $C_{20}H_{38}B_2FeKP_2$ (M+K$^+$) 457.1630, found 457.1631.

*4.2.4. Crystal data of (*S,S*)-1,1′-bis[boranato(*t*-butyl)methylphosphino]ferrocene*

An orange, thin plate crystal of dimensions 0.2×0.06×0.7 mm was mounted on a glass fiber. All measurements were made using a Rigaku AFC7S with graphite monochromated Cu-Kα radiation (λ=1.54178 Å) at 25°C. Cell constants and an orientation matrix for data collection were obtained from a least-squares refinement using the setting angles of 20 carefully centered reflections in the range 38.55<2θ<41.38°. The data were collected using a ω–2θ scan technique to a maximum 2θ value of 138.2°. Scans of (1.31+0.3tan θ)° were made at a speed of 8.0°/min (in omega). Crystal data: $C_{20}H_{38}B_2FeP_2$, Mw=417.93, monoclinic, space group $P2_1$ (#4), a=7.267(2), b=12.441(2), c=13.314(4) Å, β=93.56(2)°, V=1201.3(4) Å^3, Z=2, D_{calcd}=1.15 g/cm^3, F(000)=448.0, μ(Cu-Kα)=62.7 cm^{-1}. The structure was solved by direct methods and expanded using Fourier techniques. The non-hydrogen atoms were refined anisotropically, and the hydrogen atoms were included but not refined. The final cycle of full matrix least-squares refinement was based on 4433 observed reflections (I>1.00σ(I)) and 227 variable parameters and converged with unweighted and weighted agreement factors of: R=0.074, R_w=0.089. The absolute configuration was determined by the Flack parameter method, value=0.005(6).

*4.3. Removal of the boranato group of (*S,S*)-**2***

A solution of bisphosphine-borane (*S,S*)-**2** (54 mg, 0.13 mmol) in pyrrolidine (1 mL) was stirred at 70°C under argon. After 90 min, pyrrolidine was removed in vacuo, and the residue was passed through a column of silica using degassed toluene. The eluent was evaporated in vacuo to leave practically pure bisphosphine in almost quantitative yield.

*4.4. Preparation of the rhodium complex of (*S,S*)-**1***

The phosphine prepared above was dissolved in THF (6 mL), and the solution added to a stirred suspension of [Rh(nbd)$_2$]BF$_4$ (42 mg, 0.11 mmol) in THF (6 mL) under argon. After 90 min, the resulting, almost clear solution, was filtered under argon and the filtrate evaporated in vacuo. The residual pasty oil was washed with ether to give orange powder which was dried in vacuo.

4.5. A typical procedure for rhodium-catalyzed asymmetric hydrosilylation

In a 20 mL Schlenk tube was placed the rhodium catalyst (3.2 mg, 0.005 mmol) under argon. Freshly distilled THF (1 mL) and acetophenone (60 μL, 0.5 mmol) were added, and the solution was cooled to −20°C. To the solution was added 1-naphthylphenylsilane (160 μL, 0.75 mmol), stirred at −20°C

until the ketone disappeared. The reaction mixture was quenched with 1 M HCl (3 mL) and stirred at rt for 2 h. The mixture was extracted with ether, washed with brine, dried over Na_2SO_4, and evaporated. The residue was purified by TLC to give (*S*)-1-phenylethanol (59 mg, 96%). The ee value (92%) was determined by HPLC analysis using a chiral column (Daicel Chiralcel OJ, 2-propanol:hexane=1:9).

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