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Correlation of X-Ray Crystal Structures of Chiral Bisphosphine-Rhodium Catalysts and the Absolute Configuration of the Products Resulted by Their Asymmetric Hydrogenations[1]

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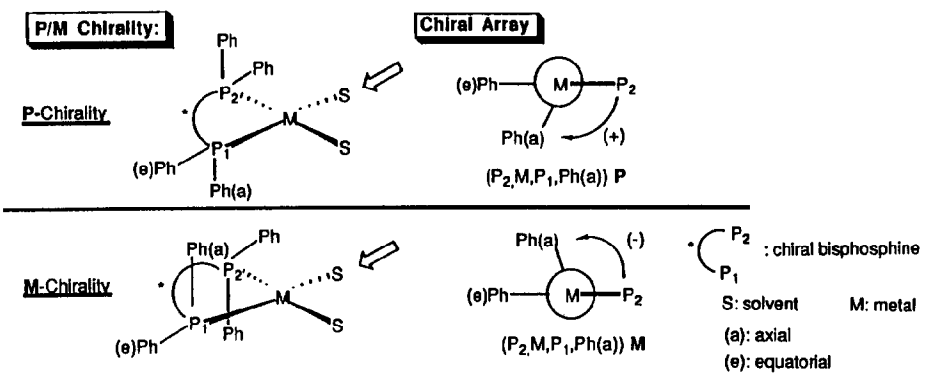
Abstract: The chiral positioning array (P/M-chirality) of four phenyl rings in the rhodium-chiral bisphosphine catalyst has been revealed to play an important role in determining the absolute configuration of the asymmetric hydrogenation product.

Many reports on the asymmetric hydrogenation of prochiral olefinic and ketonic substrates catalyzed by rhodium complexes of chiral bisphosphine ligands have been published[2]. Especially, the asymmetric hydrogenation of (*Z*)-α–acetamidocinnamic acid was carried out with most of chiral bisphosphine-rhodium catalysts, and the mechanism of this asymmetric hydrogenation was clearly elucidated by Halpern[3,4]. From these experimental results, Knowles *et al.* examined the correlation of the X-ray crystal structures of chiral bisphosphine-rhodium catalysts and the absolute configuration of the *N*-acetylphenylalanine produced with assumption that the edge-face array of four phenyl groups around the rhodium center is more important for determining the stereochemistry of the product than the positioning array of four phenyl groups in pseudo-axial or equatorial position in a chelate ring[5].

In this communication, we wish to discuss that the positioning array of four phenyl rings in pseudo-axial or equatorial manners[6] is sufficient to explain the observed stereochemical effect.

Now we wish to suggest new concept of P/M-chirality[7] in order to distinguish two species of the positioning arrays of four phenyl groups in the chiral bisphosphine-rhodium catalysts as shown in Chart 1.

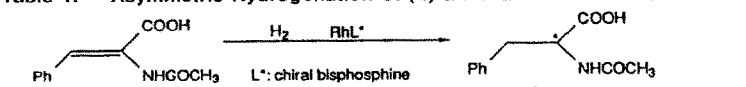
Chart 1. P/M Chirality of Chiral Bisphosphine-Metal Catalysts



Brown and his coworkers already proposed the concept of P/M-chirality to distinguish two chiral conformers of seven membered chelate ring, the chair and the twist-boat form[8,9]. However, our concept of P/M-chirality can apply to all bisphosphine ligand-Rh complexes, regardless of the size of chelate ring. The X-ray crystal structures of the rhodium complexes with chiral bisphosphines((*S*,*S*)-DIOP[10a], (*R*,*R*)-DIPAMP[10b], (*R*,*R*)-CHIRAPHOS[10c], (*R*)-BINAP[10d], (*R*)-PROPHOS[10e], (*R*)-CYCPHOS[10f], (2*R*,4*R*)-BPPM[10g], and (*R*)(*S*)-BPPFA[10h]) indicated to have P-chirality in the positioning array of their four phenyl groups.

The reported and present data of the asymmetric hydrogenation of (*Z*)-α-acetamidocinnamic acid and 2-aminoacetophenone hydrochloride catalyzed by several typical chiral bisphosphine-Rh complexes are listed in Table 1 and 2.

Table 1. Asymmetric Hydrogenation of (*Z*)-α-Acetamidocinnamic acid



entry	chiral bisphosphine	P/M-chirality	confign.	%ee
1[a]	(*S,S*)-DIOP	P	*S*	82
2[b]	(*R,R*)-DIPAMP	P	*S*	94
3[c]	(*S,S*)-CHIRAPHOS	M	*R*	89
4[d]	(*S*)-BINAP	M	*R*	84
5[e]	(*R*)-PROPHOS	P	*S*	90
6[f]	(*R*)-CYCPHOS	P	*S*	88
7[g]	(2*S*,4*S*)-BPPM	M	*R*	91
8[h]	(*S*)(*R*)-BPPFA	M	*S*	93
9[i]	(*R*)(*S*)-BPPFOH	P	*R*	65
10[j]	(*S*)-BPPEF	P	*R*	16

a-h): ref. 11 *i* and *j*) present work : ref 12

Table 2. Asymmetric Hydrogenation of 2-Aminoacetophenone Hydrochloride

L*: chiral bisphosphine

entry	catalyst: chiral bisphosphine	P/M-chirality	confign.	convn.	%ee	condition: [subst.]/[Rh]	atm/°C/h.
11[a]	(*R,R*)-MOD-DIOP	M	*R*	100	19.0	10^2	50/50/72
12[b]	(*S*)-BIMOP	M	*R*	78	11.3	10^3	50/50/48
13[c]	(*R,R*)-PPCP	P	*S*	100	15.1	10^2	50/50/72
14[d]	(2*S*,4*S*)-BCPM	M	*S*	100	81	10^3	20/50/20
15[e]	(*R*)(*S*)-BPPFOH	P	*R*	100	43.4	10^3	50/50/48
16[f]	(*S*)(*S*)-BPPFOH	P	*R*	100	46.7	10^3	50/50/48
17[g]	(*S*)-BPPEF	P	*S*	100	26.7	10^2	50/50/72

a-c) , *e-g*) present work : ref 13 *d*): ref 14

All C_2-symmetric bisphosphine-rhodium catalysts and usual non C_2-symmetric bisphosphine-rhodium catalysts of P(M)-chirality gave the *S* (*R*)-products both in the asymmetric hydrogenation of (*Z*)-α-acetamidocinnamic acid(entry 1-6)and 2-aminoacetophenone hydrochloride (entry 11,12, and 13), whereas unusual non-C_2-symmetric bisphosphine-rhodium catalysts, pyrrolidine bisphosphine(BPPM, BCPM)and ferrocenyl bisphosphine(BPPFOH, BPPFA, BPPEF), gave the complex result (entry 7-10,14-17).

In the asymmetric hydrogenation of dehydroalanine, it is widely known that the major enantiomer of the product aries from the less stable diastereomer of the catalyst-substrate adduct because the less stable diastereomer is more reactive than the more stable one in the oxidative addition rate of the hydrogen molecule to the diastereomeric catalyst-substrate adducts[3] . The same view was applied to explain the asymmetric hydrogenation of the aminoketone derivatives.

The X-ray crystal structure of (2*S* ,4*S*)-BPPM-Rh complex[10g] and (*S*)-ferrocenyl phosphine-Rh[10h] complex indicate that the down-apical position of (2*S*,4*S*)-BPPM-Rh complex and the upper-apical position of (*S*)-ferrocenyl phosphine complex were sterically crowded, respectively. Therefore, the asymmetric hydrogenation catalyzed by (2*S*,4*S*)-BPPM/(2*S*,4*S*)-BCPM-Rh complex (M-chirality) can proceed to give the (*R*)-product, *via* (A)-adduct in the case of (*Z*)-α-acetamidocinnamic acid(entry 7) but (*S*)-product *via* (B)-adduct in the case of 2-aminoacetophenone hydrochloride (entry 14), because the transition state energy in the oxidative addition of the hydrogen molecule to the (A)-adduct from the upper-apical side becomes more higher than the (B)-adduct from the down-apical side due to the steric hindrance with bending of the P_2-Rh-prochiral carbonyl group moiety to the crowded down-apical position of the rhodium atom as shown in Fig. 1[16]. Similarly, the asymmetric hydrogenation of (*Z*)-α-acetamidocinnamic acid catalyzed by (*S*)-ferrocenyl phosphine-Rh catalyst can give (*R*)-product *via* (D)-adduct (entry 8,9, and 10). Otherwise, in the asymmetric hydrogenation of 2-aminoacetophenone hydrochloride, (*S*)-BPPEF-Rh complex gave the (*S*)-product (entry 17) as expected, whereas (*R*)(*S*)-BPPFOH and (*S*)(*S*)-BPPFOH-Rh complexes might be resulted in (*R*)-product from the electronic interaction of the rhodium atom with the hydroxyl group of BPPFOH, as shown in Fig. 2[17].

Fig. 1 (2*S*,4*S*)-BPPM-Rh-Subatrate Adduct (M-chirality)

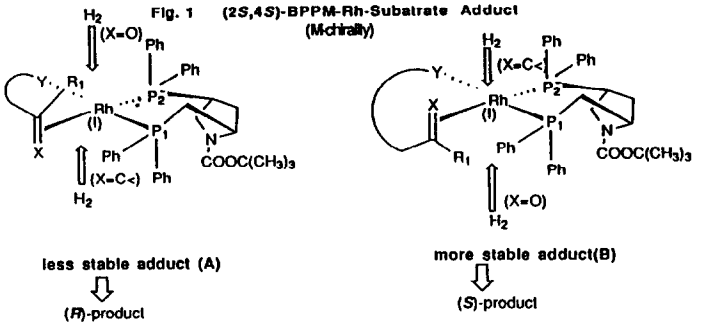
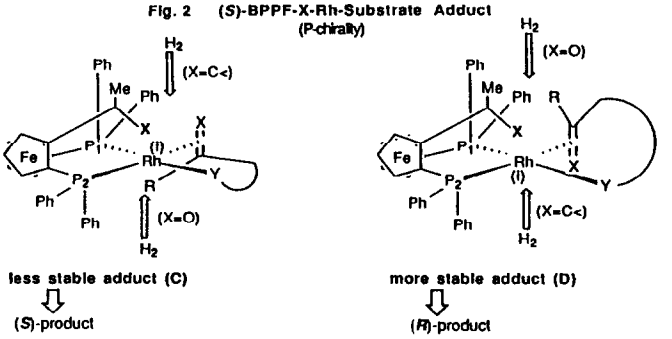


Fig. 2 (*S*)-BPPF-X-Rh-Substrate Adduct (P-chirality)



We concluded that the absolute configuration of the products depended on the P/M-chirality of the catalysts in the asymmetric hydrogenation with all types of chiral bisphosphine-rhodium complexes except the unusual non-C_2-symmetric pyrrolidine and ferrocenyl bisphosphine ligands, because the pyrrolidine and ferrocenyl bisphosphine ligands formed the unsymmetrically crowded rhodium complexes and furthermore some ferrocenyl bisphosphines(BPPFOH, BPPFA) donated the unsymmetric neighboring participation of their hydroxyethyl and aminoethyl groups.

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12. Reactions were carried out with substrate (2.5 mmol), $[Rh(COD)Cl]_2$ (0.0125 mmol) and ligand (0.03 mmol) in methanol at 50°C for 48 h under an initial hydrogen pressure of 50 atm. The chemical yields were quantitative. The optical purity was calculated on the maximum optical rotation of pure *N*-acetylphenylalanine; $[\alpha]_D$ +46.0 (*c* 1, EtOH), ref 15.

13. Reactions were carried out with substrate (5.0mmol), $[Rh(COD)Cl]_2$ (2.5×10^{-3} or 2.5×10^{-2}mmol), ligand(6.0×10^{-3} or 6.0×10^{-2}mmol) and triethylamine (25×10^{-3} or 25×10^{-2}mmol) in methanol at 50°C for 48-72h under an initial hydrogen pressure of 50 atm. The conversion was determined by ^1H NMR analysis. The optical purity was determined by HPLC analysis.

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16. The ^{31}P NMR study of the (2*S*,4*S*)-BPPM-Rh-itaconic acid complex indicated that the prochiral olefinic group occupied specifically the chelating position oriented trans to the P_2 atom[18, 19].

17. We assumed that the prochiral group occupied selectively the chelating position oriented trans to the P_2 atom in the ferrocenyl catalyst because of the steric and electron-donating effect of the hydroxyethyl substituent.

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