

## Transfer hydrogenation using recyclable polyurea-encapsulated palladium: efficient and chemoselective reduction of aryl ketones

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A robust and recyclable palladium catalyst [Pd<sup>0</sup>EnCat] has been prepared by ligand exchange of polyurea-encapsulated palladium(II) acetate with formic acid, resulting in deposition of Pd(0) in the support material; Pd<sup>0</sup>EnCat is shown to be a highly efficient transfer hydrogenation catalyst for chemoselective reduction of a wide range of aryl ketones to benzyl alcohols.

Reduction of ketones to alcohols is a synthetically important transformation, both in the laboratory and in industry. A large number of stoichiometric metal hydride reagents have been developed to effect this transformation and efforts toward further improvements continue.<sup>1,2</sup> The development of homogeneous catalysts for the reduction of carbonyl compounds using molecular hydrogen or other hydrogen donors has attracted special attention. Ruthenium-complex catalysed hydrogenation or transfer hydrogenation have proved to be particularly reliable.<sup>3,4</sup> However, the current emphasis on cleaner methods for chemical transformations requires high selectivity, low cost, easy separation and production of minimum waste. One of the recent highlights in this area involved the uncatalysed hydrogen-transfer reductions of ketones at elevated temperature.<sup>5</sup> From a practical point of view a more attractive approach is to develop a heterogeneous catalyst that is efficient for this transformation. Although the reduction of aliphatic ketones using heterogeneous catalysts remains an unanswered challenge, it has been shown that aryl ketones can be reduced, typically by Pd/H<sub>2</sub>.<sup>6</sup> The major problem associated with this system has been the further hydrogenolysis of the initially formed benzyl alcohol and the over-reduction of the aromatic ring.<sup>6</sup> This was circumvented by adding ethylenediamine.<sup>7</sup> However, this makes isolation of the product and recycling the catalyst problematic.

Palladium(II) acetate microencapsulated in polyurea [PdEnCat<sup>TM</sup>] has been demonstrated to be an accomplished recyclable catalyst for a number of key transformations.<sup>8–10</sup> As part of the continuous effort to develop environmentally benign catalytic systems, it was decided to prepare polyurea-encapsulated Pd(0) [Pd<sup>0</sup>EnCat] from [PdEnCat<sup>TM</sup>]<sup>11</sup> and investigate whether this could provide a solution to the heterogeneous transfer hydrogenation of aryl ketones. Our initial efforts were directed to establishing an efficient preparative procedure for [Pd<sup>0</sup>EnCat] that would not only exhibit high reactivity but also resist leaching. It emerged quickly that formic acid was the best reducing reagent to produce a catalyst meeting both of these criteria. It is clear that the rate of the deposition of the Pd(0) increases when the concentration of formic acid in ether is raised, and a 1 : 1 mixture of formic acid and ether was found to be the best choice.<sup>12</sup> Further investigations were carried out to establish the optimal reaction conditions. It was found that better performance in terms of reactivity and stability of the catalyst was achieved by using HCOOH, Et<sub>3</sub>N in the molar ratio of 1 : 1 (instead of 5 : 2 used conventionally for other catalysts).<sup>13</sup> The stability of the catalyst was further improved by adding ethyl acetate as a solvent.

The efficiency and stability of the newly established catalytic system was examined in detail with acetophenone as a substrate. Reduction proceeds to completion giving excellent isolated

yields through five successive recycle runs (Table 1). Pleasingly, no traces of methylene compounds from further hydrogenolysis or products from the over-reduction of the aromatic ring were detected by either NMR or GC. A clear advantage of this catalyst over Pd/C was also noticed when propiophenone was reduced using Pd/C (10%) under otherwise identical conditions. (Scheme 1).

The newly prepared catalyst [Pd<sup>0</sup>EnCat] is clearly more reactive than Pd/C with higher conversion within the same reaction time (Table 2). A mechanistic study was conducted to probe the electronic property of this palladium catalyst by using a reported assay.<sup>14</sup> It was found the metal centre is more electron rich than Pd/C, which could account for this superior catalytic property.<sup>15</sup>

The scope of this catalytic method was established by using a wide range of aryl ketones and in all cases the reactions reach completion within 21–48 h with exceedingly high yields (Table 2). It is worth noting that the hetero-aromatic ketones are also reduced in almost quantitative yields.

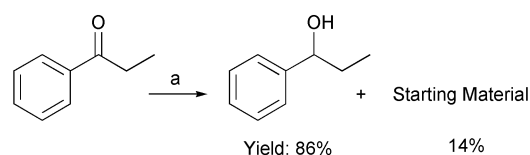
The selective and rapid reduction of nitro groups in the presence of carbonyl functionalities is also a highly valuable transformation in organic synthesis. The development of an efficient catalytic system to achieve this goal has attracted considerable effort recently.<sup>16</sup> Therefore it was decided to investigate whether [Pd<sup>0</sup>EnCat] could provide a better solution to this challenge. The result showed that [Pd<sup>0</sup>EnCat] mediated transfer hydrogenation can effect highly efficient reduction of nitro groups in the presence of carbonyl functionalities (Scheme 2). Importantly, the chemoselectivity was found to be significantly higher than Pd/C catalysed transfer hydrogenation (99% vs. 85%).<sup>17</sup>

In summary, a highly efficient heterogeneous palladium catalyst [Pd<sup>0</sup>EnCat] for transfer hydrogenation was prepared by treatment of [PdEnCat<sup>TM</sup>] with HCOOH leading to deposition

Table 1 Recycling experiments<sup>a</sup>

Run	1	2	3	4	5
Yield (%)	99	98	98	97	96
Time/h	21	22	24	26	28

<sup>a</sup> Reagents and conditions: 10 mol% Pd<sup>0</sup>-EnCat, 200 μL EtOAc, 0.8 mmol HCOOH, 0.8 mmol Et<sub>3</sub>N, 0.016 mmol acetophenone, 24 °C.



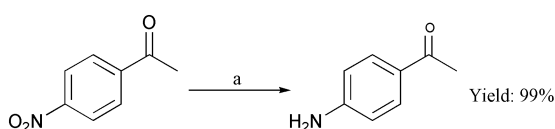
Scheme 1 (a) Reagents and conditions: 10 mol% Pd/C (10%), 200 μL EtOAc, 0.8 mmol HCOOH, 0.8 mmol Et<sub>3</sub>N, 0.016 mmol Propiophenone, 24 °C, 22 h.

of Pd(0) in the polyurea support material. This catalyst has been proven to be highly efficient and chemoselective in the reduction of carbonyl and nitro groups. The stability of the catalyst has also been demonstrated convincingly by conducting

**Table 2** Reduction of aromatic ketones using Pd<sup>0</sup>-EnCat/HCOOH/Et<sub>3</sub>N<sup>ab</sup>

Entry	Ketone	Reduced product	Time/h	Yield (%)
1			21	99
2			22	97
3			36	90
4			48	99
5			48	90
6			68	99
7			48	95
8			24	92
9			48	94
10			18	99
11			18	99

<sup>a</sup> Reagents and conditions: 10 mol% Pd<sup>0</sup>-EnCat, 200 μL EtOAc, 0.8 mmol HCOOH, 0.8 mmol Et<sub>3</sub>N, 0.016 mmol Ketone, 24 °C. <sup>b</sup> Catalyst was reused for 5 times.



**Scheme 2** (a) Reagents and conditions: 10 mol% Pd<sup>0</sup>-EnCat, 200 μL EtOAc, 0.8 mmol HCOOH, 0.8 mmol Et<sub>3</sub>N, 0.016 mmol acetophenone, 24 °C, 2.5 h.

five successive runs without an obvious drop in the reaction rate. Further application of the newly constructed catalytic system to many other key transformations are currently being explored.

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- The Pd(OAc)<sub>2</sub> polyurea encapsulated catalyst PdEnCat™ is available from Dr D. Pears, Avesial Ltd., P. O. Box 42, Hexagon House, Blackley, Manchester M9 82S. The cross-linking of the polyurea is ensured by the addition of ethylene diamine and the material takes the form of spherical microcapsules. The average loading of Pd is determined by Inductively Coupled Plasma (ICP) MS to be approximately 0.4 mmol g<sup>-1</sup>.
- Preparation of Pd<sup>0</sup>EnCat: 0.5 g PdEnCat™ was introduced to a mixture of 3 mL diethyl ether and 1 mL formic acid. The reaction mixture was allowed to reflux for 5 hours with vigorous stirring. The solvent was removed by pipette. The black beads (100–200 microns) were washed by diethyl ether and dried under vacuum overnight.
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