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Short Communication

# Heterogeneous asymmetric hydrogenation of aromatic ketones enhanced by silanols on highly monodispersed silica spheres



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## A R T I C L E I N F O

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## ABSTRACT

A triphenylphosphine-stabilized  $Ir/SiO_2$  catalyst modified by a chiral diamine was synthesized with four silica spheres as support for the asymmetric hydrogenation of aromatic ketones. The H-bond between substrate and silanols and the interaction between substrate and modifier commonly affected the steric configuration of asymmetric hydrogenation of aromatic ketones. With the silanols increasing, the activity of asymmetric hydrogenation significantly increased. This is the first report of heterogeneous asymmetric hydrogenation of aromatic ketones on highly monodispersed silica spheres with >99.9% ee and >99% conversion.

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## 1. Introduction

Since 1968, silica materials have been widely used in high-tech applications owing to their excellent physicochemical, mechanical and optical properties [1]. Silica-supported mesoporous heterogeneous catalysts for asymmetric hydrogenation have attracted a great deal of interest [2-4]. Chuang and Maciel have recently found that approximately 60% of the single silanols and 50% of the geminal silanols in the silica surface were non-hydrogen bonded (isolated species) at 25 and 200 °C [5]. Katz [6] found that surface silanol groups affected heterogeneous catalysis activity, and Lin [7] reported higher reaction rates in cyanosilylation than AEP-MSN alone owing to the increased number of surface silanol groups in cooperative catalysis reactions. In our recent work, we had also shown that high performance of heterogeneous catalysts was related to surface hydroxyl [8-11]. We attributed this to developing highly active and enantioselective catalytic systems enhanced by silanols on support. Herein we report the synthesis of a TPP-stabilized and chiral diamine modified Ir/SiO<sub>2</sub> catalyst with four silica spheres as support which provided >99.9% ee and >99% conversion for heterogeneous asymmetric hydrogenation of simple ketones. The experimental results demonstrated that the surface silanol in the silica significantly enhanced the activity and enantioselectivity of this reaction through the hydrogen bonding between substrates and silanol. To our knowledge, this is the first report of the heterogeneous asymmetric hydrogenation of simple aromatic ketones enhanced by silanols on highly monodispersed silica spheres.

## 2. Experimental

## 2.1. General information

Tetraethoxysilane (TEOS, Aldrich), cinchonine (Acros), triphenylphosphine (tpp, Aldrich), aromatic ketones (Aldrich) and H<sub>2</sub>IrCl<sub>6</sub>·6H<sub>2</sub>O (Institute of Kunming Noble Metals, China) were used as-received without further purification. Other reagents were of analytical grade. The purity of hydrogen was over 99.99%. High-resolution transmission electron microscopy (HTEM) graph was recorded by FEI Tecnai G2 F20 S-Twin TEM with an accelerating voltage of 200 kV. X-ray photoelectron spectroscopy data was taken on Kratos XSAM 800 XPS. Inductively coupled plasma (ICP) data was tested by Intrepid IIXSP ICP. Scanning electron microscopy (SEM) graph was obtained by JEOL JSM-7500F SEM. N<sub>2</sub> adsorption-desorption isotherms were tested on a Micrometitics ASAP 2020 M + C analyzer at 77 K. The BET (Brunauer-Emmett-Teller) method was adopted to calculate the special surface areas using adsorption data. The pore size distributions were derived from the adsorption branches of isotherms using the BJH (Barret-Joyber-Halenda) model. Products were analyzed by GC instrument with an FID detector and  $\beta$ -DEX120 capillary column.

## 2.2. The preparation of four monodispersed silica spheres

Firstly, ethanol (6 mL), aqueous ammonia (10, 20, 30 and 40 mL) and TEOS (6 mL) were added into a round flask of 100 mL and stirred for 8 h at 35  $^{\circ}$ C. Then the mixture was filtrated and washed with ethanol and water a few times. The solid was dried under vacuum at room temperature for 24 h.



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Table 1

## 2.3. The prepareation of 2%Ir/SiO<sub>2</sub>/2tpp

Under an argon atmosphere, silica spheres (1 g),  $H_2IrCI_6$  (0.104 mmol), tpp (0.208 mmol) and *i*PrOH (30 mL) were added into a round flask of 100 mL and stirred for 24 h at room temperature. Formal-dehyde (5 mL) was then added and the mixture was heated at 110 °C for 5 h. The mixture was cooled to room temperature and the solid was filtrated and dried under vacuum at room temperature for 6 h to afford the catalyst.

## 2.4. General procedure for the asymmetric hydrogenation reaction

Asymmetric hydrogenation of aromatic ketones was performed in a 60 mL stainless steel autoclave with a magnetic stirred bar at room temperature, by using 9-amino(9-deoxy)epicinchonine as modifier, which is derived from cinchonine. In a typical run, the catalyst, chiral diamine, solvent, base and acetophenone were placed in the autoclave, followed by five purges hydrogen. The hydrogen pressure was thereafter increased to desired level. The mixture was stirred at room temperature for the appropriate duration.

## 3. Results and discussion

Initially, four monodispersed silica spheres were prepared as a support for the asymmetry hydrogenation of aromatic ketones according to Chen's research [12]. The four diameters of the silica particles were synthesized depending on the reagent concentrations used. Increased concentration of ammonia correlated with the decrease in average particle sizes of the silica spheres. The SEM graph of silica spheres ((a), (b), (c) and (d)) is shown in Fig. 1. The silica spheres are monosize with the average particle size about 46, 290, 400 and 560 nm respectively.

Table I			
The effect of surface sile	anols for asymmetric	hydrogenation o	f acetophenone.

		area/m <sup>2</sup> g <sup>-1</sup>	Average pore/Å	X/mmol/g	Conv. (%)	Ee (%)	Config.
1	46	109.2	63.1	14.5	63.7	90.0	S
2 2	290	22.9	35.4	11.7	38.9	89.7	S
3 4	400	13.2	24.6	12.5	58.4	90.3	S
4 5	560	69.2	18.3	15.0	71.8	90.0	S

 $^{a}$  Substrate/Ir = 300/1, acetophenone: 0.856 mol/L,9-amino(9-deoxy)epicinchonine: 2.8  $\times$  10 $^{-3}$  mol/L, LiOH: 0.025 mol/L, 25 °C, 6 MPa, 3 h.

<sup>b</sup> 3%lr/SiO<sub>2</sub>/2tpp.

The amount of surface silanols on the silica particles was estimated by chemical titration [13]. The surface silanol amount of four silicas was respectively 14.5, 11.7, 12.5 and 15.0 millimole/g (Table 1). The results indicate that there were substantial amounts of silanols in the silica, and the silanol amount of four silicas was in the order: (d) > (a) > (c) > (b). Nitrogen adsorption isotherms indicated that the silica particles had a low BET surface area being 109.2, 22.9, 13.2 and  $69.2 \text{ m}^2\text{g}^{-1}$  and their corresponding BJH average pore diameters were 63.1, 35.4, 24.6 and 18.3 Å respectively.

3%Ir/SiO<sub>2</sub>/2tpp was prepared with four silicas as supports according to our previously reported method [14–19]. The results of asymmetric hydrogenation were summarized in Table 1. In general, the large surface areas and pore diameters of support were beneficial for the activity in heterogeneous catalytic systems. However, 3%Ir/SiO<sub>2</sub>(a)/2tpp performed 63.7% conversion lower than 3%Ir/SiO<sub>2</sub>(d)/2tpp, although the former had the largest surface areas and the largest average pore diameters (Table 1, entries 1, 4). In addition, 3%Ir/SiO<sub>2</sub>(c)/2tpp with the lowest surface areas and slighter average pore diameters exhibited 58.4% conversion higher than 3%Ir/SiO<sub>2</sub>(b)/2tpp (Table 1, entries 2, 3). In



Fig. 1. SEM graph of high monodispersed silica spheres.



Scheme 1. Proposed hydrogen model. X: F, Cl, Br, OCH<sub>3</sub>, and CF<sub>3</sub>.

addition, the activity of acetophenone significantly increased from 38.9% to 71.8% (Table 1, entries 1–4) with silanols increasing from 11.7 to 15.0 millimole/g. In particular, the catalyst 3%Ir/SiO<sub>2</sub>(d)/2tpp with the most silanols exhibited the highest activity (71.8%) (Table 1, entry 4). These results suggest that the effect of silanols was higher than the effect of surface areas and pore diameters. Interestingly, the surface silanols vastly enhanced the activity but had no effect on the enantioselectivity of asymmetric hydrogenation of acetophenone. This prompted us to study the model of asymmetric hydrogenation.

As early as 1979, Orito et al. reported the first asymmetric hydrogenation of prochiral ketocarbonyls using chiral modified supported platinum catalysts [20]. Subsequently, a number of mechanisms have been proposed for the Orito reaction and recent surface science studies indicate that a second H-bonding interaction may occur in the adsorbed 1:1 modifier-substrate complex [21-26]. According to the generalized two-point H-bonding model [27], we speculate that there was an interaction carried out through H-bond between substrate and silanols for the heterogeneous asymmetric hydrogenation of aromatic ketones (Scheme 1). IR spectroscopy was one of standard methods to investigate hydrogen bonds in the solid state [28]. 1-(2-Fluorophenyl)ethanone was selected as subject of study because of its strong electronegativity. As shown in Fig. 2, the red line was the IR spectrum of 3%Ir/SiO<sub>2</sub>(d)/2tpp adsorbing 1-(2-fluorophenyl)ethanone. A new weak sharp peak at 3680 cm<sup>-1</sup> was confirmed by FTIR methods. The peak was due to the H-F interaction between fluoro- and silanols compared to experimental  $(3687 \text{ cm}^{-1})$  and theoretical frequencies  $(3640 \text{ cm}^{-1})$  [29–31]. This demonstrated that a hydrogen bond was formed between substrates and catalyst. Due to the hydrogen bonding, steric effects influence the asymmetry of hydrogenation as shown in Scheme 1. It is noteworthy



**Fig. 2.** The IR spectrum. A: The IR spectrum of 3/lr/SiO<sub>2</sub>(d)/2tpp; B: the IR spectrum of 3/lr/SiO<sub>2</sub>(d)/2tpp adsorbing 1-(2-fluorophenyl)ethanone; and. C: the IR spectrum of 1-(2-fluorophenyl)ethanone.

## Table 2

The effect of different iridium loadings for hydrogenation of acetophenone<sup>a</sup>.

Entry	Load capacity/%	Conv./%	Ee/%	Config.
1	1	2.5	79.2	S
2	2	86.3	91.6	S
3	3	71.8	90.0	S

 $^a$  Substrate/Ir = 300/1, acetophenone: 0.856 mol/L,9-amino(9-deoxy)epicinchonine: 2.8  $\times$  10 $^{-3}$  mol/L, LiOH: 0.025 mol/L, 25 °C, 6 MPa, 3 h.

that the enantioselectivity of acetophenone had little variation (Table 1, entries 1–4) over the range of silanol concentration increasing from 11.7 to 15.0 millimole/g. According to the proposed hydrogen model, the steric effect was not different when the substrate was same. That was the reason the amount of surface silanols had no significant effect on asymmetry of the same substrate hydrogenation. However, the experiment data suggests that increased concentration of silanols improved the activity.

According to the catalytic activity from Table 1, the  $SiO_2$  (d) was chosen to be the best support. The catalysts at various iridium loadings (1, 2 and 3%) were prepared. The reaction solution was tested by ICP and no iridium ions were detected after the catalysts were prepared demonstrating that all iridium ions were adsorpted on the supports. The asymmetric hydrogenation data was summarized in Table 2. The  $2%Ir/SiO_2(d)/2tpp$ performed the highest catalytic activity and enantioselectivity (Table 2, entry 2) and was selected as the catalyst in the following examinations.

The HTEM picture of 2%Ir/SiO<sub>2</sub>(d)/2tpp showed that iridium nanoclusters were highly dispersed on the SiO<sub>2</sub>. The average diameter of iridium nanoclusters was about 3.0 nm. XPS analysis indicated that Ir 4f<sub>7/2</sub> core level centered at 61.6 eV which is a reduced state compared to Ir (0) (Ir 4f<sub>7/2</sub> core level centered at 60.8 eV) [32]. The full range XPS spectra indicated that the amount of Ir supported on the SiO<sub>2</sub> is 2%wt./wt.

The effect of the different reaction factors on the asymmetric hydrogenation of acetophenone was tested (see supporting information). Methanol and LiOH were the best solvent and base respectively in the reaction. >99% conversion and good enantioselectivity of up to 87.6% were obtained while MeOH/LiOH was examined. The combination of iPrOH and KOH was also investigated in our catalytic system. Just 11.0% conversion and 48.9% enantioselectivity were obtained, although the iPrOH/KOH was identified as the best combination for hydrogenation of aromatic ketones. A high concentration of the base and modifier was needed in our catalytic system. The effect of hydrogen pressure on the reaction was also examined. When the reactions were run at high hydrogen pressure (6-7 MPa), the activity and enantioselectivity of the catalytic system were maintained (>99% conversion, 87.6-88.9% ee). However, when the hydrogen pressure decreased to 5 MPa, the conversion dropped (79.4%) while the enantioselectivity (89.7%) remained. When the pressure was further reduced to 4 MPa, the conversion (47.3%) and the enantioselectivity (72.8%) were reduced. In addition, less than 1% conversion was observed with no hydrogen when the base and the solvent were instead KOH and iPrOH. According to the procedures reported by G. Szőllősi et al. [33], additional experiments were carried out to clarify the effect of support acidity on activity and enantioselectivity. The acetophenone was hydrogenated with the catalyst treated by 5% aqueous NaOH solution and low conversion and low enantioselectivity were obtained.

A representative range of simple aromatic ketones divided into three categories (ortho-substituted, para-substituted and un-substituted substrate) respectively was hydrogenated with the catalyst 2%Ir/SiO<sub>2</sub>(d)/2tpp. The results obtained were shown in Table 3. In general, excellent conversions and high enantioselectivities were obtained for all tested aromatic ketones. When the steric bulk of substituent was larger, the enantioselectivity and activity were lower. As previously reported research, the steric and the electronic effect commonly influences the activity and the enantioselectivity in the asymmetric

#### Table 3

Asymmetric hydrogenation of aromatic ketones catalyzed by 2%Ir/SiO<sub>2</sub>(d)/2tpp.<sup>a</sup>

0	2%Ir/	SiO <sub>2</sub> /2TPI		OH		
R <sub>1</sub>	∕ <sub>R₂</sub> chiral	diamine	R <sub>1</sub>	R <sub>2</sub>		
Entry	R <sub>1</sub>	R <sub>2</sub>	Con (%)	ee (%)	Config.	
1	C <sub>6</sub> H <sub>5</sub>	Me	99.3	90.1	S	
2	$2-FC_6H_4$	Me	50.1	90.7	S	
3	2-ClC <sub>6</sub> H <sub>4</sub>	Me	52.9	91.7	S	
4	2-BrC <sub>6</sub> H <sub>4</sub>	Me	66.9	92.2	S	
5	2-CF <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	Me	81.2	79.5	S	
6	2-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	Me	6.3	>99.9	S	
7	2-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	Me	99.7 <sup>b</sup>	>99.9	S	
8	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	Me	99.8	82.6	S	
9	C <sub>6</sub> H <sub>5</sub>	Et	98.9	90.2	S	
10	C <sub>6</sub> H <sub>5</sub>	i-Pr	35.8	42.7	S	

<sup>a</sup> Substrate/Ir = 300/1, acetophenone: 0.856 mol/L, 9-amino(9-deoxy)epicinchonine: 2.8 × 10<sup>-3</sup> mol/L, LiOH: 0.05 mol/L, 25 °C, 6 MPa, 3 h.

Reaction time: 48 h.

hydrogenation of simple aromatic ketones. However, there were some interesting phenomena found and these phenomena might be explained by the H-bond between substrate and silanols. As shown in entries 2–5 in Table 3, the prochiral ketone group (p-CO) was activated by a group in the ortho-position in the aromatic ring. In addition to p-CO, all effective substrates contain a group (X) that is capable of forming H-bonds with the silanols in the silica surface. When the substituent on the benzene ring was changed to F, Cl and Br, the H-bond energy decreased gradually. The activities of hydrogenation were obviously improved to up to 50.1%, 52.9%, and 66.9% conversion, together with a reasonably high enantioselectivity of up to 92.2% (Table 3, entries 2-4).

As shown in the Scheme 1, the H-bond between the X and silanols and the H-bond between p-CO and the modifier effectively controlled the stereo-structure commonly. Meanwhile, the strong H-bond between the X and silanols limited the move of the substrates on the supports and leads to low activities. The same phenomenon was observed with other substrates. The CH<sub>3</sub>O substituent not only has strong H-bond, but also has a large suitable steric effect, for which it was hydrogenated with low only 6.3% conversion but highest >99.9% enantioselectivity in the same reaction conditions (Table 3, entry 6). After 48 h reaction, the CH<sub>3</sub>O substituent was completely hydrogenated with >99% conversion and >99.9% enantioselectivity (Table 3, entry 7). Owing to the largest steric effect, low enantioselectivity (79.5%) and conversion (81.2%) were obtained in the hydrogenation of 2-trifluoromethylacetophenone (Table 3, entry 5). The para-substituted substrate also exhibited strong hydrogen bongding, but it was not beneficial to the controlling of the stereostructure. Hence, just 82.6% enantioselectivity and >99% conversion were obtained. Un-substituted substrates just having the H-bond between p-CO and the modifier, gave lower enantioselectivities compared to the ortho-substituted substrate (Table 3, entries 1, 9–10). Similarly, the largest bulk led to the lowest 42.7% enantioselectivity and 35.8% activity (Table 3, entry 10). The above experimental results demonstrate that surface silanols effectively control the activity and enantioselectivity in the heterogeneous asymmetric hydrogenation of aromatic ketones.

## 4. Conclusion

In summary we have synthesized four monodispersed and rich silanol silicas that are used as support and demonstrated that silanols enhanced the activity and enantioselectivity via hydrogen bonding between substrates and silanol in the heterogeneous asymmetric hydrogenation of aromatic ketones, especially for ortho-substituted aromatic ketones. By increasing the concentration of silanols, the activity of asymmetric hydrogenation was significantly increased. This was the first report of the heterogeneous asymmetric hydrogenation of aromatic ketones enhanced by silanols on highly monodispersed silica spheres with >99.9% ee and >99% conversion. The work reported herein provides a new direction for asymmetric hydrogenation.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx. doi.org/10.1016/j.catcom.2014.05.009. This data include MOL file and InChiKey of the most important compounds described in this article.

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