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ASYMMETRIC HYDROGENATION CATALYZED BY BIS(DIMETHYLGLYOXIMATO)COBALT(II)-ACHIRAL BASE COMPLEX AND CHIRAL AMINOALCOHOL CONJUGATED SYSTEMS.
AN OXIDO-REDUCTASE MODEL WITH ENANTIOSELECTIVITY*

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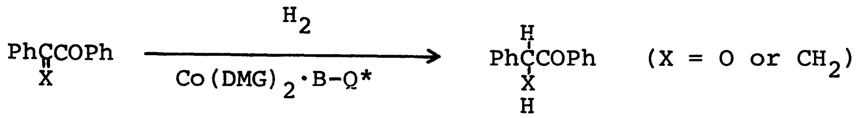
A new effective catalyst-system for asymmetric hydrogenation was found, which resembles oxido-reductases in functions. The effects of protonated chiral base in this system made possible to present the mechanism of this catalytic hydrogenation and the enantioselection. The optical yield of benzoin at -10°C reached 78%.

Catalytic asymmetric reactions with homogeneous metal complexes are attracting much interest.$^{1)}$

From the viewpoint of chemical evolution, we intend to explore more and more excellent catalyst in both the catalytic activity and the selectivity (especially enantioselectivity) approaching progressively to enzymes, and have already reported several asymmetric hydrogenations catalyzed by cyanocobalt-chiral amine complexes$^{2)}$ and bis(dimethylglyoximato)cobalt(II)-chiral amine complexes.$^{3)}$

The asymmetric induction with the latter catalyst had, first, been assumed to arise from an asymmetric field induced at the site trans to chiral base through hydrogen bonding between the oxygen atom of DMG and the hydroxyl group of aminoalcohol, from consideration of CD and NMR spectra of β-cyanoethyl(D(-)-erythro-1,2-diphenylethanolamine)bis(dimethylglyoximato)cobalt (A̲) and related compounds, and from the importance of OH group of chiral amine for asymmetric induction. However, crystal structure of compound A̲ determined by X-ray method$^{4)}$ showed the absence of such a hydrogen bonding. This fact and some results from studies on structures of effective chiral amines suggested the possibility that asymmetric induction was brought about by aminoalcohol molecules other than that coordinated to cobalt atom. Thus, we tried the asymmetric hydrogenation of benzil and α-phenylacrylophenone in the coexistence of easily coordinating achiral base and chiral aminoalcohol, and found a new catalyst system resembling enzymes.

As seen from comparison of runs 4 and 7 (Table 1), the optical yield did not decrease, but the reaction rate was extremely enhanced on addition of benzylamine (BA) to $Co(DMG)_2$-quinine system (run 4), and the optical yield at -10°C reached 78% (in mesitylene). $Co(DMG)_2 \cdot$BA-quinidine system gave the same result. Addition of triphenylphosphine as an achiral base also gave the same optical yield, but the reaction rate was considerably depressed; in most cases, reaction rates increased in the order of increasing electron donor ability of the achiral base



$$\mathrm{Ph\underset{\underset{X}{\|}}{C}COPh} \xrightarrow[\mathrm{Co(DMG)_2 \cdot B\text{-}Q^*}]{\mathrm{H_2}} \mathrm{Ph\overset{H}{\underset{\underset{H}{X}}{C}}COPh} \quad (\mathrm{X = O\ or\ CH_2})$$

Table 1. Asymmetric Hydrogenation of Benzil Catalyzed by $\mathrm{Co(DMG)_2 \cdot B\text{-}Q^*}$[a)]

Run	Base	React. temp. (°C)	B/Co[c)]	Q*/Co[d)]	Q*HCl/Co[e)]	Benzoin $[\alpha]_D^{22}$	Benzoin O.Y.[f)h)] (%)	Benzoin Conf.	v[g)] $10^{-3}\mathrm{sec}^{-1}$
1	quinidine	RT	0	2	0	-56	47	R	
2	BA[b)] quinidine	26-27	1	1	0	-57	48	R	6.0
3	BA quinidine	30	1	3	0	-60	51	R	12.0
4	quinine	30	0	1	1	+73	61.5	S	1.5
5	BA quinine	30	1	1	0	+54	45.6	S	
6	BA quinine	30	1	0	1	+70	59	S	6.5
7	BA quinine	30	1	1	1	+72.3	61	S	13.6
8	$\mathrm{Ph_3P}$ quinine	RT	1	1	1	+72.8	61.5	S	0.3
9	BA quinine	-10	1	1	1	+92	78	S	

a) Every experiment was carried out in benzene solution except for run 9 (in mesitylene); Substrate/Cobalt = 10. b) BA: benzylamine. c) B: achiral base (BA or $\mathrm{Ph_3P}$). d) Q*: chiral aminoalcohol (quinine, quinidine etc.). e) Q*HCl: hydrochloride of Q*. f) O.Y.: optical yield. g) V (initial velocity): ($\mathrm{H_2}$ moles consumed/sec)/mole of catalyst. h) In every case, chemical yield was almost quantitative.

Table 2. Effect of HCl Salt on the Asymmetric Hydrogenation of α-Phenylacrylophenone

Run	React. temp. (°C)	BA/Co[a)]	Q*/Co[b)]	Q*HCl/Co	Product $[\alpha]_D^{22}$	Product Opt. yield (%)	Product Conf.
1	RT	0	1	1	+99.4°[c)]	49	S
2	30	1	0	1	+91.4°	45	S
3	30	1	1	0	+20.2°	10	S

a) BA: benzylamine. b) Q*: quinine. c) Optical rotation of pure (S)-α-phenylpropiophenone, $[\alpha]_D$ +202° (c 3.5, chloroform).

added (V, $0.3 \times 10^{-3}\mathrm{sec}^{-1}$ for Ph_3P, $2.0 \times 10^{-3}\mathrm{sec}^{-1}$ for pyridine, and $13.6 \times 10^{-3}\mathrm{sec}^{-1}$ for BA). This suggests that the base coordinating at axial position is not chiral aminoalcohol but achiral base in these systems. Furthermore, the presence of an equilibrium between coordinated and non-coordinated states of quinidine to $CH_3Co(DMG)_2$ was shown by the fact that $|\Delta\varepsilon|$ of CD spectrum of their mixture was increased with increasing molar ratio of quinidine to Co. Addition of an equimolar amount of benzylamine to the above system erased the CD absorption. This clearly indicates that benzylamine coordinates selectively to Co in this system:

$$[\ CH_3Co(DMG)_2{\cdot}Q^* \rightleftharpoons CH_3Co(DMG)_2 + Q^*\ ] \xrightarrow{BA} CH_3Co(DMG)_2{\cdot}BA + Q^*$$

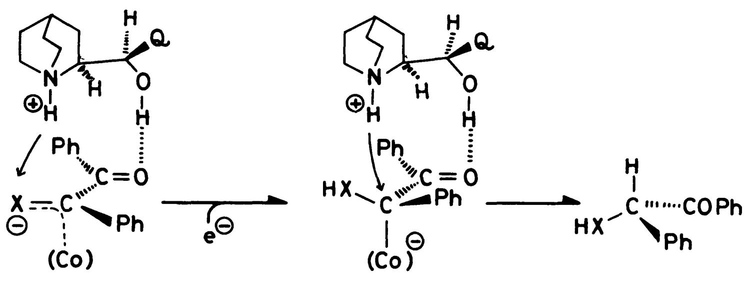
This fact is quite surprising in view of how asymmetric induction is brought about.

As seen from comparison of runs 5 and 6 (1 and 4) in Table 1, Q*HCl gave higher enantioselectivity than its free base (Q*), and addition of HCl salt of achiral amine (quinuclidine hydrochloride) caused a remarkable decrease in enantioselectivity. A similar effect of HCl salt was also observed in the hydrogenation of α-phenylacrylophenone (Table 2). These facts suggest that protonated chiral aminoalcohol plays an important role in this enantioselection, and also the proton pulled out of $HCo(DMG)_2{\cdot}B$ by amine reacts with substrate or substrate-binding complexes in a bound state and proton itself does not swim away from base in these systems. If so, addition of an achiral stronger base[5)] than chiral base (Q*) gives protonated achiral base ($t\text{-}BH^+$) in competition with Q^*H^+ and is expected to cause a decrease in optical yield.

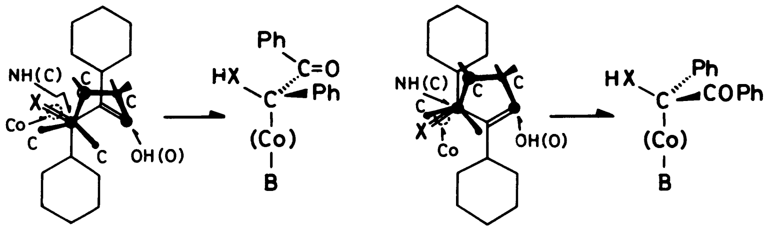
$$[\ Q^* + t\text{-}B + HCo(DMG)_2{\cdot}B \rightleftharpoons Co(DMG)_2{\cdot}B^{\ominus} + Q^*H^{\oplus} + t\text{-}BH^{\oplus}\ ]$$

As expected, addition of stronger base to the $Co(DMG)_2{\cdot}BA$-quinidine system caused a remarkable decrease in optical yield (none, 51%; tri-n-hexylamine, 37%; triethylamine, 32%; quinuclidine, 12% O.Y.). Thus, protonated chiral aminoalcohol must recognize enantiotopic face on giving its proton to the substrate or substrate-binding complexes. This, in turn, requires electron donor at some stages. The species must be $Co(I)^-$ anion released by abstraction of H^+ from $HCo(DMG)_2{\cdot}B$. Rate accelerations with increasing basicity and with addition of proton sources are in accord with the mechanism comprised of electron donor, $Co(I)^-$, and proton donors (protonated bases and $HCo(DMG)_2{\cdot}B$, although the latter seems to be a poorer proton donor). Further evidences for the mechanism have also been provided by studies on the mechanism of catalytic reductive dimerization of α-oxocarbonyl compounds.[3d,6)] Besides, on approach of Q^*H^+ to the substrate, the OH group may have a specific interaction with carbonyl group of substrate, since the OH of chiral base is extremely important in this enantioselection.[3c)]

A possible mechanism for this asymmetric hydrogenation is presented as follows, taking benzil or α-phenylacrylophenone as the substrate and quinine as the chiral base.



I II III



I'_S II_S I'_R II_R

At first stage, nucleophilic Co(I) anion and protonated quinine bite the substrate with weakly attractive interaction between oxygen of carbonyl and OH group of quinine, and also that between anionic part (X: O or CH_2) of substrate and positively charged part of Q^*H^+ to give the alkyl complex (II), and at the second stage, this undergoes cleavage of Co-C bond by the back side attack with inversion of configuration to give S-isomer. We have a preliminary result illustrating the back side attack,7) and some data supporting carbanionic cleavage of Co-C bond.6) At first stage, there are two transition states which give S and R isomers. I'_S and I'_R are the projections which are obtained by viewing I from above. I'_S leading to S isomer is well fitting and has no substantial repulsion, while I'_R will result in a serious steric repulsion. From the same situation, II_S is more favored for the approach of Q^*H^+ than II_R

The enantioselectivity of other chiral aminoalcohols previously reported can also be explained likewise.

As described above, this catalyst system resembles enzymes, oxido-reductases, whose catalytic site and specificity-determining site are generally separated; $Co(DMG)_2 \cdot B$ and chiral aminoalcohol are considered to correspond NAD (NADP) and apoenzyme, respectively.

References and Notes

* A part of this work was presented at 6th Internatl. Conference on Organometal. Chem., Amherst (U.S.A.), Abstracts 55 (August, 1973).

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4) Y. Ohashi, Y. Sasada, Y. Tashiro, Y. Ohgo, S. Takeuchi, and J. Yoshimura, Bull. Chem. Soc. Jap., 46, 2589 (1973).

5) Weaker bases such as benzylamine, pyridine and triphenylphosphine can hardly pull out proton of $HCo(DMG)_2 \cdot B$ and therefore, excess of such bases does not decrease enantioselectivity.

6) Y. Natori, Master's thesis, Tokyo Institute of Technology, 1974.

7) (+)-Methylpropionate-2-d was obtained by deuterogenation of R-α-methoxycarbonylethyl(pyridine)bis(dimethylglyoximato)cobalt whose absolute configuration was determined by X-ray method; (+)-propionic acid-2-d has S-configuration.

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