

# Catalytic Flow Hydrogenation of Aromatic Nitro Compounds Using Polysilane-Supported Palladium

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Continuous-flow hydrogenation of aromatic nitro compounds was successfully performed by using polysilane-supported palladium catalysts to afford the corresponding amino compounds in high yields. Productivity was high, and a wide variety of nitro compounds were applicable under the continuous-flow conditions. It is noted that no leaching of palladium was observed by inductively coupled plasma analysis.

**Keywords:** hydrogenation, catalytic flow, palladium, polysilane, supported catalyst, nitro compound, amino compound

## 1. Introduction

Continuous-flow reactions have advantages over batch reactions in terms of productivity, heat and mixing efficiency, and safety, as well as reproducibility; furthermore, automation and multistep reactions are possible. Moreover, the amount of waste can be minimized by using continuous-flow conditions with solvent-free reagents, leading to green sustainable chemistry [1]. Continuous-flow reactions using heterogeneous catalysts (catalytic continuous-flow reactions) can constitute ideal reaction systems because the desired products, which are easily separated from catalysts, are obtained continuously [2]. Several examples of catalytic flow hydrogenation have been reported; however, in most cases, especially for nitro compounds, metal leaching is problematic and the lifetime of catalysts is often limited because the amino group of the product interacts with the metal surface and decreases the catalytic activity [3].

We have been developing various continuous-flow systems with immobilized catalysts [4–6]. Here, we report continuous-flow hydrogenation reactions of aromatic nitro compounds using novel polysilane-supported palladium catalysts that we recently developed [4a, 4d, 5b, 7]. The flow system is efficient for the synthesis of a range of nitrogen-containing compounds, which are key intermediates of many biologically active compounds and functional materials.

## 2. Results and Discussion

Polysilane-supported palladium catalysts can be prepared from polysilane, aluminum oxide, and palladium acetate, but it is also commercially available [8]. This catalyst (Pd/PMPSi- $\text{Al}_2\text{O}_3$ ) is easy to handle and shows high catalytic activity in the hydrogenation of olefins in continuous-flow systems.

We placed Pd/PMPSi- $\text{Al}_2\text{O}_3$  in a column reactor (5 or 10 mm inner diameter, 50 or 100 mm length) and fitted the column to a flow-reaction system composed of a mass-flow controller, a peristaltic pump, and a pressure monitor (Figures 1 and 2). The pressure monitor was used for monitoring the clogging in the tube or column. The system was controlled by a PC, and the temperature range of the system was between room temperature and 200 °C (aluminum heating block). A back-pressure regulator is not attached.

The reaction conditions were optimized by using 4-nitrobenzylalcohol as substrate (Table 1). Almost full conversions were

obtained at 25 °C using several solvent systems (entries 1, 4, and 6). Removal of the hydroxyl group was also observed by tuning the reaction conditions (entry 8).

We then surveyed the substrate scope of the reaction by using a range of aromatic nitro compounds (Table 2). Nitro compounds bearing hydroxyl groups (entries 1–3) and methoxy groups (entries 4 and 5) reacted smoothly. Selective reduction of the nitro groups proceeded quantitatively in the case of carbonyl compounds such as esters and ketones (entries 6–10). Interestingly, a ketone moiety was tolerant under the conditions (entry 10). Dinitro compounds could also be used in this flow-reaction system without product inhibition (entries 11 and 12). The reduction of 2-nitroanisole proceeded quantitatively to give 2-aminoanisole under neat conditions without deactivation of the catalyst (entry 13). It is noted that leaching of palladium was not observed in any of the reactions (detection limit: 0.03 ppm).

To obtain higher productivity, the flow rate of starting material **1 k** was increased (Table 3). Flow rates of 130  $\mu\text{L}/\text{min}$  (5  $\varphi \times 50$  mm column) and 480  $\mu\text{L}/\text{min}$  (10  $\varphi \times 100$  mm column) were found to be the maximum flow rates at which the desired product was obtained quantitatively. Yields of 9.7 g/h (entry 3) or 36.0 g/h

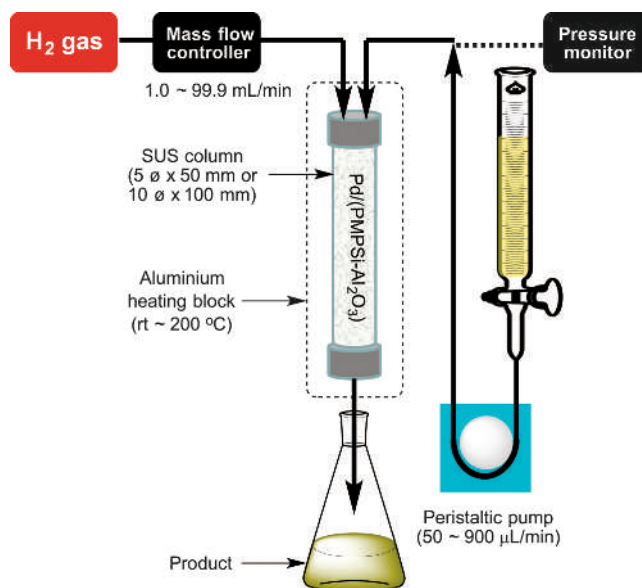
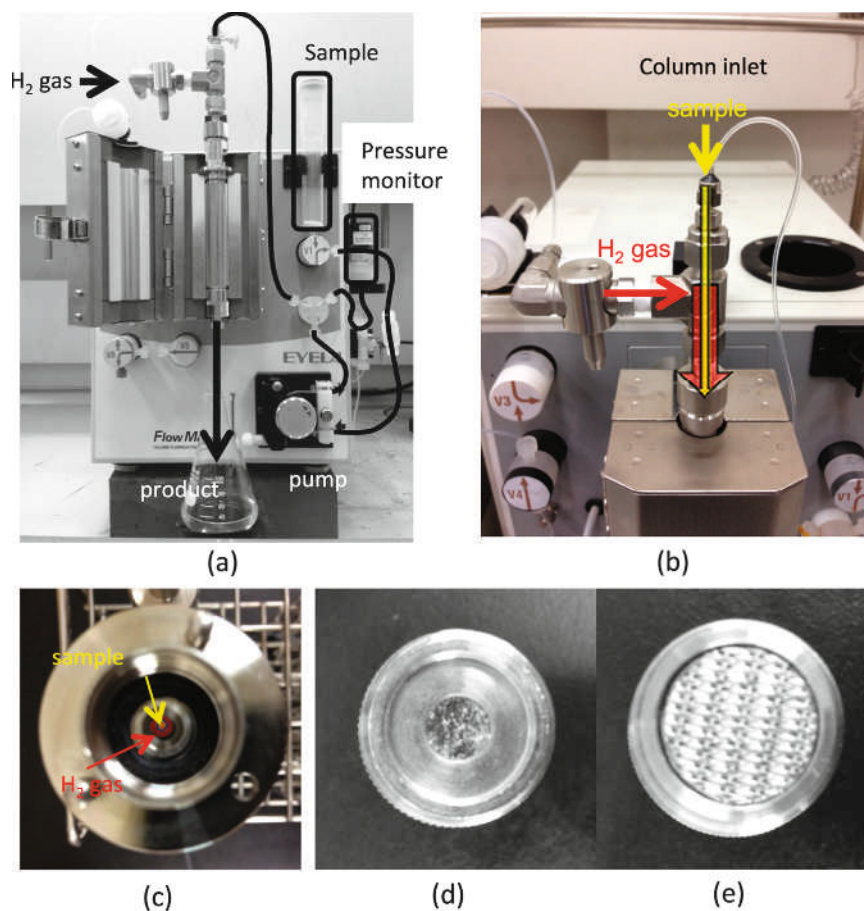


Figure 1. System diagram of the continuous-flow reactor

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**Figure 2.** Photographs of the reaction apparatus ((a) whole reaction system [some parts were clarified by black color], (b) column inlet, (c) column inlet [bottom view], (d) column top [without SUS filter], (e) column top [with SUS filter])

(entry 5) of 2-aminoanisole were obtained in each case, and the space-time yield (sty) reached 75.2 (mmol/g·h) (entry 2).

### 3. Conclusion

Polysilane-supported palladium catalyst was applied to the continuous-flow hydrogenation of a range of nitro compounds, and high catalytic activity was obtained. This system is efficient and scalable, and is expected to be applied to industrial-scale hydrogenation reactions.

### 4. Experimental

The continuous-flow reactor system (EYELA CCR-1000G; Figure 1) comprised of an EYELA CCR-1000G flow reactor fitted with a peristaltic roller tube pump and mass-flow controller. A 5 × 50 mm SUS column (EYELA) was filled with Pd/(PMPSi–Al<sub>2</sub>O<sub>3</sub>) (0.9 g) and fitted on the top and bottom with SUS filters (pore size 10 μm) and screw caps. Teflon tubing (1 × 1.6 mm) was used throughout.

**4.1. Typical Procedure for Hydrogenation of 2-Nitroanisole by Pd/PMPSi–Al<sub>2</sub>O<sub>3</sub> (Table 3, Entry 3).** Pd/PMPSi–Al<sub>2</sub>O<sub>3</sub> (885 mg, Pd 56.6 μmol/g) was packed into the SUS

**Table 1.** Optimization of reaction conditions<sup>a</sup>

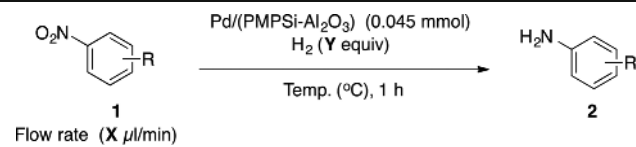
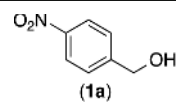
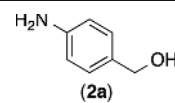
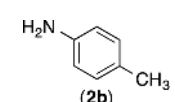
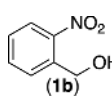
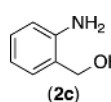
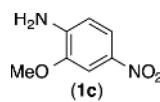
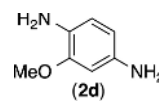
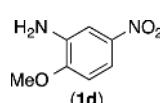
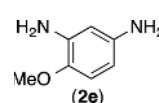
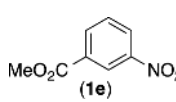
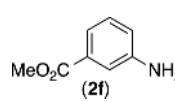
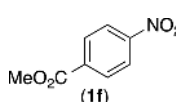
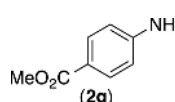
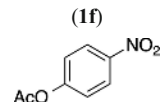
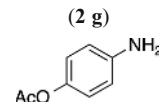
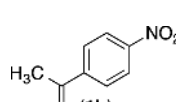
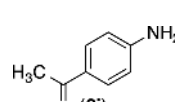
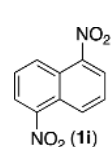
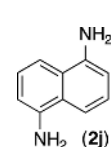
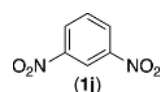
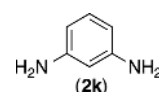
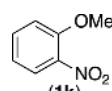
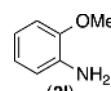
Entry	Solvent (M)	X (equiv.)	T (°C)	Conversion (%) <sup>b</sup>			
				2a	2b	1a	–CHO
1	EtOAc (0.1)	18	25	97	3	ND	ND
2	EtOH (0.1)	18	25	95	2	3	Trace
3	EtOH (0.1)	18	75	62	37	ND	1
4	EtOH (0.2)	9	25	99	1	Trace	Trace
5	EtOH (0.4)	4.5	25	89	1	10	Trace
6	Toluene–IPA=9:1 (0.1)	18	25	98	1	1	Trace
7	Toluene–IPA=9:1 (0.1)	18	50	94	5	1	Trace
8	Toluene–IPA=9:1 (0.1)	18	100	15	82	1	2
9	Toluene–IPA=9:1 (0.4)	4.5	25	95	2	3	ND

ND=not detected.

<sup>a</sup> Reaction conditions: a 5 φ × 50 mm (0.982 mL) column was used as a packed catalyst column and Pd/(PMPSi–Al<sub>2</sub>O<sub>3</sub>) catalyst (840 mg, Pd loading: 53.7 μmol/g) was packed. Flow rate of substrate: 250 μL/min.

<sup>b</sup> Determined by <sup>1</sup>H NMR analysis.

Table 2. Substrate scope<sup>a</sup>

							
Entry	1	Solvent (M)	X (μL/min)	Y (equiv.)	Temp. (°C)	2	Conv. (%) <sup>b</sup>
1	 (1a)	EtOH (0.2)	250	7.5	20	 (2a)	99
2	(1a)	Toluene-IPA 9:1 (0.1)	250	10	100	 (2b)	82
3	 (1b)	EtOH (0.2)	250	7.5	60	 (2c)	99
4	 (1c)	EtOH (0.1)	400	5	70	 (2d)	Quant
5	 (1d)	EtOH (0.1)	400	5	50	 (2e)	99
6	 (1e)	EtOH (0.1)	400	5	50	 (2f)	Quant
7	 (1f)	EtOH (0.1)	400	5	50	 (2g)	95
8 <sup>c</sup>	(1f)	MeOH (0.2)	400	6	50	(2g)	Quant
9 <sup>c</sup>	 (1g)	Toluene-IPA 9:1 (0.2)	200	5	50	 (2h)	99
10 <sup>d</sup>	 (1h)	EtOH (0.2)	400	6	50	 (2i)	Quant
11	 (1i)	Toluene-EtOH 9:1 (0.02)	450	18	70	 (2j)	Quant
12	 (1j)	Toluene-EtOH 9:1 (0.2)	400	9	50	 (2k)	Quant
13	 (1k)	Toluene-IPA 9:1 (5.0)	200	3.6	50	 (2l)	Quant

<sup>a</sup> Reaction conditions: a 5 φ × 50 mm (0.982 mL) column was used as a packed catalyst column and Pd/(PMPSi-Al<sub>2</sub>O<sub>3</sub>) catalyst (840 mg, Pd loading: 53.7 μmol/g) was packed.

<sup>b</sup> Determined by <sup>1</sup>H NMR analysis.

<sup>c</sup> Reaction time: 1.5 h.

<sup>d</sup> Reaction time: 2 h.

**Table 3.** Optimizing productivity at quantitative conversion

COc1cccc([N+](=O)[O-])c1 (1k)  $\xrightarrow[85\text{ }^\circ\text{C}, 2\text{ h}]{\text{Pd}/(\text{PMPSi}-\text{Al}_2\text{O}_3), \text{H}_2 (3.6\text{ equiv})}$  COc1cccc(N)c1 (2l)

neat (8.18 M)  
Flow rate (X μl/min)

Entry	Column <sup>a</sup>	X (μL/min)	H <sub>2</sub> (mL/min)	Conversion (%) <sup>b</sup>	Space-time Yield <sup>c</sup> (mmol/g·h)
1	5 φ×50 mm	150	98.7	93	75.6
2	5 φ×50 mm	140	91.9	99	75.2
3	5 φ×50 mm	130	85.6	Quant	70.6
4	10 φ×100 mm	500	329	99	33.7
5	10 φ×100 mm	480	316	Quant	32.7

<sup>a</sup> Pd/(PMPSi–Al<sub>2</sub>O<sub>3</sub>) catalyst (Pd loading: 53.7 μmol/g) was packed in 5 φ×50 mm (885 mg, 0.051 mmol) or 10 φ×100 mm (7.20 g, 0.40 mmol) columns.  
<sup>b</sup> Determined by <sup>1</sup>H NMR analysis.  
<sup>c</sup> The amount of product (mmol) per 1 g of the catalyst and 1 h of reaction time.

column (5 φ×50 mm), and the column temperature was kept at 85 °C by using an aluminum heating block. 2-Nitroanisole (neat) was fed into the column using the peristaltic roller tube pump (130 μL/min), and H<sub>2</sub> gas was introduced into the column by using the mass-flow controller (85.6 mL/min). The system was allowed to stabilize for 30 min, and then product formation was sampled over 2 h. The sample was analyzed by <sup>1</sup>H NMR spectroscopy, which confirmed complete conversion of 2-nitroanisole into *o*-anisidine.

*o*-anisidine: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz) δ: 3.36 (brs, 2H), 3.86 (s, 3H), 6.72–6.76 (m, 2H), 6.79–6.82 (m, 2H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz) δ: 55.4, 110.5, 115.0, 118.5, 121.1, 136.2, 147.3.

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