HYDROGENATION AND HYDROSILYLATION OF QUINOXALINE BY HOMOGENEOUS RHODIUM CATALYSTS

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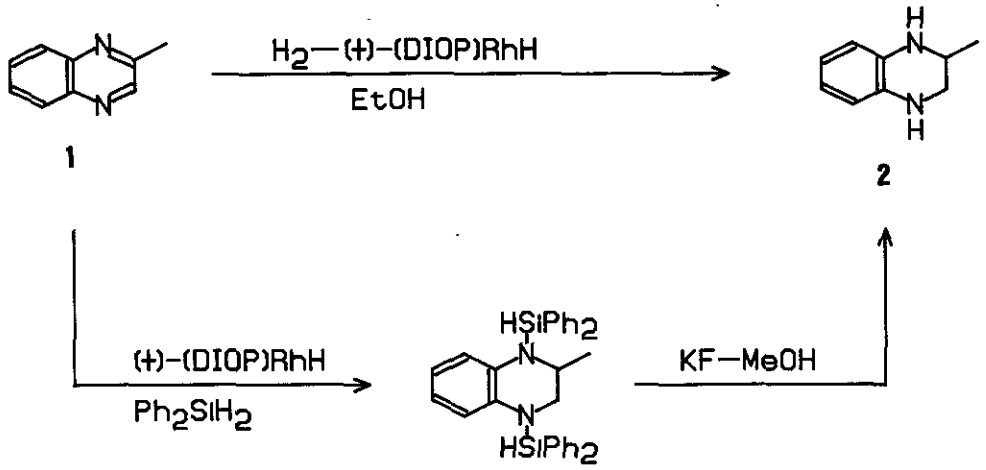
Abstract——Hydrogenation of quinoxalines by a homogeneous rhodium catalyst gives tetrahydroquinoxalines. The catalytic process is applicable for hydrosilylation of quinoxalines. 2-Methylquinoxaline is asymmetrically hydrosilylated by a chiral catalyst.

Catalytic homogeneous hydrogenation has been used as an important procedure in organic synthesis. It is the greatest merit that the catalyst can be modified for asymmetric synthesis. There have been reported various examples of asymmetric hydrogenation of olefins, dehydroamino acids, and carbonyl compounds and, in some cases, a perfect enantioselectivity has been achieved.[1] On the contrary, a few examples have been reported on the application for imines and nitrogen heterocyclic compounds.[2] In this paper, we report homogeneous hydrogenation and hydrosilylation of quinoxalines with an easily available rhodium complex and its application for asymmetric reduction.

Hydrogenation of 2-methylquinoxaline [1] with a hydridorhodium catalyst containing 1,4-bis(diphenylphosphino)butane (DPPB) ligand [(DPPB)RhH] proceeded in ethanol under H_2 (7-10 kg/cm^2) at 25 °C to give 2-methyltetrahydroquinoxaline [2]. Triphenylphosphine, 1,2-bis(diphenylphosphino)ethane, and 1,3-bis(diphenylphosphino)propane were ineffective as the ligand, and the best ligand was (+)-2,3-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane [(+)-DIOP].[3] The hydrogenation was applicable for quinoxaline and 2-propylquinoxaline.

The catalyst [(+)-(DIOP)RhH] was also effective for hydrosilylation of these quinoxalines by diphenylsilane and were obtained *N*,*N*′-bis(diphenylsilyl)tetrahydroquinoxalines which were easily desilylated to tetrahydroquinoxalines by



methanolic potassium fluoride. 2-Methyltetrahydroquinoxaline obtained via hydrosilylation by (+)-(DIOP)RhH catalyst was converted to a diastereomeric mixture of diamides of (+)-α-methoxy-α-trifluoromethylphenylacetic acid [(+)-MTPA][4] to determine the enantioselectivity by HPLC.[5] (S)-2-Methyltetrahydroquinoxaline was formed predominantly (19 % ee) and the selectivity was improved to 36 % ee by using monosodium amide of (R)-2,2′-diamino-1,1′-binaphthyl[6] as the ligand. 2,3-Dimethylquinoxaline was predominantly reduced to trans-2,3-dimethyltetrahydroquinoxaline (63:37 selectivity) and this result is opposite to the cis-selective $LiAlH_4$ reduction[7] and heterogeneous hydrogenation over PtO_2 (cis/trans = 95:5).[8] Results of hydrogenation and hydrosilylation are summarized in Table I.

Because both the substrate and product could strongly coordinate toward the transition metal by nitrogen atom, the catalyst seemed to be inactivated by substitution of the effective ligand and coordinative saturation except the strongly coordinative bidentate ligands which form a 7-membered ring chelate.[9] Thence, the anionic ligand which bonds more tightly to the metal atom than neutral ligands gave better enantioselectivity. Also, the better enantioselectivity on hydrosilylation can be attributed to the high affinity of silicon atom toward nitrogen atom of the heterocycles, same as those observed on the homogeneous reduction of carbonyl compounds. [10]

EXPERIMENTAL

Hydrogenation——To a mixture of tetracarbonyldi-μ-chlorodirhodium(I) (8 mg, 0.02 mmol) and (+)-DIOP (20 mg, 0.04 mmol) in ethanol (0.2 ml) was added KBH_4 (3 mg,

Table I. Hydrogenation and Hydrosilylation of Quinoxalines.[a]

substrate	% yield of the product[b]	
	hydrogenation	hydrosilylation[c]
quinoxaline	81[d]	65[d]
2-methylquinoxaline	52[e]	35[e]
2-methylquinoxaline	84 (2 % ee)	74 (19 % ee, S)
2-methylquinoxaline	72 (3 % ee)[f]	66 (36 % ee, R)[f]
2-propylquinoxaline	55	62
2-phenylquinoxaline	<2[g]	5
2,3-dimethylquinoxaline	<2[g]	18 (trans/cis = 63:37)

[a]Unless otherwise stated reaction proceeded by 2-3 mol % of (+)-(DIOP)RhH in ethanol under H_2 (7 kg/cm^2, hydrogenation) or in diphenylsilane (hydrosilylation) at 25 °C for 36-72 h. [b]Yields of tetrahydroquinoxalines. [c]Isolated yield. [d]Determined by GLC. [e]2 mol % of (DPPB)RhH was employed. [f]Mono sodium amide of (R)-2,2'-diamino-1,1'-binaphthyl was used as the ligand. [g]The product was detected by TLC analysis.

0.06 mmol) at 25 °C. After 30-min stirring, the gas evolution ceased and a dark brown solution of the catalyst [(+)-(DIOP)RhH] was obtained. To this was added **1** (144 mg, 1.0 mmol) and the mixture was placed in a stainless pressure bottle. This was stirred under hydrogen (7 kg/cm^2) at 25 °C for 18 h, and then concentrated. Pure **2** (125 mg, 84%) was obtained as colorless crystals (mp 70-72 °C) by a column chromatography on silica gel eluting with 5% EtOAc in CH_2Cl_2.

Hydrosilylation——After removal of the solvent, the (+)-(DIOP)RhH catalyst (0.04 mmol) was dissolved in diphenylsilane (0.8 ml) and to this was added **1** (144 mg, 1.0 mmol). The mixture was stirred for 48 h at 25 °C and the dark brown solution was added in a suspension of KF[11] (300 mg) in methanol (5 ml) and this was stirred for 2 h. The mixture was dried and the residue was extracted three times with ether (2 ml). The combined extracts were concentrated and purified by a silica-gel column. Pure **2** (109 mg, 74%) was obtained.

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(5) HPLC conditions: column, Develosil ODS 5 (4.5 i.d. x 250 mm); eluant, 55% CH_3CN in H_2O. Retention volumes: R, 33.2 ml; S, 35.3 ml. ^1H NMR ($CDCl_3$) of $(MTPA)_2$-(±)-2: δ 8.1-6.4 (m, aromatic H), 3.81 (s, CH_3O), 3.76 (s, CH_3O), 3.0-2.4 (m, CHN), 0.83 (d, CH_3), 0.64 (d, CH_3). Authentic (S)-2: S. Matsuura, T. Sugimoto, H. Hasegawa, S. Imaizumi, and A. Ichiyama, J. Biochem., 1980, **87**, 951.

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