



Significant supplier-dependent disparity in catalyst activity of commercial Pd/C toward the cleavage of triethylsilyl ether

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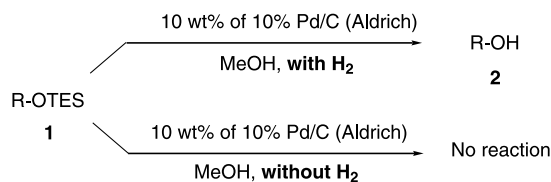
Abstract—Pd/C catalysts exhibit remarkable supplier-dependent difference in catalyst activity and property. Some commercial Pd/C catalysts are quite acidic. Although a TES ether cleavage reaction using 10% Pd/C in the absence of hydrogen was quite recently published, we could conclude it was only an acid, released from the catalyst, catalyzed solvolysis, and hydrogen is essential for the actual 10% Pd/C-catalyzed cleavage of a TES ether.

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Pd/C has been considered as one of the most universally applicable catalysts for hydrogenation.¹ However, to the best of our knowledge, although there have been some reports suggesting several distinctive features among Pd/C catalysts prepared by different methods¹ or purchased from different suppliers,² there have been no examples of the conflicting reports in the literature concerning this subject. Here we would like to introduce such discrepant papers, including ours, and to report on the outcome of the verification of such. We also caution that catalyst activity and properties of Pd/C differ greatly depending on the supplier. Because the acidity of some commercial Pd/C catalysts is quite high, particular attention should be given to choose and use them.

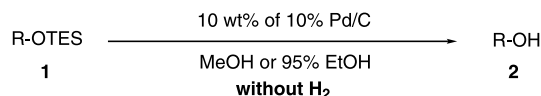
Most recently, we have reported³ a remarkable solvent effect toward the Pd/C-catalyzed cleavage of TES and TBDMS ethers, and it was applied to the development of a chemoselective hydrogenation method for other reducible functionalities distinguished from the TES and TBDMS protective groups of a hydroxyl group by the employment of MeCN or EtOAc as a solvent. While, particularly, TES ethers can be easily cleaved under mild hydrogenation conditions using 10 wt% (versus substrate) of 10% Pd/C (Aldrich product number 20,569-9) in MeOH at room temperature **under an ambient hydrogen atmosphere**, the desilylation **did not occur in the absence of hydrogen** (Scheme 1).

On the other hand, Rotulo-Sims and Prunet published⁴ during the review of our manuscript,³ a simple palla-



Scheme 1.

dium-catalyzed cleavage method of TES ethers. In contrast to our results, their method allows easy removal of alkyl TES ethers using 10 wt% of 10% Pd/C⁵ in MeOH or 95% EtOH as a solvent **without hydrogen conditions** even under an argon atmosphere (Scheme 2).



Scheme 2.

Prompted by the great discrepancy between the two papers, we pursued the reaction in further detail. From their results it occurred to us that certain distinctions of the property of various commercial 10% Pd/C catalysts might have caused the serious conflicting results. Actually, the reaction of 1-triethylsiloxydecane (**1a**) in the presence of 10 wt% of 10% Pd/C purchased from various suppliers in MeOH without hydrogen at room temperature for 24 h gave scattered results (Table 1). Complete cleavage of the TES protective group, as well as Prunet's report,⁴ took place in 1 h when 10% Pd/C (Merck or ACROS) was used in 10 wt% of the sub-

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Table 1. Supplier-dependent 10% Pd/C catalyst activity toward the cleavage of the TES ether **1a**

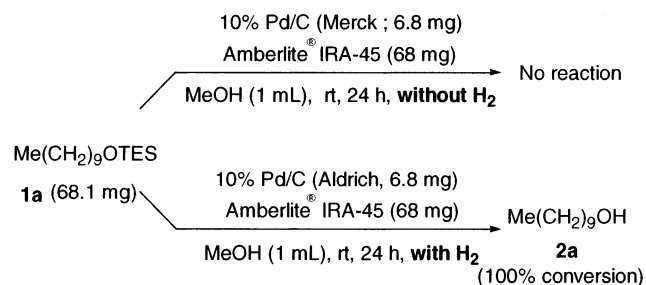
$\text{Me}(\text{CH}_2)_9\text{OTES} \xrightarrow[\text{MeOH, 24 h, rt, without H}_2]{10\% \text{ Pd/C (6.8 mg)}} \text{Me}(\text{CH}_2)_9\text{OH}$ <p>1a (68.1 mg) 2a</p>		
Entry	10% Pd/C ^a	1a:2a
1	Aldrich (20,569-9)	100:0 ^b
2	Wako (163-15272)	87:13
3	N. E. Chemcat (dry)	78:22
4	Nacalai (25928-84)	75:25
5	Kishida (400-59095)	59:41
6	ACROS (19503-0100)	0:100 ^c
7	Merck (807104-0010)	0:100 ^d

^a Supplier's product number is indicated in parentheses.^b The reproducibility of the data was confirmed in experiments using different lots of the Pd/C (Lot. AI 05401JS and Lot. KA 13921CA).^c The reaction was completed in approximately 1 h.^d The reaction was completed within 1 h.

strate **1a**, respectively (entries 6 and 7). 10% Pd/C catalysts from Wako, N. E. Chemcat, Nakarai and Kishida (entries 2–5) were less effective in promoting the TES cleavage. Needless to say, the cleavage of the TES protective group of **1a** did not proceed upon employment of 10% Pd/C (Aldrich) while smooth cleavage was observed under a hydrogen atmosphere.

In view of these undesirable results, we believed that the cleavage reaction of TES ethers with 10% Pd/C without hydrogen conditions was promoted by the contaminated acid in the Pd/C catalysts although Prunet asserted aggressively that the cleavage was a palladium-catalyzed reaction.⁴ To explore the influence of the contaminated acid during the production process of the Pd/C, a basic gel-type resin, Amberlite® IRA-45, as an acid scavenger was added into the reaction mixture using 10% Pd/C (Merck). As consequences of the reaction, no desilylation occurred at all even after 24 h⁶ while no depression of the cleavage of TES ethers using 10% Pd/C (Aldrich) under a hydrogen atmosphere was observed in the presence of Amberlite® IRA-45 (Scheme 3).

Further, the acid-catalyzed methanolysis of **1a** (0.25 mmol) in the presence of a non-stoichiometric amount

**Scheme 3.**

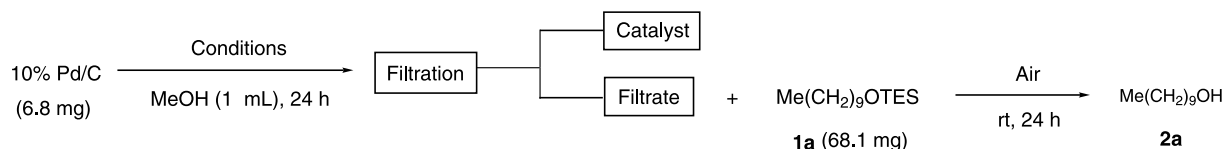
(0.014 mmol) of HCl resulted in 87% loss of the TES protective group of **1a** within 1 h without hydrogen at room temperature (Table 2, entry 1). We then investigated whether the TES cleavage reaction in the absence of hydrogen conditions⁴ is certainly a palladium-catalyzed (assisted) reaction or only an acid-catalyzed solvolysis. The addition of Aldrich's 10% Pd/C, having no TES-cleaving tendency under neutral non-hydrogen conditions, to above acid catalyzed reaction conditions was examined (entry 2). The cleavage of the TES ether of **1a** was slightly enhanced (98% loss) although the addition of only activated charcoal (Norit® SX-3) or Pd black resulted no acceleration of the cleavage (entries 3 or 4). Next, 10% Pd/C (Merck, 6.8 mg) in MeOH (1.0 mL) was stirred at room temperature under several conditions for 24 h and then the catalyst was filtered off using a membrane filter (Millipore, Millex®-L9, 0.20 μm). The TES ether (**1a**, 68.1 mg, 0.25 mmol) was stirred in the resulting filtrate under an air atmosphere at room temperature for 24 h. Table 3 summarizes the effect of various catalyst pretreatments and reaction conditions on the reaction rate. After stirring the suspension of 10% Pd/C (Merck) for 24 h, partial cleavage of the TES group of **1a** was observed even in the filtrate (entry 1). When the suspension of 10% Pd/C in MeOH was sonicated or stirred under an H₂ atmosphere before filtration, enhanced cleavage of the TES group took place in 24 h (entries 3 and 5), although the addition of Amberlite® IRA-45 (6.8 mg) into the suspension perfectly suppressed the cleavage (entries 2, 4 and 6). On the other hand, no cleavage was identified under identical reaction conditions when Aldrich's Pd/C was used instead of Merck's Pd/C (entries 7–9).

Pd/C catalysts are usually prepared by the reduction of PdCl₂ in the presence of heavy metal-free activated charcoal in concentrated hydrochloric acid.¹ Since the acidity of the suspension of 10% Pd/C is enhanced under a hydrogen atmosphere, the retained acids may be driven away from the fine pores of the charcoal by the hydrogen molecule⁷ and/or residual PdCl₂ by the incomplete reduction during the preparation process maybe reduced by hydrogen.^{2,8} From these results it is obviously concluded the TES cleavage reaction in the absence of hydrogen conditions⁴ is substantially acid-catalyzed solvolysis because the TES cleavage reaction progresses even in the 0.05% HCl–MeOH solution

Table 2. Influence of additives toward the acid catalyzed methanolysis of the TES ether **1a**

$\text{Me}(\text{CH}_2)_9\text{OTES} \xrightarrow[\text{rt, for 1 h without H}_2]{\text{Additives 0.05\% HCl-MeOH (1 mL, 0.014 mmol)}} \text{Me}(\text{CH}_2)_9\text{OH}$ <p>1a (68.1 mg, 0.25 mmol) 2a</p>		
Entry	Additives	1a:2a
1	None	13:87
2	10% Pd/C (Aldrich, 6.8 mg)	2:98
3	Norit® SX3 (6.8 mg)	22:78
4	Pd black (Kishida, 0.7 mg)	37:63

Table 3. Cleavage of the TES ether **1a** in the filtrate



Entry	10% Pd/C	Conditions	1a:2a
1	Merck	Air	74:26
2	Merck	Air+Amberlite® IRA-45	100:0
3	Merck	Sonication	67:33 ^a
4	Merck	Sonication+Amberlite® IRA-45	100:0
5	Merck	H ₂ (balloon)	23:77 ^a
6	Merck	H ₂ (balloon)+Amberlite® IRA-45	100:0
7	Aldrich	Air	100:0
8	Aldrich	Sonication	100:0
9	Aldrich	H ₂ (balloon)	100:0

^a Average of 2 times.

(Table 2, entry 1) and the Pd/C-free filtrate (Table 3, entries 1, 3, 5).

Recently, we reported the smooth reduction of Pd(OAc)₂ to zero valent palladium by MeOH as a reductant at room temperature.⁸ Although Rotulo-Sims and Prunet also reported in their paper⁴ the TES cleavage reaction in the absence of hydrogen conditions could be greatly enhanced in MeOH by the use of PdCl₂ instead of 10% Pd/C, PdCl₂ was presumably reduced to Pd(0) by MeOH and a very small amount of hydrogen chloride should be generated during the short reaction period.

In addition, our attention was directed to gaining more precise insight into the acidity of Pd/C catalysts. Thus, we determined the pH of the aqueous suspension after stirring for 24 h (Table 4). As can be seen, the suspension of 10% Pd/C catalysts purchased from Merck and ACROS having a high TES-cleaving tendency indicate a quite acidic property (entries 1, 2, 4 and 5). Surprisingly, the suspension of Merck's Pd/C recorded pH <3 under the a H₂ atmosphere (entry 4)⁷ while Aldrich's Pd/C indicates a rather slightly basic to neutral range (entries 3 and 6), compared with the pH value of ion-exchanged water (ca. 6.0, entry 7).^{9,10}

Since the unexpected loss of other acidic-sensitive protective groups from the mother molecule would cause extensive damage to a multi-step synthetic process, the acid-catalyzed solvolysis of THP ether (**3**) was also examined with 10 wt% of 10% Pd/C at room temperature in MeOH. Although no cleavage of the THP ether (**3**) occurred when Pd/C (Aldrich) was used as a catalyst (Table 5, entries 1 and 2),¹¹ partial deprotection (**3:4** = 56:44) of the THP ether (**3**) under atmospheric conditions (entry 3) and complete cleavage under H₂ conditions (entry 4) proceeded with Merck's 10% Pd/C. Consequently, the cleavage of TES ethers using 10% Pd/C under no hydrogen conditions is not a neutral reaction and restricted the use of acid-sensitive functionalities.

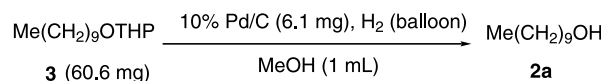
Table 4. Comparison of the acidity of commercial 10% Pd/C

10% Pd/C (1.0 g)		Conditions Ion-exchanged H ₂ O (10 mL) rt for 24 h	pH measurement
Entry	10% Pd/C	Conditions	pH ^a
1	Merck	Air	4.82 (23.4°C) 4.79 (24.2°C)
2	ACROS	Air	5.75 (24.8°C) 5.82 (24.9°C)
3	Aldrich	Air	6.28 (24.6°C) 6.34 (24.5°C)
4	Merck	H ₂ (balloon)	2.96 (26.5°C) 2.88 (26.1°C)
5	ACROS	H ₂ (balloon)	3.34 (25.0°C) 3.38 (24.6°C)
6	Aldrich	H ₂ (balloon)	5.91 (26.5°C) 5.98 (26.2°C)
7	pH of ion-exchanged H ₂ O ^b		5.92 (23.5°C) 5.99 (23.5°C)

^a pH was determined with Horiba D-21 pH meter.

^b Ion-exchanged H₂O indicates slightly acidic pH by the dissolved atmospheric CO₂.

Table 5. Cleavage of the THP ether in the presence of 10% Pd/C



Entry	10% Pd/C	H ₂ (balloon)	3:2a
1	Aldrich	None	100:0
2	Aldrich	○	100:0
3	Merck	None	56:44
4	Merck	○	0:100

In conclusion, we have clearly demonstrated the unreliability of the palladium-catalyzed cleavage of TES ethers in the absence of hydrogen conditions.⁴ The cleavage should be interpreted as an acid-catalyzed solvolysis. This methodology will be an attractive tool for the organic chemist if the supplier of Pd/C is specified and the reproducibility of the data is indicated using some different lots of the Pd/C. Furthermore, we were also able to demonstrate Pd/C catalysts exhibit remarkable supplier-dependent difference in the property and quality. When a Pd/C catalyst is used in an article, the name of the supplier and the product number of the catalyst must be clarified. Finally, it is noteworthy that hydrogen is an obligatory condition for the real palladium-catalyzed cleavage of silyl ethers in MeOH and that 10% Pd/C of Aldrich (20,569-9) is a quite safe and nearly neutral catalyst within our investigation. According to all of the results indicated in this paper, the 10% Pd/C (Aldrich)-catalyzed TES cleavage mechanism under hydrogen conditions³ can involve a direct hydrogenolysis of the silyl group or a true palladium-catalyzed methanolysis by the 10% Pd/C activated by hydrogen.

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- Supplier of the 10% Pd/C was not indicated in their paper.⁴
- The addition of 68 mg of Amberlite® IRA-45 as an acid scavenger into the reaction mixture caused no cleavage of the TES ether (**1a**), even after 24 h.
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- The palladium content of the commercial 10% Pd/C was determined by the inductively-coupled plasma (ICP) spectrometry. As shown in Table 6, some scatter of the Pd content were observed.

Table 6. The palladium content of the commercial 10% Pd/C

Entry	10% Pd/C ^a	Pd content (%)
1	Merck (807104-0010, Lot: S2328 4835)	8.7
2	ACROS (19503-0100, Lot: A012028901)	8.5
3	Aldrich (20,569-9, Lot: KA 13921CA)	9.2

^a Supplier's product and Lot. numbers are indicated in parentheses.

- A milky precipitate was formed by addition of one drop of 0.1 mol/L silver nitrate (AgNO₃) solution to the filtrate of the pH-determined suspension (ca. 2 mL) in Table 4. An amount of the precipitate was increased with the drop in pH. Consequently, the causes of the high acidity of the 10% Pd/C purchased from Merck or ACROS are contamination of HCl and PdCl₂.
- Kaisalo and Hase previously reported² a cleavage reaction of the THP protective group under Pd/C-catalyzed hydrogenation conditions using an equal amount to the substrate of 10% Pd/C (Aldrich) in EtOH. In contrast to their report, no reproducibility of their results was indicated in our study using an equal amount to the substrate of 10% Pd/C (Aldrich product number 20,569-9). Since two kinds of dry 10% Pd/C (20,569-9 and 52,088-8, Engelhard code C3645) is inserted in an Aldrich catalog, it is contemplated that the different kind of 10% Pd/C (52,088-8) was used for their reaction [The easy cleavage of THP ether using 10% Pd/C (Aldrich product number 52,088-8) was confirmed in our laboratory].