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Unsupported Nanoporous Gold Catalyst for Highly Selective Hydrogenation of Quinolines

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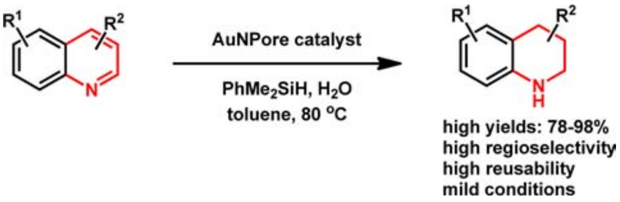
ABSTRACT



For the first time, the highly efficient and regioselective hydrogenation of quinoline derivatives to 1,2,3,4-tetrahydroquinolines using unsupported nanoporous gold (AuNPore) as a catalyst and organosilane with water as a hydrogen source is reported. The AuNPore catalyst can be readily recovered and reused without any loss of catalytic activity.

The interesting features of nanoporous gold (AuNPore), such as the three-dimensional (3D) bicontinuous network structure, high surface area, nontoxic nature, high fabrication reproducibility, high recyclability, and rather simple recovery, make it an attractive candidate for a new heterogeneous catalyst.[1−4] In comparison with the gold nanoparticles supported on metal oxides,[5] the unsupported AuNPore catalyst system offers the opportunity to understand the intrinsic catalytic activity more easily by elimination of the support effect and to extend the catalytic application widely through relaxation of aggregation. Recent advances in catalytic applications of AuNPore, such as CO oxidation and alcohol oxidations as well as organosilane oxidation, demonstrated its excellent catalytic performance on selective oxidation reactions.[1−4] However, a nanoporous gold catalyst has not been used for selective hydrogenation so far because of the limited ability of H_2 dissociation with gold as compared to its counterpart for the Pd group metals.[6] Most recently, we

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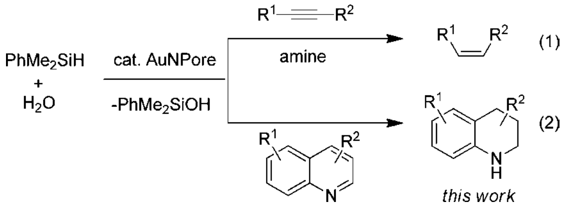
have demonstrated for the first time that AuNPore is able to be used as a robust catalyst for the semihydrogenation of alkynes to alkenes with excellent *Z*-selectivity without over-reduced alkanes by using organosilane and water as a hydrogen source and an appropriate amine as an additive (eq 1).[7]



1,2,3,4-Tetrahydroquinoline (py-THQ) is an important framework that exists in numerous biologically active natural products and pharmacologically relevant therapeutic agents.[8] Direct hydrogenation of quinoline is regarded as an efficient and straightforward approach to access py-THQ. Both homo- and heterogeneous catalysis based on Ru, Rh, Pd, Pt, and Ir have been studied extensively with H_2 but suffer from either high H_2 pressures (>1 atm) or high temperatures (>100 °C).[9,10] Moreover, the strong adsorption of quinolines and their hydrogenated products on heterogeneous catalysts influences the catalytic activity and selectivity.[10] In contrast, a gold catalyst has attracted less attention for this hydrogenation due to its low adsorption ability toward quinoline.[11,12] In continuation of our interest in nanoporous metal catalysis,[13] herein, we report for the first time the highly regioselective hydrogenation of quinolines catalyzed by the unsupported AuNPore using organosilane and water as a hydrogen source, affording the corresponding py-THQs in high yields (eq 2).

The unsupported AuNPore catalyst was prepared by dealloying a homogeneous $Au_{30}Ag_{70}$ alloy with a thickness of 40 μm in 70 wt % of nitric acid as an electrolyte at rt for 18 h.[7] A scanning electron microscopy (SEM) image reveals that the ligament and nanopore channnel are formed uniformly across the entire AuNPore with an average ligament size of ~30 nm (Figure 1a). An energy dispersive X-ray (EDX) study showed that the residual Ag composition of AuNPore is 2%. The representative bright-field transmission electron microscopy (TEM) image of AuNPore shows the multiple layers of gold ligaments with convex and concave columnar curvatures, indicating the bicontinuous 3D network nanoporous structure (Figure 1b). Ligament size is determined to be ~30 nm, which is consistent with the values estimated from the SEM image.

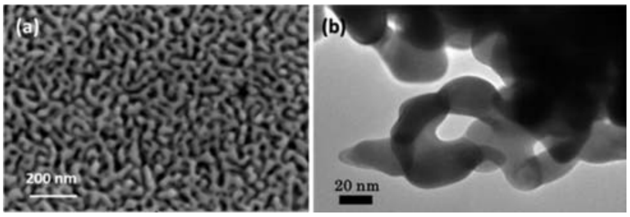


Figure 1. (a) SEM image of AuNPore. (b) Representative bright-field TEM image of AuNPore.

Recently we reported that AuNPore is an effective catalyst for the oxidation of organosilanes with water to produce organic silanols in high yields along with the vigorous liberation of H_2 gas.[4] Furthermore, as aforementioned in eq 1, we have found that the use of pyridine as an additve in the AuNPore-catalyzed semihydrogenation of alkynes using organosilane and water as a hydrogen source suppressed the evolution of H_2, giving the corresponding alkenes in high selectivity.[7] During the screening of amine additives, we noticed that when quinoline was used as an additive, py-THQ was produced as a byproduct in 30% yield. This result encouraged us to further investigate the reaction conditions to achieve an efficient and selective hydrogenation of quinolines by using AuNPore as the catalyst. Initially, quinoline (**1a**) was treated with the AuNPore catalyst, $PhMe_2SiH$, and water in the presence of various organic solvents as shown in Table 1. The use of dimethylformamide (DMF) and acetonitrile (CH_3CN), which were employed successfully in the previous alkyne hydrogenation, afforded the corresponding 1,2,3,4-tetrahydroquinoline (**2a**) as the sole product, but the yields were

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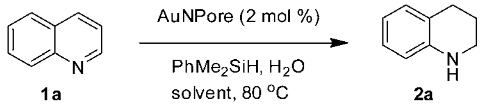
low (entries 1 and 2). Further examination with tetrahydrofuran (THF) and ethanol did not improve the yield of **2a** (entries 3 and 4). Fortunately, the use of nonpolar solvent such as toluene gave **2a** in high yield without formation of 5,6,7,8-tetrahydroquinoline (bz-THQ) and decahydroquinoline (DHQ) byproducts (entry 5). It was noted that the hydrogenation of **1a** with H_2 in toluene by using AuNPore as a catalyst did not proceed at all (entry 6). It is noteworthy that a nanoporous silver (AgNPore) catalyst was totally inactive for the present hydrogenation of quinoline. AgNPore was fabricated by the dealloying of $Ag_{23}Al_{77}$ alloy under basic conditions following the reported method (see Supporting Information (SI)).[14] When the reaction was treated with the AgNPore catalyst instead of AuNPore as shown in entry 7 in Table 1, the reaction did not proceed and **1a** was recovered in quantitative yield. This result implied that gold was a real catalytic species in the AuNPore catalyst for the present hydrogenation of quinoline and the residual Ag component in AuNPore was inactive.

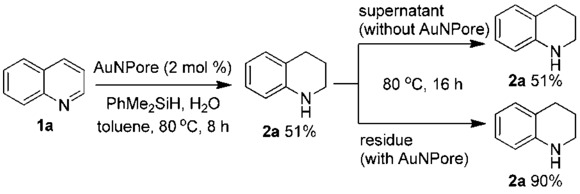
Table 1. Screening of Solvents for Selective Hydrogenation of Quinoline (**1a**) to 1,2,3,4-Tetrahydroquinoline (**2a**)[a]



entry	solvent	**2a**, yield (%)[b]
1	DMF	12
2	CH_3CN	30
3	THF	26[c]
4	EtOH	38
5	toluene	91
6	toluene	0[d]
7[e]	toluene	0

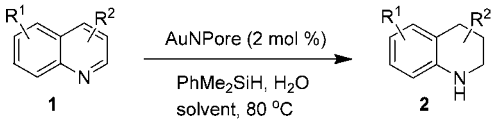
[a] Reaction conditions: Quinoline (**1a**, 0.5 mmol), $PhMe_2SiH$ (1.25 mmol), H_2O (1.5 mmol), solvent (0.5 mL), AuNPore (2 mol %), 80 °C for 24 h. [b] ^1H NMR yield determined using anisole as an internal standard. [c] Reaction temperature was 60 °C. [d] H_2 (1 atm) balloon was used instead of $PhMe_2SiH$ and H_2O. [e] 2 mol % of AgNPore was used instead of AuNPore.

To clarify whether the AuNPore catalyst leached to the reaction mixture or not, we carried out the following leaching experiments (eq 3). **1a** was treated with $PhMe_2SiH$ and water in the presence of the AuNPore catalyst (2 mol %) in toluene at 80 °C. After 8 h, the supernatant was transferred to the other reaction vessel and **2a** was produced in 51% yield at this time. The supernatant was continuously heated at 80 °C in the absence of the catalyst for 16 h, affording **2a** in 51% yield. In contrast, the residual containing the AuNPore catalyst was completed in 16 h, giving **2a** in 90% yield. These results, together with our previous X-ray photoelectron spectroscopy (XPS) analysis that the binding energies of AuNPore and Au mica are almost the same,[7] clearly indicated that the present hydrogenation was catalyzed by metallic gold(0), and inductively coupled plasma (ICP-AES) analysis indicates that no gold catalyst was leached after reaction.



(3)

Table 2. AuNPore-Catalyzed Hydrogenation of Various Quinolines[a]



entry	substrate	1	time (h)	2	yield (%)[b]
1	R^1 = H, R^2 = H	**1a**	24	**2a**	86[c]
2	R^1 = H, R^2 = 2-Me	**1b**	7	**2b**	91
3	R^1 = H, R^2 = 3-Me	**1c**	18	**2c**	96
4	R^1 = 8-Me, R^2 = H	**1d**	6	**2d**	83
5	R^1 = 3-Me, R^2 = 6-Me	**1e**	7	**2e**	98
6	R^1 = H, R^2 = 2-*n*-Pr	**1f**	3	**2f**	97
7	R^1 = H, R^2 = 2-Ph	**1g**	10	**2g**	98
8	R^1 = 6-Cl, R^2 = H	**1h**	39	**2h**	97
9	R^1 = 2-Me, R^2 = 3-Me	**1i**	24	**2i**	78[d]
10	R^1 = H, R^2 = 2-CHCHPh	**1j**	18	**2j**	85[e]

[a] Reaction conditions: Quinolines (**1**, 0.5 mmol), $PhMe_2SiH$ (2.0 mmol), H_2O (2.0 mmol), toluene (0.5 mL), AuNPore (2 mol %), 80 °C. [b] Isolated yield. [c] $PhMe_2SiH$ (1.25 mmol) and H_2O (1.5 mmol) were used. [d] A 2.5:1 mixture of *syn* and *anti* isomers. [e] The product is 2-phenethyl-1,2,3,4-tetrahydroquinoline.

The catalytic activity of AuNPore was further examined with various substituted quinolines under the aforementioned conditions (Table 2). Monomethylsubstituted quinolines were hydrogenated regioselectively to give the corresponding py-THQ in high isolated yields regardless of the methyl substituent at the benzene or pyridine ring (entries 2–4). Quinolines bearing 3,6-dimethyl (**1e**), 2-propyl (**1f**), and 2-phenyl (**1g**) were also suitable substrates for the present hydrogenation, providing the corresponding py-THQs (**2e**–**g**) in high yields with exclusive regioselectivity (entries 5–7). Remarkably, the AuNPore catalyst exhibited excellent selectivity with the hydrogenation of 6-chloroquinoline (**1h**), affording the desired **2h** in high yield without formation of the dehalogenated product (entry 8). When the 2,3-dimethyl-quinoline **1i** was employed under the standard conditions, the corresponding product **2i** was obtained in 78% yield with a 2.5:1 mixture of *syn* and *anti* isomers, in which the *syn*-isomer was obtained as a major product (entry 9). However, it should be noted that quinoline derivatives with a hydroxy or carbonyl group, such as quinoline-4-ol (poor solubility in toluene) or 2-quinolinecarbaldehyde, were not compatible under the standard conditions, resulting in the total

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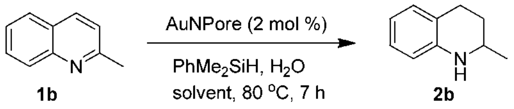
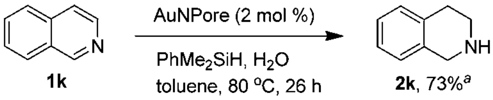
recovery of substrates. Quinoline derivatives with an alkynyl or alkenyl moiety did not show good chemoselectivity; 2-(oct-1-yn-1-yl)quinoline produced a mixture of products with alkyne-reduced quinoline[7] and alkynyltetrahydroquinoline as major products, and 2-styrylquinoline (**1j**) afforded both alkene and pyridine moiety reduced 2-phenethyl-1,2,3,4-tetrahydroquinoline (**2j**) in 85% yield by using excess amounts of organosilane and water (entry 10). Note that isoquinoline (**1k**) showed a relatively lower reactivity compared with quinoline, affording the corresponding 1,2,3,4-tetrahydroisoquinoline (**2k**) in 70% yield along with some amounts of recovered **1k** (eq 4). It was noted that no trace of bz-THQs or DHQs was detected in the present hydrogenation.

Table 3. Reusability of AuNPore Catalyst



run	**2b**, yield (%)[a]
1	95
2	98
3	98
4	97
5	98

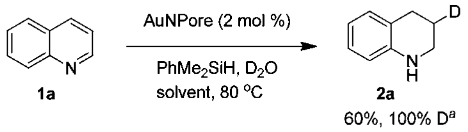
[a] ^{1}H NMR yield determined using CH_2Br_2 as an internal standard.



(4)

[a] Yield was determined by ^{1}H NMR spectra using CH_2Br_2 as an internal standard.

The AuNPore catalyst was reused for five cycles without any loss of catalytic activity and selectivity in the hydrogenation of 2-methylquinoline (**1b**) under the standard conditions; the yield was still 98% even for the fifth cycle (Table 3). The catalyst was recovered through simple filtration of the reaction mixture washing with acetone and reused without further purification. It is noteworthy that the nanoporous structure of the recovered catalyst did not show structural changes after the fifth cycle (see SI).



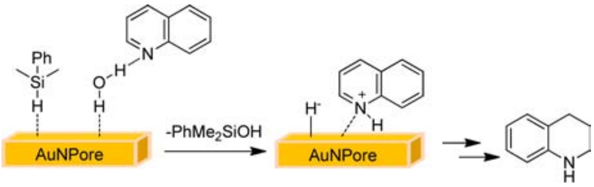
(5)

[a] Yield was determined by ^{1}H NMR spectra using CH_2Br_2 as an internal standard.

To gain further insight into the reaction details, we carried out the deuterium labeling experiments. The reaction of quinoline **1a** with $PhMe_2SiH$ and D_2O in the presence of the AuNPore catalyst in toluene gave the corresponding 3-D-tetrahydroquinoline **2a′** as the sole product in 60% yield containing 100% one deuterium atom and **1a** was recovered in 28% yield (eq 5 and SI). This result clearly indicated that both $PhMe_2SiH$ and water are the hydrogen source in the present reaction.

On the basis of the present results and our previous study of the amine effect on the hydrogenation of alkynes,[7] the ionic hydrogenation pathway is proposed as shown in Scheme 1. Due to the moderate adsorption energy of quinoline on Au,[12] the H-bond forms preferably between quinoline and water. The reaction of adsorbed $PhMe_2SiH$ and water may produce [AuNPore-H]$^-$ and [H-quinoline]$^+$ species, in which the latter reacts subsequently with hydride on AuNPore to form the corresponding py-THQ. Although the detailed mechanism of the following hydride addition into [H-quinoline]$^+$, such as 1,4- or 1,2-addition, remains unclear at this stage, the formation of a H-bond between quinoline and water is crucial to suppress the vigorous liberation of H_2 gas which is inactive toward the unsupported AuNPore catalyst.

Scheme 1. Reaction Pathway for the AuNPore-Catalyzed Hydrogenation of Quinoline



In conclusion, we have demonstrated for the first time that the unsupported AuNPore can catalyze the hydrogenation of quinolines. By using organosilane and water as the hydrogen source, various quinoline derivatives were hydrogenated to give the py-THQs in high yields with excellent regioselectivity. The AuNPore catalyst can be easily recoverable and reused several times without any loss of catalytic activity and leaching. Further extension of this hydrogenation method to other unsaturated multiple bonds is in progress.

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Supporting Information Available. Experimental procedures and characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.