PB149 Synthesis of Chiral Ruthenium Complexes Bearing Primary Amines and Their Catalytic Activities

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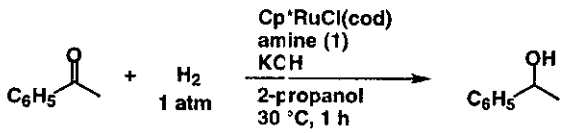
Abstract: Cp*Ru complexes (Cp* = η^5-C_5Me_5) with chelate ligands bearing NH moiety effect hydrogenation of ketones effectively under mild condition. Among the ligands tested, *N,N*-dialkylaminoethylenediamine exhibited a significant acceleration effect on the reaction. Asymmetric hydrogenation of prochiral ketones have been investigated by introducing stereogenic centers into *N,N*-dialkylaminoethylenediamine skeleton. The mechanism of the asymmetric hydrogenation has been studied on the basis of the catalyst performance and the structure of isolable Cp*RuCl(chiral diamine) complexes.

Since it was suggested that an NH moiety in the ligand coordinated to metal center participates in formation of a cyclic transition state through hydrogen bonding to a ketone substrate in the Ru(II) catalyzed transfer hydrogenation of ketones,[1] much attention has been given to the design of transition metal catalyst bearing an NH moiety. Although such "NH effect" has been successfully applied to asymmetric transfer hydrogenation using 2-propanol,[2] there have been no hydrogenation catalyst system which may involve the "NH effect" except Ru(II)–phosphine–1,2-diamine combined system.[3] We disclose herein a new type of hydrogenation catalyst system based on Cp*Ru complexes, which shows a significant "NH effect".

First, we have examined the acceleration effect of several amines (**1**) on hydrogenation of acetophenone in 2-propanol in the presence of catalytic amount of Cp*RuCl(cod) and KOH. The reaction was carried out in 2-propanol containing acetophenone, Cp*RuCl(cod), a primary amine, and KOH (acetophenone:Ru:amine:KOH = 100:1:1:1) under atmospheric pressure of H_2 at 30 °C for 1 h (Scheme 1).

Scheme 1



acetophenone:Ru:1:KOH = 100:1:1:1

Cp*RuCl(cod) has no catalytic activity even with KOH (<1% conv). The presence of etherea oxygen (**1a**) or phosphine (**1b**) functionality in the ligand molecule resulted in a slight increase in the reaction rate, while the reaction was greatly accelerated when diamines **1d–1f** were used as ligands, as shown in Figure 1. *N,N*-dimethylaminoethylenediamine (**1f**) provides a remarkable acceleration effect among them.

The hydrogen pressure influences strongly the reaction rate. Table 1 shows the hydrogen pressure dependence of the initial rate of the hydrogenation using Cp*RuCl(cod)–**1f**–KOH catalyst system. In the absence of H_2, alcoholic product was hardly obtainable (entry 1), indicating that this reductive transformation is a net hydrogenation. The TOF reached 1170 when the reaction was performed under 20 atm of H_2 (entry 4).

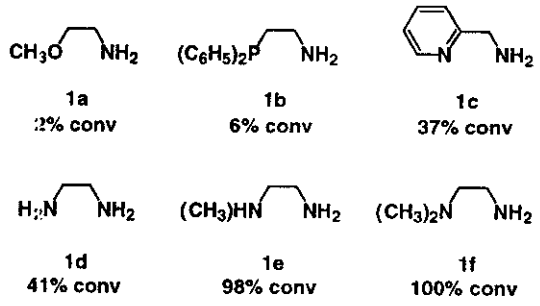


Figure 1. Effect of ligand structure on the hydrogenation.

Table 1. Effect of the Pressure of Hydrogen on Cp*Ru Catalyzed Reductive Transformation of Acetophenone.

entry	H_2 atm	time h	conv %	TOF h^{-1}
1	0	1	0	0
2	1	1	5	50
3	10	0.5	26	520
4	20	0.5	58	1170

Conditions: cat = Cp*RuCl(cod) + **1f** + KOH, acetophenone:Ru:**1f**:KOH = 1000:1:1:1, 30 °C, 2-propanol, TOF = product mol/cat mol·h.

Encouraged by the marked acceleration with **1f**, we then tried the asymmetric hydrogenation of acetophenone using chiral diamine ligands derived from L-proline (Figure 2). If the diamines possess the NH moiety on the each nitrogen like **2a**, the corresponding phenethyl alcohol with low enantiomeric purity (3% *ee* (*R*)) was obtained. However, moderate to good *ee* values were observed by fixing NH moiety onto either of the two nitrogen atoms (**2b**: 13% *ee* (*S*), **2c**: 40% *ee* (*S*), **2d**: 72% *ee* (*R*), **2e**: 13% *ee* (*R*)). Noteworthy is that the sense of enantioselectivity was reversed depending on the position of the

NH moiety. Thus, *Re* face of acetophenone was preferentially attacked by hydride to yield (*S*)-phenethyl alcohol when the H-bearing nitrogen is located at α-position of the stereogenic center, whereas *Si* face was favored when its position is β. This may lead to the low enantioselectivity obtained in the case of **2a**, since it can be assumed that the opposite selectivity caused by two NH groups in the different position was compensated.

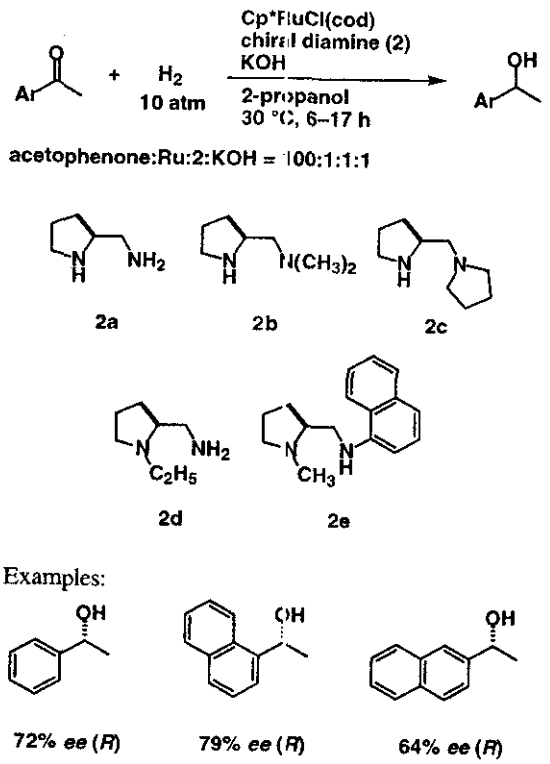


Figure 2. Asymmetric hydrogenation of ketones catalyzed by Cp*RuCl(cod)–**2**–KOH system.

1'-Acetonaphthone and 2'-acetonaphthone were also hydrogenated by Cp*RuCl(cod)–**2d**–KOH catalyst system to give the corresponding chiral alcohols with 79% *ee* (*R*) and 64% *ee* (*R*), respectively.

In order to gain deeper insight on the reaction mechanism, Cp*RuCl(**2d**) was prepared and its structure was unequivoally confirmed by X-ray crystallography (Figure 3). This complex could be prepared by mixing an equimolar amount of Cp*RuCl(cod) and **2d** in ether at room temperature, or more conveniently from 1/4 $(Cp^*RuCl)_4$ and **2d**. Recrystallization of the reaction products from CH_2Cl_2–toluene gave orange crystals suitable for X-ray crystal structure analysis. Figure 3 indicates that the Cp*Ru complex has a distorted octahedral coordination environment with Cp*, NR_3, RNH_2, and Cl ligands as observed in RuCl(η^6-arene)(diamine) complexes.[1b] It should be noted that Cl---HN bond distance is very short, 2.67 Å (expected van der Waals separation, 3.0 Å), which is ascribable to an *intramolecular hydrogen bond*.[1b] *We believe that Cl is replaced* by H with retention of configuration upon treatment of KOH in the presence of H_2, and then the aryl methyl ketones approach to the resulting H–Ru–N–H linkage to form 6-membered cyclic transition state, in which steric repulsion between the ethyl group of the ligand and the substituent of the ketone becomes minimum.

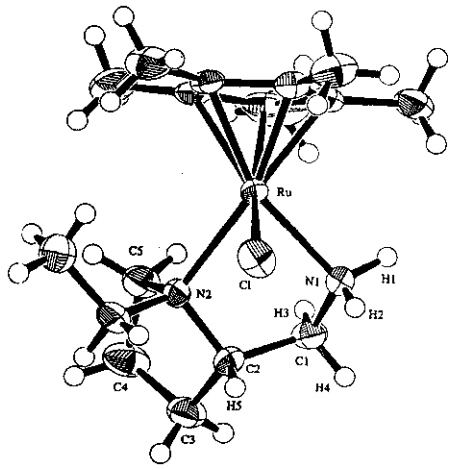


Figure 3. Structural view of [Cp*RuCl(**2d**)].

In conclusion, we have found that Cp*RuCl(cod)–diamine–KOH combined system are effective catalysts for hydrogenation of ketones. Asymmetric hydrogenation using chiral diamines was also achieved with moderate to good enantioselectivities. The mechanism of the asymmetric hydrogenation will be discussed.

References.

1) a) Noyori, R.; Hashiguchi, S. *Acc. Chem. Res.* **1997**, *30*, 97. b) Haack. K-. J.; Hashiguchi, S.; Fujii, A.; Ikariya, T.; Noyori, R. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 285.
2) For example, see a) Jiang, Y.; Jiang, Q.; Zhang, X. *J. Am. Chem. Soc.* **1998**, *120*, 3817. b) Pamer, M.; Walsgrove, T.; Wills, M. *J. Org. Chem.* **1997**, *62*, 5226.
3) a) Doucet, H.; Ohkuma, T.; Murata, K.; Yokozawa, T.; Kozawa, M.; Katayama, E.; England, A. F.; Ikariya, T.; Noyori, R. *Angew. Chem.* **1998**, *110*, 1792 and references therein.