Supplementary Data

Supplementary Data For Expanding the Utility of Flow Hydrogenation – A Robust Protocol Restricting Hydrodehalogenation

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Abstract

A commonly observed limitation of conducting hydrogenations under flow chemistry conditions is hydrodehalogenation. In a bid to circumvent this limitation a series of hydrogenation catalysts were screened, with 5 % Pt/C (sulfided) catalyst identified as an effective catalyst to selectively effect reductive aminations, nitro reduction, and alkene reductions in the presence of halogen atoms. Additionally the optimised protocol to effect reductive aminations, which utilised the ThalesNano H-cube pro™, cleanly reduced an imine functionality in the presence of furan moiety indicating potential amenability with other labile functionalities.

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GRAPHICAL ABSTRACT

Supporting Information

1. GC-MS Traces
2. NMR Spectra
1. GCMS Data

Gas chromatography-mass spectrometry (GC-MS) was performed using a Schimadzu GC-MS QF2010 EI/NCI System fitted with a ZB-5MS column [30 m x 0.25 mm], 5% phenyl-arylene stationary phase. The injector temperature was set at 250 °C and an oven program starting at 160 °C, with a hold time of 1 min. The temperature was then rapidly increased to 230 °C (35 °C/min) and it was held for 18.5 – 22 min. The flow rate was set at 23mL/min, with a column flow rate of 0.95 mL/min.

Table S1: Details of compounds including molecular weight and retention times observed in GC-MS traces (A – K, Table S2).

<table>
<thead>
<tr>
<th>Compound</th>
<th>Structure</th>
<th>Retention Time (mins)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td><img src="image1" alt="Chemical Structure" /></td>
<td>2.15</td>
</tr>
<tr>
<td>10</td>
<td><img src="image2" alt="Chemical Structure" /></td>
<td>1.61</td>
</tr>
</tbody>
</table>

Table S2: Evaluation of commercially available catalysts for the hydrogenation of 7 at 1.0 mL.min⁻¹ flow rate, 50 °C, 50 bar H₂. Reactions were conducted for 10 minutes and analysed using GC-MS.

A. Entry 1, Table 1  
B. Entry 2, Table 1  
C. Entry 3, Table 1  
D. Entry 4, Table 1  
E. Entry 5, Table 1  
F. Entry 6, Table 1
Table S3: Details of compounds including molecular weight and retention times observed in GC-MS traces (A-K, Table S4).

<table>
<thead>
<tr>
<th>Compound</th>
<th>Structure</th>
<th>Retention Time (mins)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td><img src="image" alt="Structure 8" /></td>
<td>2.54</td>
</tr>
<tr>
<td>11</td>
<td><img src="image" alt="Structure 11" /></td>
<td>2.61</td>
</tr>
<tr>
<td>12</td>
<td><img src="image" alt="Structure 12" /></td>
<td>1.86</td>
</tr>
<tr>
<td>13</td>
<td><img src="image" alt="Structure 13" /></td>
<td>1.73</td>
</tr>
</tbody>
</table>
**Table S4**: Evaluation of commercially available catalysts for the hydrogenation of 8 at 1.0 mL.min\(^{-1}\) flow rate, 50 °C, 50 bar H\(_2\). Reactions were conducted for 10 minutes and analysed using GC-MS.

A. Entry 1, Table 2
B. Entry 2, Table 2
C. Entry 3, Table 2
D. Entry 4, Table 2
E. Entry 5, Table 2
F. Entry 6, Table 2
G. Entry 7, Table 2
H. Entry 8, Table 2
I. Entry 9, Table 2
J. Entry 10, Table 2
K. Entry 11, Table 2
**Table S5:** Details of compounds including molecular weight and retention times observed in GC-MS traces (A – K, Table S6).

<table>
<thead>
<tr>
<th>Compound</th>
<th>Structure</th>
<th>Retention Time (mins)</th>
</tr>
</thead>
</table>
| 9        | ![Structure](image1)  
Chemical Formula: C₈H₆BrN  
Molecular Weight: 196.54 | 3.88 |
| 14       | ![Structure](image2)  
Chemical Formula: C₈H₈BrN  
Molecular Weight: 198.06 | 3.45 |
| 15       | ![Structure](image3)  
Chemical Formula: C₈H₇N  
Molecular Weight: 117.15 | 2.47 |
| 16       | ![Structure](image4)  
Chemical Formula: C₈H₉N  
Molecular Weight: 119.16 | 2.23 |

**Table S6:** Evaluation of commercially available catalysts for the hydrogenation of 9 at 1.0 mL.min⁻¹ flow rate, 50 °C, 50 bar H₂. Reactions were conducted for 10 minutes and analysed using GC-MS.
Table S7: Details of compounds including molecular weight and retention times observed in GC-MS traces (A – E, Table S8).

<table>
<thead>
<tr>
<th>Compound</th>
<th>Structure</th>
<th>Retention Time (mins)</th>
</tr>
</thead>
<tbody>
<tr>
<td>17</td>
<td><img src="image" alt="Structure" /> Chemical Formula: C_{7}H_{5}BrO Molecular Weight: 185.02</td>
<td>2.61</td>
</tr>
<tr>
<td>18</td>
<td><img src="image" alt="Structure" /> Chemical Formula: C_{7}H_{5}N Molecular Weight: 107.15</td>
<td>1.80</td>
</tr>
<tr>
<td>22</td>
<td><img src="image" alt="Structure" /> Chemical Formula: C_{14}H_{12}BrN Molecular Weight: 274.16</td>
<td>8.08</td>
</tr>
<tr>
<td>21</td>
<td><img src="image" alt="Structure" /> Chemical Formula: C_{14}H_{13}N Molecular Weight: 195.26</td>
<td>4.49</td>
</tr>
<tr>
<td>24</td>
<td><img src="image" alt="Structure" /> Chemical Formula: C_{7}H_{5}O Molecular Weight: 108.14</td>
<td>1.81</td>
</tr>
<tr>
<td>26</td>
<td><img src="image" alt="Structure" /> Chemical Formula: C_{14}H_{13}N Molecular Weight: 197.28</td>
<td>4.33</td>
</tr>
<tr>
<td>4</td>
<td><img src="image" alt="Structure" /> Chemical Formula: C_{12}H_{12}BrNO Molecular Weight: 266.13</td>
<td></td>
</tr>
</tbody>
</table>
Table S8: Evaluation of hydrogenation reactions in Scheme 3 - 6

A. Scheme 3 results

B. Scheme 4 results

C. Scheme 5 – 10% Pd/C

D. Scheme 5 – 5% Pt/C (sulfided)

E. Scheme 6 results

Table S9: Details of compounds including molecular weight and retention times observed in GC-MS traces (A-C, Table S8 and S9).

<table>
<thead>
<tr>
<th>Compound</th>
<th>Structure</th>
<th>Retention Time (mins)</th>
</tr>
</thead>
<tbody>
<tr>
<td>27</td>
<td><img src="image" alt="Chemical Structure" /> Chemical Formula: C₆H₅BrNO₂ Molecular Weight: 202.01</td>
<td>2.57</td>
</tr>
<tr>
<td>28</td>
<td><img src="image" alt="Chemical Structure" /> Chemical Formula: C₆H₅BrN Molecular Weight: 172.02</td>
<td>2.46</td>
</tr>
<tr>
<td>29</td>
<td><img src="image" alt="Chemical Structure" /> Chemical Formula: C₆H₅N Molecular Weight: 93.13</td>
<td>1.71</td>
</tr>
</tbody>
</table>
**Table S10:** Evaluation of hydrogenation catalysts for selective nitro reduction, conditions were set to 1.0 mL/min flow rate, 30 °C, 30 bar H₂. Reactions were conducted for 10 minutes and analysed using GC-MS.

A. Entry 1, Table 4  
B. Entry 2, Table 4 (10% Pd/C)  
C. Entry 3, Table 4

**Table S11:** Evaluation of residence time for selective nitro reduction, conditions were set to 30 °C, 30 bar H₂ and variable flow rate. Reactions were conducted for 10 minutes and analysed using GC-MS.

A. Entry 1, Table 5  
B. Entry 2, Table 5  
C. Entry 3, Table 5
2. NMR Spectra