Selective hydrogenation of arenes to cyclohexanes in water catalyzed by chitin-supported ruthenium nanoparticles†

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The selective hydrogenation of aromatic compounds to cyclohexanes was found to be promoted by chitin-supported ruthenium nanoparticles (Ru/chitin) under near-neutral, aqueous conditions without the loss of C–O/C–N linkages at benzylic positions.

The catalytic hydrogenation of arenes is a straightforward and hugely important method by which cyclohexanes are produced.1,2 However, a major issue with this transformation is the need to suppress the competitive hydrogenolysis of reactive carbon–heteroatom linkages (e.g. C–O and C–N bonds) at benzylic positions.3,4 Attempts to address this problem typically focus on using acetic acid as a (co-)solvent in the presence of late transition metal catalysts such as PtO2,5 and Rh–PtO2,6 RuO2,7 and Rh/Al2O3.7 The most frequently used catalysts are Ru/Al2O3 or, substantially more expensive, Rh/Al2O3. However, irrespective of the choice of catalyst, the use of acidic reaction media is incompatible with substrates bearing acid-sensitive functionalities such as epoxides and tertiary benzylic alcohols. Recently studied catalysts that have allowed the selective arene hydrogenation of benzylic alcohols or ethers in the absence of acidic additives include Rh/AlO(OH),8b Ru/MCM-41,8b,b Ru/CNF-P,9a,b Rh/CNF-T9c and Ru/HPS-NR3Cl.10 In particular, Motoyama and Nagashima elegantly demonstrated the simultaneous tolerance of epoxide and benzylic C–O functionalities using Rh/CNF-T or Ru/HPS-NR3Cl.9c,d However, with the exception of the Ru/HPS-NR3Cl system, which utilized H2O as a solvent,9d these reactions were typically run in hydrocarbons or polyethylene glycol.10,11

The development of catalytic systems that operate under aqueous conditions remains strongly in demand, since it promises a route to functionalized, water-soluble cyclohexanes for applications in materials and biological sciences.9c,12

We here disclose that chitin-supported ruthenium nanoparticles (Ru/chitin) efficiently catalyze arene hydrogenation under aqueous conditions without hydrogenolyzing C–O/C–N bonds at the benzylic positions.

In recent work we established that Ru/chitin serves as an efficient catalyst for the hydration of nitriles to amides under aqueous conditions.13,14 Based on this result, we reasoned that Ru/chitin should also be suited to the chemoselective hydrogenation of functionalized arenes because the nitrile hydration operated under near-neutral conditions13 and supported ruthenium nanoparticles are known to be good catalysts for arene hydrogenation.6,8,9,b,a,b,10a–d,15 As shown in Table 1, the activity of Ru was tested in the hydrogenation of benzyl glycidyl ether (1a) to cyclohexylmethyl glycidyl ether (2a). This reaction allowed the monitoring of both reactivity and selectivity for arene hydrogenation over hydrogenolysis at the benzylic position or acid-/base-mediated opening of the oxirane ring.9c,e,16 Currently known catalysts effective in this transformation are limited to just two tailor-made systems: Rh/CNF-T (rt, 12 h)9c and Ru/HPS-NR3Cl (30 °C, 24 h).15,17 Ru/chitin can be prepared by simple impregnation–reduction using inexpensive RuCl3·3H2O, NaBH4 and commercially available chitin under aqueous conditions and in the absence of capping agents.13 Results demonstrate that the hydrogenation of 1a was effectively catalyzed by Ru/chitin. When a mixture of 1a (1.0 mmol), H2O (5 mL) and Ru/chitin (0.8 wt%, 0.008 mmol of Ru, 0.8 mol% Ru) was stirred at 50 °C under a H2 atmosphere (2 MPa), the hydrogenation was completed within 1.5 h and cyclohexane 2a was obtained in 98% yield (Table 1, entry 1). ICP-AES on the Ru/chitin catalyst before and after the hydrogenation cycle established that only negligible leaching of Ru (4.2 ppm) took place during the catalytic test. The hydrogenation proceeded in water with no detectable loss of the C–O linkages in the substrates, there being no appreciable formation of side products 3a–6a. This result was reproducible (1H NMR yields of 2a in separate runs: 97, 95, and 97%). Product 2a could be isolated in 84%...
yield after removal of the catalyst and SiO₂ column chromatography, with Ru contamination proving lower than the detection limit of ICP-AES (<1 ppb). Results demonstrate that both ruthenium and chitin were necessary for selective arene hydrogenation (entry 1 vs. entries 2–5). Moreover, heterogeneous catalysts prepared analogously to Ru/chitin but using cellulose, chitosan, γ-Al₂O₃, or carbon promoted arene hydrogenation but with lower selectivity (entries 6–9). Among these, hydrogenation with Ru/cellulose¹² was also found to be distinctly effective, although appreciable amounts of side-products were formed through hydrogenolysis (Table 1, entry 6). Results obtained using commercially available catalysts are summarized in entries 10–14. Rh/Al₂O₃ (Sigma-Aldrich) proved efficient (2a: 92% yield) but induced partial hydrogenolysis to 3a or 4a (entry 11). Lastly, Ru/C (TCI)¹⁸ was also a moderately good catalyst (2a: 87% yield) but caused competing epoxide ring-opening (entry 12).¹⁹

Results in Table 2 demonstrate that Ru/chitin-promoted selective arene hydrogenation was compatible with benzylic C–O or C–N linkages in alcohol, ether, amide and amino functionalities in a wide range of substrates (1b–kNa). The corresponding cyclohexanes 2b–kNa were obtained in good-to-excellent isolated yields, with the products typically being isolated by distillation or column chromatography after simply removing the catalyst by filtration or centrifugation. Hydrogenation of significantly acid-sensitive benzylic alcohols 1d and

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Conv. of 1a (%)</th>
<th>Yield of 2a (%)</th>
<th>Combined yield of 3a (%)</th>
<th>Combined yield of 4a (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ru/chitin</td>
<td>&gt;99</td>
<td>&gt;98</td>
<td>&lt;1</td>
<td>&lt;1</td>
</tr>
<tr>
<td>2</td>
<td>None</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>&lt;1</td>
</tr>
<tr>
<td>3</td>
<td>Chitin</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>&lt;1</td>
</tr>
<tr>
<td>4</td>
<td>RuCl₃·3H₂O</td>
<td>&gt;99</td>
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<td>6</td>
<td>12</td>
</tr>
<tr>
<td>5</td>
<td>RuO₂</td>
<td>1</td>
<td>&lt;1</td>
<td>1</td>
<td>&lt;1</td>
</tr>
<tr>
<td>6</td>
<td>Ru/cellulose</td>
<td>&gt;99</td>
<td>97</td>
<td>2</td>
<td>&lt;1</td>
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<tr>
<td>7</td>
<td>Ru/chitosan</td>
<td>47</td>
<td>41</td>
<td>&lt;1</td>
<td>&lt;1</td>
</tr>
<tr>
<td>8</td>
<td>Ru/γ-Al₂O₃</td>
<td>40</td>
<td>36</td>
<td>3</td>
<td>&lt;1</td>
</tr>
<tr>
<td>9</td>
<td>Ru/C</td>
<td>51</td>
<td>43</td>
<td>4</td>
<td>1</td>
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<tr>
<td>10</td>
<td>Ru/Al₂O₃</td>
<td>19</td>
<td>15</td>
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<tr>
<td>11</td>
<td>Rh/Al₂O₃</td>
<td>&gt;99</td>
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<td>5</td>
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<tr>
<td>12</td>
<td>Ru/C⁰</td>
<td>&gt;99</td>
<td>87</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>13</td>
<td>Rh/C⁰</td>
<td>&gt;99</td>
<td>24</td>
<td>25</td>
<td>38</td>
</tr>
<tr>
<td>14</td>
<td>Pd/C⁰</td>
<td>96</td>
<td>&lt;1</td>
<td>25</td>
<td>69</td>
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<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate (1)</th>
<th>Conv. (%)</th>
<th>Product (2)</th>
<th>Yield (%)</th>
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<tbody>
<tr>
<td>1</td>
<td>(R)-1Na</td>
<td>&gt;99</td>
<td>2b</td>
<td>90 [66]</td>
</tr>
<tr>
<td>2</td>
<td>(S)-1e</td>
<td>&gt;99</td>
<td>2b</td>
<td>95 [92]</td>
</tr>
<tr>
<td>3</td>
<td>(S)-2e</td>
<td>&gt;99</td>
<td>2d</td>
<td>90 [88]</td>
</tr>
<tr>
<td>4</td>
<td>(S)-2f</td>
<td>&gt;99</td>
<td>2e</td>
<td>79 [75]</td>
</tr>
<tr>
<td>5</td>
<td>(R)-2fNa</td>
<td>&gt;99</td>
<td>2ea</td>
<td>85 [82]</td>
</tr>
<tr>
<td>6</td>
<td>1h</td>
<td>&gt;99</td>
<td>2g</td>
<td>99 [93]</td>
</tr>
<tr>
<td>7</td>
<td>1g</td>
<td>&gt;99</td>
<td>2h</td>
<td>97 [95]</td>
</tr>
<tr>
<td>8</td>
<td>1iHCl</td>
<td>&gt;99</td>
<td>2i-HCl</td>
<td>96 [91]</td>
</tr>
<tr>
<td>9</td>
<td>(S)-1jHCl</td>
<td>&gt;99</td>
<td>2kNa</td>
<td>96 [90]</td>
</tr>
</tbody>
</table>

Table 1: Hydrogenation of 1a to 2a

Table 2: Catalytic hydrogenation of arenes (1) to cyclohexanes (2) with Ru/chitin

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1. ruthenium and chitin were necessary for selective arene hydrogenation (entry 1 vs. entries 2–5).
2. Determined by ¹H NMR using mesitylene as an internal standard.
3. GC-MS yield using n-octane as an internal standard.
4. Purchased from commercial suppliers.
The reusability of the Ru/chitin catalyst was tested over seven consecutive reductions of 1a, with the catalyst being recovered by centrifugation each time. Results indicated only a modest loss of catalytic activity and selectivity (hydrogenation of 1a: 1st run, 98% yield; 2nd run, 96% yield; 3rd run, 94%; 4th run, 90%; 5th run, 89%; 6th run, 87%; 7th run, 87%, Table S4†). This behavior was investigated by HRTEM analysis (Fig. 1). Analysis after either 1 or 6 hydrogenation cycles suggested that the nanoparticles continued to incorporate pristine metal, with an observed d-spacing of 2.14–2.17 Å attributed to the Ru(002) plane of Ru. However, nanoparticle sintering was clearly observed after repeated testing, with the mean particle size growing from 2.3 ± 0.3 nm in the fresh catalyst (Fig. 1a) to 3.5 ± 0.8 nm after 6 hydrogenation cycles (Fig. 1c). TEM, EDX and XRD analyses of the as-prepared Ru catalysts (Fig. S1–S9†) suggest that 2–3 nm nanoparticles represent both the most efficient and selective of the catalysts tested. Interestingly, results point to the inexpensive polysaccharide supports chitin and cellulose accommodating such particles (Table S5 and Fig. S10†) more readily than other commercially available supports do when using the same preparative route. Though one commercially sourced Ru/C catalyst

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate (1) (conditions)</th>
<th>Conv. (a) (%)</th>
<th>Yield (c) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>(S)-1Na (100 °C, 6 h)</td>
<td>&gt;99</td>
<td>95 [91]</td>
</tr>
<tr>
<td>4d</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6e</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2f</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The hydrogenation of toluene (3a) by Ru/chitin in water showed a turnover frequency (TOF) of 6000 h⁻¹ and a turnover number (TON) of 3000 based on the amount of consumed H₂ (eqn (1)). These values are higher than or comparable to those in previously reported hydrogenations of 3a in water with other Ru or Rh catalysts (Ru: TOF and TON, 10–2700 h⁻¹ and 240–2700; Rh: 100–11 000 h⁻¹ and 300)."
contains comparably-sized nanoparticles, the selectivity is lower than Ru/chitin or Ru/cellulose (Fig S8 and Table S5).

In summary, we have prepared 2–3 nm chitin-supported ruthenium nanoparticles in the absence of additional capping agents. They have promoted efficient hydrogenation of arenes to cyclohexanes under near-neutral, aqueous conditions, with hydrogenation taking place to the exclusion of hydrogelenolysis of normally reactive C–O and C–N linkages. Of importance, preliminary data point to the use of this readily available, environmentally benign support material being synonymous with the generation of nanoparticles whose dimensions provide both excellent conversion and selectivity. Ongoing work is seeking to more precisely investigate morphological changes exhibited by Ru/chitin in order to counteract the modest loss of activity after multiple hydrogenation cycles and to assess the possibility of developing these systems in a microfluidic context.

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Notes and references


During the review process for this manuscript, arene hydrogenation of benzyl ethers by the Ru/carbon-nitrogen matrix was reported: X. Cui, A.-E. Surkus, K. Junge, C. Topf, J. Radnik, C. Kreyenschulte and M. Beller, Nat. Commun., 2016, 7, 11326.


16 2a can also be a (co-)monomer for preparing epoxide resins.

17 (a) Ref 9c: 1a (0.5 mmol), Rh/CNF-T (10 mg, 0.2 wt% Rh, 0.04 mol% Rh), H2 (1 MPa), n-hexane (1 mL), rt, 12 h; 2a, >99% yield; (b) Ref 9d: 1a (1 mmol), Ru/HPS-NR3Cl (0.3 mol% Ru), H2 (3 MPa), H2O (1 mL), 30 °C, 24 h; 2a, 96% yield.


19 The origin of high selectivity in the hydrogenation of 1a with Ru/chitin remains unclear. Coordination of hydroxyl groups in chitin to the Ru metal does not seem to suppress catalytic activity for side reactions; the selectivity in the hydrogenation with Rh/Al2O3, Ru/C or Rh/C was not significantly altered by adding ethylene glycol (Table S2,† entries 1–3). Meanwhile, the coordination of acetamide groups to the Ru metal may partly account for the high selectivity of Ru/chitin; addition of N-acetylethanolamine increased the selectivity for arene hydrogenation with Rh/C (Table S2,† entry 5).


21 The reason for a small amount of racemization in Table 2, entries 2 and 9 is not entirely clear, but we assume it to result from dehydrogenation of alcohol or amine-HCl followed by hydrogenation of the resulting ketones and iminium salts. This view is based on the following observations: (1) in Table 2, entry 4, ketone 6e formed in 7% yield; (2) hydrogenation of acetophenone with Ru/chitin under the standard conditions yielded cyclohexyl methyl ketone (20%), 1c (27%) and 2c (52%).

22 Hydrogenation of dibenzyl ether (100 °C, 6 h, 91% conv.) gave a mixture of bis(cyclohexylmethyl) ether (27%), benzyl cyclohexylmethyl ether (38%), 2b (7%) and other unidentified products. Hydrogenation of dibenzylamine-HCl (100 °C, 5 h, >99% conv.) gave a mixture of bis(cyclohexylmethyl)amine-HCl (21%) and 2i-HCl (74%).