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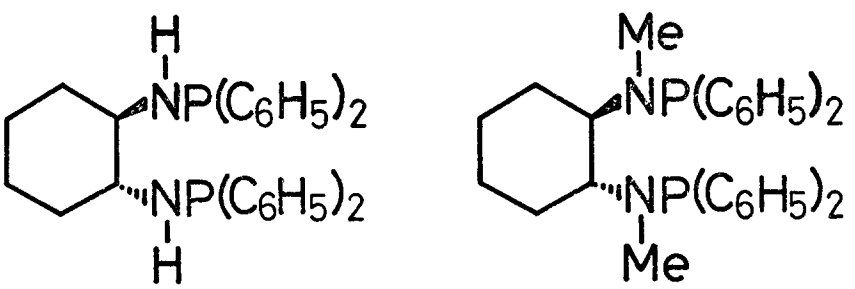
CHIRAL RECOGNITION BY VARIOUS BISPHOSPHINE-RHODIUM COMPLEXES IN ASYMMETRIC HYDROGENATION OF OLEFINS THROUGH HELICAL CONFORMATION OF PHENYL GROUPS ON THE PHOSPHOROUS ATOM

Ken-ichi Onuma*, Tomiyasu Ito and Asao Nakamura
Central Research Laboratories, Ajinomoto Co., Inc.
1-1 Suzuki-cho, Kawasaki, 210, Japan

Chiral reversion of the stereoselectivity of the rhodium complex of (1R,2R)-bis(diphenylphosphinamino)cyclohexane by N-methylation of the ligand in asymmetric hydrogenation was described.

In recent years, catalytic asymmetric hydrogenations of α-acylaminocinnamic acids have been investigated for obtaining chiral α-amino acids. Considerable efforts have been devoted not only to developing new chiral ligands[1], but also to studying the mechanisms of asymmetric hydrogenations[2]. However, little is known about the structural correlation of the ligands to the chirality of the products.

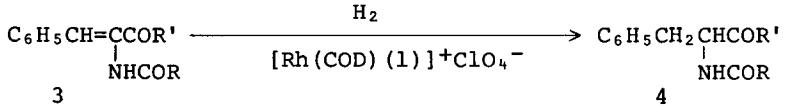
(1R,2R)-Bis(diphenylphosphinamino)cyclohexane, (R,R)-1, has been found to be an effective ligand for the rhodium catalyzed asymmetric hydrogenation, to give preferentially (R)-amino acids[3]. Interestingly, Hanaki et al.[4] have reported that the rhodium complex of (1R,2R)-bis(N-diphenylphosphino-N-methyl-amino)cyclohexane, (R,R)-2, which is N,N'-dimethyl derivative of (R,R)-1 gives preferentially (S)-amino acids. In view of subtlety of the structural divergence between these two ligands, the origin of this marked difference in stereo-selectivity should be further explored.



(R,R)-1 (R,R)-2

Figure 1. Chiral Aminophosphines, (R,R)-1 and (R,R)-2.

(R,R)-1 and (S,S)-1[5] were prepared in dry benzene by reaction of chlorodiphenylphosphine with (1R,2R)-diaminocyclohexane and with (1S,2S)-diaminocyclohexane, respectively. Each of the aminophosphines was used as the chiral ligand in the cationic rhodium complex[6], $[Rh(COD)(l)]^+ClO_4^-$. The following catalytic reaction always proceeded quantitatively.



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3a,4a R=CH_3 R'=OH
3b,4b R=CH_3 R'=NH_2
3c,4c R=C_6H_5 R'=OH
3d,4d R=C_6H_5 R'=NH_2

The reaction product was carefully isolated and the optical purity was determined either by measuring the optical rotation[7] or by liquid chromatography[8]. The results are summarized in Table 1.

Table 1. Asymmetric hydrogenation[a] of α-acylaminocinnamic acids and their amides

Substrate	Solvent	Optical yield (configuration) (R,R)-1	(S,S)-1	(R,R)-2
3a	EtOH	41(R)	41(S)	89(S)[b]
3a	EtOH-C_6H_6(1:1)	70(R)	72(S)	
3b	EtOH-C_6H_6(1:1)	92(R)	92(S)	
3c	EtOH	43(R)	43(S)	92(S)[b]
3c	EtOH-C_6H_6(1:1)	62(R)	60(S)	
3d	EtOH-C_6H_6(1:1)		70(S)	

a) All hydrogenations were run with 1g of substrate and 9μmol of a cationic complex under initial pressure of 8Kg/cm^2 at room temperature.
b) Hanaki et al.[9].

As can be seen in Table 1, (R)-amino acids are the major product in the hydrogenation with the rhodium complex of (R,R)-1, while (S)-amino acids are formed preferentially when the rhodium complex of (S,S)-1 is used, although the optical yields are dependent on the substrate structures and solvents. The most striking feature is that (S)-amino acids have been obtained in the hydrogenation with the rhodium complex of (R,R)-2, in contrast with the results of (R,R)-1.

In order to clarify the origin of the chiral reversion of the stereoselectivity by N-methylation of ligand, stereochemistry of the complexes has been considered.

The seven-membered chelate ring containing the rhodium atom may take predominantly a twist-chair conformation[10] to reduce repulsion between phenyl groups

and cyclohexane ring. The hydrogen atoms on the nitrogen atoms in the (R,R)-1 complex may occupy axial positions, and the methyl groups in (R,R)-2 complex may occupy equatorial positions in the twist-chair conformation, deduced from analogy of the preferred conformation of piperazine derivatives[11]. The preferable conformations can be also satisfactorily understood from the consideration with CPK molecular models. This difference of the conformation around the nitrogen atoms may exert significant effects on the orientation of equatorial phenyl groups to give reverse helical conformation as shown in Fig. 2. The phenyl groups are supposed to be skewed in left-handed orientation in (R,R)-1 complex and in right-handed orientation in (R,R)-2 complex.

We are going to propose that the reversion of stereoselectivity in asymmetric hydrogenation is mainly caused by the difference of the helical conformation: the complex having left-handed helicity would give (R)-amino acids and the complex having right-handed helicity would give (S)-amino acids. With this hypothesis concerning the structural correlation between the helical conformation of phenyl groups and the chirality of the products, other results previously reported[1a,b] have been satisfactorily interpreted. The structure of the rhodium complex of (2S,3S)-bis(diphenylphosphino)butane has been determined by X-ray analysis[12]. This complex has the left-handed helicity and has been reported surely to give (R)-amino acids[1b]. The conformation of phenyl groups has been observed to be skewed in right-handed orientation in the rhodium complex of (1R,2R)-bis(o-anisylphenylphosphinyl)ethane[1a], which has been reported certainly to give (S)-amino acids.

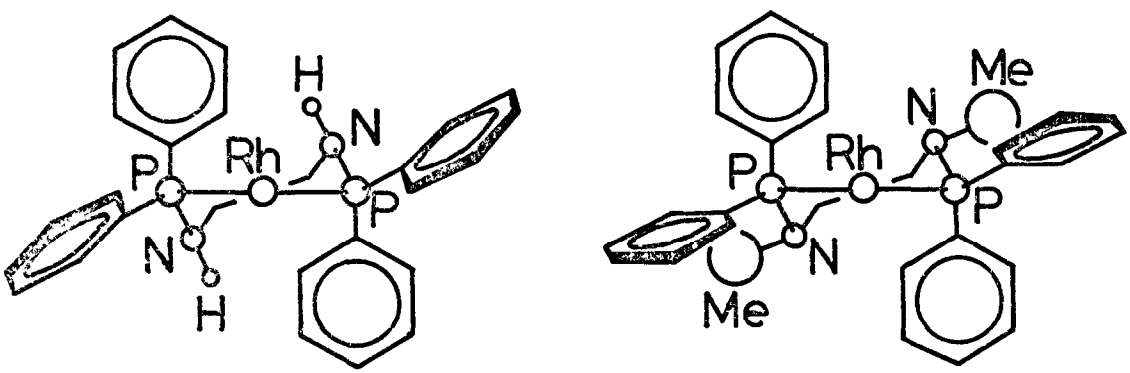

Figure 2. Chiral skew conformation of equatorial phenyl groups in rhodium complex of (R,R)-1 and (R,R)-2, the skelton of cyclohexane ring omitted for simplicity.

The contribution of the coordination of the amide group[13] in a substrate should be also taken into account for the study of the correlation between the helicity of the complex and the chirality of a product.

Stereochemistry of phenyl groups of the complexes is currently being studied by X-ray analysis. Further investigations are in progress on the structural correlation between the complex and the substrate, and the effect of solvents.

References and Footnotes

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5) (R,R)-1: mp 130-132°, $[\alpha]_D^{20}$=-4.51°(C=1.0,C_6H_6). Anal. ($C_{30}H_{32}N_2P_2$) C,H,N,P; Cald. 74.67,6.68,5.81,12.84. Found 74.47,6.65,5.79,12.81. (S,S)-1: mp 130-132°, $[\alpha]_D^{20}$=+4.48°(C=1.0,C_6H_6). Anal. ($C_{30}H_{32}N_2P_2$) C,H,N,P; Cald. 74.67,6.68, 5.81,12.84. Found 74.60,6.68,5.75,12.50.

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7) The value of specific rotations of pure enantiomers was taken from ref. 1)(b)

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