Available online at www.sciencedirect.com

ScienceDirect

Tetrahedron Letters

Tetrahedron Letters 48 (2007) 8128–8131

Palladium nanoparticles-catalyzed chemoselective hydrogenations, a recyclable system in water

Nuria Miro Callis, Emilie Thiery, Jean Le Bras* and Jacques Muzart

UMR 6519 'Réactions Sélectives et Applications', Boîte 44, CNRS-Université de Reims, Champagne-Ardenne, BP 1039, 51687 Reims cedex 2, France

Received 11 July 2007; revised 11 August 2007; accepted 18 September 2007
Available online 21 September 2007

Abstract—Chemoselective hydrogenation of double bonds in the presence of various functional groups occurred in high yields using water or toluene as solvent, and Pd nanoparticles as catalyst. Up to nine recyclings were achieved in water without decrease of the catalyst activity.

Chemoselective reduction of a double bond in the presence of a functional group is of great interest in synthetic organic chemistry. The well-known Pd/C catalyst leads to poor selectivities, but associated to additives such as amines, ammonia, pyridine, ammonium acetate or sulfides, it mediates the chemoselective reduction of olefins without concomitant reduction of benzyl groups,[1a–f] aromatic carbonyls,[1e,f] aromatic halogens,[1e,f] *N*-Cbz groups[1d–g] and epoxides.[2] Recently, silk-fibroin supported palladium catalyst also showed chemoselectivity in hydrogenation of olefins.[3] However, all catalytic systems are used in organic media, and the recycling of the catalyst has only been performed over few number of cycles.[1g,2]

Water is an attractive alternative to traditional organic solvents because it is inexpensive, non-flammable, non-toxic and environmentally sustainable. However, most organic substrates are hydrophobic and, consequently, sparingly soluble in water. To overcome this problem, a cosolvent[4] or a micellar system[5] is often used, but products separation from crude reaction mixtures containing surfactants can be difficult because these systems readily form emulsions during standard work-ups.[6] The often requirement of water-soluble ligands for metallic catalysis under aqueous conditions is also an obstacle to general applications. In our opinion, nanoparticles have great potential as catalysts since they could combine high reactivity and selectivity, simple preparation and easy catalyst recovery by association with non-usual media. Only few studies have been devoted to chemoselective hydrogenations with nanoparticles, especially in pure water. Dendrimer-encapsulated Pd nanoparticles and Pd–Rh bimetallic clusters have been used in alcohol/water mixtures for the size-selective hydrogenation of allylic alcohols[7] and the partial hydrogenation of 1,3-cyclooctadiene, respectively.[8] Hydrogenation of allylic alcohols and alkenes in aqueous mixtures have been carried out using nano-size Pd catalysts generated in multilayer polyelectrolyte films,[9] or Pd nanoparticles stabilized by either polymers[10] or alkylated branched polyethyleneimines.[11] Selective reductions of 2-butyne-1,4-diol into 2-butene-1,4-diol, and dehydrolinalool into linalool have been performed in alcohol/water, with Pd nanoclusters and Pd nanoparticles formed in micelles, respectively.[12] The catalytic systems used for the hydrogenation of 1,3-cyclooctadiene,[8] sterically hindered alkenes[11] and olefinic alcohols[9b] are recyclable. Recently, we found that particles, namely, $Pd_{OAc,N}$, easily prepared from a mixture of n-Bu_4NBr, n-Bu_3N and $Pd(OAc)_2$, are efficient catalysts for (i) the selective hydrogenation in methanol, toluene and ionic liquids of olefins in the presence of *O*-benzyl protective groups,[13] and (ii) the regioselective hydrogenolysis in water of benzylic epoxides.[14] Our continuing interest in the use of aqueous media[15] led us to examine the catalytic potential of $Pd_{OAc,N}$ as a chemoselective and recyclable catalyst in water for the hydrogenation of C=C bonds of the functionalized alkenes.

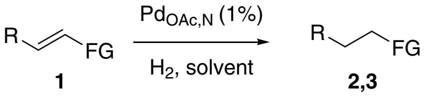
Keywords: Hydrogenation; Chemoselectivity; Palladium; Nanoparticles; Water.

---

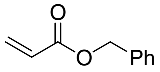
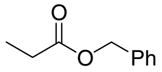
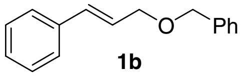
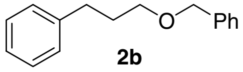
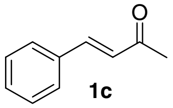
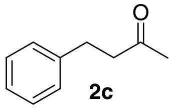
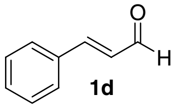
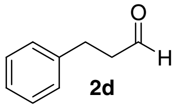
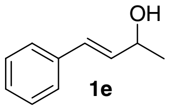
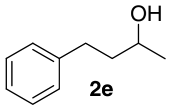
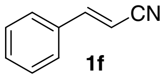
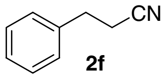
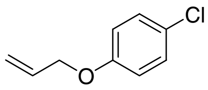
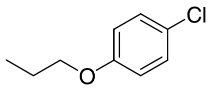
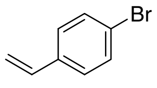
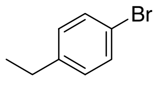
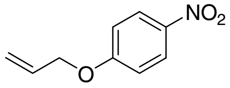
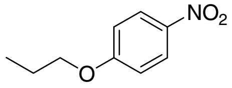
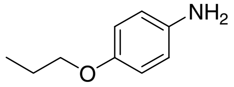
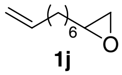
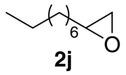
* Corresponding author. Tel.: +33 3 26 91 32 46; fax: +33 3 26 91 31 66; e-mail: jean.lebras@univ-reims.fr

0040-4039/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2007.09.121

Table 1. $Pd_{OAc,N}$-catalyzed hydrogenations in water and toluene[a]



1 **2,3**

Entry	Substrate	Time (h)	Product	Yield[b] (%)	
				H_2O	PhMe
1	 **1a**	4	 **2a**	98	80[c]
2		24		97	99
3	 **1b**	4	 **2b**	54[c]	10[c]
4		24		93	70[c]
5	 **1c**	4	 **2c**	94	96
6		24		93	99
7	 **1d**	4	 **2d**	98	95[c]
8		24		98	96
9	 **1e**	4	 **2e**	78[c]	99
10		24		93	99
11	 **1f**	4	 **2f**	93	99
12		24		92	99
13	 **1g**	4	 **2g**	90	96
14		24		92	97
15	 **1h**	4	 **2h**	81	70[c]
16		24		62	90
17	 **1i**	4	 **2i**	75	99
18		24	 **3i**	98	[d]
19	 **1j**	4	 **2j**	92	94
20		24		91	94

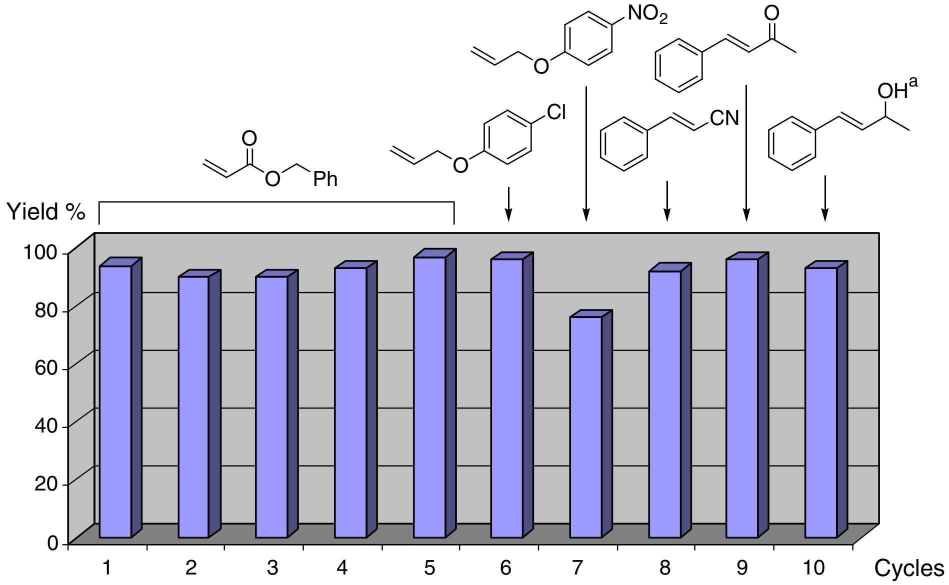
[a] Substrate (1 mmol), $Pd_{OAc,N}$ (0.01 mmol), solvent (2 mL), H_2 (gas bag), rt.

[b] Isolated yield.

[c] Uncompleted reaction, NMR yield.

[d] A mixture of **2i**/**3i** (91/9) was obtained.

The hydrogenation of benzyl acrylate (**1a**) has been firstly examined. The use of a catalytic amount of $Pd_{OAc,N}$ in water and a gas bag filled with hydrogen led, in 4 h at room temperature, to benzyl propionate in 98% yield (Table 1, entry 1). Prolonging the reaction time to 24 h led to a similar yield (entry 2) indicating the



Graph 1. Recycling of the catalyst in water (substrate (1 mmol), $Pd_{OAc,N}$ (0.01 mmol), water (2 mL), H_2 (gas bag), rt, 4 h). The product was extracted with Et_2O (5 × 5 mL). The next reaction was carried out using the crude aqueous phase as both catalyst and solvent. [a]Performed over 24 h.

high chemoselectivity of the process. To compare, the reaction has been carried out in toluene: the reaction rate decreased but high selectivities were also obtained (entries 1 and 2). These results are particularly interesting because benzyl esters are widely used in organic synthesis, but are hydrogenolyzed with Pd/C as the catalyst.[1,16,17] Benzyl ethers are also commonly used to protect alcohols. While cleavage of the *O*-benzyl bond of cinnamyl benzyl ether (**1b**) was observed with $Pd_{OAc,N}$ in methanol,[13] the selective reduction of its double bond proceeded in high yield in water (entry 4). The sluggish reaction observed in toluene (entries 3 and 4) illustrates in this case the clear advantage of water as the solvent. The C=C bond of 4-phenylbut-3-en-2-one (**1c**), cinnamaldehyde (**1d**) and (*E*)-4-phenylbut-3-en-2-ol (**1e**) has been effectively and selectively hydrogenated, the reaction of **1e** being, however, slower in water than in toluene (entries 5–10). It has to be noted that other nanocatalysts used for the hydrogenation of **1c** and **1d** in water required larger amounts of catalyst or high pressures of hydrogen.[18] The reduction of the nitrile group has been reported over Pd/C,[19] but the hydrogenation of cinnamonitrile (**1f**) with $Pd_{OAc,N}$ as the catalyst led to 3-phenylpropanenitrile (**2f**) in 92–99% yield (entries 11 and 12).[20] The discrepancy of reactivity between aromatic halogens and olefins was examined with 1-(allyloxy)-4-chlorobenzene (**1g**) and 4-bromostyrene (**1h**). High yields of 1-chloro-4-propoxybenzene (**2g**) were isolated from the hydrogenation of **1g** in water as in toluene (entries 13 and 14). In contrast, some hydrogenolysis of the C–Br bond of **1h** occurred, particularly in water (entries 15 and 16). Nevertheless, 1-bromo-4-ethylbenzene (**2 h**) has been isolated in 81% yield in water when the reaction time was limited to 4 h. These results illustrate the advantage of $Pd_{OAc,N}$ as catalyst over Pd/C in terms of chemoselectivity.[21,22] The reduction of the double bond of 1-(allyloxy)-4-nitrobenzene (**1i**) is more selective in toluene than in water (entry 17). In fact, both the nitro and the olefinic groups have been quantitatively reduced in water over 24 h (entry 18). Although the chemoselective reduction of a C=C bond in the presence of an epoxy ring function is generally difficult,[2,23] this occurs in high yield from **1j** over the $Pd_{OAc,N}$ catalyst (entries 19 and 20).

Given the above results, water is a good solvent to carry out chemoselective $Pd_{OAc,N}$-catalyzed hydrogenations. As observed for the regioselective hydrogenolysis in water of benzylic epoxides,[14] the dispersion of the nanoparticles in a water–oil system led to the formation of 'black aqueous droplets' in which palladium is probably adsorbed on the surface. This urged us to perform recycling experiments, and **1a**,**c**,**e**–**g** and **1i** have been successively hydrogenated in water with the same batch of catalyst. Up to 10 cycles were achieved without decrease of the catalyst activity (Graph 1) and with results similar to those obtained using new batches of catalyst (Table 1). In toluene, the catalyst is supported by the Teflon® magnetic stirring bar and the surface of the reaction flask. Recycling experiments have shown a decrease in the activity after the 4th cycle.[24]

In conclusion, palladium nanoparticles, $Pd_{OAc,N}$, easily obtained from $Pd(OAc)_2$ and an unsophisticated ammonium salt, constitute a chemoselective hydrogenation catalyst of olefins, in water, under mild reaction conditions. This efficient and environmentally sustainable catalytic system combines the advantages of homogeneous and heterogeneous catalysts.

Acknowledgements

We are indebted to 'Ville de Reims' for a Ph.D. studentship to E.T. and the Erasmus Program for a financial support to N.M.C. who was on leave from Universitat Autónoma de Barcelona.

References and notes

1. (a) Czech, B. P.; Bartsch, R. A. *J. Org. Chem.* **1984**, *49*, 4076–4078; (b) Sajiki, H. *Tetrahedron Lett.* **1995**, *36*, 3465–3468; (c) Sajiki, H.; Kuno, H.; Hirota, K. *Tetrahedron Lett.* **1997**, *38*, 399–402; (d) Sajiki, H.; Hattori, K.; Hirota, K. *J. Org. Chem.* **1998**, *63*, 7990–7992; (e) Mori, A.; Miyakawa, Y.; Ohashi, E.; Haga, T.; Maegawa, T.; Sajiki, H. *Org. Lett.* **2006**, *8*, 3279–3281; (f) Mori, A.; Mizusaki, T.; Miyakawa, Y.; Ohashi, E.; Haga, T.; Maegawa, T.; Monguchi, Y.; Sajiki, H. *Tetrahedron* **2006**, *62*, 11925–11932; (g) Hattori, K.; Sajiki, H.; Hirota, K. *Tetrahedron* **2000**, *56*, 8433–8441.
2. Sajiki, H.; Hattori, K.; Hirota, K. *Chem. Eur. J.* **2000**, *6*, 2200–2204.
3. (a) Sajiki, H.; Ikawa, T.; Hirota, K. *Tetrahedron Lett.* **2003**, *44*, 8427–8439; (b) Ikawa, T.; Sajiki, H.; Hirota, K. *Tetrahedron* **2005**, *61*, 2217–2231.
4. Cornils, B.; Herrmann, W. A. Aqueous-Phase Organometallic Catalysis; Wiley: New York, 1998.
5. Dwars, T.; Paetzold, E.; Oehme, G. *Angew. Chem., Int. Ed.* **2005**, *44*, 7174–7199.
6. Cerritelli, S.; Chiarini, M.; Cerichelli, G.; Capone, M.; Marsili, M. *Eur. J. Org. Chem.* **2004**, 623–630.
7. (a) Niu, Y.; Yeung, L. K.; Crooks, R. M. *J. Am. Chem. Soc.* **2001**, *123*, 6840–6846; (b) Oh, S.-K.; Niu, Y.; Crooks, R. M. *Langmuir* **2005**, *21*, 10209–10213.
8. Chung, Y.-M.; Rhee, H.-K. *J. Mol. Catal. A: Chem.* **2003**, *206*, 291–298.
9. (a) Kidambi, S.; Dai, J.; Li, J.; Bruening, M. L. *J. Am. Chem. Soc.* **2004**, *126*, 2658–2659; (b) Wang, Y.; Lee, J.-K. *J. Mol. Catal. A: Chem.* **2007**, *263*, 163–168.
10. Nakao, R.; Rhee, H.; Uozumi, Y. *Org. Lett.* **2005**, *7*, 163–165.
11. Vasylyev, M. V.; Maayan, G.; Hovav, Y.; Haimov, A.; Neumann, R. *Org. Lett.* **2006**, *8*, 5445–5448.
12. (a) Telkar, M. M.; Rode, C. V.; Chaudhari, R. V.; Josgi, S. S.; Nalawade, A. M. *Appl. Catal. A: Gen.* **2004**, *273*, 11–19; (b) Semagina, N. V.; Bykov, A. V.; Sulman, E. M.; Matveeva, V. G.; Sidorov, S. N.; Dubrovina, L. V.; Valetsky, P. M.; Kiselyova, O. I.; Khokhlov, A. R.; Stein, B.; Bronstein, L. M. *J. Mol. Catal. A: Chem.* **2004**, *208*, 273–284.
13. Le Bras, J.; Mukherjee, D. K.; González, S.; Tristany, M.; Ganchegui, B.; Moreno-Mañas, M.; Pleixats, R.; Hénin, F.; Muzart, J. *New J. Chem.* **2004**, *28*, 1550–1553.
14. Thiery, E.; Le Bras, J.; Muzart, J. *Green Chem.* **2007**, *9*, 326–327.
15. (a) Le Bras, J.; Muzart, J. *Tetrahedron Lett.* **2002**, *43*, 431–433; (b) Le Bras, J.; Muzart, J. *Tetrahedron: Asymmetry* **2003**, *14*, 1911–1915; (c) Chevrin, C.; Le Bras, J.; Hénin, F.; Muzart, J. *Synthesis* **2005**, 2615–2618; (d) Thiery, E.; Chevrin, C.; Le Bras, J.; Harakat, D.; Muzart, J. *J. Org. Chem.* **2007**, *72*, 1859–1862.
16. Green, T. W.; Wuts, P. G. M. Protective Groups in Organic Synthesis, 3rd ed.; Wiley: New York, 1999.
17. We observed that the hydrogenation of **1a** in water with Pd/C was completed over 4 h and afforded a mixture of **2a** and propanoic acid; **2a** was isolated in 74% yield.
18. **1c** and **1d** have been hydrogenated, respectively, in 97% and 87% in 24 h using 5% of an amphiphilic-polymer-supported nanopalladium catalyst: see Ref. 10. Compound **1d** has been hydrogenated over β-cyclodextrin immobilized on Pd nanoparticles in 99% yield under 20 bar hydrogen pressure: Mhadgut, S. C.; Palaniappan, K.; Thimmaiah, M.; Hackney, S. A.; Toeroek, B.; Liu, J. *Chem. Commun.* **2005**, 3207–3209.
19. (a) Hénin, F.; Létinois, S.; Muzart, J. *Tetrahedron Lett.* **1997**, *38*, 7187–7190; (b) Diker, K.; Döé de Maindreville, M.; Lévy, J. *Tetrahedron Lett.* **1995**, *36*, 2497–2500; (c) Rylander, P. *Catalytic Hydrogenation in Organic Syntheses*; Academic Press: New York, 1979; pp 138–152.
20. Similar results were obtained with Pd/C in water over 24 h.
21. For examples of Pd/C-catalyzed hydrodehalogenation, see: (a) Marques, C. A.; Selva, M.; Tundo, P. *J. Org. Chem.* **1994**, *59*, 3830–3837; (b) Marques, C. A.; Selva, M.; Tundo, P. *J. Org. Chem.* **1995**, *60*, 2430–2435; (c) Bomben, A.; Marques, C. A.; Selva, M.; Tundo, P. *Synthesis* **1996**, 1109–1114; (d) Sajiki, H.; Kume, A.; Hattori, K.; Hirota, K. *Tetrahedron Lett.* **2002**, *43*, 7247–7250; (e) Li, J.; Wang, S.; Crispino, G. A.; Tenhuisen, K.; Singh, A.; Grosso, J. A. *Tetrahedron Lett.* **2003**, *44*, 4041–4043.
22. We observed that the hydrogenation of **1h** in water with Pd/C was completed over 4 h and afforded a mixture of **2h** and ethylbenzene; **2h** was isolated in 15% yield.
23. We observed that the hydrogenation of **1j** in water with Pd/C was completed over 4 h and afforded a mixture of **2j**, 1-octanol and 2-octanol; **2j** was isolated in 60% yield.
24. Compound **1a** (1 mmol), $Pd_{OAc,N}$ (0.01 mmol), toluene (2 mL), H_2 (gas bag), rt, 4 h. The organic phase was passed through a Celite pad. The next reaction was carried out with the same reaction flask and the same magnetic stirring bar. Total conversion was obtained for the first four cycles and **2a** was isolated, respectively, in 95, 97, 96 and 95% yield. In the 5th cycle, conversion dropped to 85%.