Asymmetric transfer hydrogenation of ketones catalyzed by rhodium and iridium complexes with chiral bidentate Schiff's bases

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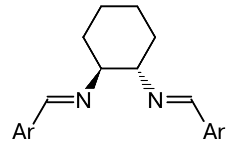
Rhodium and iridium complexes of Schiff's bases derived from (1*R*,2*R*)- and (1*S*,2*S*)-diaminocyclohexane catalyze asymmetric transfer hydrogenation of alkyl aryl ketones in Pr^{i}OH at room temperature to give chiral secondary alcohols (up to 65% *ee*).

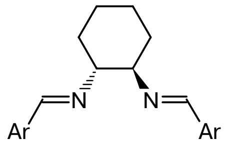
Key words: asymmetric hydrogenation of ketones, hydrogen transfer, catalysis, rhodium complexes, iridium complexes, chiral Schiff's bases, (1*R*,2*R*)- and (1*S*,2*S*)-diaminocyclohexane derivatives.

Considerable progress has been recently achieved in asymmetric transfer hydrogenation catalyzed by complexes of transition metals (Rh, Ir, and Ru) in Pr^{i}OH or in a mixture of HCOOH with Et_3N.[1] Chiral bidentate ligands such as 1,2-diamines, their *N*-acetyl derivatives, and bisoxazolines are successively used in the preparation of catalysts for the reactions of this type.[2—8] However, the use of complexes with bidentate Schiff's bases for this purpose is scarcely reported in the literature and only in a ruthenium-catalyzed reaction.[9]

The goal of this paper is to present the results of asymmetric hydrogenation of ketones in Pr^{i}OH in the presence of rhodium and iridium complexes with Schiff's bases, namely, (1*R*,2*R*)- and (1*S*,2*S*)-diaminocyclohexane derivatives. The catalysts were prepared *in situ* by the reaction of $[M(COD)Cl]_2$ (M = Rh and Ir, and COD is cycloocta-1,5-diene) with ligands **1** or **2**.



(*S*,*S*)-**1a—c**



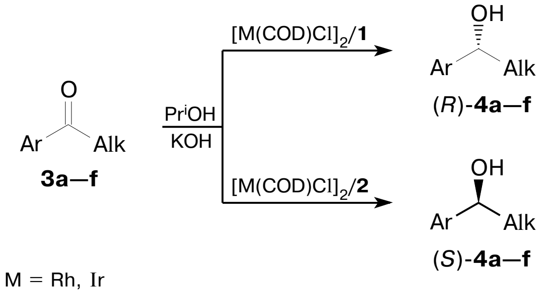
(*R*,*R*)-**2a**

Ar = Ph (**a**), 2-$MeOC_6H_4$ (**b**), 1-naphthyl (**c**)

Results and Discussion

The stereochemistry of this reaction is shown in Scheme 1. It is of note that the reaction catalyzed by analogous ruthenium complexes yields the same stereoisomer, *i.e.*, (*S*)-**4** in the presence of ligands (*R*,*R*)-**2**.[9] Enantioselectivities of the Rh- and Ir-containing catalysts in the hydrogenation of ketones **3** in Pr^{i}OH (Table 1) is moderate but much higher than that of Ru catalysts, for the latter it did not exceed 40% *ee*.[9] The maximum yield and the highest level of asymmetric induction in the reduction of most of the ketones studied was provided by the Ir/**1b** system (see Table 1).

Scheme 1



3, 4	a	b	c	d	e	f
Ar	Ph	Ph	Ph	1-Naphthyl	2-Naphthyl	2-Fluorenyl
Alk	Me	Et	Pr^i	Me	Me	Me

Experimental

Polarimetric measurements were carried out on a JASCO DIP-360 instrument in 1-cm cells.

Commercial alkyl aryl ketones **3**, (1*S*,2*S*)-diaminocyclohexane and its enantiomer (Aldrich), and $[Rh(COD)Cl]_2$ and $[Ir(COD)Cl]_2$ (Fluka) were used in the syntheses.

(1*S*,2*S*)-*N*,*N*′-Dibenzylidene-1,2-diaminocyclohexane (1a). A solution of (1*S*,2*S*)-1,2-diaminocyclohexane (5.5 g, 50 mmol) and benzaldehyde (11 g, 140 mmol) in anhydrous benzene (250 mL) was refluxed with a Dean—Stark trap for 3 h.

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Table 1. Yield (*Y*) and enantiomeric excess (*ee*) of secondary alcohols **4** (%) in the asymmetric transfer hydrogenation of ketones **3a—f** in the presence of $[M(COD)Cl]_2$/**1** and $[M(COD)Cl]_2$/**2** as catalysts

M	Schiff's base	**4a**		**4b**		**4c**		**4d**		**4e**		**4f**	
		Y	*ee*	*Y*	*ee*	*Y*	*ee*	*Y*	*ee*	*Y*	*ee*	*Y*	*ee*
Rh	**1a**	43	45 (*R*)	55	43 (*R*)	—	—	60	34 (*R*)	73	35 (*R*)	70	60 (*R*)
Rh	**2a**	46	48 (*S*)	60	46 (*S*)	46	46 (*S*)	60	32 (*S*)	60	35 (*S*)	64	65 (*S*)
Rh	**1b**	51	36 (*R*)	55	26 (*R*)	20	40 (*R*)	44	28 (*R*)	43	42 (*R*)	34	43 (*R*)
Rh	**1c**	19	44 (*R*)	34	40 (*R*)	—	—	40	31 (*R*)	44	35 (*R*)	69	50 (*R*)
Ir	**2a**	88	41 (*S*)	84	43 (*S*)	30	32 (*S*)	68	34 (*S*)	65	48 (*S*)	85	50 (*S*)
Ir	**1b**	91	55 (*R*)	86	51 (*R*)	—	—	90	59 (*R*)	74	48 (*R*)	88	61 (*R*)

Benzene was evaporated, and the solid residue was suspended in hexane, filtered off, and washed with hexane to decolorization. The product was recrystallized from hexane (100 mL). The white crystals were dried at 70 °C *in vacuo* (1—2 Torr) to give compound **1a**, yield 8.5 g (61%), m.p. 98—99 °C, $[\alpha]_D^{20}$ +205 (*c* 1, $CHCl_3$).

Ligands **2a**, **1b**, and **1c** were prepared in a similar manner.

(1*R*,2*R*)-*N*,*N*′-Dibenzylidene-1,2-diaminocyclohexane (2a). Yield 63%, m.p. 98—99 °C (*cf.* Ref. 9: m.p. 99—100 °C), $[\alpha]_D^{20}$ −208 (*c* 1, $CHCl_3$).

(1*S*,2*S*)-*N*,*N*′-Bis(2-methoxybenzylidene)-1,2-diaminocyclohexane (1b). Yield 56%, m.p. 102—104 °C, $[\alpha]_D^{20}$ +68.4 (*c* 0.5, MeOH) (*cf.* Ref. 9: m.p. 105—106 °C, $[\alpha]_D^{25}$ −69.2 (*c* 0.5, MeOH) for the (1*R*, 2*R*)-enantiomer).

(1*S*,2*S*)-*N*,*N*′-Bis(1-naphthylmethylidene)-1,2-diaminocyclohexane (1c). Yield 80%, m.p. 130—133 °C, $[\alpha]_D^{20}$ +233.5 (*c* 0.25, CH_2Cl_2) (*cf.* Ref. 9: m.p. 131—132 °C, $[\alpha]_D^{25}$ −202 (*c* 0.25, CH_2Cl_2) for the (1*R*, 2*R*)-enantiomer).

The ^{1}H NMR spectra of the ligands obtained coincide with the published ones.[9]

Asymmetric transfer hydrogenation of ketones 3 (general procedure). A mixture of $[M(COD)Cl]_2$ (M = Rh or Ir) (28.4 μmol) and a chiral ligand (62.5 μmol) was placed in a flask equipped with a magnetic stirrer in an atmosphere of Ar. A solution of KOH (0.196 mmol) in Pr^iOH (10 mL) was added through a silicone septum by a syringe. The reaction mixture was stirred for 1 h, and a solution of ketone **3** (0.625 mmol) in Pr^iOH (10 mL) was added in the same manner. The resulting solution was stirred at ~20 °C for five days, neutralized with HCl, passed through a 2-cm layer of activated carbon, and analyzed by GLC or HPLC. For the detailed conditions of chromatographic analyzes, see Ref. 10.

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References

1. R. Noyori and S. Hashiguchi, *Acc. Chem. Res.*, 1997, **30**, 97.
2. P. Gamez, F. Fache, P. Mangeney, and M. Lemaire, *Tetrahedron Lett.*, 1993, **34**, 6897.
3. K. Puntener, L. Schwink, and P. Knochel, *Tetrahedron Lett.*, 1996, **37**, 8165.
4. S. Inoue, K. Nomura, S. Hashiguchi, R. Noyori, and Y. Izawa, *Chem. Lett.*, 1997, 957.
5. P. Gamez, B. Dunjic, and M. Lemaire, *J. Org. Chem.*, 1996, **61**, 5196.
6. A. Fujii, S. Hashiguchi, N. Uematsu, T. Ikariya, and R. Noyori, *J. Am. Chem. Soc.*, 1996, **118**, 2521.
7. K. Mashita, T. Abe, and K. Tani, *Chem. Lett.*, 1998, 1199; 1201.
8. D. Muller, G. Umbricht, B. Weber, and A. Pfaltz, *Helv. Chim. Acta*, 1991, **74**, 232.
9. P. Krasik and H. Alper, *Tetrahedron*, 1994, **50**, 4347.
10. M. G. Vinogradov, L. S. Gorshkova, V. A. Pavlov, O. V. Mikhalev, G. V. Chel′tsova, I. V. Razmanov, V. A. Ferapontov, O. R. Malyshev, and G. L. Heise, *Izv. Akad. Nauk, Ser. Khim.*, 2000, 459 [*Russ. Chem. Bull., Int. Ed.*, 2000, **49**, 460].

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