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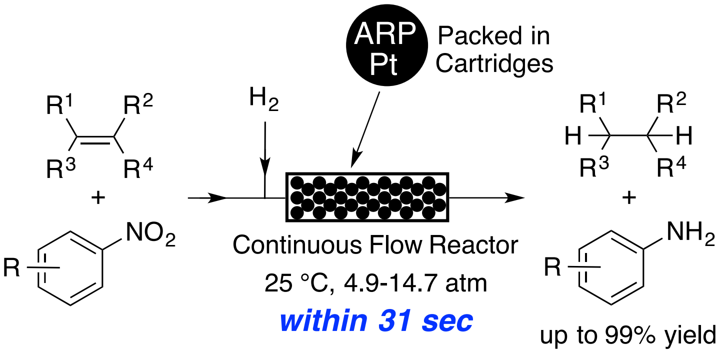

Continuous-Flow Hydrogenation of Olefins and Nitrobenzens with ARP-Pt

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Continuous-flow hydrogenation of olefins and nitrobenzenes catalyzed by platinum nanoparticles dispersed in an amphiphilic polymer

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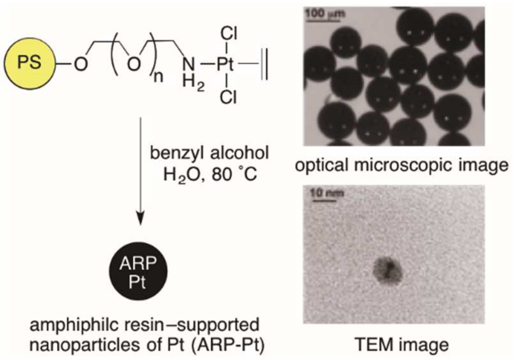
A method for the flow hydrogenation of olefins and nitrobenzenes in a continuous-flow reactor containing platinum nanoparticles dispersed on an amphiphilic polystyrene–poly(ethylene glycol) resin (ARP-Pt) was developed. The hydrogenation of olefins and nitrobenzenes was completed within 31 seconds in the continuous-flow system containing ARP-Pt, giving the corresponding hydrogenated products in up to 99% yield with good chemoselectivity. Moreover, long-term (63-70 h) continuous-flow hydrogenation of styrene and nitrobenzene produced more than ten grams of ethylbenzene and aniline, respectively, without significant loss of catalytic activity. The flow hydrogenation system provides an efficient and practical method for the chemoselective reduction of olefins and nitrobenzenes.

Introduction

Organic transformations under continuous-flow conditions have become increasingly important in synthetic organic chemistry.[1] Continuous-flow processes provide significant advantages in regard to safety, efficiency, reproducibility, and waste reduction, and allow for practical, efficient, and green/sustainable organic transformations. Therefore, the replacement of conventional batch organic reactions with continuous-flow reactions represents a major challenge in modern organic chemistry.

The development of continuous-flow systems for the catalytic hydrogenation of carbon-carbon unsaturated bonds and nitro groups with heterogeneous catalysts has attracted significant attention because of the potentially widespread applications in the synthesis of valuable organic compounds.[2-5] Conventional heterogeneous catalysts such as Pd/C and Pt/C have been applied in continuous-flow hydrogenation reactions using molecular hydrogen.[3,4a,4d,4e,4g,5] However, the hydrogenation of olefins and nitrobenzenes bearing other substituents that can be reduced using conventional catalysts, such as chloro, carbonyl, and cyano moieties, is likely to suffer from the undesired reduction of all substituents. New continuous-flow systems are desired in order to facilitate chemoselective, efficient, and practical flow hydrogenation reactions.

Metal nanoparticles supported on solid supports such as polymers, carbon, and metal oxides have been recognized as advanced nanomaterials, which can be applied as efficient heterogeneous catalysts in various organic reactions, such as hydrogenation, oxidation, and coupling reactions.[6] The catalytic activity of supported metal nanoparticles can be regulated by the appropriate selection of solid supports and preparation of the nanoparticles. Therefore, many supported nanoparticles have been synthesized by various methods and have been applied in a wide range of organic transformations including hydrogenation.[7,8] As part of our continuous efforts to advance this research objective,[9] we previously developed novel supported platinum nanoparticles dispersed in amphiphilic polystyrene–poly(ethylene glycol) resin (PS-PEG) (Amphiphilic Resin-supported nanoparticles of Platinum; ARP-Pt), which were readily prepared by the reduction of a PS-PEG supported platinum ethylene complex with benzyl alcohol in water at 80 °C (Scheme 1).[10] ARP-Pt efficiently catalyzed the aerobic



Scheme 1 Preparation of amphiphilic resin-supported nanoparticles of Pt.

oxidation of various alcohols in water under batch conditions.[10a,b] Very recently, we successfully developed a technique for the efficient, aerobic oxidation of alcohols under continuous-flow conditions, using a flow reactor containing ARP-Pt.[10c] Various primary and secondary alcohols including aliphatic, aromatic, and heteroaromatic alcohols were completely oxidized within 73 sec in a continuous-flow reactor (X-Cube™, ThalesNano Inc.) equipped with two catalyst cartridges (ϕ 4 x 70 mm) of ARP-Pt (Fig 1) to give the corresponding carboxylic acids and ketones, respectively, in up to 99% isolated yields. Moreover, a practical gram-scale synthesis of surfactants was realized in the aqueous aerobic continuous-flow oxidation over long reaction times (36-116 h) without significant loss of catalytic activity. The successful results prompted us to utilize the flow reaction system containing ARP-Pt in other organic transformations. Herein, we report the continuous-flow hydrogenation of olefins and nitrobenzenes with molecular hydrogen catalyzed by ARP-Pt. The continuous-flow hydrogenation of various olefins and nitrobenzenes was completed within 31 sec to give the corresponding hydrogenated products in up to 99% isolated yields with excellent chemoselectivity. Notably, ARP-Pt has dual functions in that it can catalyze the reduction of olefins and nitrobenzenes with H_2 as well as the oxidation of alcohols with O_2 under flow conditions.[11] To our best knowledge, the continuous-flow system showing such dual functions is unprecedented. Moreover, the high catalytic activity of ARP-Pt during flow hydrogenation was preserved over a long reaction time (at least 70 h) to produce more than 10 grams of the hydrogenated products. The turnover number (TON) of the catalyst reached 4400 in the continuous-flow reaction conducted over 70 h. The continuous-flow hydrogenation system provides an efficient and practical method for the chemoselective hydrogenation of olefins and nitrobenzenes.

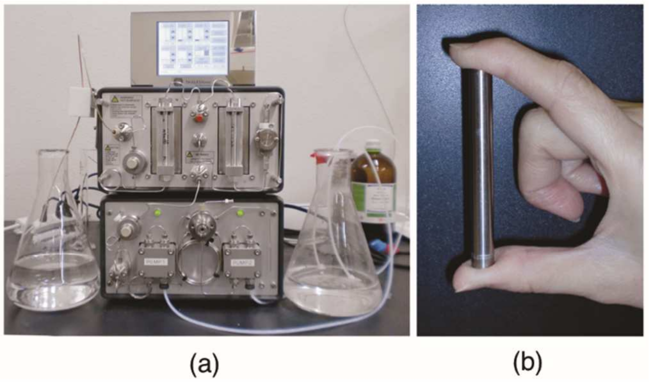


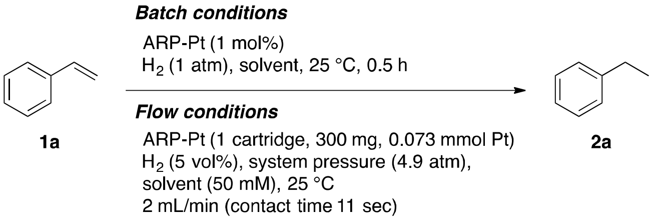
Fig. 1 (a) A picture of the flow-oxidation reactor (X-Cube™). (b) View of the catalyst cartridge (ϕ 4 x 70 mm).

Results and Discussion

Hydrogenation of olefins with ARP-Pt

Before the investigation of the flow hydrogenation was initiated, the catalytic activity of ARP-Pt was evaluated in the hydrogenation of styrene in various solvents under batch conditions (Table 1, entries 1-8). The reaction of styrene **1a** was performed in the presence of ARP-Pt (1 mol% Pt) in EtOH under 1 atm of H_2 at 25 °C for 0.5 h, to give ethylbenzene **2a** in 99% GC yield (entry 1). The reaction conducted in H_2O was sluggish at 25 °C (14% conversion, entry 2). When the hydrogenation of **1a** in H_2O was performed at a higher temperature (80 °C) and over a longer reaction time (1 h), **1a** was converted into **2a** in 98% yield (entry 3). This result indicated that ARP-Pt acted as a viable catalyst in the aqueous hydrogenation of olefins under batch conditions. The reactions of **1a** in THF, toluene, and CH_3CN proceeded smoothly at 25 °C in 0.5 h to provide **2a** in 94-99% yields (entries 4, 5, and 8, respectively). The use of $CHCl_3$ and 1,4-dioxane afforded **2a** in a moderate yield (entries 6 and 7).

Table 1 Optimization of the hydrogenation of styrene **1a.**

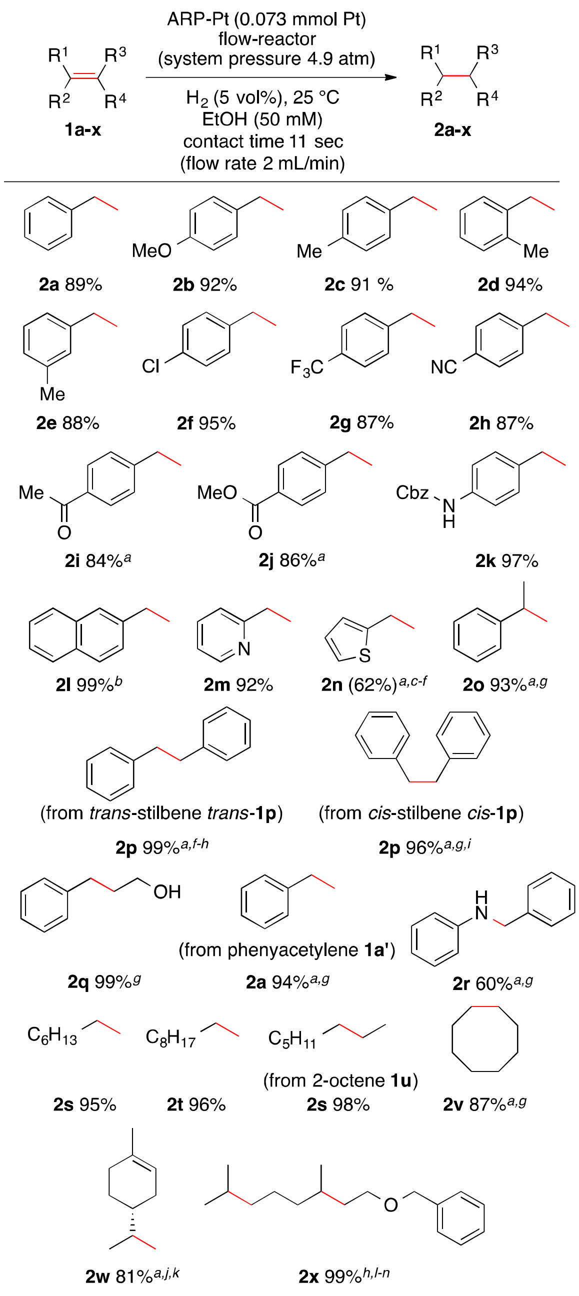


Entry	Solvent	Conversion (%)[a]	Yield of **2a** (%)[a]
Batch conditions			
1	EtOH	>99	99
2	H_2O	14	14
3[b]	H_2O	>99	98
4	THF	98	95
5	toluene	94	94
6	$CHCl_3$	55	54
7	1,4-dioxane	42	42
8	CH_3CN	>99	99
Flow conditions			
9	EtOH	>99	99 (89)[c]
10	H_2O	–[d]	–[d]
11	THF	>99	99
12	toluene	93	92
13	$CHCl_3$	>99	94
14	1,4-dioxane	77	77
15	CH_3CN	83	83

Conditions for the batch reaction: **1a** (0.2 mmol), ARP-Pt (1 mol% Pt), solvent (2 mL), H_2 (1 atm), 25 °C, 0.5 h.
Conditions for the flow reaction: 50 mM solution of **1a**, ARP-Pt (1 cartridge; ϕ 4.0 x 70 mm, 300 mg, 0.073 mmol Pt), H_2 (5 vol% in flow stream), 4.9 atm system pressure, 2 mL/min flow rate (contact time: 11 sec, LHSV: 333 h^{-1}).
[a] Determined by GC with an internal standard. [b] The reaction was performed at 80 °C for 1 h. [c] Isolated yield shown in parenthesis. [d] Blockage of the solution stream occurred in the flow system.

Next, the hydrogenation of styrene **1a** catalyzed by ARP-Pt was carried out in various solvents using a flow reactor (Fig. 1(a), X-Cube™, ThalesNano Nanotechology, Inc.).[12] A 50 mM solution of styrene (**1a**) was introduced into the reactor at a flow rate of 2.0 mL/min, and was passed through a catalyst cartridge (internal diameter 4 mm, length 70 mm, Fig. 1(b)), which was charged with ARP-Pt (300 mg, 0.073 mmol Pt).[13] Under these conditions, the total contact time between the solution and catalyst was 11 sec (LHSV = 333 h^{-1}).[14] The flow hydrogenation of **1a** in EtOH at 25 °C at a system pressure of 4.9 atm (minimum setting pressure of X-Cube; 5 vol% nanosize bubbles of H_2 in the flow steam) gave ethylbenzene (**2a**) in 99% GC yield and 89% isolated yield, with a complete conversion of **1a** (entry 9). The flow hydrogenation in H_2O failed due to blockage of the solution stream, which was caused by insolubility of styrene in aqueous solutions in the flow system (entry 10). THF, toluene, and $CHCl_3$ were also effective solvents for the flow hydrogenation of **1a** (92-99% yield of **2a**) (entries 11-13). The activity of ARP-Pt slightly deceased when the reaction was carried out using 1,4-dioxane and CH_3CN, and afforded **2a** in 77% and 83% yields, respectively (entries 14 and 15). Considering the environmental and toxicological impact of the solvents,[15] we selected EtOH as the optimal solvent for subsequent investigations.

With the optimized conditions at hand, the substrate scope of olefins **1** was investigated in the flow hydrogenation (Scheme 2). Styrenes **1b**, **1c**, **1f**, and **1g** bearing methoxy, methyl, chloro, and trifluoromethyl groups in the *para*-position of the benzene ring underwent the flow hydrogenation using the flow reactor containing a cartridge of ARP-Pt (0.073 mmol Pt) at 25 °C, 4.9 atm system pressure (5 vol% of H_2), and a flow rate of 2 mL/min (contact time = 11 sec, LHSV = 333 h^{-1}) to afford the corresponding ethylbenzenes **2b**, **2c**, **2f**, and **2g** in 87-95% isolated yield. The flow hydrogenation of substrates **1d** and **1e** bearing methyl substituents in the *ortho*- and *meta*-positions proceeded efficiently to give **2d** and **2e** in 94% and 88% yield, respectively. *Para*-substituted styrenes **1h-1k** bearing cyano, acetyl, methoxylcarbonyl, and Cbz-protected amino groups were also tolerated, and provided the corresponding ethylbenzenes **2h-2k** in 84-97% yields; hydrogenation of the substituents was not observed. 2-Vinylnaphtalene **1l** and 2-vinylpyridine **1m** were also viable and furnished hydrogenated products **2l** and **2m** in 99% and 92% yield, respectively. Although the hydrogenation of 2-vinylthiophene **1n** required harsher reaction conditions (25 mM solution, 70 °C, system pressure = 14.7 atm, flow rate = 0.7 mL/min; contact time = 31 sec, LHSV = 117 h^{-1}), **2n** was obtained in 62% NMR yield and the unreacted starting material could be recovered. Disubstituted aromatic olefins **1o-q** were not fully consumed under the standard reaction conditions. Slight modification of the conditions (reaction temperature, concentration of the solution, and/or flow rate) allowed olefins **1o-q** to be fully converted into the desired hydrogenated products **2o-q** in 93-99% yield. The hydrogenation of *trans*-stilbene (*trans*-**1p**) required a slower flow rate (1.0 mL/min; contact time = 22 sec, LHSV = 167 h^{-1}) than that of *cis*-stilbene (*cis*-**1p**) (1.5 mL/min; contact time = 14 sec, LHSV = 250 h^{-1}) in order for a complete conversion to occur. The flow system could be applied in the hydrogenation of phenylacetylene **1a** and imine **1r** to give the hydrogenated products **2a** and **2r** in 94% and 60% yield, respectively.



Scheme 2 Flow hydrogenation of various olefins **1** in EtOH.
Reaction conditions: 50 mM solution of **1** in EtOH, APR-Pt (1 cartridge, 300 mg, 0.073 mmol Pt), H_2 (5 vol% in flow stream), system pressure = 4.9 atm, flow rate = 2 mL/min; contact time = 11 sec; LHSV = 333 h^{-1}, 25 °C. Isolated yields are given, except for **2n**. The yield of **2n** (shown in parenthesis) was determined by ^{1}H NMR with an internal standard. [a] 25 mM solution of **1** was used. [b] A mixture of EtOH/THF (1:2) was used. [c] 70 °C. [d] System pressure = 14.7 atm. [e] Flow rate = 0.7 mL/min (contact time: 31 sec, LHSV: 117 h^{-1}). [f] A mixture of EtOH/THF (1:1) was used. [g] 40 °C. [h] Flow rate = 1 mL/min (contact time: 22 sec, LHSV: 167 h^{-1}). [i] Flow rate = 1.5 mL/min (contact time: 14 sec, LHSV: 250 h^{-1}). [j] A mixture of EtOH/THF (4:1). [k] Flow rate = 2.5 mL/min (contact time: 9 sec, LHSV: 417 h^{-1}). [l] 12.5 mM solution of **1** was used. [m] 50 °C. [n] System pressure = 9.8 atm.

The flow hydrogenation of aliphatic olefins **1s-u** efficiently proceeded under the standard conditions (50 mM EtOH solution, 25 °C, system pressure = 4.9 atm, flow rate = 2 mL/min; contact time = 11 sec, LHSV = 333 h^{-1}). Although modification of the reaction conditions was required, aliphatic olefins **1v-x** were also viable substrates and afforded products **2v-x** in good yields. Trisubstituted olefins **1x** were completely converted into alkanes, while trisubstituted olefin **1w** remained intact.

The continuous-flow hydrogenation of styrene was carried out over a long reaction time under the optimized conditions (50 mM EtOH solution, 25 °C, system pressure = 4.9 atm, flow rate = 2.0 mL/min, contact time = 11 sec, LHSV = 333 h^{-1}). The flow hydrogenation of styrene with ARP-Pt could be conducted for 63 h without significant loss of catalytic activity, producing ethylbenzene **2a** in over 91% GC yield (Fig. 2). The flow hydrogenation conducted for 63 h provided 7560 mL of the solution of **2a** (50 mM, 39.4 g). The turnover number of ARP-Pt for the flow hydrogenation of styrene reached 5180. ICP analysis showed that 97% of the Pt content still remained on the used catalyst after the long-term continuous-flow hydrogenation. Therefore, leaching of Pt from the catalyst did not occur during long-term flow reaction. A TEM study of the used catalyst revealed that the morphology of the Pt nanoparticles changed during the long-term hydrogenation, and larger nanoparticles (ca. 40 nm) were generated (Fig S1(b)). Because the catalyst still exhibited high catalytic activity after 63 h, the resulting large Pt nanoparticles also showed catalytic activity in the flow hydrogenation of olefins.

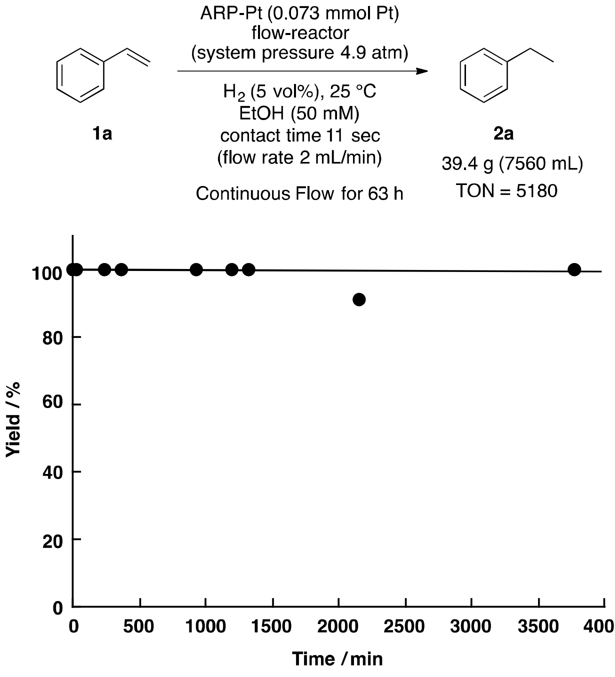
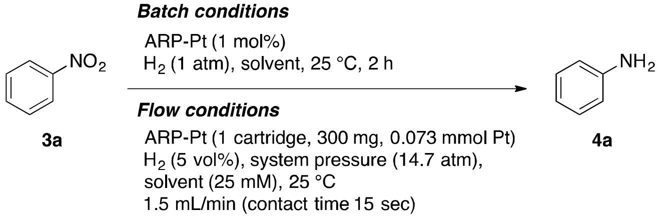


Fig. 2 Long-term continuous-flow hydrogenation of styrene **1a**. Bottom: GC yield of ethylbenzene **2a** over time (min).

Hydrogenation of nitrobenzenes with ARP-Pt

In order to expand the substrate scope in the hydrogenation reaction using ARP-Pt, the hydrogenation of nitrobenzenes was also investigated under batch and flow conditions. The batch hydrogenation of nitrobenzene **3a** with H_2 (1 atm) was performed in the presence of ARP-Pt (1 mol% Pt) in various solvents at 25 °C for 2 h (Table 2, entries 1-8). Nitrobenzene **3a** was efficiently converted into aniline **4a** in EtOH, THF, toluene, and CH_3CN under batch conditions to give aniline **4a** in 92-99% GC yield (entries 1, 4, 5, and 8, respectively), while the batch hydrogenation in H_2O, 1,4-dioxane, and $CHCl_3$ exhibited a moderate conversion (entries 2, 6, and 7, respectively). A longer reaction time (12 h) was required for the complete hydrogenation of **3a** in water at 25 °C, giving **4a** in 98% GC yield (entry 3). ARP-Pt could be also applied in the aqueous hydrogenation of nitrobenzenes under batch conditions.

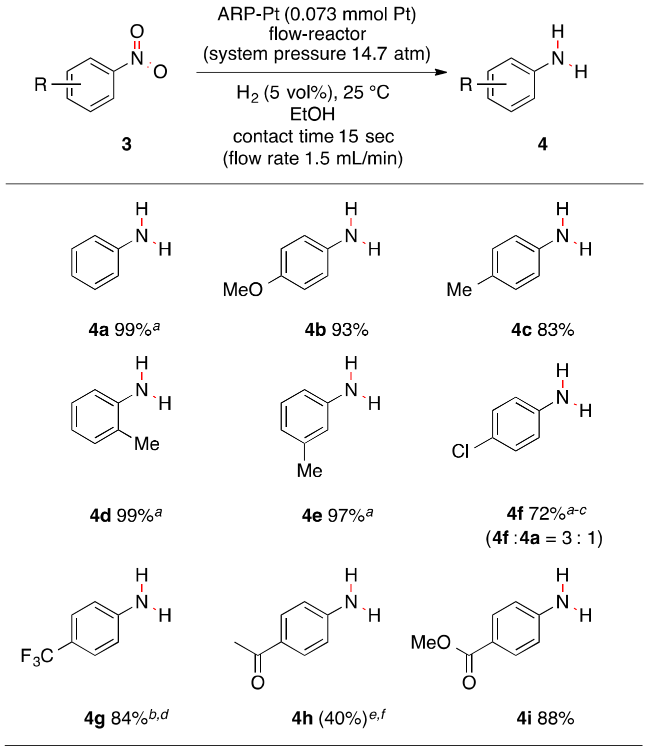
Table 2 Optimization of hydrogenation of nitrobenzene **3a**.



Entry	Solvent	Conversion (%)[a]	Yield of **4a** (%)[a]
Batch conditions			
1	EtOH	>99	99
2	H_2O	39	36
3[b]	H_2O	>99	98
4	THF	>99	94
5	toluene	>99	98
6	$CHCl_3$	46	36
7	1,4-dioxane	41	37
8	CH_3CN	>99	92
Flow conditions			
9	EtOH	>99	>99 (99)[c]
10	H_2O	–[d]	–[d]
11	THF	90	90
12	toluene	>99	99
13	$CHCl_3$	84	64
14	1,4-dioxane	66	62
15	CH_3CN	>99	87

Conditions for the batch reaction: **3a** (0.2 mmol), ARP-Pt (1 mol% Pt), solvent (2 mL), H_2 (1 atm), 25 °C, 2 h.
Conditions for the flow reaction: 25 mM solution of **3a**, ARP-Pt (1 cartridge; ϕ 4.0 x 70 mm, 300 mg, 0.085 mmol Pt), H_2 (5 vol% in flow stream), 14.7 atm of system pressure, 25 °C, 1.5 mL/min of flow rate (contact time: 14 sec, LHSV: 250 h^{-1}).
[a] Determined by GC-MS with an internal standard. [b] The reaction was performed for 12 h. [c] Isolated yield is shown in parenthesis. [d] Blockage of the solution stream occurred in the flow system.

The flow hydrogenation of **3a** in various solvents was carried out using the flow system containing ARP-Pt (entries 9-15). Introduction of 25 mM solutions of **3a** in EtOH, THF, and CH_3CN to the flow reactor containing a cartridge of ARP-Pt (300 mg) at 25 °C, under a system pressure of 14.7 atm (5 vol% of H_2) and a flow rate of 1.5 mL (contact time = 14 sec, LHSV = 250 h^{-1}), afforded aniline **4a** in 90->99% conversion and 87-99% GC yield (entries 9, 11, 12, and 15). The flow hydrogenation of **3a** in $CHCl_3$ and 1,4-dioxane provided a moderate yield of **4a** (entries 13 and 14). However, the use of water caused a blockage of the solution stream in the flow system, due to the low solubility of **3a** in water (entry 10). Based on the aforementioned results, we selected EtOH as the optimal solvent for the flow hydrogenation of nitrobenzenes.



Scheme 3 Flow hydrogenation of nitrobenzenes **3** in EtOH.
Standard reaction conditions: 25 mM solution of **3** in EtOH, APR-Pt (1 cartridge, 300 mg, 0.073 mmol Pt), H_2 (5 vol% in flow stream), system pressure = 14.7 atm, flow rate = 1.5 mL/min, contact time = 14 sec, LHSV = 250 h^{-1}, 25 °C. Isolated yields are given. [a]Isolated as the HCl salt. [b]Flow rate = 1.0 mL/min (contact time = 22 sec, LHSV = 167 h^{-1}). [c]System pressure = 9.8 atm. [d]40 °C. [e]Flow rate = 2.0 mL/min (contact time = 11 sec, LHSV = 333 h^{-1}). [f]GC yield is shown in parenthesis.

With the optimized conditions at hand, the substrate scope of nitrobenzenes **3** was investigated (Scheme 3). The flow hydrogenation of nitrobenzenes **3b** and **3c** bearing *para*-methoxy and *para*-methyl groups gave anilines **4b** and **4c** in 92% and 83% isolated yield, respectively. *Ortho*- and *meta*-methyl substituents (**3d** and **3e**) did not interfere with the flow hydrogenation. In the flow hydrogenation of *p*-chloronitrobenzene **3f**, the dechlorination reaction competed to afford a mixture of *p*-chloroaniline **4f** and aniline **4a** (3:1) in 72% yield. *Para*-trifluoromethylnitrobenzenes **3g** underwent the flow hydrogenation to give aniline **4g** in 84% yield. In the flow hydrogenation of nitrobenzenes **3h** bearing acetyl groups, the nitro group was selectively reduced without hydrogenation of the acetyl group. However, polymerization of the resulting acetyl aniline **4h** proceeded under the flow conditions. Therefore, **4h** was obtained in only 40% GC yield. The flow hydrogenation of **3i** readily proceeded to afford **4i** in 88% yield, without concomitant reduction of the ketone and ester groups.

The continuous-flow hydrogenation of nitrobenzene **3a** was conducted over a long reaction time under the standard conditions (25 mM EtOH solution, 25 °C, system pressure = 14.7 atm, flow rate = 1.5 mL/min; contact time = 14 sec, LHSV = 250 h^{-1}). The flow hydrogenation of nitrobenzene with ARP-Pt efficiently proceeded for 70 h without significant loss of catalytic activity, giving aniline **4a** in over 96% yield (Fig. 3). The flow hydrogenation for 70 h produced 6300 mL of the solution of **4a** (25 mM, 19.4 g). The turnover number of ARP-Pt during the flow hydrogenation of nitrobenzene was 2160. ICP analysis of the used catalyst revealed that no Pt leaching occurred during the long-term continuous-flow hydrogenation. However, TEM analysis revealed that Pt nanoparticles formed large aggregates (ca. 400 nm) during the long-term reaction (Fig S1(c)). In the long-term flow hydrogenation of nitrobenzene, the desired aniline was still obtained after 70 h in good yield, suggesting that the large aggregates could also catalyze the hydrogenation of nitrobenzene under the flow conditions.

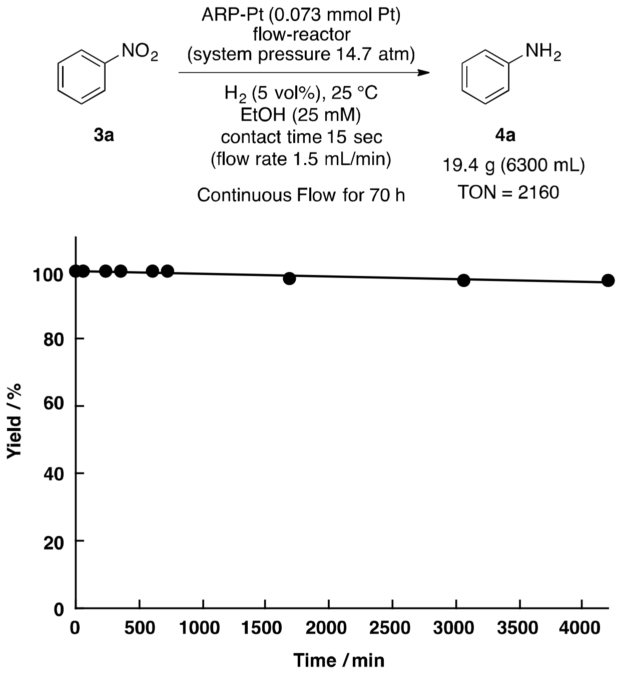


Fig. 3 Long-term continuous-flow hydrogenation of nitrobenzene **3a**.
Bottom: GC yield of aniline **4a** over time (min).

Conclusions

A method for the flow hydrogenation of olefins and nitrobenzenes in a continuous-flow reactor containing platinum nanoparticles dispersed on a PS–PEG resin (ARP-Pt) was developed. The flow hydrogenation of olefins and nitrobenzenes efficiently proceeded within 31 sec to give the corresponding alkanes and anilines, respectively, in excellent yields with good efficiency and chemoselectivity. Moreover, the long-term continuous-flow hydrogenation of olefins and nitrobenzenes was realized, and afforded more than 10 grams of the hydrogenated products. One of the advantageous points for the flow system containing ARP-Pt is to show dual functions in that it can catalyze the reduction of olefins and nitrobenzenes with H_2 as well as the oxidation of alcohols with O_2 under flow conditions. Therefore, this flow system provides efficient, and practical methods for the chemoselective hydrogenation of olefins and nitrobenzenes as well as aerobic oxidation of alcohols.

Experimental Section

General

All chemicals were commercially available and used as received without purification. Water was deionized with a Millipore system (Milli-Q grade). The flow hydrogenation was carried out with an X-Cube™ reactor system (ThalesNano Nanotechnology Inc, Hungary). ^{1}H and ^{13}C{^{1}H} NMR spectra were recorded on a JEOL JNM-ECS 400. GC analysis was carried out on a Hewlett Packard 4890 system. Mass spectra were recorded on an Agilent 6890/5973 GCMS system (GC EI-MS) or a JEOL AccuTOF GC JMS-T100GC equipped with an Agilent 6890N GC (GC TOF-MS). ICP analysis was performed on a LEEMAN LABS Profile plasma spectrometer. TEM analysis was carried out with a JEOL JEM-2100F transmission electron microscope.

Typical procedure for the batch hydrogenation

The substrate (0.2 mmol) and ARP-Pt (1 mol% Pt) were charged into a reaction tube. After the solvent was added, the inside atmosphere in the reaction tube was replaced with an H_2 balloon. The contents of the reaction tube were stirred at 25 °C. After the reaction, the catalyst was removed by filtration and the resulting solution was analyzed with GC and GC-MS.

Typical procedure for the flow hydrogenation of olefins

An ethanolic solution of styrene (**1a**, 50 mM) was pumped into the X-Cube reactor system installed with a catalyst cartridge (ARP-Pt: 300 mg; 0.073 mmol Pt) at a flow rate of 2.0 mL/min. The flow hydrogenation of **1a** with H_2 gas (5 vol% of the nanobubbles) was conducted at 25 °C under a system pressure of 4.9 atm. The resulting solution was collected for 5 min (10 mL). After pentane (20 mL) was added, the solution was washed with H_2O (20 mL x 3). The combined organic phases were dried over Na_2SO_4 and carefully concentrated by evaporation to afford a colorless oil (**2a**, 89% yield). In the isolation of **2k**, **2l**, and **2x**, the resulting EtOH solution from the flow reaction was directly concentrated to give the products.

Typical procedure for the flow hydrogenation of nitrobenzenes

An ethanolic solution of nitrobenzene (**3a**, 25 mM) was pumped into the X-Cube reactor system installed with a catalyst cartridge (ARP-Pt: 300 mg; 0.073 mmol Pt) at a flow rate of 1.5 mL/min. The flow hydrogenation of **3a** with H_2 gas (5 vol% of the nanobubbles) was conducted at 25 °C under a system pressure of 14.7 atm. The resulting solution was collected for 7 min (10 mL). A solution of HCl in EtOH (0.15 mL, 2 M) was added and the solvent was removed by evaporation to give aniline hydrochloride **4a•HCl** (99% yield). In the isolation of **4b**, **4c**, **4g**, and **4i**, the resulting EtOH solution from the flow reaction was directly concentrated to give the products.

ICP analysis of the catalyst after flow hydrogenation

After the flow hydrogenation of styrene for 63 h, the used catalyst was removed from the catalyst cartridge. The catalyst was added into aqua regia (5 mL). The solution was heated at 80 °C for 12 h. The resulting solution was diluted with water to a total volume of 50 mL. The aqueous solution was analyzed via ICP.

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Notes and references

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† Electronic Supplementary Information (ESI) available: characterization data and NMR charts for the products. See DOI: 10.1039/b000000x

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13 The Pt loading of ARP was determined by ICP analysis (0.242 mmol/g).

14 The reaction space volume in the catalyst cartridge was determined as follows. A preweighed catalyst cartridge was packed with ARP-Pt (300 mg, 0.085 mmol Pt) and sealed on either end with 8 mm filters. After wetting the cartridge with EtOH, the wet catalyst cartridge was weighed. The reaction volume was determined from the weight difference between the dry and the wet cartridges to be 0.36 mL. Then, the contact time was calculated from the following equation: contact time [sec] = 0.36 [mL; reaction space volume in the catalyst cartridge] x 60 / flow rate [mL/min].

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