A Microfluidic Device for Conducting Gas–Liquid–Solid Hydrogenation Reactions

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Supporting Online Information

Table of Contents

<table>
<thead>
<tr>
<th>Table of Contents</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experimental</td>
<td>S-1</td>
</tr>
<tr>
<td>Determination of the amount of the Pd catalyst</td>
<td>S-3</td>
</tr>
<tr>
<td>Control experiment</td>
<td>S-3</td>
</tr>
<tr>
<td>Average thickness of the liquid thin layer</td>
<td>S-4</td>
</tr>
</tbody>
</table>

Experimental

**General Methods:** $^1$H and $^{13}$C NMR spectra were recorded on a JEOL JNM-LA300, JNM-LA400 or JNM-LA500 spectrometer in CDCl$_3$ unless otherwise noted. Tetramethylsilane (TMS) served as internal standard ($\delta = 0$) for $^1$H NMR, and CDCl$_3$ was used as internal standard ($\delta = 77.0$) for $^{13}$C NMR. All solvents and chemicals were purified based on standard procedures.

**Immobilization of the Pd catalyst on the wall of the microchannel:** A microchannel (200 µm in width, 100 µm in depth, and 40-45 cm in length) was first treated with 1N NaOH aq./ethanol (1/1 (= v/v)), water, ethanol, and methanol successively to wash
and activate the surface of the channel. A 3-aminopropyltriethoxysilane methanol solution (10%, 1.0 mL) was then added slowly to the channel for 15 hours, and the channel was washed with methanol to afford microchannel 3. On the other hand, copolymer 1 (50 mg) and tetrakis(triphenylphosphine)palladium(0) (Pd(PPh₃)₄, 50 mg) were dissolved in dichloromethane (1.0 mL) and t-amyl alcohol (5.0 mL) at room temperature, and the mixture was stirred overnight at this temperature. Pd solution 2 thus prepared (2.0 mL) was added slowly to the channel 3 for 40 hours, and the channel 4 thus prepared was treated with air to remove an excess amount of the solution inside the channel. The microchannel 4 was then heated at ca. 150 °C for 5 hours. This procedure (the addition of the polymer solution and heating) was carried out four times to give the desired Pd-immobilized microchannel.

**Hydrogenation using the Pd-immobilized microchannel:** A typical experimental procedure is described for the hydrogenation of benzalacetone. Through one inlet of the Pd-immobilized microchannel, benzalacetone in THF (0.1 mol/L, 0.5 mL) was added using a syringe pump at a constant speed (0.1 mL/hr). Through the other inlet, H₂ was applied via a massflow controller at a constant flow rate (1 mL/min). The reaction mixture was diluted with hexane at the end of the channel. The reaction was stopped after 5 hours to afford 4-phenyl-2-butanone (97%) and 4-phenyl-2-butanol (3%). The yields were determined by ¹H NMR analysis. After the reaction, the microchannel was washed with hexane and THF, and was reused several times.

**4-Phenyl-2-butanone (I):** ¹H NMR (CDCl₃) δ = 2.12 (s, 3H), 2.74 (t, 2H, J = 7.7 Hz), 2.88 (t, 2H, J = 7.7 Hz), 7.10-7.30 (m, 5H); ¹³C NMR (CDCl₃) δ = 29.6, 29.9, 45.0, 126.0, 128.2, 128.4, 140.9, 207.8.

**4-Phenyl-2-butanol (J):** ¹H NMR (CDCl₃) δ = 1.23 (d, 3H, J = 6.3 Hz), 1.47 (brs, 1H), 1.70-1.84 (m, 2H), 2.55-2.85 (m, 2H), 3.75-3.90 (m, 2H), 7.15-7.33 (m, 5H); ¹³C NMR (CDCl₃) δ = 23.6, 32.1, 40.8, 67.5, 125.8, 128.4, 142.0.

**1,2-Diphenylethane:** ¹H NMR (CDCl₃) δ = 2.90 (s, 4H), 7.10-7.29 (m, 10H); ¹³C NMR
\[ (\text{CDCl}_3) \delta = 37.9, 125.9, 128.3, 128.4, 141.7. \]

**1,4-Diphenylbutane (1):** \(^1\text{H} \text{NMR (CDCl}_3\) \(\delta = 1.65 \text{ (m, 4H), 2.61(m, 4H), 7.10-7.30 \text{ (m, 10 H); \(}^{13}\text{C NMR (CDCl}_3\) \(\delta = 31.1, 35.8, 125.6, 128.2, 128.4, 142.5.}\]

**3-Phenyl-1-propanol:** \(^1\text{H} \text{NMR (CDCl}_3\) \(\delta = 1.85-1.95 \text{ (m, 2H), 2.71 (t, 2H, } J = 7.7 \text{ Hz), 3.68 (t, 2H, } J = 6.4 \text{ Hz), 7.17-7.32 \text{ (m, 5H); \(}^{13}\text{C NMR (CDCl}_3\) \(\delta = 32.0, 34.2, 62.2, 125.8, 128.4, 128.4, 141.8.}\]

**Cyclohexylbenzene:** \(^1\text{H} \text{NMR (CDCl}_3\) \(\delta = 1.21-1.89 \text{ (m, 10H), 2.45-2.52 \text{ (m, 1H), 7.15-7.31 \text{ (m, 5H); \(}^{13}\text{C NMR (CDCl}_3\) \(\delta = 26.2, 26.9, 34.5, 44.6, 125.7, 126.8, 128.3, 148.1.}\]

**2-Methyl-2,4-diphenylpentane (2):** \(^1\text{H} \text{NMR (CDCl}_3\) \(\delta = 1.03 \text{ (d, 3H, } J = 7.1 \text{ Hz), 1.16 (s, 3H), 1.25 (s, 3H), 1.96 (dd, 1H, } J = 14.1, 5.1 \text{ Hz), 2.06 (dd, 1H, } J = 14.1, 7.1 \text{ Hz), 2.50-2.59 \text{ (m, 1H), 7.02-7.31 \text{ (m, 10H); \(}^{13}\text{C NMR (CDCl}_3\) \(\delta = 25.1, 28.2, 31.0, 37.0, 38.4, 52.7, 125.4, 125.5, 126.0, 127.0, 127.9, 128.2, 149.2, 149.3.}\]

**1-Benzyl-3-phenylpropane (3):** \(^1\text{H} \text{NMR (CDCl}_3\) \(\delta = 1.91-1.98 \text{ (m, 2H), 2.70-2.74 \text{ (t, 2H, } J = 7.8 \text{ Hz), 3.48-3.51 \text{ (t, 2H, } J = 6.4 \text{ Hz), 4.51 (s, 2H), 7.17-7.38 \text{ (m, 10H); \(}^{13}\text{C NMR (CDCl}_3\) \(\delta = 31.4, 32.4, 69.5, 72.9, 125.7, 127.5, 127.7, 128.3, 128.4, 128.5, 138.6, 142.0.}\]

**2-Benzyl (2-Phenylethyl)carbamate (4):** \(^1\text{H} \text{NMR (CDCl}_3\) \(\delta = 2.80-2.84 \text{ (t, 2H, } J = 6.9 \text{ Hz), 3.44-3.50 \text{ (m, 2H), 5.10 (s, 2H), 7.17-7.35 \text{ (m, 10H and NH); \(}^{13}\text{C NMR (CDCl}_3\) \(\delta = 36.0, 42.1, 66.5, 126.4, 128.0, 128.4, 128.5, 128.7, 136.5, 138.6, 156.2.}\]

**Phenethylamine:** \(^1\text{H} \text{NMR (CDCl}_3\) \(\delta = 2.71-2.74 \text{ (t, 2H, } J = 6.8 \text{ Hz), 2.93-2.96 \text{ (t, 2H, } J = 6.8 \text{ Hz), 7.18-7.31 \text{ (m, 5H); \(}^{13}\text{C NMR (CDCl}_3\) \(\delta = 40.0, 43.5, 126.0, 128.3, 128.7, 139.7.}\]

**1-Undecanol:** \(^1\text{H} \text{NMR (CDCl}_3\) \(\delta = 0.86-0.90 \text{ (t, 3H, } J = 6.7 \text{ Hz), 1.26-1.33 \text{ (m, 16H), 1.52-1.59 \text{ (m, 2H), 3.62-3.66 \text{ (t, 2H, } J = 6.6 \text{ Hz); \(}^{13}\text{C NMR (CDCl}_3\) \(\delta = 14.1, 22.7, 25.7, 29.3, 29.4, 29.6, 31.9, 32.8, 63.1.}\]

**Ethyl Undecanoate:** \(^1\text{H} \text{NMR (CDCl}_3\) \(\delta = 0.86-0.89 \text{ (t, 3H, } J = 6.8 \text{ Hz), 1.24-1.43 \text{ (m, 17H), 1.57-1.65 \text{ (m, 2H), 2.26-2.30 \text{ (t, 2H, } J = 7.5 \text{ Hz), 4.10-4.15 \text{ (q, 2H, } J = 7.1 \text{ Hz); \(}^{13}\text{C NMR (CDCl}_3\) \(\delta = 14.1, 14.3, 22.7, 25.0, 29.1, 29.26, 29.30, 29.46, 29.55, 31.9, 34.4, 60.1, 173.9.}\]

Determination of the amount of the Pd catalyst immobilized on the
**microchannel:** Pd was loaded on a model microchannel based on the standard method shown above. The model microchannel was then cut into pieces and treated with conc. sulfuric acid and conc. nitric acid at 180 °C for ca. 1 hour. The residue was diluted with water, and ICP analysis was conducted. The amount of the Pd catalyst immobilized on the chip for the reactions was calculated based on the surface area of the channel wall.

**Hydrogenation using Pd on carbon as a catalyst (control experiment):** A 10 mL ordinary flask for laboratory use was used as a reaction vessel with a magnetic stirrer. A solution of 1-phenyl-1-cyclohexene (0.25 mmol, 39.6 mg) in THF (1 mL) was added to a suspension of palladium on carbon (5 wt. % wet type, 28 mol%, 311.4 mg) in THF (1.5 mL) under almost the same H₂ pressure as that in the experiments with the microchannel (almost 1 atm, according to the gauge of the bomb). The mixture was stirred vigorously for 2 min. The mixture was then poured into hexane with a syringe and was treated with a celite filtration. The filtrate was concentrated and dried under reduced pressure. The yield (11%) was determined by \(^1\)H NMR analysis.

**Average thickness of the liquid thin layer:** According to the calculation, average thickness of the liquid thin layer is 18 µm.

**References**