Asymmetric Hydrogenation Catalyzed by Bis(disubstituted glyoximato)-cobalt(II)(L)-Chiral Cocatalyst System. Effect of Structural Variation of Ligands and Hydrogen Pressure[1)]

Yoshiaki Ohgo,* Yasuhisa Tashiro,† and Seiji Takeuchi
Niigata College of Pharmacy, 5829 Kamishin'ei-cho, Niigata 950-21
(Received August 25, 1986)

Synopsis. The reaction rate was extremely enhanced by increasing the basicity of the axial ligand of [Co(dmgH)$_2$(L)] and by increasing the hydrogen pressure without decreasing the enantioselectivity. Substituting one and two methyl groups of the dimethylglyoxime ligand in [Co(dmgH)$_2$(L)] with a phenyl group enhanced and retarded the reaction rate, respectively. The chirality at the cobalt did not affect the enantioselectivity.

The authors have reported asymmetric hydrogenations of diketones, α-ketocarboxylates and olefinic compounds[2-6)] catalyzed by bis(dimethylglyoximato)-cobalt(axial ligand)-chiral cocatalyst systems and have proposed a mechanism for the catalysis of the asymmetric hydrogenations.[4,5)] The proposed mechanism involves an electron-donating site and an enantiodifferentiating site that are separated in these systems (Fig. 1).

We examined the effects of a structural variation of inplane and axial ligands as well as hydrogen pressure in order to determine a guideline for finding a better catalyst and to provide further support regarding the mechanism.

Results and Discussion

Effect of Structural Variation of Inplane and Axial Ligands. In Table 1 are summarized the results for asymmetric hydrogenations of benzil that were catalyzed by several catalyst systems in which inplane and axial ligands were varied (Eq. 1 and Fig. 2).

$$\mathrm{PhCOCOPh} \xrightarrow[\mathrm{Co(PL)_2L\text{-}B^*}]{\mathrm{H_2}} \mathrm{Ph\overset{*}{C}HCOPh}\ (\mathrm{OH}) \qquad (1)$$

The chemical yields were almost quantitative. An increase in the sigma-donor character of an axial ligand accelerates the reaction rate (as already reported in part);[5)] an increase in the steric bulkiness decreases it. A steric hinderance of the inplane ligand is considered to decrease the rate, but the electronic effect of an inplane substituent is somewhat complicated. Since the plane of a phenyl group is oriented almost perpendicular to the glyoxime plane,[7)] the electronic influence of the phenyl group is considered to be inductive rather than resonance; thus, the phenyl group will act as an electron-withdrawing group, which can bring about a decrease in the electron density of cobalt atoms. In fact, the Co-CH_3 proton signal in the series of complexes shifts to a lower field (^{1}H NMR spectrum) with an increase in the phenyl substituent (Table 1). The fact that the substitution of one of the two methyl groups of the dimethylglyoxime ligand in Co(dmgH)$_2$L with a phenyl group causes some rate enhancement seems to be incompatible with the fact that the sigma-donor character of the axial ligand enhances the reaction rate. The reason has not yet been clarified.

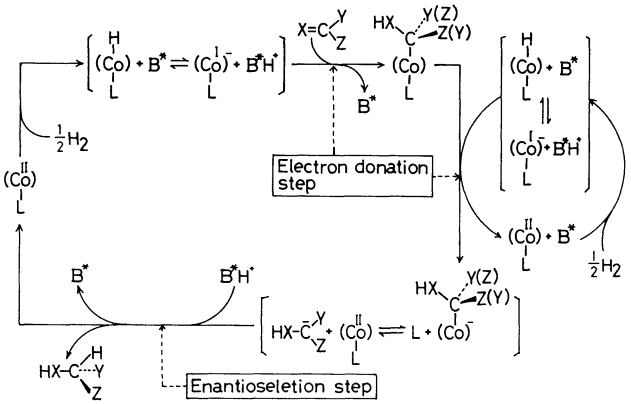

Fig. 1. Catalytic cycle.

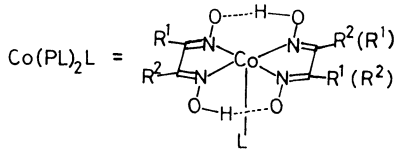

Fig. 2. Structures of Catalysts.

Planar Ligand (PL)	Substituent	
	R^1	R^2
dmgH	CH_3	CH_3
chdH	$-CH_2CH_2CH_2CH_2-$	
mpgH	CH_3(Ph)	Ph (CH_3)
dpgH	Ph	Ph

We have shown that chiral amine coordinates preferentially to one of the two prochiral faces of bis[(*E,E*)-1-phenyl-1,2-propanedione dioximato]cobalt-(I).[8)] If a cobalt complex is involved in the enantiodifferentiating transition state, the enantioselectivities should vary by changing an achiral axial ligand to a chiral one. The results showed that a chiral axial ligand did not alter the enantioselectivity. This provides further support for the proposed mechanism regarding the enantioselection described in previous papers.[4,5)]

Effect of Pressure. Asymmetric hydrogenation catalyzed by chiral rhodium complexes are sensitive to the hydrogen pressure: a high hydrogen pressure decreases the enantioselectivity remarkably.[9,10)] The hydrogen

†Present address: Tokyo Plant, Nippon Kayaku Co., Shimo 3-31-12, Kita-ku, Tokyo 115.

Table 1. Effect of Structural Variation of Inplane and Axial Ligands on the Asymmetric Hydrogenation of Benzil Catalyzed by Bis(glyoximato)cobalt(II)(L)-Quinine System At 30°C[a]

Planar ligand (PL)	Axial ligand[h] (L)	$CH_3(PL)_2Co(L)$ chem. shift (δ/ppm)	V[b] 10^{-3} s^{-1}	(S)-(+)-benzoin Enantioselectivity/%ee[c]
dmgH[d]	Ph_3P	1.19	0.3#	61#
	Py	0.84	2.5#	57#
	$PhCH_2NH_2$	0.74	13.6#	61.5#
	(*R*)-PEA	0.68	11.5	61.5
	(*S*)-PEA		11.5	61.5
chdH[e]	$PhCH_2NH_2$	0.75	10.0	61
mpgH[f]	Bu_3P		1.17	56
	Ph_3P		0.07	53
	Py	1.14 (achiral) i) 1.15 (chiral)	9.8	60.5
	$PhCH_2NH_2$	1.06 (achiral) i) 1.07 (chiral)	18.0	62
	(R)-PEA		8.1	62
	(*S*)-PEA		8.5	62
dpgH[g]	Py	1.44	2.5	59
	$PhCH_2NH_2$	1.33	2.8	57

See Ref. 5).

a) Catalytic hydrogenation was carried out in benzene under atmospheric pressure of hydrogen. In every experiment, equimolar amounts of quinine (Q*) and its HCl salt (Q*HCl) were used (Q*/Co=Q*HCl/Co=1) as the chiral cocatalyst. b) *V*: initial rate (H_2 moles consumed/s/mol of catalyst). c) The enantioselectivity (%ee: % enantiomeric excess) in every reaction was calculated from the specific rotation of the product based on the specific rotation of pure *S*(+)-benzoin, $[\alpha]_D$ +118.5° (*c* 1, acetone).[5] d) dmgH: dimethylglyoxime monoanion. e) chdH: cyclohexanedione dioxime monoanion. f) mpgH: methylphenylglyoxime monoanion=(*E*,*E*)-1-phenyl-1,2-propanedione dioxime monoanion. g) dpgH: diphenylglyoxime monoanion. h) Ph_3P: triphenylphosphine. Py: pyridine. (*R*)-PEA: (*R*)-1-phenylethylamine. Bu_3P: tributylphosphine. i) Achiral and chiral complexes are formed in the ratio of 1 (achiral): 1.2—1.4 (chiral) when methyl iodide is added to the catalyst solution prepared according to the usual method. Methyl signals (^{1}H NMR) of achiral complexes appear at a higher field than those of corresponding chiral complexes.

Table 2. Pressure Effect on Asymmetric Hydrogenation of Ethyl 2-(Acetylamino)propenoate Catalyzed by Bis(dimethylglyoxomato)cobalt(II)-Quinine[a]

Entry	Pressure Kg/cm^2	S/Co[b]	Solvent	React. temp.	React. time	%ee[c]
1	atm.	10	Benzene	RT[d]	10 h	18.0
2	20	10	Benzene	RT	17 min	17.7
3	40	10	Benzene	RT	12 min	19.7
4	60	10	Benzene	RT	5 min	18.4
5	60	6.8	THF	−14°C	1.5 h	16.0

a) Catalytic hydrogenation was carried out in a 100 ml autoclave. In every experiment, equimolar amounts of quinine (Q*) and its HCl salt were used (Q*/Co=Q*HCl/Co=1) as the chiral cocatalyst. b) S/Co: molar ratio of substrate to cobalt. c) Enantioselectivity (% enantiomeric excess) in every experiment was calculated from the specific rotation of the product based on that of the optically pure (*S*)-(−)-ethyl *N*-acetylalaninate, $[\alpha]_{578}^{20}=-66.4°$ (*c* 6, ethanol).[11] d) RT: Room temperature.

pressure effect was ascribed to a difference in the reactivity of the two diastereomeric complexes (leading to the two enantiomeric products) toward hydrogen.[10] However, our catalyst systems are completely different from the chiral ligand-coordinated rhodium complexes. Mechanistic studies on our systems revealed that the electron-donating site and the enantiodifferentiating site are separated:[4,5] this suggested that a higher hydrogen pressure should accelerate the reaction rate without any decrease in the enantioselectivity. When an easily ligating amine, $PhCH_2NH_2$, was used, the reaction rate was too rapid for a measurement, even at a 20 kg/cm^2 pressure of hydrogen. Consequently, experiments on pressure effect were examined in the asymmetric hydrogenation of ethyl 2-(acetylamino)propenoate by using bis(dimethylglyoximato)cobalt(II)-quinine without the addition of a simple axial base (Eq. 2).

$$H_2C{=}C\begin{matrix}\diagup NHCOCH_3\\ \diagdown COOC_2H_5\end{matrix} \xrightarrow[Co(dmgH)_2\text{-Quinine}]{H_2} H_3C\text{-}\overset{*}{C}H\begin{matrix}\diagup NHCOCH_3\\ \diagdown COOC_2H_5\end{matrix} \quad S(-)\text{-} \qquad (2)$$

As expected, the reaction rate was extremely enhanced with increasing hydrogen pressure, while the enantioselectivities were almost constant within the experi-

mental error (Table 2). The reaction rate under a 60 $kg\,cm^{-2}$ initial pressure of hydrogen became roughly 100 times that under an atmospheric pressure of hydrogen.

Experimental

Effect of Inplane and Axial Ligands on the Catalytic Asymmetric Hydrogenation of Benzil. Catalytic asymmetric hydrogenation of benzil was carried out in benzene under an atmospheric pressure of hydrogen according to the procedure described in previous papers,[5,6] except for using the inplane and axial ligands specified in Table 1. The reaction temperature was maintained at 30±0.2 °C.

Pressure Effect. The catalyst solution was prepared according to the procedure described in previous papers[5,6] under a nitrogen atmosphere. Methanol was evaporated in vacuo to give a wet paste which was dissolved in 25 ml of a degassed benzene solution of 2-(acetylamino)propenoate. The solution was transferred under a nitrogen atmosphere to a 100-ml autoclave. The nitrogen atmosphere was replaced with hydrogen. Asymmetric hydrogenation was performed in the initial pressure of hydrogen specified in Table 2. The time required to complete the reaction was determined by a pressure gauge. After carrying out the usual workup,[6] an oily product was obtained which was purified on silica gel (Kiesel gel-60) column chromatography using benzene/acetone (3/1) as an eluent. The eluate was concentrated under a reduced pressure to give a syrup whose optical rotation was measured. The enantioselectivities were calculated from the specific rotations. The results are shown in Table 2.

References

1) Asymmetric Reactions. XIII.
2) Y. Ohgo, S. Takeuchi, and J. Yoshimura, *Bull. Chem. Soc. Jpn.*, **44**, 583 (1971).
3) S. Takeuchi, Y. Ohgo, and J. Yoshimura, *Chem. Lett.*, **1973**, 265.
4) Y. Ohgo, Y. Natori, S. Takeuchi, and J. Yoshimura, *Chem. Lett.*, **1974**, 1327.
5) Y. Ohgo, S. Takeuchi, Y. Natori, and J. Yoshimura, *Bull. Chem. Soc. Jpn.*, **54**, 2124 (1981) and references cited therein.
6) S. Takeuchi and Y. Ohgo, *Bull. Chem. Soc.*, **54**, 2136 (1981); *ibid.*, **57**, 1920 (1984).
7) A. Uchida, Y. Ohashi, Y. Sasada, and Y. Ohgo, *Acta Crystallogr., Sect. C*, **41**, 25 (1985).
8) Y. Ohgo and S. Takeuchi, *Chem. Lett.*, **1985**, 407.
9) W. S. Knowles, M. J. Sabacky, and B. D. Vineyard, *Adv. Chem. Ser.*, **132**, 274 (1974); B. D. Vineyard, W. S. Knowles, M. J. Sabacky, G. L. Backman, and D. J. Weinkauff, *J. Am. Chem. Soc.*, **99**, 5946 (1977).
10) A. S. C. Chan, J. J. Pluth, and J. Halpern, *J. Am. Chem. Soc.*, **102**, 5952 (1980); J. Halpern, "Asymmetric Synthesis," ed by J. D. Morrison, Academic Press, Inc. (1985), Vol. 5, pp. 41—70 and references therein.
11) K. Freudenberg and F. Rhino, *Chem. Ber.*, **57B**, 1547 (1924).