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Preparation of silk fibroin-supported Pd(0) catalyst for chemoselective hydrogenation: reduction of palladium(II) acetate by methanol on the protein

Hironao Sajiki,[a,*] Takashi Ikawa,[a] Hiromi Yamada,[b] Kozo Tsubouchi[b] and Kosaku Hirota[a,*]

[a]*Laboratory of Medicinal Chemistry, Gifu Pharmaceutical University, Mitahora-higashi, Gifu 502-8585, Japan*
[b]*Laboratory of Biopolymer Characterization, National Institute of Agrobiological Sciences, Oowashi, Tsukuba 305-8634, Japan*

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Abstract—The Pd/fibroin (Fib) was easily prepared by the auto-reduction of the silk-fibroin conjugated $Pd(OAc)_2$ using MeOH as a solvent and a reductant and exhibited good chemoselectivity in the hydrogenation of olefins and azides in the presence of aromatic carbonyls and/or halogens or an *O*-benzyl protective group. © 2002 Elsevier Science Ltd. All rights reserved.

Since a silk protein supported and/or coordinated zero-valent metal catalyst for asymmetric hydrogenation was reported by Akabori and co-workers during 1956 to 1962,[1] few further developments in this area have been noted during the last 4 decades[2] while a core-shell nano structured gold colloid-silk fibroin bioconjugate has recently been prepared.[3] This could be due to the fact that the silk-palladium catalysed asymmetric hydrogenations are inefficient inasmuch as the reproducibility of the method was invariably poor.[1] In protein-supported metal catalysts, the amine, hydroxyl, carbonyl, aromatic, or thiol functional groups in the protein can easily bind with the metal surface, leading to the bioconjugate. However, fibroin of the silk fibroin-supported palladium catalyst was most likely denatured under the drastic reaction conditions for the reason that the fibroin was exposed to the strongly acidic conditions derived from liberating HCl from $PdCl_2$ in boiling 0.1N AcOH based upon Akabori's preparation method.[1a,b,4] To the best of our knowledge, no applicable protein-supported metal catalysts have, as yet, been reported. The aim of the present communication is to report the preparation of a highly dispersed Pd catalyst supported on the silk fibroin by the HCl and hydrogen-free mild method at room temperature that is active and chemoselective in the heterogeneous phase hydrogenation.

The silk fibroin is one of the two principal components of silk fiber which is secreted from the silk gland of the silkworm *bombyx mori* and recently has come to be considered as a useful bio-material accounting for a wide variety of interesting properties such as in food, cosmetics, medical and biological materials, not to mention fibers.[5] The total content of glycine, alanine, serine and tyrosine comprised more than 90 mol% of the whole volume of the silk fibroin, and very few residues of sulfur amino acids, which can be a strong catalyst poison of metals, are included.[6]

The Pd deposition ($1\sim10$ wt% of the silk fibroin) onto the silk fibroin was initiated by incipient wetness impregnation with a rust-colored MeOH solution of $Pd(OAc)_2$ [Fig. 1(a)]. The mixture was allowed to stand for 4 days at room temperature in air and the silk fibroin changed gradually from white to black and the solution also changed gradually from rust to thoroughly colorless-clear [Fig. 1(b–c)], indicating the slow but complete adsorption of $Pd(OAc)_2$ on the silk fibroin and the rapid formation of the zero-valent Pd catalyst on the silk fibroin (Pd/Fib) via oxidation of the silk fibroin or MeOH.[7] After simple filtration, the obtained Pd/Fib was stable for more than a year at room temperature in air (in a capped vial) and is nonpyrophoric. The Pd/Fib catalyst can be used by cutting up the Pd/Fib fiber with scissors and is removed easily from the reaction mixture using a pair of tweezers or by simple filtration.

Scanning electron microscopy (SEM) images evidenced the high dispersion of amorphous palladium metal particles on the smooth surface of the silk fibroin (Fig. 2). The variation of the Pd content only made a difference

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* Corresponding authors.

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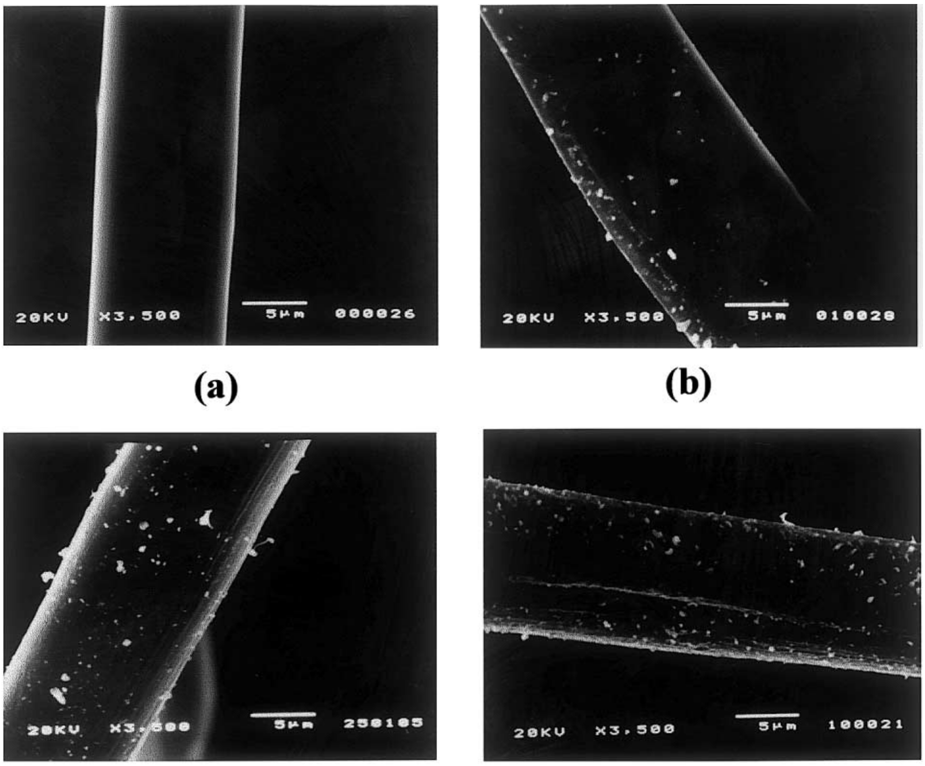
(a) (b) (c)

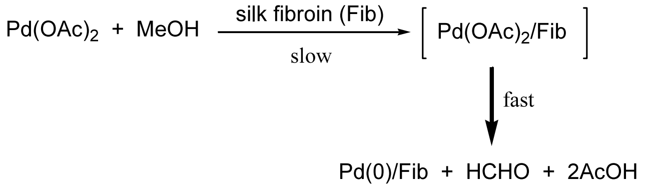
Figure 1. Preparation of Pd/Fib catalyst. Color change of the silk fibroin and the umber MeOH solution of $Pd(OAc)_2$. (a) The silk fiber and $Pd(OAc)_2$ solution in MeOH. (b) Impregnation of the fiber. (c) After 4 days impregnation. Black Pd/Fib and colorless-clear solution is observed.



(a) (b)
(c) (d)

Figure 2. SEM images of original silk fibroin fiber (a) and Pd/Fib fiber contain 1% Pd metal (b), 2.5% (c), 10% (d).

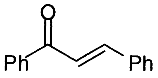
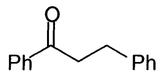
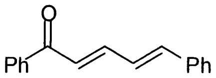
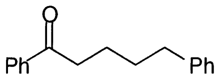
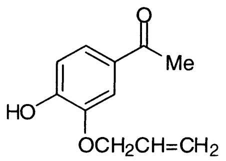
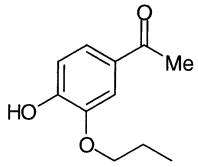
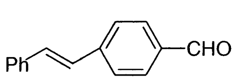
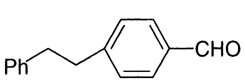
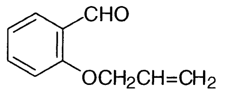
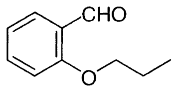
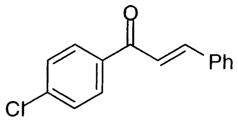
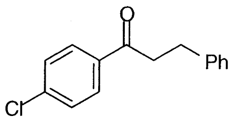
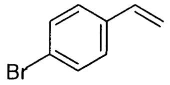
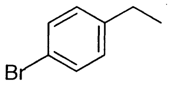
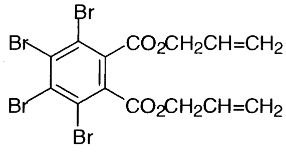
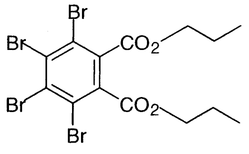
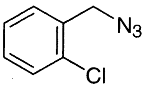
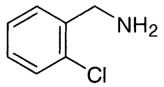
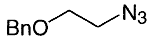
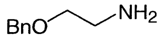
in the density of the Pd particles. This homogeneous dispersion was attributed to an interaction between the $Pd(OAc)_2$ and amino acids of the silk fibroin, increasing the resistance to the growth of the Pd cluster.[3] The quantitative analysis of the formation of acetic acid[8] and formaldehyde[9] was carried out to gain insight into the reduction of $Pd(OAc)_2$. For the reason that 90% of acetic acid and 70% of formaldehyde were determined from the filtered clear solution of Figure 1(c), MeOH contributed to the reduction of $Pd(OAc)_2$ which was strongly adsorbed and coordinated by silk fibroin,[7] while the Tyr and/or Ser residues of silk fibroin also display strong electron-donating properties (Scheme 1).[3]



Scheme 1. Generation mechanism of Pd/Fib.

To explore the scope of the 2.5% Pd/Fib catalyst,[10] the chemoselective hydrogenation of a variety of substrates was carried out at room temperature. The results shown in Table 1 demonstrate that the hydrogenation activity toward olefin and azide is retained. No hydrogenation of aromatic ketones (entries 1–3 and 6), aldehydes (entries 4 and 5), halogens (entries 6–9) or benzyl ether (entry 10) was observed. It is well known that the heterogeneous hydrogenation of aromatic carbonyls, aromatic halides except fluorides and benzyl ether occur easily.[11] Therefore, it is extremely difficult to achieve the chemoselective hydrogenation of olefin and azide functionalities leaving intact the aromatic carbonyl and halide and benzyl ether. Recently, we have reported a chemoselective hydrogenation without hydrogenolysis of the benzyl ethers[12] and a partial hydrogenation of

Table 1. Chemoselective hydrogenation of olefin or azide functionality using 2.5% Pd/Fib catalyst[a]

Entry	Substrate	Time (h)	Product	Yield (%)[b]
1		30		97 (99)[c]
2		3		100
3		37		99
4		24		100[d]
5		27		100[e]
6		20		98
7		24		100[f]
8		3		94
9		24		91
10		5		87

[a] Unless otherwise specified, the reaction was carried out using 1.0 mmol of the substrate in MeOH (5 mL) with 2.5% Pd/Fib (10% of the weight of the substrate) under hydrogen atmosphere (balloon) for the given reaction time. [b] Isolated yield. [c] The yield in parentheses is obtained from the different reaction conditions (5 atm of hydrogen for 2 h). [d] The reaction was performed under 5 atm of hydrogen. [e] Reaction performed with AcOEt as a solvent since the formations of a certain amount of the over-reduced alcohol was observed in MeOH. [f] Determined by ^{1}H NMR.

aromatic carbonyls[13] using a Pd/C–ethylenediamine complex catalyst [Pd/C(en)]. 2.5% Pd/Fib and 5% Pd/C(en) catalysts both exhibit no catalyst activity toward the hydrogenolysis of benzyl ethers (entry 10 and Ref. 12). While aromatic ketones and aldehydes were easily transformed into the corresponding benzyl alcohols by the 10%Pd/C(en)-catalyzed hydrogenation,[13] 2.5% Pd/Fib catalyst was entirely inactive toward the hydrogenation of aromatic carbonyl groups (entries 1–6). Further, the hydrogenation using 2.5% Pd/Fib catalyst also perfectly tolerates aromatic chlorides (entries 6 and 9) and bromides (entries 7 and 8).[14] Needless to say, Pd/C(en) or commercial Pd/C-catalyzed chemoselective hydrogenation with retention of aromatic halides could not be accomplished.[15] Consequently, 2.5% Pd/Fib catalyst can be applied to the development of a chemoselective hydrogenation method of olefin and azide groups which distinguishes the aromatic ketone, aldehyde, chloride and bromide functionalities although the Pd/C(en) or commercial Pd/C-catalyzed hydrogenation cannot tolerate these functionalities.

At present, detailed mechanistic studies have not been undertaken and the exact process of the chemoselectivity is unclear. It has been proposed that the formation of Pd metal particles on the surface of silk fibroin reduced the active surface area of the catalyst. Therefore, the catalyst activity of Pd/Fib was partially diminished.

In summary, the present study provides indication that the rapid reduction of the silk-fibroin conjugated $Pd(OAc)_2$ proceeded using MeOH as a reductant at room temperature. The Pd/Fib catalyst displays good chemoselectivity in the hydrogenation of olefins and azides in the presence of aromatic carbonyls and/or halogens or an *O*-benzyl protective group. This catalyst provides a simple and practical protocol for chemoselective hydrogenation and reinforces the versatility of aromatic carbonyls and halides in organic synthesis.

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