DOI: 10.1002/adsc.200800110

Enantioselective Hydrogenation of Aromatic Ketones Catalyzed by a Mesoporous Silica-Supported Iridium Catalyst

Guohua Liu,[a,*] Mei Yao,[a] Jianyao Wang,[a] Xiaoquan Lu,[a] Mouming Liu,[a] Fang Zhang,[a] and Hexing Li[a,*]

[a] Department of Chemistry, Shanghai Normal University, Shanghai 200234, People's Republic of China
Fax: (+86)-21-6432-2511; e-mail: ghliu@shnu.edu.cn or HeXing-Li@shnu.edu.cn

Received: February 19, 2008; Revised: April 3, 2008; Published online: June 2, 2008

Supporting information for this article is available on the WWW under http://asc.wiley-vch.de/home/.

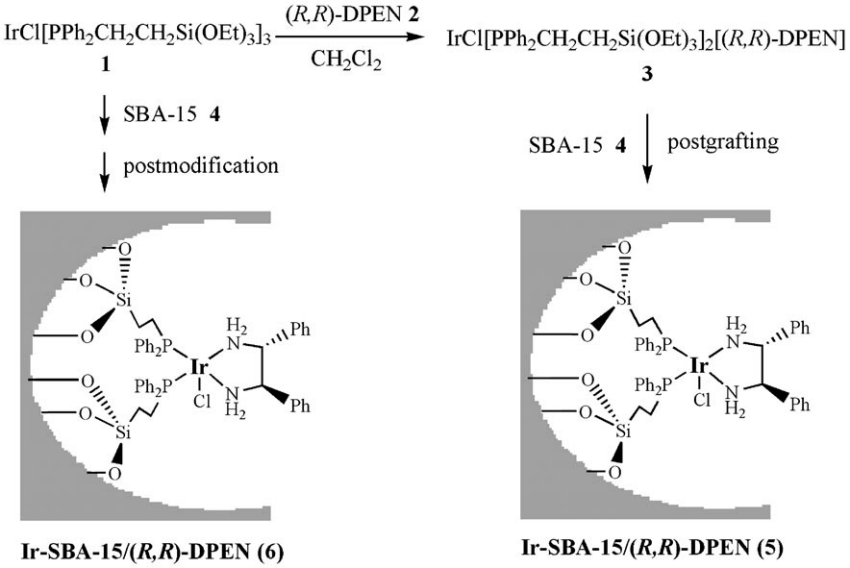
Abstract: A mesoporous, silica-supported, chiral iridium catalyst with a highly ordered dimensional-hexagonal mesostructure was prepared by postgrafting the organometallic complex (1-diphenylphosphino-2-triethylsilylethane)[(*R,R*)-1,2-diphenylethylenediamine]iridium chloride {IrCl[$PPh_2(CH_2)_2Si(OEt)_3$]$_2$[(*R,R*)-DPEN] (DPEN = 1,2-diphenylethylenediamine)} on SBA-15 silica. During the asymmetric hydrogenation of various aromatic ketones under 40 atm of hydrogen, the mesoporous, silica-supported, chiral iridium catalyst exhibited high catalytic activity (more than 95% conversions) and excellent enantioselectivity (up to more than 99% *ee*). The catalyst could be recovered easily and used repetitively seven times without significantly affecting the catalytic activity and the enantioselectivity.

Keywords: asymmetric catalysis; catalyst recycling; enantioselectivity; hydrogenation; mesoporous materials

The asymmetric hydrogenation of prochiral ketones is an important method to prepare enantiomerically pure secondary alcohols, which are very valuable synthetic intermediates for pharmaceuticals or materials. Although a variety of homogeneous chiral Ru, Rh and Ir catalysts have been demonstrated to be highly enantioselective in the hydrogenation of prochiral ketones,[1,2] their practical applications in industrial process are hindered due to the difficulty in recovery and reuse of the expensive catalyst, as well as product contamination caused by metal leaching. To overcome these problems, a practical strategy[3] is to immobilize them onto polymer supports[4] or on inorganic materials.[5] However, these heterogeneous catalysts often suffer from lowered catalytic activity and enantioselectivity. Furthermore, their catalytic sites are randomly oriented among the supports and microenvironment around the active sites is usually not clear. It is thus difficult, or even impossible, to fine-tune both catalytic activity and enantioselectivity through systematically adjusting the microenvironment of the catalytic sites in these supports. Recently, mesoporous materials as supports have attracted much attention.[6] These mesoporous materials possess a high density and high dispersion of active sites due to the large surface area and ordered mesopore channels. More attractively, it is possible to improve the catalytic activity and enantioselectivity through controlling the microenvironment of the active sites in regular and adjustable mesopores. Thus, the design of the mesoporous silica-supported chiral catalyst represents a promising strategy in the field of asymmetric catalysis.[7]

We have been interested in mesoporous silica-supported catalysts.[8] Recently, we reported a mesoporous, silica-supported, chiral ruthenium catalyst, which showed high catalytic activity and enantioselectivity for the asymmetric transfer hydrogenation of ketones.[8a] As an extension of our previous study, we have now prepared a mesoporous, silica-supported, chiral iridium catalyst and applied it to the asymmetric hydrogenation of ketones under 40 atm H_2. The key feature was that such a catalyst was synthesized by immobilizing directly the organometallic complex on SBA-15 *via* a postgrafting method in order to maintain its highly ordered mesostructure. Our research focused on the investigation of the different stereocontrol performance and comparison of its catalytic property with those obtained through the *in situ* complexing approach reported in the literature.

The mesoporous, silica-supported, chiral iridium catalyst, abbreviated as Ir-SBA-15/(*R,R*)-DPEN (**5**), was synthesized by a postgrafting method. As shown in Scheme 1, the organometallic complex **3** was prepared by the reaction of IrCl[$Ph_2P(CH_2)_2Si(OEt)_3$]$_3$ (**1**)[9] with (*R,R*)-DPEN (**2**) in a high yield. Ir-SBA-15/



Scheme 1. Syntheses of immobilized catalysts **5** and **6**.

(*R,R*)-DPEN (**5**) was successfully obtained by anchoring **3** onto the SBA-15 **4** under reflux in toluene for 24 h. The FT-IR spectrum of the catalyst **5** displayed the characteristic bands of **3** around 2980, 2937, 1604, 1442 and 694 cm^{-1} for ν_{as}(C–H), ν_s(C–H), ν_s(C–C), ν(P–C) and ω(C–H), respectively.[10] Strong Q^3(δ = −104 ppm) and Q^4 (δ = −112 ppm) peaks in the ^{29}Si MAS NMR spectrum (Figure 1) suggested that the catalyst **5** possessed mainly a network structure of {(HO)Si(OSi)$_3$} and{Si(OSi)$_4$},[9] while the relatively weak T^2 (δ = −58 ppm) and T^3 (δ = −67 ppm) peaks indicated the formation of {R(HO)Si(OSi)$_2$} and {RSi(OSi)$_3$}[9] (R = organometallic complexes **3**) as a part of the wall in the mesoporous structure.[11] In addition, ^{13}C (Figure 1) and ^{31}P CP MAS NMR spectra clearly displayed peaks at 129, 58, 30, 15 ppm and at 70.2, 34.5, −4.6 ppm. All these confirmed the successful incorporation of the organometallic complex **3** onto the SBA-15. The inductively coupled plasma (ICP) optical emission spectrometric analysis showed that the Ir loading amount in the catalysts **5** was 5.56 mg per gram of catalyst, which was nearly consistent with the results of elemental analysis (5.49 mg/g) calculated from mass% of N (0.08%).

The powder XRD patterns revealed that the catalyst **5** and the SBA-15 showed one similar intense d_{100} diffraction peak along with two similar weak diffraction peaks (d_{110}, d_{200}) in Figure 2, suggesting that the dimensional-hexagonal pore structure (*p6mm*) could be preserved after the postgrafting.[12] The decreases of the peak intensity of the catalyst **5**, compared to the SBA-15, implied that the postgrafting might disturb the highly ordered mesoporous structure to a certain degree. The TEM morphology further confirmed

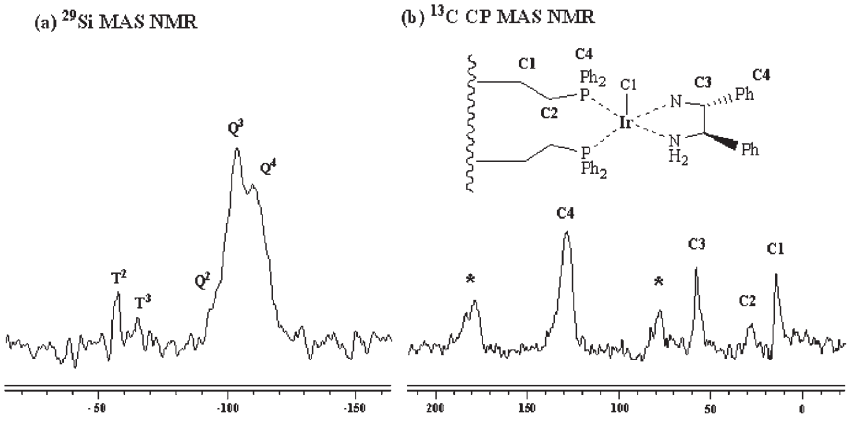


Figure 1. Solid-state NMR spectra of the mesoporous, silica-supported, chiral catalyst **5** (a) ^{29}Si MAS NMR and (b) ^{13}C CP MAS NMR.

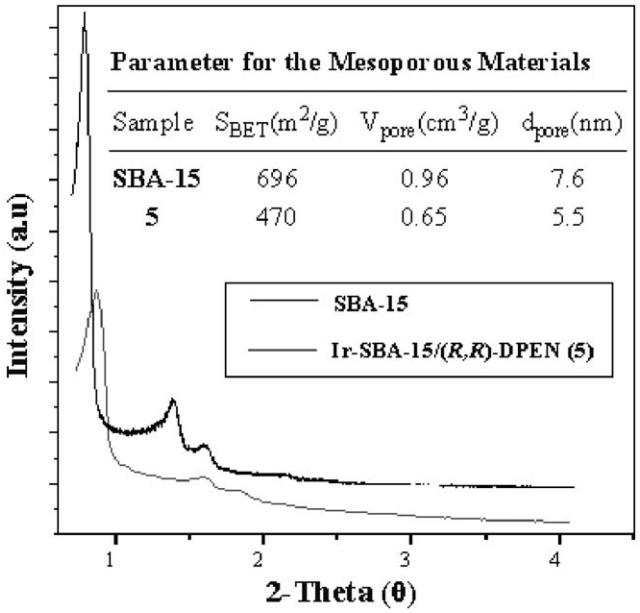


Figure 2. Powder XRD patterns of the SBA-15 (*upper curve*) and the mesoporous, silica-supported, chiral catalyst **5** (*lower curve*).

that the catalyst **5** had a well-ordered mesostructure with the dimensional-hexagonal arrangement as shown in Figure 3. The nitrogen adsorption-desorption isotherm of the catalysts **5** exhibited a typical IV type isotherm with a steep increase in adsorption at $P/P_0 = 0.57$. From the structural parameters listed in Figure 2, it was found easily that the postgrafting of **3** resulted in a decrease in nanopore size, surface area, and pore volume. This was attributed to the occupation of **3** in the pore channels to make the pore narrow and the coverage of **3** on the channel surface to result in an increase of the wall thickness.[8b,c]

Hydrogen serving as H-donor was applied in the Ir-catalyzed asymmetric hydrogenation of ketones.[13] During the asymmetric hydrogenation of ketones carried out at 50 °C under 40 atm H_2 in the presence of isopropyl alcohol, the catalyst **5** provided (*R*)-1-phenyl-1-ethanol with 99% conversion and more than 99% *ee* using acetophenone as a substrate (Table 1, entry 1). Such an enantioselectivity was higher than that achieved with the corresponding organometallic complex **3** (entry 2) and higher even than that obtained by using {IrHCl[(*R*)-BINAP][(*R*,*R*)-DPEN]} as a homogeneous catalyst (84% *ee* of **9a**).[13a] Apparently, the regular and adjustable pores in such a catalyst are beneficial to control the microenvironment of the active sites and retain the excellent stereocontrol performance. On the basis of this excellent result, the catalyst **5** was further investigated using a series of aromatic ketones as substrates (entries 3–6). In general, high conversions and no side products, and excellent enantioselectivities were obtained under similar conditions. In addition, the structures and electronic properties of substituents on the acetophenone did not affect significantly the enantioselectivity. Of particular note was that the reaction could be run at a high substrate/catalyst ratio without affecting the *ee* value, as exemplified by the hydrogenation of **8a** at a substrate/catalyst ratio = 500 (entry 7). More importantly, the heterogeneous catalyst **5** could be easily separated from the reaction mixture *via* simple filtration and used repetitively. For example, upon completion of the reaction, the heterogeneous catalyst **5** was quantitatively recovered *via* filtration. In seven consecutive reactions using 4-methoxyacetophone (**8a**) as

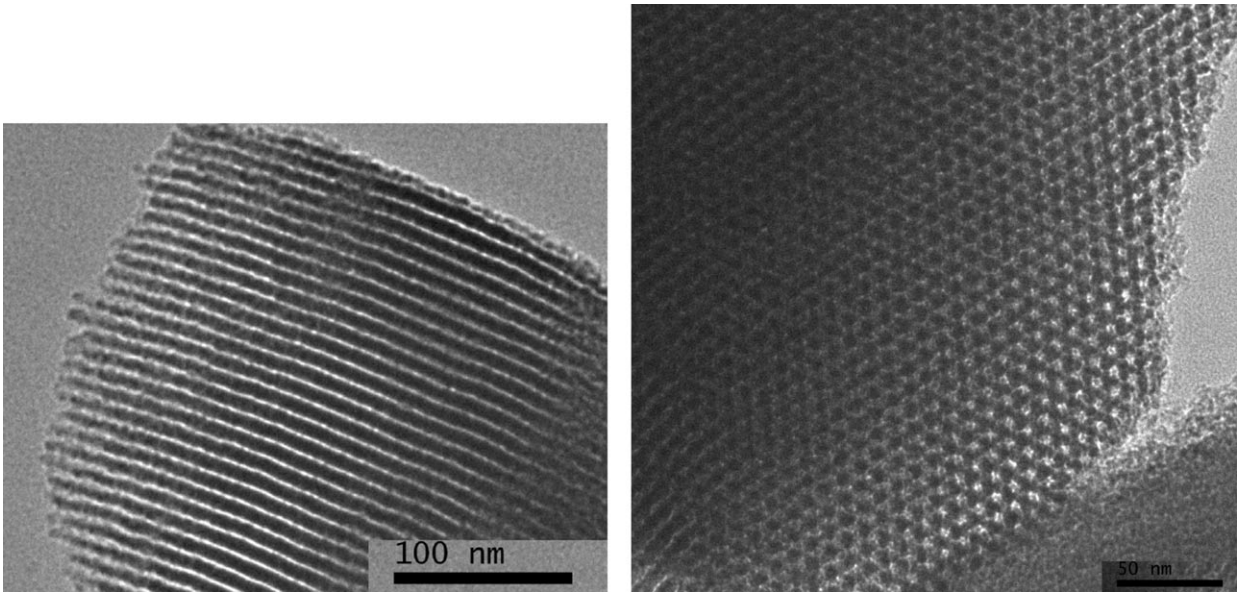
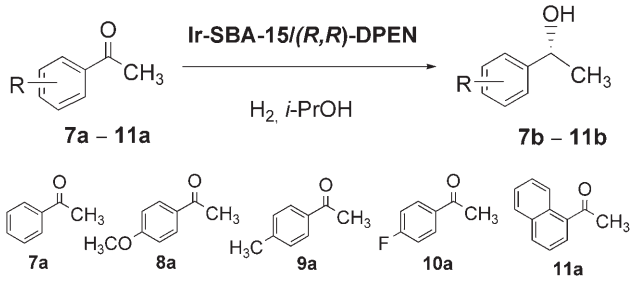


Figure 3. TEM images of the mesoporous, silica-supported, chiral catalyst **5** viewed along [100] and [001] directions.

Table 1. Asymmetric hydrogenation of aromatic ketones.[a]



Entry	Substrate	Run	Conversion [%][b]	*ee* [%][b]
1	**7a**	1	99	>99
2	**7a**	1	99	35
3	**8a**	1	>99	99
4	**9a**	1	>99	>99
5	**10a**	1	95	>99
6	**11a**	1	>99	>99
7	**8a**	1	90	>99[c]
8	**8a**	2	>99	97[d]
9	**8a**	3	>99	96[d]
10	**8a**	4	>99	96[d]
11	**8a**	5	>99	94[d]
12	**8a**	6	>99	88[d]
13	**8a**	7	99	92[d]
14	**7a**	1	92	64[e]

[a] *Reaction conditions:* catalyst (1.60 μmol), *i*-PrOH (5 mL), ketone (0.4 mmol), 40 atm, reaction temperature (50 °C), reaction time (16–24 h).
[b] Determined by chiral GC analysis. The absolute configuration of the product is *R*.
[c] Data were obtained at S/C = 500.
[d] Recovered catalyst was used.
[e] Data was obtained using catalyst (**6**) prepared by a postmodified method.

substrate, the catalyst **5** afforded more than 98% conversions and more than 91% *ee* values with the exception of the sixth recycling experiment (entries 8–13). The catalytic activity and enantioselectivity decreased gradually as the catalyst **5** was recycled, which was due to the slight loss of Ir metal as confirmed by ICP analyses.

Although the relationship between the mesoporous structure and catalytic property is complex, the following factors could be taken into consideration when using the heterogeneous catalyst **5**. Firstly, on comparing the catalyst **5** with the respective homogeneous catalysts,[13a,b] the higher enantioselectivity of catalyst **5** was attributed to fact that the organometallic complexes in catalyst **5** were mainly incorporated in the highly ordered mesopores of the SBA-15 support. This kind of immobilization is useful to form a regularly dispersive arrangement and to reduce aggregation of the active species, leading to excellent stereocontrol performance owing to the favorable catalytic microenvironment for chiral recognition. This explains why the catalyst **5** showed higher enantioselectivity than the corresponding homogeneous catalysts. Secondly, on comparing the catalyst **5** with the SBA-supported catalyst reported by Liu et al.,[7b] the higher catalytic efficiency in recovery and reuse of the catalyst **5** may be attributed to fact that the covalent immobilization of the organometallic complexes on the SBA-15 avoided the loss of metal. In our catalytic system, the metal loading occurred in the formation of the organometallic complexes before they were anchored on the SBA-15 *via* covalent immobilization. Thus, this avoided non-covalent adsorption leading to the loss of metal during the catalytic process. According to the ICP analyses, the loss of metal could be neglected in our catalytic system. This explains why the activity of the SBA-supported catalyst reported by Liu et al. decreased abruptly after three recycling-experiments due to a significant loss of Ru metal. On the other hand, the *in situ* complexing approach may be another factor to affect the recycling efficiency. From entry 14, one could see that the catalyst prepared by *in situ* coordination *via* a postmodified method afforded the corresponding secondary alcohol with 92% conversion and 64% *ee* when using acetophenone as a substrate. However, both the conversion and enantioselectivtiy decreased abruptly in the second recycling test. This result suggested that the postmodified organic groups [(*R,R*)-DPEN] were mainly near the mouth of the mesopores[14] and were easy to leach due to the *in situ* complexing approach, which should be a main factor accounting for catalyst deactivation.

In conclusion, we have developed a facile approach to prepare mesoporous, silica-supported, chiral iridium catalyst **5** by a postgrafting method. The catalyst **5** exhibited more than 95% conversions for all tested ketones and the excellent enantioselectivities (up to more than 99% *ee*) during the asymmetric hydrogenation of various aromatic ketones under 40 atm H_2 were higher than those of other corresponding silica-supported catalysts and even the corresponding organometallic complex. Furthermore, such a catalyst could be recovered and reused seven times without affecting obviously the *ee* value, showing a good potential in industrial applications.

Experimental Section

General Procedures for Asymmetric Hydrogenation of Ketones

The solid **5** (55.3 mg, 1.60 μmol based on Ir from ICP) was added to a stainless steel autoclave at room temperature in a glovebox, into which anhydrous 2-propanol (5 mL, 0.065 mol) and the ketone (0.4 mmol) were charged beforehand. The hydrogenation was performed at 50 °C under H_2 (40 atm) for 16–24 h. After completion of the reaction, hydro-

gen was carefully released. Dry CH_2Cl_2 (1 mL) was added and the mixture was stirred for 1 min. The reactor then was centrifuged (2000 r/min) for 1–2 min. The solution was purified by column chromatography using ether as the eluent. The main peaks were concentrated to afford a mixture of ketone and the corresponding alcohol as a colorless liquid for determination of conversion and enantiomeric excess. The conversion and enantiomeric excess were determined *via* GC analysis using a Supelco β-Dex 120 chiral column (30 m × 0.25 mm(i.d.), 0.25 μm film) (see Supporting Information for details).

Supporting Information

Complete experimental procedures and full characterization data are given in the Supporting Information.

Acknowledgements

We are grateful to China National Natural Science Foundation (20673072), 973 Pre-program (2005CCA01100), Shanghai Sciences and Technologies Development Fund (071005119 and 06JC14060), and Shanghai Municipal Education Commission (No. 08YZ71) for financial support.

References

[1] a) E. N. Jacobsen, A. Pfaltz, H. Yamamoto, (Eds.), *Comprehensive Asymmetric Catalysis*, Springer, Berlin, **1999**; b) I. Ojima, *Catalytic Asymmetric Synthesis*, 2nd edn., Wiley, New York, **2000**; c) G. Q. Lin, Y. M. Li, A. S. C. Chan, *Principles and Applications of Asymmetric Synthesis*, Wiley-Interscience, New York, **2001**.

[2] a) C. A. Sandoval, T. Ohkuma, K. Muñiz, R. Noyori, *J. Am. Chem. Soc.* **2003**, *125*, 13490; b) S. Burk, G. Francio, W. Leitner, *Chem. Commun.* **2005**, 3460; c) K. Mikami, K. Wakabayashi, K. Aikawa, *Org. Lett.* **2006**, *8*, 1517; d) X. F. Wu, D. Vinci, T. Ikariya, J. L. Xiao, *Chem. Commun.* **2005**, 4447; e) L. Dahlenburg, R. Götz, *Eur. J. Inorg. Chem.* **2004**, *4*, 888; f) Z. R. Dong, Y. Y. Li, J. S. Chen, B. Z. Li, Y. Xing, J. X. Gao, *Org. Lett.* **2005**, *7*, 1043; g) Z. E. Clarke, P. T. Maragh, T. P. Dasgupta, D. G. Gusev, A. J. Lough, K. Abdur-Rashid, *Organometallics* **2006**, *25*, 4113.

[3] a) M. Heitbaum, F. Glorius, I. Escher, *Angew. Chem.* **2006**, *118*, 4850; *Angew. Chem. Int. Ed.* **2006**, *45*, 4732; b) D. E. DeVos, I. F. J. Vankelecom, P. A. Jacobs, *Chiral Catalyst Immobilization and Recycling*, Wiley-VCH, Weinheim, **2000**; c) J. A. Gladysz, *Chem. Rev.* **2002**, *102*, 3215; d) Q. H. Fan, Y. M. Li, A. S. C. Chan, *Chem. Rev.* **2002**, *102*, 3385; e) J. Horn, F. Michalek, C. C. Tzschucke, W. Bannwarth, *Top. Curr. Chem.* **2004**, *242*, 43; f) P. McMorn, G. Hutchings, *Chem. Soc. Rev.* **2004**, *33*, 108.

[4] a) D. E. Bergbreiter, *Chem. Rev.* **2002**, *102*, 3345; b) T. J. Dickerson, N. N. Reed, K. D. Janda, *Chem. Rev.* **2002**, *102*, 3325; c) X. G. Li, W. P. Chen, W. Hems, F. King, J. L. Xiao, *Org. Lett.* **2003**, *5*, 4559; d) Y. X. Liang, Q. Jing, X. Li, L. Shi, K. L. Ding, *J. Am. Chem. Soc.* **2005**, *127*, 7694; e) S. Bräse, F. Lauterwasser, R. E. Ziegert, *Adv. Synth. Catal.* **2003**, *345*, 869; f) X. W. Wang, K. L. Ding, *J. Am. Chem. Soc.* **2004**, *126*, 10524; g) H. M. L. Davies, A. W. Walji, *Org. Lett.* **2005**, *7*, 2941; h) S. M. Lu, H. Alper, *J. Am. Chem. Soc.* **2003**, *125*, 13126.

[5] a) C. E. Song, S. G. Lee, *Chem. Rev.* **2002**, *102*, 3495; b) A. G. Hu, G. T. Yee, W. B. Lin, *J. Am. Chem. Soc.* **2005**, *127*, 12486; c) P. N. Liu, J. G. Deng, Y. Q. Tu, S. H. Wang, *Chem. Commun.* **2004**, 2070; d) J. A. M. Brandts, P. H. Berben, *Org. Process Res. Dev.* **2003**, *7*, 393.

[6] a) D. E. DeVos, M. Dams, B. F. Sels, P. A. Jacobs, *Chem. Rev.* **2002**, *102*, 3615; b) P. Yang, D. Zhao, D. I. Margolese, B. F. Chmelka, G. D. Stucky, *Nature* **1998**, *396*, 152; c) Y. Tao, H. Kanoh, L. Abrams, K. Kaneko, *Chem. Rev.* **2006**, *106*, 896.

[7] a) I. Domínguez, V. Fornés, M. J. Sabater, *J. Catal.* **2004**, *228*, 92; b) P. N. Liu, P. M. Gu, F. Wang, Y. Q. Tu, *Org. Lett.* **2004**, *6*, 169; c) J. Y. Ying, C. P. Mehnert, M. S. Wong, *Angew. Chem.* **1999**, *111*, 58; *Angew. Chem. Int. Ed.* **1999**, *38*, 56; d) D. M. Jiang, Q. H. Yang, J. Yang, L. Zhang, G. R. Zhu, W. G. Su, C. Li, *Chem. Mater.* **2005**, *17*, 6154; e) D. M. Jiang, J. S. Gao, Q. H. Yang, J. Yang, C. Li, *Chem. Mater.* **2006**, *18*, 6012; f) B. Pugin, H. Landert, F. Spindler, H. U. Blaser, *Adv. Synth. Catal.* **2002**, *344*, 974; g) Y. Izumi, K. Konishi, M. Tsukahara, D. M. Obaid, K. I. Aika, *J. Phys. Chem. C* **2007**, *111*, 10073; h) K. Mukhopadhyay, A. B. Mandale, R. V. Chaudhari, *Chem. Mater.* **2003**, *15*, 1766; i) J. P. K. Reynhardt, Y. Yang, A. Sayari, H. Alper, *Chem. Mater.* **2004**, *16*, 4095.

[8] a) G. H. Liu, M. Yao, F. Zhang, Y. Gao, H. X. Li, *Chem. Commun.* **2008**, 347; b) H. X. Li, F. Zhang, Y. Wan, Y. F. Lu, *J. Phys. Chem. B* **2006**, *110*, 22942; c) Y. Wan, F. Zhang, Y. F. Lu, H. X. Li, *J. Mol. Catal. A: Chem.* **2007**, *267*, 165; d) H. X. Li, Y. D. Wu, Y. Wan, J. Zhang, W. L. Dai, M. H. Qiao, *Catal. Today* **2004**, *93–95*, 493; e) H. X. Li, Q. F. Zhao, Y. Wan, W. L. Dai, M. H. Qiao, *J. Catal.* **2006**, *244*, 251; f) H. X. Li, Z. F. Bian, J. Zhu, Y. N. Huo, H. Li, Y. F. Lu, *J. Am. Chem. Soc.* **2007**, *129*, 4538.

[9] O. Krőcher, O. A. Kőppel, M. Frőba, A. Baiker, *J. Catal.* **1998**, *178*, 284.

[10] a) A. S. M. Chong, X. S. Zhao, *J. Phys. Chem. B.* **2003**, *107*, 12650; b) Q. Y. Hu, J. E. Hampsey, N. Jiang, C. J. Li, Y. F. Lu, *Chem. Mater.* **2005**, *17*, 1561.

[11] S. L. Burkett, S. D. Sims, S. Mann, *Chem. Commun.* **1996**, *11*, 1367.

[12] D. Zhao, Q. Huo, J. Feng, B. F. Chmelka, G. D. Stucky, *J. Am. Chem. Soc.* **1998**, *120*, 6024.

[13] a) L. Dahlenburg, R. Menzel, F. W. Heinemann, *Eur. J. Inorg. Chem.* **2007**, 4364; b) E. L. Roux, R. Malacea, E. Manoury, R. Poli, L. Gonsalvi, M. Perruzini, *Adv. Synth. Catal.* **2007**, *349*, 309; c) C. Maillet, T. Praveen, P. Janvier, S. Minguet, M. Evain, C. Saluzzo, M. L. Tommasino, B. Bujoli, *J. Org. Chem.* **2002**, *67*, 8191; d) L. Dahlenburg, R. Götz, *Eur. J. Inorg. Chem.* **2004**, 888.

[14] a) I. K. Mbaraka, B. H. Shanks, *J. Catal.* **2005**, *229*, 365; b) A. Stein, M. H. Lim, *Chem. Mater.* **1999**, *11*, 3285.

