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Asymmetric Transfer Hydrogenation Catalyzed by Mesoporous MCM-41-Supported Chiral Ru-Complex

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Chiral *N*-sulfonyldiamine was successfully anchored on mesoporous MCM-41 silica. The MCM-41-supported chiral *N*-sulfonyldiamine was used as an efficient heterogeneous chiral ligand in the asymmetric transfer hydrogenation of ketones. This heterogeneous system offered satisfactory enantioselectivities up to 94% with excellent conversions.

Keywords: *N*-sulfonyldiamine; MCM-41; Immobilization; Asymmetric catalysis; Transfer hydrogenation.

INTRODUCTION

The reduction of ketones to the corresponding secondary alcohols is one of the most important chemical processes in industry and in synthesis-related research laboratories. Usually, ketones can be reduced into alcohols involving a number of reducing reagents, including molecular hydrogen, metal hydrides, and dissolving metals.[1] The transfer hydrogenation of organic compounds has attracted much attention because it is a much safer and more environmentally benign process.[2-8] Homogeneous noble metal catalysts, such as Ru complexes,[9–13] are known to be effective for these kinds of reactions, but they suffer from difficulties in the recovery and reuse of expensive catalysts, and the necessity for co-catalysts. Successful development of homogeneous catalyst has been sometimes followed by attempts to attach the catalyst on an insoluble support. Noble metal-based heterogeneous catalysts were also considered because of their advantages in catalyst recovery and recycling. Supported nanoparticle catalysts, such as Ni,[14–16] Pt[17] and carbon nanotubes[18] have been reported to act as effective and reusable catalysts for these kinds of hydrogen transfer reactions. However, such heterogeneous processes need to be improved because the usage of the catalysts has been very high (i.e. 10–20 mol% Ni), while the conversion of the reactant and the selectivity of the desired product have been very low. The use of well-defined nanostructured mesoporous materials[19-22] magnetic materials,[23] zeolites,[24] organic polymers,[25] or high surface area carbon[26] for catalytic transformations of organic substrates is an exciting and rapidly growing area. Recently, mesoporous MCM materials with uniform nanosized pore diameters and high specific surface areas have become of high interest as inorganic supports.[27-29] Organic groups, in particular, can be robustly anchored to the surface. The attachment of optically active complex with catalytic activity onto such ordered mesoporous materials can create a heterogeneous chiral catalyst.[30]

In general, the sulfonamides and their derivatives have attracted the interest of many researchers due to their importance in the development of coordination chemistry, their application in medicinal chemistry, catalytic fields, etc.[31–39] For example, metal complexes containing sulfonamide ligands have been used as catalysts in different organic reactions.[40–43] The transfer hydrogenation of ketones catalyzed by Ru(II) complexes bearing N-donor ligands has been attracting more and more attention from the catalysis community[44-53] since the success of Noyori's catalyst, bearing 1,2-diamine ligands.[54] Many derivatives of Ru(II) complexes containing N-donor ligands have been aimed to identify a good Ru(II) catalyst for the transfer hydrogenation of ketones. In this paper, we report MCM-41 supported chiral Ru-complex for asymmetric transfer hydrogenation of ketones.

EXPERIMENTAL DETAILS

General: All manipulations were performed under atmospheric conditions otherwise noted. Reagents and solvents were obtained from commercial suppliers and were used without further purification. Water was deionized with a Millipore system as a Milli-Q grade. (1*R*,2*R*)-diaminocyclohexane and 2-(4-chlorosulfonylphenyl)-ethyltrimethoxysilane were purchased from TCI Chemical Industries, Ltd. and [Ru(*p*-cymene)Cl_2]$_2$ was purchased

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from Aldrich. Proton nuclear magnetic resonance (^{1}H NMR, 300 MHz) and carbon nuclear magnetic resonance (^{13}C NMR, 75 MHz) spectra were measured with a JEOL JNM ECA-300 spectrometer. The ^{1}H NMR chemical shifts were reported relative to tetramethylsilane (TMS, 0.00 ppm). The ^{13}C NMR chemical shifts were reported relative to deuterated chloroform ($CDCl_3$ 77.0 ppm). Elemental analysis was performed on a Yanaco CHN Corder MT-6 elemental analyzer by the chemical analysis team in Rikagaku Kenkyūjo (RIKEN), Wako, Japan. Inductively coupled plasma atomic emission spectrometry (ICP-AES) was performed on a Shimadzu ICPS-8100 equipment by the chemical analysis team in RIKEN Wako, Japan. The gas chromatography-mass spectrometry (GC-MS) was measured by an Agilent 7860A/JEOL JMS-T100GC equipped with a capillary column (DB-Wax, 0.25 mm i.d. × 30 m or HP-1, 0.32 mm i.d. × 30 m). Thin layer chromatography (TLC) analysis was performed on Merck silica gel 60 F_{254}. Enantiomeric access was carried out using daicel OD-H column. Column chromatography was carried out on silica gel (Wakogel C-300).

Preparation of the mesoporous silica MCM-41: The MCM-41 silica was prepared similarly to the reported method[55] using cetyltrimethylammonium bromide as a surfactant and tetraethoxysilane as a silicate source. The MCM-41 was characterized by XRD and TEM.

Preparation of the trimethoxysilated *N*-sulfonyl-1,2-diamine 2: To a stirred solution of (1*R*,2*R*)-diaminocyclohexane **1** (200 mg, 1.74 mmol) and triethylamine (176 mg, 1.74 mmol) in CH_2Cl_2 (14 mL), 2-(4-chlorosulfonylphenyl)-ethyltrimethoxysilane (564 mg, 1.74 mmol) was slowly added at -10 °C. The reaction mixture then warmed slowly to room temperature. After stirring for 2 h, the mixture was diluted with CH_2Cl_2 and washed with cold water. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography to give (1*R*,2*R*)-*N*-(trimethoxysilylpropyl-*N*-sulfonyl)-1,2-cyclohaxanediamine **2** in 87% yield. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.84 (t, *J* = 3.4 Hz, 2 H), 1.32-1.45 (m, 4 H), 1.51-1.58 (m, 4 H), 2.12-2.35 (br, 3 H), 2.75 (t, *J* = 3.43 Hz, 2 H), 2.87 (m, 2 H), 3.57 (s, 9 H), 7.45 (d, *J* = 8.52 Hz, 2 H), 7.78 (d, *J* = 8.54 Hz, 2 H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 12.7, 20.5, 22.8, 27.3, 31.8, 49.6, 53.7, 56.8, 127.4, 127.6, 128.1, 128.2, 137.1, 143.2.

Preparation of the MCM-41-supported chiral *N*-sulfonyldiamine 3: Fresh calcinated MCM-41 silica (0.7 g) was added to a starred solution of compound **2** (80 mg, 0.2 mmol) in hot toluene (15 mL) and the mixture was refluxed for 18 h. After filtration, the powder was washed several times with methylene chloride and dried under vacuum at 70 °C to give MCM-41-supported chiral *N*-sulfonyldiamine **3**. Weight gain showed that 0.25 mmol of *N*-sulfonyldiamine moiety was grafted in 1.0 g of MCM-41 silica **3**.

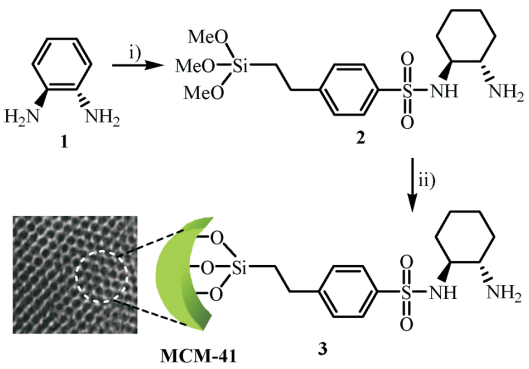
General procedure for the asymmetric transfer hydrogenation: In argon atmosphere, MCM-41-supported chiral *N*-sulfonyldiamine ligand **3** (68 mg, 0.017 mmol) was suspended in water (2 mL) and heated with [Ru(*p*-cymene)Cl_2]$_2$ (6.1 mg, 0.01 mmol) at 80 °C for 1 h. The solution was cooled to room temperature, and then ketone (1 mmol) and HCO_2Na (340 mg, 5 mmol) were added. The mixture was stirred at 40 °C for 15 h and the conversion was measured by GC analysis. The reaction mixture was cooled and diluted with water and ethyl acetate. The organic layer was dried over $MgSO_4$ and evaporated under reduced pressure and the crude product was purified by short-column chromatography. Chiral HPLC (Daicel OD-H column) was used for the determination of enantiomeric excess of the product.

RESULTS AND DISCUSSION

Synthesis and characteristics of the supported chiral ligand

Tu and coworkers have exploited asymmetric transfer hydrogenation of ketones with immobilized Ru-TsDPEN catalysts.[56] Similar to the reported method, the immobilization of *N*-(*p*-toluenesulfonyl)-1,2-diaminocyclohexane onto MCM-41 silica was easily performed through two steps as shown in Scheme 1. Reaction of optically active (1*R*,2*R*)-diaminocyclohexane with 2-(4-chlorosulfonylphenyl)ethyltrimethoxysilane afforded (1*R*,2*R*)-*N*-(trimethoxysilylpropyl-*N*-sulfonyl)-1,2-cyclohaxanediamine **2** in high yield. Subsequent treatment of MCM-41 silica with **2** in refluxing toluene gave MCM-41-supported *N*-sulfonyldiamine **3** (0.25 mmol/g). Some physical proper-

Scheme 1 Preparation of the MCM-41-supported chiral ligand **3**



i) 2-(4-chlorosulfonylphenyl)ethyltrimethoxysilane, Et_3N, CH_2Cl_2 -10 °C, 2 h; ii) MCM-41, toluene, reflux, 18 h.

Table 1. Physical properties of MCM-41-supported chiral ligand **3**

Sample	Surface area	Pore diameter	Pore volume	Loading amount
MCM-41	1130 m^2/g	4.15 nm	0.65 cm^3	-
3	685 m^2/g	3.25 nm	0.53 cm^3	0.25 mmol/g

ties of the immobilized *N*-sulfonyldiamine are summarized in Table 1. The data show that the functionalized MCM-41 possesses characteristic pore structure of mesoporous material containing high specific surface area and high mesoporous volumn. Pore size distribution of MCM-41 silica **3** was similar to parent MCM-41. Surface area and pore diameter of MCM-41 silica **3** decreased due to the grafting of organic functional group. The HRTEM image obtained after the modification of the parent MCM-41 silica is presented in Fig. 1. The hexagonal symmetry of the pore arrays is conserved after the immobilization of *N*-sulfonyldiamine chiral ligand **3** onto MCM- 41 silica, which was also confirmed by XRD (Fig. 2).

Catalytic asymmetric transfer hydrogenation using MCM-41 supported ligand 3

The MCM-41-supported chiral Ru(II) complex was prepared *in situ* by treatment of the supported *N*-sulfonyldiamine **3** with $[Ru(p\text{-cymene})Cl_2]_2$ in H_2O at 80 ºC for 1 h. With the heterogeneous Ru catalyst, we attempted the asymmetric transfer hydrogenation of ketones. The asymmetric transfer hydrogenation of acetophenone was carried out using MCM-41-supported chiral *N*-sulfonyldiamine **3** (1 mol% of Ru complex and 1.7 mol% of chiral ligand) in presence of HCO_2Na (5 mol equiv) at 40 ºC for 15 h in pure water to give the corresponding alcohol in 85% yield with 86% enentiomeric excess (Table 2 **5a**). Then we extended asymmetric transfer hydrogenation reaction to the other ketones. Table 2 summarizes the catalytic performances for asymmetric transfer hydrogenation of aromatic ketones in aqueous medium. When propiophenone and substituted acetophenones were employed as substrates, the catalyst gave satisfactory enantioselectivities with high yield. The enantioselectivity seems to depend on the structure of the ketone. The enantiomeric access increased with decreasing of steric hindrance around the carbonyl group and electron donating group connected to the benzene ring (**5c-f**). It may be because the electron withdrawing groups give lower LUMO values, which accelerates the catalytic reaction. Reactions of chloro and methoxy-substituted acetophenone exhibited high hydrogen transfer rates and comparable enantioselectivities to acetophenone. However, the

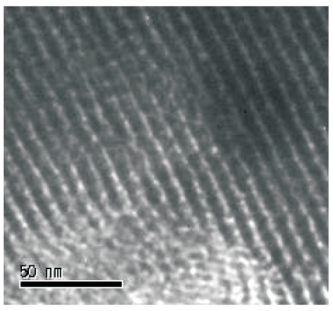


Fig. 1. TEM image of MCM-41 supported ligand **3**.

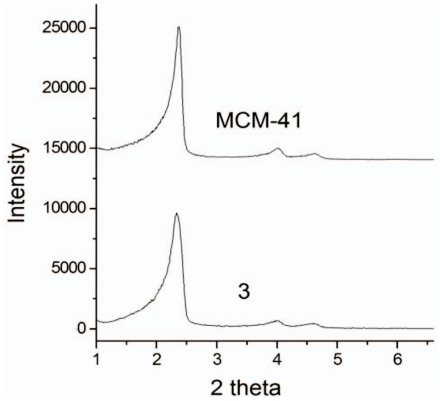
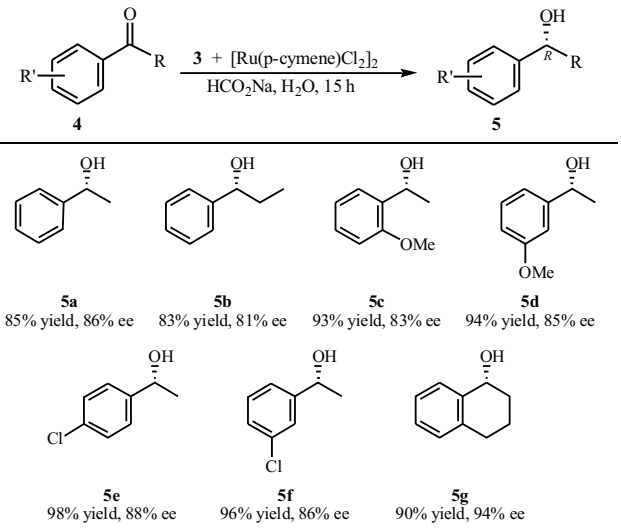


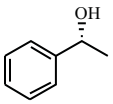
Fig. 2. XRD pattern of MCM-41 supported ligand **3**.

Table 2. Asymmetric transfer hydrogenation of ketones with supported chiral ligand **3**[a]



[a] All reactions were carried out at 40 ºC; ketone:Ru:ligand: HCO_2Na = 100:1:1.7:500. Yield was determined by GC analysis. Ee was determined by HPLC analysis using Daicel OD-H column (3% of 2-propanol in hexane, 1 mL/min).

Table 3. Recycling of the MCM-41-supported chiral ligand **3**[a]

Ketone	Cycle	Conv. (%)[b]	E.e. (%)[c]
	1	85 (99)[d]	86 (94)[d]
	2	86 (99)[d]	85 (94)[d]
	3	81 (25)[d]	82
	4	85	78

[a] Reaction was carried out at 40 °C; ketone:Ru:ligand:HCO_2Na = 100:1:1.7:500. [b] Determined by GC analysis. [c] Determined by HPLC analysis using Daicel OD-H column (3% 2-propanol in hexane, 1mL/min). [d] See ref. 57.

highest enantioselectivity (94%) was observed for the transfer hydrogenation of α-tetralone (**5g**). Recently, G-H Liu *et al.*[57] reported the asymmetric transfer hydrogenatin reaction of aromatic ketone using glass as a solid support, which required 33 mol% of Ru-catalyst. It is noteworthy here that our MCM-41-supported chiral *N*-sulfonyldiamine **3** provided excellent results in terms of yield (98%), enantoselectivity (94%).

Recycle of the MCM-41-supported chiral *N*-sulfonyldiamine 3

The reusability of the immobilized catalyst is one of the important factors for the practical application of heterogeneous catalyst. In order to test the factor, we carried out the transfer reaction of acetophenone in the same reaction conditions (Table 2 **5a**). The supported catalyst was recovered by simple filtration and washed by water-ethyl acetate and directly used to the next reaction without further addition of Ru-complex. It is noteworthy that the catalyst could be used for four times (Table 3) without significance loss of its catalytic activity as well as enantioselectivity.

CONCLUSIONS

We have synthesized MCM-41-supported chiral *N*-sulfonyldiamine **3** as a heterogeneous chiral catalyst, derived from relatively cheap optically pure (1*R*,2*R*)-diaminocyclohexane, for the asymmetric transfer hydrogenation of ketones. The catalyst displayed good catalytic activity and enantioselectivity in the asymmetric transfer hydrogenation of aromatic ketones in aqueous medium, and the substrates with electron-donating groups had less enantioselectivity than those with electron withdrawing groups. Further synthesis on mesoporous silica-supported chiral ligands and their use to asymmetric catalysis are underway.

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