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ASYMMETRIC HYDROGENATION OF α-OXOCARBONYL COMPOUNDS CATALYZED BY BIS(DIMETHYLGLYOXIMATO)COBALT(II)- CHIRAL AMINE COMPLEX*

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

Bis(dimethylglyoximato)cobalt(II)- quinine-catalyzed asymmetric hydrogenation of α-diketones afforded optically active reduction products, while that of α-oxocarboxylates and diacetyl gave not only simple reduction products but also reductive dimerization products with optical activity. In general, the optical yields of simple reduction products in cases of α-diketones (56 - 73%) were higher than those in cases of α-oxocarboxylates (12 - 20%).

In previous papers we have reported cyanocobalt-chiral amine system-catalyzed asymmetric hydrogenation of olefinic compounds,$^{1,2)}$ and bis(dimethylglyoximato)-cobalt(II)- chiral amine complex-catalyzed asymmetric hydrogenation of benzil$^{3,4)}$ and olefinic compounds.$^{5)}$

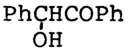
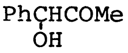
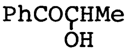
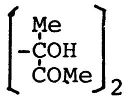
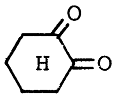
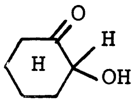
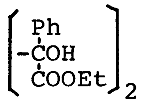
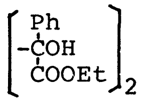
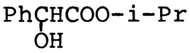
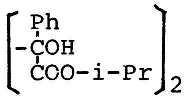
We now wish to report catalytic asymmetric hydrogenation of several α-diketones and α-oxocarboxylic acid esters. Several catalytic asymmetric hydrogenations of ketones using chiral metal complexes have also been reported.$^{6)}$

Catalytic hydrogenation was carried out in benzene solution under atmospheric pressure of hydrogen. The products from methyl phenyl diketone (1), diacetyl (2) and isopropyl phenylglyoxylate (5) were purified by silica gel column chromatography, and those from ethyl phenylglyoxylate (4) were purified by preparative thin layer chromatography. The structures of these products were confirmed by ir, nmr, and/or mass spectra. Optical yields were calculated from the specific rotations of the products and the corresponding optically pure isomers.

As shown in Table 1, the carbonyl group adjacent to the phenyl group of methyl phenyl diketone was preferentially reduced to give S(+)-α-hydroxy-α-phenylacetone in 56% optical yield. This compound was shown to racemize easily; Fig. 1 shows linear correlation between log $[\alpha]_D$ and reaction time (t). The true asymmetric yield (about 67%) was obtained by the extrapolation of the linear log $[\alpha]_D$ vs. Reaction time to t = 0.

Hydrogenation of diacetyl (2) gave not only the simple reduction products, R(-)-acetoin of 2.5% optical purity, but also reductive dimerization products, in 55% yield, which were consisted of erythro isomer (78%) and threo isomer (22%). The ratio was determined from the intensity of nmr signals of C-CH_3 [δ 1.25 (erythro) and δ 1.30 (threo)] and CH_3CO [δ 2.36 (erythro) and δ 2.23 (threo)].$^{7)}$ The low optical yield of acetoin may be attributed to racemization during the reac-

Table 1. Asymmetric Hydrogenation of α-Ketocarbonyl Compounds Catalyzed by $Co(DMG)_2$-quinine[g]

Substrate	S/Co	React. temp. (°C)	Products				
			Structure	Yield,%	$[\alpha]_D$	Opt. yield,%	Conf.
PhCOCOPh	10	-10[f]	 $PhCH(OH)COPh$	95	+86°	73	S
PhCOCOMe (1)	10	RT	 $PhCH(OH)COMe$	87-88	+88.8°[a]	56	S
			 $PhCOCH(OH)Me$	7-8			
MeCOCOMe (2)	10	30	 $MeCH(OH)COMe$		-2.0°[b]	2.5	R
			 $\left[-\overset{\text{Me}}{\underset{\text{COMe}}{\text{C}}}\text{OH}\right]_2$ erythro	42.9			
			threo	12.1	-33°[c]		
 (3)	10	RT		54	-2.44°		
PhCOCOOEt (4)	20	30	 $PhCH(OH)COOEt$	32	+28.2°[d]	13.7	S
			 $\left[-\overset{\text{Ph}}{\underset{\text{COOEt}}{\text{C}}}\text{OH}\right]_2$ erythro	13			
			threo	41	+8.2°		
PhCOCOOEt (4)	10	15	 $PhCH(OH)COOEt$	71-73	+40°	19.5	S
			 $\left[-\overset{\text{Ph}}{\underset{\text{COOEt}}{\text{C}}}\text{OH}\right]_2$	20-23			
PhCOCOO-i-Pr (5)	10	15	 $PhCH(OH)COO\text{-}i\text{-}Pr$	62	+18°[e]	11.5	S
			 $\left[-\overset{\text{Ph}}{\underset{\text{COO-i-Pr}}{\text{C}}}\text{OH}\right]_2$	24			

a) Specific rotation of optically pure R(-)-α-hydroxy-α-phenylacetone, $[\alpha]_D^{20}$ -158.3° (c 2.5, ethanol).[8] b) Specific rotation of pure R(-)-acetoin, $[\alpha]_D$ -82° (c 0.844, water).[9] c) This value was based upon the concentration of threo derivative calculated from the ratio of threo to erythro. d) Specific rotation of pure ethyl S(+)-mandelate, $[\alpha]_D^{20}$ +205.1° (c 0.7, carbon disulfide).[10] e) Specific rotation of mandelic acid derived by hydrolysis of the product (isopropyl mandelate). f) In toluene. g) In these experiments equimolar amounts of quinine (Q*) and its HCl salt (Q*HCl) were used (Q*/Co = Q*HCl/Co = 1).

tion and purification procedure. Reduction of 1,2-cyclohexanedione gave 2-hydroxycyclohexanone with $[\alpha]_D$ -2.44° in 54% yield. The reaction with phenylglyoxylic acid esters also gave not only simple reduction product, mandelic acid esters, but also reductive dimerization products, erythro- and (+)-threo-diphenyltartaric acid esters.

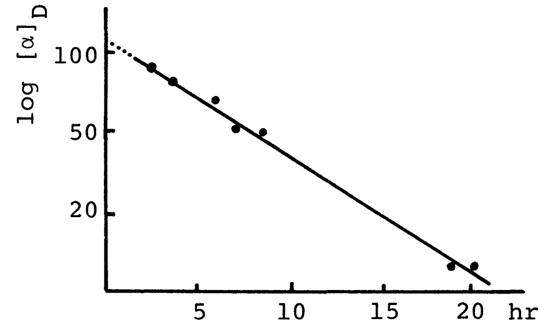
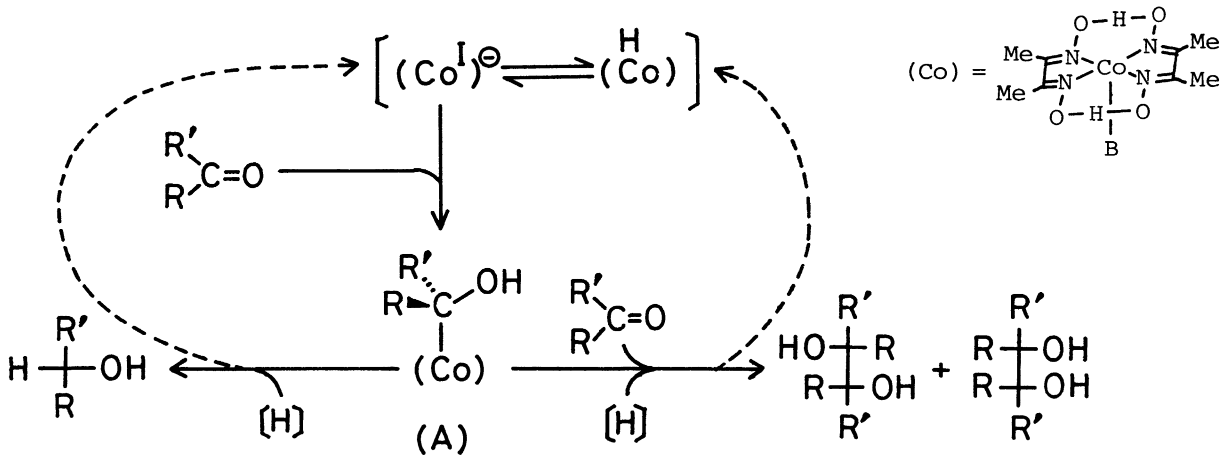


Fig. 1. Linear correlation between log $[\alpha]_D$ and reaction time.

The formation of reductive dimerization products must proceed through an intermediate with Co-C bond which may be formed by the reaction of substrate with the nucleophilic bis(dimethylglyoximato)-cobalt(I) anion. The fact that the dimers have their optical activities seems to suggest that the intermediate alkyl complexes may react with another substrate molecule prior to cleavage of Co-C bond to give dimers. The intermediates can also afford the simple reduction products by reductive cleavage. An alternative mechanism (for simple reduction), in which hydrido complex reacts with the substrate to give an intermediate with O-Co bond followed by reductive cleavage, would be improbable, since increase in alkalinity[11)] does not decrease the ratio of monomer to dimer in the case of the reaction in aprotic solvent.[12)] Thus, simple reduction and reductive dimerization are considered to proceed by competitive one-sided attack of hydrogen and another substrate molecule, respectively, to the alkyl complex (A) with the same chirality, if so, configurations of (-)-threo-3,4-dimethyl-3,4-dihydroxyhexane-2,5-dione and diethyl (+)-threo-diphenyltartrate should be (S:S) and (R:R), respectively. Studies on the assignment of these configurations are in progress.



Generally, the optical yields of simple reduction products in cases of α-diketones (56 - 73%) were higher than those in cases of α-oxocarboxylates (12 - 20%), similarly as observed in the hydrogenation of olefinic compounds.5)

It is also worth noting that asymmetric induction occurred in the catalytic reductive dimerization. To our knowledge, this is the first example of catalytic asymmetric dimerization of ketones.

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$$\mathrm{HCo(DMG)_2B} \underset{\text{neutral}}{\overset{\text{alkaline}}{\rightleftharpoons}} \mathrm{Co(DMG)_2B^{\ominus}}$$

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