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Novel Palladium-on-Carbon/Diphenyl Sulfide Complex for Chemoselective Hydrogenation: Preparation, Characterization, and Application

Akinori Mori,[a] Tomoteru Mizusaki,[a,b] Masami Kawase,[a] Tomohiro Maegawa,[a] Yasunari Monguchi,[a] Shinobu Takao,[b] Yukio Takagi,[b] and Hironao Sajiki[a,]*

[a] Laboratory of Medicinal Chemistry, Gifu Pharmaceutical University, 5-6-1 Mitahora-higashi, Gifu 502-8585, Japan
Fax: (+81)-58-237-5979; e-mail: sajiki@gifu-pu.ac.jp
[b] N. E. Chemcat Corporation, 678 Ipponmatsu, Numazu, Shizuoka 410-0314, Japan

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Abstract: A diphenyl sulfide immobilized on palladium-on-carbon system, Pd/C[Ph_2S], was developed to achieve the highly chemoselective hydrogenation of alkenes, acetylenes, azides, and nitro groups in the presence of aromatic ketones, halides, benzyl esters, and N-Cbz protective groups. Instrumental analyses of the heterogeneous catalyst demonstrated that diphenyl sulfide was embedded on Pd/C *via* coordination of its sulfur atom to palladium metal or physical interaction with graphite layers of the activated carbon. The catalyst could be recovered and reused at least five times without any significant loss of the reactivity.

Keywords: chemoselectivity; diphenyl sulfide; heterogeneous catalysis; hydrogenation; palladium

The development of chemoselective transformations of functional groups has been of great importance in synthetic organic chemistry.[1] Chemoselective hydrogenation, in particular, contributes to the synthesis of complicated natural products, pharmaceuticals, and functional materials.[2] A number of selective hydrogenation methods has been reported that minimize undesired reductions, e.g., platinum metal sulfides[3] and the ZnX_2-Pd/C or Pt/C systems[4] have been applied to the selective hydrogenation of nitro groups in the presence of aromatic halides to obtain haloaniline derivatives. A recent study reported that a polymer-incarcerated platinum species worked for the selective reduction of olefins, acetylenes, and aromatic nitro groups while leaving benzyl ethers and aromatic halides untouched.[5] Other methods for the chemoselective hydrogenation of aromatic nitro groups using vanadium-promoted Raney nickel,[6] Ir/C-MgO,[7] and Pt/Al_2O_3-$P(OPh)_3$[7] were also reported to give aniline derivatives which bear aromatic chlorides and aromatic carbonyl groups. Semihydrogenations of acetylenes to olefins was also achieved by use of nickel[8] or gold[9] nanoparticles. However, only a few catalyst systems such as the Lindler and Rosenmund methods are practically useful.[10] During the course of our study on the heterogeneous transition metal-catalyzed chemoselective hydrogenation during the past decade, we have established a chemoselective hydrogenation method using a nitrogen-containing base and Pd/C,[11] which hydrogenates olefins, acetylenes, nitro groups and so on, while leaving benzyl ethers untouched. Recently, we reported that the addition of diphenyl sulfide (Ph_2S) to the Pd/C-catalyzed hydrogenation system achieved the chemoselective hydrogenation of olefin, acetylene and azide functionalities in the presence of other functional groups, such as aromatic carbonyls, and halides, benzyl esters, N-Cbz (benzyloxycarbonyl) protecting groups and cyano groups.[12] In spite of such unique chemoselectivities, this method requires the removal of Ph_2S from the reaction mixture using silica gel column chromatography. Therefore, the development of a Pd/C-Ph_2S complex, Pd/C-[Ph_2S], by immobilization of Ph_2S onto Pd/C[13] as a heterogeneous and chemoselective hydrogenation catalyst possessing a chemoselectivity similar to the addition of Ph_2S to the Pd/C-catalyzed hydrogenation system was strongly desired.

Detailed investigations of Ph_2S on Pd/C led us to establish the preparation method of the Pd/C-Ph_2S complex (Pd/C[Ph_2S]). A suspension of 10% Pd/C and Ph_2S (2.0 equiv. *vs.* Pd metal of Pd/C) in methanol was stirred for 5 days at room temperature under an argon atmosphere, and then the resulting black powder was collected by filtration, washed successive-

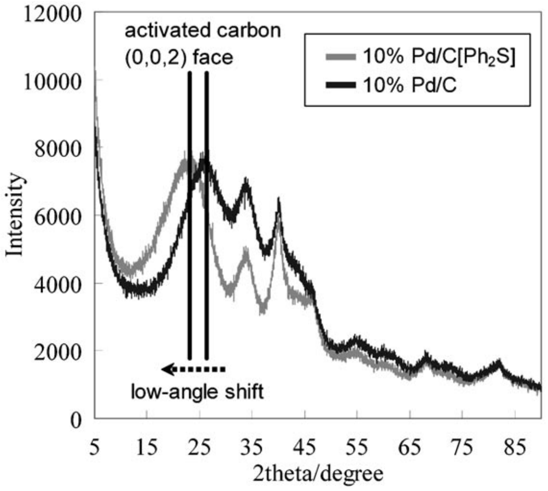


Figure 1. XRD analysis of Pd/C[Ph_2S].

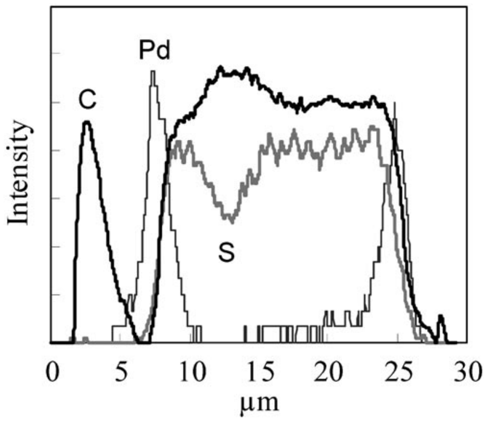


Figure 2. EPMA analysis of Pd/C[Ph_2S].

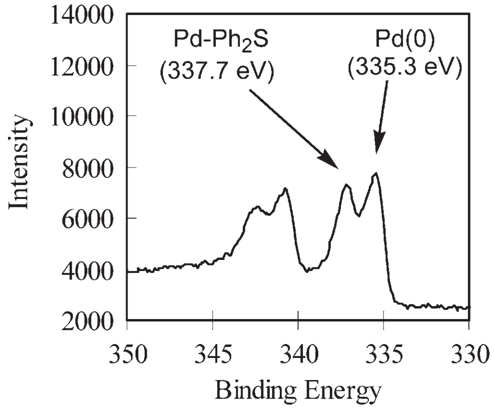


Figure 3. XPS analysis of Pd/C[Ph_2S].

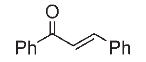
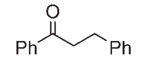
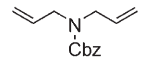
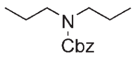
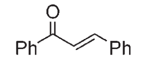
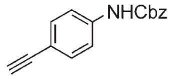
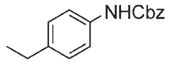
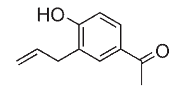
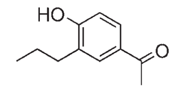
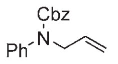
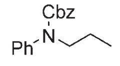
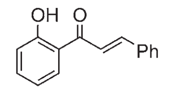
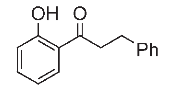
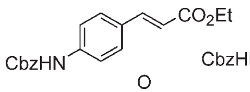
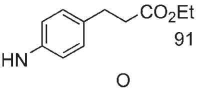
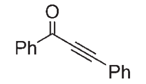
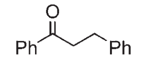
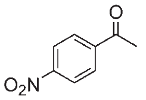
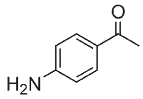
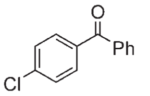
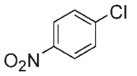
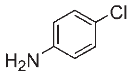
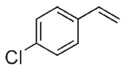
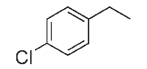
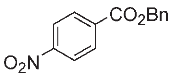
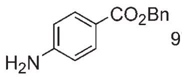
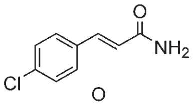
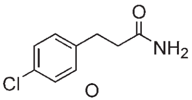
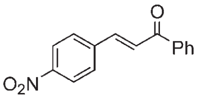
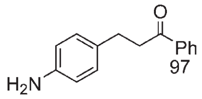
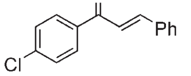
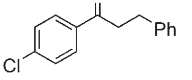
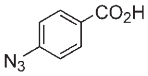
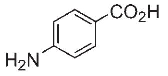
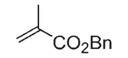
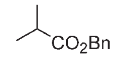
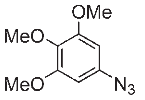
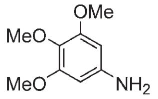
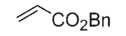
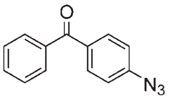
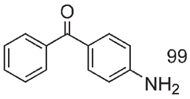
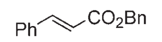
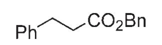
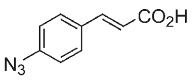
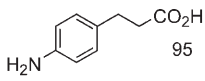
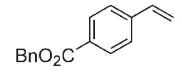
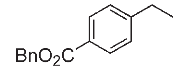
ly with methanol and ether, and finally dried under reduced pressure to give a complex which consists of Pd/C and Ph_2S. The elemental analysis of the complex indicated that the ratio of Pd metal and Ph_2S was 1:1.27. As the result of the XRD (X-ray diffraction) analysis,[14] it was observed that the (0,0,2) face of the activated carbon of this complex was shifted to a lower angle compared to that of commercial Pd/C (Figure 1). This result means that a certain amount of Ph_2S penetrates into the graphite layers of the activated carbon.[15] Furthermore, EPMA (electron probe micro analyzer[16]) data (Figure 2) showed that Ph_2S and the Pd metal are not necessarily evenly distributed on the carbon support.

The XPS (X-ray photoelectron spectroscopy) spectrum of Pd 3*d* of Pd/C[Ph_2S] indicates a certain and partial interaction of Ph_2S with the Pd metal. One of the binding energy peaks of the Pd metal of Pd/C-[Ph_2S] was observed at 337.7 eV which is obviously higher than that of the Pd(0) standard (335.1–335.5 eV) (Figure 3),[17] suggesting that the peak should be derived from the Pd–S complex, and a portion of the Pd metal is strongly bound to Ph_2S. Furthermore, a comparison of the effective Pd metal surface area,[18] determined by measurement of the CO absorbability, between Pd/C and Pd/C[Ph_2S] indicated that 47% of the active sites on the Pd surface of Pd/C[Ph_2S] were covered by Ph_2S. These results indicated that about one-half of the fresh Pd(0) surface (active sites) of the original Pd/C still remained intact and the other half had interacted with Ph_2S by the Pd–S bond based upon the moderately-occluded sulfur lone pair. Therefore, Pd/C[Ph_2S] should possess a very weak catalyst activity and was expected to produce chemoselective hydrogenation among some reducible functionalities.

To explore the catalyst activity of Pd/C[Ph_2S], the hydrogenation of various substrates was carried out (Table 1). Both olefin and acetylene functionalities were selectively hydrogenated without any reduction of the aromatic ketones by Pd/C[Ph_2S] (entries 1, 3–5), although aromatic ketones are very smoothly hydrogenolyzed to methylene compounds *via* the formation of the intermediary benzyl alcohols using commercial Pd/C as a catalyst (entry 2).[13b,h] It is well known that aromatic chlorides are partially hydrogenated under the Pd/C-catalyzed hydrogenation conditions.[2a] In contrast, Pd/C[Ph_2S] did not catalyze the hydrogenolysis of aromatic chlorides at all (entry 6), and the selective hydrogenation of olefins with retention of the aromatic chlorides was available (entries 7–9). Benzyl esters and N-Cbz protecting groups are widely used in organic synthesis as protecting groups,[19] because of their easy introduction to carboxylic acids and amines, respectively, as well as easy deprotection using the Pd/C-catalyzed hydrogenation, therefore, it is extremely difficult to keep such groups intact during a synthetic process including the hydrogenation steps. If these protecting groups survive under the hydrogenation conditions, Pd/C[Ph_2S] would provide new applications. We then examined

Table 1. Chemoselective hydrogenation of olefin or acetylene in the presence of aromatic ketone using Pd/C[Ph_2S].[a]

Substrate $\xrightarrow[\text{MeOH, 24 h}]{\text{10\% Pd/C[Ph}_2\text{S]},\ \text{H}_2\text{ (balloon)}}$ Product

Entry	Substrate	Product	Yield [%][b]	Entry	Substrate	Product	Yield [%][b]
1			98	14			98
2[c]			100	15			94
3			88	16			80
4			97	17			91
5			94	18			97
6		Recovery	99	19			91
7			100[d]	20			97
8			100	21			97
9			99	22			91
10			100[d]	23			91
11			100[d]	24			99
12			99	25			95
13			99				

[a] Unless otherwise noted, the reaction was carried out using 500 μmol of the substrate in MeOH (1.0 mL) with 10% Pd/C[Ph_2S] (10 wt% of the substrate) with vigorous stirring at room temperature (*ca.* 20 °C) under ordinary hydrogen pressure (balloon) for 24 h.

[b] Isolated yield.

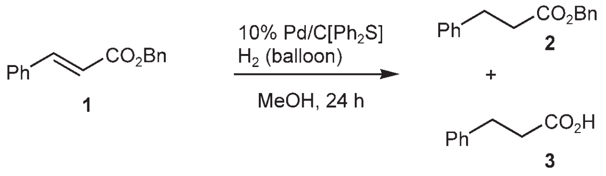
[c] The reaction was carried out using 10% Pd/C (10 wt% of the substrate) instead of Pd/C[Ph_2S].

[d] The reaction was carried out in CD_3OD (1.0 mL) and the yield was determined by ^1H NMR because of the low-boiling point property of the product.

the application of Pd/C[Ph_2S] to the chemoselective hydrogenation of olefin and acetylene functionalities in the presence of benzyl ester and N-Cbz protecting groups (entries 10–17). No hydrogenolysis of either the benzyl ester or N-Cbz protecting groups was observed during the smooth hydrogenation of olefin or acetylene moieties.[20]

While nitro groups are easily reduced to amines under the Pd/C-catalyzed hydrogenation conditions,[2a] the addition of Ph_2S to the reaction led to an incomplete hydrogenation and produced a complex mixture,[12] because hydroxylamine-accumulation followed by dimerization probably took place.[6,7,21] On the other hand, Pd/C[Ph_2S] was able to be applied to the hydrogenation of the nitro groups without any side reaction. The desired amine was obtained in a nearly quantitative yield as the sole product (entries 18–21) with the coexisting aromatic carbonyl (en-

Table 2. Reuse test of Pd/C[Ph_2S].



Run	Ratio of **1**:**2**:**3**	Yield of **2**[a]	Yield of Recovered Pd/C-[Ph_2S]
1	0:100:0	100	99
2	0:100:0	92	98
3	0:100:0	97	97
4	0:100:0	99	100
5	0:100:0	99	100

[a] Isolated yield.

tries 18 and 21), aromatic chloride (entry 19) and benzyl ester (entry 20) functionalities intact. The hydrogenation of the azide moiety using Pd/C[Ph_2S] was also investigated (entries 22–25) and they were efficiently hydrogenated to the corresponding amines regardless of the electronic circumstances of the aromatic ring.

We next investigated the reusability of Pd/C[Ph_2S] in the chemoselective hydrogenation of benzyl cinnamate. Pd/C[Ph_2S] could be reused at least until the fifth run without significant loss of the selectivity and yield (Table 2).[22]

In summary, we have developed a novel and isolable diphenyl sulfide-supported Pd/C catalyst (Pd/C-[Ph_2S]) possessing an excellent chemoselectivity toward hydrogenation; olefin, acetylene, nitro, and azide functionalities were smoothly hydrogenated, while aromatic carbonyl and halide, benzyl ester and N-Cbz functionalities were not. Such an efficient expression of the chemoselectivity has its roots in the catalyst properties based upon the reasonable and partial interaction with Ph_2S on the active sites of the Pd surface (Pd–S bonding). These findings reinforce the versatility of such reducible functionalities in synthetic chemistry, and the Pd/C[Ph_2S] catalyst has been recognized as a chemoselective and convenient catalyst for hydrogenation.

Experimental Section

Preparation of Pd/C[Ph_2S]

A suspension of 532 mg of 10% Pd/C and Ph_2S (166 μL, 2.00 equiv. *vs.* Pd metal of Pd/C) in MeOH (5 mL) was stirred for 5 days at room temperature under an argon atmosphere, and then the resulting solid was collected on filter paper, washed successively with methanol (10 mL × 2) and ether (10 mL × 2), and then dried under reduced pressure for 24 h to give Pd/C[Ph_2S]. The Pd/C[Ph_2S] could be stored in a regular reagent bottle at room temperature without any special handling and alternation of the catalyst activity.

General Procedure for the Chemoselective Hydrogenation using Pd/C[Ph_2S]

A substrate (0.50 mmol), Pd/C[Ph_2S] (10 wt% of the substrate), and MeOH (1 mL) were added to a test tube containing a stir bar and sealed with a septum. After two vacuum/H_2 cycles to replace the air inside with hydrogen, the mixture was vigorously stirred at room temperature under ordinary hydrogen pressure (balloon) for 24 h. The reaction mixture was filtered using a membrane filter (Millipore, Millex®-LH, 0.45 mm) and the filtrate was concentrated under vacuum to provide the pure product without further purification.

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