suspension in the hybridization buffer (13000 rpm, ×3). Particles were stored in 500 μL of the hybridization buffer.

Enzymatic digestion of particle-bound DNA: The first enzymatic reaction step was carried out by incubating the particles overnight at 37°C in a 100 μL solution containing NaCl (50 mM), Tris-HCl (100 mM, pH 7.5), and $MgCl_2$ (10 mM) containing 200 units of *Eco*RI enzyme (New England Biolabs Ltd.).

Enzymatic ligation of particle-bound DNA: The enzymatic ligation step was carried out by incubating the particles overnight at room temperature in a buffer solution comprised of Tris-HCl (50 mM, pH 7.5), $MgCl_2$ (10 mM), and ATP (1 mM) containing 1600 units of T4 DNA ligase (New England Biolabs Ltd.).

Gel electrophoresis: After the first enzymatic reaction the enzyme was deactivated by addition of EDTA (20 mM final concentration). The particles were isolated by repeated centrifugation and redispersion into an aqueous EDTA solution (20 mM) and then incubated overnight in 20 μL of an aqueous solution of dithiothreitol (0.5 M) and EDTA (20 mM). Gel electrophoresis was carried out using a 20% polyacrylamide (19:1 acrylamide:bisacrylamide) gel in TBE (Tris-borate (90 mM, pH 8.0) and EDTA (1 mM)) and the bands were visualized by staining with ethidium bromide.

Transmission electron microscopy: Specimens for inspection by TEM were prepared by the slow evaporation of one drop of an aqueous solution of the particles onto a carbon-coated copper mesh grid. All samples were examined in a JEOL 2000 EX TEM operating at 200 kV.

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Oxidation of Alcohols in Water

Catalytic Oxidation of Alcohols in Water under Atmospheric Oxygen by Use of an Amphiphilic Resin-Dispersion of a Nanopalladium Catalyst

Yasuhiro Uozumi and Ryu Nakao*

Oxidation of alcohols to form carbonyl compounds is one of the most fundamental and important yet immature processes in organic chemistry. Thus, although a variety of methods and reagents for the oxidation have been developed, until recently the traditional oxidation reactions have been performed with stoichiometric amounts of heavy metal reagents (e.g. Cr, Mn)[1] or moisture-sensitive expensive oxidants (e.g., *N,N'*-dicyclohexylcarbodiimide (DCC), oxalyl chloride),[2] and often in environmentally undesirable media like chlorinated solvents which render them impractical. There is good reason to believe that alcohol oxidation might be feasible by aerobic oxidation in water in a reaction promoted by a heterogeneous catalyst under atmospheric pressure conditions. This would represent a much cheaper, safer, and more environmentally benign oxidation protocol. Recently, much work has appeared on the catalytic oxidation of allylic or benzylic alcohols with molecular oxygen,[3,4] and several palladium catalyst systems have been developed for the oxidation.[5,6]

We have previously reported that amphiphilic polystyrene-poly(ethylene glycol) (PS-PEG) resin-supported palladium–phosphane complexes catalyzed various palladium-mediated reactions smoothly in water.[7] With the resin-supported catalyst in aqueous media, organic substrates must

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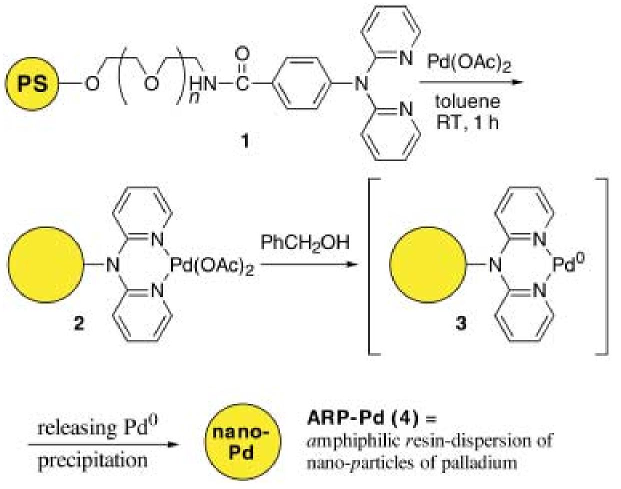
diffuse into the hydrophobic PS matrix to form the highly concentrated reaction sphere in which the anchored catalyst performs efficient organic transformations in water. These observations prompted us to design and prepare PS-PEG resin-supported palladium nanoparticles,[8,9] which should combine high catalytic activity owing to the large surface area of the nanoparticles[10] and water-based reactivity provided by the amphiphilicity of the PS-PEG matrix. Catalytic oxidation of alcohol was achieved in water under an atmospheric pressure of molecular oxygen by use of amphiphilic polymer-supported palladium nanoparticles.[11]

An amphiphilic resin-dispersion of palladium nanoparticles was readily prepared by reduction of a PS-PEG resin-supported palladium(II) complex (Scheme 1). Thus, the bis-pyridine chelating ligand **1** anchored on PS-PEG amino-resin was complexed to palladium by treatment with an equimolar amount of $Pd(OAc)_2$ in toluene at 25 °C to give the stable 16-electron divalent palladium complex **2**. The complex **2** was treated with benzyl alcohol in refluxing water for 12 h to generate palladium complex **3** in situ which should readily release the neutral palladium species. The nanopalladium particles were precipitated out in a PS-PEG matrix to give the desired amphiphilic PS-PEG resin-dispersion of palladium nanoparticles (**4**, ARP-Pd) (loading value: 0.37 mmol Pd per g). Transmission electron microscopy (TEM) of the resulting palladium-resin (Figure 1 a, b)shows that the palladium particles have a mean diameter of 9.1 nm with a narrow size distribution (Figure 1 c).



Scheme 1. Preparation of amphiphilic resin-dispersion of nanoparticles of palladium (ARP-Pd; **4**).

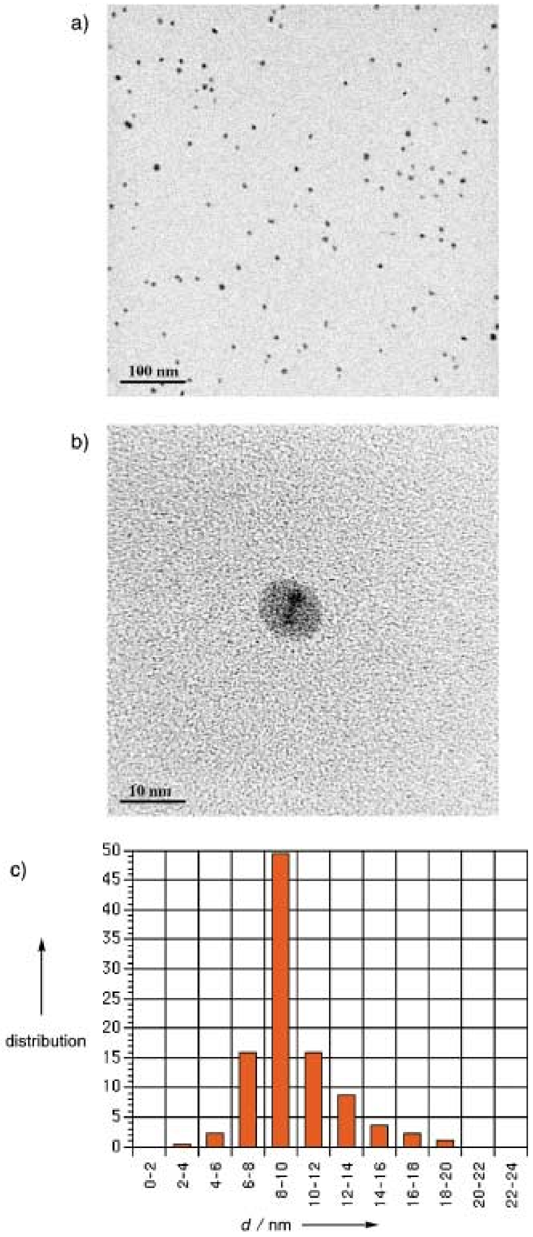
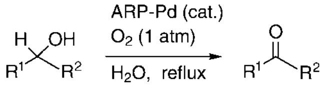


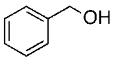
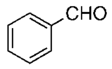
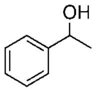
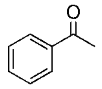
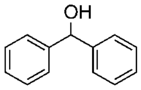
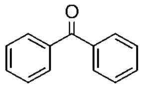
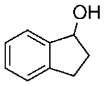
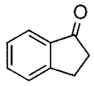
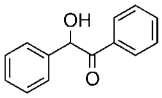
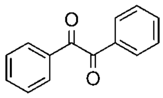
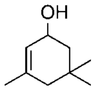
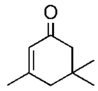
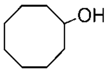
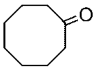
Figure 1. TEM images (a and b), and the respective histogram of particle size distribution (c) of **4**.

The catalytic activity of the amphiphilic resin-dispersion of palladium nanoparticles (ARP-Pd) was examined for the catalytic aerobic oxidation of alcohols in water. Representative results are shown in Table 1. Thus, a mixture of 1 mol% palladium of ARP-Pd and benzyl alcohol was refluxed in water under an atmospheric pressure of oxygen gas for 90 min. After being cooled, the mixture was filtered and the catalyst resin was rinsed twice with a small portion of diethyl ether. The washings were concentrated in vacuo to give benzaldehyde almost quantitatively, the purity of which was analyzed by ^{1}H NMR spectroscopy and gas chromatography (GC) to be 97% without any chromatographic purification (Table 1, entry 1). During the reaction, no deposit of palladium black on the glass wall (a palladium mirror) was observed. The recovered ARP-Pd showed essentially the same TEM image and was reused with negligible loss of catalytic activity. After the workup, the aqueous filtrate exhibited no catalytic activity for the oxidation. These observations indicate that the palladium species does not leach into the aqueous phase under the reaction conditions.[12]

Secondary alcohols gave the corresponding ketones under essentially the same conditions. Thus, phenethyl alcohol, diphenylmethanol, and 1-hydroxyindane underwent catalytic oxidation in water to give acetophenone, benzophenone, and indanone in >99%, 85%, and 95% yield, respectively

Table 1: ARP-Pd catalyzed oxidation of alcohols in water.[a]



Entry	Substrate	Product	Pd [mol %]	*t* [h]	Yield [%][b]
1			1	1.5	97
2			5	20	>99
3			5	20	85
4			5	20	95
5			1	2.5	98
6			5	20	78
7			20	20	88
8			(second run)	20	86
9			(third run)	20	83
10			(forth run)	20	87
11	*n*-$C_8H_{17}OH$[c]	*n*-$C_7H_{15}COOH$	20	40	90
12	*n*-$C_6H_{13}OH$[c]	*n*-$C_5H_{11}COOH$	20	40	98
13	*n*-C_4H_9OH[c]	*n*-C_3H_7COOH	20	40	93

[a] All reactions were carried out in refluxing water under 1 atm of oxygen gas. Pd mol%/reaction time (h): entries 1 and 5: 1/2, entries 2–5: 5/20, entry 7: 20/20, entries 11–13: 20/40; ratio of alcohol (mmol)/water (mL): 1/1.3. [b] All yields are for the pure products. [c] Oxidation of 1-alkanols were performed in 0.2 м aqueous solution of potassium carbonate.

(Table 1, entries 2, 3, and 4). The catalytic oxidation of benzoin bearing an α-ketohydroxy group and isophorol bearing an allylic hydroxy group also proceeded smoothly to give benzil and isophorone in 98% and 78% yields (Table 1, entries 5 and 6). It is noteworthy that this catalyst system was also effective for the oxidation of nonactivated alkanols. Thus, the oxidation of cyclooctanol took place in water under an atmospheric pressure of oxygen gas to give cyclooctanone in 88% yield (Table 1, entry 7). Catalytic aerobic oxidation of primary alcohols was carried out in an aqueous solution of potassium carbonate (0.2 м) under otherwise similar conditions. Thus, 1-octanol, 1-hexanol, and 1-butanol were oxidized by using 20 mol% palladium of the ARP-Pd catalyst under oxygen gas (1 atm) in refluxing water in the presence of potassium carbonate. The mixture was filtered, and the filtrate was acidified with hydrochloric acid and extracted with diethyl ether to give excellent yields of the corresponding carboxylic acids (Table 1, entries 11, 12, and 13).

Recycling experiments were examined for the oxidation of cyclooctanol. Thus, after the first run, which gave cyclooctanone in 88% yield (Table 1, entry 7), the ARP-Pd catalyst was subjected to a second oxidation from which it gave cyclooctanone in 86% yield (Table 1, entry 8); the average chemical yield for four consecutive runs was 86%, which clearly demonstrates the practical recyclability of this catalyst (Table 1, entries 7–10).

In conclusion, catalytic oxidation of alcohols was achieved in water by oxygen gas by using a novel amphiphilic resin-dispersion of palladium nanoparticles (ARP-Pd), which was designed and prepared with a view toward using it for palladium catalysis in water. Similarly, nanoparticles of various transition metals can be envisaged in a PS-PEG matrix, which would provide a wide variety of high catalytic abilities in water. We are currently investigating the scope and mechanism of this catalytic oxidation.

Experimental Section

PS-PEG resin-supported bispyridine ligand **1.** A mixture of PS-PEG amino-resin (5.0 g; average diameter = 170 μm, 1% divinylbenzene cross-linked, loading value of amino residue = 0.4 mmol g^{-1}), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI) (709 mg, 3.70 mmol), 1-hydroxybenzotriazole hydrate (HOBt)

(625 g, 4.63 mmol), and 4-(bis(pyrid-2-yl)amino)benzoic acid (808 mg, 2.78 mmol) in DMF (60 mL) was shaken at room temperature for 10 h. The mixture was filtered and the resulting resin beads were rinsed three times with DMF and three times with dichloromethane, then dried in vacuo to give **1**. Swollen gel-phase ^{13}C MAS NMR (100 MHz, $CDCl_3$, 25 °C, TMS; characteristic signals; signals of PS and PEG moieties are omitted for simplicity): $\delta = 117.2$, 118.5, 125.4, 128.2, 130.5, 137.4, 147.4, 148.3, 157.6, 166.4 ppm.

PS-PEG resin-supported palladium acetate bispyridine complex **2**: A mixture of **1** (5.5 g; loading value of ligand residue = 0.37 mmol g^{-1}) and palladium diacetate (457 mg, 2.04 mmol) in toluene (60 mL) was shaken at room temperature for 1 h. The mixture was filtered and the resulting resin beads were rinsed three times with dichloromethane and then dried in vacuo to give **2**. Swollen gel-phase ^{13}C MAS NMR (100 MHz, $CDCl_3$, 25 °C, TMS; characteristic signals; signals of PS and PEG moieties are omitted for simplicity): $\delta = 23.0$, 116.4, 117.2, 120.1, 129.7, 135.7, 140.0, 142.1, 150.3, 150.7, 165.5, 177.5 ppm.

PS-PEG resin-dispersion of palladium nanoparticles **4** (ARP-Pd): A mixture of **2** (5.6 g; loading value of palladium residue = 0.37 mmol g^{-1}) and benzyl alcohol (18 mL) in water (56 mL) was refluxed for 12 h (no leaching of palladium to the water phase was observed, which would have resulted in the formation of palladium black). The mixture was filtered and the resulting resin beads were rinsed three times with water and three times with acetone, then dried in vacuo to give ARP-Pd.

Catalytic oxidation of alcohols in water: Typical procedure given for the oxidation of 1-hexanol: A mixture of ARP-Pd (106 mg, 39 μmol of palladium), 1-hexanol (22 μL, 0.17 mmol), and potassium carbonate (24 mg, 0.17 mmol) in water (0.9 mL) was refluxed for 40 h under an atmospheric pressure of oxygen gas. After being cooled, the mixture was filtered, and the resin beads were rinsed three times with saturated aqueous sodium bicarbonate solution. The combined filtrate was acidified with 5 % hydrochloric acid and extracted with diethyl ether. The extract was dried over magnesium sulfate and concentrated in vacuo to give hexanoic acid (20 mg; 98 %) as a pure compound (> 99 % purity based on GC and ^{1}H NMR analysis).

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[8] For a recent review on catalytic reactions by metal nanoparticles, see: M. Králik, A. Biffis, *J. Mol. Catal. A* **2001**, *177*, 113.

[9] For examples of polymer-stabilized palladium nanoparticles, see: a) N. Toshima, Y. Shiraishi, T. Teranishi, M. Miyake, T. Tominaga, H. Watanabe, W. Brijoux, H. Bönnemann, G. Schmid, *Appl. Organomet. Chem.* **2001**, *15*, 178; b) T. Teranishi, M. Miyake, *Chem. Mater.* **1998**, *10*, 594; c) D. E. Bergbreiter, B. Chen, T. J. Lynch, *J. Org. Chem.* **1983**, *48*, 4179.

[10] J. S. Bradley in *Clusters and Colloids: From Theory to Applications* (Ed.: G. Schmid), VCH, Weinheim, **1994**, pp. 523–536.

[11] It has been reported that palladium cluster catalysts promote oxidation of allylic alcohols under an oxygen atmosphere, see: a) K. Kaneda, M. Fujii, K. Morioka, *J. Org. Chem.* **1996**, *61*, 4502; b) K. Kaneda, Y. Fujii, K. Ebitani, *Tetrahedron Lett.* **1997**, *38*, 9023.

[12] A referee has argued that the oxidation with leached homogeneous palladium species could still be plausible where the metal species may redeposit back on the heterogeneous surface. For recent examples of metal colloids as reservoirs for homogeneous metal species, see: a) S. Tasler, B. H. Lipshutz, *J. Org. Chem.* **2002**, ASAP; b) I. W. Davies, L. Matty, D. L. Hughes, P. J. Reider, *J. Am. Chem. Soc.* **2001**, *123*, 10139. See also ref. [8].