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Fine Tuning of Pd^0 Nanoparticle Formation on Hydroxyapatite and Its Application for Regioselective Quinoline Hydrogenation

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Fine control of the formation of Pd^0 nanoparticles with diameters between 1 and 1.5 nm on hydroxyapatite (HAP) was achieved by adjusting the temperature at which the Pd^{II} species on the HAP surface (Pd^{II}HAP) was reduced in the presence of 1 atm of molecular hydrogen. The HAP-supported Pd^0 nanoparticles (Pd^{0}HAP) having an average diameter of 1.5 nm exhibited significantly high catalytic activity for the regioselective hydrogenation of quinolines to the corresponding 1,2,3,4-tetrahydroquinolines under mild reaction conditions. Moreover, the Pd^{0}HAP catalyst was reusable without appreciable loss of its high catalytic activity or selectivity.

Size-selective synthesis of metal nanoparticles (NPs) is of great interest in the areas of materials chemistry and physics because of the high potential for application of NPs in catalysis, optics, and electronics.[1] In the catalysis area in particular, much effort has been devoted to improving methods for precisely controlling metal NP size using various stabilizers such as solid supports, polymers, and surfactants in order to design high performance catalysts.[2] Systematic control of the size of metal NPs, however, remains a valuable challenge. We have developed unique heterogeneous catalysts using hydroxyapatite (HAP), $Ca_{10}(PO_4)_6(OH)_2$, as a macroligand for catalytically active species that are effective in various environmentally benign organic transformations.[3] By using HAP as a catalyst support, a structurally uniform $(P{=}O)_2PdCl_2$ precursor species is easily created, which is further reduced to size-controlled Pd^0 NPs with narrow size distribution. It has been demonstrated that Pd^{0}HAPs with specific particle sizes act as an effective heterogeneous catalysts for aerobic alcohol oxidations (effective Pd^0 NP size: 3.8 or 7.8 nm),[4a] dehydrogenation of indolines (9 nm),[4b] hydrogenolysis of Z-groups (3 nm),[4c] and hydrodechlorination of organic halides (3 and 1.2 nm) and DDT derivatives (4 nm).[4d–4f]

Herein, we found that the fine tuning of the formation of Pd^0 NPs on HAP surfaces in the size range 1–1.5 nm was achieved by changing the reduction temperatures and that Pd^{0}HAP with a diameter of 1.5 nm exhibited significantly high catalytic activity for the regioselective hydrogenation of quinolines to the corresponding 1,2,3,4-tetrahydroquinolines under mild reaction conditions.

1,2,3,4-Tetrahydroquinoline derivatives have attracted considerable attention due to their importance as synthetically valuable intermediates for pharmaceuticals,[5] agrochemicals,[6] and dyes.[7] Among several possible methods for the synthesis of the 1,2,3,4-tetrahydroquinolines such as cyclization of 3-aminopropyl-*o*-haloarenes,[8a,8b] Beckmann rearrangement of oxime sulfonates,[8c] borohydride reduction of quinolones,[8d] the catalytic hydrogenation of quinolines is the most straight forward and promising approach due to its high atom efficiency and the availability of a wide variety of quinolines. There are many reports on homogeneous and heterogeneous catalyst systems for the hydrogenation of quinolines. These systems, however, have often suffered from low catalytic activity or poor selectivity and the need for harsh conditions such as high hydrogen pressures and acidic solvents.[9] It is desirable, therefore, to develop highly active heterogeneous catalysts for the regioselective hydrogenation of quinolines to 1,2,3,4-tetrahydroquinolines under greener process conditions.[10]

HAP-bound $PdCl_2$ (Pd^{II}HAP) was synthesized according to a procedure described in our previous report.[4a] To prepare the Pd^0 NPs, Pd^{II}HAP (0.2 g, Pd: 4 μmol) was treated under 1 atm of H_2 for 30 min to reduce the Pd(II) species giving grayish brown powders (Pd^{0}HAP(*T*) (*T*: reduction temperature of 30, 60, or 90 °C)). Palladium K-edge XAFS analysis of the Pd^{0}HAP(*T*) was conducted on the samples taken after reduction with H_2. XANES spectra showed that the reduction of the Pd^{II} species occurred within 30 min to form Pd^0 species on HAP during the pretreatment. In the Fourier transforms of the Pd K-edge EXAFS spectra (Figure 1), a peak around 0.25 nm corresponding to the Pd–Pd bond was observed in all Pd^{0}HAP(*T*) catalysts.

A second coordination peak based on the Pd–(Pd)–Pd bond, however, did not appear in the range between 0.4 and 0.5 nm. These results confirm the formation of Pd^0 NPs on the HAP surface. The intensity of the peak around 0.25 nm decreased with increasing reduction temperature, indicating that the particle size becomes smaller at higher reduction temperatures (Figures 1a–1c). A curve fitting analysis of the Pd K-edge EXAFS spectra

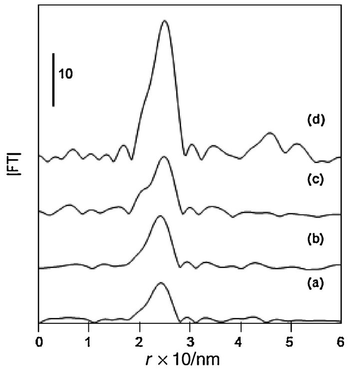


Figure 1. Fourier transforms of k^3-weighted Pd K-edge EXAFS experimental data for (a) Pd^{0}HAP(90), (b) Pd^{0}HAP(60), (c) Pd^{0}HAP(30), and (d) Pd foil.

Table 1. Curve-fitting results of the Pd K-edge EXAFS[a]

Catalyst	Shell	CN[b]	R/nm[c]	σ/nm[d]	d/nm[e]
Pd^{0}HAP(30)	Pd–Pd	6.5	0.275	0.070	1.5
Pd^{0}HAP(60)	Pd–Pd	6.2	0.276	0.077	1.2
Pd^{0}HAP(90)	Pd–Pd	6.1	0.277	0.080	1.0
Pd foil	Pd–Pd	12	0.275	0.060	—

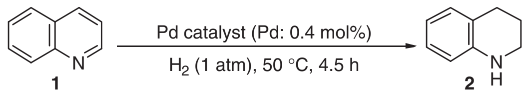
[a]The region of 0.178 (nm) $< r <$ 0.285 (nm) in the FT was inversely transformed. [b]Coordination number. [c]Bond distance. [d]Debye-Waller factor. [e]Diameter of Pd^0 NPs estimated from the CN.

revealed that the coordination number of the nearest Pd–Pd shell for the Pd^{0}HAP(T) was 6.5, 6.2, and 6.1 at 30, 60, and 90 °C, respectively (Table 1). Assuming the formation of cubooctahedral Pd^0 NPs,[11] average particle sizes of the Pd NPs on Pd^{0}HAP (30, 60, and 90) were estimated to be 1.5, 1.2, and 1.0 nm, respectively.[12] These results indicate that high temperature for reduction of the HAP-grafted Pd(II) species favors the formation of small Pd^0 NPs. Conclusively, fine tuning of the size of the Pd^0 NPs can be achieved using H_2 at varying reduction temperatures.

After the preparation of Pd^{0}HAPs by appropriate reduction procedures, toluene (6 mL) was added into a reaction vessel in the presence of Pd^{0}HAP(T), and then the mixture was stirred for 30 min at 50 °C under 1 atm of H_2. Following the addition of quinoline (**1**), the hydrogenation reaction was investigated, as shown in Table 2. To compare the catalytic activity, Pd^{0}HAPs having a diameter of 3.8 or 7.8 nm, which were synthesized according to our previous literature,[4a] were also examined in the above hydrogenation. A specific size effect of Pd^0 NPs was observed on this hydrogenation, i.e., Pd^{0}HAP(30) with a mean diameter of 1.5 nm prepared at 30 °C exhibited a higher catalytic activity than either the smaller or larger Pd^0 NPs (Entries 1–3, 6, and 7). An evaluation of various solvents showed that the reaction proceeded best in toluene, providing 1,2,3,4-tetrahydroquinoline (**2**) in 98% yield without formation of other hydrogenation products such as 5,6,7,8-tetrahydroquinoline and decahydroquinoline (Entry 3). Hydrogenolysis of the C–N bond and hydrodenitrogenization also did not occur at all. The use of n-heptane and methylcyclohexane in place of toluene gave moderate yields (Entries 8 and 9), while reactions in ethyl acetate, water, and methanol provided poor yields of **2** (Entries 10–12). Pd^{0}HAP(30) was filtered from the reaction mixture after ca. 50% conversion of **1**. Further stirring of the filtrate under similar reaction conditions did not afford any products. No Pd species in the filtrate were detected by inductively coupled plasma (ICP) analysis (detection limit: 0.1 ppm). These results reveal that the present hydrogenation clearly took place on the Pd^0 NPs located on the HAP surface.

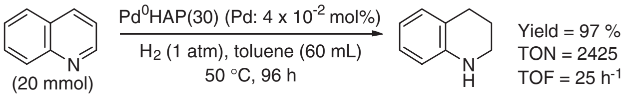
After the reaction, the Pd^{0}HAP(30) catalyst was recovered from the reaction mixture and could be reused at least twice without loss of its high catalytic activity or selectivity for **2** (Entries 4 and 5). Notably, Pd^{0}HAP(30) showed much higher catalytic activity than commercially available heterogeneous Pd catalysts such as 5% Pd/Al_2O_3 (4.4 nm), 5% Pd/C (4.3 nm), and 5% Pd/TiO_2 (3.6 nm) (Entries 13–15). As exemplified in Scheme 1, this Pd^{0}HAP(30) catalyst system can be also applied to scale-up conditions; **1** (20 mmol, 2.6 g) was successfully converted to **2** (96% isolated yield) with a TOF of 25 h^{-1} and a TON of up to 2425.

Table 2. Regioselective hydrogenation of **1** to **2** under various conditions[a]



Entry	Catalyst	d /nm[b]	Solvent	Convn /%[c]	Yield /%[c]
1	Pd^{0}HAP(90)	1.0	toluene	70	70
2	Pd^{0}HAP(60)	1.2	toluene	90	90
3	Pd^{0}HAP(30)	1.5	toluene	98	98
4[d]	Pd^{0}HAP(30)	1.5	toluene	98	98
5[e]	Pd^{0}HAP(30)	1.5	toluene	98	94
6[f]	Pd^{0}HAP	3.8	toluene	43	41
7[f]	Pd^{0}HAP	7.8	toluene	17	16
8	Pd^{0}HAP(30)	1.5	n-heptane	54	52
9	Pd^{0}HAP(30)	1.5	methylcyclohexane	50	48
10	Pd^{0}HAP(30)	1.5	EtOAc	25	25
11	Pd^{0}HAP(30)	1.5	H_2O	22	14
12	Pd^{0}HAP(30)	1.5	MeOH	18	16
13[g]	5% Pd/Al_2O_3	4.4	toluene	28	15
14[g]	5% Pd/TiO_2	3.6	toluene	17	8
15[g]	5% Pd/C	4.3	toluene	7	6

[a]Reaction conditions: **1** (0.5 mmol), Pd catalyst (Pd: 0.4 mol %), solvent (6 mL). [b]Mean diameter. [c]Determined by GC using an internal standard. [d]1st reuse. [e]2nd reuse. [f]Pd^{II}HAP was reduced by alcohol at 90 °C (See ref 4a). [g]Purchased from WAKO Pure Chemicals.



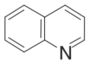
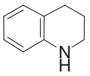
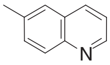
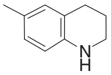
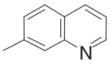
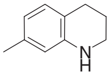
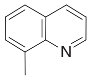
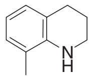
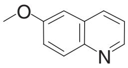
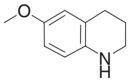
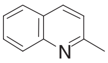
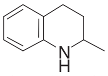
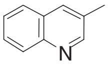
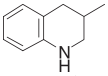
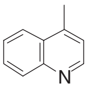
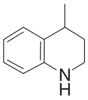
Scheme 1.

These values are considerably greater than those reported for other catalyst systems under an atmospheric H_2 conditions: PI Pt (TOF and TON: 1.0 h^{-1}, 82),[10a] PI Pd (0.8 h^{-1}, 20),[10b] Rh/AlO(OH) (3.1 h^{-1}, 18),[10c] SiO_2–Rh_3O (2.6 h^{-1}, 8),[10d] and $NiCl_2$–Li–naphthalene (0.1 h^{-1}, 2).[10e]

Various quinolines could be hydrogenated by the Pd^{0}HAP(30) catalyst to form the corresponding tetrahydroquinolines in high yields, as shown in Table 3. Quinolines bearing a methyl group at the 6-, 7-, or 8-position proceeded successfully to give the corresponding 1,2,3,4-tetrahydroquinolines in excellent yields (Entries 1–5). Introduction of substituents such as a methyl group on the N-ring and a methoxy group on the benzene ring retarded the rate of hydrogenation, but regioselective hydrogenation could proceed under 10 atm of H_2 (Entries 6–8).

In summary, fine tuning of Pd^0 NP sizes in the range of 1–1.5 nm can be achieved via hydrogen reduction of $PdCl_2$ species on HAP by varying temperatures. The HAP-supported Pd^0 NPs with a mean diameter of 1.5 nm showed the highest activity and selectivity among the Pd^{0}HAPs for the regioselective hydrogenation of quinolines to 1,2,3,4-tetrahydroquinolines with H_2. Moreover, the solid Pd^{0}HAP was reusable. The continuous study on the control synthesis of various sizes of Pd^0 NPs on HAP will be applicable to other selective transformation of functional groups.

Table 3. Regioselective hydrogenation of quinolines using $Pd^0HAP(30)$ catalyst[a]

Entry	Substrate	Time /h	Product	Convn /%[b]	Yield /%[b]
1		4.5		98	98(88)
2		8		95	95(85)
3		8		94	93(85)
4		6		94	92(84)
5		16		95	92(87)
6[c]		36		99	96(84)
7[c]		36		>99	98(84)
8[c]		36		99	95(85)

[a] Reaction conditions: substrate (1 mmol), $Pd^0HAP(30)$ catalyst (Pd: 0.4 mol %), toluene (6 mL), H_2 (1 atm), 50 °C. [b] Determined by GC using an internal standard. The values in parentheses are isolated yields. [c] Reaction was carried out at 30 °C under 10 atm of H_2. Product was determined by HPLC with an internal standard.

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12 The FE-SEM image of $Pd^0HAP(30)$ catalyst revealed the formation of Pd^0 NPs having 1.5 nm diameter on the HAP surface, see Supporting Information, which is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.