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The application of diferrocenylimine ligands for asymmetric transfer hydrogenation of ketones

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ABSTRACT

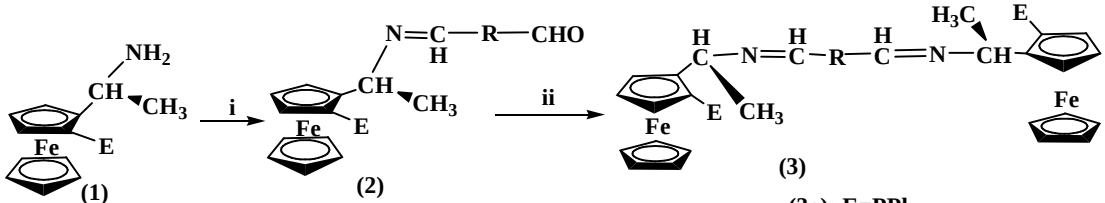
Two Novel planar chiral diferrocenylimine **(3a)** and **(3b)** were prepared for the Iridium catalyzed asymmetric transfer hydrogenation of aromatic ketones. The results show that the activity and enantioselectivity of the chiral iridium catalyst are very sensitive to the substrate structure. Ir(I)-catalyzed asymmetric transfer hydrogenation of acetophenone resulted in moderate to good yield and lower enantioselectivity; asymmetric transfer hydrogenation of proopiophenone and 2- benzoylpridine resulted in lower yield and lower enantioselectivity; as for 4-benzoylpridine, Good results have been achieved.

KEYWORDS

Diferrocenylimine;
Asymmetric transfer hydrogenation;
Chiral iridium complex;
Synthesis;
Chiral.

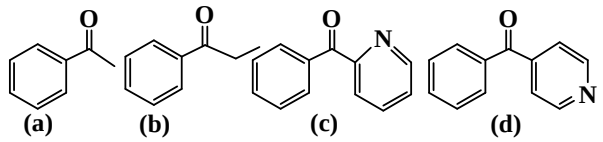
INTRODUCTION

In recent years chiral ferrocene ligands incorporating both planar and central chirality have attracted considerable attentions[1-3]. Despite a large variety of planar-chiral ferrocene derivatives are known to be highly effective in the asymmetric catalysis[4-8], only a few examples have been developed into industrial processes. The lack of application of homogeneous asymmetric catalysis is partly due to the problems of separation and recycling of the expensive chiral catalysis. With an effort to design an efficient and recoverable ferrocene ligand for asymmetric transfer hydrogenation of ketones, herein, we designed and synthesized two novel diferrocenyliimines ligands **(3a)** and **(3b)**, (SCHEME 1) which incorporates both planar and central chirality and applied them in asymmetric transfer hydrogenation of ketones. It is expected that the steric effect of the



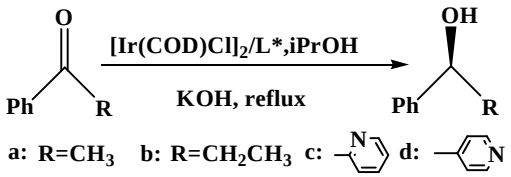
SCHEME 1: Preparation of Chiral diferrocenylphosphine-diimines ligands 3

TABLE 1: Asymmetric transfer hydrogenation of ketones in i-Propanol catalyzed by Chiral Ir(I) complexes



Entry[a]	Ligand	ketones	Time/h	Temp /°C	Yield[b] (%)	Ee (%)[c]
1		a	4	50	75	48.9
2		b	4	50	20	41.7
3	(3a)	c	6	50	40	13.1
4		d	4	25	>99	19.9
5		a	6	50	60	21.9
6		b	6	50	20	30.8
7	(3b)	c	6	50	35	4.0
8		d	4	25	80	81.9

a: Reactions were carried out in the presence of 2.0 mmol acetophenone, L:M =1:1(L= Ligand£¬M= Metal); b: Yield was calculated as alcohol after chromatography, c: ee values were determined by HPLC analysis of the isolated alcohol with Chiralcel OD columns



SCHEME 2

specific microenvironment created by the ferrocene skeletone structure could modulate the catalytic behaviors of the chiral diferrocenylimines.

RESULTS AND DISCUSSION

Asymmetric transfer hydrogenation of prochiral ketones to provide chiral alcohols has received a great deal of attention in the last decade or so. The new developed diferrocenylimine ligands**(3a and 3b)** were applied to Ir-catalyzed asymmetric transfer hydrogenation of various aromatic ketones(acetophenone, proopiophenone, 2- benzoylpridine, 4-benzoylpridine) using 2-propanol as a source of hydrogen..

The results of asymmetric transfer hydrogenation of ketones by Ir(I)/ 3a and Ir(I)/ **(3b)** are listed in TABLE 1. It can be seen from TABLE 1 that The results obtained clearly demonstrate that the title compounds has moderate catalytic activity and low enantioselectivity Ir(I) towards catalytic transfer hydrogenation. The results show that the activity and enantioselectivity of the chiral iridium catalyst are very sensitive to the substrate structure. Ir(I)-catalyzed asymmetric transfer hydrogenation of acetophenone resulted in moderate yield and lower enantioselectivity(entry 1 and 5, TABLE 1, 60-75%yield, 21.9-48.9% e.e.); asymmetric transfer hydrogenation of proopiophenone (entry 2 and 6, TABLE 1, 20%yield, 30.8-41.7% e.e.) and 2- benzoylpridine resulted in lower yield and lower enantioselectivity(entry 3 and 7, TABLE 1, 35-40%yield, 4.0-13.1% e.e.); as for 4-benzoylpridine, Good results have been achieved(entry 4 and 8, TABLE 1, 80-99%yield, 19.9-81.9% e.e.).

Chiral diferrocenylimine-diols ligand 3b is efficient ligand in asymmetric transfer hydrogenation reaction. It catalyzed asymmetric transfer hydrogenation of 4-benzoylpridine with good enantioselectivity (81.9%ee).

EXPERIMENTAL

General procedure

All reactions were carried out under argon and monitored by thin-layer chromatograph (TLC). Diethyl ether was dried using Na under reflux. Melting point (uncorrected) was measured with a XT4 melting point apparatus. ^{1}H NMR spectra were recorded on a Varian EM-360 spectrometer, using $CDCl_3$ as solvent and TMS as the internal standard. Optical rotations were measured on a WZZ-3 polarimeter.

Synthesisi of planar chiral diferrocenylimines (3a) and (3b)

The title compounds was prepared according to SCHEME 1, primary amine 1a ($[\alpha]_D^{20}$+337 (c 0.9, $CHCl_3$), mp. 117-118 ^{0}C) and 1b ($[\alpha]_D^{20}$ 25.0 (c 0.667, CH_2Cl_2) mp 159-161^{0}C(lit. 162-163^{0}C).were prepared by literature methods[9,10]. Starting with **(1a)** and **(1b)**, diferrocenyphosphine-diimine ligand 3a and diferrocenylimine-diols ligand **(3b)** were designed and synthesized.

(3a): (1a)(820 mg, 2.0 mmol) and p-phthaldehyde (560 mg, 4.17 mmol) were dissolved in anhydrous ethanol and mixed with molecular sieve**(5g)** refluxed for 4h, concentrated in vacuo washed with hot water (10ml×2), filtered and evaporated to dryness, the crude material **(2)** and **(1a)** (820 mg, 2.0 mmol) were dissolved in

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anhydrous ethanol refluxed for 2h, filtered, the crude material was recrystallized from dichloromethane/petroleum ether giving orange crystals **(3a)** (754mg, 82%). mp 248-250^{0}C, ($[\alpha]_D^{20}$+543.9 (c 0.4, CH_2Cl_2)). The IR spectrum indicated the presence of the unsubstituted cyclopentadienyl ring (1100.9 and 997.6cm-1), 1022.0~1147.6 cm^{-1} (single substituted cyclopenta dienyl), 486.1cm^{-1} and 509.9cm^{-1}(ν_{Fe-C}), 1621 and 1639 cm^{-1}(N=CH); ^{1}H NMR spectrum ($CDCl_3$) δ_H: (ppm) 1.63 (d, J=6.7, 6H, $CHCH_3$), 3.73 (m, 2H, $CHCH_3$), 4.02 (s, 10H, Fc-unsubst. Ring), 4.23-4.75 (m, 6H, FeC_5H_3), 6.72-6.94 (s, 4H, C_6H_4), 7.24-7.67(m, 20H, C_6H_5), 7.88(s, 2H, N=CH); ^{31}P NMR: -23.283; HRMS (TOF): 924.4.

(3b): It was prepared in similar manner to that for the preparation of **(3a)**, starting with **(1b)** (803 mg, 86%). mp 172-174^{0}C, ($[\alpha]_D^{20}$-237.3 (c 0.153, CH_2Cl_2). The IR spectrum indicated the presence of the unsubstituted cyclopentadienyl ring (1103.9 and 996.6cm^{-1}), 1022.0~1147.6 cm^{-1} (single substituted cyclopenta dienyl), 486.1 cm^{-1} and 509.9 cm-1(ν_{Fe-C}), 1621 and 1639 cm^{-1}(N=CH); ^{1}H NMR spectrum ($CDCl_3$) δ_H: (ppm) 0.72 (d, J=6.7, 6H, $CHCH_3$), 3.48 (s, 2H, OH), 4.10 (s, 10H, Fc-unsubst. Ring), 4.06-4.22 (m, 8H, FeC_5H_3CH), 7.22-7.60(m, 40H, C_6H_5), 8.06 (s, 4H, C_6H_4), 8.31(s, 1H, N=CH), 8.84(s, 1H, N=CH); Calc. for $C_{58}H_{52}Fe_2N_2O_2$: C, 75.65; H, 5.65; N, 3.04. Anal. Found: C, 75.60; H, 5.63; N, 2.98; MS (TOF): 920.6.

Application of these new chiral ferrocene ligands in Ir-catalyzed asymmetric transfer hydrogenation

The catalyst was generated in situ by refluxing ligands 3a and 3b (1.0 mmol%) with $[Ir(COD)Cl]_2$ (1.0 mmol%) in 2-propanol at 50^{0}C under argon for 4h. After being cooled down to room temperature, acetophenone (2.0 mmol) was added, followed by KOH (1.5 mg, 0.03 mmol) under argon. The transfer hydrogenation was conducted at desired temperature under argon for a given time. The resulting solution was purified by flash chromatography on a silica gel column eluted by petroleum ether/ethyl acetate (9/1) and the product was analyzed by HPLC.

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