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Journal of Molecular Catalysis A: Chemical 256 (2006) 219–224

JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL

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Siliceous mesocellular foam-supported chiral bisoxazoline: Application to asymmetric cyclopropanation

Su Seong Lee[a,b], Jackie Y. Ying[a,b,*]

[a] *Department of Chemical Engineering, Massachusetts Institute of Technology, Cambridge, MA 02139, USA*
[b] *Institute of Bioengineering and Nanotechnology, 31 Biopolis Way, The Nanos, Singapore 138669, Singapore*

Received 8 November 2005; received in revised form 3 April 2006; accepted 10 April 2006

Abstract

Chiral bisoxazolines were covalently immobilized onto siliceous mesocellular foams (MCF) by a simple method. The heterogenized bisoxazoline-copper catalysts showed high enantioselectivity (up to 85% enantiomeric excess (ee)) and excellent recyclability in asymmetric cyclopropanation reactions.

Keywords: Bisoxazoline; Mesoporous; Cyclopropanation; Immobilization

1. Introduction

Chiral bisoxazolines have been used in various asymmetric catalytic reactions [1]. They can be synthesized easily from chiral aminoalcohols, which are derived from amino acids. Recently, several new asymmetric reactions by chiral bisoxazolines have been reported [2], showing that these catalysts are very useful. However, these ligands are expensive, and high catalyst-to-substrate ratios are required to achieve good enantioselectivities and reactivities.

Several research groups have reported on heterogenizing chiral bisoxazolines [3]. Most heterogenized bisoxazolines are polymer-supported [4,5], although a few silica-supported bisoxazolines [6–8] have been reported. Silica-supported catalysts are more easily recycled, and have better stability than polymer-supported catalysts. However, silica has a high density of surface silanol groups, which can adversely impact the catalytic reactions [7,8], and silica is a more difficult support for the covalent immobilization of ligands.

Nitrogen-containing chiral ligands, such as chiral bisoxazolines, have a low Rf value on TLC plate. This indicates a strong interaction between the ligands and silica surface. After ligand immobilization, the strong interaction between ligand and silica surface may impact the formation of metal complexes, leading to low enantioselectivity. Some previous studies showed that capping of free silanol groups after immobilization of chiral ligands improved the enantioselectivity and regioselectivity by preventing strong interaction between the ligands and silanol groups [7,8].

Herein, we report the immobilization of chiral bisoxazolines onto MCF, which is a stable mesoporous silica with interconnected pores [9]. The effect of capping the free silanol groups on the MCF support, and the role of linker group in immobilizing the bisoxazoline ligand onto MCF were investigated.

2. Experimental

2.1. General

MCF, MCM-48, and SBA-15 were synthesized according to the literature procedures [9,10]. A commercial silica (60 Å pores, BET surface area ~500 m^2/g, pore volume = 0.75 cm^3/g) was purchased from Aldrich. Other chemicals were purchased from commercial suppliers, and were used without further purification. *Tert*-butyl-bisoxazolines (tBBOX) (**1**), anhydrous tetrahydrofuran (THF), anhydrous toluene, anhydrous CH_2Cl_2, styrene, phenylhydrazine and ethyldiazoacetate (EDA) were purchased from Aldrich. 3-Iodopropyltrimethoxysilane and [(chloromethyl)phenylethyl]trimethoxysilane were purchased

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[*] Corresponding author. Tel.: +65 6824 7100; fax: +65 6478 9020.
E-mail address: jyying@ibn.a-star.edu.sg (J.Y. Ying).

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doi:10.1016/j.molcata.2006.04.018

from Gelest Inc. Photoacoustic Fourier-transform infrared (PA-FTIR) spectra were obtained with a MTEC Model 200 photoacoustic cell on a Bio-Rad FTS-60A spectrometer.

2.2. Preparation of MCF-supported bisoxazoline

2.2.1. Preparation of 2

n-Butyllithium (*n*-BuLi) (1.6 M in hexane, 980 μL, 1.57 mmol) was added to a solution of tBBOX (**1**) (209 mg, 0.78 mmol), diisopropylamine (*i*-Pr_2NH) (110 μL, 0.78 mmol, 1 equiv.) and tetramethylethylenediamine (TMEDA) (237 μL, 1.57 mmol, 2 equiv.) in THF (15 mL) at −78 °C [11]. The reaction mixture was warmed to −20 °C and stirred for 1 h. The solution was cooled down to −78 °C, and 3-iodopropyltrimethoxysilane (309 μL, 1.57 mmol, 2 equiv.) was added dropwise. The mixture was warmed to room temperature and stirred for 3 days, after which the solvent was evaporated under vacuum. Toluene was added, and the soluble portion was collected by centrifuge and washed with toluene. The solution was added to MCF (1.5 g), which had been dried under vacuum at 180 °C for 1 day. The suspension was stirred at 80 °C for 3 days, filtered through a filter funnel, and washed with toluene (3 × 20 mL), acetone (3 × 20 mL), water (10 × 20 mL), methanol (3 × 20 mL) and CH_2Cl_2 (3 × 20 mL). After drying in vacuum, the desired product (**2**) was obtained.

- PA-FTIR (cm^{-1}): 3427, 2958, 1659, 1085, 809, 459.
- Elemental analysis: C: 11.07%; H: 1.42%; N: 1.21%.
- Loading of tBBOX: 0.432 mmol/g.

2.2.2. Preparation of 3

Methyllithium (MeLi) (1.4 M in ether, 2.27 mL, 3.18 mmol, 2.1 equiv.) was added to a solution of tBBOX (403 mg, 1.51 mmol) in THF (20 mL) at −50 °C. After stirring the mixture at −50 °C for 1 h, [(chloromethyl)phenylethyl]trimethoxysilane (743 μL, 3.02 mmol, 2 equiv.) was added dropwise. The mixture was stirred at room temperature for 2 h, and then heated to 50 °C. It was stirred at 50 °C for 3 days, and the solvent was evaporated under vacuum. Toluene was added, and the toluene phase was collected by centrifugation and washing. The resulting solution was added to MCF (3.0 g), which had been dried under vacuum at 180 °C for 1 day. The suspension was stirred at 80 °C for 3 days, filtered through a filter funnel, and washed with toluene (3 × 20 mL), acetone (3 × 20 mL), water (10 × 20 mL), methanol (3 × 20 mL) and CH_2Cl_2 (3 × 20 mL). After drying in vacuum, the desired product (**3**) was obtained.

- PA-FTIR (cm^{-1}): 3381, 2958, 1656, 1608, 1085, 807, 459.
- Elemental analysis: C: 12.54%; H: 1.28%; N: 0.91%.
- Loading of tBBOX: 0.325 mmol/g.

2.2.3. Capping of free silanol groups with hexamethyldisilazane (HMDS) (4 and 5)

Catalyst **2** or **3** (700 mg) was dried at 80 °C for 2 days. Excess HMDS (700 μL) was added to the dried catalyst in hexane (10 mL). The suspension was stirred at room temperature for 2 days, filtered through a filter funnel, and washed with hexane (3 × 10 mL), acetone (3 × 10 mL), methanol (3 × 10 mL) and CH_2Cl_2 (3 × 10 mL). After drying in vacuum, the desired product (**4** or **5**) was obtained.

Catalyst **4**: PA-FTIR (cm^{-1}): 3449, 2957, 1663, 1089, 842, 811, 460; elemental analysis: C: 13.25%; H: 1.98%; N: 1.09%; loading of tBBOX: 0.389 mmol/g.

Catalyst **5**: PA-FTIR (cm^{-1}): 3443, 2958, 1663, 1608, 1089, 844, 809, 459; elemental analysis: C: 14.92%; H: 1.88%; N: 0.84%; loading of tBBOX: 0.300 mmol/g.

2.3. Preparation of bisoxazoline supported on other silica supports

2.3.1. Immobilization of the chiral bisoxazoline

The same procedure described for **2** was followed, except that the conventional silica supports were activated by refluxing them in 1.0 M aq. HCl solution for 6 h. PA-FTIR spectra of these silica-supported catalysts were similar to that of the MCF-supported catalyst.

Elemental analysis:

- MCM-48-supported bisoxazoline: C: 3.32%; H: 0.42%; N: 0.34%.
- SBA-15-supported bisoxazoline: C: 9.01%; H: 1.17%; N: 0.98%.
- Commercial silica-supported bisoxazoline: C: 6.97%; H: 0.96%; N: 0.76%.

Loading of tBBOX:

- MCM-48-supported bisoxazoline: 0.12 mmol/g.
- SBA-15-supported bisoxazoline: 0.35 mmol/g.
- Commercial silica-supported bisoxazoline: 0.27 mmol/g.

2.3.2. Capping of free silanol groups with HMDS

The same procedure described for **4** was followed for the silica-supported bisoxazoline catalysts. The PA-FTIR spectra of the post-capped catalysts were similar to that of **4**.

Elemental analysis:

- MCM-48-supported bisoxazoline: C: 7.28%; H: 1.03%; N: 0.31%.
- SBA-15-supported bisoxazoline: C: 12.54%; H: 1.62%; N: 0.87%.
- Commercial silica-supported bisoxazoline: C: 10.72%; H: 1.53%; N: 0.71%.

Loading of tBBOX:

- MCM-48-supported bisoxazoline: 0.11 mmol/g.
- SBA-15-supported bisoxazoline: 0.31 mmol/g.
- Commercial silica-supported bisoxazoline: 0.25 mmol/g.

2.4. Cyclopropanation

$(CuOTf)_2$·toluene (0.011 mmol) or $Cu(OTf)_2$ (0.022 mmol) was added to the immobilized bisoxazolines (0.022 mmol) in