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CATALYTIC ASYMMETRIC HYDROGENATION OF BENZIL WITH BIS(DIMETHYLGLYOXIMATO)COBALT-(II)-CHIRAL AMINE COMPLEX. EFFECTS OF STRUCTURAL VARIATION OF CHIRAL AMINE AND REACTION TEMPERATURE

Yoshiaki OHGO, Seiji TAKEUCHI, Yukikazu NATORI, and Juji YOSHIMURA
Laboratory of Chemistry for Natural Products, Faculty of Science,
Tokyo Institute of Technology, Ookayama, Meguro-ku, Tokyo 152

It was found in the titled reaction that (1) the configuration of the predominant isomer is unequivocally determined by those of the vicinal carbons attaching amino and hydroxyl groups, (2) the hydroxyl group of chiral aminoalcohols plays an extremely important role in this asymmetry-transfer, and (3) the optical yield increases with lowering the reaction temperature (O.Y.: 71% at 10°C).

Metal complexes with enantioselectivity are regarded as metalloenzyme models. Studies on the metal complex catalyzed asymmetric reactions will make a basic contribution not only to the field of synthetic organic chemistry of natural products but also to rationalization of extremely high reactivity and specificity of enzymes.

The authors have reported that cyanocobalt-optically active amine systems catalyzed asymmetric hydrogenation of olefinic compounds,[1,2] and that bis(dimethylglyoximato)cobalt(II)-quinine complex catalyzed the asymmetric hydrogenation of benzil,[3] several olefinic compounds[4] including acylaminoacrylate derivatives under atmospheric pressure of hydrogen at room temperature. Several reports[5] on catalytic asymmetric hydrogenations using metal complex catalysts, chiral phosphines or chiral amides complexes of Rh(I), Ni, Pd, and Pt, have also been reported.

This paper describes the effects of temperature and structural variation of chiral amine on the enantioselectivity of the asymmetric hydrogenation of benzil catalyzed by bis(dimethylglyoximato)cobalt(II)-chiral amine.

Effects of Structural Variation of Chiral Amine.

In order to clarify effects of the structural variation of amine on the enantioselectivity of this asymmetric hydrogenation, 9 amines were used for the asymmetric hydrogenation of benzil in several solvents.

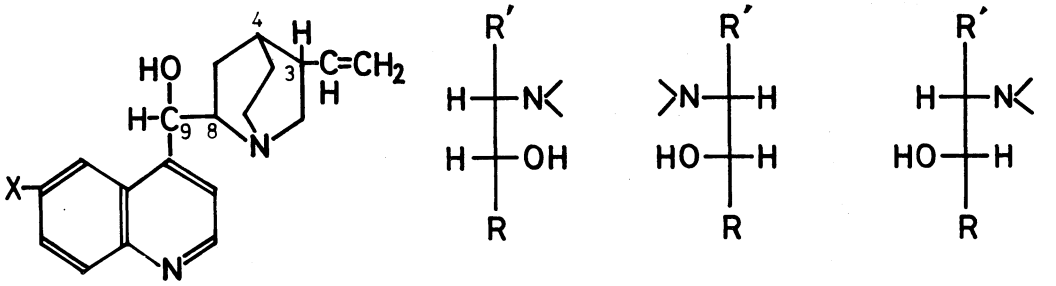
Catalytic hydrogenation was carried out under atmospheric pressure of hydrogen at room temperature. Optical yields were calculated from the specific rotation of the product and that of the optically pure benzoin.[6] The results are summarized in Table 1, and the structures of amines necessary for explanation are shown in Fig. 1. In this series of experiments only free bases were used.

Table 1. Effects of Structural Variation of Chiral Amine on the Asymmetric Hydrogenation of Benzil to Benzoin[a]

Run	Amine	Solvent (ratio)	Yield (%)	$[\alpha]_D^{21}$	Optical yield(%)	Conf.[b]
1	quinine	T/B (0.6)[c]		+40	33.8	S(+)
2	quinidine	T/B (0.64)	92	-39.4	33.2	R(-)
3	cinchonidine	T/B (0.64)	98	+39.9	33.6	S(+)
4	quinidine	B	95	-56.0	47	R(-)
5	ephedrine	M/B (0.36)	99.5	+12.6	10.6	S(+)
6	ephedrine	B	94	+19.8	16.7	S(+)
7	Ψ-ephedrine	B	96	-9.2	7.8	R(-)
8	N-Me-ephedrine	B	95	+33.2	28.0	S(+)
9	brucine	T/B (0.64)	96	-1.55	1.3	R(-)
10	O-Ac-quinine	T/B (0.6)	99	-5.35	4.5	R(-)
11	(-)-α-Me-benzylamine	T/B (0.6)	95	0.00	0	

a) In this series of experiments free bases were used (Base/Cobalt = 2; Substrate/Cobalt = 20). b) Configuration of predominant isomer. c) T= tetrahydrofuran; B = benzene; M = methanol.

Comparison of runs 1 - 6 shows that the configuration of the predominant isomer is unequivocally determined by those of the vicinal carbons attaching amino and hydroxyl groups. Brucine and O-acetylquinine gave extremely low enantioselec-



quinine (X = OCH_3) quinine quinidine Ψ-ephedrine

quinidine (X = OCH_3) cinchonidine

cinchonidine (X = H) ephedrine (R = Ph)

Fig. 1. Structures and configurations of chiral amines

tivity, and moreover, S(-)-α-methylbenzylamine could not bring about the asymmetric hydrogenation. These facts show that the hydroxyl group of the optically active amines plays an important role in the asymmetry-transfer.

It is worth noting that optically pure benzoin was easily obtained by recrystallization of the crude product.[7] Thus, this sort of phenomenon will make catalytic asymmetric syntheses more promising methods of acquiring optical isomers.

Effect of Temperature. The hydrogenation was carried out in benzene solution at 10 , 20, and 30°C by use of bis(dimethylglyoximato)cobalt(II)-equimolar amount of quinine and quinine hydrochloride. The reaction rate was followed by the amount of hydrogen absorbed.

Table 2. Optical yield with variation of temperature

React. temp. (°C)	Chem. yield(%)	$[\alpha]_D$	Opt. yield(%)
10	95	+84°	71
20	95	+79°	66.7
30	99	+73°	61.5

The reaction was carried out in benzene solution, and equimolar amounts of quinine and its hydrochloride were used as chiral substances.

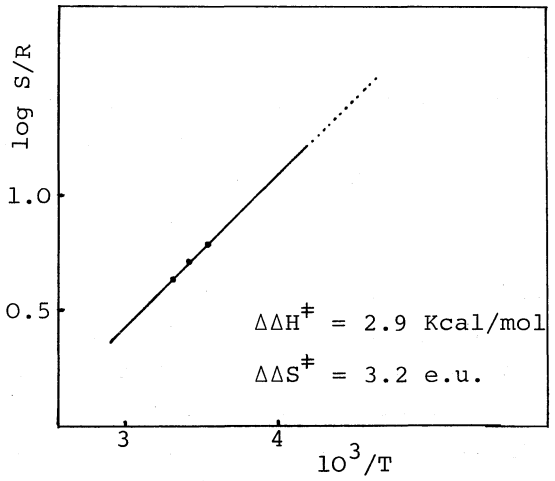


Fig. 2. Linear correlation between log S/R and 1/T

The pseudo first order rate constants were 14.0 x 10^{-3}/min, 9.08 x 10^{-3}/min, and 5.19 x 10^{-3}/min, at 30 , 20 , and 10°C respectively. From the Arrhenius plot of these rate constants activation energy and activation entropy were estimated; E_a = 8.3 Kcal/mol, $\Delta S^{\ddagger}$ = -50 e.u. The optical yields were shown in Table 2. The ratios of S-isomer to R-isomer (calculated from the corresponding optical yield) were plotted against 1/T, which gave approximately good linearity. From the slope, the difference between activation enthalpies for the formation of S-isomer and that of R-isomer ($\Delta\Delta H^{\ddagger}_{rs}$), and the corresponding entropy difference of activation ($\Delta\Delta S^{\ddagger}_{rs}$) were estimated to be 2.9 Kcal/mol and 3.2 e.u., respectively. If the linearity is assumed to hold for a rather wide range of temperature, the optical yield at a lower temperature can be predicted.

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6) Specific rotation of optically pure benzoin, $[\alpha]_D \pm 118.5^{\circ}$ (acetone, c 1); I. V. Hopper and F. J. Wilson, J. Chem. Soc., 1928, 2483.
7) When benzoin with a low optical purity was recrystallized from benzene-methanol with stirring, benzoin with much lower optical purity (0-5% optical purity) crystallized, and the optical purity of benzoin in the filtrate was raised by this method until that reached about 70% optical purity. When benzoin (thus obtained) with rather high optical purity was recrystallized from methanol slowly, optically pure benzoin was obtained as crystals.

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