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Efficient rhodium and iridium-catalysed asymmetric transfer hydrogenation using water-soluble aminosulfonamide ligands

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Abstract—A range of aromatic ketones was reduced asymmetrically under transfer hydrogenation conditions using enantiomerically pure catalysts derived from water-soluble diamine ligands and $[Cp*MCl_2]_2$ (Cp*=pentamethylcyclopentadienyl, M=Rh, Ir). High catalytic activity and enantioselectivity were observed in systems containing up to 51% water. © 2001 Elsevier Science Ltd. All rights reserved.

1. Introduction

Asymmetric catalytic transfer hydrogenation using 2propanol as a source of hydrogen is an attractive method for the preparation of chiral alcohols and amines.¹ The majority of work carried out in this area has used ruthenium catalysts in combination with a variety of phosphine and amine ligands.² Of these, the most notable transfer hydrogenation system incorporates the Ru(II)–TsDPEN (TsDPEN = N-(p-toluenesulfonyl)-1,2-diphenylethylenediamine) catalyst, first reported by Noyori et al.³ More recently, the synthesis and application of efficient rhodium-based catalysts has been reported in the literature.⁴ Whilst the utility of irridium catalysts for transfer hydrogenation has been documented, there are few results that compare with those obtained from ruthenium or rhodium-based systems.4b,5

Recently, we have used the water-soluble aminosulfonic acid ligands 1 and 2 with ruthenium for the transfer reduction of various aromatic ketones.⁶ Herein, we report on the synthesis and application of efficient water-soluble rhodium and iridium-based catalysts for asymmetric transfer hydrogenation under aqueous conditions. Our research interests lie in the area of supported liquid phase (SLP) catalysis⁷ and this work is a step further in the development of a SLP transfer hydrogenation catalyst.



2. Results and discussion

The chiral rhodium or iridium complexes were prepared by reacting $[Cp^*MCl_2]_2$ (M = Rh, Ir) with ligands 1 or 2 in the presence of base at 40°C ($[Cp^*MCl_2]_2$ /diamine/



Scheme 1.

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Table 2. Asymmetric transfer hydrogenation of acetophenones catalysed by polar iridium complexes

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Ketone	Ligand	Reaction time (h)	Conversion (%)	Enantiomeric excess (%)	Configuration
3	1	140	90	82	R
	2	26	88	96	R
4	1	43	95	86	R
	2	4	98	93	R
5	1	51	83	85	R
	2	26	99	94	R
6	1	150	22	78	R
	2	141	80	95	R
7	1	91	93	76	R
	2	20	99	95	R
8	1	139	77	73	R
	2	45	96	96	R
9	1	139	41	91	R
	2	45	55	97	R

base = 1:8:8) and were used immediately without isolation.⁸ A range of aromatic ketones was reduced at room temperature under transfer hydrogenation conditions (Scheme 1). Tables 1 and 2 show the results from systems containing 15% water.

Both the choice of metal and ligand affected the rate and enantioselectivity of the reaction in the expected manner.² Rhodium-based complexes proved to be superior catalysts in terms of rate and enantioselectivity, with ligand **2** systems providing higher reactivity. The electronic properties of the substrate had a significant effect on the outcome of the reaction. Electron deficient ketones were reduced rapidly to the corresponding alcohols with high conversion and enantioselectivity. Electron-rich ketones were reduced more slowly but also with high enantioselectivity.

In order to determine the effect of an increase in water concentration, the iridium-catalysed transfer hydrogenation experiments were carried out in a 2-propanol– water mixture containing 34 and 51% water. The overall volume of reaction solvent remained unchanged. The results (Table 3) were quite surprising. An expected rate decrease relating to the lower concentration of 2-propanol was not seen. Instead, a significant rate increase was noted for both systems. In addition to this, a large increase in enantiomeric excess was observed for ligand 1 systems when the concentration of water was increased from 15 to 34%. The reason for these results is not clear at this time.

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In conclusion, we have used water-soluble rhodium and iridium complexes to efficiently catalyse the asymmetric reduction of various aromatic ketones. Our future work will concentrate on the development of biphasic and supported liquid phase systems that utilise these catalysts.

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Table 3. Transfer hydrogenation using iridium catalysts in systems containing (i) 34% and (ii) 51% water

Ketone	Ligand	Reaction time (h)	Conversion (%)		Enantiomeric excess (%)	
5	1	22	(i)	74	92	
			(ii)	90	92	
5	2	2.5	(i)	82	94	
			(ii)	94	93	
6	1	115	(i)	20	91	
			(ii)	33	92	
6	2	116	(i)	76	92	
			(ii)	89	87	
8	1	42	(i)	47	91	
			(ii)	66	93	
8	2	18	(i)	92	95	
			(ii)	92	94	

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- 8. A solution of potassium *tert*-butoxide in isopropanol (0.8 cm³ of a 0.1 M solution, 0.08 mmol) was added to a suspension of ligand (1) (34.6 mg, 0.08 mmol) in water (1 cm³) and stirred at room temperature until a clear solution was obtained. To this solution [Cp*IrCl₂]₂ (8.0 mg, 0.01 mmol) was added and the mixture stirred under argon at 40°C for 2 hours and then allowed to cool to room temperature. Acetophenone (240 mg, 2 mmol) in isopropanol (10 cm³) was then added along with water (1 cm³) and potassium tert-butoxide in isopropanol (2 cm³ of a 0.1 M solution, 0.20 mmol). This mixture was then stirred at 22°C. Samples (approx. 0.05 cm³) were taken out of the reaction mixture after the given time, passed through a small column of silica using Et_2O (3×1 cm³) as the eluent and finally concentrated to approx. 0.5 cm³. Analysis was undertaken by GC using a Supelco beta-dex 120 column. Configuration was determined from the sign of rotation of the isolated product.