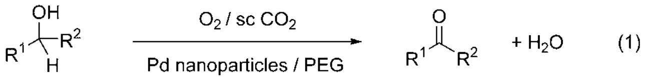
Multiphase Catalysis

Biphasic Aerobic Oxidation of Alcohols Catalyzed by Poly(ethylene glycol)-Stabilized Palladium Nanoparticles in Supercritical Carbon Dioxide**

*Zhenshan Hou, Nils Theyssen, Axel Brinkmann, and Walter Leitner**

The aerobic oxidation of alcohols to aldehydes and ketones is a fundamental chemical transformation for the production of a large variety of important intermediates and fine chemical products. Catalytic methods for this reaction are being investigated intensively to replace stoichiometric oxidation processes that generate large amounts of heavy metal and solvent waste.[1] Among the transition metals, palladium shows very promising catalytic properties in the form of complexes,[2] heterogeneous metal catalysts,[3,4] or nanoparticles.[5] Significant progress has been made in improving activity, substrate scope, and selectivity with multifunctional substrates for the individual catalytic systems. Two of the major general limitations of the catalytic approach relate to rapid catalyst deactivation by aggregation and formation of Pd-black[6] and the need for large amounts of organic solvents in batchwise solution-phase processes involving molecular oxygen.[7]

Herein, we report on a new highly efficient catalytic system for the biphasic aerobic oxidation of alcohols by using palladium nanoparticles in a poly(ethylene glycol) (PEG) matrix as the catalyst and supercritical carbon dioxide ($scCO_2$) as the substrate- and product-phase [Eq. (1)].[8,9] The design of this system was based on the assumption that the PEG matrix might help to prevent aggregation and deactivation of the catalytically active nanoparticles while $scCO_2$ could provide a safe environment for the use of molecular oxygen under essentially solvent-free conditions and could allow continuous operation, even with substrates of low volatility. The results disclosed herein confirm the feasibility of this approach, provide insight into the formation of the catalytically active particles within the matrix, and demonstrate that activity, selectivity, and substrate scope of this new system compare favorably to other catalytic approaches for selective alcohol oxidation.



In an exploratory study, the oxidation of 3-methyl-2-butene-1-ol (**1a**) to 3-methyl-2-butene-1-al (**2a**) was used as a test reaction [Eq. (2)]. The giant palladium cluster [$Pd_{561}phen_{60}(OAc)_{180}$][5a,b,10,11] (**3**; phen = 1,10-phenanthroline) was found to lead to a particularly active and selective catalyst for aerobic oxidation of alcohols in $scCO_2$ when embedded in a PEG-1000 matrix (Figure 1). PEG of molecular weight 1000 is a waxy solid under ambient conditions but melts under CO_2 pressures at temperatures above approximately 40 °C.[8,12] In a typical procedure, PEG-1000, cluster **3**, and substrate **1a** were charged into a window-equipped high-pressure reactor, which was then pressurized with CO_2 and O_2, either sequentially or as a preformed mixture from a high-pressure reservoir. The Pd clusters were well dispersed in the liquid PEG-1000 matrix over a period of about 1–2 h under the reaction conditions summarized in Figure 1. Substrate **1a** and product **2a** are contained preferentially in the supernatant "supercritical" CO_2 phase, as demonstrated by online GC monitoring. The conversion/time profile reveals a significant induction period in the first run, which can be associated with the dispersion process (see below). The oxidation occurs exclusively on the hydroxy function and with no significant over-oxidation to yield **2a** with selectivities well above 99 % at quantitative conversion.

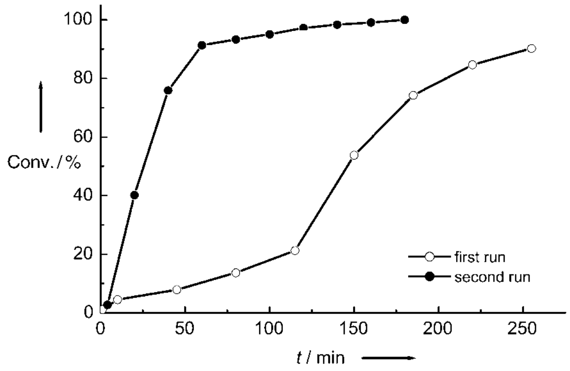
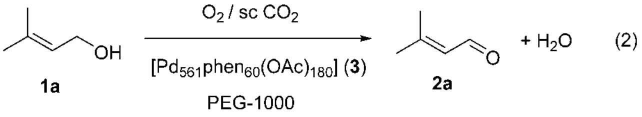


Figure 1. Conversion/time profile of the biphasic selective aerobic oxidation of 3-methyl-2-butene-1-ol (**1a**) by using a catalyst formed from [$Pd_{561}phen_{60}(OAc)_{180}$] (**3**) and PEG-1000 with $scCO_2$ as the reaction medium ($T = 50\,°C$, $d(CO_2/O_2) = 0.55\ g\,mL^{-1}$).



After conversion is completed, the products **2a** and water can be extracted quantitatively with $scCO_2$ (80 °C, 14.5 MPa, 5 $L\,h^{-1}$, 7 h) with the Pd-doped PEG phase left in the reactor. Only very small amounts of PEG-1000 are extracted by $scCO_2$

---

[*] Prof. Dr. W. Leitner
Institut für Technische und Makromolekulare Chemie
Lehrstuhl für Technische Chemie und Petrolchemie
RWTH Aachen, Worringerweg 1, 52064 Aachen (Germany)
Fax: (+49) 241-80-22177
E-mail: leitner@itmc.rwth-aachen.de

Dr. Z. Hou, Dr. N. Theyssen, A. Brinkmann, Prof. Dr. W. Leitner
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1, 45470 Mülheim an der Ruhr (Germany)

[**] This work was supported by the Max-Planck-Gesellschaft and the Fonds der Chemischen Industrie. We thank Axel Dreier and Dr. B. Tesche, MPI Mülheim, for the transmission electron microscopy analysis and Prof. U. Simon, RWTH Aachen, for fruitful discussions.

DOI: 10.1002/ange.200461493

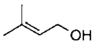
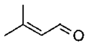
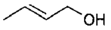
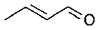
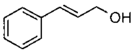
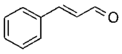
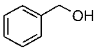
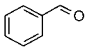
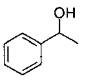
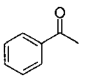
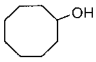
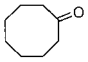
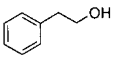
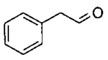
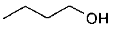
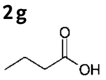
under these conditions (8 mg according to the method described in ref. [8]), and the product is contaminated with less than 2.3 ppm of Pd according to atomic absorption spectroscopy. Most notably, the reaction starts again without any noticeable induction period in the second run, thereby leading to complete conversion within less than 200 min at 50 °C (Figure 1). This high activity is fully retained or even seems to increase slightly in subsequent runs. The same qualitative behavior is observed at somewhat higher reaction temperatures and for benzyl alcohol **1d**, another prototypical substrate (Table 1).

The activity and selectivity of the catalytic system formed from **3** and PEG-1000 are remarkably higher than those of conventional heterogeneous catalysts under the same reaction conditions with $scCO_2$ as the reaction medium.[4] In control experiments ($T = 65$ °C, $d(CO_2/O_2) = 0.55\ g\,mL^{-1}$), palladium on charcoal gives only 34 % conversion of **1a** after 1.5 h reaction time. Higher conversion can be obtained upon prolonged reaction times, but only at the expense of significantly reduced selectivity towards the unsaturated aldehyde **2a** (5 h: conversion = 75 %, selectivity = 78 %). The same negative trend is even more pronounced with palladium on alumina, which gives only 45 % selectivity at 88 % conversion within 5 h. Interestingly, the addition of PEG-1000 results in a certain improvement of the performance of the heterogeneous catalyst, as shown for palladium on carbon (5 h: conversion = 82 %, selectivity = 89 %). However, neither activity nor selectivity can rival the performance of the PEG-stabilized nanoparticle catalyst.

Table 1 summarizes representative results obtained with the catalytic system **3**/PEG-1000 in $scCO_2$ for a variety of alcohols under a standard set of reaction conditions. Conversion and selectivity from the second run is given unless noted otherwise. Allylic alcohols **1a–c** are transformed into the corresponding α,β-unsaturated aldehydes **2a–c** in excellent yields under mild conditions. Somewhat longer reaction times are required for primary and secondary benzylic alcohols **1d** and **1e**, but selectivities remain close to 99 %. The cyclic alcohol **1f** and even 2-phenylethanol (**1g**) give very high selectivities for the corresponding ketone **2f** and aldehyde **2g**, respectively, and quantitative conversion is obtained after appropriate reaction times. The only exception, so far, was found with 1-butanol (**1h**), which is oxidized rapidly but forms butyric acid **5** as the major product under the present conditions.

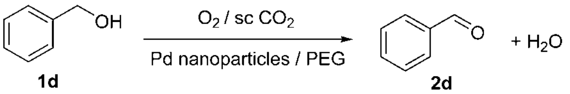
It is important to note that the giant palladium cluster **3** is known to oxidize allylic alcohols in conventional organic solvents, whereas benzylic alcohols are not effectively transformed with **3** under conventional conditions.[11] Thus, the broad substrate scope summarized in Table 1 indicates that the catalytically active species is different in the catalytic system formed from **3**/PEG-1000 in $scCO_2$. We were therefore interested in whether it is possible to generate PEG-stabilized Pd nanoparticles for the selective oxidation of alcohols from other precursors as well. Indeed, a material with almost identical catalytic properties was obtained by simply heating a mixture of $[Pd(acac)_2]$ (**4**; acac = acetylacetonate; 20 mg), the commercial surfactant Brij 35 (0.8 g), and PEG-1000 (2.7 g) to 130 °C for 1 h under an argon atmosphere.

Table 1: Biphasic catalytic oxidation of alcohols **1a–h** by using PEG-stabilized palladium nanoparticles in $scCO_2$.[a]

Substrate	Product	T [°C]	t [h]	Run	Conv. [%]	Sel. [%]
 **1a**	 **2a**	65	1.5	1	81.0	99.8
				2	99.2	99.3
				3	100	99.1
 **1b**	 **2b**	65	1.5	2	100	98.1
 **1c**	 **2c**	65	1.5	2	99.8	99.2
 **1d**	 **2d**	80	13	1	83.1	99.8
				2	96.2	98.8
				3	99.8	97.5
				4	100	98.7
 **1e**	 **2e**	80	13	2	56.9	98.8
 **1f**	 **2f**	80	26	2	99.5	98.9
 **1g**	 **2g**	80	13	2	45.8	95.5
 **1h**	 **5**	80	4	1	65.5	57.5[b]

[a] Reaction conditions: palladium cluster **3** (0.1 mmol Pd), PEG-1000 (2.40 g), substrate **1a–h** (1.99 mmol), $d(CO_2/O_2) = 0.55\ g\,mL^{-1}$. [b] Butyric acid butyl ester is formed as a second product, together with small amounts of butanal.

As we were encouraged by the promising results obtained from batchwise recycling, the aerobic oxidation of benzylic alcohol **1d** was carried out as a continuous-flow process [Eq. (3)]. The set-up was largely identical to previously described equipment,[13] with a 36 mL stainless-steel reactor as the central part. Owing to the unique combination of gas-like mixing and liquid-like solvent properties provided by $scCO_2$, a homogeneous feed of CO_2, O_2, and **1d**/**2d** can be transported through the PEG phase by using a capillary.



1d **2d** (3)

In the absence of CO_2, **1d** and **2d** are liquids at the reaction temperature and are largely miscible with PEG-1500. Consequently, separation of catalysts and products would be tedious, if not impossible. Furthermore, great care would have to be taken to stay outside the explosive regime for all mixtures of the organic substrates and products and the molecular oxygen.

As judged by visual inspection, the catalyst material remains physically intact inside the reactor and no significant extrusion of PEG or Pd is observed, even during long operation times with $scCO_2$ as the mobile phase. Even with the very basic reaction engineering used in these bench-scale experiments, significant single-pass conversions are achieved with substrate **1d** under the nonoptimized conditions summarized in Figure 2. The initial conversion with both Pd nanoparticle/PEG-1500 catalysts reaches 15% at a total pressure of 15.5 MPa. Most notably, a small but continuous increase in activity occurs for both catalytic materials over the course of a 40 h continuous operation (Figure 2). The increase is somewhat more strongly pronounced for the system **3**/PEG-1500 where a conversion of 27% at nearly perfect selectivity is reached after 36 h.

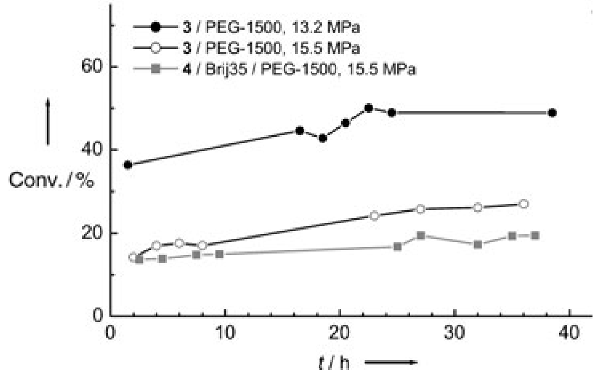


Figure 2. Continuous-flow aerobic oxidation of benzylic alcohol **1d** in $scCO_2$ by using PEG-stabilized Pd nanoparticles formed from $[Pd_{561}phen_{60}(OAc)_{180}]$ (**3**) and $[Pd(acac)_2]$ (**4**), respectively ($T = 80\,°C$, $p(CO_2/O_2$, 92:8) = 15.5 MPa and 13.2 MPa, respectively; flow rates: **1d**: 0.5 $mL\,h^{-1}$; exit flow: 5 $L\,h^{-1}$).

Interestingly, the CO_2 pressure has a distinct influence on the performance of the system. A small reduction of the pressure level (13.2 MPa instead of 15.5 MPa) leads to a significant increase in conversion by a factor of almost two (Figure 2), thereby resulting in a maximum single-pass conversion of approximately 50%. Most likely, the increased conversion results from a shift of the partition coefficient of the substrate in the biphasic medium in favor of the PEG phase at lower supercritical fluid density, thus increasing substrate availability in the catalyst phase. This explanation is supported by the fact that the solubility power of $scCO_2$ becomes insufficiently low for continuous operation with substrate **1d** at approximately 11 MPa. In general, these results indicate the possibility for significant optimization of single-pass conversion by variation of engineering parameters such as flow rates, CO_2 density, O_2/substrate ratio, and residence time.

It seems plausible to associate the high activity and long-term stability of the new catalytic system with a high dispersion of Pd nanoparticles, which are prevented from agglomeration within the PEG matrix.[14] This interpretation is strongly supported by transmission electron microscopy (TEM) studies of catalyst material formed from **3** and PEG-1000 before and after the reaction (Figure 3).

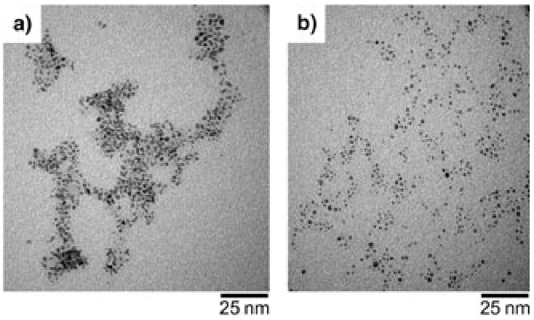


Figure 3. TEM images of the catalytically active material formed from the giant palladium cluster **3** and PEG-1000 before (a) and after (b) the selective biphasic oxidation of **1a** ($T = 65\,°C$, $d(CO_2/O_2) = 0.55\ g\,mL^{-1}$).

As shown in Figure 3a, the mixing of cluster **3** with PEG-1000 leads to a dispersion of particles that is far from uniform with significant agglomeration in certain areas of the matrix. In a sample taken after catalytic oxidation of **1a**, this situation has changed significantly (Figure 3b). The particles are now much more equally dispersed throughout the whole matrix. The average particle sizes were determined to be around 3.6 nm and 2.9 nm before and after the reaction, respectively. These values are consistent with values given for giant Pd clusters in other environments (3.0–3.6 nm,[10] 2.6 ± 0.35 nm[11a]). At this stage of investigation, we believe that interactions between the giant cluster and PEG are favoring dispersion of the particles within the matrix during the course of the reaction. The formation of pseudo-crown-ether structures between PEG and the nanoparticles has been suggested[14a,c] and was recently confirmed for a $ZnCl_2$–PEG complex by X-ray diffraction analysis.[15] The supercritical-phase-induced viscosity reduction may help to facilitate the necessary mass transport for the dispersion process in this multiphase approach to continuous-flow nanoparticle catalysis.

We have developed a novel catalytic system for the selective aerobic oxidation of alcohols based on highly dispersed Pd nanoparticles in a poly(ethylene glycol) (PEG) matrix with supercritical carbon dioxide ($scCO_2$) as the substrate and product phase. These catalytic materials show high activity, selectivity, and stability for a broad range of substrates. Catalytically active particles can be formed from various palladium sources and their dispersion appears to be aided by the presence of the supercritical reaction medium. The PEG matrix effectively stabilizes and immobilizes the catalytically active particles, whereas the unique solubility and mass-transfer properties of $scCO_2$ allow continuous processing at mild conditions, even with low-volatility substrates. This system nicely exemplifies the potential benefits resulting from the combination of molecular design and reaction engineering in advanced multiphase catalysis. Finally, it seems worth noting that both the catalyst matrix and the mobile phase used in this approach are toxicologically innocuous and environmentally benign materials that are applied in commercial applications in the nutrition industry, thus making this approach of general interest for "green" nanoparticle catalysis.

Experimental Section

Safety warning: Experiments using large amounts of compressed gases, especially molecular oxygen, are potentially hazardous and must only be carried out by using appropriate equipment and safety precautions.

The palladium cluster **3** was prepared under argon according to a known procedure.[10a] [Pd(acac)$_2$] (**4**), Brij 35, PEG-1000, and **1a**–**h** were obtained from commercial suppliers. The oxidation products were identified by comparison of ^{1}H NMR spectra and GC data with those of authentic samples. A preformed mixture of CO_2 and O_2 (molar ratio 92:8) was prepared in a temperature-controlled 5 L autoclave at 35 °C and 20.0 MPa and used throughout most of the oxidation experiments.

Batchwise catalytic oxidation of **1a**–**h**: A solution of **3** (9.98×10^{-5} mol) in acetic acid (1 mL) was introduced into a 10 mL window-equipped stainless-steel high-pressure reactor. The solvent was evaporated; PEG-1000 (2.40 g) and then the appropriate substrate **1a**–**h** (2.0×10^{-3} mol) were added. The reactor was pressurized with the CO_2/O_2 mixture (5.50 g) and heated to the desired temperature under vigorous stirring for the given reaction time (see Figure 1 and Table 1). After the reaction, CO_2 at 80 °C and 14.5 MPa was flushed through the liquid PEG phase for 7 h by use of a capillary with a compressor at an outlet flow-rate of approximately 5 L h^{-1}. The products were collected from the gas stream in two serial traps kept at −35 °C and analyzed by ^{1}H NMR spectroscopy and GC. Before starting the next run, the reactor was vented to ambient pressure and then new substrate was charged, followed by the CO_2/O_2 mixture.

Continuous-flow catalytic oxidation of **1d**: The catalytically active material formed from **3** or **4** and PEG-1500 (3.5 g) was charged into a 36 mL stainless-steel high-pressure reactor which was kept at 80 °C. A prewarmed (50 °C) continuous stream of CO_2/O_2 was passed through the liquid PEG phase at a flow rate of approximately 5 L h^{-1} by use of a capillary (exit flow at ambient conditions, total pressure of 15.5 MPa and 13.2 MPa in the reactor, respectively; Figure 2). The substrate was fed into the CO_2 stream before it entered the reactor with an HPLC pump at a rate of 0.5 mL h^{-1}. The mixture of **1d** and **2d** was isolated in two sequential cold traps (−35 °C) from the exit flow upon depressurization of the supercritical solvent. The cold traps were replaced periodically after about 2 h and their combined content was analyzed by ^{1}H NMR spectroscopy and GC.

Received: July 30, 2004
Revised: October 15, 2004

Keywords: aerobic oxidation · multiphase catalysis · nanoparticles · palladium · supercritical fluids

---

[1] a) R. A. Sheldon, I. W. C. E. Arends, G.-J. T. Brink, A. Dijksman, *Acc. Chem. Res.* **2002**, *35*, 774–781; b) J. Muzart, *Tetrahedron* **2003**, *59*, 5789–5816; c) B.-Z. Zhan, A. Thompson, *Tetrahedron* **2004**, *60*, 2917–2935.

[2] For recent examples, see: a) G.-J. T. Brink, I. W. C. E. Arends, M. Hoogenraad, G. Vespui, R. A. Sheldon, *Adv. Synth. Catal.* **2003**, *345*, 497–505; b) B. A. Steinhoff, S. R. Fix, S. S. Stahl, *J. Am. Chem. Soc.* **2002**, *124*, 766–767; c) N. Kakiuchi, Y. Maeda, T. Nishimura, S. Uemura, *J. Org. Chem.* **2001**, *66*, 6620–6625; d) D. R. Jensen, M. J. Schultz, J. A. Mueller, M. S. Sigman, *Angew. Chem.* **2003**, *115*, 3940–3943; *Angew. Chem. Int. Ed.* **2003**, *42*, 3810–3813; e) K. P. Peterson, R. C. Larock, *J. Org. Chem.* **1998**, *63*, 3185–3189; f) A. Haimov, R. Neumann, *Chem. Commun.* **2002**, 876–877; g) E. M. Ferreira, B. M. Stoltz, *J. Am. Chem. Soc.* **2001**, *123*, 7725–7726; h) S. Paavola, K. Zetterberg, T. Privalov, I. Csöregh, C. Moberg, *Adv. Synth. Catal.* **2004**, *346*, 237–244.

[3] For recent examples, see: a) K. Yamaguchi, N. Mizuno, *Angew. Chem.* **2002**, *114*, 4720–4724; *Angew. Chem. Int. Ed.* **2002**, *41*, 4538–4542; b) M. Musawir, P. N. Davey, G. Kelly, I. V. Kozhevnikov, *Chem. Commun.* **2003**, 1414–1415; c) C. Keresszegi, J.-D. Grunwaldt, T. Mallat, A. Baiker, *Chem. Commun.* **2003**, 2304–2305; d) B.-Z. Zhan, M. A. White, T.-K. Sham, J. A. Pincock, R. J. Doucet, K. V. Ramana Rao, K. N. Robertson, T. S. Cameron, *J. Am. Chem. Soc.* **2003**, *125*, 2195–2199; e) R. Anderson, K. Griffin, P. Johnston, P. L. Alster, *Adv. Synth. Catal.* **2003**, *345*, 517–523; f) U. R. Pillai, E. Sahle-Demessie, *Green Chem.* **2004**, *6*, 161–165.

[4] For the use of supercritical CO_2 with heterogeneous Pd catalysts for alcohol oxidation, see: a) G. Jenzer, D. Sueur, T. Mallat, A. Baiker, *Chem. Commun.* **2000**, 2247–2248; b) J.-D. Grunwaldt, M. Caravati, M. Ramin, A. Baiker, *Catal. Lett.* **2003**, *90*, 221–229; c) A. M. Steele, J. Zhu, S. C. Tsang, *Catal. Lett.* **2001**, *73*, 9–13; d) R. Gläser, R. Jos, J. Williardt, *Top. Catal.* **2003**, *22*, 31–39.

[5] For recent examples, see: a) G. Kovtun, T. Kameneva, S. L. Hladyi, M. Starchevsky, Y. Pazdersky, I. Stoarov, M. Vargaftik, I. Moiseev, *Adv. Synth. Catal.* **2002**, *344*, 957–964; b) K.-M. Choi, T. Akita, T. Mizugaki, K. Ebitani, K. Kaneda, *New J. Chem.* **2003**, *27*, 324–328; c) Y. Uozumi, R. Nakao, *Angew. Chem.* **2003**, *115*, 204–207; *Angew. Chem. Int. Ed.* **2003**, *42*, 194–197.

[6] T. Iwasawa, M. Tokunaga, Y. Obora, Y. Tsuji, *J. Am. Chem. Soc.* **2004**, *126*, 6554–6555.

[7] a) G.-J. T. Brink, I. W. C. E. Arends, R. A. Sheldon, *Science* **2000**, *287*, 1636–1639; b) K. Mori, K. Yamaguchi, T. Hara, T. Mizugaki, K. Ebitani, K. Kaneda, *J. Am. Chem. Soc.* **2002**, *124*, 11572–11573.

[8] The immobilization of Wilkinson's catalyst in PEG for biphasic hydrogenation in scCO_2 has been described recently: D. J. Heldebrant, P. G. Jessop, *J. Am. Chem. Soc.* **2003**, *125*, 5600–5601.

[9] Ru and Pd nanoparticles embedded in high density polyethylene as catalysts for hydrogenations with scCO_2: H. Ohde, M. Ohde, C. M. Wai, *Chem. Commun.* **2004**, 930–931.

[10] a) G. Schmid, M. Harms, J. O. Malm, J. O. Bovin, J. Van Ruitenbeck, H. W. Zandbergen, W. T. Fu, *J. Am. Chem. Soc.* **1993**, *115*, 2046–2048; b) G. Schmid, *Chem. Rev.* **1992**, *92*, 1709–1727.

[11] a) M. N. Vargaftik, V. P. Zagorodnikov, I. P. Stolarov, I. I. Moiseev, *J. Mol. Catal.* **1989**, *53*, 315–348; b) M. K. Starchevsky, S. L. Hladiy, Y. A. Pazdersky, M. N. Vargaftik, I. I. Moiseev, *J. Mol. Catal. A* **1999**, *146*, 229–236; c) K. Kaneda, Y. Fujie, K. Ebitani, *Tetrahedron Lett.* **1997**, *52*, 9023–9026; d) K. Ebitani, Y. Fujie, K. Kaneda, *Langmuir* **1999**, *15*, 3557–3562.

[12] E. Kokova, M. Petermann, E. Weidner, *Chem. Ing. Tech.* **2004**, *76*, 280–284.

[13] a) A. Bösmann, G. Franciò, E. Janssen, M. Solinas, W. Leitner, P. Wasserscheid, *Angew. Chem.* **2001**, *113*, 2769–2771; *Angew. Chem. Int. Ed.* **2001**, *40*, 2697–2699; b) M. T. Reetz, W. Wiesenhöfer, G. Franciò, W. Leitner, *Adv. Synth. Catal.* **2003**, *345*, 1221–1228.

[14] For example: a) L. Longenberger, G. Mills, *J. Phys. Chem.* **1995**, *99*, 475–478; b) T. Bormann, H. W. Roesky, U. Ritter, *J. Mol. Catal. A* **2000**, *153*, 31–48; c) D.-H. Chen, Y.-W. Huang, *J. Colloid Interface Sci.* **2002**, *255*, 299–302.

[15] E. Staunton, A. M. Christie, I. Martin-Litas, Y. G. Andreev, A. M. Z. Slawin, P. G. Bruce, *Angew. Chem.* **2004**, *116*, 2155–2157; *Angew. Chem. Int. Ed.* **2004**, *43*, 2103–2105.