

# Preparation and Resolution of Atropisomeric Ligand, 6, 6' -Dimethyl-2, 2'-bis (diphenylphosphino) biphenyl, and Asymmetric Hydrogenation Using the Rhodium (I) Complexes Thereof

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## Preparation and Resolution of Atropisomeric Ligand, 6, 6'-Dimethyl-2, 2'-bis(diphenylphosphino)biphenyl, and Asymmetric Hydrogenation Using the Rhodium(I) Complexes Thereof

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**Abstract** A bisphosphine, 6,6'-dimethyl-2,2'-bis(diphenylphosphino)biphenyl (DMBP) was newly prepared, and resolved into (*R*)- and (*S*)-DMBP. The maximum optical rotations of (*R*)- and (*S*)-DMBP were +18.2° and -17.0° (c 0.5, C<sub>6</sub>H<sub>6</sub>), respectively. Catalytic asymmetric hydrogenation of dehydroamino acids such as 2-acetamidoacrylic acid (AAA), (*Z*)- $\alpha$ -acetamidocinnamic acid (ACA), and itaconic acid (ITA) was investigated by using the rhodium(I) complexes containing (*R*)- and (*S*)-DMBP. Catalytic activity of the complexes toward hydrogenation was as high as, but enantioselectivity of the complexes for asymmetric hydrogenation was lower than that of the rhodium(I) complexes of (*R*)- and (*S*)-6,6'-dimethyl-2,2'-bis(diphenylphosphinoamino)biphenyl ((*R*)- and (*S*)-MABP). The reason of the differences in the enantioselectivity between both the DMBP and MABP complexes was also discussed.

### Introduction

Asymmetric hydrogenation by the use of the rhodium(I) complexes containing chiral phosphines is a matter of current interest because it is a promising method for obtaining preferentially one of a pair of enantiomers from the parent prochiral compounds containing C=C, C=O and C=N groups.

Since Kagan and Dang discovered (-)-2,3-*o*-isopropylidene-2,3-dihydroxy-1,4-bis-(diphenylphosphino)butane (DIOP) in 1971<sup>1)</sup>, many chiral bisphosphines were devised and catalytic activities of the complexes thereof were investigated. The chiral bisphosphines reported hitherto can be divided into the following four classes: (1) consists of the chiral P-atom bisphosphines such as 1, 2-bis{(*o*-methoxyphenyl)phenylphosphino}ethane (DIPAMP)<sup>2)</sup>, 1, 2-bis{( $\alpha$ -naphthyl)phenylphosphino}ethane (BNPE)<sup>3)</sup> and 1-(neomenthyl)-phenylphosphino-2-diphenylphosphinoethane(MENPHOS)<sup>4)</sup>; (2), of the chiral C-atom bisphosphines such as DIOP<sup>1)</sup>, *N-t*-butoxycarbonyl-4-diphenylphosphino-2-diphenylphosphinomethylpyrrolidine(BPPM)<sup>5)</sup> and 2,3-bis(diphenylphosphino)butane (CHIRAPHOS)<sup>6)</sup>;

(3), of the chiral ferrocenyl bisphosphines such as *N,N*-dimethyl-1-{1',2'-bis(diphenylphosphino)ferrocenyl}ethylamine(BPPFA), 1-{1',2'-bis(diphenylphosphino)ferrocenyl}ethanol(BPPFOH) and 1',2'-bis(diphenylphosphino)-2-ethylferrocene(BPPEF)<sup>7)</sup>; and (4), of the atropisomeric chiral bisphosphines such as 2,2'-bis(diphenylphosphino)-1,1'-binaphtyl(BINAP)<sup>8)</sup>, and 2,2'-bis(diphenylphosphinoamino)-1,1'-binaphtyl(BDPAB)<sup>9)</sup>. The chiralities of class (4) are due to atropisomerism, so they have the advantage of non-flexibility of conformation; they are therefore certainly useful for clarifying the mechanisms of asymmetric hydrogenation, which still remains ambiguous.

We previously succeeded in preparing (*R*)- and (*S*)-6,6'-dimethyl-2,2'-bis(diphenylphosphinoamino)biphenyl (MABP)<sup>10)</sup>, which are able to form a 9-membered chelate ring with a metal ion. The rhodium(I) complexes containing the phosphines ((*R*)- and (*S*)-MABP) showed an excellent activity for asymmetric hydrogenation of dehydroamino acids. As a continuation of the work, we tried to prepare and resolve 6,6'-dimethyl-2,2'-bis(diphenylphosphino)biphenyl (DMBP), which forms a 7-membered chelate ring with a metal ion.

The present study was primarily undertaken (1) to prepare *rac*-DMBP, (2) to resolve it into (*R*)- and (*S*)-DMBP, (3) to investigate the catalytic activities of the rhodium(I) complexes thereof for asymmetric hydrogenation of 2-acetamidoacrylic acid (AAA), (*Z*)- $\alpha$ -acetamidocinnamic acid (ACA) and itaconic acid (ITA), and to compare the catalytic activities of the DMBP complexes with those of the MABP complexes.

Figure 1 shows the chemical formulas, nomenclatures and abbreviations of the bisphosphines employed in the present work.

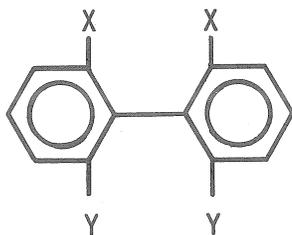


Fig. 1. The bisphosphines employed in the present study.

X : H ; Y : P(C<sub>6</sub>H<sub>5</sub>)<sub>2</sub> = 2,2'-bis(diphenylphosphino)biphenyl (BPBP).

X : CH<sub>3</sub> ; Y : P(C<sub>6</sub>H<sub>5</sub>)<sub>2</sub> = 6,6'-dimethyl-2,2'-bis(diphenylphosphino)biphenyl (DMBP).

X : CH<sub>3</sub> ; Y : NHP(C<sub>6</sub>H<sub>5</sub>)<sub>2</sub> = 6,6'-dimethyl-2,2'-bis(diphenylphosphinoamino)-biphenyl (MABP).

X : CH<sub>3</sub> ; Y : PO(C<sub>6</sub>H<sub>5</sub>)<sub>2</sub> = 6,6'-dimethyl-2,2'-bis(diphenylphosphinyl)biphenyl (DMBPO).

## Experimental

**Materials.** The prochiral substrates AAA, ACA and ITA were obtained from commercial sources and purified by recrystallization before use. (+)- $\alpha$ -phenylethylamine and

(-)- $\alpha$ -naphthylethylamine were commercially available and used without further purification.

**Measurements.** Optical rotations were measured at ambient temperatures in a 1 dm cell with a JASCO DIP-181 digital polarimeter. Infrared absorption spectra were recorded on a JASCO Model A-3 infrared spectrophotometer using samples as neat liquid, or KBr disks.  $^1\text{H}$  NMR spectra were measured with JEOL JNM-GX400 spectrometer using  $(\text{CH}_3)_4\text{Si}$  as the internal standard.  $^{31}\text{P}$  NMR spectra were recorded on a JEOL JNM-GX400 spectrometer using  $\text{H}_3\text{PO}_4$  as the external standard. Visible and ultraviolet absorption spectra were measured with a JASCO UVIDEC-505 UV/VIS recording digital spectrophotometer.

**Preparation of *rac*-DMBP.** The preparative route for the compound is outlined in Fig. 2.

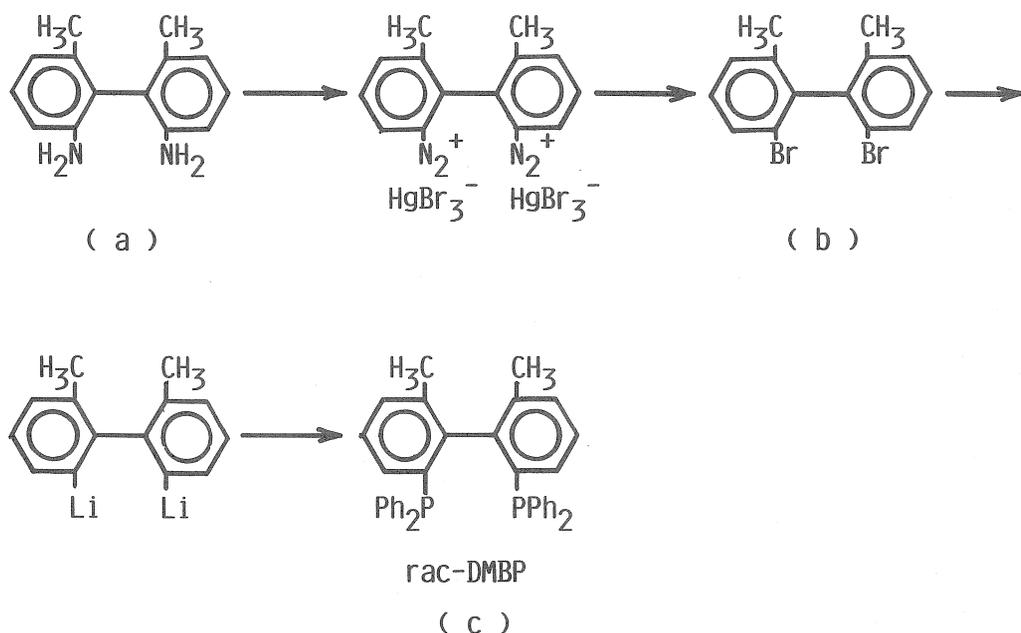


Fig. 2. Preparative route for *rac*-DMBP.

(a) 6,6'-Dimethyl-2,2'-diaminobiphenyl (DMDA). This was prepared by modifying the known method<sup>11</sup>. Freshly prepared W-2 Raney nickel catalyst<sup>12</sup> was added to a solution of 6,6'-dimethyl-2,2'-dinitrobiphenyl<sup>10b</sup> in ethanol at about 60°C. To the solution, hydrazine hydrate was added dropwise in amounts enough to completely reduce the dinitro compound. After recrystallization from aqueous ethanol, DMDA was obtained as white plates. Yield: 11.7g (92%). mp: 135-137°C (lit. 135-136°C<sup>13</sup>).

(b) 6,6'-Dimethyl-2,2'-dibromobiphenyl. This was prepared by considerably modifying the literature method.<sup>14,15</sup> The DMDA (2.12g, 10mmol) was dissolved in 50%  $\text{H}_2\text{SO}_4$

(160cm<sup>3</sup>). The solution was cooled to 0°C, to which a solution of sodium nitrite (1.50g, 21.6mmol) in water (30cm<sup>3</sup>) was added over 2-3 h. The temperature should be kept below 5°C during the addition of the sodium nitrite solution. To the solution, a solution of mercury(II) bromide (7.4g, 21mmol) in water (180cm<sup>3</sup>) containing potassium bromide (42g, 360mmol) was slowly added in ice bath. Yellow powdery products were formed immediately. After 1 h, they were collected by filtration in the dark and washed with cold water (2 × 30cm<sup>3</sup>). To the products, was added potassium bromide (40g) to stabilize them, and the mixture was washed with cold acetone (3 × 20cm<sup>3</sup>) and allowed to dry. The mixture was then thinly and uniformly spread in a pyrex tube 50 × 3cm of which one end was closed, and the other end was open and fitted with an air condenser. The tube was gently heated with a micro burner from the open end toward the closed end so that the tetrazonium salt was converted into the dibromo compound. The resulting materials in the tube were washed with ether to extract the desired dibromo compound. The ether was distilled off to give brown compounds. They were dissolved in pentane, and the solution was filtered and evaporated in vacuum. Faintly brown products were obtained. Yield: 2.11g (62.2%). The products were recrystallized twice from aqueous ethanol. They were obtained as white needles. mp: 110-112°C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, Me<sub>4</sub>Si): δ (ppm)=2.01 (s, 6H, CH<sub>3</sub>), 7.07-7.58 (m, 6H, C<sub>6</sub>H<sub>3</sub>).

(c) *rac*-DMBP. Under a nitrogen atmosphere, 1.6 M hexane solution of *n*-butyllithium (28cm<sup>3</sup>, 20mmol) was added dropwise with stirring to a solution of the dibromo compound (c) (7.0g, 21mmol) in anhydrous ether (80cm<sup>3</sup>) at 0°C. During the addition, white yellow dilithio compound was gradually precipitated. After addition was completed, the reaction mixture was allowed to stand at room temperature for 2 h. To the above suspension, a solution of chlorodiphenylphosphine (7.7cm<sup>3</sup>, 42mmol) in anhydrous ether (35cm<sup>3</sup>) was dropwise added over 30 min. The dilithio compound was then changed into the white desired products. They were collected by filtration, washed several times with methanol, and air-dried. Yield: 8.2g (71%). Recrystallization from acetone-methanol gave white crystals. mp: 240-242°C. <sup>1</sup>H NMR (CDCl<sub>3</sub>, Me<sub>4</sub>Si): δ (ppm)=1.35 (s, 6H, CH<sub>3</sub>), 6.99-7.23 (m, 26H, C<sub>6</sub>H<sub>5</sub>, C<sub>6</sub>H<sub>3</sub>). <sup>31</sup>P NMR (CDCl<sub>3</sub>, H<sub>3</sub>PO<sub>4</sub>): δ (ppm)= -14.08 (s, 2P).

**Preparation of Resolving Agents.** (-)-Di- $\mu$ -chloro-bis[(*R*)-*N,N*-dimethyl- $\alpha$ -phenylethylamine-2*C,N*] dipalladium ([PdCl{(*R*)-dmphn}]<sub>2</sub>) and (+)-Di- $\mu$ -chloro-bis[(*S*)-*N,N*-dimethyl- $\alpha$ -(2-naphtyl) ethylamine - 3*C,N*] dipalladium ([PdCl{(*S*)-dmnan}]<sub>2</sub>) were prepared according to the method of literature<sup>16</sup>.

*Dichloro-(R,R)-N,N'-dimethylcyclohexanediaminepalladium(II)* ([PdCl<sub>2</sub>{(*R,R*)-dmchxn}]). The optically active (*R,R*)-cyclohexanediamine ((*R,R*)-chxn) was obtained by resolving their commercial racemates according to the method described in the literature<sup>17</sup>. To (*R,R*)-chxn (2.8g, 15mmol) in water (50cm<sup>3</sup>) was added carbobenzoxy chloride (6.2g, 36mmol) with stirring and the solution was ice-cooled. A sufficient amount of 2 M sodium hydroxide solution was added to the mixture to make it basic, and the mixture was stirred for 4 h. The carbobenzoxyated diamine thus obtained was collected by filtration and dried in vacuo. Yield: 3.8g (65%). Under a nitrogen atmosphere, a

suspension of lithium aluminum hydride (1.0g, 50mmol) and absolute THF (25cm<sup>3</sup>) was ice-cooled and thereto was added the above diamine (1.8g, 4.6mmol). The resulting solution was refluxed for 6 h and ice-cooled. Then, a mixture of water (5cm<sup>3</sup>) and THF (20cm<sup>3</sup>) was added to decompose LiAlH<sub>4</sub>. Residue was collected by filtration and washed with hot THF (3 × 20cm<sup>3</sup>). The filtrate and washings were combined together, to which concentrated HCl (5cm<sup>3</sup>) was added. The solution was roto-evaporated to give white powders, which were dried in vacuo. The (*R,R*)-dimethylcyclohexanediamine dihydrochloride (*R,R*)-dmchxn·2HCl thus obtained was purified by dissolving it in ethanol and adding acetone. Yield: 0.63g (63%). Na<sub>2</sub>PdCl<sub>4</sub> (0.81g, 2.8mmol) was added to (*R,R*)-dmchxn·2HCl (0.59g, 2.8mmol) in water (20cm<sup>3</sup>). Then, 0.5 M NaOH (11cm<sup>3</sup>) was drop by drop added to the resulting solution to neutralize it. After 2 h, pale yellow powders were obtained, which were collected by filtration and dried in vacuo. Yield: 0.63g (71%). Found: C, 29.66; H, 5.80; N, 8.63%. Calcd for C<sub>8</sub>H<sub>18</sub>N<sub>2</sub>PdCl<sub>2</sub>: C, 30.07; H, 5.68; N, 8.77%.

**Resolution of *rac*-DMBP.** (*S*)- and (*R*)-DMBP were obtained from *rac*-DMBP as outlined in Fig. 3.

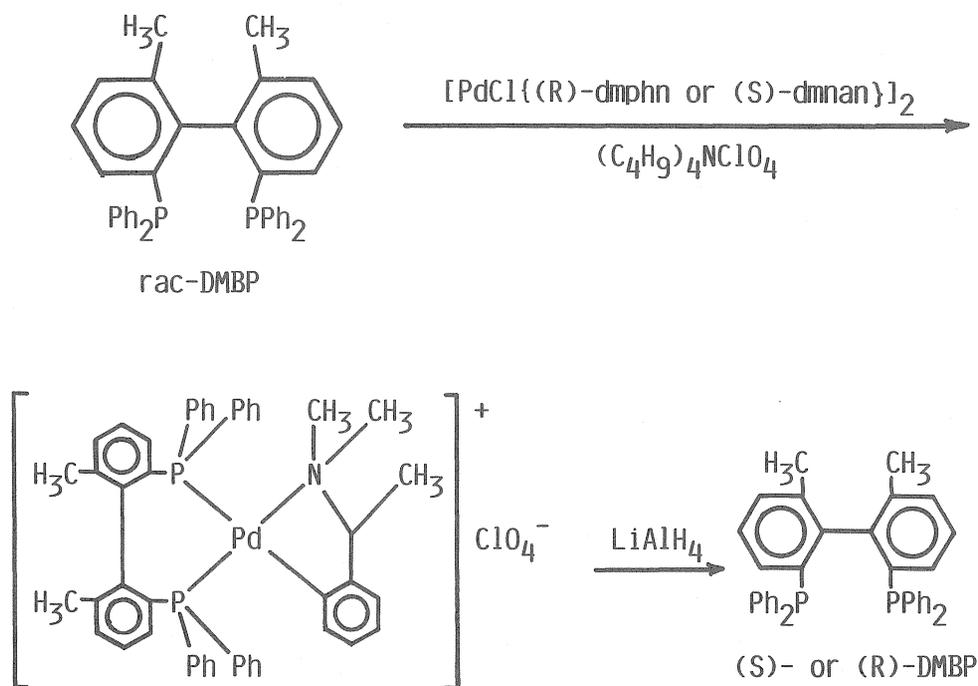


Fig. 3. Optical resolution of *rac*-DMBP.

*Preparation of (S)-DMBP by the Use of [PdCl{(R)-dmphn}]<sub>2</sub>.* *Rac*-DMBP (0.55g, 1.0mmol) was suspended in methanol (40cm<sup>3</sup>), to which was added a solution of the

resolving agent  $[\text{PdCl}\{(R)\text{-dmphn}\}]_2$  (0.29g, 0.5mmol) in methanol (10cm<sup>3</sup>). The solution was stirred at room temperature for 1 h in the dark. The pale yellow solution was once filtrated and thereto was added  $(\text{C}_4\text{H}_9)_4\text{NClO}_4$  (0.12g, 0.5mmol) in methanol (10cm<sup>3</sup>). The mixture was allowed to stand at room temperature for 24 h. Crystals formed were collected by filtration and dried over  $\text{P}_2\text{O}_5$ . The pale yellow crystals of  $[\text{Pd}\{(R)\text{-dmphn}\}\{(S)\text{-dmbp}\}]\text{ClO}_4$  were recrystallized from dichloromethane-ether. Yield: 0.27g (59%).  $[\alpha]_{\text{D}}: +287.5^\circ$  (c 0.16, acetonitrile).  $^1\text{H NMR}$  ( $\text{CDCl}_3$ ,  $\text{Me}_4\text{Si}$ ):  $\delta$  (ppm) = 1.01 (s, 3H,  $\text{NCH}_3$ ), 1.28 (s, 6H,  $\phi\text{-CH}_3$ ), 1.56 (s, 3H,  $\text{N-CH}_3$ ), 2.55 (b, 3H,  $\text{C-CH}_3$ ), 5.33 (t, 1H,  $\text{C-H}$ ), 6.25–7.60 (m, 30H,  $\text{C}_6\text{H}_5$ ,  $\text{C}_6\text{H}_4$ ,  $\text{C}_6\text{H}_3$ ). Found: C, 62.98; H, 5.03; N, 1.65%. Calcd for  $\text{C}_{48}\text{H}_{46}\text{NO}_4\text{CIPd}$ : C, 63.73; H, 5.13; N, 1.55%.

In a 200cm<sup>3</sup> 3-necked flask was placed  $\text{LiAlH}_4$  (0.25g, 6.6mmol) under nitrogen. Dry and degassed ether (100cm<sup>3</sup>) was added to it by a syringe and the flask was surrounded by an ice-water mixture. To this was carefully added the ternary complex obtained above (0.97g, 1.0mmol). The mixture was stirred for 30 min, and then the flask was removed from the ice-water mixture. The mixture was stirred at 40°C for 4 h, and then the flask was cooled in an ice-water bath. To this was added carefully 1cm<sup>3</sup> of water to decompose  $\text{LiAlH}_4$  and the mixture was stirred at room temperature for 30 min. The mixture was filtered and the residue was washed with hot benzene (3 × 30cm<sup>3</sup>). The filtrate and washings were combined together and roto-evaporated. After purification by means of silica gel chromatography with toluene as an eluent, the fractions were collected and roto-evaporated. Products thus obtained were dried in vacuo. Yield: 0.25g (45%). Recrystallization from acetone-methanol gave white crystals of (S)-DMBP. mp: 209–212°C.  $[\alpha]_{\text{D}}: -17.0^\circ$  (c 0.49, PhH).  $^1\text{H NMR}$  ( $\text{CDCl}_3$ ,  $\text{Me}_4\text{Si}$ ):  $\delta$  (ppm) = 1.35 (s, 6H,  $\text{CH}_3$ ), 6.99–7.23 (m, 26H,  $\text{C}_6\text{H}_5$ ,  $\text{C}_6\text{H}_3$ ). Found: C, 82.61; H, 5.69%. Calcd for  $\text{C}_{38}\text{H}_{32}\text{P}_2$ : C, 82.89; H, 5.86%.

*Preparation of (R)-DMBP by the Use of  $[\text{PdCl}\{(S)\text{-dmnan}\}]_2$ .* The ternary complex  $[\text{Pd}\{(S)\text{-dmnan}\}\{(R)\text{-dmbp}\}]\text{ClO}_4 \cdot \text{CH}_3\text{OH}$  was prepared by using  $[\text{PdCl}\{(S)\text{-dmnan}\}]_2$  according to the same method as that described for the above ternary complex  $[\text{Pd}\{(R)\text{-dmphn}\}\{(S)\text{-dmbp}\}]\text{ClO}_4$ . Yield: 0.60g (50%).  $[\alpha]_{\text{D}}: -366.7^\circ$  (c 0.18, acetonitrile).  $^1\text{H NMR}$  ( $\text{CDCl}_3$ ,  $\text{Me}_4\text{Si}$ ):  $\delta$  (ppm) = 1.21 (b, 6H,  $\phi\text{-CH}_3$ ), 1.61 (s, 3H,  $\text{N-CH}_3$ ), 1.68 (s, 3H,  $\text{N-CH}_3$ ), 1.91 (b, 3H,  $\text{C-CH}_3$ ), 4.45 (t, 1H,  $\text{C-H}$ ), 6.68–7.63 (m, 32H,  $\text{C}_{10}\text{H}_6$ ,  $\text{C}_6\text{H}_5$ ,  $\text{C}_6\text{H}_3$ ). Found: C, 64.08; H, 5.16; N, 1.44%. Calcd for  $\text{C}_{52}\text{H}_{48}\text{NO}_4\text{P}_2\text{CIPd} \cdot \text{CH}_3\text{OH}$ : C, 64.51; H, 5.31; N, 1.42%. The ternary complex was reduced with  $\text{LiAlH}_4$  to give (R)-DMBP. Yield: 0.25g (75%). mp. 207–210°C.  $[\alpha]_{\text{D}}: +18.2^\circ$  (c 0.50, PhH).

**Hydrogenation Experiments.** Hydrogenation was carried out as described previously<sup>10</sup>. Hydrogen was introduced into the flask through a syringe needle (hydrogen flow rate: about 50cm<sup>3</sup> min<sup>-1</sup>). The progress of hydrogenation was checked by means of TLC. All solvents were dried and degassed before use. The catalyst was prepared in situ just prior to hydrogenation by the reaction of  $[\text{RhCl}(\text{COD})]_2$  with an appropriate bisphosphine.

**Work-up of the Product.** After hydrogenation, the resulting solution were evaporated to dryness and the residue was treated as follows: (1) in the case of the hydrogenation of AAA, the residue was dissolved in water (10cm<sup>3</sup>) and the insoluble catalyst was separated by filtration. Evaporation of the filtrate afforded the product. (2), of ACA, the residue was dissolved in 0.5 M aqueous sodium hydroxide and the insoluble catalyst was separated by filtration. The filtrate was then acidified with 2 M hydrochloric acid, extracted with ether, and the ethereal extract was washed with a small amount of water. The ethereal phase was dried over anhydrous sodium sulfate and evaporated to dryness. (3), of ITA, the residue was dissolved in 2 M hydrochloric acid and the insoluble catalyst was separated by filtration. The filtrate was extracted with ether, and the ethereal extract was dried over anhydrous sodium sulfate and concentrated under reduced pressure to dryness.

### Results and Discussion

*Catalytic Activity and Enantioselectivity of the Rh(I)-DMBP Catalysts toward Asymmetric Hydrogenation.* Catalysts were prepared in situ from (S)- or (R)-DMBP and [RhCl(COD)]<sub>2</sub>, and their catalytic activities for the hydrogenation of 2-acetamidoacrylic acid (AAA), (Z)- $\alpha$ -acetamidocinnamic acid (ACA) and itaconic acid (ITA) were examined under 1 atm of hydrogen pressure at 25°C. The results were summarized in Table 1. The table also contains the results obtained by using catalysts of MABP<sup>10)</sup> and BPBP<sup>15)</sup>.

Table 1. Results of Asymmetric Hydrogenation<sup>a)</sup>

Exp. No.	Substrate	Catalyst	Substrate/Rh(I) <sup>b)</sup>	Time	$[\alpha]_D$	Opt. yield <sup>c)</sup>	Config. of product
A-1	AAA	[RhCl(COD)] <sub>2</sub> +2.2(S)-DMBP	50	2h	+ 8.8°	13%	R
A-2 <sup>10)</sup>	AAA	[RhCl(COD)] <sub>2</sub> +2.2(S)-MABP	50	2	-61.2	92	S
A-3 <sup>15)</sup>	AAA	(+)-[Rh(COD)(bpbp)]PF <sub>6</sub>	50	5	+ 8.6	13	R
A-4	AAA	[RhCl(COD)] <sub>2</sub> +2.2(R)-DMBP	50	2	- 9.9	15	S
A-5 <sup>10)</sup>	AAA	[RhCl(COD)] <sub>2</sub> +2.2(R)-MABP	50	2	+60.5	91	R
A-6	ACA	[RhCl(COD)] <sub>2</sub> +2.2(S)-DMBP	25	5	- 5.8	13	R
A-7 <sup>15)</sup>	ACA	(+)-[Rh(COD)(bpbp)]PF <sub>6</sub>	25	6	- 3.4	6.5	R
A-8	ACA	[RhCl(COD)] <sub>2</sub> +2.2(R)-DMBP	25	5	+ 5.6	12	S
A-9 <sup>10)</sup>	ACA	[RhCl(COD)] <sub>2</sub> +2.2(R)-MABP	25	5	-36.0	78	R
A-10	ITA	[RhCl(COD)] <sub>2</sub> +2.2(S)-DMBP	50	5	- 4.3	25	R
A-11 <sup>10)</sup>	ITA	[RhCl(COD)] <sub>2</sub> +2.2(S)-MABP	50	5	-12.4	73	R
A-12	ITA	[RhCl(COD)] <sub>2</sub> +2.2(R)-DMBP	50	5	+ 2.0	12	S
A-13	AAA	d)	50	2	+ 8.2	12	R
A-14 <sup>10)</sup>	AAA	e)	50	2	-53.7	81	S

a) Reaction condition: Solvent: MeOH. [Rh]: 0.75mM. Hydrogen pressure: 1 atm. Temperature: 25°C.

b) Molar ratios of substrate to Rh(I) catalyst. c) Optical yields were determined on the basis of the reported rotation for the optically pure enantiomers: (R)-N-acetylalanine,  $[\alpha]_D$ : +66.3° (c 2.0, H<sub>2</sub>O)<sup>6)</sup>; (S)-N-acetylphenylalanine,  $[\alpha]_D$ : +46.0° (c 1.0, EtOH)<sup>9)</sup>; (R)-methylsuccinic acid,  $[\alpha]_D$ : +16.88° (c 2.16, EtOH)<sup>21)</sup>. d) The catalyst recovered after work-up of Exp. A-1 was used. e) The catalyst recovered after work-up of Exp. A-2 was used.

The results obtained in the case of the hydrogenation of AAA are as follows: when the catalyst of (*S*)-DMBP was used (Exp. A-1), AAA was hydrogenated within 2 h to give (*R*)-*N*-acetylalanine in a 13% optical yield. The reaction using (*R*)-DMBP (Exp. A-4) showed similar activity for hydrogenation to that of Exp. A-1 except that (*S*)-*N*-acetylalanine was obtained in place of (*R*)-*N*-acetylalanine. The results obtained for the hydrogenation of ACA and ITA were essentially similar to those of AAA. In the case of (*S*)-DMBP (Exps. A-6 and A-10), ACA and ITA were hydrogenated within 5 h to give (*R*)-*N*-acetylphenylalanine in a 13%, and (*R*)-methylsuccinic acid in a 25% optical yield, respectively. In Exps. A-11 and A-12, the catalysts recovered after work-up of Exps. A-1 and A-2, respectively, were used. Decrease in optical yield were found in both cases, but the experiments indicate that the catalysts can be used repeatedly. These results indicate that the catalytic activity of DMBP for hydrogenation is about the same as that

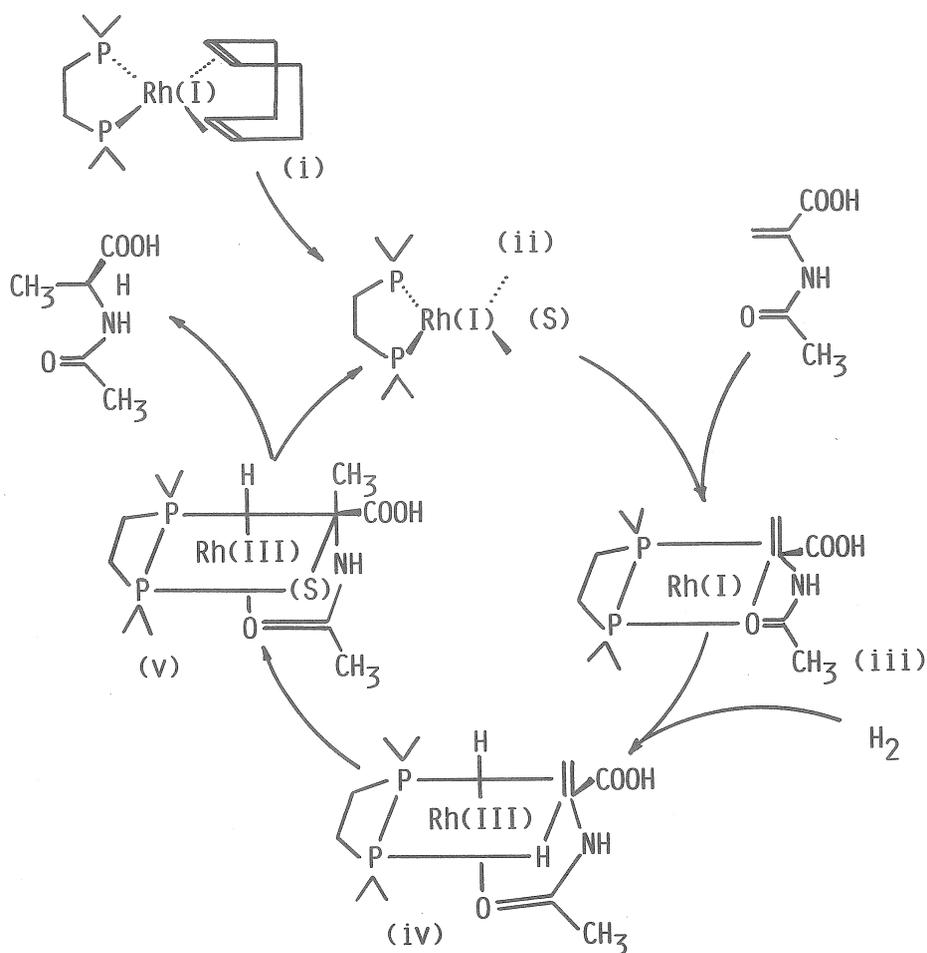


Fig. 4. Cycle of the catalyst for asymmetric hydrogenation.

of MABP, but that the enantioselectivity of the DMBP catalyst is lower than that of the latter.

*Relationship of Catalyst Structure to the Product Configuration.* Various mechanistic studies have been made on asymmetric hydrogenation of dehydroamino acids by using Rh(I)-bisphosphine complexes. Figure 4 shows the cycle for the hydrogenation of dehydroamino acid derivatives, which was proposed by Halpern et al.<sup>18,19</sup>, Ojima et al.<sup>5b</sup>., and Brown and Chaloner<sup>20</sup>. On the basis of the X-ray structural analyses of some complexes containing chiral bisphosphine such as (*R,R*)-1,2-bis(phenyl-*o*-anisoylphosphino)ethane ((*R,R*)-DIPAMP), Knowles et al.<sup>2</sup> first found that in the case of the hydrogenation of dehydroamino acid derivatives the catalyst structure is related to the configuration of the product (Fig. 5). When the face-edge arrangement of four P-aryl rings of coordinated chiral bisphosphine is of Type A which corresponds to the  $\lambda$ -conformation of chelate ring, the catalyst hydrogenates dehydroamino acid derivatives to give (*S*)-products. When the face-edge arrangement is of Type B which corresponds to the  $\delta$ -conformation of chelate ring, the catalyst hydrogenates the substrates to give (*R*)-products.

Examination of molecular model of the (*S*)-DMBP chelate suggests that four phenyl rings adopt an alternate face-edge arrangement of Type B as illustrated in Fig. 5. The experimental results that the present Rh(I)-(*S*)-DMBP catalyst affords (*R*)-product are in accordance with the previous observations described above. (+)-[Rh(COD)(bpbp)]PF<sub>6</sub> also gave (*R*)-product<sup>15</sup>. This implies that the face-edge arrangement of the (+)-bpbp chelate is also of Type B. It should be noted that Rh(I)-(*S*)-MABP catalyst gave (*S*)-products upon hydrogenation of AAA and ACA, whereas Rh(I)-(*S*)-DMBP catalyst afforded (*R*)-products, although the both bisphosphine ligands have the (*S*)-configuration. MABP forms 9-membered chelate ring with Rh(I) ion. Examination of molecular model of the (*S*)-MABP chelate suggests that the face-edge arrangement of (*S*)-MABP is of Type A as shown in Fig. 5. It is opposite with that of (*S*)-DMBP, which forms a 7-membered chelate ring with Rh(I) ion. Thus the chelate ring size of such type of bisphosphine ligands have a significant effect on the face-edge arrangement, which seems to determine the absolute configuration of the hydrogenated product.

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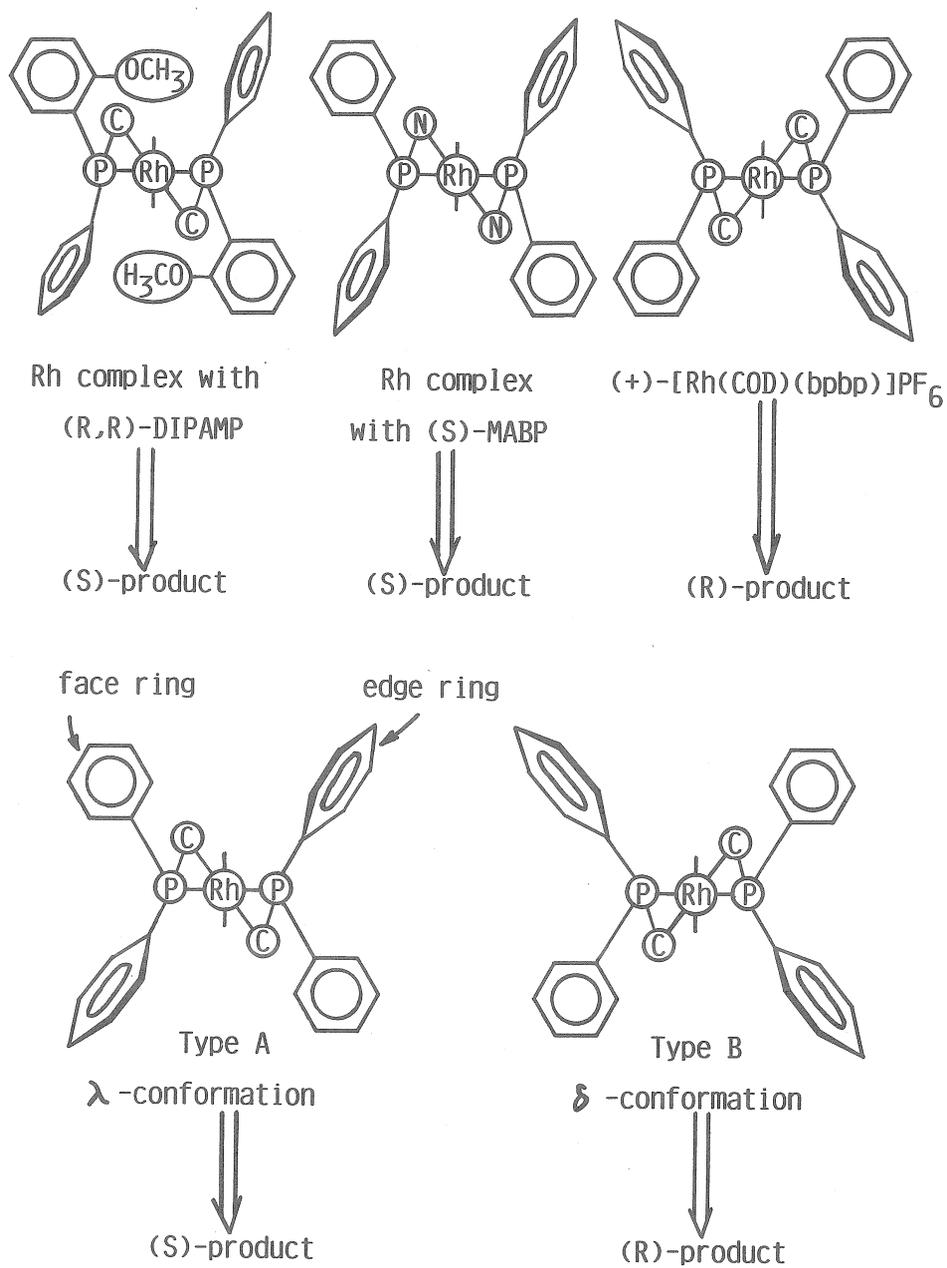


Fig. 5. Relationships of catalyst structure to the product configuration.

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