Catalysis Letters Vol. 100, Nos. 3–4, April 2005 (© 2005)
DOI: 10.1007/s10562-004-3458-1

Highly selective asymmetry transfer hydrogenation of prochiral acetophenone catalyzed by palladium–chitosan on silica

Yanxi Sun, Yun Guo, Quanzhong Lu*, Xianle Meng, Wu Xiaohua, Yanglong Guo, Yunsong Wang, Xiaohui Liu, and Zhigang Zhang

Lab for Advanced Materials, Research Institute of Industrial Catalysis, East China University of Science and Technology, Shanghai, 200237 P.R. China

Received 23 June 2004; accepted 29 November 2004

The chitosan–palladium catalyst supported on silica was prepared and used to catalyze an asymmetry transfer hydrogenation of prochiral acetophenone to alcohol with formate salts as a hydrogen donor at atmosphere. The results indicate that palladium coordinates with amino group in chitosan to form palladium–chitosan complex and its performance for an asymmetry transfer hydrogenation of acetophenone is affected greatly by the reaction temperature, hydrogen donor and solvent. For the hydrogenation of acetophenone over the palladium–chitosan–silica catalyst, the suitable solvent is ethanol and hydrogen donor is ammonium formate or sodium formate. Using ammonium formate as H-donor at atmosphere and 80 °C, an enantiomeric excess of R-1-phenylethanol reaches 68.9%.

KEY WORDS: palladium–chitosan; chiral catalyst; acetophenone; 1-phenyl ethanol; transfer hydrogenation; enantioselectivity.

1. Introduction

Many pharmaceuticals, agrochemicals, flavours, fragrances and important intermediates are only desirable to one enantiomeric form. This increasing demand for enantiomerically pure compounds has fostered to develop the preparation methods affording pure enantiomers of chiral products [1]. Among the various methods, the enantioselective catalysis is unique in a. sense that a minute quantity of the chiral catalyst is sufficient to produce large amount of the desired chiral products [2]. In an asymmetry catalytic reaction, the key factor is to design and prepare the chiral catalyst. The heterogeneous chiral catalysts have some advantages, such as facile separation of catalyst from reactants and, products, as well as handing, stability, recovering and reuse [3]. The methods of preparing heterogeneous chiral catalyst are the traditional catalyst modified with chiral molecules, immobilization of homogeneous chiral catalyst and preparation of chiral polymers, and so on. However, the preparation of a solid chiral catalyst is complicated generally and has to be operated under inert atmosphere, which leads to its cost very high.

Natural optically active polymers such as proteins and genes, owning to their specific chiral structure, have played a major role in a molecular recognition and catalytic investigation. Using their specific chiral structure to prepare the heterogeneous chiral catalyst makes the procedure of preparing chiral catalyst simple and its cost reduce, because the chiral ligands of chiral catalyst to be, not synthesized. Chitosan (CS), deacetylated chitin that is widely dispersed in living organisms, is a natural optical active biopolymer [α_{20}^{D} + 250 (C 0.5, CH_3COOH (2%, wt))] [4] with unique favourable properties and can be used in the industrial and manufacturing processes including waste water treatment, food process, medical, agriculture, pharmaceutical and textile industries. CS contains many kinds of functional group (such as amino group and hydroxyl group) that can chelate the transition metal ions (even neutral atoms) to form a metal–polymer complex that can be used as the chiral catalysts for asymmetric reactions [5–7]. This metal–CS complex catalyst can be prepared simply and used easily under atmosphere. But the researches on the CS–substrate catalyst are rare, especially as a chiral heterogeneous catalyst.

Hydrogenation of unsaturated groups is a useful method to prepare the chiral molecules [8], among, which the asymmetric hydrogenation of prochiral ketone to corresponding optically active secondary alcohols is one of the most important reactions in modern synthetic chemistry [9–11]. As an important synthetic technique, the catalytic transfer hydrogenation (CTH) has been used widely in hydrogenation of the functional groups, including nitro ketone and olefin [12]. Comparing with hydrogenation by molecular hydrogen, CTH can be operated at ambient condition simply and easy.

In this paper, the chiral heterogeneous catalyst of palladium–chitosan complex supported on silica was developed, and its performance was investigated for the asymmetric transfer reduction of acetophenone by formate salts as H-donor under atmosphere.

* To whom correspondence should be addressed.
E-mail: gzhlu@ecust.edu.cn

2. Experimental

2.1. Preparation of chiral heterogeneous catalyst

Acetophenone, ethanol, formic acid, potassium formate, sodium formate, ammonium formate, triethylamine, silica and $PdCl_2$ are of analytical grade. Chitosan with more than 85% deacetylation was purchased commercially, and needed not be pretreated before use.

One gram chitosan and 60 mL 1.5% acetic aqueous solution were placed in the 100 mL three-necked flask equipped with the mechanical stirrer, thermometer and dropping funnel. After chitosan was dissolved under stirring at 50 °C, l0 g silica was added, and then 4 N sodium hydroxide aqueous solution was added by titratation until the pH value reached to 13, while CS was deposited on silica. The solid products were filtered, washed with de-ionized water and then dried to gain fine white particles.

The white particles obtained above, $PdCl_2$ and ethanol aqueous solution were placed, in a round bottom flask equipped with the magnetic stirrer and reflux condenser. The mixture was stirred, and refluxed at 80 °C for 8 h. When $PdCl_2$ coordinated with amino group in CS completely, the particles became dark gray, and the solution became transparent and colorless. Then it was filtered, washed with ethanol and dried, and reduced with formaldehyde.

2.2. Measurement of XPS

X-ray photoelectron spectroscopy (XPS) spectrum of sample was measured on an ESCALAB 210 XPS analyzer (VG Scientific, UK) with MgKα radiation. The binding energy (BE) of adventitious C_{1s} (284.6 eV) was used as a reference.

2.3. Transfer hydrogenation of acetophenone

Hydrogen resource, chiral catalyst, acetophenone and solvent were placed in the 50 mL flask equipped with the magnetic stirrer and condenser at atmosphere. After the hydrogenation of acetophenone (figure 1) has finished at the given temperature, the reaction solution was cooled to the room temperature and filtered, the catalyst was recovered and the products were analyzed directly.

2.4. Analysis of products and enantiomeric excesses (ee)

The products were analyzed qualitatively by GC–MS (Micromass GCT and HP-6890) and determined quantitatively by gas chromatograph (PE Autosystem XL) with a chiral capillary column (CP-Chiralsil-Dex CB). The enantioselectivity to product was expressed with ee (%) = R(%) − S(%). The absolute configuration of product was determined by the sign of rotation with automatic polarmeter of WZZ-2B (China).

3. Results and discussion

3.1. The XPS analysis of catalyst

The XPS data of $PdCl_2$, CS–SiO_2 and $PdCl_2$–CS–SiO_2 are listed in table 1. Two kinds of Pd with different chemical state can be distinguished. Their BE are 337.46 and 335.34 eV, which are corresponding Pd^{2+} and Pd^0 respectively. The BE of $Pd_{3d5/2}$ in $PdCl_2$–CS–SiO_2 is 0.72 eV lower than the BE of $Pd_{3d5/2}$ in $PdCl_2$, which may be caused by Pd^{2+} coordinated with CS. As seen from table 1, the BE of N_{ls}, in $PdCl_2$–CS–SiO_2 is 0.42 eV higher than that of N_{ls} in CS–SiO_2, which indicates that the coordination bonds have formed between palladium and amino group in CS. This is in line with the results reported by Yin and co-workers [5]. Pd^0 is. produced by the reduction of some Pd^{2+} ions by ethanol during the preparation process [13, 14].

The results in table 1 show also, there is no difference in the BE of Si_{2p}, O_{ls}, between CS–SiO_2 and $PdCl_2$–CS–SiO_2, but the BE of Cl_{2p} in $PdCl_2$–CS–SiO_2 is lower than the BE of Cl_{2p} of $PdCl_2$. As an electron donor, nitrogen in the amino group of CS supplies a part of electron to Pd after coordinated with Pd, which leads to an increase of electric density of $Pd_{3d5/2}$ and Cl_{2p} and a decrease of the BE of $Pd_{3d5/2}$ and Cl_{2p}. This proves further that the coordination occurs between palladium and the amino group. The structure of the $PdCl_2$–CS–SiO_2, catalyst can be described in figure 2.

3.2. Catalytic performance for asymmetric transfer hydrogenation

3.2.1 Effect of Pd loading

In the asymmetric reaction catalyzed by the chiral organometallic catalyst the yield of product is greatly influenced by the ratio of chiral ligand to transition metal, and there is an optimal ratio of chiral ligand to transition metal. The influence of Pd loading on the catalytic property of Pd–CS–SiO_2 and the enantioselectivity of R-1-phenylethanol is shown in table 2. The results indicate that with an increase of the Pd loading, the yield of 1-phenylethanol increases slightly, and the enantioselectivity of R-1-phenylethanol is affected hardly by the Pd loading (or the ratio of chiral ligand to transition metal). Increasing the Pd loading from 1.0 to 2.1%, 3.2, 4.0, 5.1 and 10.2%, only very little difference

Table 1
The XPS data of CS–SiO_2 and $PdCl_2$–CS–SiO_2

XPS peak	Binding energy (eV)		
	CS–SiO_2	$PdCl_2$–CS–SiO_2	$PdCl_2$
$Sis_{p3/2}$	103.12	103.12	
$Pd_{3d5/2}$	–	335.34, 337.46	338.18
N_{ls}	399.14	399.56	
O_{ls}	532.52	532.48	
Cl_{2p}		198.48	199.14

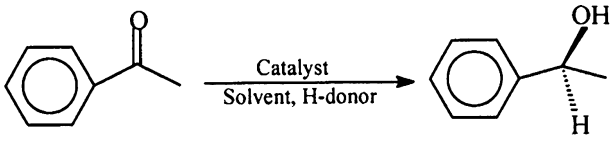

Figure 1. Asymmetric hydrogen transfer reduction of acetophenone.

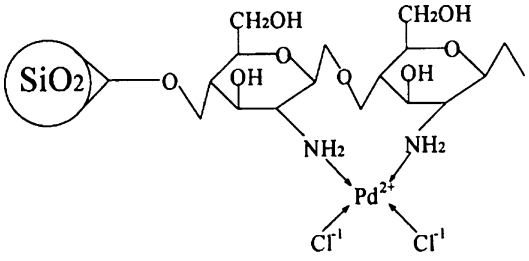

Figure 2. Structure of the $PdCl_2$–CS–SiO_2 catalyst.

of yield varying from 0.6 to 1.2% is observed and the ee value is 65.1–68.9%. The suitable loading of Pd on CS–SiO_2 is suggested about 3%.

3.2.2. *Effect of H-donor*

In the heterogeneous or homogeneous CTH, several types of hydrogen donor have been used successfully [15,16]. Among these hydrogen donors, formic acid and its salts are the most important agents, because of their cheaper cost and good properties, for example, their hydrogen donation is stronger than that of other donors [17]. Here, formic acid and its salts, sodium formate, potassium formate, ammonium formate, and, the azeotropic mixture of formic acid and triethylamine were used as the hydrogen donors.

The results in table 3 show that net formic acid or the azeotropic mixture of formic acid and triethylamine as H-donor are inactive for the transfer hydrogenation of acetophenone. In the ethanol solvent, as H-donor potassium formate or formic acid is inactive either. The best H-donor is ammonium formate or sodium formate, using which the ee values to R-1-phenylethanol may reach 68.9 or 60.4%, respectively. These results are similar to that reported by Cavinato and co-workers, formate salts are more active hydrogen donors than formic acid for the hydrogenation of C═C double bond of γ-keto-α, β-unsaturated carboxylic acids over the Pd/C catalyst [18].

The counter-ion is essential to a hydrogenolysis of the organic compounds by formate salts. The separation, of formate ion from its cation, that is necessary for an ionization of alkali metal formates, depends on both a polarity of the bond and an inter-nuclear distance between oxygen(s) of formate and alkali metal ion. The greater a polarity of bond, the easier its ionization will be. In the hydrogenolysis of $ArCH_2$–OR catalyzed by Pd/C, the hydrogen-donating ability of formic acid and formates is $K^+ > NH_4^+ > Na^+ > NHEt_3^+ > Li^+ > H^+$ [19]. For the hydrogenation of acetophenone over the Pd–CS–SiO_2 catalyst the hydrogen-donating ability is $HCOONH_4$ > HCOONa > $HCOOH/Et_3N$, HCOOK and HCOOH are inactive (table 2). This situation is different to the hydrogenolysis of $ArCH_2$–OR over the Pd/C catalyst. The difference in the ability of hydrogen donating above, we think, may attribute to a difference in the solubility and ionization of the compounds as a, hydrogen donor. A lower solubility makes lower concentration of H-donor, which decreases the rate of formate ions cooperating with Pd in Pd–CS–SiO_2. But H-donating ability of HCOOK is less than that of HCOONa, its reason is not clear now.

3.3. *Effect of the reaction condition*

3.3.1. *Reaction temperature*

The effect of reaction temperature on the hydrogenation of acetophenone is shown in table 4, in which ammonium formate and sodium formate are used as a hydrogen donor.

The results show that the Pd–CS–SiO_2 catalyst is inactive at 70 °C and the conversion of acetophenone is about 0%. With an increase of reaction temperature, the enantioselectivity to R-1-phenylethanol increases firstly and then decreases. After the reaction runs at

Table 2
Influence of Pd loading on the catalytic performance of Pd–CS–SiO_2 and the enantioselectivity of R-1-Phenylotimol at 80 °C[a]

Loading of Pd /%	Time /h	Yield /%	ee /%	Configuration
10.2	24	0.7	65.4	R
5.1	24	0.7	67.6	R
4.0	24	0.9	66.3	R
3.2.	24	1.2	68.9	R
2.1	24	0.8	67.2	R
1.0	24	0.6	65.1	R

[a] 0.1 g catalyst, 0.1 mmol acetophenone, 0.24 mmol ammonium formate and 30 mL solvent at 80 °C.

Table 3
Effect of hydrogen donor on the catalytic performance of Pd–CS–SiO_2 and the enantioselectivity of M-phenylethanol at 80 °C[a]

H-donor	Solvent	Time/h	Yield/%	ee/%	Configuration
$HCOONH_4$	Ethanol	24	1.2	68.9	R
HCOONa	Ethanol	24	0.67	60.4	R
$HCOOH/Et_3N$[b]	Ethanol	74	0.15	21.0	R
HCOOK	Ethanol	74	0	0	–
HCOOH	Ethanol	74	0	0	–
30 mL HCOOH	No	24	0	0	
30 mL $HCOOH/Et_3N$[b]	No	24	0	0	–

[a] 0.1 g catalyst, 0.1 mmol acetophenenone, 0.24 mmol formate salt and 30 mL solvent.
[b] $HCOOH/Et_3N$ = 5/2.

Table 4
Effect of the reaction temperature and solvent on the hydrogenation of acetophenone[a]

Temp./°C	H-Donor	Solvent	Time /h	Yield /%	ee /%	Configuration
70	$HCOONH_4$	Ethanol	70	0	0	–
75	$HCOONH_4$	Ethanol	24	0.4	49.0	R
80	$HCOONH_4$	Ethanol	24	1.2	68.9	R
85	$HCOONH_4$	Ethanol	24	1.0	33.4	R
85	$HCOONH_4$	Ethanol (5% H2O)	2.4	0	0	–
70	HCOONa	Ethanol	70	0	0	–
75	HCOONa	Ethanol	24	0.3	50.1	R
80	HCOONa	Ethanol	24	0.67	60.4	R
85	HCOONa	Ethanol	24	0.3	32.7	R
85	HCOONa	Ethanol (5% H2O)	24	0.4	41.1	R
85	HCOONa	Ethanol (20% H2O)	24	0	0	–
80	$HCOONH_4$	2-Propanol	24	0.3	32.3	R
80	$HCOONH_4$	Methanol	24	0	0	–
80	$HCOONH_4$	Dichloromethane	24.	0	0	–

[a] 0.1 g catalyst, 0.2 mmol acetphenone, 0.24 mmol formate salt and 30 mL solvent.

80 °C for 24 h, the maximum ee (68.9%) is obtained with ammonium formate as H-donor, using sodium formate as H-donor, the maximum of ee is 60.4%. As the reaction temperature rises to 85 °C, the former ee value decreases to 33.4%, and the latter is 32.7%. It is possible that with an increase of temperature, the solubility of formate salts increases, while the hot solvent makes chitosan expand. As a result, the cavities and ''core'' sites on the catalyst can be reached more easily by substrate, which helps the substrate to attack Pd^{2+} at two sides of chiral surface, while the higher reaction temperature may cause R-1-phenylethanol racemization. For the asymmetric catalytic hydrogenation of acetophenone, the suitable temperature is about. 80 °C, to make the cavities of chitosan have a better defined shape for the selective formation of chiral R-1-phenylethanol [20].

3.3.2. Solvent

In the catalytic liquid–solid phase reaction, the selectivity to product and the activity of catalyst are often influenced by a solvent. The different solvent can give rise to a change of the enantioselective outcome of reaction [21]. The results in table 4 show that the solvent has an influence on this transfer hydrogenation reaction greatly, and the suitable solvent is ethanol or 2-propanol, using methanol or dichloromethane as a solvent no product of alcohol can be obtained.

In order to increase the solubility of formate salts in a solvent and a suitable expansion of chitosan to favour the adsorption of substrate on active sites, the effect of water on the asymmetry transfer hydrogenation of acetophenone in the ethanol solvent was investigated. The results in table 4 show that using $HCOONH_4$ as H-donor, the presence of water is detrimental to the asymmetry hydrogenation. When sodium formate is employed as H-donor and 5% H_2O was added in the ethanol solvent at 85 °C, the ee value increased from 32.7 to 41.1%; when 20% water was added in solvent, the yield of product decreases to 0%. This indicates that the transfer hydrogenation of acetophenone is sensitive to the amount of water. It is also observed that the concentration of water affects greatly the initial rate of hydrogenation of acetophenone. Only at low concentration, water has a beneficial effect on the reaction rate [22,23].

4. Conclusions

The chitosan–palladium complex supported on silica is a very effective catalyst for the asymmetric hydrogenation of prochiral acetophenone. The preparation method of this heterogeneous chiral catalyst is simple and easy, and it can be prepared and used under atmosphere. The performance of the catalyst for the hydrogenation of acetophenone is affected greatly by the H-donor used, reaction temperature and solvent. The favourable reaction condition is that, the reaction temperature is 80 °C, ethanol is used as a solvent and ammonium formate or sodium formate is used as hydrogen donor.

Acknowledgments

This study is supported financially by the Committee of Science and Technology of Shanghai Municipality (No. 021 nm007, 03DJ14006).

References

[1] G.I.P. Daniëlle, C.J.K. Paul and L.S. Anthony, J. Org. Chem. 65 (2000) 3010.
[2] A. Baiker, Curr. Opin. Solid State Mater. Sci. 3 (1998) 86.
[3] W.K. Sang, J.B. Sung and H. Taeghwan, Micropor. Mesopor. Mater. 523 (2001) 44–45.
[4] H. Takeda and K. Kadowaki, Agric. Biol. Chem. 49 (1985) 3151.
[5] M.Y. Yin, G.L. Yuan and Y.Q. Wu, J. Mol. Catal. A: Chem. 147 (1999) 93.

[6] J. Zhang and C.G. Xia, J. Mol. Catal. (China), 16 (2002) 465.
[7] E. Piron, M. Accomintti and A. Domard, Langmuir 13 (1997) 1653.
[8] O. Takeshi, O. Hirohito and H. Shohei, J. Am. Chem. Soc. 117 (1995) 2675.
[9] C. Salazzo, R. Halle and T. Francois, J. Organomet. Chem. 603 (2000) 30.
[10] M. Tommo, K. Yoshinori and E. Kokki, J. Org. Chem. 63 (1998) 2378.
[11] R. Alice, H. Domien and T. Francois, Tetra: Asy. 12 (2001) 811.
[12] T. Nakano, J. Ando and Y. Jshii, Tech. Rep. Kansai Univ. 29 (1987) 69.
[13] S. Papp, A. Szücs and I. Dékány, Appl. Clay. Sci. 19 (2001) 155.
[14] A.K. Zharmagambetova, E.E. Ergozhin, Y.L. Sheludyakov, S.G. Mukhamedzhanova, I.A. Kurmanbayeva, B.A. Selenova and B.A. Utkelov, J. Mol. Catal. A: Chem. 177 (2001) 165.
[15] S. Kajagopal and A.F. Spatola, J. Org. Chem. 60 (1995) 1347.
[16] G. Brieger and T. Nestrick, Chem. Rev. 74 (1974) 567.
[17] R.A.W. Johnstone, A.H. Wilby and I.D. Entwistle, Chem. Rev. 85 (1985) 129.
[18] G. Cavinato and L. Toniolo, J. Mol. Catal A: Chem. 106 (1996) 25.
[19] S. Rajagopal and A.F. Spatola, Appl. Catal. A: Gen. 152 (1997) 69.
[20] J.B. Daniel, B.T. Catherine and E.C.P. Mano, Tetra.: Asy. 9 (1998) 2015.
[21] P.N. Rylander, *Catalytic Hydrogenation over Platinum Metals* (Academic Press, New York, 1976).
[22] M.V. Rajashekharam, I. Bergault, P. Fouilloux, D. Schweich, H. Delmas and R.V. Chaudhari, Catal. Today 48 (1999) 83.
[23] G. Cavinato and L. Toniolo, J. Mol. Catal. A: Chem. 106 (1996) 25.