Catalysis Communications 57 (2014) 111–114

Contents lists available at ScienceDirect

Catalysis Communications

journal homepage: www.elsevier.com/locate/catcom

Short Communication

Imidazolium ion tethered TsDPENs as efficient water-soluble ligands for rhodium catalyzed asymmetric transfer hydrogenation of aromatic ketones

Guowei Kang, Silong Lin, Atul Shiwakoti, Bukuo Ni *

Department of Chemistry, Texas A&M University-Commerce, Commerce, TX 75429-3011, USA

ARTICLE INFO

Article history:
Received 17 June 2014
Received in revised form 31 July 2014
Accepted 3 August 2014
Available online 12 August 2014

Keywords:
Asymmetric catalysis
Transfer hydrogenation reaction
Ketones
Water
Alcohols

ABSTRACT

An imidazolium ion tethered TsDPEN has been synthesized readily and used as a water-soluble ligand for $[Cp^*RhCl_2]_2$ catalyzed asymmetric transfer hydrogenation (ATH) of aromatic ketones in water. This process provided the secondary alcohols in moderate to excellent conversions (up to 100%) with high enantioselectivities (up to 98% ee) under mild reaction conditions without adding any surfactants. The catalytic system is highly effective with the substrate to catalyst (S/C) ratio of 500 and low hydride donor loading of 1.5 equiv. of HCO_2Na. The procedure presented is simple and makes this method suitable for practical use.

1. Introduction

Catalytic asymmetric reactions that can be performed in water are of current interest because water is a safe, economical, nontoxic, and environmentally benign solvent, compared to typical organic solvents [1, 2]. Moreover, when a reaction is carried out in water, the hydrophobic products can be isolated easily by simple separation. However, the use of water as reaction media is still not always practical for the field of asymmetric synthesis, essentially because most metal catalysts are unstable toward hydrolysis or water disrupts the transition state of the reactions and other polar interactions between organic substrate and catalyst in water [3, 4]. In order to overcome these drawbacks, special design of phase-transfer catalysts or additions of amphiphilic surfactants are generally required achieving high reactivity and selectivity in water [3, 4]. Therefore, development of a catalyst that is not only active in aqueous media but also stable and soluble in this solvent would be highly desirable.

Asymmetric transfer hydrogenation (ATH) of ketones is without question one of the most versatile and powerful methods for the synthesis of enantiomerically pure secondary alcohols [5–7], which are an invaluable and important class of intermediates for the fine chemicals and pharmaceuticals [8, 9]. Since the pioneering work by Noyori and coworkers by the use of N-(p-toluenesulfonyl)-1,2-diphenylethylenediamine (TsDPEN) as ligand for Ru(II) catalyzed ATH of ketones [10], a great deal of effort has been devoted to the design and synthesis of more efficient chiral ligands for this cornerstone transformation, and a significant number of new ligands have been developed for the ATH of ketones with Ru(II), Ir(III), and Rh(III) complexes as catalysts using isopropanol/KOH or $HCOOH/Et_3N$ as a hydride source [11–16]. In 2001 the first example of Ru(II)-catalyzed ATH of ketones with HCO_2Na as a hydride source in aqueous media was reported [17]. Since this discovery, a number of water-soluble ligands and catalysts have been developed for ATH in aqueous media providing the reduction products in high conversion yields and enantioselectivities [18–26]. However, a major problem associated with these catalytic systems is that the low substrate/catalyst (S/C) ratio (normally S/C = 100) and large excess amounts of hydride donor (≥5 equiv. of HCO_2Na) are generally required for the reactions to achieve good conversion in reasonable time scales with good enantioselectivity [27–29]. For example, Chung and co-workers described a water-soluble Ru(II) complex that promoted highly enantioselective ATH of aromatic ketones. However, when the amount of hydride source HCO_2Na was lowered to 2 equiv., they found that both the catalytic activity and the enantioselectivity were considerable reduced [30]. Therefore, the development of efficient catalytic systems aimed at raising S/C ratio, reducing the quantity of hydride donor and being active in aqueous media has proved to be a significant challenge. In continuation of our research interest in the development of water-compatible catalysts that are effective in aqueous media [31, 32], we herein, wish to report our recent effort in the synthesis of imidazolium ion tethered TsDPENs and their use as

* Corresponding author. Fax: +1 9034686020.
E-mail address: bukuo.ni@tamuc.edu (B. Ni).

http://dx.doi.org/10.1016/j.catcom.2014.08.006
1566-7367/

water-soluble ligands for Rh(III)-catalyzed ATH of aromatic ketones in pure water with a substrate to catalyst (S/C) ratio of 500 and only the use of 1.5 equiv. of hydride donor HCO_2Na.

2. Experimental

2.1. Material and instruments

All commercially available chemicals and solvents were used as received. NMR spectra were obtained at 400 MHz (^{1}H NMR) and 100 MHz (^{13}C NMR). Chemical shifts are reported in ppm relative to the internal standard of TMS. All the compounds synthesized (shown in Table 2) in the manuscript are known compounds. Their absolute configurations of the products were determined by comparison with the known optical rotation and chiral HPLC analysis. HPLC analysis was performed using ChiralPak columns.

2.2. (S,S)-N-Boc-N′-(4-bromomethylphenylsulfonyl)-1,2-diphenylethylenediamine *3*

To a solution of (S,S)-N-Boc-1,2-diphenylethylenediamine **1** (1.87 g, 6.0 mmol) and Et_3N (0.84 mL, 6.0 mmol) in dry CH_2Cl_2 (20 mL) cooled in an ice-bath was added dropwise 4-bromomethylphenylsulfonyl chloride **2** (1.94 g, 7.2 mmol) in CH_2Cl_2 (10 mL). After the ice-bath was removed, the reaction mixture was stirred at room temperature for 2 h. Water was added to the reaction mixture. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 20 mL), combined with the organic phase and dried over Na_2SO_4. After concentration, the solid was purified by flash chromatography on silica gel (hexane/ethyl acetate = 4:1 to ethyl acetate) to afford the product **3** (2.65 g, 81%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (d, J = 8.0 Hz, 2H), 7.20–7.13 (m, 5H), 6.98–6.92 (m, 5H), 6.72 (d, J = 8.0 Hz, 2H), 6.31 (s, 1H), 5.18 (s, 1H), 4.77 (dd, J = 10.0 and 8.0 Hz, 1H), 4.61 (dd, J = 10.0 and 6.8 Hz, 1H), 4.35 (s, 2H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.1, 141.6, 141.3, 140.7, 137.8, 137.4, 137.3, 129.0, 128.6, 128.5, 128.0, 127.6, 127.5, 127.4, 127.3, 127.2, 80.8, 64.4, 60.1, 44.9, 31.6, 28.3. This intermediate was used for the next step without further characterization.

2.3. Typical procedure for the synthesis of imidazolium ion tethered TsDPENs *5a*

A solution mixture of the intermediate **3** (818 mg, 1.5 mmol) and 1,2-dimethyl imidazole (173 mg, 1.8 mmol) in acetonitrile (2 mL) was heated at 70 °C for 30 h. The solvent was removed under reduced pressure, and the residue was washed with a mixture solvent (hexane/ethyl acetate = 10:1) and dried in vacuo to give an intermediate **4a**, to which HCl solution (3 mL, 4 M in dioxane) was added. The reaction mixture was stirred at room temperature for 5 h and the precipitation was filtered and washed with hexane to give the Boc deprotected intermediate, which was used for the next step directly without further characterization.

The Boc deprotected intermediate was subsequently neutralized by Na_2CO_3 (159 mg, 1.5 mmol) in MeOH (2 mL). The mixture was stirred for 5 h and the solvent was removed to dryness. The solid residue was dissolved in dry CH_2Cl_2 and filtered, and concentrated to give the product **5a** as a white solid (550 mg, 68% yield for 2 steps). $[\alpha]_D^{23} = -68.4$ (c = 0.8, CH_3OH); ^{1}H NMR (400 MHz, CD_3OD): δ 7.60–7.55 (m, 3H), 7.40–7.38 (m, 1H), 7.20–7.14 (m, 7H), 6.90–6.80 (m, 5H), 5.36 (s, 2H), 4.68 (d, J = 10.4 Hz, 1H), 4.50 (d, J = 10.4 Hz, 1H), 3.86 (s, 3H), 2.56 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD): δ 145.1, 140.9, 138.0, 135.6, 134.4, 128.5, 127.8, 127.6, 122.7, 121.2, 62.3, 59.4, 50.4, 34.4, 8.7; HRMS (ESI) calcd for $[C_{26}H_{29}N_4O_2S]^+$: 461.2011, found: 461.2013.

2.4. Synthesis of TsDPENs *5b*

Compound **5b** was synthesized using the same procedure as that used for **5a**, yield: 75%; $[\alpha]_D^{23} = -64.9$ (c = 0.8, CH_3OH); ^{1}H NMR (400 MHz, CD_3OD): δ 7.64 (d, J = 2.0 Hz, 1H), 7.56–7.53 (m, 2H), 7.41 (d, J = 2.0 Hz, 1H), 7.17–7.12 (m, 7H), 6.88–6.77 (m, 5H), 5.35 (s, 2H), 4.57 (d, J = 10.0 Hz, 1H), 4.30 (d, J = 10.0 Hz, 1H), 4.18 (t, J = 7.6 Hz, 2H), 2.57 (s, 3H), 1.85–1.76 (m, 2H), 1.42–1.35 (m, 2H), 0.97 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, CD_3OD): δ 146.6, 143.5, 140.1, 139.3, 139.0, 130.4, 130.2, 129.9, 129.8, 129.7, 129.3, 123.8, 65.8, 62.2, 52.7, 50.3, 33.6, 21.4, 14.7, 11.1; HRMS (ESI) calcd for $[C_{29}H_{35}N_4O_2S]^+$: 503.2481, found: 503.2483.

2.5. Synthesis of TsDPENs *5c*

Compound **5c** was synthesized using the same procedure as that used for **5a**, yield: 63%; $[\alpha]_D^{23} = -51.8$ (c = 0.6, CH_3OH); ^{1}H NMR (400 MHz, CD_3OD): δ 7.63–7.55 (m, 3H), 7.46–7.32 (m, 6H), 7.20–7.11 (m, 7H), 6.76–6.75 (m, 5H), 5.43 (s, 2H), 5.35 (s, 2H), 4.63 (d, J = 10.4 Hz, 1H), 4.41 (d, J = 10.4 Hz, 1H), 2.56 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD): δ 147.0, 143.3, 140.1, 138.0, 137.2, 135.8, 131.3, 131.0, 130.8, 130.6, 130.0, 129.9, 129.8, 129.5, 124.2, 124.1, 64.8, 61.7, 53.8, 52.8, 11.5; HRMS (ESI) calcd for $[C_{32}H_{33}N_4O_2S]^+$: 537.2319, found: 537.2326.

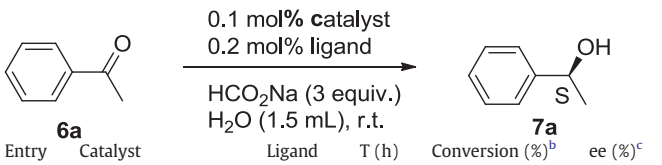
2.6. Synthesis of TsDPENs *5d*

Compound **5d** was synthesized using the same procedure as that used for **5a**, yield: 71%; $[\alpha]_D^{23} = -59.6$ (c = 0.8, CH_3OH); ^{1}H NMR (400 MHz, CD_3OD): δ 7.61 (d, J = 2.0 Hz, 1H), 7.48 (d, J = 8.4 Hz, 2H), 7.36 (d, J = 2.0 Hz, 1H), 7.17 (d, J = 8.4 Hz, 2H), 7.10–7.01 (m, 5H), 6.89–6.82 (m, 3H), 6.75 (d, J = 6.8 Hz, 2H), 5.43 (s, 2H), 4.85 (s, 2H), 4.40 (d, J = 8.8 Hz, 1H), 4.00 (d, J = 8.8 Hz, 1H), 3.95 (s, 3H); ^{13}C NMR (100 MHz, CD_3OD): δ 147.6, 143.8, 142.7, 140.5, 140.0, 130.1, 130.0, 129.7, 129.5, 129.2, 128.9, 125.8, 124.0, 67.5, 63.0, 53.3, 52.8, 36.8; HRMS (ESI) calcd for $[C_{26}H_{29}N_4O_3S]^+$: 477.1961, found: 477.1963.

2.7. General procedure for asymmetric transfer hydrogenation

To a solution of ligand **5d** (2.1 mg, 0.004 mmol) in water (1 mL) was added $[Cp^*RhCl_2]_2$ (1.2 mg, 0.002 mmol), HCO_2Na (41 mg, 3.0 mmol), and ketone (2.0 mmol). The reaction mixture was stirred at room temperature for the time as indicated in Tables 1 and 2. The reaction

Table 1
Optimization of reaction conditions for the asymmetric hydrogenation of acetophenone.[a]



6a 7a

Entry	Catalyst	Ligand	T (h)	Conversion (%)[b]	ee (%)[c]
1	$[Cp^*RhCl_2]_2$	**5a**	14	100	96
2	$[Cp^*RhCl_2]_2$	**5b**	9	100	97
3	$[Cp^*RhCl_2]_2$	**5c**	10	100	97
4	$[Cp^*RhCl_2]_2$	**5d**	7	100	97
5	$[Cp^*RhCl_2]_2$	TsDPEN	25	100	96
6	$[RuCl_2(p\text{-cymene})]_2$	**5d**	72	94	95
7	$[Cp^*IrCl_2]_2$	**5d**	72	97	94
8[d]	$[Cp^*RhCl_2]_2$	**5d**	11	100	96
9[d,e]	$[Cp^*RhCl_2]_2$	**5d**	8	100	96
10[f]	$[Cp^*RhCl_2]_2$	**5d**	36	18	96

[a] Reactions performed on a 2 mmol scale at room temperature in 1.5 mL H_2O.
[b] Determined by ^{1}H NMR.
[c] Determined by HPLC analysis.
[d] 1.5 equiv. of HCO_2Na was used.
[e] 1.0 mL H_2O was used.
[f] The second run, 2 mmol HCO_2H was added to regenerate HCO_2Na.