Development of microchannel reactors using polysilane-supported palladium catalytic systems in capillaries

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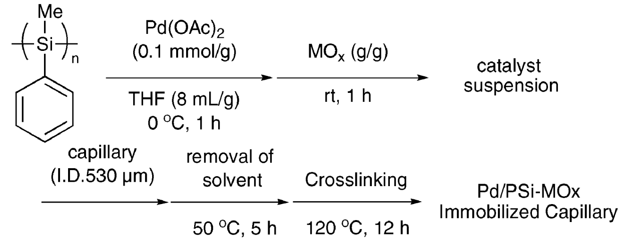
A new method of immobilizing Pd catalysts on the channel wall of a capillary by using polysilane with metal oxide has been developed, and applied to hydrogenation reactions.

Microchannel reactors, which have been used mainly in the field of analytical chemistry, have recently been applied to organic synthesis.[1–3] A microchannel reactor is a device that has a very small channel etched in a solid material. This reactor can provide many fundamental and practical advantages for organic synthesis, stemming from its small size as well as flow-reactor chemical processes. There are many general advantages of using microchannel reactors in organic synthesis. One of the most important features of microchannel reactors is a high surface area/volume ratio. The specific surface areas of microchannel reactors lie between 10 000 and 50 000 $m^2\ m^{-3}$, whereas those of traditional reactors are generally about 100 $m^2\ m^{-3}$.[2a] This feature allows suitable environments for multiphase reactions to be established on the interfacial area between different phases, such as liquid–liquid, gas–liquid, and gas–liquid–solid reactions. In particular, immobilization of catalysts on the surface of a microchannel reactor provides one of the most powerful tools for multiphase reactions.

Immobilized catalysts have been of great interest due to several advantages, such as simplification of product work-up, separation, isolation, and reuse of catalysts.[4,5] In addition, immobilized catalysts play key roles in sustainable chemistry. However, their use in organic synthesis has been relatively limited, mainly due to their low activity. To address this issue, we have developed highly active polymer-supported catalysts based on our original microencapsulation and polymer-incarcerated methods using organic polymers.[6] The catalysts have been further applied to microchannel reactors for hydrogenation.[7] In the course of our investigations to develop novel immobilized catalysts that can be applied to microchannel reactors, we have focused on polysilane[8] (PSi)-supported catalysts. We have already reported PSi-supported Pd and Pt catalysts for hydrogenation, Suzuki and Sonogashira reactions, and hydrosilylation, *etc.*[9] We reasoned that polysilane operated not only as a backbone for the immobilized catalysts but also as a connecting material between the surface of a glass wall and catalysts *via* silicon–oxygen networks. In this paper, we describe a new immobilization method for Pd catalysts on a channel wall of a capillary by using polysilane with metal oxide, and its application to hydrogenation reactions.

Polysilane-supported palladium catalysts (Pd/PSi) were prepared following our previous work (Scheme 1).[9] Accordingly, palladium acetate ($Pd(OAc)_2$) was added to a THF solution of polysilane at 0 °C. After a few minutes, the solution became black, and the mixture was then stirred for 1 h. Capillaries (530 μm i.d.) were filled with the catalyst solution, and the solvent was removed in a dry oven (50 °C, 5 h). After cross-linking (120 °C, 12 h), Pd/PSi immobilized capillary was obtained. This capillary was not very effective for hydrogenation of 2,4-diphenyl-4-methyl-1-pentene, a model substrate (Table 1, entry 1). To improve the activity of the capillary, a range of metal oxides were examined as additives (Table 1, entries 2–7):[10] after addition of $Pd(OAc)_2$, the metal oxides were added and the mixture was stirred at rt for 1 h to give a grayish suspension. Following the same procedure described above in the immobilization step on capillaries, Pd/PSi-MO_x immobilized capillaries were prepared.†

With zirconium oxide or silicon oxide as an additive, conversion of the substrate was moderate (Table 1, entries 2–4). It was also indicated from optical microscope analysis that the capillary surfaces were heterogeneous (Fig. 1b and 1c). In contrast, aluminium oxide and titanium oxide† gave excellent conversions (Table 1, entries 5–7). In the case of aluminium oxide, however, the yield of the desired product was lower, large precipitates were observed in the capillary during preparation (see also Fig. 1d), and partial disruption of the continuous reaction flow occurred (sluggish flow or liquid ring flow).[11] The conversion as well as the product yield were satisfactory in cases when (using analysis of capillary surfaces), sufficiently thick and uniform layers of palladium were observed (Fig. 1e). To increase the catalyst surface area, we employed smaller particles of titanium oxide as an additive



Scheme 1 Typical procedure for the preparation of Pd/PSi-MO_x immobilized capillaries.

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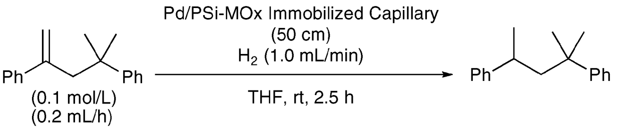
Table 1 Effect of metal oxides (MO_x)

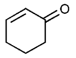
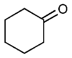
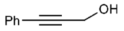
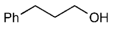
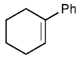
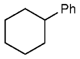
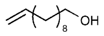
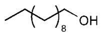
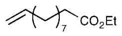
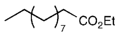
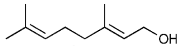
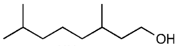
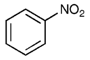
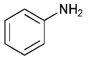
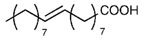
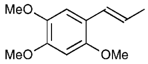
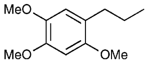
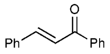
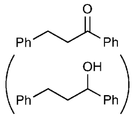


Entry	MO_x (size/nm)	Pd loading[a]	Product recovery[b] (%)	Conv.[b] (%)
1	—	0.046	80	76
2	ZrO_2 (5000)	No loading	—	—
3	ZrO_2 (20–30)	0.048	87	96
4	SiO_2 (70)	0.014	90	99
5	Al_2O_3 (40–47)	0.045	61	>99
6[c]	TiO_2 (100–300)	0.083	97 [qnt.]	>99 [98]
7[c]	TiO_2 (70)	0.22	88 [qnt.]	>99 [98]
8[d]	TiO_2 (100–300)	<0.007[e]	73	>99

[a] μmol per 20 cm. [b] Determined by GC analysis. [c] The values in square brackets are those obtained with a substrate flow rate of 1.0 mL h^{-1}; qnt. = quantitative. [d] The capillary was prepared in the absence of polysilane. [e] Loaded Pd was at the lower limit of detection. In all cases, no leaching of Pd could be detected by ICP analysis (<7.3 nmol per sample).

Table 2 Hydrogenation using the Pd/PSi-TiO_2 immobilized capillary

$$\underset{\substack{(0.1\ \text{mol/L})\\(0.1\ \text{mL/h})}}{\text{Substrate}} \xrightarrow[\text{THF, rt}]{\substack{\text{Pd/PSi-TiO}_2\ \text{Immobilized Capillary (50 cm)}\\ \text{H}_2\ \text{(2.0 mL/min)}}} \text{Product}$$

Entry	Substrate	Product	Conv.[a] (%)	Yield[a] (%)
1			>99	82
2[b]			99[c]	72[c]
3			>99	>99
4			>99	69
5			>99	84
6			>99	54
7			>99	83
8[d]		$CH_3(CH_2)_{16}COOH$	>99[c]	71[c]
9			>99[c]	>99[c]
10	$CH_2{=}CH(CH_2)_{13}CH_3$	$CH_3(CH_2)_{14}CH_3$	>99	69
11[b]			96[c]	77[ce] (19)[cf]

[a] Determined by GC analysis. [b] EtOH was used as a solvent. [c] Determined by ^{1}H-NMR analysis. [d] The reaction was conducted at 50 °C. [e] Yield of the ketone. [f] Yield of the alcohol. In all cases, leaching of Pd was not detected by ICP analysis (<6.8 nmol per sample).

(Table 1, entry 7). Although the loading of the palladium on the Pd/PSi-TiO_2 immobilized capillary was higher, almost the same activity for hydrogenation of the olefin was obtained. In addition, polysilane was found to be effective for the catalyst immobilization of capillaries. When a capillary was prepared without polysilane, no loaded Pd could be detected.

Next, we tested reduction of several substrates using the Pd/PSi-TiO_2 immobilized capillary‡ (Table 2). In most cases, hydrogenation reactions proceeded smoothly to afford the corresponding reduced compounds in excellent conversions. It is noted that the purities of the products were >99% (analyzed by GC) without purification. In addition, no leaching of Pd was detected after the reaction in each case.

We further examined reuse of the capillary in hydrogenation of 2,4-diphenyl-4-methyl-1-pentene (Table 3).§ After the reaction, the Pd/PSi-TiO_2 immobilized capillary was washed with THF and then dried. Gratifyingly, the reactivity of the catalyst was maintained after being reused 12 times. However, a slight decrease of the reactivity was observed on the 13th reuse. To address this problem, we optimized several conditions for the preparation of the Pd/PSi-TiO_2 immobilized capillary, and finally found that the most important point for the preparation was the temperature of the crosslinking. When we performed the crosslinking at 180 °C, the Pd/PSi-TiO_2 immobilized capillary could be used for the hydrogenation reaction without any decrease in the activity even after being reused 15 times.

We also conducted long-time continuous flow experiments (Table 4). When the crosslinking was performed at 180 °C, 100 h continuous flow for hydrogenation of 2,4-diphenyl-4-methyl-1-pentene could be carried without significant loss of activity.

In conclusion, we have developed a new immobilization method for Pd catalysts on the channel wall of a capillary by using polysilane with metal oxide, to prepare a Pd/PSi-TiO_2 immobilized capillary. The capillary was effective for several

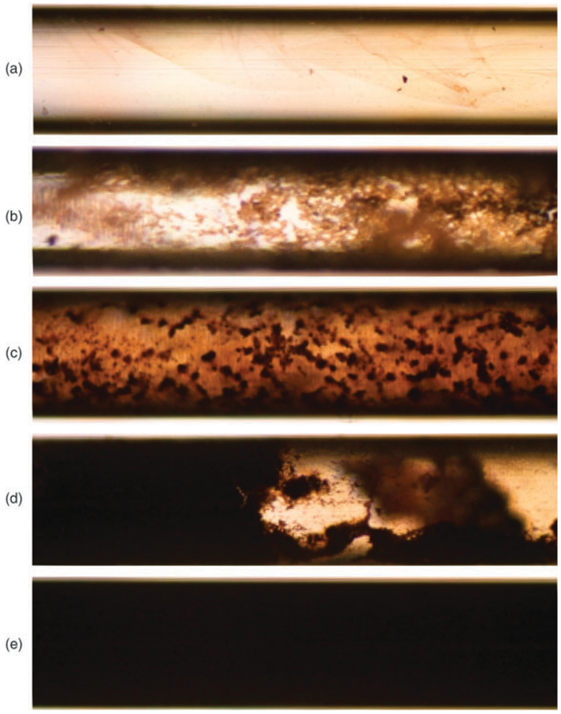


Fig. 1 Optical microscopy images of capillary surfaces. All capillaries were 530 μm i.d.; Pd/Si-MO_x appears black. (a) Pd/PSi (blank), (b) Pd/PSi-ZrO_2, (c) Pd/PSi-SiO_2, (d) Pd/PSi-Al_2O_3, (e) Pd/PSi-TiO_2.

Table 3 Reuse of the Pd/PSi-TiO_2 immobilized capillary at different crosslinking temperatures[a]

	Repeat number														
Temp.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
120 °C	>99	>99	>99	>99	>99	99	>99	>99	>99	>99	98	>99	95	93	98
160 °C	>99	>99	>99	>99	>99	>99	>99	>99	>99	>99	>99	97	99	96	>99
180 °C	>99	>99	99	>99	98	>99	>99	>99	>99	>99	>99	>99	>99	>99	>99

[a] Determined by GC analysis. In all cases, no leaching of Pd could be detected by ICP analysis (<6.8 nmol per sample).

Table 4 Long-time continuous flow experiments[a]

	Conversion (%)			
Crosslinking temp.	1 h	4 h	24 h	100 h
160 °C	>99	96	81	39
180 °C	>99	>99	>99	97

[a] Determined by GC analysis. In all cases, no leaching of Pd could be detected by ICP analysis (<3.6 nmol per sample).

hydrogenation reactions. The preparation of the capillary is simple and easy, and various kinds of solvents and substrates can be used in this system. Moreover, the capillary could be reused at least 15 times without loss of activity, and no leaching of Pd occurred under the conditions.

Notes and references

† **Preparation of Pd/PSi-TiO_2 immobilized capillaries**: The capillary column (0.530 mm I.D., 150 cm length) was washed with (successively) 1 N NaOH aq.–ethanol (1 : 1), water, ethanol, and methanol, to activate the surface of the capillary. Separately, poly(methylphenylsilane) (500 mg) was dissolved in THF (4.0 ml) and the solution was cooled to 0 °C. To this solution was added palladium(II) acetate (11.2 mg, 0.05 mmol), and the mixture was stirred for 1 h at this temperature and then allowed to warm to room temperature. After 1 h, TiO_2 (500 mg) was added and the mixture was stirred for 1 h. The Pd mixture was added to the capillary column, and the capillary was heated to 50 °C to remove excess solvent inside the capillary. The capillary was then heated to 120 °C for 12 h for crosslinking. Finally, the capillary was cut into lengths of 50 cm for hydrogenation reactions.

‡ **General procedure for hydrogenation using Pd/PSi-TiO_2 immobilized capillaries**: Through one inlet of the Pd/PSi-TiO_2 immobilized capillary, the substrate solution in THF (0.1 mol L^{-1}, 1.0 mL) was added using syringe pump at constant speed (0.1 mL h^{-1}). Through the other inlet, hydrogen gas was added *via* a massflow controller at a constant flow rate (2.0 mL min^{-1}). The reaction mixture was collected in the vessel filled with ethyl acetate at the end of the capillary. The reaction was stopped after 5 h to afford the desired compound. The conversion and the yield were determined by GC analysis (durene was used as an internal standard). After the reaction, the capillary was washed with THF and dried overnight at room temperature.

§ **Reuse of Pd/PSi-TiO_2 immobilized capillary**: This experiment was carried out under the same conditions as those in the general procedure, using 2,4-diphenyl-4-methyl-1-pentene as a substrate. The reaction was stopped after 8 h to afford 2-methyl-2,4-diphenylpentane, and the conversion determined by GC analysis. After the reaction, the capillary was washed with THF and dried overnight at room temperature.

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