CHEMISTRY LETTERS, pp. 559-562, 1989.

The Effects of cis-Coordinating Phosphine of Chiral Bisphosphine-Rhodium Complexes on the Catalytic Activities in the Asymmetric Hydrogenation of Itaconic Acid[1)]

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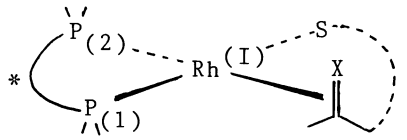
The effects of cis-coordinating phosphine of the rhodium complexes of BCPM ((2S,4S)-N-(t-butoxycarbonyl)-4-(dicyclohexylphosphino)-2-[(diphenylphosphino)methyl]pyrrolidine) analogues bearing electron donating or attracting groups on the catalytic activities in the asymmetric hydrogenation of itaconic acid are described.

Recently, we have proposed the "respective control concept"[2)] which states that one phosphino group of the bisphosphine ligands oriented cis to the prochiral group of the substrate controls the enantioselectivity and another group oriented trans to the prochiral group accelerates its reaction rate in the asymmetric hydrogenations using the rhodium complexes as catalysts. It has been applied very well to the following case. The electron-rich phosphine is important for forming rigid chelation of rhodium with electron-deficient olefins and carbonyl compounds at trans position, resulting in higher enantioselectivity by the chiral array of diarylphosphino group oriented cis to the prochiral group, and also significant for accelerating the oxidative addition of molecular hydrogen, resulting in higher catalytic activity as shown in Fig. 1.



X= C≺, O, N-

S= O-, N≺, Cl, solvent

-P(1) (cis) : enantioselection

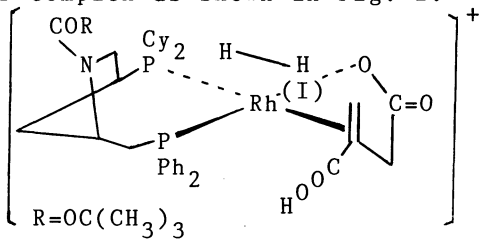
-P(2) (trans) : electron-rich → 1) acceleration of the oxidative addition of molecular hydrogen → higher catalytic activity (d-σ* interaction)

2) rigid chelation of rhodium with electron-deficient olefins or ketones by back donation (d-π*) → higher enantioselection

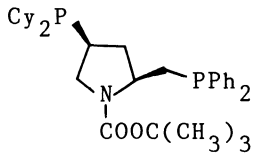
Fig. 1.

On the basis of this concept, we have developed a highly efficient chiral ligand, BCPM ((2S,4S)-N-(t-butoxycarbonyl)-4-(dicyclohexylphosphino)-2-[(diphenylphosphino)methyl]pyrrolidine) (1), and its rhodium complex is found to be one of the most effective catalysts for asymmetric hydrogenations of carbonyl compounds[3)]

and itaconic acid.[4] In the case of the asymmetric hydrogenation of itaconic acid with the cationic rhodium complex of BCPM (**1**), we have reported that the prochiral olefinic group orients predominantly trans to the electron-rich phosphino group, dicyclohexylphosphino group, and necessarily cis to the diphenylphosphino group in the rate-determining and enantioselecting step. Furthermore, we have described a possible mode of oxidative addition of molecular hydrogen which proceeds with H_2 aligned parallel to the Cy_2P-Rh-olefin axis of the Rh(I) square-planar complex as shown in Fig. 2.[4]



(A mode of oxidative addition of H_2)



(2S,4S)-BCPM (**1**)

electron-rich : $-PCy_2 \gg -PPh_2$

Fig. 2.

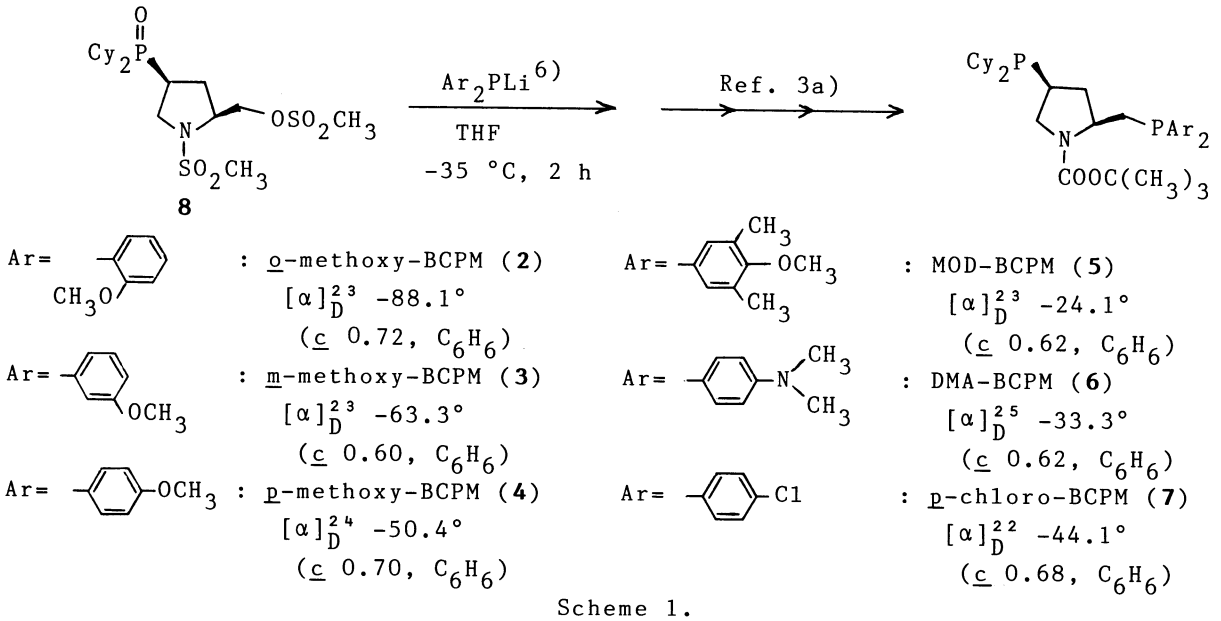
In this communication, we wish to describe the effects of cis-coordinating phosphine of BCPM analogues (**2-7**) bearing the electron donating or the attracting group at the C_2 position of pyrrolidine ring on the catalytic activities in the asymmetric hydrogenation of itaconic acid. We have reported the preparation of chiral pyrrolidinebisphosphine ligands having electron-rich dialkylphosphino group, dicyclohexylphosphino group, at the C_2 position and their effects on the asymmetric hydrogenation catalyzed by their-rhodium complexes.[3b] The optical yields are lower than BCPM (**1**) due to the comformation of the dicyclohexylphosphino group is more flexible than that of the diphenylphosphino group of BCPM (**1**).[5] Therefore, we have designed new chiral BCPM analogues (**2-7**) substituted with comformationally rigid diarylphosphino group at the C_2 position.

The BCPM analogues (**2-7**) were prepared easily from the mesylate (**8**) by the similar method reported previously[3a,6] as indicated in Scheme 1.[7]

The results of asymmetric hydrogenation of itaconic acid with the cationic rhodium complexes of newly synthesized BCPM analogues are summarized in Table 1. All hydrogenations were carried out in the presence of a cationic rhodium catalyst (0.1--x0.1 mol%) prepared in situ by mixing $[Rh(COD)_2]ClO_4$ and a ligand in a ratio of 1 : 1.2 and triethylamine ([Substrate]/[Et_3N]=1) at room temperature for 20 h in methanol under an atmospheric hydrogen pressure.

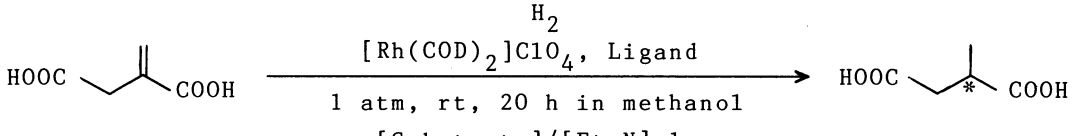
o-Methoxy-BCPM (**2**) gave a lower optical yield than the other ligands. The catalytic activity of o-methoxy-BCPM-Rh^+ was lesser than that of the other catalyst. This results may be rationalized under the steric factor of the o-methoxy group.[6a] When **4**, **5**, or **6** bearing the electron donating substituents on the diarylphosphino group at the C_2 position of pyrrolidine ring were used as ligands, the hydrogenations proceeded smoothly with a high substrate to catalyst ratio (3000 : 1) more than using BCPM (**1**)-Rh^+ complex as a catalyst. On the other hand, the rhodium complex of m-methoxy-BCPM (**3**) having the electron attracting group did not accelerate the reaction rate compared with that when rhodium complexes of **4**, **5**, or **6** were used as catalysts. In particular, the catalytic activity of the rhodium complex of p-chloro-BCPM (**7**) which has a better electron attracting

group than the m-methoxy one is fairly lesser than BCPM-Rh^+ complex. These experimental results clealy indicate that cis-coordinating phosphines of chiral bisphosphinerhodium complexes affect on the catalytic activity, although their effects may be a slight compared with trans ones.[3b] We have assumed two explanation for



Scheme 1.

Table 1. Asymmetric Hydrogenation of Itaconic Acid with the Cationic Rhodium Complexes of BCPM Analogues[a]



Ligand	[Substrate]/[Rh]	Convn./%[b]	% ee[c]	(Confign.)
1	1000	100	92.0[4]	(S)
	3000	10	—	-
2	1000	43.0	58.4	(S)
3	1000	100	93.0	(S)
	3000	<10	—	-
4	1000	100	85.7	(S)
	3000	100	74.5	(S)
5	1000	100	91.0	(S)
	3000	98.2	80.5	(S)
6	1000	100	92.5	(S)
	3000	100	83.9	(S)
7	1000	17.6	79.8	(S)

a) All hydrogenations were carried out with [Substrate]=0.5 M in methanol. b) Determined by ^{1}H-NMR analysis. c) Determined by HPLC analysis of the corresponding methyl ester with CH_2N_2 on Chiralcel OB (Daicel).

these results. One is that the variations of catalytic activities especially between **2**, **3**, **5** and **4**, **6**, **7** may be rationalized by the sterically hindering effects of the ortho- or meta-substituted diarylphosphino groups of **2**, **3**, or **5** on the formation of bisphosphine-rhodium-substrate complexes. Another is that the d-σ* orbital overlapping and d-π* back donation by the electorn-rich trans-coordinating phosphino group,[8] dicyclohexylphosphino group, may be more assisted by electorn rich cis-coordinating phosphine of **4**, **5**, or **6** as a better electron donating phosphine than that of diphenylphosphino group of BCPM (**1**).[9] Consequently, the oxidative addition of molecular hydrogen to the rhodium as the rate-determining step of the asymmetric hydrogenation of itaconic acid (Fig. 2) is accelerated by the both trans and cis-coordinating electron-rich phosphines of **4**, **5**, or **6**. On the other hand, the electron attracting effect of cis-coordinating phosphine of p-chloro-BCPM (**7**) may inhibit the d-σ* orbital interaction assisted by the trans-coordinating dicyclohexylphosphine.

Our results show that the effects of cis-coordinating phosphine of the rhodium complexes of BCPM analogues play a role in the activity of catalysts and the electron-rich phosphine is important for accelerating the reaction rate in the asymmetric hydrogenation of itaconic acid. In general, the electronic effects of trans-coordinating phosphine of bisphosphine-rhodium complexes may contribute to activating the catalysts mainely, and cis-coordinating phoshine also has been found to assist trans-effects. These asymmetric hydrogenation findings offer a new mechanistic aspect on the hydrogenation catalyzed by chiral bisphosphine-rhodium complexes.

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5) We have examined the asymmetric hydrogenation of itaconic acid with the cationic rhodium complex of chiral pyrrolidinebisphosphine bearing the dicyclohexylphosphino group at the C_2 and C_4 positions of the pyrrolidine ring (BCCP (2S,4S)-N-(t-butoxycarbonyl)-4-(dicyclohexylphosphino)-2-[(dicyclohexylphosphino)methyl]-pyrrolidine)). The optical yield is 65.6% (S).
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7) All new ligands were amorphous solids. They were fully charactetrized by the spectral data (^{1}H-NMR) and gave satisfactory elemental analyses.
8) R. H. Crabtree and R. J. Uriarte, Inorg. Chem., 22, 4152 (1983); C. E. Johnson and R. Eisenberg, J. Am. Chem. Soc., 107, 3148 (1985).
9) As unpublished data, we have calcurated the molecular orbitals of chiral pyrrolidinebisphosphine-rhodium complexes by using extended Huckel method. The energy levels of the d_{yz} orbital of rhodium and back donation between rhodium and substrate using BCCP is larger than using BCPM.

(Received December 21, 1988)