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Asymmetric transfer hydrogenation of aromatic ketones with chiral diamino-thiophene/iridium catalyst systems

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ABSTRACT

The chiral diamino-bis(bithiophene) ligands were firstly employed in the iridium(I)-catalyzed asymmetric transfer hydrogenation of aromatic ketones. The new catalyst systems, generated in situ from chiral diamino-bis(bithiophene) ligands and $IrCl(CO)(PPh_3)_2$ in ^{i}PrOH, gave the corresponding optically active secondary alcohols with high yield and fair to good enantioselectivities (up to 90% ee). The chiral Ir(I)/diamino-bis(bithiophene) complexes were also synthesized and characterized. The XPS spectra showed that the potentially multidentate ligands coordinated to the Ir atom through the nitrogen atoms, while the thiophene pendants did not participate in coordination to the Ir atom.

1. Introduction

Chiral ligands with mixed functional groups have been known to play an important role in transition metal complexes catalyzed asymmetric reactions [1]. In the past two decades, a large number of the chiral-mixed [PN], [NPN], [PNP], [PNNP], [ON] and [ONNO] ligands have been synthesized and served as excellent chiral auxiliaries for catalytic asymmetric synthesis [2–13]. Compared to the ligands with P, N or O as donor atoms, sulfur-containing based chiral mixed ligands have received much less attention. A plausible reason is that sulfur has a tendency to poison transition metal catalysts.

However, sulfur possesses a number of oxidation states available and can form some compounds that have different functional groups. Furthermore, its empty relatively low-energy d orbitals can accept back-donation of π-electron density from the metal, leading to stabilize the metal–S bond. Upon complexation of a metal, chirality can be induced at sulfur [14,15]. These promoting structural features exhibit very rich coordination chemistry towards transition metal and serve as powerful sterodirecting ligands in asymmetric synthesis [16–18]. Recently, sulfur-containing ligands have proved to be as excellent as other classical chiral ligands in the form of various groups, such as thioether [19,20], sulfoxide [14,21], sulfamide [22], thiocarbonyl [23], and aminosulfide [24].

Thiophene functional groups, as a type of extremely flexible coordination mode of the sulfur-containing five-membered ring, can coordinate to metal centers through the sulfur, carbons or all five atoms in the thiophene ring [25]. The π-electron of the aromatic thiophene ring can involve in donor–acceptor interactions with metal atoms conveniently. More recently, the chiral thiophene derivatives as ligands have been successfully used as chiral auxiliaries for a wide range of reactions, such as asymmetric reduction [26–29], allylic alkylation [30–32], hydrosilylation [32], cyclopropanation [33], Diels–Alder reaction [34], and Heck reaction [35], while the use of thiophene ligands in asymmetric transfer hydrogenation (ATH) appears to be still rather underdeveloped [36].

Previously, our lab has reported the application of chiral diamino-bis(thiophene) ligands **2** in ATH of aromatic ketones and the thiophene groups in the chiral sulfur-containing ligands enhanced chemical as well as optical yields in the final product [36]. In our present study, we further investigated the catalytic performance of chiral diamino-bis(bithiophene) ligands **4** bearing two thienyl units in each N-pendant and the coordination environment of the diamino-thiophene ligands.

2. Experimental

2.1. General methods

All experiments were carried out in a nitrogen atmosphere. NMR spectra were recorded on a Bruker AV 400 instrument. Mass spectra were carried out on a Finnigan LCQ mass spectrometer. IR spectra were recorded on a Nicolet Avatar 360 FT-IR spectrometer. CD spectra were measured with a JASCO J-810 spectrophotometer. Conductance was determined by conducto metermodec DDS-11A.

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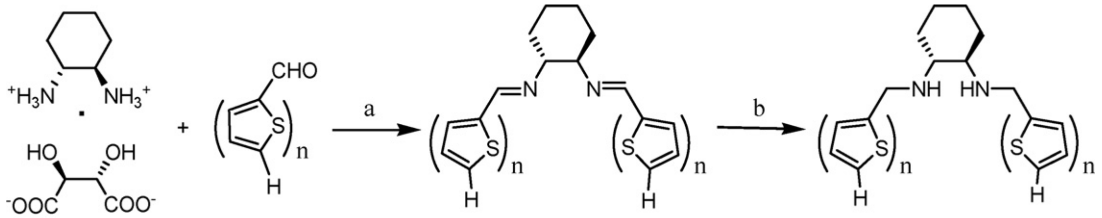

(*R*,*R*)-**1**: n = 1
(*R*,*R*)-**3**: n = 2

(*R*,*R*)-**2**: n = 1
(*R*,*R*)-**4**: n = 2

Scheme 1. Syntheses of chiral thiophene ligands. Reagents and conditions: (a) K_2CO_3, CH_3CH_2OH/H_2O, reflux; (b) $NaBH_4$, CH_3CH_2OH, reflux.

The XPS data were recorded on a Quantum 2000 spectrometer operating with Al Kα (1486.6 eV) radiation source and the binding energies were referred to the carbon C 1s peak (E_b = 284.7 eV). Optical rotations were measured with a Perkin-Elmer 341 polarimeter. The yields and ee values were determined by GC analysis with a CP-Chirasil-Dex CB column. The solvents were dried and purified according to standard methods.

2.2. Preparation of chiral thiophene ligands

H_2O (15 mL) and EtOH (30 mL) were added to a mixture of (*R*,*R*)-1,2-diammoniumcyclohexane mono-(+)-tartrate salt (1.32 g, 5 mmol) and K_2CO_3 (1.28 g, 10 mmol), and then refluxed with stirring for 5 h. A solution of 5-(thiophen-2-yl)thiophene-2-carbaldehyde in EtOH (1.94 g, 10 mmol in 10 mL) was added. Afterwards the mixture continued stirring with reflux for 2 more days, followed by a CH_2Cl_2 extraction. The combined extracts were washed with H_2O and dried over anhydrous Na_2SO_4, followed by filtration and concentration. The crude product was then recrystallised from hot ethanol to give diimino-bis(bithiophene) ligand (*R*,*R*)-**3** as a white solid (2.12 g, 91% yield).

A solution of (*R*,*R*)-**3** (2.00 g, 4.29 mmol) and $NaBH_4$ (3.25 g, 85.8 mmol) in absolute ethanol (80 mL) was refluxed with stirring for 2 days. The solution was then cooled to room temperature. H_2O was added to destroy excess $NaBH_4$, followed by a CH_2Cl_2 extraction. The combined extracts were washed with saturated NH_4Cl solution and H_2O successively. The organic layer was dried over anhydrous Na_2SO_4, followed by filtration, then concentrated to give diamino-bis(bithiophene) ligand (*R*,*R*)-**4** as a white solid (1.90 g, 94% yield).

The ligands (*S*,*S*)-**3** and (*S*,*S*)-**4** were also synthesized via the similar procedure above.

2.3. Synthesis and characterization of chiral Ir(I)/diamino-bis(bithiophene) complexes

CH_2Cl_2 (7 mL) was added to a mixture of (*R*,*R*)-**4** (0.471 g, 1.0 mmol) and $[Ir(COD)Cl]_2$ (0.336 g, 0.5 mmol). The solution was stirred at room temperature and a yellow precipitate formed immediately. After stirring for 2.5 additional hours, a solid was collected by filtration, washed with a few milliliters of CH_2Cl_2 and dried under vacuum to afford [Ir(COD)-(*R*,*R*)-**4**]Cl (0.605 g, 75% yield). $\Lambda_m = 56.23\ \Omega^{-1}\ cm^2\ mol^{-1}$. ^1H NMR (400 MHz, CD_3OD): δ 0.93–1.12 (m, 4H), 1.32–1.42 (m, 2H), 1.67 (d, J = 8.4 Hz, 2H), 2.24–2.32 (m, 4H), 2.33–2.44 (m, 4H), 2.90–3.03 (m, 2H), 3.53–3.61 (m, 2H), 3.94 (d, J = 15.2 Hz, 2H), 4.56–4.63 (m, 4H), 7.13 (dd, J_1 = 3.6 Hz, J_2 = 5.2 Hz, 2H), 7.17–7.21 (m, 4H), 7.34 (dd, J_1 = 1.2 Hz, J_2 = 3.6 Hz, 2H), 7.43 (dd, J_1 = 0.8 Hz, J_2 = 5.2 Hz, 2H). ^{13}C NMR (100 MHz, CD_3OD): δ 26.5, 28.5, 30.3, 37.0, 46.8, 64.5, 67.6, 71.7, 124.4, 125.9, 127.0, 130.0, 132.4, 136.3, 129.0, 142.0. IR (KBr): 3432, 3105, 3068, 2935, 2852, 2832, 1629, 1467, 1383, 1202, 1046, 1007, 800, 723, and 695 cm^{-1}. EIMS (m/z): 771.2 (M−Cl). $[\alpha]_D^{20} = 36.1$ (c 1.0, CH_3OH).

The complex [Ir(COD)-(*S*,*S*)-**4**]Cl was also synthesized by the same procedure. $[\alpha]_D^{20} = -36.8$ (c 1.0, CH_3OH).

2.4. Typical procedure for ATH of ketones

A solution of $IrCl(CO)(PPh_3)_2$ (3.9 mg, 0.005 mmol) and ligand (*R*,*R*)-**4** (2.6 mg, 0.0055 mmol) in ^{i}PrOH (5 mL) was stirred for 20 min. A solution of KOH in ^{i}PrOH (0.06 mmol in 0.6 mL) and isobutyrophenone (0.5 mmol) were introduced, and then the solution was stirred at 45 °C for 16 h. The reaction mixture was then filtered through a pad of silica gel and analyzed by GC using a chiral CP-Chirasil-Dex CB column, giving 96% yield and 90% ee.

3. Results and discussion

Chiral thiophene ligands **1–4** were prepared according to literature procedure [31]. We used (*R*,*R*)-1,2-diammoniumcyclohexane mono-(+)-tartrate salt instead of (*R*,*R*)-1,2-cyclohexanediamine (Scheme 1). Ligands **3** and **4** were obtained with high chemical yield (91% and 94%, respectively).

Recently, Umani-Ronchi reported the application of chiral diamine ligands (*R*,*R*)-**2** and **4** in asymmetric allylic alkylation and hydrosilylation, but the molar ratios of substrate to ligand were very low [31,32]. In our earlier studies, we used diamino-bis(thiophene) ligands **2** as chiral auxiliaries in ATH. In continuation with our findings, we decided to employed chiral diamino-bis(bithiophene) ligands **4** in ATH of aromatic ketones, giving the corresponding optically active alcohols with high yield and fair to good enantioselectivities.

Table 1
ATH of propiophenone with (*R*,*R*)-**4** and various metal complexes as catalyst precursors[a].

Entry	Metal complex	Alcohol	
		Yield[b] (%)	Ee[b] (%)
1	$Ru_3(CO)_{12}$	29	61
2	$[RuCl_2(COD)]_n$	94	22
3	$[RuCl_2(cymene)]_2$	98	19
4	*trans*-$RhCl(CO)(PPh_3)_2$	34	47
5[c]	$RhH(CO)(PPh_3)_3$	20	47
6	$Pd(CH_3CN)_2Cl_2$	0	–
7	$IrCl(COD)PPh_3$	97	56
8[c]	$IrH(CO)(PPh_3)_3$	96	68
9	$IrCl(CO)(PPh_3)_2$	97	76

[a] Reaction conditions: propiophenone, 0.5 mmol; Sub.:[M]:ligand:KOH = 100:1:1.1:8; ^{i}PrOH, 5 mL; temp., 45 °C; time, 16 h.

[b] Yield and ee were determined by GC analysis using chiral CP-Chirasil-Dex CB column.

[c] Temp., 60 °C.