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THE MECHANISM OF ASYMMETRIC HYDROGENATIONS CATALYZED BY CHIRAL PYRROLIDINEPHOSPHINE-RHODIUM COMPLEXES[1)]

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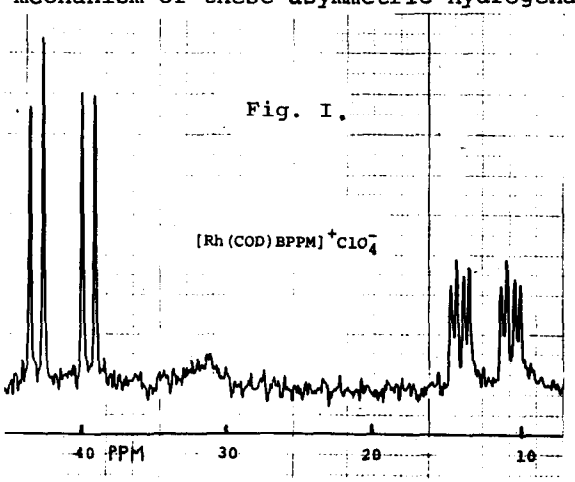
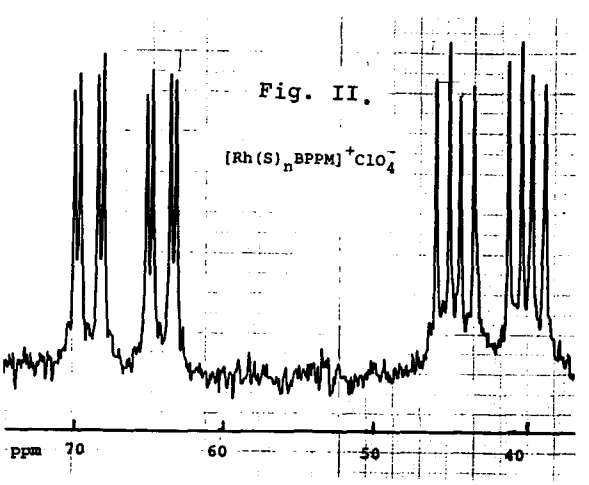
Effective catalytic asymmetric hydrogenations catalyzed by chiral pyrrolidinephosphine-rhodium complexes have been proven to be useful for the preparation of optically active α-amino acids (83-91%)[2,3)], isoquinoline salsolidine (45%)[6)] α-hydroxy esters (78.5%)[4,5)], R-(-)-pantolactone (80.5-86.7%)[7,9)], β-amino acids (53-55.2%)[8)], α-methylsuccinic acid (94.2%)[10,11)] and β-methylaspartic acid (58.2% optical yield)[12)].

We wish to describe here the chemical and ^{31}P n.m.r. evidences on the mechanism of these asymmetric hydrogenations.

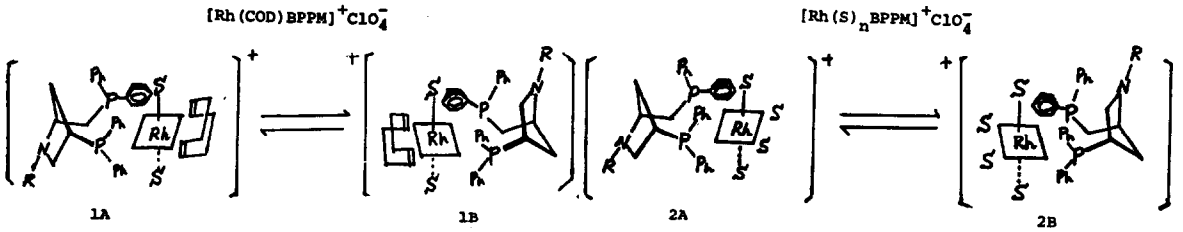




Figures. ^{31}P n.m.r. spectra recorded in p.p.m. downfield from external 85% H_3PO_4.

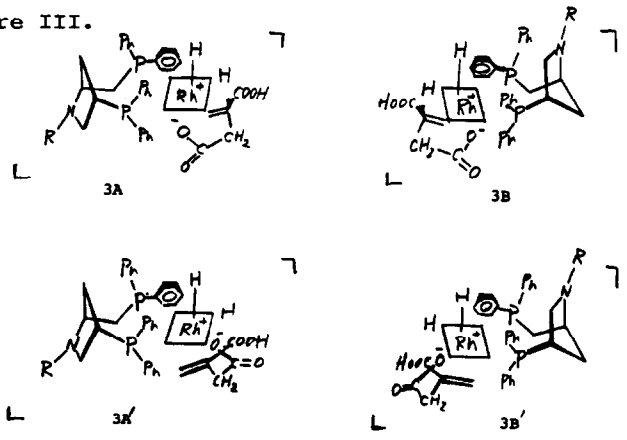
The ^{31}P n.m.r. spectra of $[Rh(COD(BPPM]^{+}ClO_4^{-}$ in CD_3OD (50 mg in 1.5 ml CD_3OD) and the hydrogenated complex, $[Rh(S)_nBPPM]^{+}ClO_4^{-}$ in CD_3OD (completely in 5 minute at atmospheric pressure of H_2) at 28°C indicated clearly that in both complex solutions two conformers are equally present as shown in Figures I and II.

From X-ray structure determination of pyrrolidinephosphine-rhodium complex, $[Rh(COD)PPPM]^{+}ClO_4^{-}$ [11,13], and these n.m.r. data, we offered the structures 1A and 1B, and 2A and 2B for the conformers in the solutions respectively.

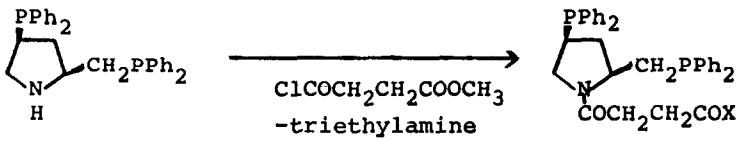


Juging from the clear evidences that (1) H_2 adds to rhodium atom in the cis manner[14], (2) chelating substrate, itaconic acid, also can fix to rhodium atom only in the cis form and (3) rhodium atom adds regiospecifically to the less substituted side of olefins while H reacts to the more substituted side[15], all structures of the stable key intermediates in the asymmetric induction can be depicted as shown in Figure III [19].

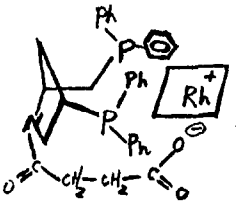
Figure III.



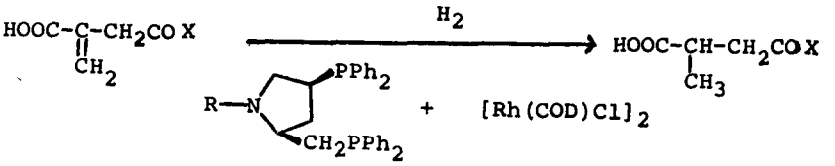
Aiming to clarify chemically the real structure of key intermediates, new chiral phosphines, HSPPM and MSPPM[16], were synthesized, because the carboxylate group of HSPPM-Rh catalyst can interact intramolecularly with rhodium atom only in the form of A-type. The intramolecular interaction of the carboxylate can depress the contribution of the conformers 3A and 3A'. Therefore, the increase of (S)-product are attributable only to the increase of the conformer 3B, whereas (R)-product derives from the conformer 3B'.

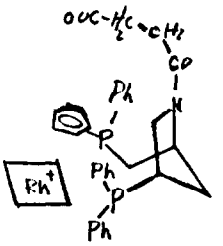


X= OCH_3, (MSPPM)
X= OH, (HSPPM)



(A)





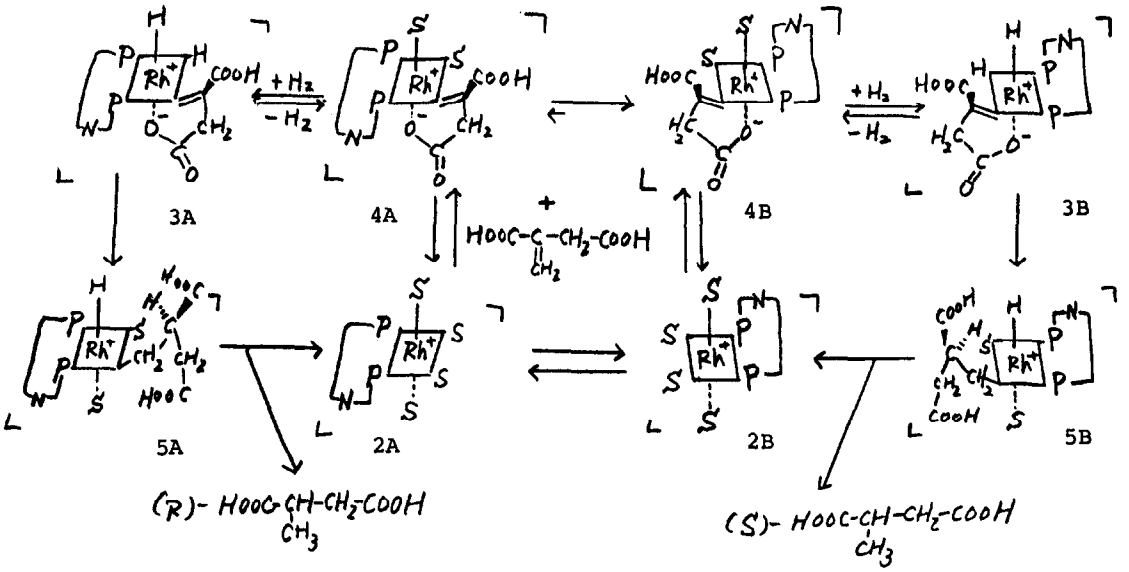
(B)

Table I Asymmetric hydrogenations of itaconic acid and its ester with modified chiral pyrrolidinephosphine-rhodium complexes[a)]

Substrate (X)	Chiral reagent (R)	Solvent	Optical y.	(con.)
OCH_3	MSPPM-Rh ($COCH_2CH_2COOCH_3$)	methanol	53.3	(S)[e)]
OCH_3	MSPPM-Rh ($COCH_2CH_2COOCH_3$)	methanol[b)]	22.8	(R)[e)]
OCH_3	HSPPM-Rh ($COCH_2CH_2COOH$)	methanol	59.9	(S)[e)]
OCH_3	HSPPM-Rh ($COCH_2CH_2COOH$)	methanol[b)]	1.4	(R)[e)]
OH [c)]	MSPPM-Rh ($COCH_2CH_2COOCH_3$)	methanol	77.6	(S)
OH [c)]	MSPPM-Rh ($COCH_2CH_2COOCH_3$)	methanol[d)]	80.0	(S)
OH	HSPPM-Rh ($COCH_2CH_2COOH$)	methanol	86.0	(S)[e)]
OH	HSPPM-Rh ($COCH_2CH_2COOH$)	methanol[d)]	93.9	(S)[e)]

a) Hydrogenations were carried out with 5 mmole of substrate, [Rh(1,5-cyclooctadiene)Cl]$_2$ (0.05 mmole) and bisphosphine (0.06 mmole) at 20°C for 20 h under an initial hydrogen pressure of 50 atom unless otherwise cited.
b) Triethylamine (half molar equivalent to substrate) was added.
c) 2 mmole scale.
d) Triethylamine (molar equivalent to substrate) was added.
e) Isolated as dimethyl ester after treatment with diazomethane.

From the Table, HSPPM-Rh gave the (S)-product more than MSPPM-Rh in all experiments. These facts may indicate that 3A and 3B are important key intermediates. This conclusion and the facts[17,18] that the chiral phosphine-rhodium asymmetric induction arises from the stereoselectivity in the binding step between the complexes and the substrate offered the following mechanism on the asymmetric hydrogenation of the chelating substrates.



Further investigations on this line are actively under way.

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16) Satisfactory spectral and analytical data were obtained for this substance.
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18) ^{31}P n.m.r. studies on the interactions between hydrogenated BPPM-Rh^+ and the substrates will be discussed in the separated papers.
19) The upper apical positions of these conformers (A and B) are sterically hindered with phenyl groups to prevent the carboxylate or olefin substitution.

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