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A novel planar chiral *N*-heterocyclic carbene–oxazoline ligand for the asymmetric hydrosilylation of ketones

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ABSTRACT

A novel ferrocene-based planar chiral *N*-heterocyclic carbene–oxazoline ligand was synthesized and applied to the rhodium(I)-catalyzed asymmetric hydrosilylation of ketones. Moderate catalytic activity and enantioselectivity were obtained.

1. Introduction

Metal-catalyzed asymmetric hydrosilylation of prochiral ketones followed by hydrolysis provides one of the most efficient methods for the preparation of chiral secondary alcohols. Dating from the pioneering work of Ojima, Kagan and Brunner [1–4], various metals, chiral ligands as well as hydride sources have been screened [5–7]. As for rhodium-catalyzed asymmetric hydrosilylation, bidentate chiral P, *N*-ligands, particularly phosphine–oxazoline ligands, have played a dominant role and some of them have achieved excellent activities and enantioselectivities [8–16].

Chiral *N*-Heterocyclic carbenes (NHCs) as effective alternatives to chiral phosphine ligands in asymmetric catalytic processes are attracting increasing attention due to their strong σ-donating and weak π-accepting properties [17,18]. Both mono-and bis-NHC ligands, of which only the carbene carbon atom(s) coordinate(s) to the metal center, have been applied to rhodium-catalyzed asymmetric hydrosilylation of ketones with excellent catalytic activities, but poor to moderate enantioselectivities [19–21]. Inspired by the good results obtained with phosphine–oxazoline ligands, several research groups have in recent years synthesized carbene–oxazoline chelating ligands and applied some of them in the asymmetric hydrosilylation of ketones [22]. In 1998, Herrmann reported the synthesis of the first chiral carbene–oxazoline ligand (Fig. 1a). In this bidentate ligand, the oxazoline ring is linked in its 2-position to the imidazole ring via a methylene bridge [23]. In 2004, Gade and co-workers reported the synthesis of a family of carbene–oxazoline ligands which were obtained by direct linkage of the two heterocycles (Fig. 1b). Their complexes with rhodium(I) achieved enantioselectivities up to 95% ee in the asymmetric hydrosilylation of prochiral dialkylketones [24,25]. In 2005, Bolm reported a series of ferrocene-based carbene–oxazoline ligands in which the imidazole ring was linked to ferrocene via a methylene bridge (Fig. 1c). All of their complexes with rhodium(I) were active giving the secondary alcohol in high yields but with very low enantioselectivities (<6% ee) [26]. With the goal of improving the catalyst performance, we designed and synthesized a novel ferrocene-based chiral carbene–oxazoline ligand precursor **1** possessing a rigid backbone by direct linkage of the imidazole ring to ferrocene (Fig. 2), and examined its efficiency in the asymmetric hydrosilylation of prochiral ketones.

2. Experimental

2.1. General remarks

Solvents were purified by standard procedures. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AV-400 spectrometer. High performance liquid chromatography (HPLC) was performed by an Agilent 1100 interfaced to a HP 71 series computer workstation with a Daicel Chiralcel OD–H chiral column. Gas chromatography analyses were performed on a chiral CP-Cyclodex-β-236 M-19 column (25 m × 0.32 mm) on Varian CP-3800. Optical rotations

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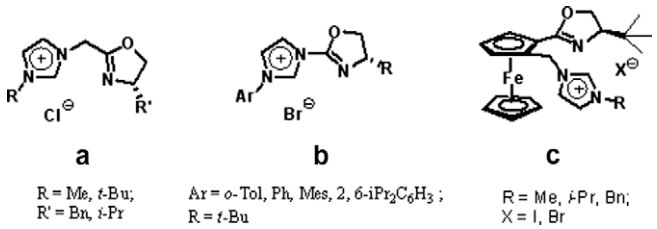

Fig. 1. Reported carbene–oxazoline ligands (imidazolium procursors).

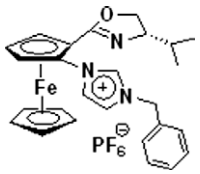

Fig. 2. Chiral carbene precursor **1**.

were measured on a Perkin–Elmer 343 Polarimeter. Commercial reagents were used as received, unless otherwise stated. THF, Et_2O and toluene were dried over sodium and freshly distilled before use. Compounds **3–5** were prepared according to published procedures [27–29].

2.2. Preparation of **6**

To a well-dried Schlenk tube, CuI (48 mg, 0.25 mmol), imidazole (0.51 g, 6 mmol) and Cs_2CO_3 (3.42 g, 10.5 mmol) were added, evacuated twice and back-filled with nitrogen. Dioxane (5 mL), **5** (2.12 g, 5 mmol) and *trans*-1,2-cyclohexane diamine (0.11 g, 1 mmol) were then successively added under nitrogen. The Schlenk tube was sealed and the reaction mixture was stirred with heating at 110 °C for 24 h. The reaction mixture was cooled to ambient temperature, diluted with 250 mL of ethyl acetate, and filtered through a plug of silica gel followed by eluting with 500 mL of ethyl acetate. The filtrate was concentrated and the resulting residue was purified by column chromatography (hexane/ethyl acetate 1:5) to provide 0.95 g of **6** (51% yield). $[\alpha]_D$ = +26.3 (*c* 0.135, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.84 (d, *J* = 6.68 Hz, 3H), 0.91 (d, *J* = 6.74 Hz, 3H), 1.70 (m, 1H), 3.90 (m, 2H), 4.17–4.30 (m, 7H), 4.53 (m, 1H), 4.70 (m, 1H), 6.99 (s, 1H), 7.21 (s, 1H), 7.83 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.3, 18.8, 32.6, 61.3, 65.7, 66.9, 67.9, 68.5, 69.6, 70.4, 71.2, 72.0, 72.6, 93.9, 122.6, 128.3, 139.8, 163.0 ppm. HRMS (ESI): calcd. for $[M+H]^+$: 364.1112, found 364.1091.

2.3. Preparation of **1**

Benzyl bromide (0.85 g, 5 mmol) in dry acetonitrile (3 mL) was added dropwise into a solution of **6** (1.82 g, 5 mmol) in dry acetonitrile (5 mL) under reflux. The mixture was further refluxed for 1.5 h. TLC showed the consumption of **6**. $TlPF_6$ (1.75 g, 5 mmol) in acetonitrile (10 mL) was added dropwise into the reaction solution under vigorous stirring. A precipitate formed promptly, and the mixture was further stirred for 20 min. After filtration, the solvent was removed *in vacuo*. The residue was purified by column chromatography (CH_2Cl_2) to give 2.13 g of **1** as a brown oil (70% yield). $[\alpha]_D$ = −43.2 (*c* 0.09, $CHCl_3$), ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.70 (d, *J* = 6.63 Hz, 3H), 0.76 (d, *J* = 6.69 Hz, 3H), 1.53 (m, 1H), 3.69 (m, 1H), 3.83 (t, *J* = 8.13 Hz, 1H), 4.09 (t, *J* = 9.41 Hz, 1H), 4.22 (s, 5H), 4.33 (s, 1H), 4.65 (s, 1H), 4.79 (s, 1H), 5.26 (m, 2H), 7.11 (s, 1H), 7.27 (s, 5H), 7.51 (s, 1H), 8.92 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.2, 18.9, 32.4, 53.6, 64.4, 65.7, 68.4, 68.5, 69.5, 69.6, 72.2, 72.5, 72.7, 92.2, 121.5, 125.9, 129.1, 129.4, 129.5, 132.6, 137.8, 162.5 ppm. HRMS (ESI): calcd. for $[M-PF_6]^+$: 454.1582, found 454.1539.

2.4. Preparation of **7**

t-BuOK (0.11 g, 0.95 mmol), $[Rh(COD)Cl]_2$ (0.22 g, 0.45 mmol) and **1** (0.54 g, 0.90 mmol) were added into dry THF (8 mL) under nitrogen. The mixture was refluxed for 12 h. After the solvent was removed *in vacuo*, the residue was purified by column chromatography (CH_2Cl_2) to afforded 0.60 g of **7** as an orange air stable solid (75% yield). $[\alpha]_D$ = −541.0 (*c* 0.083, Acetone); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.87 (t, *J* = 6.38 Hz, 6H), 1.69–1.74 (m, 3H), 1.94 (s, 3H), 2.09–2.30 (m, 2H), 2.40–2.59 (m, 1H), 3.35 (s, 1H), 3.75–3.78 (m, 2H), 4.15 (m, 1H), 4.37–4.42 (m, 6H), 4.53 (t, *J* = 9.62 Hz, 1H), 4.68 (m, 1H), 4.88–4.91 (m, 3H), 5.54 (d, *J* = 15.16 Hz, 1H), 5.67 (d, *J* = 15.15 Hz, 1H), 7.02 (s, 1H), 7.23–7.27 (m, 2H), 7.39–7.43 (m, 3H), 7.68 (s, 1H) ppm. ^{13}C NMR (100 MHz, $(CD_3)_2CO$): δ 17.4, 17.6, 27.9, 32.3, 34.3, 55.1, 67.3, 69.3, 69.4, 70.3, 70.4, 71.0, 71.3, 71.7, 73.0, 80.0, 97.6, 97.7, 98.9, 123.7, 126.7, 128.4, 129.2, 129.3, 129.8, 137.5, 166.9, 167.0, 181.2 (d, $^1J_{C-Rh}$ = 51.1 Hz, C-Rh) ppm. HRMS (ESI): calcd. for $[M-PF_6]^+$: 664.1498, found 664.1400.

2.5. General procedure for the asymmetric hydrosilylation reaction

Under nitrogen, catalyst **7** (16.0 mg, 0.02 mmol) and ketone (1 mmol) were added into THF (1 mL). Silane (1.5 mmol) in dry THF (1 mL) was added by syringe within 20 min at 25 °C. Then the mixture was stirred for 24 h at this temperature. *p*-Tolylsulfonic acid in methanol (1%, 1 mL) was added to hydrolyze the silyl ether at 0 °C, and the mixture was further stirred for 30 min at ambient temperature. After the solvent was evaporated, the product was purified by column chromatography with petroleum ether/diethyl ether (6:1–2:1). All products had *S* configuration, which were determined by comparing the optical rotations with the reported values [30]. Enantiomeric excesses were determined by HPLC with a Chiralcel OD–H column or by GC using a chiral CP-Cyclodex-β-236 M-19 column.

3. Results and discussion

The planar chiral carbene precursor **1** was synthesized from ferrocene–carboxylic acid **2** (Scheme 1). Treatment of **2** with oxalyl chloride and (*S*)-valinol successively led to the formation of amide **3** in 86% yield, which was transformed into **4** in 84% yield by cyclization using Appel's method [27]. After a highly diastereoselective *ortho*-lithiation followed by treatment with 1,2-diiodoethane, **5** was obtained in 79% yield [28,29]. Then **5** was allowed to react with imidazole in the presence of Cs_2CO_3, CuI and *trans*-1,2-cyclohexane diamine in dioxane at 110 °C. The resulting ferrocene imidazole **6** was treated with benzyl bromide followed by anion exchange with $TlPF_6$ to give ferrocene imidazolium salt **1**, which is hygroscopic upon exposure to the ambient atmosphere. This behavior, however, did not influence the transformation of imidazolium salt to its corresponding metal complex.

The ferrocene imidazolium salt **1** was treated with $[Rh(COD)Cl]_2$ in THF in the presence of *t*-BuOK to give the carbene rhodium complex **7** as an orange air stable crystal in 75% yield (Scheme 2). The analytical and spectroscopic data for **7** are consistent with its proposed structure. The ^{13}C NMR spectra showed the expected signals for the carbene carbon linking with Rh at around 181.2 ppm. The mass spectra showed strong characteristic signals for the $[M^+-PF_6]$ fragment.