THE STRUCTURE OF THE ENANTIOSELECTIVITY DETERMINING INTERMEDIATE IN THE PHOSPHINE-RHODIUM ASSISTED ASYMMETRIC HYDROGENATION OF β-METHYLENE ACIDS[1)]

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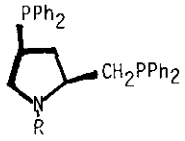
Abstract ---- The general mechanism of the phosphine-rhodium catalyzed asymmetric hydrogenation of β-methylene acid was proposed to account the chemical evidences on the structure of the enantioselectivity determining key intermediate, [Rh(BPPM)-(β-Methylene Acid)(H_2)]$^+X^-$ (3a).

I have developed the new chiral pyrrolidinephosphine-rhodium complexes which are effective catalysts for the asymmetric syntheses of α-amino acids, salsolidine, R-(-)-pantolactone, β-amino acids, methylsuccinic acid, and β-alkylbutyrolactone[2)].



Pyrrolidine-phosphine (1)

R= H, PPM ; R= COtBu, PPPM

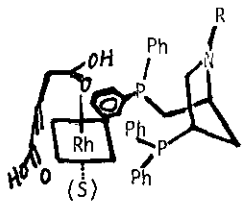
R= CH_3, MPPM ; R= $COCH_3$, APPM

R= CHO, FPPM ; R= $CONH_2$, CAPPM

R= COOtBu, BPPM ; etc.

Furthermore, ^{31}P NMR studies on the intermediates in the asymmetric hydrogenations catalyzed by the phosphine-rhodium complexes have revealed the structure of [Rh(Bisphosphine)(Itaconic Acid)]$^+$ ClO_4^- (2) as shown in Fig. I[3)].

Fig. I.



[Rh(BPPM)(Itaconic Acid)]$^+ClO_4^-$ (2a)

$J_{P(1)-Rh}$= 135 Hz

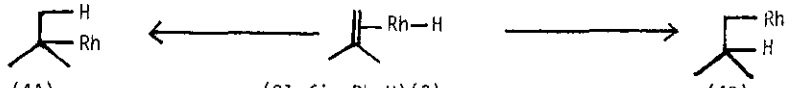
$J_{P(2)-Rh}$= 142 Hz

$J_{P(1)-P(2)}$=36 Hz

(S): Solvent

In this paper, I wish to discuss here the chemical evidences for the structure of enantioselectivity determining intermediate, [Rh(Bisphosphine)(Itaconic Acid)(H_2)]$^+ClO_4^-$ (3), which are derived from the well defined complexes, [Rh(Bisphosphine)(Itaconic Acid)]$^+ClO_4^-$ (2) and hydrogens.

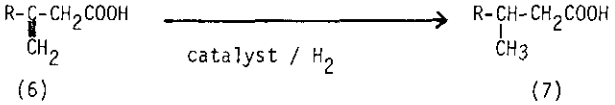
The two types of the regioselectivity are possible in the hydride-transfer from the π-complex, [Rh(Bisphosphine)(Itaconic Acid)(H_2)]$^+ClO_4^-$ (3), as shown below.



(4A) (Olefin-Rh-H)(3) (4B)

To determine which structure(4A or 4B) is the real key intermediate in the asymmetric hydrogenation of β-methylene acids, I compared the hydrogenation rates of β-methylene-propionic acid (6b) and β-methylene-γ-trimethylsilyl-propionic acid (6c)[4], because that trimethylsilyl group in the latter compound (6c) is expected to accelerate the formation of the intermediate (4B) or to restrain the intermediate (4A) due to its β-cation stabilizing effect in comparison with the reaction rate of the former (6b), on the assumption that the formation rates of both key intermediates, [Rh(BPPM)(β-Methylene Acid)(H_2)]$^+X^-$ (3a), are almost the same.

Table I. Asymmetric Hydrogenation of β-Methylene Acids[a].



(6) (7)

Substrate (R)	Chiral Catalyst	Conditions	Solvent	Conversion (%)	(7) Opt. y(%).(Abs. Conf.)
HOOC- (6a)	BPPM-Rh	20°C, 2h, 10 atom of H_2	MeOH	100	
CH_3- (6b)	BPPM-Rh	"	MeOH	100	
$(CH_3)_3SiCH_2$- (6c)	BPPM-Rh	"	MeOH	78	
HOOC- (6a)	BPPM-Rh	20°C, 20h, 20 atom of H_2	MeOH[b]	100	95.4 (S)
HOOC- (6a)	BPPM-Rh	"	MeOH	100	89.5 (S)
CH_3 CH_3 >C=CH-CH_2-CH_2- (6d)	BPPM-Rh	"	MeOH[c]	100	30 (R)
$(CH_3)_3SiCH_2$- (6c)	BPPM-Rh	"	MeOH[c]	100	10 (S)

a) All hydrogenations were carried out with 5mmole of substrate (6), 0.06 mmole of BPPM, and 0.025 mmole of [Rh(1,5-cyclooctadiene)Cl]$_2$ in 10 ml of solvent.
b) Triethylamine (5 mmole) was added.
c) Triethylamine (2.5 mmole) was added.

The stereochemistry of the trimethylsilyl product (7c) was assigned to the S-configuration by comparing its ORD curves (positive plain curve)[5] with the ORD curves of R-3,7-dimethyl-octanoic acid, and the optical purity of 7c was determined by analysis of NMR spectra of the methyl ester (methyl ester of 7c) in the presence of the chiral shift reagent Eu(hfc)$_3$.

Fig.2. (A) Mechanism for Itaconic Acid (Trifunctional Acids)

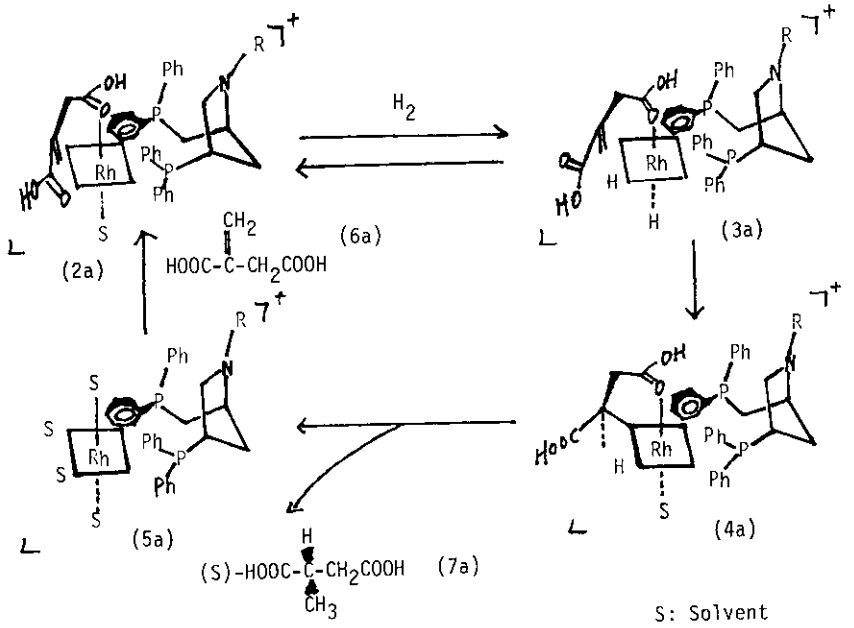
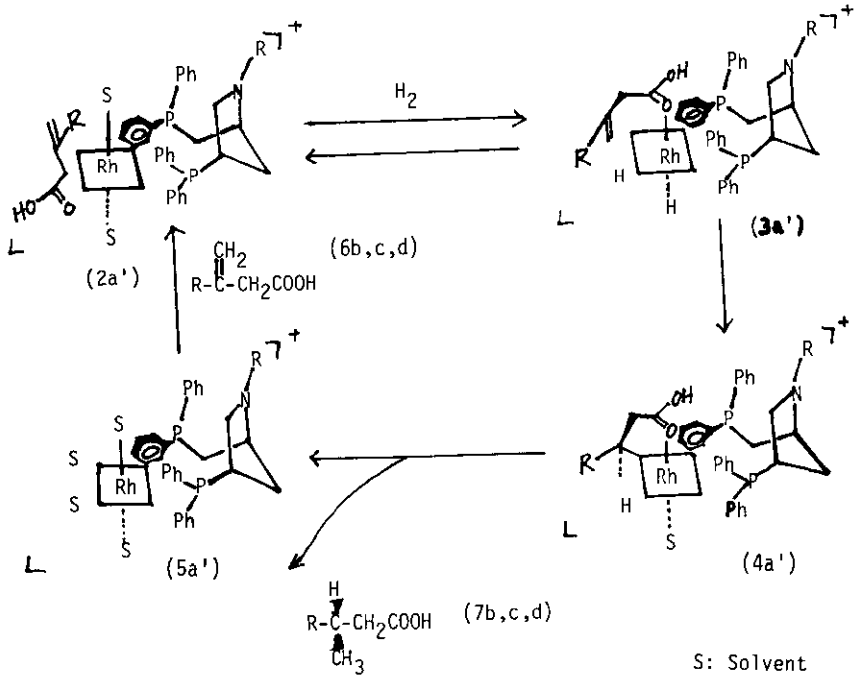


Fig. 3. (B) Mechanism for β-Methylene Acids (Bifunctional Acids)



From the table I, the trimethylsilyl group restrains the hydrogenation rate of the β-olefin. This fact may indicate that this hydrogenation proceeds via the intermediate (4A), and also the large differences of the optical yields between itaconic acid (trifunctional acid) and the simple β-methylene acids (6c,d) also suggested the effective participation of α-carboxylic acid in 6a to obtain the high optical yield.

Therefore, I proposed the general mechanisms (A for trifunctional acid, B for bifunctional acid) in Figs 2 and 3.

Further studies along this line are under way.

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