CHEMISTRY LETTERS, pp. 1331-1334, 1990. © 1990 The Chemical Society of Japan

Photocatalytic Asymmetric Reduction of 3-Methyl-2-oxobutanoic Acid with Chiral Rh(I) Complexes and Powdery Semiconductors

Hanhein WANG, Tadayoshi SAKATA,*†,††† Masashi AZUMA,†,†††† Tetsuo OHTA,†,††††† and Hidemasa TAKAYA††
Institute of Photographic Chemistry, Academia Sinica, Beijing, China
† Institute for Molecular Science, Myodaiji, Okazaki 444
†† Department of Industrial Chemistry, Faculty of Engineering, Kyoto University, Kyoto 606

Photocatalytic asymmetric reduction of 3-methyl-2-oxobutanoic acid giving 2-hydroxy-3-methylbutanoic acid has been carried out in up to 60% ee in aqueous methanol with chiral BINAP--Rh(I) complexes and semiconductor photocatalysts, TiO_2 or CdS.

Asymmetric hydrogenation of unsaturated organic compounds with a chiral ligand--metal complex as catalyst is of great interest in recent years and a remarkable progress has been made in this field.1) We have found that BINAP--Rh(I) and BINAP--Ru(II) complexes [BINAP = 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl] are highly efficient catalysts for enantioselective hydrogenation of various olefinic and ketonic substrates.2) Asymmetric hydrogenation investigated so far, however, are mostly carried out in the dark using gaseous hydrogen, or by transfer hydrogenation from alcohols. Photocatalytic asymmetric reduction using semiconductor photocatalysts and protic solvents as hydrogen sources has been another subject of interest, though only a few examples have been reported previously.3,4) Cuendet and Gratzel5) reported catalytic reduction of ketocarboxylic acids with TiO_2 as photocatalyst, which is related with the photocatalytic amino acid synthesis.3,6) Here, we report a novel photocatalytic asymmetric

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††† Present address: Department of Electronic Chemistry, Tokyo Institute of Technology at Nagatsuta, Midori-ku, Yokohama 227.

†††† Present address: Department of Applied Chemistry, Osaka Institute of Technology, Omiya, Asahi-ku, Osaka 535.

††††† Present address: Department of Industrial Chemistry, Faculty of Engineering, Kyoto University, Kyoto 606.

reduction of 3-methyl-2-oxobutanoic acid (**1**) to 2-hydroxy-3-methylbutanoic acid (**2**) using a binary system consisting of optically active [Rh((R)- or (S)-binap)(cod)]ClO_4 [(R)- or (S)-(**3**)] (cod = cycloocta-1,5-diene) and semiconductors.

Powdery semiconductors such as TiO_2 (Furuuchi Chem. Co., size, 300M), platinized TiO_2 (Pt/TiO_2) (prepared by photochemical deposition of Pt on TiO_2 surface), CdS (Furuuchi Chem. Co., treated at 600 °C in Ar), and platinized CdS (Pt/CdS) (prepared by heating a mixture of CdS and 5% Pt black at 600 °C) were used as photocatalysts. The binary catalyst was prepared by addition of the powdery semiconductor to a solution of (R)- or (S)-(**3**) in methylene chloride followed by evaporation of the solvent under reduced pressure. A mixture of (**1**) and the catalyst in aqueous methanol was irradiated with a 500W Xenon lamp in an anaerobic condition. When CdS was used, triethanolamine (TEOA) was added as a sacrificial agent. The enantiomeric excess (% ee) of the product (**2**) was determined based on the analysis of the reaction mixture by liquid chromatography on a chiral column (Daiseru Kogyo Co., Chiralpak WH). Some of the representative results are summarized in Table 1.

Table 1. Asymmetric reduction of 3-methyl-2-oxobutanoic acid (**1**) catalyzed by semiconductor photocatalysts and BINAP--Rh(I) complexes

Run	Photocat.	Cat.	Chiral product	Yield μmol	% ee a)
1	Pt/TiO_2 b,c)	(R)-3	(S)-2	32	56
2	Pt/TiO_2 b,c)	(S)-3	(R)-2	75	60
3	TiO_2 c)	(R)-3	(S)-2	55	34
4	TiO_2 c)	(S)-3	(R)-2	32	44
5	Pt/CdS d,e)	(R)-3	(S)-2	17	28
6	Pt/CdS d,e)	(S)-3	(R)-2	29	34
7	CdS e)	(R)-3	(S)-2	12	10
8	CdS e)	(S)-3	(R)-2	8	26

a) % ee = 100 x (moles of one enantiomer - moles of other enantiomer)/(moles of both enantiomers). b) TiO_2: rutile, Pt:TiO_2 = 3:100 (mol%). c) A mixture of 3-methyl-2-oxobutanoic acid (**1**) (400 mg, 3.39 mmol) and the catalyst [the photocatalyst (150 mg) and (R)- or (S)-(**3**) (30 mg)] in 80% aqueous methanol (40 ml) was irradiated at room temperature for 15 h. d) CdS: obtained from Furuuchi Chem. Co. and treated at 600 °C; Pt:CdS = 5:100 (wt%). e) A mixture of (**1**) (400 mg, 3.39 mmol), triethanolamine (1 ml), and the catalyst [the photocatalyst (150 mg) and (R)- or (S)-(**3**) (25 mg)] in 80% aqueous methanol (40 ml) was irradiated at room temperature for 15 h.

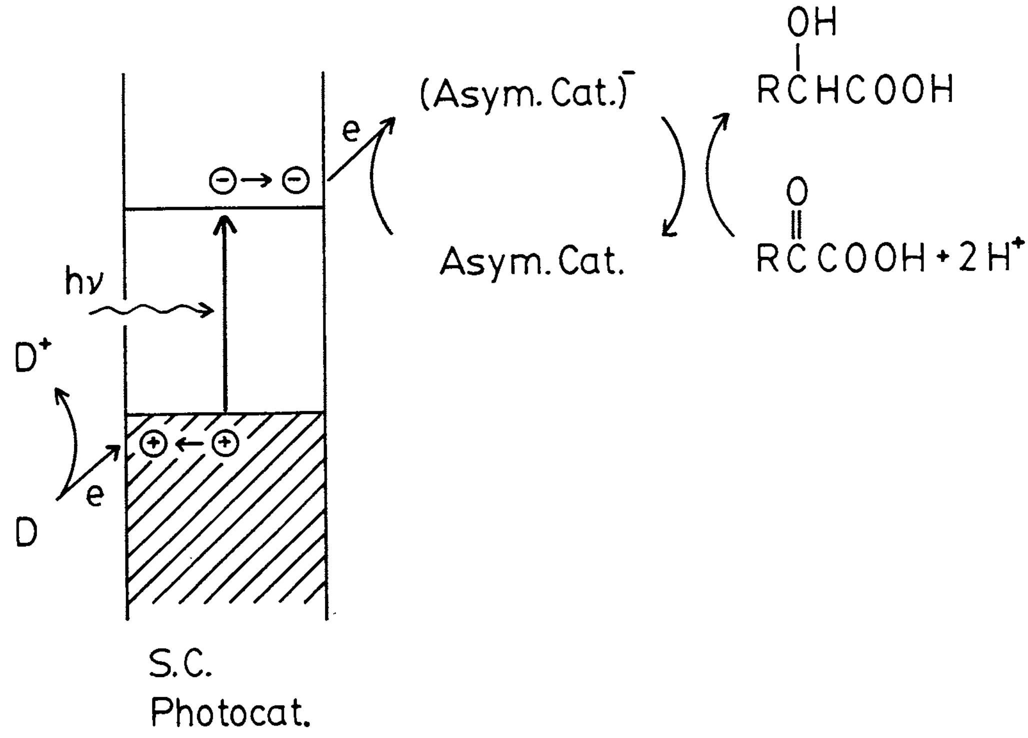

Fig. 1. Schematic illustration of asymmetric photoreduction of α-ketocarboxylic acid with a semiconductor and BINAP--Rh(I) complex under illumination. D in this figure represents a sacrificial agent.

Control experiments show that, in the absence of the chiral complex (**3**), racemic (**2**) is formed. Enantiomeric excess of up to 60% has been obtained (run 2). These results show that the catalytic system of BINAP--Rh(I) complex and certain semiconductor photocatalyst can cause asymmetric induction in the hydrogenation of α-ketocarboxylic acid.

At this stage, one can only speculate the mechanism leading to the optically active (**2**). The first event of the process involves a charge separation on the surface of the photocatalyst upon irradiation (Fig. 1). The excited electrons in the conduction band are transferred to the chiral Rh(I) complex, which in turn reduces the ketocarboxylic acid (**1**), where asymmetric induction might occur to give the product (**2**). Direct electron transfer from the semiconductor photocatalyst to the ketocarboxylic acid may compete with the above process to give racemic product.

As Seen in Table 1, efficiency of this photocatalytic reaction is low. One of the reasons of this low efficiency might be due to degradation of BINAP assymmetric catalyst caused by the photocatalytic oxidation.

As seen in Table 1, loading of Pt on the semiconductor photocatalyst does not increase the yield beyond expectation. This might be explained by the difference in the kind of reaction. Hydrogen evolution is sensitive to the presence of Pt catalyst. Consequently, Pt loading increases the rate of hydrogen evolution, i.e. reduction of water, but not the reduction rate of carboxy group of keto acids.

Although the efficiency of the asymmetric reduction is still very low, one of the new aspects of the present reaction is that asymmetric hydrogenation of α-ketocarboxylic acid has been attained without using gaseous hydrogen, but photocatalytic reaction drives the hydrogenation through electron transfer process via chiral transition metal complex. Further investigation is required for elucidation of the mechanism and improvement of both chemoselectivity and efficiency of asymmetric induction.

We thank Drs. K. Hashimoto and K. Mashima of Institute for Molecular Science for valuable discussions. Financial support from Kyowa Hakko Kogyo Co., Ltd. is also gratefully acknowledged.

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(Received April 12, 1990)