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Preparations of Chiral Pyrrolidinebisphosphines Bearing Two Different Types of Phosphino Groups and Their Use in Efficient Catalytic Asymmetric Hydrogenation[1)]

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Chiral pyrrolidinebisphosphine ligands, (2*S*-*cis*)-BCPM and (2*S*-*cis*)-BCPP, bearing two different types of phosphino groups, a dicyclohexylphosphino group and a diphenylphosphino group, were designed and prepared on the basis of our design concept for developing highly efficient ligands. The validity of the concept was confirmed experimentally in the asymmetric hydrogenation of ketopantolactone using neutral rhodium(I) complexes of BCPM, BCPP, BPPM, and BCCP. The rhodium(I) complex of (2*S*-*cis*)-BCPM was found to be the most effective catalyst (substrate/catalyst >*ca.* 10^4, >90% ee (*R*)).

Keywords catalytic asymmetric hydrogenation; chiral pyrrolidinebisphosphine; rhodium(I) complex catalyst; bisphosphine ligand; asymmetric reaction; pantolactone

Catalytic asymmetric hydrogenation is one of the most effective methods for the synthesis of optically active compounds from prochiral compounds. In the last two decades a number of rhodium or ruthenium complexes coordinated with chiral bidentate phosphine ligands have been prepared and employed as efficient catalysts for asymmetric reactions,[2)] some of them affording practical enantioselectivity (>90% ee) in the asymmetric hydrogenations of prochiral olefins and ketones.

We have developed an unsymmetrical chiral bisphosphine, (2*S*-*cis*)-4-(diphenylphosphino)-2-[(diphenylphosphino)methyl]-1-pyrrolidinecarboxylic acid 1,1-dimethylethyl ester ((2*S*-*cis*)-BPPM, **1**), which is a highly effective chiral ligand for the rhodium(I)-catalyzed asymmetric hydrogenations of *N*-acyldehydroamino acids,[3)] itaconic acid,[4)] and ketopantolactone,[5)] affording (*R*)-α-*N*-acylamino acids, (*S*)-α-methylsuccinic acid, and (*R*)-pantolactone in high optical yields, respectively.[6)] However, very few catalysts have been reported to show not only high enantioselectivity (>90% ee) but also high catalytic activity (turnover number: [substrate]/[catalyst] > *ca.*10^4) in the asymmetric hydrogenations.[7)]

We proposed a new design concept for developing chiral catalysts that are highly efficient in terms of both enantioselectivity and catalytic activity. The concept, named the "respective control concept," is based on the idea that one phosphino group of the bisphosphine ligands oriented *cis* to the prochiral group of the substrates controls the enantioselectivity and the other oriented *trans* controls the catalytic activity (Fig. 1).[8)] Our previous studies on the mechanism of the asymmetric hydrogenation of itaconic acid with a BPPM (**1**)–Rh^+ complex using ^{31}P-NMR spectroscopy indicated the intermediary key structure of the complex of BPPM (**1**)–Rh(I)-itaconate to be as shown in Fig. 2, where the prochiral olefin group of itaconic acid is oriented *trans* to the diphenylphosphino group at C_4 of the pyrrolidine ring and the carboxylate anion is oriented *cis* to the phosphino group.[9)] From these results, it was considered that the diphenylphosphino group at the C_2-methylene group situated near the prochiral olefin group played the principal role in enantioselection in the asymmetric hydrogenation. On the other hand, it was reported that the neutral rhodium(I) complexes of trialkylphosphines, being more electron-rich than diaryl-substituted phosphines, showed higher catalytic activities in the asymmetric hydrogenations of prochiral ketones. However, the enantioselectivities were lower than those obtained by using diaryl-substituted phosphines (Fig. 3).[10)]

On the basis of these facts, we designed and synthesized (2*S*-*cis*)-4-(dicyclohexylphosphino)-2-[(diphenylphosphino)methyl]-1-pyrrolidinecarboxylic acid 1,1-dimethylethyl ester (BCPM, **2**),[11)] which has a dicyclohexylphosphino group at C_4 of the pyrrolidine ring and a diphenylphosphino group at C_2-methylene. Further, we prepared (2*S*-*cis*)-2-[(dicyclohexylphosphino)methyl]-4-(diphenylphosphino)-1-pyrrolidinecarboxylic acid 1,1-dimethylethyl ester (BCPP, **3**) and (2*S*-*cis*)-4-(dicyclohexylphosphino)-2-[(dicyclohexylphosphino)methyl]-1-pyrrolidinecarboxylic acid 1,1-dimethylethyl ester (BCCP, **4**)[12)] in order to clarify the role of each phosphino group in enantioselectivity and catalytic activity in the asymmetric hydrogenations (Fig. 4). The synthetic routes

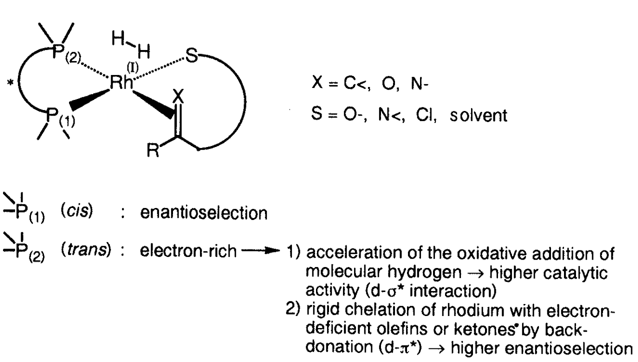

Fig. 1. New Design Concept for Developing Highly Effective Chiral Bisphosphine–Rhodium Catalysts

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This paper is dedicated to Professor Yoshifumi Maki on the occasion of his retirement from Gifu Pharmaceutical University in March 1994.

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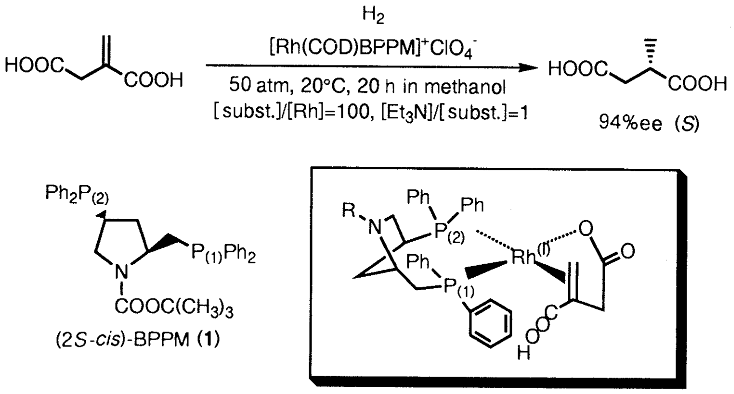


(2*S*-*cis*)-BPPM (**1**)

Fig. 2. Structure of a [BPPM-Rh(I)-Itaconate] Complex

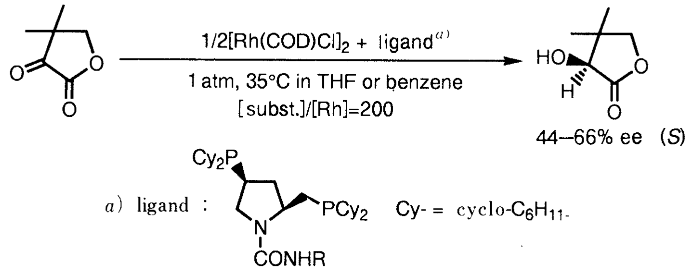
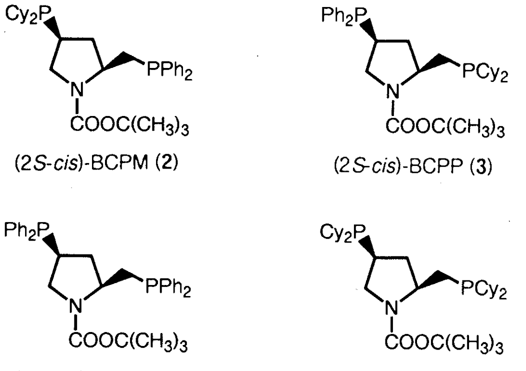


Fig. 3



(2*S*-*cis*)-BCPM (**2**)

(2*S*-*cis*)-BCPP (**3**)

(2*S*-*cis*)-BPPM (**1**)

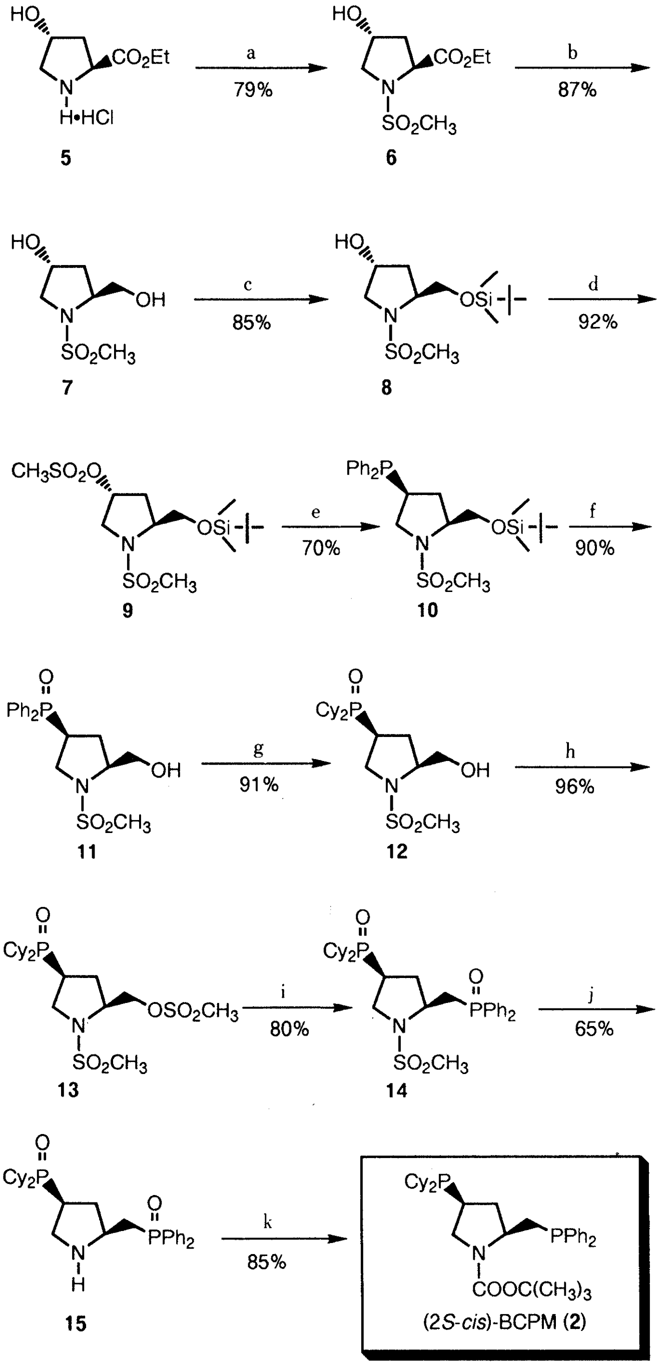
(2*S*-*cis*)-BCCP (**4**)

Fig. 4

to BCPM (**2**), BCPP (**3**), and BCCP (**4**) are shown in Charts 1, 2, and 3, respectively. We planned to synthesize **2** and **3** bearing two different phosphino groups on the pyrrolidine ring. We selected a methylsulfonyl group as the *N*-protecting group, since the protecting group was required to be stable under rather severe conditions, such as lithium aluminum hydride ($LiAlH_4$) reduction, diphenylphosphination, catalytic hydrogenation with rhodium on alumina (under a high hydrogen pressure and at a high temperature), and trichlorosilane reduction.

The chiral pyrrolidinebisphosphine, BCPM (**2**) was synthesized starting from 4-hydroxy-L-proline ethyl ester hydrochloride (**5**) (Chart 1). The *N*-protection of **5** was carried out by reaction with methanesulfonyl chloride in pyridine, yielding an *N*-methylsulfonyl derivative (**6**), which was purified by recrystallization from ethyl acetate. The ester group of **6** was reduced with $LiAlH_4$ in tetrahydrofuran (THF) to produce a diol (**7**). The selective protection of the primary alcohol of **7** was carried out by reaction with *tert*-butyldimethylsilyl chloride in THF. After mesylation of the remaining free alcohol of **8**, phosphination with sodium diphenylphosphide proceeded at 0°C in dioxane–THF to give a monophosphino compound (**10**), which was purified by column chromatography and recrystallization from a mixed solvent of ethanol and isopropyl ether. Oxidation of the phosphino group of **10** with 10% hydrogen peroxide in methanol and subsequent desilylation with 3% methanolic hydrogen chloride gave the corresponding phosphine oxide (**11**). The phenyl groups of the phosphinyl compound (**11**) were then hydrogenated with hydrogen (150 atm) over 5% rhodium on alumina in methanol at 150 °C for 2 d to give a dicyclohexylphosphinyl compound (**12**). Mesylation of the primary alcohol of **12** followed by usual diphenylphosphination and oxidation gave a bisphosphinyl compound, (2*S*-*cis*)-4-(dicyclohexylphosphinyl)-2-[(diphenylphosphinyl)methyl]-1-(methylsulfonyl)pyrrolidine (**14**), which was purified by recrystallization. Demesylation of **14** was achieved by heating with a mixture of 48% hydrobromic acid and phenol, followed by treatment with 30% sodium hydroxide to give the corresponding free amine (**15**) having ethanol as a solvent of crystallization after purification by chromatography and recrystallization. Reduction of the bisphosphine oxide (**15**) was carried out by heating with trichlorosilane–triethylamine in acetonitrile under an argon atmosphere and subsequent treatment with 30% sodium hydroxide. The resulting bisphosphino compound was converted to BCPM (**2**) by reaction with di-*tert*-butyl dicarbonate in dichloromethane under an argon atmosphere.

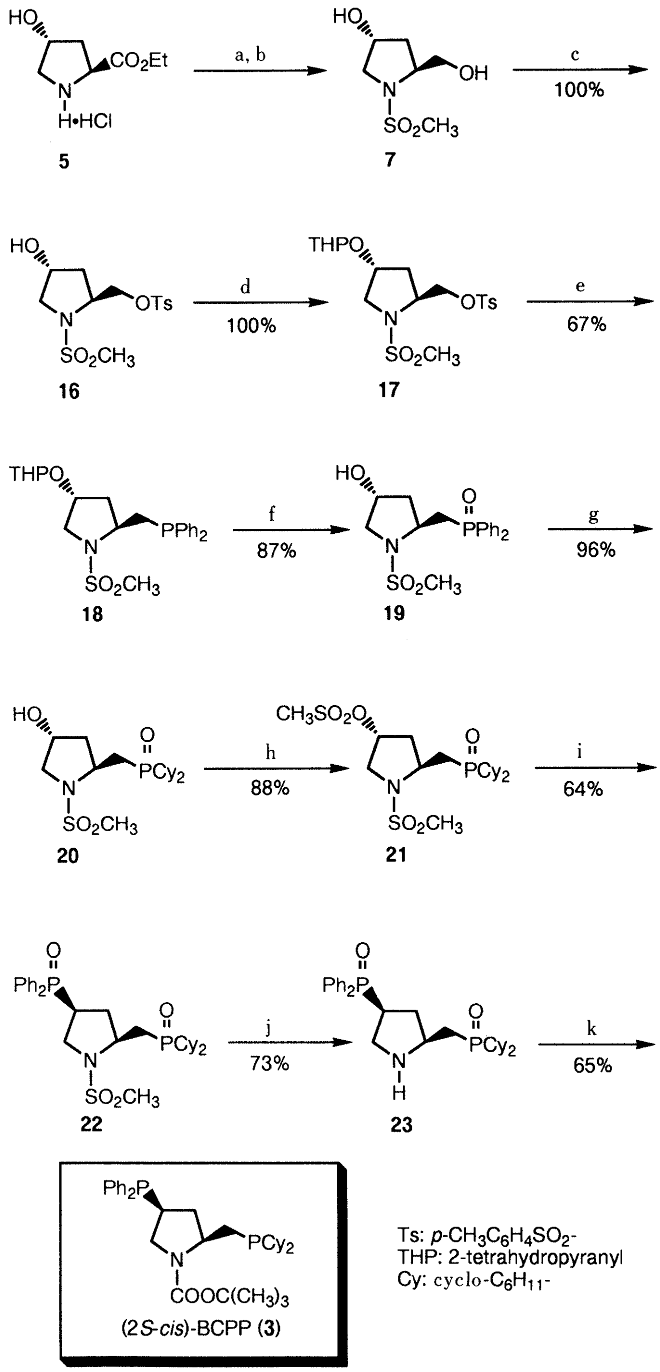
Another pyrrolidinebisphosphine, BCPP (**3**) was also synthesized starting from 4-hydroxy-L-proline ethyl ester



Cy: cyclo-C_6H_{11}-

a) methanesulfonyl chloride, pyridine; b) $LiAlH_4$, THF; c) *tert*-butyldimethylsilyl chloride, Et_3N, THF; d) methanesulfonyl chloride, pyridine; e) Ph_2PNa, dioxane-THF; f) 10% H_2O_2, then 3% HCl-methanol; g) H_2, 5% Rh on Al_2O_3, methanol; h) methanesulfonyl chloride, pyridine; i) Ph_2PNa, dioxane-THF-DMF; j) 48% HBr-phenol; k) $HSiCl_3$-Et_3N, CH_3CN, then di-*tert*-butyl dicarbonate-Et_3N, CH_2Cl_2

Chart 1



Ts: p-$CH_3C_6H_4SO_2$-
THP: 2-tetrahydropyranyl
Cy: cyclo-C_6H_{11}-

a) methanesulfonyl chloride, pyridine; b) $LiAlH_4$, THF c) p-toluenesulfonyl chloride, pyridine; d) 3,4-dihydro-2*H*-pyran, PTSA, CH_2Cl_2; e) Ph_2PNa, dioxane-THF; f) 10% H_2O_2, then PTSA, methanol; g) H_2, 5% Rh on Al_2O_3, methanol; h) methanesulfonyl chloride, pyridine; i) Ph_2PNa, dioxane-THF-DMF; j) 48% HBr-phenol; k) $HSiCl_3$-Et_3N, CH_3CN, then di-*tert*-butyl-dicarbonate-Et_3N, CH_2Cl_2

Chart 2

hydrochloride (**5**), as depicted in Chart 2. Selective tosylation of the primary alcohol of the diol (**7**) obtained above was carried out by reaction with tosyl chloride in pyridine at −25 °C overnight. The remaining hydroxyl group of **16** was protected by reaction with 2,3-dihydropyran (DHP) in the presence of p-toluenesulfonic acid (PTSA). Diphenylphosphination of **17** with sodium diphenylphosphide in dioxane–THF at room temperature gave a monophosphino compound (**18**). Oxidation of the phosphino group of **18** with 10% hydrogen peroxide in methanol and subsequent cleavage of the tetrahydro-

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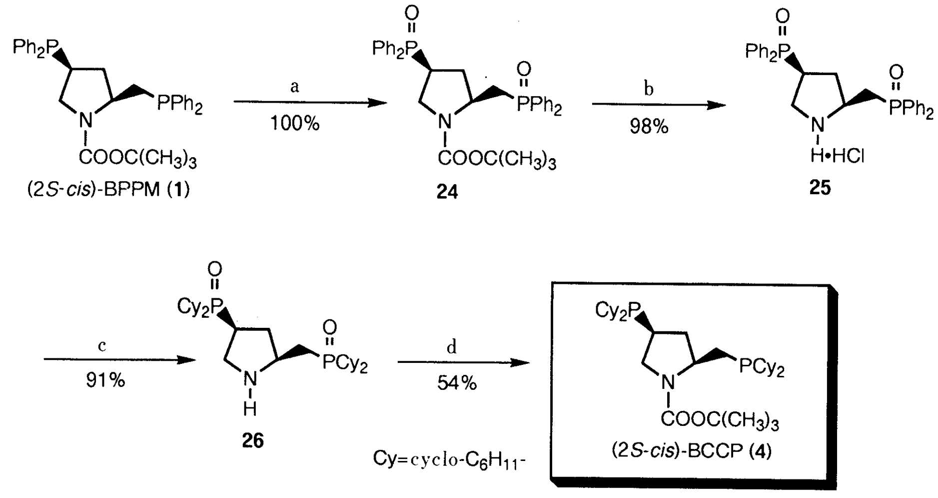
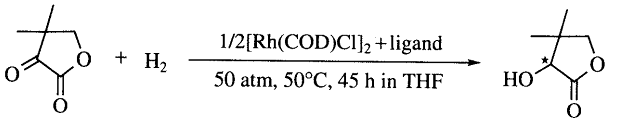


a) 10% H_2O_2, acetone; b) 3% HCl-methanol;
c) H_2, 5% Rh on Al_2O_3, methanol;
d) $HSiCl_3$-Et_3N,CH_3CN, then di-*tert*-butyl dicarbonate-Et_3N, CH_2Cl_2

Chart 3

TABLE I. Asymmetric Hydrogenation of Ketopantolactone Catalyzed by Rhodium(I) Complexes of BPPM (**1**), BCPM (**2**), BCPP (**3**), and BCCP (**4**)



Ligand	[Substrate]/ [Rh]	Convn. (%)	$[\alpha]_D^{20-24}$ (°)	Opt. yield (%)$^{a)}$	Confign.
(2*S*-*cis*)-BCPM (**2**)	1000	100	−45.9	91	*R*
	10000	100.0	−45.5	90	*R*
(2*S*-*cis*)-BPPM (**1**)	100	100	−40.8	81	*R*
	1000	44	−16.1 (−36.5)$^{b)}$	72	*R*
(2*S*-*cis*)-BCPP (**3**)	1000	75	−3.9 (−4.6)$^{b)}$	9	*R*
(2*S*-*cis*)-BCCP (**4**)	10000	100.0	+30.8	61	*S*

a) Calculated on the basis of the optical rotation value of the pure enantiomer, (*R*)-(−)-pantolactone; $[\alpha]_D^{25}$ −50.7° (*c*=2.05, H_2O). *b*) Corrected to take account of the product ratio.

pyranyl (THP) ether gave the phosphine oxide (**19**). The phenyl groups of the phosphinyl compound (**19**) were hydrogenated with hydrogen (150 atm) over 5% Rh on Al_2O_3 in methanol at 150°C for 2 d to afford the corresponding dicyclohexylphosphinyl compound (**20**). Mesylation of the hydroxyl group of **20** was followed by diphenylphosphination to give the phosphino-phosphinyl compound, which was susceptible to oxidation and converted to the bisphosphinyl compound (**22**). Demesylation of **22** by heating with a mixture of hydrobromic acid and phenol followed by treatment with sodium hydroxide gave the free amine (**23**). The bisphosphinylpyrrolidine (**23**) was transformed into BCPP (**3**) by reduction with trichlorosilane in the presence of triethylamine in toluene and subsequent reaction with di-*tert*-butyl dicarbonate under an argon atmosphere.

BCCP (**4**) was synthesized by *N*-*tert*-butoxycarbonylation of (2*S*, *cis*)-4-(dicyclohexylphosphino)-2-[(dicyclohexylphosphino)methyl]pyrrolidine, which was obtained by oxidation of BPPM (**1**), removal of the *N*-*tert*-butoxycarbonyl group, catalytic reduction with rhodium on alumina, and then reduction with trichlorosilane according to the method reported previously (Chart 3).[10]

To examine the validity of our concept, we carried out the asymmetric hydrogenation of ketopantolactone, the most conformationally rigid class of α-keto esters, using the neutral rhodium(I) complexes of BCPM (**2**), BCPP (**3**), and BCCP (**4**). The asymmetric hydrogenations were run with the substrate (10 mmol), chloro(1,5-cyclooctadiene)-rhodium(I) dimer ([Rh(COD)Cl]$_2$) (0.5×10^{-2} mmol), and the bisphosphine ligand (1.1×10^{-2} mmol) under hydrogen (50 atm) at 50 °C for 45 h in peroxide-free THF (10 ml). For BCPM (**2**) and BCCP (**4**), hydrogenation with [bisphosphine ligand]/[Rh]/[substrate] = $1.3/1.0/10^4$ was also examined. The results are summarized in Table I. The asymmetric hydrogenation using the neutral rhodium(I) complex of BCPM (**2**) prepared *in situ* gave high enantioselectivity (>90% ee) even at high ratios (*ca.* 10^4) of the substrate to the catalyst. When benzene was used as a solvent instead of THF, a somewhat lower optical yield was obtained. On the other hand, the cationic rhodium(I) complex (0.1 mol% to the substrate) prepared *in situ* by mixing BCPM (**2**) and bis(1,5-cyclooctadiene)-rhodium(I) hexafluorophosphate ($[Rh(COD)_2]^+PF_6^-$) (molar ratio, 1.1 : 1) showed very low enantioselectivity (2—3% ee (*R*)) in spite of its high catalytic activity. From the results shown in Table I, it is clear that BPPM (**1**) and BCPM (**2**) bearing the diphenylphosphinomethyl group on the C_2 position of the pyrrolidine ring gave higher optical yields than BCPP (**3**) and BCCP (**4**) bearing the dicyclohexylphosphinomethyl group on the same C_2 position. It is also clear that BCPM (**2**) and BCCP (**4**)

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bearing the dicyclohexylphosphino group (more electron-rich than the diphenylphosphino group) on the C_4 position accelerated the hydrogenation rate of the carbonyl group more dramatically ($> 10^2$ times) than BPPM (**1**) and BCPP (**4**) having the diphenylphosphino group on the same C_4 position. In conclusion, the steric effect of the phosphino group on the C_2-methylene group of the pyrrolidine ring plays a crucial role in the enantioselection, and the electronic effect of the phosphino group on the C_4 position is important for increasing the catalytic activity.

Thus we have experimentally confirmed the "respective control concept" for developing highly efficient ligands in transition metal-catalyzed asymmetric hydrogenation, and found a new bisphosphine ligand, BCPM (**2**), to be the most effective ligand in the rhodium(I) complex-catalyzed asymmetric hydrogenation of ketopantolactone.

Experimental

General Methods All melting points and boiling points are uncorrected. IR spectra were recorded on a JASCO A-202 or IR-810 spectrometer. ^{1}H-NMR spectra were measured with a JEOL FX-90Q (90 MHz) using tetramethylsilane as an internal standard. Optical rotations were measured with a JASCO DIP-140 digital polarimeter. Column chromatography was carried out on silica gel (Wakogel C-200, 100—200 mesh or Silica gel 60, 70—230 mesh, Merck). Gas-liquid chromatography (GLC) was conducted on a Hitachi 163 gas chromatograph with a 1 m × 3 mm column of 10% SE 30 or 10% poly(ethylene glycol) (PEG) 20M supported on Chromosorb W (AW-DMCS) (80—100 mesh).

Materials THF was purified by distillation from sodium benzophenone ketyl immediately prior to use. Ketopantolactone (Fuji Chemical Industries, Ltd.) was purified by recrystallization. All other solvents and reagents were obtained commercially in high purity, and were used after drying over molecular sieves or without further purification unless otherwise indicated.

(2*S*-*trans*)-4-Hydroxy-1-(methylsulfonyl)-2-pyrrolidinecarboxylic Acid Ethyl Ester (6) Methanesulfonyl chloride (12.03 g, 0.105 mol) was added dropwise to an ice-cooled solution of 4-hydroxy-L-proline ethyl ester hydrochloride (**5**) (19.56 g, 0.1 mol) in anhydrous pyridine (200 ml) with stirring, and the mixture was stirred at 0 °C for 6 h and then at room temperature for 15 h. After evaporation of the pyridine under reduced pressure, the residue was acidified to pH 4 by addition of 10% HCl and extracted with ethyl acetate (3 × 200 ml). The combined extracts were washed with brine, and dried over anhydrous $MgSO_4$. After evaporation of the solvent, the crystalline residue was recrystallized from ethyl acetate, affording white crystals of **6**. Yield, 18.70 g (79%), mp 118—120 °C, $[\alpha]_D^{20}$ −80.1° ($c=1.02$, ethanol). IR (KBr): 3540 (OH), 1745 (CO), 1324, 1151 (SO_2) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.29 (3H, t, $J=7.1$ Hz, $CH_2C\underline{H}_3$), 1.89—2.59 (2H, m, $CHC\underline{H}_2CH$), 2.44 (1H, br, OH), 3.01 (3H, s, SO_2CH_3), 3.59 (2H, m, CH_2N), 4.04 (2H, q, $J=7.1$ Hz, $C\underline{H}_2CH_3$), 4.14—4.66 (2H, OCH, NCH). *Anal.* Calcd for $C_8H_{15}NO_5S$: C, 40.49; H, 6.37; N, 5.90. Found: C, 40.49; H, 6.34; N, 5.77.

(2*S*-*trans*)-4-Hydroxy-1-(methylsulfonyl)-2-pyrrolidinemethanol (7) A solution of **6** (16.6 g, 0.07 mol) in anhydrous THF (200 ml) was added dropwise to a stirred and ice-cooled suspension of $LiAlH_4$ (3.98 g, 0.105 mol) in THF (360 ml). The mixture was stirred at 0 °C for 3 h and at room temperature for 3 h, and then a small amount of water was added to the reaction mixture with cooling in an ice bath. Filtration through Celite and evaporation under reduced pressure gave **7** (11.90 g, 87%) as a viscous liquid, which was confirmed to be almost pure by GLC, and used without further purification. An analytical sample was obtained by recrystallization from isopropyl ether–hexane; mp 55—57 °C, $[\alpha]_D^{20}$ −63.8° ($c=1.28$, ethanol). IR (KBr): 3440 (OH), 1319, 1149 (SO_2) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.57—2.33 (1H, br, OH), 1.87—2.16 (2H, m, CCH_2C), 2.96 (3H, s, CH_3), 3.52 (1H, br, OH), 2.43—4.11 (5H, m, CH_2NCHCH_2O), 4.45 (1H, br, OCH). *Anal.* Calcd for $C_6H_{13}NO_4S$: C, 36.91; H, 6.71; N, 7.13. Found: C, 37.03; H, 6.70; N, 7.13.

(3*R*-*trans*)-5-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]methyl]-1-(methylsulfonyl)-3-pyrrolidinol (8) *tert*-Butyldimethylsilyl chloride (6.63 g, 44 mmol) was added to a solution of **7** (7.81 g, 40 mmol), 4-dimethylaminopyridine (195 mg, 1.6 mmol), and triethylamine (4.86 g, 48 mmol) in anhydrous THF (160 ml) and the mixture was stirred for 16 h at room temperature. The reaction mixture was concentrated *in vacuo* and water (40 ml) was added to the residue. The mixture was extracted with ethyl acetate (3 × 120 ml). After drying over anhydrous $MgSO_4$, the solution was concentrated *in vacuo* to leave **8** as a viscous liquid, which was confirmed to be almost pure by GLC and used without further purification. An analytical sample was obtained by recrystallization from isopropyl ether–hexane; mp 55—57 °C, $[\alpha]_D^{20}$ −53.9° ($c=1.00$, ethanol). IR (KBr): 3550 (OH), 1327, 1150 (SO_2) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.07 (6H, s, $Si(CH_3)_2$), 0.89 (9H, s, $SiC(CH_3)_3$), 1.99—2.34 (3H, m, CCH_2C, OH), 2.92 (3H, s, SO_2CH_3), 3.40—3.53 (2H, m, CH_2N), 3.60—4.07 (3H, m, $NCHCH_2O$), 4.36—4.56 (1H, m, OCH). *Anal.* Calcd for $C_{12}H_{27}NO_4SSi$: C, 46.57; H, 8.97; N, 4.53. Found: C, 46.47; H, 8.73; N, 4.88.

(3*R*-*trans*)-5-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]methyl]-1-(methylsulfonyl)-3-pyrrolidinol Methanesulfonate (9) Methanesulfonyl chloride (5.05 g, 44 mmol) was added dropwise to a stirred and ice-cooled solution of **8** (10.52 g, 34 mmol) in anhydrous pyridine (100 ml), and the mixture was stirred at room temperature for 15 h. After evaporation of the pyridine, the residue was treated with cooled 10% HCl (*ca.* 40 ml) and extracted with ethyl acetate (3 × 150 ml). The combined extracts were washed successively with water (50 ml), saturated sodium bicarbonate (75 ml), and brine (75 ml). After drying over anhydrous $MgSO_4$, the solution was concentrated under reduced pressure to leave a crystalline residue, which was purified by recrystallization from isopropyl ether–hexane to give pure **9** (12.13 g, 92% yield); mp 51.5—52.5 °C, $[\alpha]_D^{20}$ −28.6° ($c=1.00$, ethanol). IR (KBr): 1363, 1173 (OSO_2), 1329, 1140 (NSO_2) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.08 (6H, s, $Si(CH_3)_2$), 0.89 (9H, s, $SiC(CH_3)_3$), 2.27—2.48 (2H, m, CCH_2C), 2.92 (3H, s, NSO_2CH_3), 3.06 (3H, s, OSO_2CH_3), 3.41—4.15 (6H, m, $CHCH_2NCHCH_2O$). *Anal.* Calcd for $C_{13}H_{29}NO_6S_2Si$: C, 40.29; H, 7.54; N, 3.61. Found: C, 40.39; H, 7.52; N, 3.49.

(3*S*-*cis*)-2-[[[(1,1-Dimethylethyl)dimethylsilyl]oxy]methyl]-4-(diphenylphosphino)-1-(methylsulfonyl)pyrrolidine (10) Sodium diphenylphosphide was prepared by heating chlorodiphenylphosphine (11.39 g, 52 mmol) and sodium metal (2.60 g, 114 mmol) in dry, degassed dioxane (150 ml) under an argon atmosphere for 3—4 h. After ice-cooling of the resultant suspension, peroxide-free THF (50 ml) was added and the mixture was cooled in an ice-bath. Then a solution of **9** (10.45 g, 27 mmol) in peroxide-free THF was added dropwise, and the mixture was stirred at 0° C for 2 h and at room temperature overnight. After filtration through Celite and concentration *in vacuo*, brine (50 ml) was added to the residue and the mixture was extracted with ethyl acetate (3 × 150 ml). The combined extracts were washed with brine (50 ml) and dried over $MgSO_4$. Concentration *in vacuo* and chromatography on silica gel (eluent: benzene–5% ethyl acetate) gave crystals, which were recrystallized from ethanol–isopropyl ether to afford pure **10** (8.94 g, 70% yield); mp 56.5—58 °C, $[\alpha]_D^{21}$ −28.9° ($c=1.02$, ethanol). IR (KBr): 1328, 1145 (SO_2) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.05 (6H, s, $Si(CH_3)_2$), 0.89 (9H, s, $SiC(CH_3)_3$), 1.85—2.42 (2H, m, CCH_2C), 2.86 (3H, s, SO_2CH_3), 2.56—2.95 (1H, m, PCH), 3.01—4.07 (5H, m, CH_2NCHCH_2O), 7.23—7.58 (10H, m, Ar-H). *Anal.* Calcd for $C_{24}H_{36}NO_3PSSi$: C, 60.35; H, 7.51; N, 2.93. Found: C, 60.38; H, 7.59; N, 2.91.

(2*S*-*cis*)-4-(Diphenylphosphinyl)-1-(methylsulfonyl)-2-pyrrolidinemethanol (11) Hydrogen peroxide (10%) (11.85 g, 34.8 mmol) was added to a stirred and ice-cooled solution of **10** (8.39 g, 17.6 mmol) in methanol (180 ml), and the mixture was stirred at 0 °C for 1 h and at room temperature for 1 h. Then methanolic 3% hydrogen chloride (12 g) was added, and the whole mixture was stirred at room temperature for 2 h. After concentration under reduced pressure at a low temperature, water (50 ml) was added to the residue and the organic layer was extracted with dichloromethane (3 × 150 ml). The combined extracts were washed with saturated sodium bicarbonate (50 ml), and dried over $MgSO_4$. Evaporation of the solvent and recrystallization from ethanol–isopropyl ether gave pure **11** (6.01 g, 90% yield) as white crystals; mp 138—139°C, $[\alpha]_D^{21}$ −32.7° ($c=0.72$, ethanol). IR (KBr): 3320 (OH), 1325, 1148 (SO_2), 1175 (PO) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.08—2.66 (2H, m, CCH_2C), 2.26 (1H, br, OH), 2.97 (3H, s, CH_3), 2.86—3.11 (1H, m, PCH), 3.37—3.88 (3H, m, CH_2NCH), 3.91—4.46 (2H, m, CH_2O), 7.33—7.96 (10H, m, Ar-H). *Anal.* Calcd for $C_{18}H_{22}NO_4PS$: C, 56.98; H, 5.84; N, 3.69. Found: C, 56.72; H, 5.88; N, 3.43.

(2*S*-*cis*)-4-(Dicyclohexylphosphinyl)-1-(methylsulfonyl)-2-pyrrolidinemethanol (12) Compound **11** (1.70 g, 4.5 mmol), 5% rhodium on alumina powder (850 mg), and methanol (20 ml) were placed in an

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autoclave, and the mixture was stirred and heated at 150 °C for 48 h under an initial hydrogen pressure of 150 atm. The autoclave was cooled to room temperature, then the reaction mixture was centrifuged to remove the catalyst and the supernatant layer was separated by decantation. The catalyst was washed three times with methanol in the same way. The combined methanol solutions were concentrated *in vacuo*. The residue was purified by silica gel chromatography (eluent: ethanol) and recrystallization from ethanol–isopropyl ether to give pure **12** (1.62 g, 91%); mp 211—212 °C, $[\alpha]_D^{22}$ $-25.4°$ ($c=0.80$, ethanol). IR (KBr): 3180 (OH), 1337, 1141 (SO_2), 1160 (PO) cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 0.80—2.66 (25H, m, $P(C_6H_{11})_2$, OH, CCH_2C), 2.83—3.03 (1H, m, PCH), 3.02 (3H, s, CH_3), 3.36—4.35 (5H, m, CH_2NCH_2O). *Anal.* Calcd for $C_{18}H_{34}NO_4PS$: C, 55.22; H, 8.75; N, 3.58. Found: C, 55.01; H, 8.76; N, 3.37.

(2*S*-*cis*)-4-(Dicyclohexylphosphinyl)-1-(methylsulfonyl)-2-pyrrolidinemethanol Methanesulfonate (13) Methanesulfonyl chloride (0.82 g, 7.2 mmol) was added dropwise to a stirred and ice-cooled solution of **12** (1.40 g, 3.6 mmol) in pyridine (20 ml), and the mixture was stirred at 0 °C for 3 h and at room temperature for 14 h. Then 10% HCl (70 ml) was added, and the mixture was extracted with ethyl acetate (3 × 80 ml). The combined extracts were washed with saturated sodium bicarbonate (30 ml) and water (30 ml), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel chromatography (eluent: ethyl acetate–ethanol (5 : 1)) and recrystallization from ethanol–isopropyl ether to give **13** (1.61 g, 96%) as crystals; mp 181—182 °C, $[\alpha]_D^{22}$ $-15.2°$ ($c=1.10$, ethanol). IR (KBr): 1360, 1182 (OSO_2), 1324, 1160 (NSO_2), 1159 (PO) cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 1.03—2.75 (24H, $P(C_6H_{11})_2$, CCH_2C), 2.86—3.11 (1H, m, PCH), 2.99 (3H, s, NSO_2CH_3), 3.09 (3H, s, OSO_2CH_3), 3.25—4.12 (3H, m, CH_2NCH), 4.31 (2H, br, CH_2O). *Anal.* Calcd for $C_{19}H_{36}NO_6PS_2$: C, 48.60; H, 7.73; N, 2.98. Found: C, 48.65; H, 7.22; N, 2.93.

(2*S*-*cis*)-4-(Dicyclohexylphosphinyl)-2-[(diphenylphosphinyl)methyl]-1-(methylsulfonyl)pyrrolidine (14) A solution of **13** (1.00 g, 2.13 mmol) in *N*,*N*-dimethylformamide (DMF) was added at −20 °C to a stirred, yellow suspension of sodium diphenylphosphide which was prepared from sodium (329 mg, 17.0 mmol) and chlorodiphenylphosphine (1.88 g, 8.52 mmol) in dioxane (20 ml), followed by addition of THF (20 ml). The mixture was stirred at −20 °C for 13 h, then filtered through Celite and the filtrate was concentrated to dryness. Brine (20 ml) was added to the residue and the mixture was extracted with ethyl acetate (3 × 50 ml). The combined extracts were washed with brine (50 ml), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was dissolved in methanol (20 ml) and to the solution was added 10% hydrogen peroxide (excess) with ice-cooling. The mixture was stirred at 0 °C for 0.5 h and at room temperature for 0.5 h. After evaporation of the solvent (not completely), the residue was dissolved in ethyl acetate (20 ml). This solution was washed with brine (10 ml), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel chromatography (eluent: ethyl acetate–ethanol (5 : 1)) and recrystallization from ethanol to give **14** (1.14 g, 93%); mp 281—284 °C (dec.), $[\alpha]_D^{24}$ $-39.4°$ ($c=1.00$, ethanol). IR (KBr): 1340, 1160 (SO_2), 1182 (PO) cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 0.94—2.65 (25H, m, $P(C_6H_{11})_2$, CCH_2C, H_a or H_b of CH_2P), 2.69—2.90 (1H, m, PCH), 2.85 (3H, s, CH_3), 3.55 (1H, ddd, H_c or H_d of CH_2N), 3.50—3.91 (2H, m, H_a or H_b of CH_2P, H_c or H_d of CH_2N), 3.99—4.58 (1H, m, NCH), 7.23—8.00 (10H, m, Ar-H). *Anal.* Calcd for $C_{30}H_{43}O_4P_2S$: C, 62.59; H, 7.53; N, 2.43. Found: C, 63.15; H, 7.12; N, 2.21.

(2*S*-*cis*)-4-(Dicyclohexylphosphinyl)-2-[(diphenylphosphinyl)methyl]-pyrrolidine (15) A mixture of **14** (3.49 g, 6.06 mmol), phenol (6.97 g), and 48% hydrobromic acid (53 ml) was heated under reflux for 10 h under an argon atmosphere. After ice-cooling, the reaction mixture was basified by addition of 30% NaOH, and extracted with ethyl acetate (2 × 200 ml). The combined extracts were washed with saturated sodium bicarbonate, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel chromatography (eluent: ethyl acetate–ethanol) and recrystallization from ethanol–isopropyl ether to give **15** (2.14 g, 65%) having ethanol as a solvent of crystallization; mp 203—204 °C, $[\alpha]_D^{22}$ $-35.3°$ ($c=1.00$, ethanol). IR (KBr): 3400 (OH of ethanol), 3270 (NH), 1184 (PO) cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 0.96—3.63 (31H, m, $P(C_6H_{11})_2$, CCH_2C, CH_2P, PCH, CH_2NCH, $CH_3CH_2O\underline{H}$), 1.23 (3H, t, $J=7.08$ Hz, $C\underline{H}_3CH_2OH$), 2.14 (1H, s, NH), 3.82 (2H, q, $J=7.08$ Hz, $CH_3C\underline{H}_2OH$), 7.36—7.97 (10H, m, Ar-H). *Anal.* Calcd for $C_{29}H_{41}NO_2P_2 \cdot CH_3CH_2OH$: C, 68.49; H, 8.71; N, 2.57. Found: C, 68.24; H, 8.52; N, 2.60.

(2*S*-*cis*)-4-(Dicyclohexylphosphino)-2-[(diphenylphosphino)methyl]-1-pyrrolidinecarboxylic Acid 1,1-Dimethylethyl Ester (BCPM, 2) Trichlorosilane (1.355 g, 10.0 mmol) was added dropwise to a stirred and ice-cooled solution of **15** (500 mg, 1.00 mmol) and triethylamine (1.113 g, 11.0 mmol) in dry and degassed acetonitrile (40 ml) under an argon atmosphere, and the mixture was heated under reflux for 3 h. After cooling, the reaction mixture was concentrated under reduced pressure. Degassed benzene (30 ml) and then degassed 30% NaOH (10 ml) were added to the residue, and the mixture was stirred and heated at 60 °C for 30 min under an argon atmosphere, resulting in a clear two-phase solution. The organic layer was separated, washed successively with degassed water, saturated sodium bicarbonate, and brine, and dried over anhydrous $MgSO_4$. Evaporation of the solvent under reduced pressure gave a solid residue. Di-*tert*-butyl dicarbonate (240 mg, 1.10 mmol) was added dropwise to an ice-cooled solution of the residue and triethylamine (111 mg, 1.10 mmol) in dry and degassed dichloromethane (20 ml) under an argon atmosphere. After the mixture had been stirred at room temperature for 2 h, the reaction mixture was concentrated under reduced pressure. The solid residue was recrystallized from degassed ethanol to give **2** (480 mg, 85%) as needles; mp 126—127 °C $[\alpha]_D^{21}$ $-40.9°$ ($c=0.24$, benzene). IR (KBr): 1692 (C=O) cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 0.85—2.00 (25H, m, $P(C_6H_{11})_2$, CCH_2C, H_a or H_b of CH_2P), 1.45 (9H, s, $C(CH_3)_3$, 2.00—2.97 (2H, m, CH_2NCH), 7.15—7.60 (10H, m, $P(C_6H_5)_2$). *Anal.* Calcd for $C_{34}H_{49}NO_2P_2$: C, 72.19; H, 8.73; N, 2.48. Found: C, 72.39; H, 8.78; N, 2.49.

(2*S*-*trans*)-4-Hydroxy-1-(methylsulfonyl)-2-pyrrolidinemethanol α-(4-Methylbenzenesulfonate) (16) A solution of *p*-toluenesulfonyl chloride (11.06 g, 58 mmol) in dry pyridine (30 ml) was added dropwise at −30 °C to a stirred solution of **7** (10.74 g, 55 mmol) in dry pyridine (100 ml), and the mixture was stirred at −25 °C for 15 h, at 0 °C for 4 h, and at room temperature for 1 h. Hydrochloric acid (10%) (560 ml) was added dropwise to the reaction mixture with cooling in an ice bath. The mixture was extracted with ethyl acetate (3 × 250 ml). The combined extracts were washed with water, saturated sodium bicarbonate, and brine, and dried over anhydrous $MgSO_4$. Evaporation of the solvent gave **16** (19.36 g, quantitative yield) as a viscous liquid, which was revealed by ^1H-NMR to be almost pure. IR (neat): 3560 (OH), 1338, 1147 (NSO_2), 1345, 1174 (OSO_2) cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 1.88—2.29 (2H, m, CCH_2C), 2.05 (1H, br s, OH), 2.45 (3H, s, Ar-CH_3), 2.88 (3H, s, SO_2CH_3), 3.27—3.57 (2H, m, CH_2N), 3.86—4.36 (3H, m, $NCHCH_2O$), 4.38—4.58 (1H, m, OCH), 7.35 (2H, d, $J=8.3$ Hz, Ar-H), 7.79 (2H, d, $J=8.3$ Hz, Ar-H).

(2*S*-*trans*)-1-(Methylsulfonyl)-4-[(tetrahydro-2*H*-pyran-2-yl)oxy]-2-pyrrolidinemethanol 4-Methylbenzenesulfonate (17) PTSA monohydrate (713 mg, 3.75 mmol) was added to a solution of **16** (8.90 g, 25.5 mmol) and 3,4-dihydro-2*H*-pyran (5.37 g, 64 mmol) in dichloromethane (150 ml), and the mixture was stirred at room temperature for 3 h. The reaction mixture was washed with saturated sodium bicarbonate and water, and dried over anhydrous $MgSO_4$. Evaporation of the solvent gave **17** (11.40 g, quantitative yield) as a viscous liquid, which was revealed by ^1H-NMR to be pure enough to use without further purification. IR (KBr): 1340, 1151 (NSO_2), 1360, 1130 (OSO_2) cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 1.34—2.59 (8H, m, $CH_2CH_2CH_2$, CCH_2C), 2.45 (3H, s, Ar-CH_3), 2.82 and 2.87 (1.41H and 1.59H, s and s, SO_2CH_3), 3.24—5.03 (9H, m, CH_2OCH, $OCHCH_2NCHCH_2O$), 7.34 (2H, d, $J=8.3$ Hz, Ar-H), 7.79 (2H, d, $J=8.3$ Hz, Ar-H).

[2*S*-*trans*]-2-[(Diphenylphosphino)methyl]-1-(methylsulfonyl)-4-[(tetrahydro-2*H*-pyran-2-yl)oxy]pyrrolidine (18) A yellow suspension of sodium diphenylphosphide was prepared from sodium (0.91 g, 39.6 mmol) and chlorodiphenylphosphine (3.97 g, 18 mmol) in fresh dioxane (60 ml) as described above. To the suspension were added THF (30 ml) and a solution of **17** (4.33 g, 10 mmol) in THF with cooling in an ice bath under an argon atmosphere. The mixture was stirred at 0 °C for 6 h and at room temperature for 13 h. Usual work-up as described above and purification by column chromatography (silica gel, benzene–ethyl acetate) gave **18** as a viscous liquid (3.01 g, 67%). IR (neat): 1337, 1147 (SO_2) cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 1.21—2.56 (9H, m, $CCH_2CH_2CH_2CH_2C$, CCH_2C, H_a or H_b of CH_2P), 2.77 and 2.80 (1.26H and 1.74H, s and s, SO_2CH_3), 3.28 (1H, m, H_a or H_b of CH_2P), 3.31—5.05 (7H, m, CH_2OCH, $OCHCH_2NCH$), 7.16—7.76 (10H, m, Ar-H).

(3*R*-*trans*)-5-[(Diphenylphosphinyl)methyl]-1-(methylsulfonyl)-3-pyrrolidinol (19) Hydrogen peroxide (10%) (2.50 g, 7.37 mmol) was added to an ice-cooled solution of **18** (3.00 g, 6.70 mmol) in methanol (60 ml) and the mixture was stirred at room temperature for 1 h. PTSA

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monohydrate (127 mg, 0.67 mmol) was added to the reaction mixture. After heating under reflux for 1 h, the reaction mixture was cooled and concentrated (not completely). Usual work-up as described above and recrystallization from ethanol–isopropyl ether gave **19** (2.22 g, 87%); mp 188—189°C, $[\alpha]_D^{20}$ $-79.4°$ ($c=1.10$, ethanol). IR (KBr): 3220 (OH), 1337, 1155 (SO_2), 1178 (PO) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.78—2.90 (3H, m, CCH_2C, H_a or H_b of CH_2P), 2.80 (3H, s, CH_3), 3.31—3.75 (3H, m, CH_2N, H_a or H_b of CH_2P), 3.82—4.26 (1H, m, NCH), 4.33—4.55 (1H, m, OCH), 4.92 (1H, br, OH), 7.24—7.96 (10H, m, Ar-H). *Anal.* Calcd for $C_{18}H_{22}NO_4PS$: C, 56.98; H, 5.84; N, 3.69. Found: C, 57.21; H, 5.96; N, 3.41.

(3*R-trans*)-5-[(Dicyclohexylphosphinyl)methyl]-1-(methylsulfonyl)-3-pyrrolidinol (20) Hydrogenation of two phenyl groups of **19** (1.434 g, 3.78 mmol) was carried out under similar conditions to those described above using 5% rhodium on alumina powder (717 mg) in methanol (20 ml). Usual work-up and recrystallization from ethanol–isopropyl ether gave **20** (1.427 g, 96%); mp 206—208 °C, $[\alpha]_D^{23}$ $-72.9°$ ($c=1.08$, ethanol). IR (KBr): 3200 (OH), 1339, 1146 (SO_2), 1163 (PO) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.91—2.19 (24H, m, $P(C_6H_{11})_2$, CCH_2C), 2.50—3.00 (2H, m, CH_2P), 2.93 (3H, s, CH_3), 3.28—3.60 (3H, m, CH_2NCH), 3.88—4.30 (1H, m, OCH), 5.23 (1H, br s, OH). *Anal.* Calcd for $C_{18}H_{34}NO_4PS$; C, 55.22; H, 8.75; N, 3.85. Found: C, 55.22; H, 8.85; N, 3.40.

(3*R-trans*)-5-[(Dicyclohexylphosphinyl)methyl]-1-(methylsulfonyl)-3-pyrrolidinol Methanesulfonate (21) Methanesulfonyl chloride (571 mg, 4.99 mmol) was added to an ice-cooled solution of **20** (976 mg, 2.49 mmol) in pyridine (15 ml). The mixture was stirred at the same temperature for 3 h and at room temperature overnight, then the product was isolated in a similar manner to that described above. Recrystallization from ethanol–hexane gave **21** (1.09 g, 88%); mp 130—131 °C, $[\alpha]_D^{23}$ $-41.7°$ ($c=1.04$, ethanol). IR (KBr): 1364, 1178 (OSO_2), 1341, 1145 (NSO_2), 1162 (PO) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.05—3.16 (26H, m, $P(C_6H_{11})_2$, CCH_2C, CH_2P), 2.92 (3H, s, NSO_2CH_3), 3.01 (3H, s, OSO_2CH_3), 3.53—4.01 (3H, m, CH_2NCH), 5.07—5.24 (1H, m, OCH). *Anal.* Calcd for $C_{19}H_{36}NO_6PS_2$; C, 48.60; H, 7.73; N, 2.98. Found: C, 48.72; H, 7.78; N, 2.81.

(2*S-cis*)-2-[(Dicyclohexylphosphinyl)methyl]-4-(diphenylphosphinyl)-1-(methylsulfonyl)pyrrolidine (22) A yellow suspension of sodium diphenylphosphide in dioxane was prepared from chlorodiphenylphosphine (246 mg, 1.2 mmol) and sodium (55 mg, 2.4 mmol) in the same manner as described above. THF (5 ml) was added and the mixture was chilled to −30 °C. A solution of **21** (149 mg, 0.3 mmol) was added and the whole mixture was stirred at the same temperature overnight. After oxidation with hydrogen peroxide, usual work-up and isolation by column chromatography (silica gel, ethyl acetate–ethanol (5 : 1)) gave **22** (bearing 1 mol of ethanol as a solvent of crystallization), which was further purified by recrystallization from ethanol–isopropyl ether. Yield: 123 mg (64%); mp 222—223°C, $[\alpha]_D^{23}$ $-42.8°$ ($c=1.02$, ethanol). IR (KBr): 3330 (OH of ethanol), 1158 (PO) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.81—2.10 (22H, m, $P(C_6H_{11})_2$), 1.22 (3H, t, $J=7.1$ Hz, $\underline{CH_3}CH_2OH$), 2.01 (1H, br s, $CH_3H_2O\underline{H}$), 2.00—3.22 (5H, m, CCH_2C, CH_2P, PCH), 2.88 (3H, s, SO_2CH_3), 3.20—3.48 (2H, m, CH_2N), 3.69 (2H, q, $J=7.1$ Hz, $CH_3\underline{CH_2}OH$), 3.99—4.44 (1H, m, NCH), 7.30—7.90 (10H, m, $2\times C_6H_5$). *Anal.* Calcd for $C_{30}H_{43}NO_4P_2S\cdot CH_3CH_2OH$: C, 61.82; H, 7.94; N, 2.25. Found: C, 61.76; H, 7.99; N, 2.18.

(2*S-cis*)-2-[(Dicyclohexylphosphinyl)methyl]-4-(diphenylphosphinyl)-pyrrolidine (23) The bisphosphine oxide (**22**) (300 mg, 0.52 mmol) was treated with a mixture of phenol (700 mg) and 48% hydrobromic acid (5.3 ml) under similar conditions to those described above. The *N*-demesylated product was purified by column chromatography and recrystallization from ethanol–isopropyl ether, yielding **23** (having 1/2 mol of water of crystallization) as white crystals. Yield: 220 mg (73%); mp 168—169 °C, $[\alpha]_D^{24}$ $-26.0°$ ($c=1.05$, ethanol). IR (KBr): 3260 (NH), 1192 (PO) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.87—2.55 (26H, m, $P(C_6H_{11})_2$, CCH_2C, CH_2P), 2.16 (2H, br, NH, $1/2H_2O$), 2.78—3.67 (4H, m, CH_2NCH, PCH), 7.30—7.90 (10H, m, $2\times C_6H_5$). *Anal.* Calcd for $C_{29}H_{41}NO_2P_2\cdot 1/2H_2O$: C, 68.75; H, 8.94; N, 2.77. Found: C, 68.51; H, 8.92; N, 2.72.

(2*S-cis*)-2-[(Dicyclohexylphosphino)methyl]-4-(diphenylphosphino)-1-pyrrolidinecarboxylic Acid 1,1-Dimethylethyl Ester (BCPP, 3) A solution of trichlorosilane (108 mg, 0.80 mmol) in toluene (3 ml) was slowly added to an ice-cooled solution of **23** (100 mg, 0.20 mmol) and triethylamine (89 mg, 0.88 mmol) with stirring under an argon atmosphere and the mixture was heated for 5 h. After the usual work-up as described above, the crude reduction product was dissolved in dry, degassed dichloromethane (6 ml), and triethylamine (24 mg, 0.24 mmol) was added under an argon atmosphere. Then di-*tert*-butyl dicarbonate (48 mg, 0.22 mmol) was added, and the whole mixture was stirred at room temperature for 2 h. After evaporation of the solvent *in vacuo*, the residue was purified by short-column chromatography on alumina using degassed benzene as an eluent. Recrystallization from degassed ethanol–hexane under an argon atmosphere gave pure **3** as white needles. Yield: 73 mg (65%); mp 126—127 °C, $[\alpha]_D^{21}$ $-40.9°$ ($c=0.24$, benzene). IR (KBr): 1692 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.85—2.00 (25H, m, $P(C_6H_{11})_2$, CCH_2C, H_a or H_b of CH_2P), 1.45 (9H, s, $C(CH_3)_3$), 2.00—2.97 (2H, m, PCH, H_a or H_b of CH_2P), 3.00—3.37 and 3.54—4.09 (1H and 2H, m, CH_2NCH), 7.15—7.60 (10H, m, $2\times C_6H_5$). *Anal.* Calcd for $C_{34}H_{49}NO_2P_2$: C, 72.19; H, 8.73; N, 2.48. Found: C, 72.39; H, 8.78; N, 2.49.

(2*S-cis*)-4-(Dicyclohexylphosphino)-2-[(dicyclohexylphosphino)methyl]-1-pyrrolidinecarboxylic Acid 1,1-Dimethylethyl Ester (BCCP, 4) (2*S-cis*)-4-(Dicyclohexylphosphinyl)-2-[(dicyclohexylphosphinyl)methyl]-pyrrolidine (**26**) was prepared from (2*S-cis*)-BPPM (**1**) (Chart 3 in the text) according to the reported procedure. A solution of trichlorosilane (1.355 g, 10.0 mmol) in dry, degassed acetonitrile (10 ml) was added dropwise to a stirred and ice-cooled solution of **26** (509 mg, 1.0 mmol) and triethylamine (1.113 g, 11.0 mmol) in acetonitrile (30 ml) under an argon atmosphere. The mixture was stirred and heated under reflux for 3 h. After the usual work-up as described above, the crude reduction product was dissolved in dry, degassed dichloromethane (10 ml), and triethylamine (223 mg, 2.2 mmol) was added under an argon atmosphere. Then di-*tert*-butyl dicarbonate (240 mg, 1.1 mmol) was slowly added, and the whole mixture was stirred at room temperature for 2 h. After evaporation of the solvent *in vacuo*, the residue was purified by column chromatography on alumina using degassed benzene as an eluent, yielding **4** as a white amorphous solid. Yield; 308 mg (54%), $[\alpha]_D^{21}$ $-40.9°$ ($c=0.24$, benzene). IR (KBr): 1690 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.81—2.71 (49H, m, $2\times P(C_6H_{11})_2$, PCH, CCH_2C, CH_2P), 1.47 (9H, s, $C(CH_3)_3$), 2.96—4.19, m, CH_2NCH). *Anal.* Calcd for $C_{34}H_{61}NO_2P_2$: C, 70.68; H, 10.64; N, 2.42. Found: C, 70.91; H, 10.50; N, 2.33.

Catalytic Asymmetric Hydrogenation of Ketopantolactone General Procedure: A solution of a neutral rhodium(I) complex catalyst was prepared *in situ* by mixing chloro(1,5-cyclooctadiene)rhodium(I) dimer ($[Rh(COD)Cl]_2$) (5×10^{-3} mmol) and pyrrolidinebisphosphine ligand, BCPM (**2**) (BCPP (**3**) or BCCP (**4**)), (1.1×10^{-2} mmol) in dry THF. The asymmetric hydrogenation of ketopantolactone (10 mmol) was carried out in the presence of the above catalyst (molar ratio: substrate/catalyst $=10^3$) in THF (10 ml) under hydrogen (50 atm) at 50 °C for 45 h. The hydrogenations at other molar ratios of the catalyst to the substrate (10^2 or 10^4) were similarly performed. The conversion rate of the substrate was determined by gas-liquid chromatographic analysis (column, PEG 20M). The product was obtained by bulb-to-bulb distillation as a solid, whose optical rotation was measured in H_2O ($c=ca.$ 2). The optical yield was calculated by using the maximum optical rotation value, $[\alpha]_D^{20}$ $-50.7°$ ($c=2.05$, H_2O), for pure (*R*)-(−)-pantolactone reported in the literature.[13] The results are summarized in Table I.

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