New Chiral Rhodium and Iridium Complexes with Chiral Diamine Ligands for Asymmetric Transfer Hydrogenation of Aromatic Ketones

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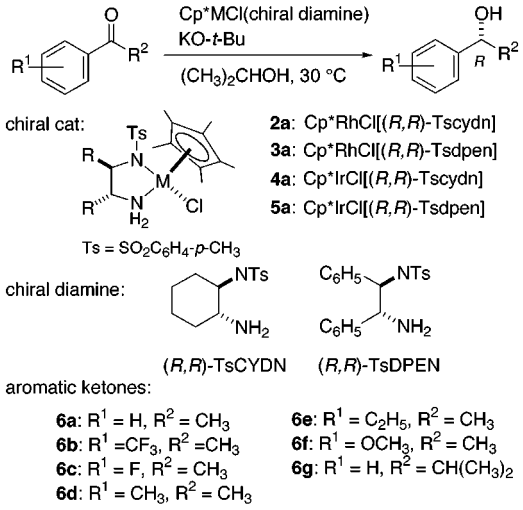
Catalytic asymmetric transfer hydrogenation using 2-propanol or formic acid as a hydrogen source is a useful complement to catalytic asymmetric hydrogenation as a practical tool for the stereoselective synthesis of chiral alcohols or amines.[1,2] We have recently developed highly efficient chiral diamine-based Ru(II) catalysts, RuCl(Tsdpen)(μ^6-arene) (**1a**) (TsDPEN: *N*-(*p*-toluenesulfonyl)-1,2-diphenylethylenediamine) for the asymmetric transfer hydrogenation of ketones and imines to chiral alcohols and amines with excellent enantiomeric purities.[3] The Ru(II)-catalyzed hydrogen transfer reaction was found to be promoted by an isolable 18-electron chiral Ru hydride (**1b**) or 16-electron Ru amide (**1c**) complex, which is a catalyst or intermediate derived from catalyst precursor **1a**. The conversion of **1b** to **1c** in the catalysis takes place by the action of ketones or imines possibly via a six-membered cyclic transition state stabilized by a hydrogen bond between an NH moiety in the ligand and C=X (X = O, NR).[3f,i] This metal/ligand bifunctional effect, therefore, results in excellent catalyst performance in terms of the rate and the enantioselectivity for the catalytic reduction using molecular hydrogen[4] or organic hydrogen sources.[5] We now disclose a synthesis of a new type of rhodium or iridium complex, Cp*MCl(Tsdiamine) (M = Rh, Ir), which has a structure isoelectronic with the chiral Ru complex (**1a**).[3a,f] These isolable complexes have proved to efficiently catalyze the asymmetric hydrogen transfer of simple aromatic ketones in 2-propanol containing a base.



The chiral Rh or Ir complexes with Cp* and chiral diamine ligands were prepared as orange to yellow crystals (**2a**−**4a**) by reacting $[Cp^*MCl_2]_2$ with (*R*,*R*)-TsCYDN or (*R*,*R*)-TsDPEN ($[Cp^*MCl_2]_2$/diamine/base = 1:2:4.2, Cp*: pentamethylcyclopentadienyl, M = Rh, Ir; (*R*,*R*)-TsCYDN: (1*R*,2*R*)-*N*-(*p*-toluenesulfonyl)-1,2-cyclohexanediamine) in the presence of $(C_2H_5)_3N$ at room temperature. ^1H NMR analysis of these complexes confirms the diastereoselective formation of a single stereoisomer.[6] The single-crystal X-ray crystallographic analysis of Cp*RhCl[(*R*,*R*)-Tscydn] (**2a**) illustrated in Figure 1 shows that **2a** has a distorted octahedral coordination environment with Cp*, amino, sulfonamido, and chloro ligands.[6] The chirality of the (*R*,*R*)-diamine ligand that forms a λ-configured five-membered ring determines the *S* configuration at the central metal as observed in the chiral Ru complex (**1a**). It should be noted that there is a very short Cl···N distance (**2a**: 2.70, **3a**: 2.66, **4a**: 2.70 Å) that is ascribed to intramolecular hydrogen bonding. Since Cp*MCl(diamine) has an acidic proton on the N atom, the facile elimination of HCl with a base in alcohols gave an isolable hydride complex through the amide complex. For example,

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(6) Crystal structure analysis of **2a**·H_2O: $C_{23}H_{36}ClN_2O_3SRh$, M_t = 558.97, triclinic, space group *P*1 (#1), a = 11.353(2) Å, b = 13.086(2) Å, c = 9.123(2) Å, α = 92.19(2)°, β = 93.68(1)°, γ = 100.93(1)°, V = 1326.2(4) Å^3, Z = 2, D_c = 1.40 g/cm^3, μ(Mo Kα) = 8.48 cm^{-1}, R (R_w) = 0.040 (0.043) for 5574 observed reflections ($I > 3.00\sigma(I)$). **4a**·H_2O: $C_{23}H_{36}ClN_2O_3SIr$, M_t = 648.28, triclinic, space group P1 (#1), a = 11.365(4) Å, b = 13.042(7) Å, c = 9.162(4) Å, α = 92.07(5)°, β = 93.99(4)°, γ = 100.85(4)°, V = 1328(1) Å^3, Z = 2, D_c = 1.62 g/cm^3, μ(Mo Kα) = 52.41 cm^{-1}, R (R_w) = 0.062 (0.065) for 5167 observed reflections ($I > 3.00\sigma(I)$). After submission of this paper, a report from Tani describing related work on TsDPEN complexes of Rh and Ir appeared. Mashima, K.; Abe, T.; Tani, K. *Chem. Lett.***1998**, 1199−1200.

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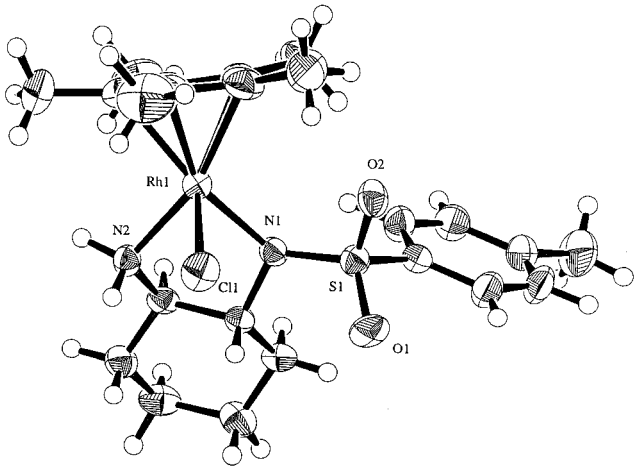

Figure 1. ORTEP view of Cp*RhCl[(1*R*,2*R*)-*N*-(*p*-toluenesulfonyl)-1,2-cyclohexanediamine) (**2a**). One crystal water molecule has been omitted for the sake of clarity. Selected bond lengths (Å): Rh1−Cl1, 2.447(2); Rh1−N1, 2.152(7); Rh1−N2, 2.116(7); Cl1−H1, 2.70. Selevted bond angles (deg): Cl1−Rh1−N1, 89.9(2); Cl1−Rh1−N2, 83.3(2); N1−Rh1−N2, 78.1(3).

the reaction of **4a** with 1 equiv of NaOH in 2-propanol gave Cp*IrH[(*R*,*R*)-Tscydn] (**4b**) as a single stereoisomer.[7] The complex **4b** readily reacted with acetone to provide quantitatively the 5-coordinate amide complex **4c** where the amine ligand is deprotonated.[7] The single-crystal X-ray crystallographic analysis of **4b** indicates that it has a structure similar to that of the chloride complex **4a**.

These well-defined Rh and Ir complexes effect the asymmetric transfer hydrogenation of aromatic ketones to the corresponding chiral alcohols in 2-propanol containing a base. The reaction of acetophenone (**6a**) (0.1 M) in 2-propanol containing (*R*,*R*)-**2a** and KO-*t*-Bu at 30 °C (ketone/**2a**/KO-*t*-Bu = 200:1:1.2) for 12 h gave (*R*)-1-phenylethanol with 97% ee in 85% yield. The rate and enantioselectivity of the reaction are strongly affected by the central metals and the structure of the chiral diamine ligands (Table 1). The Rh complex with TsCYDN is the better catalyst in terms of the rate and enantioselectivity in comparison to the Ir complex with the same amine. The TsCYDN complexes provide higher reactivity than the TsDPEN complexes. The analogous preformed chiral Ru complex (**1a**) with the TsDPEN ligand has a somewhat higher reactivity with a comparable to lower enantioselectivity (92% yield, 94% ee) for reduction of **6a**. *m*-(Trifluoromethyl)acetophenone (**6b**) (substrate/catalyst ratio (S/C) = 200−500) was readily reduced almost quantitatively to an intermediate of the fungicide, (*R*)-1-(*m*-trifluoromethylphenyl)ethanol, with 97% ee. A reaction using a 0.1 M solution with a S/C of 1000 gave the optically active alcohol in a good yield without a significant deterioration of the enantiomeric purity. Since the transfer hydrogenation of ketone with 2-propanol is reversible, the reaction using a 1 M solution of **6b** resulted in a decrease in the stereoselectivity to ca. 80% ee after 95% conversion for 12 h. To attain high catalysis performance the reaction using a 0.1 M solution is recommended. The structures and electronic properties of the ketonic substrates significantly affect the outcomes of the reactions (Table 1). The reduction of acetophenones with electron-withdrawing substituents, **6b** or **6c**, proceeds rapidly to the corresponding chiral alcohols with excellent yield and high ee. Electron-donating substituents resulted in a slower reaction as expected but with a high enantioselectivity. The bulkiness of the R^2 group in **6g** caused a strong retardation of the reaction, giving the product with a low ee (1% conv, 29% ee). The cyclic substrates, 1-tetralone and 1-indanone, are also converted to the corresponding alcohols with high enantiomeric purities and in moderate yields.

Table 1. Asymmetric Transfer Hydrogenation of Acetophenones Catalyzed by Preformed Chiral Catalysts and KO-*t*-Bu System in 2-Propanol[a]

cat.	ketone	time (h)	convn[b] (%)	ee[c] (%)	config[d]
(*R*,*R*)-**1a**	6a	12	92	94	*R*
(*R*,*R*)-**2a**	6a	12	85	97	*R*
(*R*,*R*)-**3a**	6a	12	14	90	*R*
(*R*,*R*)-**4a**	6a	12	36	96	*R*
(*R*,*R*)-**2a**	*m*-**6b**	12	>99	97	*R*
(*R*,*R*)-**2a**	*m*-**6b**[e]	24	>99	97	*R*
(*R*,*R*)-**2a**	*m*-**6b**[f]	66	90	96	*R*
(*R*,*R*)-**2a**	*m*-**6b** (1M)	12	95	80	*R*
(*R*,*R*)-**1a**	*m*-**6b**	6	>99	90	*R*
(*R*,*R*)-**4a**	*m*-**6b**	24	99	94	*R*
(*R*,*R*)-**2a**	*o*-**6b**	12	>99	96	*R*
(*R*,*R*)-**2a**	*o*-**6c**	12	97	91	*R*
(*R*,*R*)-**2a**	*o*-**6d**	24	20	94	*R*
(*R*,*R*)-**2a**	*p*-**6e**	24	58	>99	*R*
(*R*,*R*)-**2a**	*p*-**6f**	24	22	>99	*R*
(*R*,*R*)-**2a**	1-tetralone	24	53	95[g]	*R*
(*R*,*R*)-**2a**	1-indanone	24	43	97[g]	*R*
(*R*,*R*)-**2a**	1′-acetonaphthone	48	48	87	*R*

[a] The reaction was carried out at 30 °C using a 0.1 M solution of the ketone in 2-propanol. Ketone/cat./KO-*t*-Bu = 200:1:1.2. [b] Conversion was determined by GLC. [c] Determined by GLC analysis using a Chirasil-DEX CB (25m). [d] Determined from the sign of rotation of the isolated product. [e] The reaction with S/C = 500. [f] The reaction with S/C = 1000. [g] Determined by HPLC analysis using a Daicel Chiralcel OB column.

Noticeably, both the isolable Ir hydride complex (**4b**)[7] and the amide complex (**4c**)[7] catalyzed the asymmetric transfer hydrogenation of **6b** in 2-propanol without any bases to give (*R*)-1-(*m*-trifluoromethylphenyl)ethanol with the same enantioselectivity in comparison to the catalyst system consisting of **4a** and KO-*t*-Bu (S/C = 500, 12 h reaction: 95% conversion, 95% ee with **4b**, 83% conversion, 94% ee with **4c**; 87% conversion, 94% ee with **4a**/KO-*t*-Bu). Successful isolation of the complex **4b** or **4c** as well as their catalytic performance confirms that this asymmetric reduction takes place by the action of the hydride or amide complex as the catalyst or intermediate, as observed in the same reaction promoted by the chiral Ru complex system.[3f]

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Supporting Information Available: The $[\alpha]_D$ values of the reaction products, the experimental procedure for the transfer hydrogenation reaction of *m*-**6b**, and the single-crystal X-ray information for **2a** and **4a**.

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(7) Ir amide complex **4c** was obtained quantitatively by a reaction of Ir hydride **4b** with acetone. A yellow crystalline complex is obtained by recrystallization from toluene. The direct conversion of **4a** to **4c** in toluene containing a base caused a lower yield. The details of the structures and chemical properties of **4b** and **4c** will be reported soon. **4b**: ^{1}H NMR (270 MHz, toluene-d_8) δ −10.4 (s, 1H, Ir-*H*), 0.8−2.4 (11H, cyclohexane ring protons plus 1H, N*H*), 1.72 (s, 15H, $C_5(CH_3)_5$), 2.08 (s, 3H, CH_3 of Ts), 3.18 (m, 1H, N*H*), 7.0, 8.07 (4H, aromatic ring protons). The crystallization from THF provides pale yellow crystals suitable for X-ray analysis. Crystal structure analysis of **4b**·2THF: $C_{31}H_{51}N_2O_4SIr$, M_t = 740.04, orthorhombic, space group $P2_12_12_1$ (#19), a = 10.170(1) Å, b = 14.969(1) Å, c = 22.454(3) Å, V = 3418.1(6) Å^3, Z = 4, D_c = 1.44 g/cm^3, μ(Mo Kα) = 40.2 cm^{-1}, R (R_w) = 0.047 (0.066) for 2676 observed reflections ($I > 3.00\sigma(I)$). **4c**: ^{1}H NMR (270 MHz, acetone-d_6) δ 0.7−2.7 (10H, cyclohexane ring protons), 1.70 (s, 15H, $C_5(CH_3)_5$), 2.35 (s, 3H, CH_3 of Ts), 5.10 (br, 1H, N*H*), 7.21, 7.74 (4H, aromatic ring protons).