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Asymmetric Hydrogenation of *N,N'*-Dimethyl-5-alkylidene- and arylmethylenehydantoins Catalyzed by (Achiral Base)bis(dimethylglyoximato)cobalt(II)-Chiral Cocatalyst System[1)]

Seiji TAKEUCHI* and Yoshiaki OHGO
Niigata College of Pharmacy, 5-13-2 Kamishin'ei-cho, Niigata 950-21
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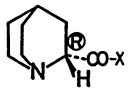
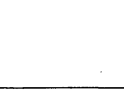
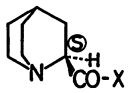
Asymmetric hydrogenation of *N,N'*-dimethyl-5-alkylidene- and arylmethylenehydantoins catalyzed by an achiral base coordinated bis(dimethylglyoximato)cobalt(II)-chiral 2-quinuclidinecarboxamide was examined. Attempts resulted in a maximum optical yield in this system (82.1% ee), strongly supporting a proposed asymmetric hydrogenation mechanism in which the chiral base acts as a proton donor, namely, a cocatalyst.

The authors have previously reported the asymmetric hydrogenation of activated ketones and olefins catalyzed by an achiral base coordinated bis(dimethylglyoximato)cobalt(II)-chiral base system (abbreviated as $Co(Hdmg)_2 \cdot B\text{-}B^*$; B and B* are achiral and chiral bases, respectively).[2)] For example, $Co(Hdmg)_2 \cdot B$-quinine catalyzes the hydrogenation of benzil to benzoin with 78% ee[3)] and $Co(Hdmg)_2 \cdot B$-(*S*)-*N*[(*R*)-1-phenylethyl]-2-quinuclidinecarboxamide catalyzes the hydrogenation of *N,N'*-dimethyl-5-benzylidenehydantoin with 79.1% ee.[4)] In the course of our study regarding asymmetric hydrogenation, we proposed an asymmetric hydrogenation mechanism in which $Co(Hdmg)_2 \cdot B$ acts as an electron donor to the substrate or intermediate and a protonated chiral base acts as a chirality-recognizing proton donor to the intermediate carbanion.[3)]

Here, we wish to describe our attempts to obtain a higher optical yield and to find supporting evidence for the proposed asymmetric hydrogenation mechanism.

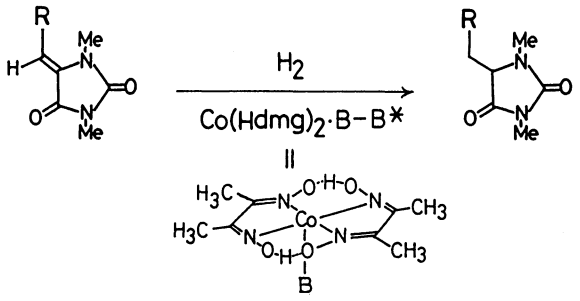
Table 1. Structures and Abbreviations of Chiral Cocatalysts

B*	X	Abbreviation
	OC_2H_5	QC-(*R*)-OEt
	$NHCH_3$	QC-(*R*)-$NHCH_3$
		QC-(*R*)*S*
		QC-(*R*)*R*
		QC-(*S*)*R*
		QC-(*S*)*R*-NCH_3
		QC-(*S*)*R*-Naph

Results and Discussion

The preparation method for chiral 2-quinuclidinecarboxamides are described in the Experimental section. Structures and their abbreviations are summarized in Table 1.

An asymmetric hydrogenation of *N,N'*-dimethyl-5-alkylidene- and arylmethylenehydantoins with $Co(Hdmg)_2 \cdot B\text{-}B^*$ was examined under various conditions (Scheme 1). The enantioselectivity was affected by the structure of B*, the structure of the substrate, the molar ratio of B* to the cobalt complex, the character of the axial base, the reaction temperature and the basicity of B*.



Scheme 1. Asymmetric hydrogenation of *N,N'*-dimethyl-5-alkylidene- and arylmethylenehydantoins with $Co(Hdmg)_2 \cdot B\text{-}B^*$.

Effect of Structure of B*. Hydrogenation of *N,N'*-dimethyl-5-benzylidenehydantoin was carried out using the chiral 2-quinuclidinecarboxamides as B*. The results are shown in Table 2.

The configuration of the predominant enantiomer of the hydrogenated product in every case is determined with that of the chiral center of the 2-quinuclidinecarboxylic acid moiety (Runs 1—7) and in the case of using the chiral secondary amides, the enantioselectivity is little affected by the structure of the amine moiety (Runs 1—5) (QC-(*S*)*R* is the most effective cocatalyst). However, the lack of N-H of amide group causes a remarkable decrease in the enantioselectivity (Runs 6 and 7). Accordingly, a structure excluding the alkyl group of the amine moiety mainly determines the enantioselectivity; also, the presence of N-H of amide group is extremely important.

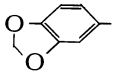
These indicate the importance of the hydrogen bond

Table 2. Effect of Structure of B* on the Asymmetric Hydrogenation of *N,N'*-Dimethyl-5-benzylidenehydantoin[a]

Run	B	B*	*N,N'*-Dimethyl-5-benzylhydantoin			
			Yield/%	$[\alpha]_D$/°	Conf.[b]	%ee[c]
1	PPh_3	QC-(*S*)*R*	93.0	−68.0	*S*	79.1
2	PPh_3	QC-(*R*)*R*	96.5	+60.7	*R*	70.6
3	$P(Bu^n)_3$	QC-(*R*)*S*	96.0	+63.2	*R*	73.5
4	$P(Bu^n)_3$	QC-(*S*)*R*-Naph	95.0	−58.0	*S*	67.7
5	$P(Bu^n)_3$	QC-(*R*)-$NHCH_3$	94.0	+56.7	*R*	65.9
6	$P(Bu^n)_3$	QC-(*S*)*R*-NCH_3	95.0	−15.0	*S*	17.4
7	$P(Bu^n)_3$	QC-(*R*)-OEt	95.0	+4.3	*R*	5.0

a) The molar ratio of substrate to cobalt was 10:1, while those of triphenylphosphine (PPh_3), tributylphosphine ($P(Bu^n)_3$), chiral cocatalysts and their hydrochlorides to cobalt were all 1:1. Solvent was benzene. b) Configuration. c) Optically pure *S* enantiomer: $[\alpha]_D^{24.0}$ −86.0° (*c* 1.018, $CHCl_3$).

Table 3. Effect of Substituent of *N,N'*-Dimethyl-5-alkylidene- and Arylmethylenehydantoins on the Asymmetric Hydrogenation[a]

Run	R	B	B*	5-Substituted *N,N'*-dimethylhydantoin				
				Yield/%	$[\alpha]_D$/°	Conf.[b]	%ee	V[c]
1	Isopropyl	$P(Bu^n)_3$	QC-(*R*)*S*	84.6	+8.2	*R*	43.8	2.5
2	1-Naphthyl	$P(Bu^n)_3$	QC-(*R*)*S*	95.0	+15.0	*R*	69.3	1.1
3	*p*-NC-C_6H_4[d]	$P(Bu^n)_3$	QC-(*R*)*S*	95.3	+39.0	*R*	74.0	2.5
4	*p*-Br-C_6H_4[e]	$P(Bu^n)_3$	QC-(*R*)*S*	96.0	+37.4	*R*	67.6	2.5
5	*p*-F_3C-C_6H_4[f]	$P(Bu^n)_3$	QC-(*R*)*S*	97.5	+34.9	*R*	69.6	2.1
6	*p*-H_3CO-C_6H_4[g]	$P(Bu^n)_3$	QC-(*R*)*S*	95.0	+54.8	*R*	72.2	2.1
7		$P(Bu^n)_3$	QC-(*R*)*S*	98.0	+48.5	*R*	66.7	2.1
8	Ph	$P(Bu^n)_3$	QC-(*R*)*S*	96.0	+63.2	*R*	73.5	2.5

a) The molar ratios of substrates to cobalt were 6—10:1, while those of $P(Bu^n)_3$, QC-(*R*)*S* and QC-(*R*)*S*·HCl to cobalt were all 1:1. Solvent was benzene. b) Configuration. c) Maximum velocity (H_2 moles consumed/s/mol of catalyst: $10^{-3}s^{-1}$). d) *p*-Cyanophenyl. e) *p*-Bromophenyl. f) *p*-Trifluoromethylphenyl. g) *p*-Methoxyphenyl.

between N-H of the chiral cocatalysts and the carbonyl group of the substrates.[4]

Effect of Substituent of Substrate. The results of the hydrogenation of *N,N'*-dimethyl-5-alkylidene- and arylmethylenehydantoins are shown in Table 3.

Enantiomeric excesses of the hydrogenated products (except for *N,N'*-dimethyl-5-benzylhydantoin) were determined by ^1H NMR spectra in the presence of a chiral lanthanoid shift reagent.

Enantioselectivity for 5-(arylmethylene)hydantoins was higher than that of 5-isobutylidenehydantoin. Among the 5-(arylmethylene)hydantoins there is little difference in the enantioselectivity. The difference between 5-(arylmethylene)- and 5-isobutylidenehydantoin can be explained by a conformation of their intermediate carbanion[4] (depicted in Fig. 1).

Conformation A is preferred to B for 5-(arylmethyl)-hydantoin carbanion because of an electrostatic repulsion between a lone pair on the asymmetric carbon atom and the π-electron on the aromatic ring. However, conformation B is rather preferred to A for 5-isobutylhydantoin carbanion because of a steric repulsion between the isobutyl group and the hydantoin ring and of a decrease in the electrostatic repulsion. One of the two enantiomers in conformation A is smoothly protonated by protonated QC-(*R*)*S* (abbreviated as QC-(*R*)*S*·H^+) to give (*R*)-5-(arylmethyl)hydantoin predominantly via a transition state having a hydrogen bond between N-H of QC-(*R*)*S*·H^+ and C=O of the carbanion of 5-(arylmethyl)hydantoin (CPK model C in Fig. 1). On the other hand, such hydrogen bonding is impossible in conformation B; this should cause a decrease in the enantioselectivity.

Effect of Molar Ratio of B* to the Cobalt Complex. Hydrogenation of *N,N'*-dimethyl-5-benzylidenehydantoin was carried out in various molar ratios of QC-(*R*)*S* (or QC-(*S*)*R*) to the cobalt complex (abbreviated as QC-(*R*)*S*/Co). The results are shown in Table 4.

The optical yield increases with increasing ratio QC-(*R*)*S*/Co and reaches a maximum value (82.1% ee) when the ratio is 7 (Run 5). This can be explained as follows.

A simplified catalytic cycle of this hydrogenation is shown in Fig. 2.[5]

The point of contact of reaction ② and cycle ④ is the enantioselectivity-determining step: protonation to the intermediate carbanion. Although the electron-

Table 4. Effect of the Molar Ratio of B* to Cobalt Complex on the Asymmetric Hydrogenation of *N,N'*-Dimethyl-5-benzylidenehydantoin[a)]

Run	B	B* (B*/Co)[b)]	*N,N'*-Dimethyl-5-benzylhydantoin				
			Yield/%	$[\alpha]_D$/°	Conf.[d)]	%ee	V[c)]
1	$P(Bu^n)_3$	QC-(*R*)*S* (1)	96.0	+63.0	*R*	73.5	2.2
2	$P(Bu^n)_3$	QC-(*R*)*S* (7)	94.0	+67.0	*R*	77.9	2.6
3	PPh_3	QC-(*S*)*R* (1)	93.0	−68.0	*S*	79.1	0.49
4	PPh_3	QC-(*R*)*S* (2)	92.5	+68.2	*R*	79.3	
5	PPh_3	QC-(*R*)*S* (7)	94.0	+70.6	*R*	82.1	0.27
6	PPh_3	QC-(*R*)*S* (14)	94.5	+70.4	*R*	81.9	0.17

a) The molar ratio of substrate to cobalt was 10:1, while those of PPh_3, $P(Bu^n)_3$, and QC-(*R*)*S*·HCl (or QC-(*R*)*S*·HCl) to cobalt were all 1:1. Solvent was benzene. b) Values in parentheses represent the molar ratio of B* to cobalt. c) Maximum velocity: 10^{-3} s^{-1}. d) Configuration.

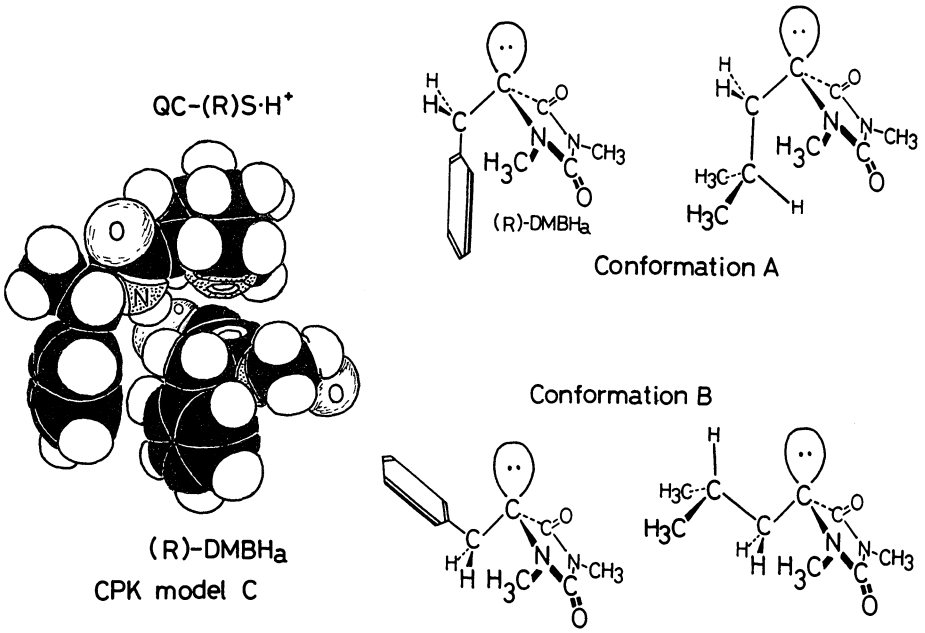


Fig. 1. Conformations of isobutyl- and benzylhydantoin (as representative of 5-(arylmethyl)hydantoin), and CPK model of the chirality-recognizing transition state (the hydrogen atom attached on the nitrogen atom of quinuclidine and the lone pair on the asymmetric carbon atom of (*R*)-*N,N'*-dimethyl-5-benzylhydantoin carbanion, (*R*)-$DMBH_a$, are not depicted).

donating cycle ③ and the proton-donating cycle ④ are independently conjugated with the reductive alkylation ① and the reduction of the alkyl complex ②, the two cycles ③ and ④ are joined by the following equilibrium. QC-(*R*)*S*·HCl in the reaction

$$H\cdot Co(Hdmg)_2\cdot B + QC\text{-}(R)S \rightleftharpoons \bar{C}o(Hdmg)_2\cdot B + QC\text{-}(R)S\cdot H^+$$

solution is included in the equilibrium as QC-(*R*)*S*·H^+. The equilibrium remains constant under a stationary state and, therefore, the optical yield is determined by the ratio of QC-(*R*)*S*·H^+ to H·Co(Hdmg)$_2$·B and other protonated achiral base (B·H^+) in the reaction system. If the ratio has reached a value near the maximum, even in QC-(*R*)*S*/Co=1, the increasing degree of the optical yield should be small and the optical yield should readily reach a maximum even though the ratio QC-(*R*)*S*/Co increases to a great extent.

Effect of σ-Donor Character of Axial Base. Hydrogenation of *N,N'*-dimethyl-5-benzylidenehydantoin was carried out using benzylamine (BA), $P(Bu^n)_3$ and PPh_3 as B. The results are shown in Table 5.

As outlined above, QC-(*R*)*S*·H^+ acts as a chirality-recognizing proton donor. On the other hand, H·Co(Hdmg)$_2$·B or B·H^+ can also act as a proton donor; hence, they competitively disturb the enantioselective proton-donation reaction by QC-(*R*)*S*·H^+ to decrease the optical yield. Since BA is a stronger base than QC-(*R*)*S*, the enantioselective protonation is strongly disturbed by BA·H^+ and decreases the optical yield (Run 1). PPh_3 and $P(Bu^n)_3$ can scarcely act as a proton acceptor since they are considerably weaker and more soft base than QC-(*R*)*S*. The lower optical yield in

Table 5. Effect of σ-Donor Character of Axial Base on the Asymmetric Hydrogenation of *N,N'*-Dimethyl-5-benzylidenehydantoin[a]

Run	B	B* (B*/Co)[b]	*N,N'*-Dimethyl-5-benzylhydantoin				
			Yield/%	$[\alpha]_D$/°	Conf.[c]	%ee	V[d]
1	BA	QC-(*S*)*R* (1)	98.0	−15.6	*S*	18.1	2.6
2	$P(Bu^n)_3$	QC-(*R*)*S* (1)	96.0	+63.0	*R*	73.5	2.5
3	PPh_3	QC-(*S*)*R* (1)	93.0	−68.0	*S*	79.1	0.49
4	PPh_3	QC-(*R*)*S* (7)	94.0	+70.6	*R*	82.1	0.27
5	—[e]	QC-(*S*)*R* (2)	93.5	−58.7	*S*	68.2	0.19
6	—	QC-(*S*)*R* (7)	94.5	−55.4	*S*	64.4	0.52
7	PPh_3 (4)[f]	QC-(*S*)*R* (7)	91.0	−69.4	*S*	80.7	0.09

a) The molar ratio of substrate to cobalt was 10:1, while those of PPh_3, $P(Bu^n)_3$, BA and QC-(*S*)*R*·HCl (or QC-(*R*)*S*·HCl) to cobalt were all 1:1 except for Run 7. Solvent was benzene. b) Values in parentheses represent the molar ratio of B* to cobalt. c) Configuration. d) Maximum velocity: $10^{-3}s^{-1}$. e) No base other than QC-(*S*)*R* was used. f) The molar ratio of PPh_3 to cobalt was 4.

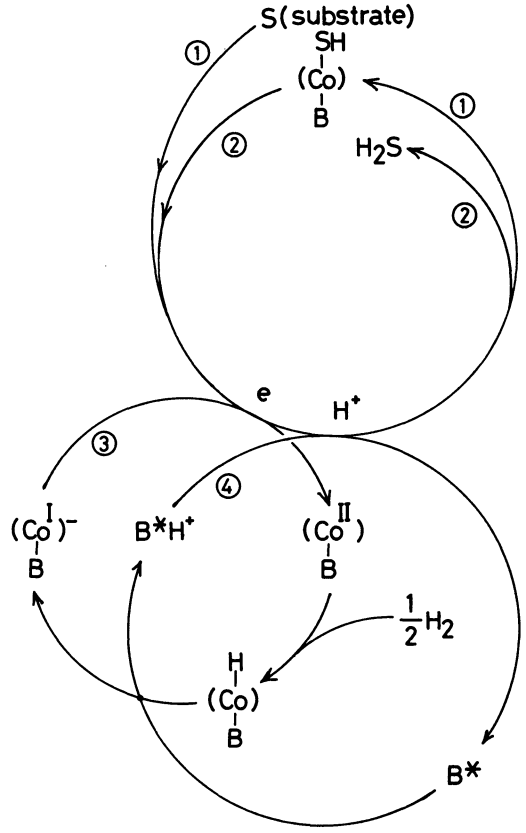
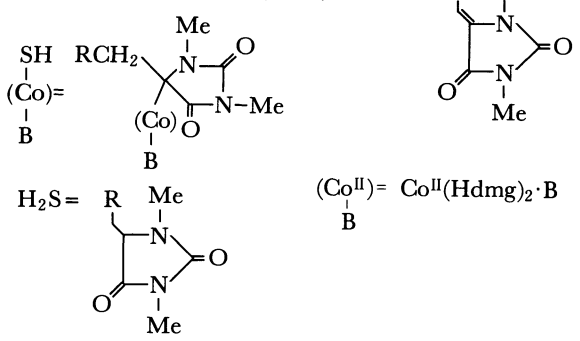


Fig. 2. Simplified catalytic cycle: S= R Me



Run 2 than that in Run 3 should be due to the stronger basicity of $P(Bu^n)_3$ than PPh_3. Needless to say, QC-(*R*)*S*·H^+ can not disturb the enantioselective protonation of itself and, hence, the low optical yield in Run 5 compared with those in Runs 2 and 3 must be due to a disturbance by H·Co(Hdmg)$_2$·QC-(*R*)*S*. A comparison of the results in Runs 3 and 4 with those in 5 and 6, respectively, clarifies the role of QC-(*R*)*S*. The optical yield increases in Run 4 but decreases in Run 6 with increasing ratio QC-(*R*)*S*/Co. The axial ligand of the cobalt complex is chiefly PPh_3 in Runs 3 and 4, whereas it is QC-(*R*)*S* in Runs 5 and 6. Consequently, it is clear that coordination of QC-(*R*)*S* to the cobalt complex decreases the optical yield.

Effect of Reaction Temperature. Hydrogenation of *N,N'*-dimethyl-5-benzylidenehydantoin was carried out at room temperature and at −10 °C in benzene and in mesitylene, respectively. The results are shown in Table 6.

The optical yield increases upon using quinine as a cocatalyst (Run 2) but decreases upon using QC-(*R*)*S* as a cocatalyst (Run 4) with decreasing reaction temperature. This should be due to the solubility of QC-(*R*)*S*·HCl in mesitylene, since the optical yield increases upon using only QC-(*R*)*S* (Run 6), but decreases upon using only QC-(*R*)*S*·HCl (Run 8) with decreasing reaction temperature. Since QC-(*R*)*S*·HCl is slightly soluble in such a nonpolar solvent as benzene and mesitylene (even at room temperature), it becomes much less soluble at −10 °C. Such a decreased solubility should result in a decreasing optical yield, since both the chiral base and its hydrochloride are required to obtain a maximum optical yield in this system.[3]

If this deduction is correct, it is possible to attain a much higher optical yield in nonpolar and aprotic solvent systems which easily dissolve QC-(*R*)*S*·HCl, even at low temperatures.

Effect of Basicity of B*. Hydrogenation of *N,N'*-dimethyl-5-benzylidenehydantoin was carried out using quinine and/or QC-(*R*)*S* as cocatalyst. The results are shown in Table 7.

(*S*)-Configuration product with 51.4%ee was obtained upon using a system mixed with quinine, QC-(*R*)*S* and their hydrochlorides (Run 3) although an opposite configuration and a higher optical yield

Table 6. Effect of Reaction Temperature on the Asymmetric Hydrogenation of *N,N'*-Dimethyl-5-benzylidenehydantoin[a]

Run	Temp[b]	Solvent	B	B*	B*·HCl	*N,N'*-Dimethyl-5-benzylhydantoin			
						Yield/%	$[\alpha]_D$/°	Conf.[c]	%ee
1	RT[d]	Benzene	$P(Bu^n)_3$	Quinine (1)	Quinine (1)[e]	91.0	−47.4	*S*	54.7
2	−10°C	Mesitylene	$P(Bu^n)_3$	Quinine (1)	Quinine (1)	90.0	−52.8	*S*	61.4
3	RT	Benzene	$P(Bu^n)_3$	QC-(*R*)*S* (1)	QC-(*R*)*S* (1)	96.0	+63.0	*R*	73.5
4	−10°C	Mesitylene	$P(Bu^n)_3$	QC-(*R*)*S* (1)	QC-(*R*)*S* (1)	97.5	+54.6	*R*	63.5
5	RT	Benzene	$P(Bu^n)_3$	QC-(*R*)*S* (1)	—[f]	94.5	+41.6	*R*	48.4
6	−10°C	Mesitylene	$P(Bu^n)_3$	QC-(*R*)*S* (2)	—	93.5	+49.0	*R*	57.0
7	RT	Benzene	$P(Bu^n)_3$	—[f]	QC-(*R*)*S* (1)	93.0	+42.8	*R*	49.8
8	−10°C	Mesitylene	$P(Bu^n)_3$	—	QC-(*R*)*S* (1)	92.0	+28.9	*R*	33.6

a) The molar ratio of substrate to cobalt was 10:1, while that of $P(Bu^n)_3$ to the cobalt was 1:1. b) Reaction temperature. c) Configuration. d) Room temperature. e) Values in the parentheses represent the molar ratio of B* or B*·HCl to cobalt. f) B*·HCl or B* were not used.

Table 7. Effect of Basicity of B* on the Asymmetric Hydrogenation of *N,N'*-Dimethyl-5-benzylidenehydantoin[a]

Run	B	B*	B*·HCl	*N,N'*-Dimethyl-5-benzylhydantoin				
				Yield/%	$[\alpha]_D$/°	Conf.[b]	%ee	V[c]
1	$P(Bu^n)_3$	Quinine (1)	Quinine (1)[d]	91.0	−47.4	*S*	54.7	1.9
2	$P(Bu^n)_3$	QC-(*R*)*S* (1)	QC-(*R*)*S* (1)	96.0	+63.2	*R*	73.5	2.2
3	$P(Bu^n)_3$	Quinine (1) + QC-(*R*)*S* (1)	Quinine (1) + QC-(*R*)*S* (1)	94.5	−44.2	*S*	51.4	2.1
4	$P(Bu^n)_3$	Quinine (1)	—[e]	93.5	−23.0	*S*	26.7	2.1
5	$P(Bu^n)_3$	QC-(*R*)*S* (1)	—	94.5	+41.6	*R*	48.4	2.5
6	$P(Bu^n)_3$	Quinine (1) + QC-(*R*)*S* (1)	— + —	95.0	−31.8	*S*	37.0	2.1

a) The molar ratio of substrate to cobalt was 10:1, while that of $P(Bu^n)_3$ to cobalt was 1:1. Solvent was benzene. b) Configuration. c) Maximum velocity: 10^{-3} s^{-1}. d) Values in the parentheses represent the molar ratio of B* or B*·HCl to cobalt. e) B*·HCl was not used.

were obtained in Run 2 compared with those in Run 1. A similar tendency was observed in the absence of the hydrochlorides, except for a higher optical yield upon using a system mixed with quinine and QC-(*R*)*S* (Run 6) than that using only quinine (Run 4). Thus, the enantioselectivity of QC-(*R*)*S* is masked and that of quinine predominates in a mixed system. Since QC-(*R*)*S* is a weaker base (namely, a weaker proton acceptor than quinine), it should hardly act as a proton acceptor in mixed systems.

This can be demonstrated by the ^{13}C NMR spectra of a mixed system in $CDCl_3$. The ^{13}C NMR spectra of quinine·HCl(I), quinine(II), QC-(*R*)*S*·HCl(III), QC-(*R*)*S*(IV) and their mixture (V and VI) are shown in Fig. 3.

The values near the peaks represent the chemical shift (ppm) of C-9 in quinine or quinine·HCl and that of carbonyl carbon in QC-(*R*)*S* or QC-(*R*)*S*·HCl. From these data the ratio of the components in the solution was estimated. For example, quinine exists almost as hydrochloride (96.9%) in a solution of QC-(*R*)*S*·HCl (3.56×10^{-5} mol) and quinine (3.545×10^{-5} mol) (V); and QC-(*R*)*S* exists completely as free base in that of QC-(*R*)*S*·HCl (1.70×10^{-5} mol), QC-(*R*)*S* (1.66×10^{-5} mol) and quinine (3.45×10^{-5} mol) (VI).[6] These results demonstrate that quinine is a much stronger proton acceptor than QC-(*R*)*S*.

Conclusion

The main problem regarding the mechanism of this asymmetric hydrogenation is what role the chiral base performs. Since the chiral base can coordinate to the cobalt complex, one may think that the chiral cobalt complex is a chirality-recognizing species itself. However, we have proposed another unique asymmetric hydrogenation mechanism (described above). Although the possibility of an enantioselective reaction by the chiral cobalt complex[7] can not be completely excluded, the results obtained above strongly support the proposed asymmetric hydrogenation mechanism. These are summarized as follows: (1) The optical yield increases with increasing ratio QC-(*R*)*S*/Co and reaches a maximum value, (2) coordination of QC-(*R*)*S* to the cobalt complex decreases the optical yield, and (3) the enantioselectivity for a stronger proton acceptor (quinine) predominates in a system mixed with quinine and QC-(*R*)*S*.

Experimental

The melting points were determined by a Yanagimoto micro-melting point apparatus and were uncorrected. The IR spectra were recorded on a JASCO A-3 spectrometer. The ^1H and ^{13}C NMR spectra were obtained on a JEOL-FX 200 spectrometer. The optical rotations were measured with a

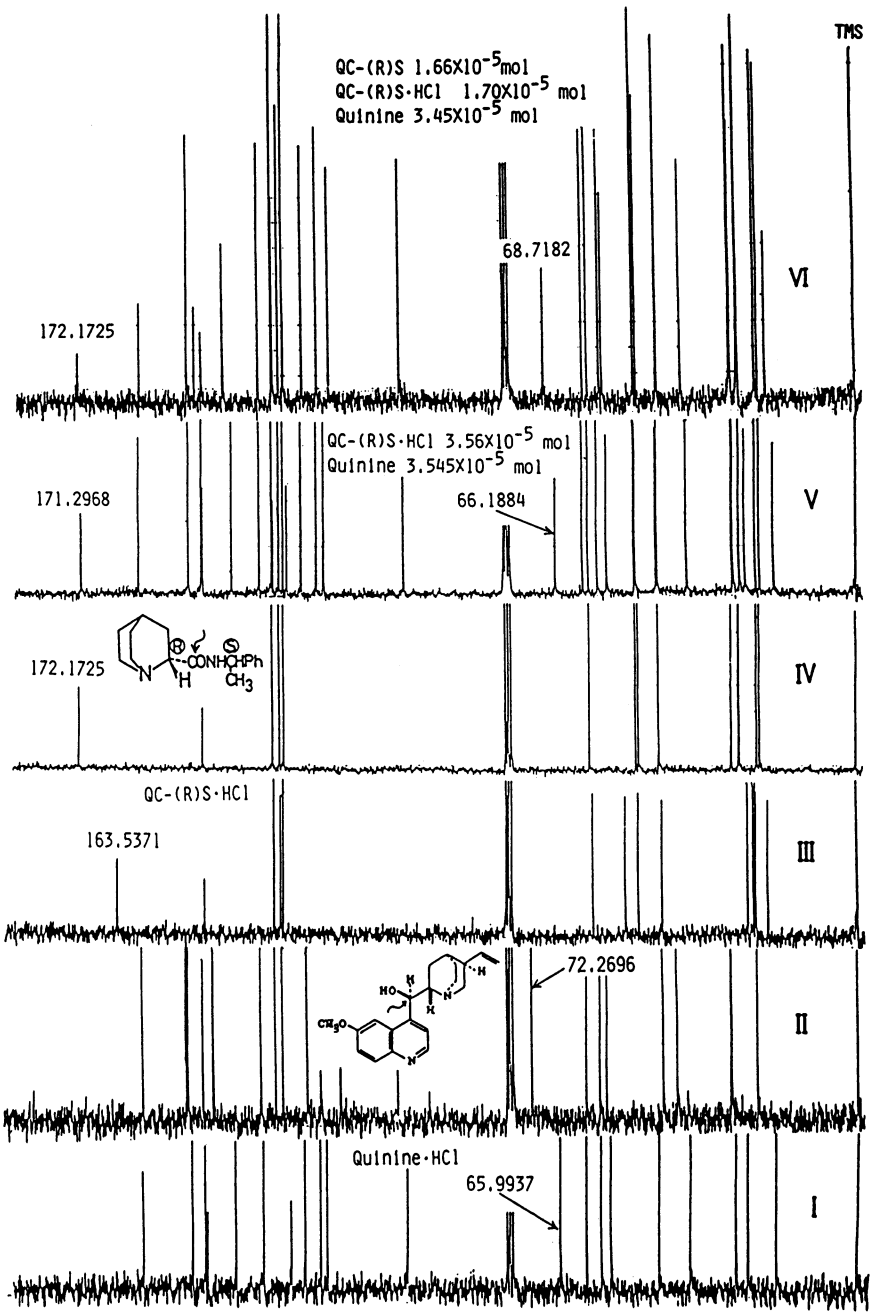


Fig. 3. ^{13}C NMR spectra in $CDCl_3$(0.6 ml).

Perkin Elmer 241 polarimeter.

Preparation of Cocatalyst. As the preparation of QC-(*R*)*S* and its enantiomer were described in a previous paper,[4] only those of QC-(*S*)*R*-NCH_3, QC-(*S*)*R*-Naph and QC-(*R*)-$NHCH_3$ are described below.

(*S*)-*N*-Methyl-*N*-[(*R*)-1-phenylethyl]-2-quinuclidinecarboxamide (QC-(*S*)*R*-NCH_3). Thionyl chloride (25 g) and (*S*)-2-quinuclidinecarboxylic acid hydrochloride (1.5 g, 7.8 mmol; $[\alpha]_D^{20.1}$ −96.8° (*c* 1.022, H_2O), lit,[8] $[\alpha]_D$ −96.2° (*c* 1, H_2O)) were refluxed for 20 min and the homogeneous solution was concentrated *in vacuo* to remove excess thionyl chloride. To the residue was added dry benzene and concentrated to dryness (repeated twice). To the crystalline residue dry ether was added and then (*R*)-*N*-methyl-1-phenylethylamine (3.6 g, 26.6 mmol) were added on ice cooling with stirring.[9] Stirring was continued for 3 d at room temperature and then to the solution was added a 50% aqueous potassium carbonate solution until the water layer became basic. The ether layer was decanted and the water layer was extracted twice with ether (200 ml×2) and the ether layers were combined and dried (Na_2SO_4). The ether solution was concentrated in order to also remove any excess (*R*)-*N*-methyl-1-phenylethylamine to give oil (1.73 g, 6.3 mmol). The oil and *p*-toluenesulfonic acid monohydrate (1.2 g, 6.3 mmol) were dissolved in methanol and concentrated to dryness. The residue was gradually solidified in ether. After standing overnight the ether was decanted and the residual solid was recrystallized from ethyl acetate to give prisms. The prisms were dissolved in water and the solution was made basic with a 50% aqueous potassium carbonate solution. The solution

was extracted twice with ether (200 ml×2) and then dried (Na_2SO_4). The concentration of the ether solution gave oil (0.79 g).

The oil (0.13 g, 0.48 mmol) was dissolved in methanol and to the solution was added 0.04 ml of concentrated hydrochloric acid. The solvent was removed and the residue was dried by evaporation with dry benzene to give crystals. These were recrystallized from ethanol-ether to give needles (0.1 g): mp>250 °C (sublimed from ca. 220 °C); $[\alpha]_D^{22.0}$ +45.0° (*c* 0.511, CH_3OH); IR (KBr) 2300—2500 (N^+H) and 1640 cm^{-1} (amide C=O); ^1H NMR ($CDCl_3$ and DMSO-d_6) δ=1.50 (2.3H,[10] d, *J*=7.34 Hz, $C\underline{H}_3$-CH), 1.60 (0.7H, d, *J*=6.60 Hz, $C\underline{H}_3$-CH), 1.76 (5H, m), 2.12 and 2.36 (2H, m), 2.63 (0.7H, s, N-$C\underline{H}_3$), 2.73 (2.3H, s, N-$C\underline{H}_3$), 3.28 (3H, m), 4.81 (1H, t, *J*=9.6 Hz, C-2 methine proton), 5.17 (0.23H, q, *J*=6.60 Hz, CH_3-$C\underline{H}$), 5.80 (0.77H, q, *J*=7.34 Hz, CH_3-$C\underline{H}$) and 7.24 (5H, m, Ph). Found: C, 66.11; H, 8.16; N, 9.09. Calcd for $C_{17}H_{25}ClN_2O$: C, 65.77; H, 8.26; N, 8.93.

(*S*)-*N*-[(*R*)-1-(1-naphthyl)ethyl]-2-quinuclidinecarboxamide (QC-(*S*)*R*-Naph). Thionyl chloride (25 g) and (*S*)-2-quinuclidinecarboxylic acid hydrochloride (2.0 g, 10.4 mmol; $[\alpha]_D^{18.2}$ −90.0° (*c* 1.026, H_2O)) were treated as described above. The crystalline residue were suspended in dry ether (200 ml) and to the solution (*R*)-1-(1-naphthyl)ethylamine (1.79 g, 10.5 mmol) and triethylamine (3.3 g, 32.6 mmol) were added on ice cooling with stirring. Stirring was continued for 6 d at room temperature and followed a similar procedure as that for QC-(*S*)*R*-NCH_3 to give syrup (2.84 g, 9.2 mmol). The syrup was reacted with *p*-toluenesulfonic acid monohydrate (1.87 g, 9.8 mmol) and treated similarly as QC-(*S*)*R*-NCH_3 to give crystals (0.92 g). These were recrystallized from petroleum ether to give large columns (0.7 g): mp 134.0—136.0 °C; $[\alpha]_D^{22.4}$ −43.4° (*c* 1.008, $CHCl_3$); IR (KBr) 3370 (NH) and 1662 cm^{-1} (amide C=O); ^1H NMR ($CDCl_3$) δ=1.28 (2H, m), 1.44 (2H, m), 1.64 (3H, d, *J*=6.85 Hz, $C\underline{H}_3$-CH), 1.84 (3H, m), 2.42 (2H, t), 2.83 (2H, m), 3.34 (1H, t, *J*=9.17 Hz, C-2 methine proton), 5.96 (1H, quintet, *J*=6.85 Hz, CH_3-$C\underline{H}$), 7.44 (5H, m, naphthyl and NH), 7.76 (2H, m, naphthyl) and 8.08 (1H, d, naphthyl). Anal. ($C_{20}H_{24}N_2O$)-C,H,O.

(*R*)-*N*-Methyl-2-quinuclidinecarboxamide (QC-(*R*)-$NHCH_3$). Ethyl (*R*)-2-quinuclidinecarboxylate (1.0 g; $[\alpha]_D^{24.6}$ +89.4° (*c* 1.013, ethanol), lit,[8] $[\alpha]_D^{22}$ −88.4° (*c* 1, abs ethanol)) was dissolved in an aqueous 35-41% methylamine solution (150 ml); the solution was allowed to react overnight. The solution was concentrated and the residue was extracted with ether (200 ml). The ether solution was dried (Na_2SO_4) and concentrated to give crystals (0.66 g). These were recrystallized from petroleum ether to give large needles (0.47 g): mp 85.0—87.0 °C; $[\alpha]_D^{24.5}$ +117.1° (*c* 1.008, $CHCl_3$); IR (KBr) 3350 (NH) and 1660 cm^{-1} (amide C=O); ^1H NMR ($CDCl_3$) δ=1.48 (4H, m), 1.87 (3H, d), 2.71 (2H, t), 2.82 (3H, d, *J*=4.9 Hz, $C\underline{H}_3$-NH), 2.89 (2H, m), 3.28 (1H, t, *J*=9.3 Hz, C-2 methine proton), 6.96 (1H, broad s, NH). Anal. ($C_9H_{16}N_2O$)C,H,O.

Asymmetric Hydrogenation of *N,N'*-Dimethyl-5-alkylidene- and Arylmethylenehydantoins with $Co(Hdmg)_2$·B-B*. The hydrogenation (under 1 atm of H_2) and the isolation of the hydrogenated product were carried out according to the procedure described in a previous paper,[4] except for the following case. When a cocatalyst with more than an equimolar amount of the cobalt complex was used, it was dissolved in a solution of the substrate to be injected into the reaction vessel[4] together with the substrate. When PPh_3 and $P(Bu^n)_3$ are not used as B, the purification by column chromatography was not carried out.[11]

Determinations of enantiomeric excesses of the hydrogenated products were similarly performed as that described in a previous paper using tris(3-trifluoroacetyl-*d*-camphorato)-europium(III).[4]

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5) As this scheme is too simplified, see reference 3) where the detailed asymmetric hydrogenation mechanism is described.

6) Since proton exchange is rapid on the NMR time scale, the observed chemical shift of C-9 or carbonyl carbon should be that in a weighted average of free base and its hydrochloride. Accordingly, the percentage of quinine·HCl in the mixed system (V) can be evaluated by the equation:

$$\frac{72.2696-66.1884}{72.2696-65.9937}\times 100 = 96.9(\%).$$

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10) The separation of signals ($C\underline{H}_3$-CH, $C\underline{H}_3$-N and CH_3-$C\underline{H}$) is due to rotational isomerization of QC-(*S*)*R*-NCH_3·HCl, which is confirmed by comparison of the ^1H NMR spectrum with that of QC-(*R,S*)*R*-NCH_3·HCl (QC-(*R,S*) represents racemate). Thus the ratio of the number of protons (2.3 : 0.7) represents that of the rotational isomers in the solution. The similar phenomenon was observed for QC-(*R*)*S*-NCH_3 and the ratio was 2.1 : 0.9 in $CDCl_3$.

11) The purification resulted in little change of optical rotation in this case. For example, 1.64 g of *N,N'*-dimethyl-5-benzylhydantoin (in Run 6 of Table 5) whose optical rotation is −55.4° was purified by the column chromatography to give 1.62 g of $[\alpha]_D$ −56.0°. This also indicates that enantiomeric enrichment does not occur in the purification procedure.