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Unexpected deprotection of silyl and THP ethers induced by serious disparity in the quality of Pd/C catalysts and elucidation of the mechanism

Takashi Ikawa, Hironao Sajiki* and Kosaku Hirota*

*Laboratory of Medicinal Chemistry, Gifu Pharmaceutical University, 5-6-1 Mitahora-higashi, Gifu 502-8585, Japan*

Abstract—Commercial Pd/C catalysts show different catalytic activity toward the deprotection of silyl and THP ethers. The Pd/C purchased from Merck and ACROS exhibits marked tendency to cleave these protective groups unexpectedly without hydrogen conditions although Aldrich's Pd/C (20,569-9) is inactive in the absence of hydrogen. It was proved that the Pd/C disparity toward the deprotection of TES and THP ethers results from residual acids and/or palladium chloride in the production process of Pd/Cs. Although a TES ether cleavage reaction in the absence of hydrogen and a THP ether cleavage reaction in the presence of hydrogen using 10% Pd/C were recently published, we could conclude they were only an acid-catalyzed solvolysis, the acid being released from the catalyst. Hydrogen is essential for the actual 10% Pd/C-catalyzed cleavage of TES ethers and THP ethers which must be stable under the true Pd/C-catalyzed hydrogenation conditions.
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1. Introduction

Silyl and THP (tetrahydropyranyl) ethers are extensively used protective groups for alcohols in synthetic chemistry because of its low cost, efficiency of preparation, stability under the intended reaction conditions and easy and selective removal.[1] A variety of methods for the selective deprotection of their protective groups have been developed including treatment with fluoride ion,[1] acid,[1] hydride[2,3] and palladium catalyst.[4] As a rule, protective groups must be stable under the intended reaction conditions as the unexpected removal of protective groups would cause serious damage to a synthetic process. On the other hand, catalytic hydrogenation is one of the most useful and widely applicable methods for the reduction of chemical substances, and has been applied in numerous synthetic processes in laboratories and industries. Hydrogenation using Pd/C as catalyst has many advantages such as stability of the catalyst, ease of removal from the reaction mixture, a wide range of applicable reaction conditions and high catalytic activity.[5] Although many preparative methods of Pd/C catalysts have been reported,[5] there have been some reports suggesting several distinctive features among Pd/C catalysts prepared by different methods[5] or purchased from different suppliers[6] to date.

Recently, we have reported TBDMS (*tert*-butyldimethylsilyl) and TES (triethylsilyl) ethers are frequently cleaved under hydrogenation conditions using 10% Pd/C (Aldrich product number 20,569-9) in MeOH at room temperature under hydrogen atmosphere (balloon),[7] although these silyl ethers were entirely intact without hydrogen atmosphere (under air or Ar) (Scheme 1).[7]
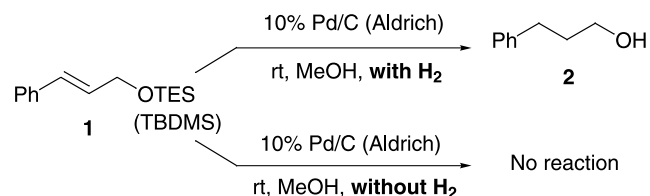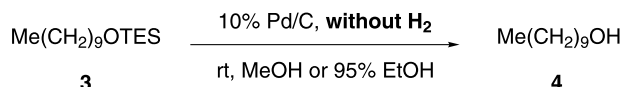

Scheme 1.

In contrast, Rotulo-Sims and Prunet have reported, during the review of our manuscript,[7c] a simple deprotection method of TES ether using 10% Pd/C in MeOH or 95% EtOH at room temperature in the absence of hydrogen atmosphere (Scheme 2).[8] Their data are apparently in conflict with our conclusion. In a preliminary communication,[9] we have suggested the cleavage of TES ethers in the absence of hydrogen conditions should be interpreted as an acid-catalyzed solvolysis. Herein, we provide a detailed discussion regarding the unreliability of the Pd/C-catalyzed cleavage of TES ethers in the absence of hydrogen conditions reported by Prunet et al. and further disclose

$$Me(CH_2)_9OTES \xrightarrow[\text{rt, MeOH or 95\% EtOH}]{\text{10\% Pd/C, \textbf{without H}}_2} Me(CH_2)_9OH$$
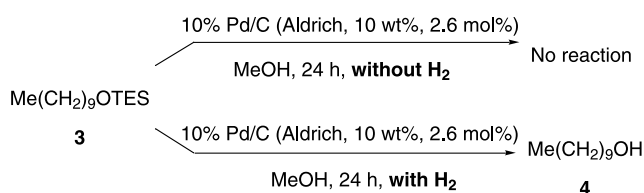
3 → **4**

Scheme 2.

Pd/C catalysts exhibit remarkable supplier-dependent difference in the property and quality (acidity).

2. Results and discussion

In our initial investigations, the reproducibility of Prunet's results using triethylsilyloxydecane (**3**) which was employed as a substrate in their paper[8] and 10% Pd/C (Aldrich) as a catalyst was reevaluated. The silyl group (**3**) has been recovered quantitatively in the absence of hydrogen even after 24 h, whereas quite ready cleavage of the TES ether under a hydrogen atmosphere (our conditions[7c]) was observed (Scheme 3). Consequently, reproducibility of Prunet's deprotection method[8] is quite poor. From these results it occurred to us that certain disparity in the property of various commercial 10% Pd/C catalysts might have caused the serious conflicting results. It is obvious that Prunet et al. have used 10% Pd/C catalyst obtained from a different supplier[10] from ours (Aldrich, 20,569-9).

$$Me(CH_2)_9OTES$$

3

$$\xrightarrow[\text{MeOH, 24 h, \textbf{without H}}_2]{\text{10\% Pd/C (Aldrich, 10 wt\%, 2.6 mol\%)}} \text{No reaction}$$

$$\xrightarrow[\text{MeOH, 24 h, \textbf{with H}}_2]{\text{10\% Pd/C (Aldrich, 10 wt\%, 2.6 mol\%)}} Me(CH_2)_9OH \quad \textbf{4}$$

Scheme 3.

Next, we investigated catalyst activity of various commercial 10% Pd/C toward the deprotection of TES ether (**3**) in the absence of hydrogen (Table 1). Most commercial Pd/C, except for Aldrich's catalyst (entry 2), showed catalyst

Table 1. Cleavage of the TES ether (**3**) using 10% Pd/C purchased from various suppliers in the absence of hydrogen

$$Me(CH_2)_9OTES \xrightarrow[\textbf{without H}_2\text{, MeOH, rt, 24 h}]{\text{10\% Pd/C (10 wt\%, 2.6 mol\%)}} Me(CH_2)_9OH$$

3 → **4**

Entry	10% Pd/C[a]	3:4[b]
1	None	100:0
2	Aldrich (20,569-9)	100:0[c]
3	WAKO (163-15272)	87:13
4	N. E. ChemCat (dry)	78:22
5	Nakalai (25928-84)	75:25
6	Kishida (400-59095)	59:41
7	Engelhard C3645[d]	40:60
8	ACROS (19503-0100)	0:100[e]
9	Merck (807104-0010)	0:100[f]

[a] Supplier's product number is indicated in parentheses.
[b] Determined by ^{1}H NMR.
[c] The reproducibility of the data was confirmed in experiments using different lots of the Pd/C (Lot. AI 05401JS and Lot. KA 13921CA).
[d] This catalyst was purchased from Aldrich (Aldrich product number 52,088-8).
[e] The reaction was completed in approximately 1 h.
[f] The reaction was completed within 1 h.

activity at room temperature toward the cleavage of TES ether in varying degrees, albeit without hydrogen (entries 3–9). Especially, 10% Pd/C purchased from Merck and ACROS cleaved the TES ether (**3**) completely within an hour as well as in Prunet's report[8] (entries 8 and 9).

Our attention next turned to the mechanism of the deprotection of the TES group of **3** using 10% Pd/C as a catalyst dispensing with hydrogen. 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 strongly that the cleavage was Pd-catalyzed reaction.[8] In general, palladium chloride in concentrated hydrochloric acid solution is used for the preparation of Pd/C catalysts as a starting material. The palladium chloride is held by adsorption on heavy metal-free activated charcoal and reduced using a suitable reductant.[5] So it may be contaminated by a trace amount of retained hydrochloric acid, and/or residual $PdCl_2$ by the incomplete reduction during the production process even after being washed repeatedly with distilled water.[5] In order to elucidate the deprotection mechanism we examined the cleavage reaction of the TES ether (**3**) in the presence of a basic gel-type resin, Amberlite®IRA-45, as an acid scavenger (Table 2). 10% Pd/C (Merck or Aldrich) was stirred with Amberlite®IRA-45 in MeOH under air for 10 min and then the reaction mixture was stirred with the TES ether (**3**) under air or hydrogen atmosphere. Pre-treatment with Amberlite®IRA-45 under air conditions resulted in no cleavage of TES ether (**3**) without hydrogen conditions with either catalyst (Merck and Aldrich, entries 1 and 3) while the TES ether (**3**) was completely cleaved under hydrogen conditions without any depression of the catalyst activities toward the cleavage of TES ethers even with coexisting Amberlite®IRA-45 (entries 2 and 4).

Table 2. Cleavage of the TES ether (**3**) in the presence of Amberlite®IRA-45

10% Pd/C (6.8 mg, 2.6 mol%) + Amberlite®IRA-45 (68 mg) $\xrightarrow[\text{MeOH, 10 min}]{\text{Under Air}}$ | Conditions, 24 h, $Me(CH_2)_9OTES$ **3** (68.1 mg) → $Me(CH_2)_9OH$ **4**

Entry	10% Pd/C	Conditions	3:4
1	Merck	Air	100:0
2	Merck	H_2	0:100
3	Aldrich	Air	100:0
4	Aldrich	H_2	0:100

We then investigated whether the TES cleavage reaction in the absence of hydrogen conditions[8] is certainly a palladium-catalyzed (mediated) reaction or only an acid-catalyzed solvolysis (Table 3). 10% Pd/C (Merck) in MeOH was stirred under various conditions for 24 h and then the catalyst was removed by filtration using a membrane filter (Millipore, Millex®-LG, 0.20 μm). TES ether (**3**) was stirred in the resulting filtrate for 24 h (entries 1–6). In the filtrate stirred with 10% Pd/C (Merck) under air atmosphere, 59% cleavage of the TES protective group

Table 3. Cleavage of the TES ether (**3**) in the filtrate
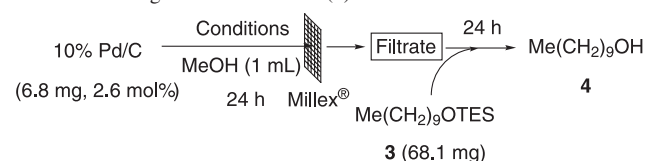
| Entry	10% Pd/C	Conditions	3:4[a]
1	Merck	Air	59:41[b]
2	Merck	Air+Amberlite®IRA-45	100:0
3	Merck	Sonication	50:50[c]
4	Merck	Sonication+Amberlite®IRA-45	100:0
5	Merck	H_2	37:63[c]
6	Merck	H_2+Amberlite®IRA-45	100:0
7	Aldrich	Air	100:0
8	Aldrich	Sonication	100:0
9	Aldrich	H_2	100:0

[a] Determined by ^1H NMR.
[b] Average of 6 times.
[c] Average of 4 times.

was observed on the average of 6 experiments (entry 1). The deprotection was slightly enhanced by the pre-treatment of 10% Pd/C (Merck) under sonication or hydrogen conditions (entries 3 and 5). Since the cleavage rates of the filtrates were enhanced under sonication or hydrogen conditions, the retained acids may be driven away from the fine pores of the charcoal[11] and/or residual $PdCl_2$ by the incomplete reduction during the production process may be reduced by hydrogen.[6] This deprotection reaction was depressed completely by the addition of Amberlite®IRA-45 into the pretreatment suspension of Pd/C in MeOH (entries 2, 4 and 6). On the other hand, TES was not cleaved at all in the filtrate stirred with 10% Pd/C (Aldrich) even under sonication and hydrogen conditions (entries 7–9). These results strongly suggest that the cleavage of TES ether using Merck's 10% Pd/C without hydrogen conditions[8] is only an acid-catalyzed methanolysis.

Further, the acid-catalyzed methanolysis of **3** in the presence of non-stoichiometric hydrochloric acid (0.06 equiv. against the substrate) resulted in 87% loss of the TES protective group of **3** within 1 h without hydrogen (Table 4, entry 1). The addition of Aldrich's 10% Pd/C which possesses no TES-cleaving activity under neutral non-hydrogen conditions, to the above acid-catalyzed reaction conditions was examined (entry 2). The cleavage of the TES ether was slightly enhanced (98%) although the addition of activated carbon (Norit®SX3) or Pd-black resulted in no acceleration of the cleavage (entries 3 and 4).

Table 4. Acid-catalyzed cleavage of the TES ether (**3**)
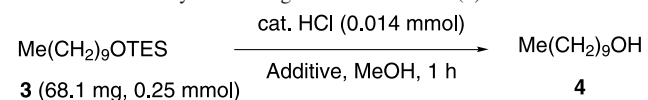
Entry	Additive	3:4[a]
1	None	13:87
2	10% Pd/C (Aldrich, 6.8 mg, 2.6 mol%)	2:98
3	Norit®SX3 (6.8 mg)	22:78
4	Pd-black (Kishida, 0.7 mg, 2.6 mol%)	37:63

[a] Determined by ^1H NMR.

In addition, we determined the pH of aqueous suspension of commercial 10% Pd/C catalysts after stirring at room temperature for 24 h using pH meter (Table 5). The suspension of 10% Pd/C catalysts purchased from Merck and ACROS, having a quite high TES-cleaving tendency, indicates a quite acidic property (entries 6–10). Under sonication conditions, the acidity of the suspension was slightly enhanced (compare entries 8 and 9) as well as an enhancement of TES cleavage activity in the filtrate (Table 3, entries 1 and 3). Surprisingly, the suspension of Merck's Pd/C recorded pH<3 under the H_2 atmosphere (entry 10) while Aldrich's Pd/C indicates a rather slightly basic to neutral range (entries 1–3), compared with the pH value of ion-exchanged water (ca. 6.0, entry 11).[12,13] These results also strongly indicate Merck's Pd/C includes significant amounts of residual $PdCl_2$ together with acids. Recently, we reported the smooth reduction of $Pd(OAc)_2$ to zero valent palladium by MeOH as a reductant at room temperature.[14] Consequently, the residual $PdCl_2$ in Merck's Pd/C should be smoothly reduced during the TES cleavage reaction in MeOH or 95% EtOH without hydrogen conditions (Scheme 2)[8] and a certain amount of hydrogen chloride should be generated.[15] Acidity of the slurry of commercial 10% Pd/Cs increases in the following order, Aldrich<Kishida<ACROS<Merck. These results are approximately parallel to the order of the catalyst activity of 10% Pd/Cs toward the cleavage of TES ether (**3**) without hydrogen conditions (compare Tables 1 and 5).

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

Table 5. Comparison of acidity of commercial 10% Pd/C

Entry	10% Pd/C	Conditions	pH[a]	Temperature (°C)
1	Aldrich	Air	6.28	24.6
			6.34	24.5
2		Sonication	6.17	25.1
			6.19	25.1
3		H_2	5.91	26.5
			5.98	26.2
4	Kishida	Air	5.97	23.0
			6.00	23.0
5		H_2	5.38	23.3
			5.36	22.6
6	ACROS	Air	5.75	24.8
			5.82	24.8
7		H_2	3.34	25.0
			3.38	24.6
8	Merck	Air	4.82	24.3
			4.79	24.2
9		Sonication	4.67	25.1
			4.63	25.0
10		H_2	2.96	26.5
			2.88	26.1
11	Ion-exchanged H_2O[b]		5.92	23.5
			5.99	23.5

[a] The pH measurements were carried out on a Horiba D-21 pH meter.
[b] Ion-exchanged H_2O indicates slightly acidic pH by the dissolved atmospheric CO_2.

acid-catalyzed solvolysis of THP ether (**5**) was also examined with 10 wt% (2.3 mol%) of 10% Pd/C at room temperature in MeOH. Table 6 summarizes the stability of THP ether (**5**) in the presence of a commercial 10% Pd/C. Although no cleavage of the THP ether (**5**) occurred in the presence and absence of hydrogen conditions when Aldrich's Pd/C was used as a catalyst (Table 6, entries 1–4), partial deprotection (**5**:**4**=56:44) of the THP ether (**5**) under atmospheric air conditions (entry 9) and complete cleavage under hydrogen conditions (entry 10) occurred by the use of 10 wt% (2.3 mol%) of Merck's Pd/C. Without hydrogen Pd/C (Engelhard) has no cleaving activity (entries 5 and 7), whereas under hydrogenation conditions the THP ether (**5**) was cleaved (entries 6 and 8). Further, while no cleavage of the THP protective group of **5** occurred with Engelhard's 10% Pd/C (Engelhard code C3645) without hydrogen conditions (entries 5 and 7), the deprotection was observed under hydrogen atmosphere and the deprotection ratio was increased with increasing the amount of the catalyst (entries 6 and 8).

Table 6. Cleavage of the THP ether (**5**) in the presence of 10% Pd/C

Me(CH₂)₉OTHP → 10% Pd/C, Solvent, 24 h → Me(CH₂)₉OH

5 (60.8 mg)   **4**

Entry	10% Pd/C	Loading wt% (mol%)	Solvent (mL)	Condition	5:4[a]
1	Aldrich[b]	10 (2.3)	MeOH (1 mL)	Air	100:0
2		10 (2.3)	MeOH (1 mL)	H₂	100:0
3		100 (23)	EtOH (10 mL)	Air	100:0
4		100 (23)	EtOH (10 mL)	H₂	100:0
5	Engelhard[c]	10 (2.3)	MeOH (1 mL)	Air	100:0
6		10 (2.3)	MeOH (1 mL)	H₂	58:42
7		100 (23)	EtOH (10 mL)	Air	100:0
8		100 (23)	EtOH (10 mL)	H₂	0:100
9	Merck[d]	10 (2.3)	MeOH (1 mL)	Air	56:44
10		10 (2.3)	MeOH (1 mL)	H₂	0:100

[a] Determined by ¹H NMR.
[b] Aldrich product number; 20,569-9.
[c] This catalyst was purchased from Aldrich (Aldrich product number; 52,088-8, Engelhard code C3645).
[d] Merck product number; 807104-0010.

To confirm whether the deprotection of the THP ether (**5**) with Merck or Engelhard's 10% Pd/C is due to the contaminated acids or not, we examined the cleavage of the THP ether (**5**) in the filtrate after pre-stirring of the suspension of 10% Pd/C catalyst in MeOH (Table 7). After stirring the suspension of 10% Pd/C (Merck or Engelhard) for 24 h, significant cleavage of the THP protective group of **5** was observed in the Pd/C-free filtrate (entries 2 and 4). In contrast, when the suspension of 10% Pd/C (Merck or Engelhard) was stirred in the presence of Amberlite®IRA-45, the cleavage was completely depressed (entries 3 and 5). Needless to say, THP-cleavage did not proceed in the filtrate of the stirred suspension of Aldrich's Pd/C (entry 1).

Kaisalo and Hase previously reported[6] the cleavage of the THP protective group of **6** under hydrogenation conditions using an equal amount (100 wt%) to the substrate of Aldrich's Pd/C-catalyzed in EtOH (Scheme 4). In contrast to their report, no reproducibility of their results was

**Table 7**. Cleavage of the THP ether (**5**) in the filtrate
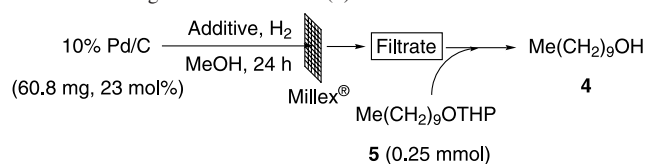
Entry	10% Pd/C	Additive	5:4[a]
1	Aldrich[b]	None	100:0
2	Engelhard[c]	None	25:75
3		Amberlite®IRA-45	100:0
4	Merck[d]	None	8:92
5		Amberlite®IRA-45	100:0

[a] Determined by ¹H NMR.
[b] Aldrich product number; 20,569-9.
[c] This catalyst was purchased from Aldrich (Aldrich product number; 52,088-8, Engelhard code C3645).
[d] Merck product number; 807104-0010.
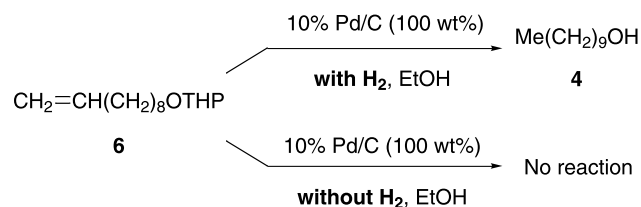
Scheme 4.

indicated in our study using 10% Pd/C (Aldrich product number 20,569-9) (Table 6, entry 4). Since two kinds of dry 10% Pd/C [Aldrich product numbers, 20,569-9 and 52,088-8 (Engelhard code C3645)] are inserted in an Aldrich catalog, it is contemplated that the different kinds of dry 10% Pd/C (52,088-8) described as 10% Pd/C (Engelhard) in this paper was used in their paper[6] (Table 6, entries 6 and 8). It is obvious that their cleavage of the THP protective group of **6** also is only an acid-catalyzed ethanolysis and THP protective groups must be stable under the true Pd/C-catalyzed hydrogenation conditions.

Finally, we investigated the stability of TIPS (triisopropyl-silyl) group under the hydrogenation conditions using acidic (Merck) and neutral (Aldrich) 10% Pd/C. The selective hydrogenation of the olefin functionality of 1-triisopropyl-silyloxy-3-phenyl-2-propene (**7**) was achieved with Aldrich's 10% Pd/C under ambient hydrogen pressure, although the deprotection of the TIPS protective group and the hydrogenation of the olefin proceeded simultaneously with acidic Merck's 10% Pd/C catalyst (Scheme 5). It should be noted that the TIPS protective group which is more stable than the TBDMS or the TES ethers is also frequently used as a protective group of hydroxyl groups in organic synthetic chemistry and it seems likely that the
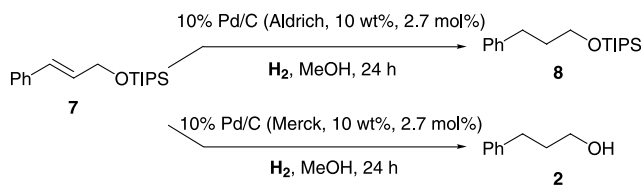
Scheme 5.

acidity of commercial Pd/C catalysts results in a variety of serious problems including unexpected deprotection of acid somewhat sensitive protective groups.

3. Conclusion

We have disclosed some commercial 10% Pd/C are quite acidic and exhibit marked tendency to cleave silyl and THP ethers unexpectedly without hydrogen conditions. It was clearly proved that the deprotection methods of TES ethers in the absence of hydrogen reported by Prunet et al.[8] and THP ethers in the presence of hydrogen reported by Kaisalo et al.[6] are not palladium-catalyzed reaction and only an acid, released from the catalysts, catalyzed solvolysis and hydrogen is absolutely essential for the real 10% Pd/C-catalyzed cleavage of TES (silyl) ethers. THP ethers must be stable under the true Pd/C-catalyzed hydrogenation conditions. Furthermore, we have also demonstrated commercial Pd/C catalysts exhibit remarkable supplier-dependent disparity in the property and quality. Since the unexpected loss of protective groups would cause serious damage to a synthetic process, especially in multi-step synthesis of complex natural products, therefore, 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 to avoid wasted efforts in the organic chemistry community. It is noteworthy that 10% Pd/C of Aldrich (20,569-9) is a quite safe, nearly neutral and useful hydrogenation catalyst. According to all of the results indicated in this paper, the 10% Pd/C (Aldrich)-catalyzed TES cleavage mechanism under hydrogen conditions[7c] can involve a direct hydrogenolysis of the silyl group or a true palladium-catalyzed methanolysis by the 10% Pd/C activated by hydrogen.

4. Experimental

4.1. General

^{1}H and ^{13}C NMR spectra were recorded on a JEOL EX 400 spectrometer ([1]H: 400 MHz, [13]C: 100 MHz). Chemical shifts (δ) are given in ppm relative to residual solvent or tetramethylsilane as an internal standard. Low and high-resolution mass spectra were taken on a JEOL JMS-SX 102 machine. The pH measurements were carried out on a Horiba D-21 pH meter that was calibrated before each set of measurements. Methylene chloride was distillated from CaH_2. Methanol for HPLC (Wako Pure Chemical Industries, Ltd.) was used without further purification. Ethanol, dehydrated (Wako Pure Chemical Industries, Ltd.) was used without purification. Amberlite®IRA-45 (basic gel-type resin) was used after washing with water and methanol. All reagents were commercially available and used without purification. All new compounds were further characterized by HRMS. Compounds known in the literature were characterized by comparison of their ^{1}H NMR data with the previously reported data.

4.1.1. Preparation of triethylsilyloxydecane (3).[16] To a solution of 1-decanol (4) (1.58 g, 10 mmol) in dichloromethane (20 mL) at room temperature was added triethylamine (1.7 mL, 12 mmol) and DMAP (224.3 mg, 2 mmol)

followed by triethylsilyl chloride (2.0 mL, 12 mmol). The mixture was stirred for 8 h at room temperature. Methanol (1 mL) was added to quench the excess amount of triethylsilyl chloride, and after 30 min a saturated aqueous NH_4Cl solution (20 mL) was added to the mixture. The aqueous layer was extracted with ether (20 mL×3), then the combined organic layer was washed with brine (20 mL), dried with anhydrous Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash column chromatography on silica gel elution with hexane to afford 2.61 g (96%) of triethylsilyloxydecane (3) as a colorless oil.

^{1}H NMR (CDCl₃): δ 3.59 (t, $J=6.8$ Hz, 2H), 1.55–1.51 (m, 2H), 1.28–1.26 (m, 14H), 0.96 (t, $J=8.1$ Hz, 9H), 0.88 (t, $J=6.8$ Hz, 3H), 0.60 (q, $J=7.8$ Hz, 6H). ^{13}C NMR (CDCL₃): δ 63.0, 32.9, 31.9, 29.6, 29.6, 29.5, 29.3, 25.8, 22.7, 14.1, 6.8, 4.4. MS (FAB, NBA) m/z 273 (M⁺+H, 18%), 271 (17), 243 (40). HRMS (FAB, NBA) calcd for $C_{16}H_{37}OSi$ (M⁺+H) 273.2614. Found 273.2610.

4.1.2. General procedure for cleavage of the TES ether (1) accompanying hydrogenation of the olefin using 10% Pd/C (Aldrich; 20,569-9) in the presence of hydrogen (Scheme 1).[7] After two vacuum/H₂ cycles to remove air from the reaction tube, a stirred mixture of the substrate (0.25 mmol), 10% Pd/C (Aldrich product number 20,569-9; 10 wt% of the substrate) in methanol (1 mL) was hydrogenated at ambient pressure (balloon) and temperature (ca. 20 °C) for 24 h. The reaction mixture was filtered through a membrane filter (Millipore, Millex®-LG, 0.20 µm), and the filtrate was concentrated in vacuo to afford 35 mg (100%) of 3-phenyl-1-propanol (2) as a colorless oil.

4.1.3. General procedure for cleavage of the TES ether (3) using 10% Pd/C purchased from various suppliers in the absence of hydrogen (Table 1). To a solution of triethylsilyloxydecane (3) (68.1 mg, 0.25 mmol) in methanol (1 mL) was added 10% Pd/C (6.8 mg, 10 wt% of the substrate) and then stirred at room temperature for 24 h. The solution was filtered through a membrane filter (Millipore, Millex®-LG, 0.20 µm), and MeOH was removed in vacuo. The ratio of the substrate (3) and 1-decanol (4) was confirmed by ^{1}H NMR of the crude mixture in CDCl₃.

4.1.4. General procedure for cleavage of the TES ether (3) in the presence of Amberlite®IRA-45 (Table 2). A suspension of 10% Pd/C (6.8 mg, 10 wt% of the substrate) and Amberlite®IRA-45 (68 mg) in methanol (1 mL) was stirred at room temperature for 10 min. After two vacuum/H₂ or Ar cycles to remove air from the reaction tube, triethylsilyloxydecane (3) was added to the mixture and then stirred at room temperature for 24 h. The reaction mixture was filtered through a membrane filter (Millipore, Millex®-LH, 0.45 µm) and the filtrate was concentrated in vacuo. The ratio of the substrate (3) and 1-decanol (4) was confirmed by ^{1}H NMR of the crude mixture in CDCl₃.

4.1.5. General procedure for cleavage of the TES ether (3) in the filtrate (Table 3, part 1, entries 1–4, 7 and 8). A suspension of 10% Pd/C (6.8 mg, 10 wt% of the substrate) [and Amberlite®IRA-45 (68 mg)] in methanol (1 mL) was stirred for 24 h (under sonication). The reaction mixture was filtered through a membrane filter (Millipore, Millex®-LG,

0.20 μm). Triethylsilyloxydecane (**3**) was added to the filtrate and then stirred at room temperature for 24 h. The reaction mixture was concentrated under reduced pressure. The ratio of the substrate (**3**) and 1-decanol (**4**) was confirmed by ^{1}H NMR of the crude mixture in CDCl$_3$.

4.1.6. General procedure for cleavage of the TES ether (3) in the filtrate (Table 3, part 2, entries 5, 6 and 9). After two vacuum/H$_2$ cycles to remove air from the reaction tube, [a suspension of the Amberlite®IRA-45 (68 mg) and] 10% Pd/C (6.8 mg, 10 wt% of the substrate) in methanol (1 mL) was stirred under hydrogen atmosphere at ambient pressure (balloon) and temperature (ca. 20 °C) for 24 h. The solution was filtered through a membrane filter (Millipore, Millex®-LG, 0.20 μm). Triethylsilyloxydecane (**3**) was added to the filtrate and then stirred under air at room temperature for 24 h. The solution was concentrated under reduced pressure. The ratio of the substrate (**3**) and 1-decanol (**4**) was confirmed by ^{1}H NMR of the crude mixture in CDCl$_3$.

4.1.7. General procedure for acid catalyzed cleavage of the TES ether (3) (Table 4). To a mixture of hydrogen chloride (10 μL of 5% HCl in MeOH, 0.014 mmol) with an additive indicated in Table 4 in methanol (1 mL) was added triethylsilyloxydecane (**3**) (68.1 mg, 0.25 mmol) and stirred at room temperature for 24 h. [The solution was filtered through a membrane filter (Millipore, Millex®-LG, 0.20 μm)] The solution (or filtrate) was concentrated under reduced pressure. The ratio of the substrate (**3**) and 1-decanol (**4**) was confirmed by ^{1}H NMR of the crude mixture in CDCl$_3$.

4.1.8. General procedure for the pH measurement of the suspension of commercial 10% Pd/C (Table 5). A suspension of 10% Pd/C (1.0 g) in 10 mL of methanol was stirred at room temperature under each condition for 24 h. The pH of the slurry was measured by Horiba D-21 pH meter that was calibrated before each set of measurements.

4.1.9. Preparation of 2-tetrahydropyranyl-1-decanyl ether (5).[17] To an ice-cold solution of 1-decanol (**4**) (1.58 g, 10 mmol) and dihydropyrane (3.7 mL, 40 mmol) in dry dichloromethane (10 mL) was added *p*-toluene-sulfonic acid monohydrate (19.0 mg, 0.1 mmol). The mixture was stirred at 0 °C for 10 min, the ice bath was removed, and the solution was stirred at room temperature for 1.5 h. The mixture was partitioned between ether (20 mL) and brine (20 mL). The organic layer was washed with saturated sodium carbonate solution (20 mL), water (40 mL) and brine (20 mL×2), dried with anhydrous Na$_2$SO$_4$, and evaporated in vacuo. The crude product was purified by flash column chromatography on silica gel elution with hexane/ether 20:1 to afford 2.30 g (95%) of 2-tetrahydropyranyl-1-decanyl ether (**5**) as a colorless oil.

^{1}H NMR (CDCl$_3$): δ 4.58 (t, *J*=3.4 Hz, 1H), 3.90–3.85 (m, 1H), 3.76–3.70 (m, 1H), 3.53–3.47 (m, 1H), 3.41–3.35 (m, 1H), 1.87–1.79 (m, 1H), 1.75–1.69 (m, 1H), 1.63–1.49 (m, 6H), 1.35–1.26 (m, 14H), 0.88 (t, *J*=6.8 Hz, 3H). ^{13}C NMR (CDCL$_3$): δ 98.8, 67.7, 62.3, 31.9, 30.8, 29.7, 29.6, 29.5, 29.3, 26.2, 25.5, 22.6, 19.7, 14.1. MS (FAB, NBA) *m/z* 243

(M$^+$+H, 40%), 241 (32), 238 (23). HRMS (FAB, NBA) Calcd for C$_{15}$H$_{31}$O$_2$ (M$^+$+H) 243.2317. Found 243.2324.

4.1.10. General procedure for cleavage of the THP ether (5) using commercial 10% Pd/C in the absence of hydrogen (Table 6, part 1, entries 1, 3, 5, 7 and 9). A mixture of the THP ether (**5**) (60.6 mg, 0.25 mmol) and 10% Pd/C (6.1 or 60.8 mg) in methanol (1 mL) or ethanol (10 mL) was stirred at room temperature for 24 h. The reaction mixture was filtered through a membrane filter (Millipore, Millex®-LG, 0.20 μm or -LH, 0.45 μm), and the solvent was removed in vacuo. The ratio of the substrate (**5**) and 1-decanol (**4**) was confirmed by ^{1}H NMR of the crude mixture in CDCl$_3$.

4.1.11. General procedure for cleavage of the THP ether (5) using 10% Pd/C in the presence of hydrogen (Table 6, part 2, entries 2, 4, 6, 8 and 10). After two vacuum/H$_2$ cycles to remove air from the reaction tube, a stirred mixture of the 2-tetrahydropyranyl-1-decanyl ether (**5**) (60.6 mg, 0.25 mmol) and 10% Pd/C (6.1 or 60.8 mg) in methanol (1 mL) or ethanol (10 mL) was hydrogenated at ambient pressure (balloon) and temperature (ca. 20 °C) for 24 h. The reaction mixture was filtered through a membrane filter (Millipore, Millex®-LG, 0.20 μm or -LH, 0.45 μm), and the filtrate was concentrated in vacuo. The ratio of the substrate (**5**) and 1-decanol (**4**) was confirmed by ^{1}H NMR of the crude mixture in CDCl$_3$.

4.1.12. General procedure for cleavage of the THP ether (5) in the filtrate (Table 7). After two vacuum/H$_2$ cycles to remove air from the reaction tube, a suspension of [the Amberlite®IRA-45 (61 mg) and] 10% Pd/C (60.8 mg, 100 wt% of the substrate) in methanol (1 mL) was stirred under hydrogen atmosphere at ambient pressure (balloon) and temperature (ca. 20 °C) for 24 h. The reaction mixture was filtered through a membrane filter (Millipore, Millex®-LH, 0.45 μm). 2-Tetrahydropyranyl-1-decanyl ether (**5**) was added to the filtrate and then stirred under air at room temperature for 24 h. The reaction mixture was concentrated under reduced pressure. The ratio of the substrate (**5**) and 1-decanol (**4**) was confirmed by ^{1}H NMR of the crude mixture in CDCl$_3$.

4.1.13. Preparation of 1-triisopropylsilyloxy-3-phenyl-2-propene (7).[18] To a solution of cinnamylalcohol (671 mg, 5 mmol) and imidazole (408 mg, 6 mmol) in dichloro-methane (20 mL) at room temperature was added triiso-propylsilyl chloride (1.16 g, 6 mmol). The mixture was stirred at room temperature for 24 h. Methanol (1 mL) was then added to quench the excess of triisopropylsilyl chloride, and after 30 min a saturated aqueous NH$_4$Cl solution (20 mL) was added. The aqueous layer was extracted with ether (20 mL×3) and the combined the organic layer was washed with brine (20 mL), dried with anhydrous Na$_2$SO$_4$, filtered and concentrated in vacuo. The crude product was purified by flash column chromatography on silica gel elution with hexane to afford 593 mg (41%) of 1-triisopropylsilyloxy-3-phenyl-2-propene (**7**) as a colorless oil.

^{1}H NMR (CDCl$_3$): δ 7.42–7.24 (m, 5H), 6.67 (d, *J*=15.6 Hz, 1H), 6.34 (dt, *J*=15.6, 4.9 Hz, 1H), 4.46 (dd,

J=4.9 Hz, 1.5 Hz, 2H), 1.21–1.12 (m, 3H and 18H). ^{13}C NMR (CDCl$_3$): δ 137.3, 129.4, 129.0, 128.5, 127.2, 126.4, 63.9, 18.0, 12.1. MS (EI) *m/z* 290.5 (M$^+$, 20%), 248 (21), 247 (100), 117 (47), 115 (15). HRMS (EI) calcd for C$_{18}$H$_{30}$OSi (M$^+$) 290.2066. Found 290.2057.

4.1.14. General procedure for investigation of the stability of the TIPS ether (7) (Scheme 5).

After two vacuum/H$_2$ cycles to remove air from the reaction tube, a stirred mixture of 1-triisopropylsilyloxy-3-phenyl-2-pro-pene (**7**) (72.6 mg, 0.25 mmol) and 10% Pd/C (Aldrich or Merck, 7.3 mg, 10 wt% of the substrate) in methanol (1 mL) was hydrogenated at ambient pressure (balloon) and temperature (ca. 20 °C) for 24 h. The reaction mixture was filtered through a membrane filter (Millipore, Millex®-LG, 0.20 µm) and the filtrate was concentrated in vacuo. The quantitative conversion of the substrate (**7**) into 1-triiso-propylsilyloxy-3-phenyl-2-propane (**8**) or 3-phenylpropanol (**2**) was confirmed by ^{1}H NMR in CDCl$_3$. 3-Phenylpropanol (**2**) agreed with the analytical data of commercially available sample.

4.1.14.1. 1-Triisopropylsilyloxy-3-phenylpropane (8).

93% Yield as a colorless oil. ^{1}H NMR (CDCl$_3$): δ 7.29–7.17 (m, 5H), 3.71 (t, J=6.1 Hz, 2H), 2.71 (t, J=7.8 Hz, 2H), 1.89–1.82 (m, 2H), 1.12–1.04 (m, 3H and 18H). ^{13}C NMR (CDCL$_3$): δ 142.4, 128.5, 128.2, 125.6, 62.6, 34.7, 32.1, 18.0, 12.0, 11.8. MS (EI) *m/z* 249 (M$^+$−C$_3$H$_7$, 100%). HRMS (EI) calcd for C$_{15}$H$_{25}$OSi (M$^+$−C$_3$H$_7$) 249.1675. Found 249.1667.

References and notes

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12. The palladium content of the commercial 10% Pd/C was determined by the inductively-coupled plasma (ICP) spectrometry. As shown in the following Table, some scattering of the Pd content was observed

Entry	10% Pd/C[a]	Pd content (%)
1	Merck (807104-0010, Lot: S23284 835)	8.7
2	ACROS (19503-0100, Lot: A012028901)	8.5
3	Kishida (400-59095, Lot: F26175K)	8.2
4	Aldrich (20,569-9, Lot: KA 13921CA)	9.2

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

13. A milky precipitate was formed by addition of one drop of 0.1 mol/L silver nitrate (AgNO$_3$) solution to the filtrate of the pH-determined suspension (ca. 2 mL) in Table 5. The amount of the precipitate was increased with the drop in pH. Consequently, the cause of the high acidity of the 10% Pd/C purchased from Merck or ACROS is contamination of HCl and PdCl$_2$.
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