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Chemoselective Hydrogenation Catalyzed by Pd on Spherical Carbon

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We have developed a highly chemoselective hydrogenation method using a novel palladium catalyst supported on spherical carbon (0.5% Pd/SC). The 0.5% Pd/SC exhibited a novel catalytic activity and could achieve the chemoselective hydrogenation of alkynes, alkenes, azides, nitro groups, and aliphatic *O-tert*-butyldimethylsilyl (TBS) ethers without hydrogenolysis of benzyl esters, benzyl ethers, nitriles, aromatic ketones, *N*-carbobenzyloxy (*N*-Cbz) protective groups, and aromatic *O*-TBS ethers.

Introduction

The transition-metal-catalyzed hydrogenation method in the presence of hydrogen gas or a hydrogen transfer agent is a powerful tool for functional group transformations in both the laboratory and industrial syntheses. Palladium on activated carbon (Pd/C) is one of the most widely used catalysts for hydrogenations owing to its stability, ease of the separation from the reaction mixture, possible recyclability, and high catalyst activity. Although the high catalyst activity of Pd/C leads to the substrate's versatility, it is incompatible with chemoselectivity in the hydrogenation of specific functional groups among other functionalities within the molecules. It is known that catalytic hydrogenations are usually suppressed by so-called catalyst poisons, such as sulfur- or nitrogen-containing materials, based on covering the catalyst's active sites by the strong coordination of sulfur and nitrogen atoms to the catalyst metal.[1,2] Although chemoselective hydrogenations among some reducible functionalities have been successfully achieved by the addition of several catalyst poisons, these methods are difficult to control and usually poorly reproducible except for a few examples, such as the Lindlar catalyst[3] and Rosenmund reaction.[4]

During the course of our studies involving the heterogeneous transition metal-catalyzed hydrogenation, we revealed that the addition of an appropriate kind and quantity of the nitrogen- or sulfur-containing molecules as catalyst poisons to the Pd/C-catalyzed hydrogenation system selectively suppressed the catalyst activity toward the hydrogenation of the specific functionalities.[5] These findings led to the development of novel catalysts, which contain a nitrogen or sulfur component, for the chemoselective hydrogenations without any addition of catalyst poisons; for example, the Pd/C–ethylenediamine complex [Pd/C(en) (Wako: 169-21443)],[6] fibroin (a protein produced by silkworms)-supported Pd catalyst [Pd/Fib (Wako: 163-22183)],[7] Pd–polyethyleneimine complex [Pd/PEI (Wako: 167-22223)],[8] and Pd/C–diphenylsulfide complex [Pd/C(Ph_2S) (N.E. Chemcat: SGS-10DR)].[9] Furthermore, palladium catalysts supported on molecular sieves (Pd/MS)[10] and boron nitride (Pd/BN)[11] were developed for the chemoselective hydrogenation of alkynes, alkenes, and azides leaving the coexisting benzyl ester, aromatic carbonyl, *N*-carbobenzyloxy (*N*-Cbz), and nitro functionalities intact, based on the characteristics of the supports. The Pd/BN could also be used for the efficient semihydrogenation of alkynes to the corresponding alkenes in the presence of diethylenetriamine.[11] Although the chemoselective hydrogenation of specific reducible functionalities has been catalyst-dependently achieved, the further development of new catalysts exhibiting different chemoselectivities will reinforce the versatility of the synthetic processes.

In the context of our ongoing study on the development of new heterogeneous catalysts for hydrogenation reactions, we found that a zero-valent palladium catalyst supported on spherical carbon (Pd/SC from YMC Co., Ltd.), which was developed for a pre-packed catalyst cartridge for a continuous-flow hydrogenation device, is useful for the chemoselective hydrogenation using the batch reaction system without the addition of catalyst poisons. We herein discuss the utility of the Pd/SC

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for the chemoselective hydrogenation, including detailed scope and limitations among the reducible functionalities.

Results and Discussion

Characterization of Pd/SC

The SEM images of the spherical carbon (SC) and 0.5% Pd/SC are shown in Figure 1 and Figure 2, respectively. Figure 1 reveals that the activated carbon is nearly spherical in shape and has dents in places on the surface (Figure 1a and b, respectively). The average diameter of SCs is 0.36 mm, and the average pore size is 1.7 nm. The BET specific surface area of the activated carbon was determined to be 1371 m^2g^{-1}. It is shown in Figure 2 that small white Pd metal particles of 0.5% Pd/SC are preferentially located in the pores of the spherical carbon.

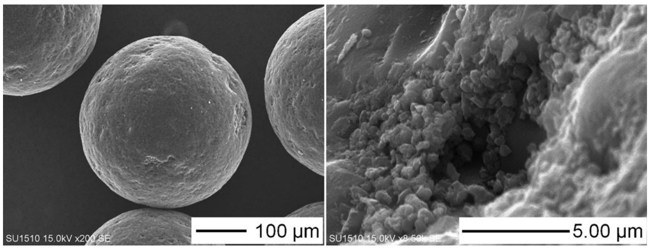


Figure 1. a) SEM image of spherical carbon at 200× magnification. b) SEM image of spherical carbon at 8500× magnification.

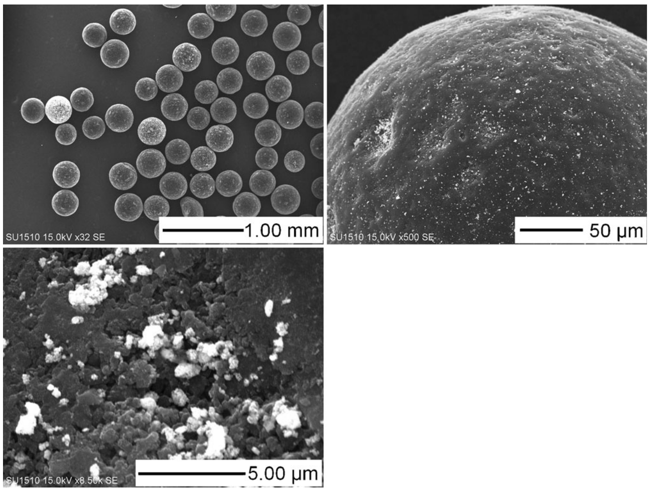


Figure 2. a) SEM image of 0.5% Pd/SC at 32× magnification. b) SEM image of 0.5% Pd/SC at 500× magnification. c) SEM image of 0.5% Pd/SC at 8500× magnification.

The palladium metal supported on SC was also observed by TEM measurements (Figure 3). In Figure 3a and b, a bright-field image of Pd particles formed on an SC and the corresponding selected-area electron diffraction pattern are shown, respectively. The Debye–Scherrer rings in the selected-area electron diffraction pattern are consistently indexed as those of face-centered cubic Pd. The mean size of the palladium clusters is 5.6 nm in diameter. The Pd metal surface area of 0.5% Pd/SC was found to be 152 m^2g^{-1}-Pd by a surface area analysis using the CO adsorption method.

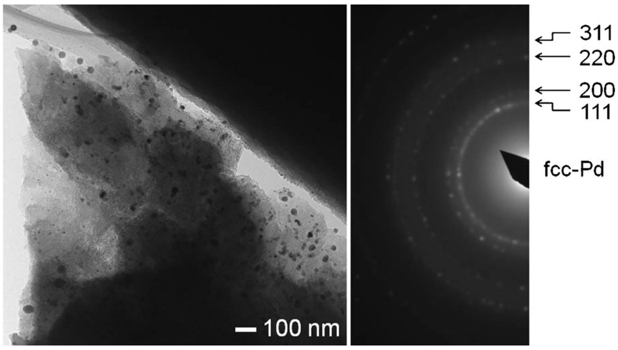


Figure 3. a) Bright-field image of 0.5% Pd/SC at 60000× magnification. b) The corresponding selected-area electron-diffraction pattern.

Electron probe microanalysis (EPMA) of 0.5% Pd/SC clarified that the Pd particles are exclusively located on the surface of the SC (Figure 4).

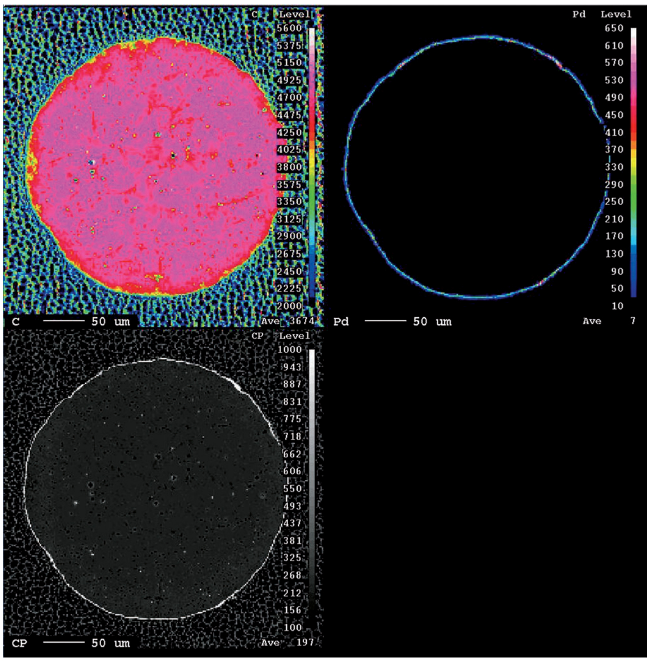


Figure 4. EPMA of 0.5% Pd/SC.

The X-ray photoelectron spectra and XRD pattern of 0.5% and 5% Pd/SCs are shown in Figure 5 and Figure 6, respectively. Figure 5 reveals large Pd $3d_{3/2}$ and Pd $3d_{5/2}$ peaks at approximately 340 eV and 335 eV, respectively, both of which are derived from the Pd^0. Although a clear XRD spectrum of 0.5% Pd/SC could not be obtained with 0.5% Pd/SC, owing to the low palladium concentration, the peaks of 5% Pd/SC were found to be identical to the reported Pd peaks of Pd/C (Figure 6).[12] The peaks at $2\theta = 40.1°$, 46.7°, 68.3°, and 82.3° in Figure 6 correspond to the Pd planes (111), (200), (220), and

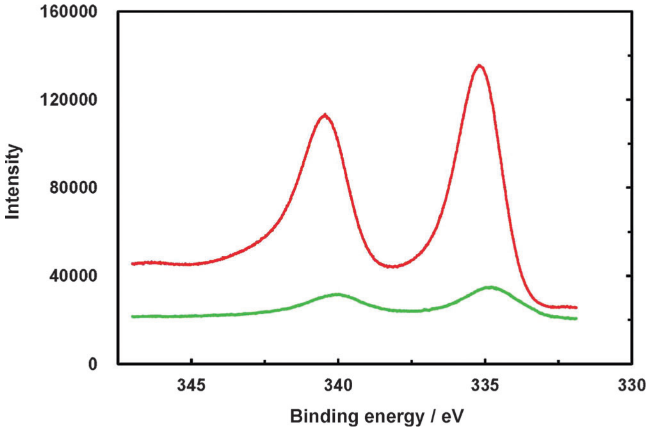


Figure 5. X-ray photoelectron spectra of Pd/SCs. 0.5 % Pd/SC (–), 5 % Pd/SC (–).

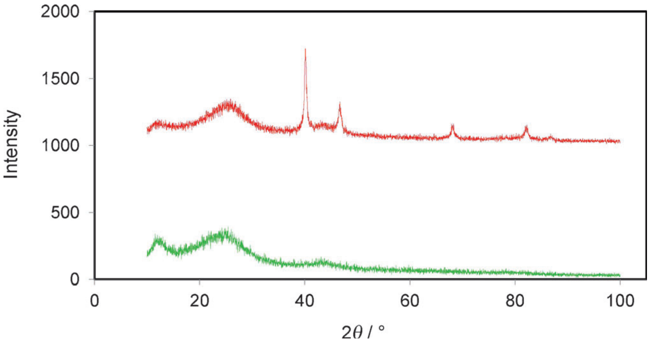


Figure 6. XRD patterns of Pd/SCs. 0.5 % Pd/SC (–), 5 % Pd/SC (–).

(3 1 1), respectively.[13] The peaks derived from other metals were not detected in the XRD spectra.

0.5 % Pd/SC as a hydrogenation catalyst

0.5 % Pd/SC was used as a catalyst for the hydrogenation of a variety of reducible functionalities (Table 1) and indicated an excellent catalyst activity for the hydrogenation of azide (entries 1–4 and 16), nitro (entries 5, 6, and 22), olefin (entries 7, 10, 11, 13, 18, 20, 21, and 24–26), and acetylene (entry 23) functionalities. On the other hand, benzyl ethers and benzyl esters were found to partially undergo the hydrogenolysis in methanol. We have reported that the choice of solvent was an important factor to control the selective suppression under the hydrogenation conditions.[5e–g, 6a,d,f,h,i, 7, 8, 14a] Thus, several solvents possessing a weak coordinative ability as a bulk configuration, such as EtOAc, THF, acetonitrile, and 1,4-dioxane, could mildly and appropriately decrease the catalyst activity, and the chemoselective hydrogenations would be achieved if using such solvents. With the expectation of the complete suppression of the hydrogenolysis of benzyl ether, the hydrogenation reaction in a wide variety of solvents was investigated (Table 2). The reaction of 4-benzyloxyphenylacetic acid **1** in methanol by using the general procedure for the chemoselective hydrogenation resulted in the formation of 8 % 4-hydroxyphenylacetic acid **2** as an over-hydrogenation product together with a 92 % recovery of the substrate **1** (^{1}H NMR data, Table 2, entry 1), whereas EtOAc, THF, and acetonitrile indicated comparatively suppressive effects (Table 2, entries 2–4), and the benzyl ether completely survived in 1,4-dioxane (Table 2, entry 5). Equally good results have been achieved for the hydrogenation of a variety of benzyl ethers by using 1,4-dioxane instead of methanol (Table 1, entries 7–9). No hydrogenolysis of the benzyl ester could be accomplished in 1,4-dioxane or acetonitrile as the solvent (Table 1, entries 9–11 and 28). Unexpectedly, the nitro and benzyl ester functionalities were completely tolerated even in methanol in the presence of an azido functionality within the molecule (Table 1, entries 2–4). This is probably owing to the catalyst's poisonous effect of the liberated amine moiety produced by the reduction of the coexisting azide group.

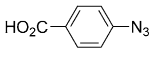
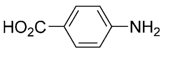
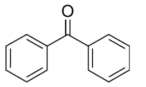
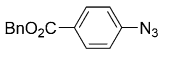
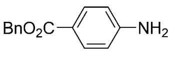
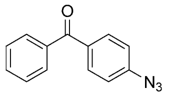
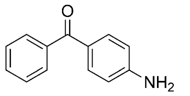
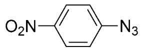
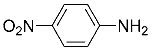
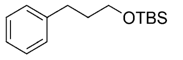
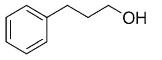
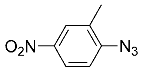
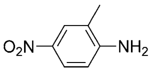
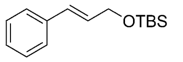
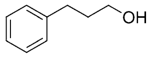
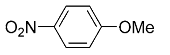
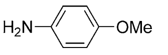
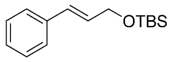
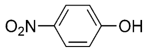
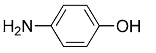
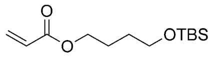
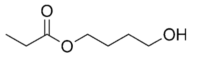
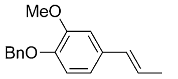
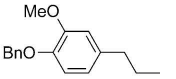
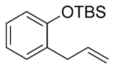
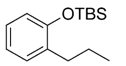
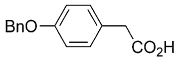
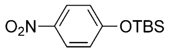
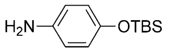
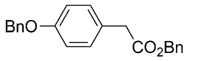
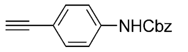
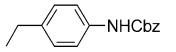
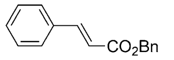
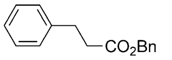
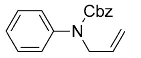
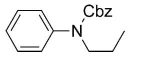
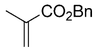
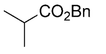
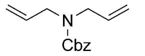
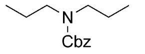
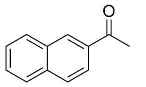
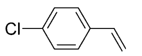
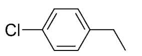
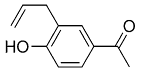
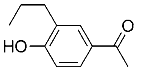
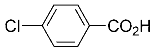
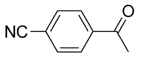
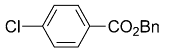
Although it is well-known that aromatic carbonyls are easily reduced to the corresponding methylene compounds through the formation of intermediary benzyl alcohols under Pd/C-catalyzed hydrogenation conditions, the carbonyl groups of the benzophenone derivatives were untouched under the present conditions (entries 15 and 16). On the other hand, reduction of the aromatic carbonyls of acetophenone or acetonaphthone derivatives proceeded in part, but the use of 1,4-dioxane as a solvent resulted in the complete suppression (entries 12 and 13). In the case of 4-acetylbenzonitrile, no hydrogenation of the carbonyl group took place even in methanol as the solvent, probably because the catalytic poisonous effect of the nitrile group within a molecule is similar to the above-mentioned solvent effect of acetonitrile (entry 14).

tert-Butyldimethylsilyl (TBS) ether, which is one of the widely used protecting groups of hydroxyl groups, is generally removed by an acid treatment. We previously demonstrated that Pd/C smoothly catalyzed the hydrogenolysis of *O*-TBS ethers under neutral conditions.[6g, 14] When 0.5 % Pd/SC was used for the hydrogenolysis of 1-*tert*-butyldimethylsilyloxy-3-phenylpropane, the hydrogenolysis of the *O*-TBS group readily proceeded and the corresponding 3-phenylpropane was obtained in 91 % isolated yield (entry 17). Other alkyl TBS ethers also underwent a similar smooth hydrogenolysis, together with the hydrogenation of the alkene moieties (entries 18 and 20), while the aryl TBS ethers were tolerant to their cleavage, leading to the chemoselective reduction of alkenes and nitro groups to the corresponding alkanes and amines, respectively (entries 21 and 22). The pH value of the filtrate after stirring of the aqueous suspension of 0.5 % Pd/SC (500 mg in 5.0 mL of H_2O) under a hydrogen atmosphere at room temperature for 24 h was measured to be 5.96, which is roughly equal to the pH value of ordinary purified water[15] and would not be acidic enough to cleave the *O*-TBS groups.[14b,c] Furthermore, the silyl group of the aliphatic *O*-TBS ether, 1-*tert*-butyldimethylsilyloxy-3-phenyl-2-propene, was found to be never cleaved in methanol at room temperature under an argon atmosphere even after 48 h (entry 19). These results indicated that 0.5 % Pd/SC possesses a catalyst activity toward the hydrogenolysis of the alkyl *O*-TBS ethers.

The *N*-Cbz protecting group is widely used for the protection of amino groups in organic synthesis because of their

Table 1. Chemoselective hydrogenation.[a]

$$\text{Substrate} \xrightarrow[\text{MeOH, RT, 24 h}]{\text{0.5\% Pd/SC, H}_2\text{ (balloon)}} \text{Product}$$

Entry	Substrate	Product	Yield [%][b]	Entry	Substrate	Product	Yield [%][b]
1[c]			100	15		recovery	96[g] [96][d,j]
2			96	16			99
3			95 [98][d,e]	17[k]			91
4			96	18[l]			87 [–][m]
5			95	19[l,n]		recovery	98[g]
6			100	20[k]			82[o]
7[f]			98	21[l]			94
8[f]		recovery	100[g]	22[l]			100
9[f]		recovery	93[g]	23			100 [22][d,p]
10[h]			99	24[q]			97[r]
11[h]			86	25[q]			93
12[f]		recovery	97[g]	26[s]			–
13[f]			92	27		recovery	95[g]
14		recovery	99[g] [92][d,i]	28[h]		recovery	97[g]

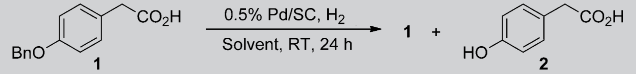
[a] Unless otherwise noted, the reactions were performed by using substrate (1.0 mmol) in methanol (1.0 mL) with 0.5% Pd/SC (0.05 mol% of the substrate) with stirring under ordinary hydrogen pressure and at room temperature for 24 h. [b] Isolated yield. [c] Methanol (3 mL) of was used. [d] 0.5% Pd/C was used instead of 0.5% Pd/SC. The yield of the desired product [or recovered starting material (entries 14 and 15)] in the mixture was determined by the calculation based on the ^{1}H NMR ratio, total weight of the mixture, and molecular weight of each material. [e] A 98:2 mixture of 4-nitroaniline and *p*-phenylenediamine was obtained. [f] 1,4-Dioxane was used as the solvent. [g] Yield of recovered starting material. [h] Acetonitrile was used as the solvent. [i] A 94:3:3 mixture of 4′-cyanoacetophenone, 4-(1-hydroxyethyl)benzonitrile, and 1-[4-(aminomethyl)phenyl]ethanone was obtained. [j] A 98:2 mixture of benzophenone and benzhydrol was obtained. [k] The reaction time for was 72 h. [l] The reaction time was 48 h. [m] 0.5% Pd/C was used instead of 0.5% Pd/SC. A complex mixture including the substrate and 3-phenyl-1-propanol was obtained. [n] The reaction was performed under an argon atmosphere. [o] 9% of 4-(*tert*-butyldimetylsilyloxy)butyl propionate was obtained. [p] A 40:60 mixture of *N*-(benzyloxycarbonyl)-4-ethylaniline and 4-ethylaniline was obtained. [q] The reaction time was 3 h. [r] A 98:2 mixture of *N*-benzyloxycarbonyl-*N*-propylaniline and *N*-propylaniline was obtained. The yield of the desired product in the mixture was determined by the calculation based on the ^{1}H NMR ratio, total weight of the mixture, and molecular weight of each material. [s] CD_3OD was used as the solvent, owing to the low boiling point of the products.

easy introduction as well as easy removal under the Pd/C-catalyzed mild hydrogenolysis conditions. Therefore, the development of the hydrogenation method of alkynes and alkenes without the hydrogenolysis of the *N*-Cbz groups would increase the utility of the *N*-Cbz protective group and offer new possible synthetic routes. The results in entries 23–25 demonstrate that the selective hydrogenation of olefins and acetylene can be achieved by using 0.5% Pd/SC under ordinary hydrogen pressures and temperatures in the presence of the *N*-Cbz group within the molecules.

We next investigated the hydrogenation of aromatic chlorides. Aromatic chlorides are partially hydrodehalogenated under the Pd/C-catalyzed conditions,[16] whereas 0.5% Pd/SC has no catalytic activity toward the hydrodechlorination (entries 26–28).

The 0.5 wt% palladium catalyst supported on activated carbon powder (0.5% Pd/C) was also used for the hydrogenation for comparison with 0.5% Pd/SC. Although 0.5% Pd/C in general exhibited weak catalyst activity compared with more highly Pd-loaded 5% or 10% Pd/C, the complete chemoselec-

Table 2. The effect of solvent on the hydrogenolysis.



Entry	Solvent	**1**:**2**[a]
1	MeOH	92:8
2	EtOAc	95:5
3	THF	97:3
4	MeCN	97:3
5	1,4-dioxane	100:0

[a] Determined by using ^{1}H NMR spectroscopy.

tivity was not achieved and the over-reduction proceeded (see the brackets in entries 3, 14, 15, 18, and 23, and footnotes). In particular, the hydrogenation of *N*-benzyloxycarbonyl-4-ethynylaniline afforded a 40:60 mixture of *N*-(benzyloxycarbonyl)-4-ethylaniline and 4-ethylaniline product (brackets in entry 23). The difference in the catalyst activity between 0.5% Pd/SC and 0.5% Pd/C would be presumably arisen from that of their structural characteristics, such as the Pd distribution on the support and morphology.

A summary table comparing the activity of Pd/SC and other chemoselective hydrogenation catalysts developed by us is shown in Figure 7. The 0.5% Pd/SC can catalyze the hydrogenation of unsaturated C–C multiple bonds, azido groups, and nitro groups in the presence of benzyl ethers, benzyl esters, nitriles, aromatic ketones, *N*-Cbz protective, and aromatic chloride functionalities. The significant future of the 0.5% Pd/SC is the catalytic ability regarding the hydrogenolysis of alkyl *O*-TBS ethers, as shown in Figure 7, for the chemoselective hydrogenation. Another characteristic of Pd/SC is the distinction between the azido and nitro groups within the same molecule. If azido groups coexist in the nitro compounds, only azides could be reduced to the corresponding amines derived from the hydrogenation of azides with the nitro groups intact caused by the suppressive effect of the amine.

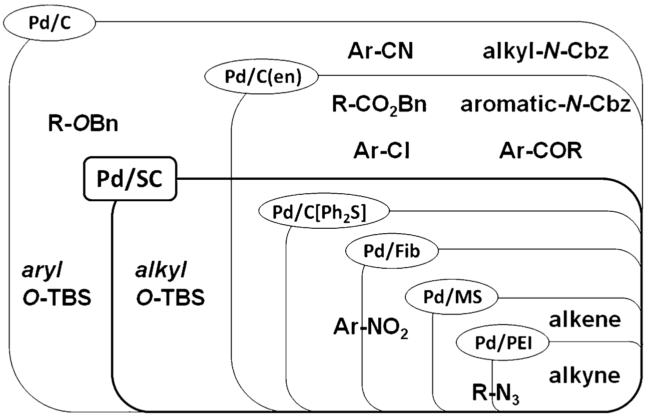
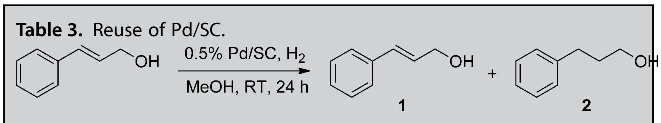


Figure 7. Comparison of catalytic activities of various catalysts for the chemoselective hydrogenation: functional groups of the framework could be reduced by each captioned catalyst.

The reuse of the heterogeneous catalysts is one of the most important properties owing to cost-performance and environmental considerations. We then investigated the reuse test of 0.5% Pd/SC for the hydrogenation of cinnamyl alcohol (Table 3). The 0.5% Pd/SC could be reused at least until the second run without any loss of catalyst activity, although it significantly decreased after the third run.[17]

Table 3. Reuse of Pd/SC.



Run	Recovered Pd/SC [%]	**1**:**2**[a]
1st	100	0:100 [92]
2nd	91	0:100 [98]
3rd	99	79:21
4th	95	99:1

[a] The ratio was determined by ^{1}H NMR spectroscopy. Isolated yield is indicated in parentheses.

The leaching of Pd metal from 0.5% Pd/SC was next investigated. After completion of the 0.5% Pd/SC-catalyzed hydrogenation of cinnamyl alcohol in methanol (12 h), the catalyst was removed by filtration by using a membrane filter (Millipore; Millex-LG, 0.20 μm) and the Pd concentration in the filtrate was measured by inductively coupled plasma atomic emission spectrometry (ICP–AES). As no leached Pd was detected within the limit of detection (<1 ppm), the reduced catalyst activity of 0.5% Pd/SC during the reuse would be attributed to the mechanical damage of the catalyst during the vigorous stirring. The mechanical damage of the catalyst was confirmed by the observation of many small cracked particles of the catalyst in the SEM image measured after the 2nd reuse test (Figure 8).

Conclusions

In summary, we have developed a mild and chemoselective hydrogenation method using commercially available 0.5% Pd/SC as a catalyst, which is applicable for the reduction of alkyne, alkene, azido, nitro, and alkyl *O*-TBS functionalities leav-

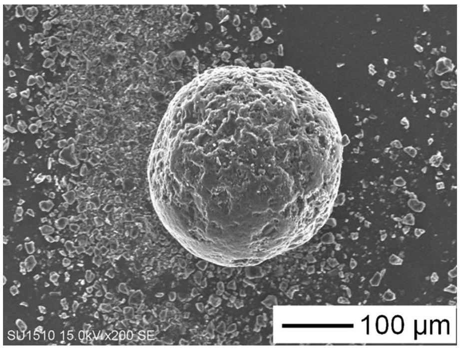


Figure 8. SEM image of 0.5% Pd/SC after 2nd reuse test at 200× magnification.

ing the benzyl ether, benzyl ester, nitrile, aromatic ketones, aromatic chlorides, *N*-Cbz, and aryl *O*-TBS groups intact. The present method could be expected to be of practical use as a general chemoselective hydrogenation process in synthetic and process chemistries.

Experimental Section

General experimental

The novel 0.5% Pd/SC catalyst (wet-type, containing 36.3 wt% H_2O) is commercially available from YMC Co., Ltd. (Kyoto, Japan). The XRD patterns were recorded by a Rigaku RINT2000 using monochromatic $Cu_{K\alpha}$ radiation at 40 kV and 20 mA. The $2\theta/\theta$ range from 10 to 100° was converted at a scan speed of $0.1^\circ\,min^{-1}$. The XPS spectrum was recorded by a Shimadzu AXIS-165 using a non-monochromatic $Al_{K\alpha}$ X-ray source (1486.6 eV) and collected in the binding energy range of 331.89–347.01 eV. The SEM images were captured by a Hitachi SU1510 microscope operated at 30 kV. The TEM images were obtained with a Hitachi H-800 microscope operated at 200 kV. EPMA was performed by using a JEOL JXA-8100. The ^1H and ^{13}C NMR spectra were recorded by a JEOL JNM-ECX 400P or JNM-ECA 400 spectrometer (400 MHz for ^1H NMR and 100 MHz for ^{13}C NMR).

General procedure for the chemoselective hydrogenation

After three vacuum/H_2 cycles to replace air inside the test tube with hydrogen, the mixture of the substrate (1.00 mmol) and 0.5% Pd/SC (16.7 mg, 0.500 μmol, 0.05 mol% of the substrate) in methanol (1.00 mL) was stirred under ordinary hydrogen pressure (balloon) and at RT for 24 h. After dilution with an appropriate solvent, which can dissolve the product, the reaction mixture was filtered by using a membrane filter (Millipore Corporation, Billerica, MA, USA; Milex-LG, 0.20 μm), and then the collected catalyst was washed with the solvent (3×10 mL). The combined filtrates were concentrated under reduced pressure to give the analytically pure product. The product ratio was determined by ^1H NMR analysis. The ^1H NMR spectra of all products were identical to those in the literature or commercial sources (see the Supporting Information).

Procedure for the confirmation of the catalytic activity of 0.5% Pd/SC toward the hydrogenolysis of aryl *O*-TBS ethers

pH measurement of the filtrate obtained from the aqueous suspension of 0.5% Pd/SC: A suspension of 0.5% Pd/SC (500 mg) in H_2O (5.00 mL) under a hydrogen atmosphere was stirred at RT for 24 h, then the mixture was filtered by using a membrane filter (Millipore; Milex-LG, 0.20 μm). The pH value of the aqueous filtrate was measured by using a Horiba pH meter F-21 and found to be 5.96.

Treatment of 1-*tert*-butyldimethylsilyloxy-3-phenyl-2-propene under an argon atmosphere: 1-*tert*-Butyldimethylsilyloxy-3-phenyl-2-propene (248 mg, 1.00 mmol) was treated with 0.5% Pd/SC (16.7 mg, 0.500 μmol) in a manner similar to that described in the general procedure for the chemoselective hydrogenation except for stirring under an argon atmosphere instead of a hydrogen atmosphere. No reaction took place and the unchanged 1-*tert*-butyldimethylsilyloxy-3-phenyl-2-propene (243 mg, 98%) was recovered.

Reuse test of 0.5% Pd/SC

Five test tubes were prepared. Each test tube was charged with cinnamyl alcohol (134 mg, 1.00 mmol), 0.5% Pd/SC (16.7 mg, 0.500 μmol, 0.05 mol%), and methanol (1.00 mL). Each mixture was stirred at RT under a hydrogen atmosphere for 24 h, then passed through a filter paper (Kiriyama, No. 5C (1 μm), diameter = 8 mm). The catalyst on the filter paper was washed with methanol (3× 10 mL) and used for the 2nd run (83.4 mg, 100%). The combined filtrates were concentrated in vacuo to give 3-phenyl-1-propanol (627 mg, 92%) as the single product.

Four test tubes were prepared for the 2nd run. Each test tube was charged with cinnamyl alcohol (134 mg, 1.00 mmol), 0.5% Pd/SC (16.7 mg, 0.500 μmol, 0.05 mol%), and methanol (1.00 mL). Each mixture was stirred at RT under a hydrogen atmosphere for 24 h, then passed through a filter paper (Kiriyama, No. 5C (1 μm), diameter = 8 mm). The catalyst on the filter paper was washed with methanol (3×10 mL) and used for the 3rd run (60.6 mg, 91%). The combined filtrates were concentrated in vacuo to give 3-phenyl-1-propanol (528 mg, 98%) as the single product.

Three test tubes were prepared for the 3rd run. Each test tube was charged with cinnamyl alcohol (134 mg, 1.00 mmol), 0.5% Pd/SC (16.7 mg, 0.500 μmol, 0.05 mol%), and methanol (1.00 mL). Each mixture was stirred at RT under a hydrogen atmosphere for 24 h, then passed through a filter paper (Kiriyama, No. 5C (1 μm), diameter = 8 mm). The catalyst on the filter paper was washed with methanol (3×10 mL) and used for the 4th run (49.4 mg, 99%). The combined filtrates were concentrated in vacuo to give a 79:21 ratio mixture of cinnamyl alcohol and 3-phenyl-1-propanol (^1H NMR).

Two test tubes were prepared for the 4th run. Each test tube was charged with cinnamyl alcohol (134 mg, 1.00 mmol), 0.5% Pd/SC (16.7 mg, 0.500 μmol, 0.05 mol%), and methanol (1.00 mL). Each mixture was stirred at RT under a hydrogen atmosphere for 24 h, then passed through a filter paper (Kiriyama, No. 5C (1 μm), diameter = 8 mm). The catalyst on the filter paper was washed with methanol (3×10 mL), and 31.6 mg (95%) of the catalyst was recovered. The combined filtrates were concentrated in vacuo to give a 99:1 ratio mixture of cinnamyl alcohol and 3-phenyl-1-propanol (^1H NMR analysis).

Assay of residual palladium in the reaction mixture

A suspension of cinnamyl alcohol (671 mg, 5 mmol) and 0.5% Pd/SC (83.5 mg, 2.50 μmol, 0.05 mol%) in methanol (5 mL) was stirred at RT under a hydrogen (balloon) atmosphere for 12 h, then passed through a membrane filter (Millipore; Millex-LH, 0.20 μm). The filtrate was diluted with methanol to 20 mL of total volume and the residual palladium was assayed using a Shimadzu ICP-8001 (Shimadzu, Kyoto, Japan). No palladium species were detected within the detection limit (< 1 ppm).

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Keywords: chemoselectivity · heterogeneous catalysis · hydrogenation · palladium · solvent effects

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