Nanocatalyst **Hot Paper**

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A Palladium-Nanoparticle and Silicon-Nanowire-Array Hybrid: A Platform for Catalytic Heterogeneous Reactions**

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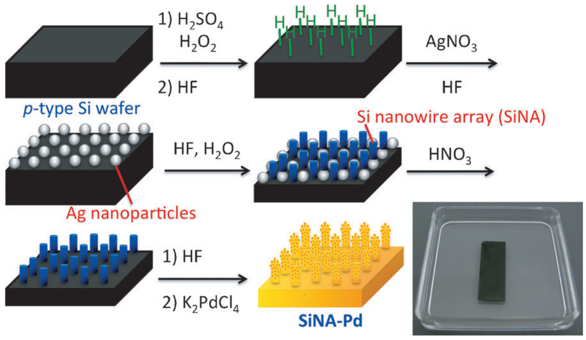
Abstract: *We report the development of a silicon nanowire array-stabilized palladium nanoparticle catalyst, SiNA-Pd. Its use in the palladium-catalyzed Mizoroki-Heck reaction, the hydrogenation of an alkene, the hydrogenolysis of nitrobenzene, the hydrosilylation of an α,β-unsaturated ketone, and the C-H bond functionalization reactions of thiophenes and indoles achieved a quantitative production with high reusability. The catalytic activity reached several hundred-mol ppb of palladium, reaching a TON of 2 000 000.*

Development of highly active and reusable solid catalysts is among the most important topics not only for organic syntheses but also for chemical and pharmaceutical process. Innovative nanodevices for catalytic transformations are expected to realize instantaneous, selective catalytic reaction systems.[1] One approach is to downsize the reaction field/space from macroscopic to microscopic scale (e.g., from flask size to microreactor size) to achieve high reactivity and novel selectivity with safety.[2,3] Another is to develop a closed porous space, such as mesoporous silica materials or metal–organic frameworks (MOFs), in which heterogeneous catalysts are attached.[4] While acknowledging the pioneering work in this area, we believe that it remains difficult to create a novel nanospace/field-mediated catalytic transformation system exhibiting high catalytic activity, reusability, safety, and selectivity as well as macroscopic accessibility of a large amount of substrates and reactants under mild and aqueous conditions.



Scheme 1. Preparation of the SiNA-stabilized Pd nanoparticle catalyst (SiNA-Pd).

We envisioned that the development of hybrid catalysts of palladium nanoparticles[5] and a silicon nanowire array (SiNA) as a macroscopic and nanoscopic hybrid catalyst would be promising for this purpose (Scheme 1). The silicon nanowire array, such as those used in silicon-based optoelectronics, fuel cells, solar cells, and photoelectrodes,[6] was readily obtained by the metal-assisted chemical etching of silicon wafers.[7] Copious nanospaces can be provided on the surface of a silicon wafer whose area is on the order of square centimeters. The hybrid catalysts should be equipped with confined nano-size reaction fields surrounded a lot of Pd nanoparticles (which should entropically drive the organic transformation in the nanospaces) on the square centimeter sized silicon wafer (which should afford plenty of reaction capacity).

Herein, we report a new platform for the catalytic reactions, a silicon nanowire array-stabilized palladium-nanoparticle catalyst, SiNA-Pd. Its use in the palladium-catalyzed Mizoroki–Heck reaction, where the quantitative production of coupling compounds was achieved with 490 mol ppb (0.000049 mol %) Pd, is presented. The hybrid catalyst was readily reused without the loss of catalytic activity. Moreover, SiNA-Pd promoted the hydrogenation of an alkene, the hydrogenolysis of nitrobenzene, the hydrosilylation of an α,β-unsaturated ketone, and the C−H bond functionalization reactions of thiophenes and indoles.

The silicon nanowire array-stabilized Pd nanoparticle catalyst was prepared as follows (Scheme 1):[8,9] A *p*-type silicon wafer was treated with H_2SO_4/H_2O_2, and aqueous HF for cleaning and installation of Si−H surface groups (H-termination), respectively.[10] $AgNO_3$ reacted with the H-

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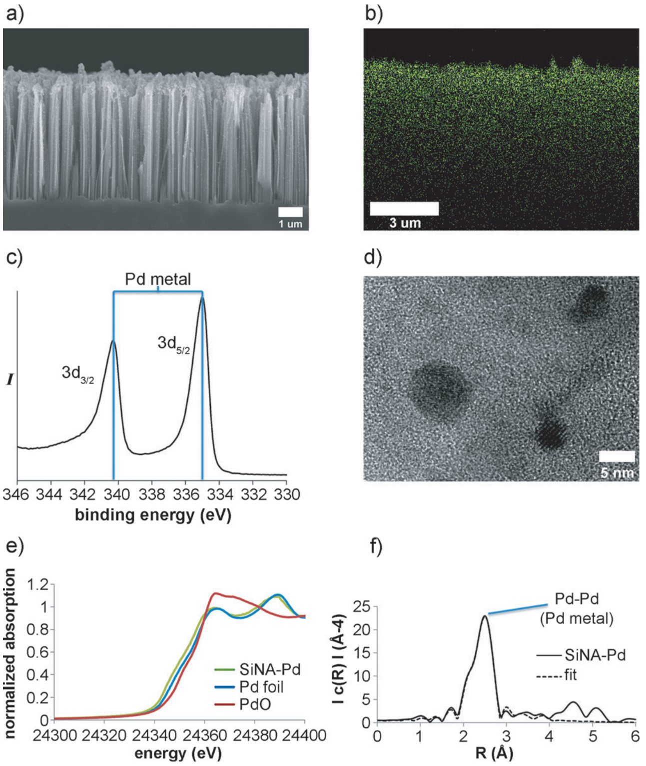
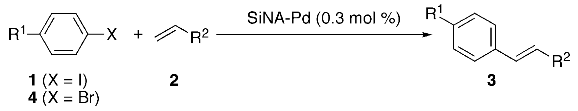


Figure 1. a) SEM, b) SEM/EDX, c) XPS, d) TEM, e) XANES, and f) FT-EXAFS of SiNA-Pd.

Table 1: Mizoroki-Heck reaction with SiNA-Pd.[a]



Entry	1 or 4 (R^1)	2 (R^2)	3	Yield [%]
1	**1a** (H)	**2a** (CO_2Bu)	**3a**	98 (99[d])
2 (2th use)	**1a**	**2a**	**3a**	96 (47[d])
3 (4th use)	**1a**	**2a**	**3a**	97 (9[d])
4 (6th use)	**1a**	**2a**	**3a**	97[e]
5 (8th use)	**1a**	**2a**	**3a**	95
6(10th use)	**1a**	**2a**	**3a**	98
7	**1b** (CH_3)	**2a**	**3b**	99
8	**1c** (MeO)	**2a**	**3c**	94
9	**1d** (CF_3)	**2a**	**3d**	99
10	**1e** (CH_3CO)	**2a**	**3e**	88
11	**1f** (NO_2)	**2a**	**3f**	85
12	1-I-naph **1g**	**2a**	**3g**	98
13	**1a**	**2b** (Ph)	**3h**	72
14	**1c**	**2b** (Ph)	**3i**	72
15	**1d**	**2b** (Ph)	**3j**	84
16	**1e**	**2b** (Ph)	**3k**	83
17	**1g**	**2b** (Ph)	**3l**	81
18[b]	**4a** (H)	**2a**	**3a**	82
19[b]	**4b** (MeO)	**2a**	**3c**	70
20[b,c]	**4c** (CF_3)	**2a**	**3d**	87
21[b,c]	**4d** (CH_3CO)	**2a**	**3e**	92
22[b,c]	**4e** (NO_2)	**2a**	**3f**	90
23[b]	1-Br-naph **4f**	**2a**	**3g**	89

[a] **1** (1.0 mol equiv), **2** (2.0 mol equiv), Et_3N (3.0 mol equiv), TBAA (0.2 mol equiv), SiNA-Pd (0.3 mol %), 1-BuOH, 100 °C, 24 h. [b] **4** (1.0 mol equiv), **2a** (1.3–2.0 mol equiv), NaOAc (1.2 mol equiv), TBAB (0.2–1.0 mol equiv), SiNA-Pd (0.3 mol %), 140 °C, 24–48 h. [c] Using DMA as a solvent. [d] The yields in parenthesis in entries 1–3 are from the use of a Pd nanoparticle catalyst on a non-etched flat silicon wafer. [e] Pd was not detected in the reaction mixture (ICP-AES).

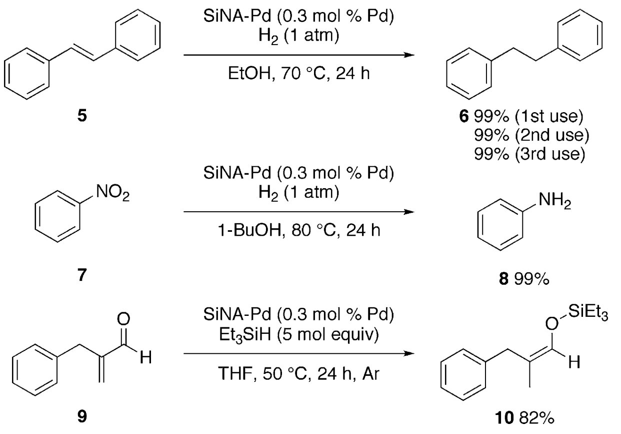
terminated wafer to give an Ag nanoparticle-coated wafer that was treated with aqueous HF/H_2O_2, yielding the Ag nanoparticle-deposited silicon nanowire array. Removal of Ag nanoparticles and regeneration of Si-H surface of the silicon nanowire array were carried out with HNO_3 and aqueous HF, respectively. Immobilization of Pd nanoparticles was performed with K_2PdCl_4 on the silicon nanowire array to obtain the silicon nanowire array-stabilized palladium nanoparticle catalyst (SiNA-Pd). An SEM image of the section of SiNA-Pd (Figure 1) revealed that the length and width of its nanospace were 5 μm and less than 800 nm, respectively, where the aspect ratio was approximately 60. BET analysis indicated that the specific surface area of SiNA-Pd was 30 times larger than the original flat silicon wafer (S_{BET} 117 cm^2/cm^2 vs. 4 cm^2/cm^2 (Kr absorption-BET analysis). An SEM/EDX image (Figure 1 b) of the section of SiNA-Pd showed that the installation of Pd onto the silicon nanowire array was located mainly on the upper part of the array. A TEM image of SiNA-Pd (Figure 1 d) showed the dispersion of Pd nanoparticles with a diameter of approximately 5–10 nm. Pd 3d XPS of Pd nanoparticles suggested the formation of zero-valent Pd species. Pd K-edge XANES (Figure 1 e) of SiNA-Pd, Pd^0 foil, and $Pd^{II}Cl_2$ supported the suggestion that the Pd species in SiNA-Pd was zero valent. FT-EXAFS of SiNA-Pd and Pd foil (Figure 1) showed signals corresponding to Pd–Pd bonds.[11] The peak at 2.5 Å was attributed to the first neighboring shell of Pd metal. The FT-EXAFS intensity of SiNA-Pd was lower than that of Pd foil, which suggests the formation of Pd nanoparticles on SiNA. These results indicate that K_2PdCl_4 is reduced to Pd^0 by Si–H on the silicon nanowires on which the resulting Pd^0 nanoparticles are readily immobilized.

We applied SiNA-Pd to the Mizoroki–Heck reaction.[12–16] The Mizoroki-Heck reaction is among the most important coupling reactions for synthetic organic and process chemistry including pharmaceuticals, agricultural chemicals, and sophisticated materials.[17] Thus, the reaction of iodobenzene (**1a**) and butyl acrylate (**2a**) was carried out with SiNA-Pd (0.3 mol % Pd) with triethylamine and tetrabutylammonium acetate (TBAA) in 1-butanol at 100 °C. The coupling proceeded smoothly to give butyl cinnamate (**3a**) with 98 % yield (Table 1, entry 1). Electron-rich and electron-deficient aromatic iodides **1b**–**g** were readily converted to the corresponding cinnamates **3b**–**g** with 85–99 % yield, respectively (entries 7–12). The coupling of **1a**–**g** and styrene (**2b**) also proceeded smoothly to give the corresponding stilbenes **3h**–**l** with 72–84 % yield (entries 13–17). Moreover, aryl bromides were also suitable substrates for the coupling. When the reaction of bromobenzene (**4a**) and **2a** was performed with sodium acetate and tetrabutylammonium bromide (TBAB), the reaction proceeded to give **3a** with 82 % yield (entry 18). The coupling of a variety of aryl bromides **4b**–**f** and **2a** led to the formation of the corresponding cinnamates **3c**–**g** with 70–92 % yield (entries 19–23).

Since SiNA-Pd efficiently promoted the Mizoroki–Heck reaction, recycling of SiNA-Pd was investigated under similar conditions. After the reaction in Entry 1 was completed, SiNA-Pd was recovered, and reused for the identical reactions. SiNA-Pd was reused nine times without loss of catalytic activity, giving 98 % yield of **3a** in the 10th use of the catalyst. Pd leaching was investigated in the reaction mixture in the 6th use of SiNA-Pd and no leaching of Pd was detected under ICP-AES analysis (Entry 4).[18] The hot-filtration test showed the termination of the reaction by use of the filtrate (Figure S1, Supporting Information). The results strongly suggested that SiNA-Pd worked as a heterogeneous catalyst.[19] In contrast, when a Pd nanoparticle catalyst on a non-etched flat silicon wafer was used under similar conditions, the catalytic activity significantly decreased to give **3a** in 99 % (1st use), 47 % (2nd use), and 9 % (4th use), respectively.

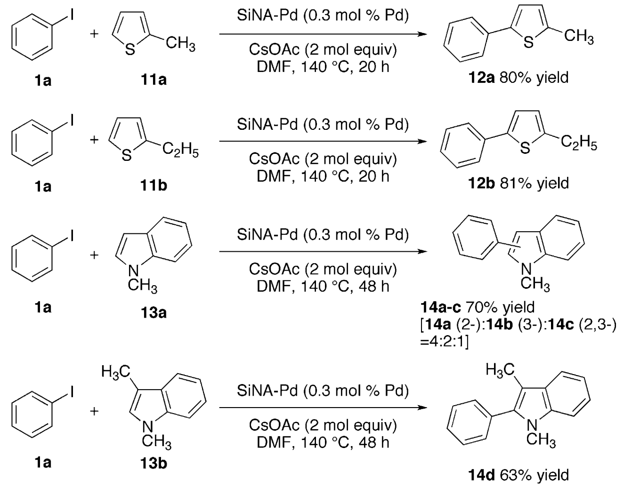
A SEM image of the reused SiNA-Pd showed that the morphology of the catalyst did not change during the reaction (Figure S1). These results indicated that silicon nanowire array stabilized the palladium nanoparticles to provide a highly active and reusable catalyst.

SiNA-Pd was applied to a variety of organic transformations. The hydrogenation of an alkene, stilbene (**5**), proceeded in the presence of SiNA-Pd (0.3 mol % Pd) in EtOH under hydrogen (1 atm) to give 1,2-diphenylethane (**6**) with 99 % yield. The catalyst was readily recovered and reused to afford **6** in 99 % (2nd use) and 99 % (3rd use) yield. The hydrogenolysis of nitrobenzene (**7**) was performed to give aniline (**8**) with 99 % yield. The hydrosilylation of an α,β-unsaturated aldehyde **9** and Et_3SiH was carried out to give the enolsilyl ether **10** with 82 % yield (Scheme 2).[20]

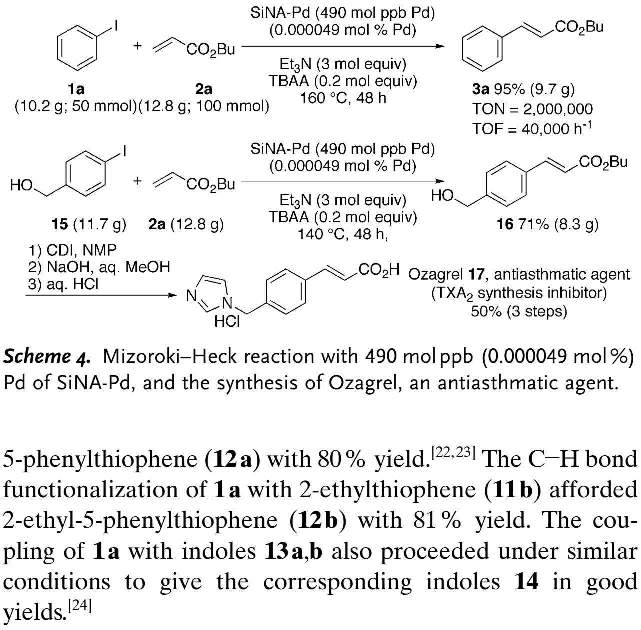


Scheme 2. Hydrogenation of stilbene, hydrogenolysis of nitrobenzene, and hydrosilylation of an α,β-unsaturated aldehyde.

The development of C–H bond functionalization reactions (C–H bond activation) is an important topic, thus we applied SiNA-Pd for the C–H bond functionalization reactions of thiophenes and indoles (Scheme 3).[21] Thus, the reaction of **1a** with 2-methylthiophene (**11a**) was carried out with SiNA-Pd (0.3 mol %) and CsOAc in DMF, we were pleased to find that the reaction proceeded to give 2-methyl-5-phenylthiophene (**12a**) with 80 % yield.[22,23] The C–H bond functionalization of **1a** with 2-ethylthiophene (**11b**) afforded 2-ethyl-5-phenylthiophene (**12b**) with 81 % yield. The coupling of **1a** with indoles **13a,b** also proceeded under similar conditions to give the corresponding indoles **14** in good yields.[24]



Scheme 3. C–H bond functionalization reactions of thiophenes and indoles.



Scheme 4. Mizoroki–Heck reaction with 490 mol ppb (0.000049 mol %) Pd of SiNA-Pd, and the synthesis of Ozagrel, an antiasthmatic agent.

To attain the highest catalytic activity for the heterogeneous catalyst-promoted Mizoroki–Heck reaction, SiNA-Pd with 490 mol ppb Pd (0.000049 mol % Pd) was used for the reaction of the 10-gram scale substrate (Scheme 4). When the reaction of **1a** (10.2 g) and **2a** was performed with 490 mol ppb Pd of SiNA-Pd, TBAA, Et_3N at 160 °C for 48 h, the desired product **3a** was obtained with 95 % yield. The turnover number (TON) and turnover frequency (TOF) were two million and 40 000 h^{-1}, respectively. To our knowledge, this is the highest TON for the Mizoroki–Heck reaction with heterogeneous catalysts.

Ozagrel **17**, an important antiasthmatic agent (thromboxane A_2 synthesis inhibitor),[25] was synthesized by the 490 mol ppb Pd SiNA-Pd-catalyzed Mizoroki–Heck reaction. Thus, the reaction of 4-iodobenzylalcohol (**15**) (11.7 g) and **2a** was carried out with 490 mol ppb Pd of SiNA-Pd under similar conditions to give the cinnamate **16** with 71 % yield. Installation of an imidazole unit, alkaline hydrolysis, and acidification provided ozagrel hydrochloride **17** with 50% yield (3 steps).

In conclusion, we have developed a highly active and reusable novel catalytic platform SiNA-Pd, a silicon nanowire array stabilized palladium-nanoparticle catalyst. SiNA-Pd was readily applied to the Mizoroki–Heck reaction, the hydrogenation, hydrogenolysis, and hydrosilylation as well as the C–H bond functionalization reactions of thiophenes and indoles. A use of SiNA-Pd in the Mizoroki–Heck reaction achieved a quantitative production of coupling compounds with several hundred-mol ppb of palladium, reaching a TON of 2000000. The hybrid catalyst was readily reused without the loss of catalytic activity.

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Keywords: C–H bond functionalization · Mizoroki–Heck reaction · ozagrel · palladium nanoparticle · silicon-nanowire array

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