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Palladium on graphene: the *in situ* generation of a catalyst for the chemoselective reduction of α,β-unsaturated carbonyl compounds†

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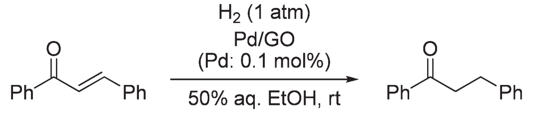
Palladium-supported graphene oxide has been successfully applied as a catalyst precursor for the selective reduction of α,β-unsaturated carbonyl compounds. Pd nanoparticles were formed during the course of the reduction with only negligible leaching of the Pd species into the reaction mixture.

The selective reduction of an olefin in the presence of other reactive functional groups represents a challenging task for the synthesis of fine chemicals. The most promising method currently available for this transformation involves the use of a palladium species as a catalyst. Palladium on activated carbon (Pd/C) is widely used as a heterogeneous catalyst, both in the laboratory and on the industrial scale, because of its high catalytic activity and ease of handling. Unfortunately, however, the level of chemoselectivity exhibited by Pd/C can sometimes be low, especially when it is applied to starting molecules containing several reducible functionalities, where mixtures of multi-reduced products can be obtained.[1] To overcome the problem of chemoselectivity, various additives, such as pyridine,[2] ethylenediamine,[3] and sulfur-containing compounds[4] have been used in combination with Pd/C. Furthermore, a range of inorganic oxides[5] and organic polymers[6] have been used as supports for the Pd to provide idiosyncratic functions. Disappointingly, however, these protocols have tended towards a reduction in the catalytic activity of Pd.

As part of our own work towards the development of improved catalytic systems, we developed an interest in the use of graphene oxide (GO) as a support for a Pd species.[7] GO is a carbon nanosheet with a one carbon atom-thickness (*ca.* 0.8 nm), good solubility in water and polar solvents, high surface area (>2000 m^2 g^{-1}), and high strength.[8] GO possesses a variety of different oxygen-containing functionalities, such as hydroxy, epoxy, and carboxyl groups, and it was envisaged that these groups would be able to coordinate to the Pd species and prevent them from aggregating and leaching.[9] Similar to clay minerals, GO readily undergoes interlayer swelling and exfoliation, and is therefore suitable for the preparation of nanocomposites.[10] As related to its pronounced cation exchange capacity and intercalation ability, GO can be regarded as an ideal catalyst support material and a host for the intercalation of catalytically active Pd species.

Our initial investigation began with an evaluation of several different Pd precursors in the presence of GO for their ability to chemoselectively reduce C=C and C=O moieties using chalcone (**1**) as a model substrate. $Pd(OAc)_2$ was found to be the optimum catalyst precursor because of its appropriate solubility in the reaction solvent, ligand exchange ability, and the ease of Pd(0) formation (Table 1, entries 1–4). The results of time course analyses of the selective hydrogenation reactions revealed that the yields increased dramatically after 2 h (Table 1, entries 5–7). The reduction of Pd(II) to Pd(0) occurred during the induction period,

Table 1 Investigation of palladium precursors for the chemoselective reduction of chalcone (**1a**)[a]



1a **2a**

Entry	Pd precursor	Time (h)	Yield (%)[b]
1	$Pd(OAc)_2$	24	99
2	$PdCl_2$	24	63
3	$Pd(acac)_2$	24	22
4	$Pd(NO_3)_2$	24	42
5	$Pd(OAc)_2$	2	10
6	$Pd(OAc)_2$	4	57
7	$Pd(OAc)_2$	12	95

[a] General conditions: Pd/GO (Pd 0.1 mol%), **1a** (0.3 mmol), H_2O (1.5 mL), and EtOH (1.5 mL) were mixed and stirred under a H_2 atmosphere (1 atm, balloon). [b] The yields were determined by GC using dodecane as an internal standard.

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† Electronic supplementary information (ESI) available: Experimental procedure and product data. See DOI: 10.1039/c3ra42150c

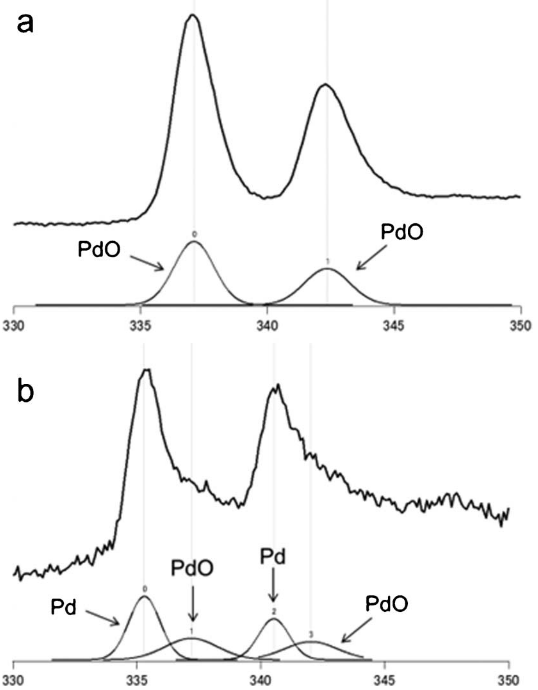


Fig. 1 XPS spectra of Pd/GO in the Pd 3d region (a) before and (b) after the hydrogenation reaction.

which was supported by X-ray photoelectron spectroscopy (XPS) analysis of the palladium species on the GO support (Fig. 1).

It is noteworthy that the catalytic activity of the Pd(II)/GO precatalyst remained largely unchanged six months after its initial preparation, because similar Pd(II) species, $Pd(OAc)_2$, quickly forms Pd black in the presence of EtOH. Furthermore, these samples had been stored in air at ambient temperature to allow greater ease of handling, providing an excellent demonstration of the overall stability and robust nature of this catalyst. Analysis of the structure of Pd(II)/GO by transmission electron microscopy (TEM) revealed that the Pd(II)/GO precatalyst prepared from $Pd(OAc)_2$ did not form any particles (Fig. 2a), indicating that a ligand exchange reaction had occurred on the GO involving the exchange of an acetate for carboxylate.[11] In contrast, Pd nanoparticles with an average diameter of 6 nm were observed on the recovered catalyst (Fig. 2b). Interestingly, the GO was also reduced during the process to form reduced graphene oxide (rGO) (Fig. 3).[12] Residual oxygen-containing functionalities (19%, determined by XPS survey scan) must have remained in the rGO to stabilize the Pd nanoparticles, because pure graphene cannot be used as a support for metal nanoparticles.[13] The potential leaching of Pd species into the reaction mixture was analyzed by inductively coupled plasma mass spectrometry (ICP-MS). Thus, upon completion of the reaction, the solvents and products were removed under vacuum with heating, and the resulting residue was treated with concentrated nitric acid before being analyzed by ICP-MS. The results revealed only 19 ppb (0.18 wt% of the initial Pd) was leached into the reaction mixture. Encouraged by this result, the recyclability of the catalyst was studied for the reduction

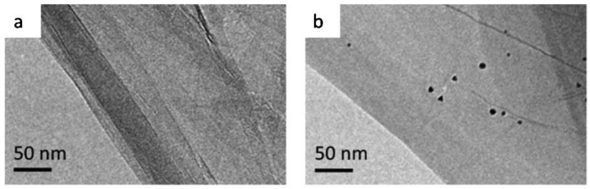


Fig. 2 TEM image of Pd/GO (a) before and (b) after the hydrogenation reaction.

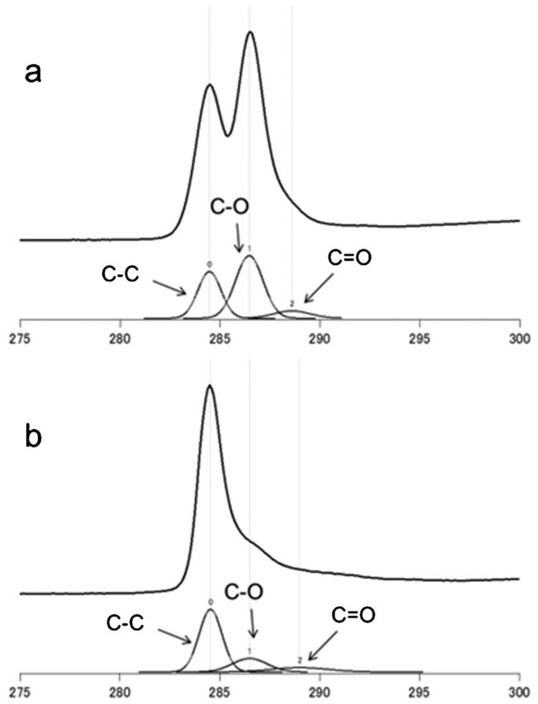
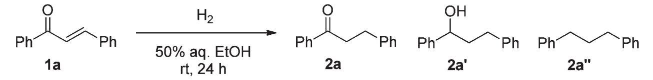


Fig. 3 XPS spectra of Pd/GO at C 1s region (a) before and (b) after the reaction.

Table 2 Optimization of the reduction of chalcone (**1a**)[a]



Entry	H_2 (atm)	T (°C)	Catalyst	Yield (%)[b] 2a	2a′	2a′′
1	1	25	Pd/GO	>99	0	0
2	5	25	Pd/GO	>99	0	0
3	5	60	Pd/GO	>99	0	trace
4[c]	1	25	Pd/GO	95	0	0
5[d]	1	25	Pd/C	5	87	3
6	1	25	Pt/C	99	0	0
7[d]	1	60	Pt/C	0	66	17
8	1	25	Pt/GO	99	0	0
9[d]	1	60	Pt/GO	0	90	10

[a] General conditions: Pd (0.1 mol%), **1a** (0.3 mmol), H_2O (1.5 mL), and EtOH (1.5 mL) were mixed and stirred under a H_2 atmosphere. [b] The yields were determined by GC using dodecane as an internal standard. [c] EtOH was used as a solvent. [d] The yields were determined by NMR.

Table 3 Substrate scope of Pd/GO-catalyzed selective reduction[a]

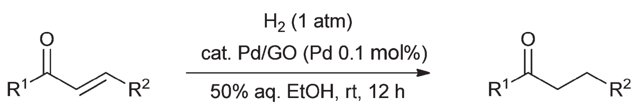
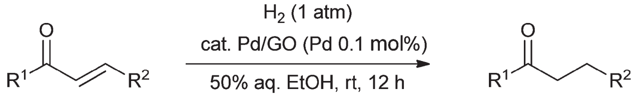
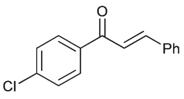
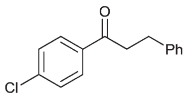
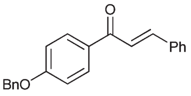
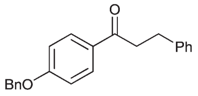
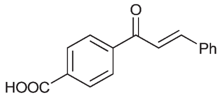
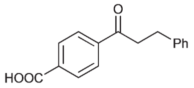
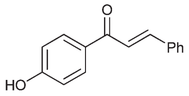
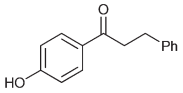
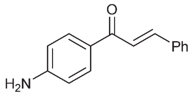
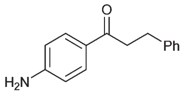
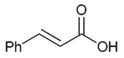
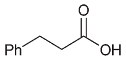
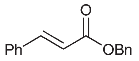
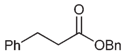
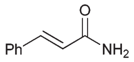
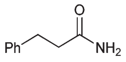
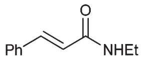
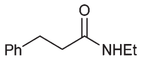
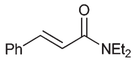
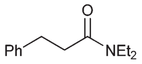
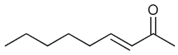
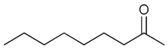
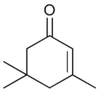
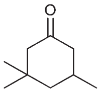
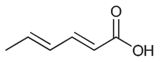
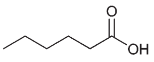
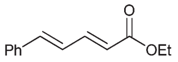
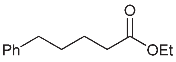
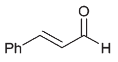
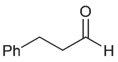
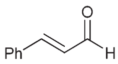
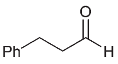


Table 3 (Continued)



Entry	Substrate	Product	Yield (%)[b]
1	 **1b**	 **2b**	96
2	 **1c**	 **2c**	100
3[c]	 **1d**	 **2d**	92
4	 **1e**	 **2e**	96
5	 **1f**	 **2f**	89
6[c]	 **1g**	 **2g**	92
7	 **1h**	 **2h**	99
8	 **1i**	 **2i**	93
9	 **1j**	 **2j**	100
10	 **1k**	 **2k**	98
11	 **1l**	 **2l**	88
12[d]	 **1m**	 **2m**	100
13[c]	 **1n**	 **2n**	84
14[d]	 **1o**	 **2o**	98
15	 **1p**	 **2p**	75[e]
16[f]	 **1p**	 **2p**	98[g]

[a] General conditions: Pd (0.1 mol%), **1** (0.3 mmol), H_2O (1.5 mL), and EtOH (1.5 mL) were mixed and stirred under a H_2 atmosphere. [b] Isolated yield. [c] THF was used as the solvent. [d] 0.5 mol% of Pd was used. [e] The corresponding alcohol was obtained in 20% yield. [f] A mixture of DMA (1.5 mL), H_2O (0.75 mL), and EtOH (0.75 mL) was used as the solvent system. [g] The corresponding alcohol was obtained in 2% yield.

of chalcone (**1a**). The reaction mixture was centrifuged three times with THF, and the recovered catalyst was then used without any reactivation process to give **2a** in quantitative yield. We have confirmed that the catalyst could be reused at least five consecutive times without any reduction in the yield of the product or the chemoselectivity.

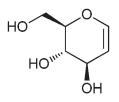
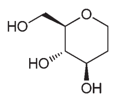
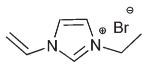
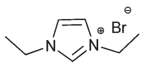
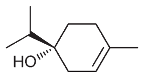
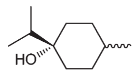
When the Pd(II)/GO precatalyst prepared from Pd(OAc)$_2$ was used for the reduction of chalcone **1a**, the olefin moiety of **1a** was selectively reduced to give **2a** (Table 2, entry 1). The catalyst showed excellent selectivity, even when the reaction was performed under 5 atm of H_2 (Table 2, entry 2) or at 60 °C (Table 2, entry 3). Although the effect of water remains unclear, the yield of **2a** was reduced slightly when only EtOH was used as the reaction solvent (Table 2, entry 4). In contrast, commercial Pd/C provided a mixture of multi-reduced products (**2a**, **2a′**, and **2a′′**) (Table 2, entry 5) and effectively demonstrated the importance of the GO support to the observed selectivity of the reduction reaction. The replacement of Pd with Pt also provided **2a** selectively at ambient temperature (Table 2, entries 6 and 8). Unfortunately, however, the carbonyl and hydroxy groups were also reduced in the presence of Pt at 60 °C (Table 2, entries 7 and 9).

With the optimized conditions in hand, we investigated the substrate scope of this selective reduction (Table 3). 4′-Chlorochalcone (**1b**) was selectively reduced to **2b** without any loss of the chlorine atom (Table 3, entry 1). In contrast, however, the application of the optimized conditions to 4′-bromochalcone resulted in a mixture of debrominated products. When benzyloxy (**1c**), carboxyl (**1d**), hydroxy (**1e**), or amino (**1f**) groups were attached to the 4′-position of the chalcone, the reaction proceeded smoothly and selectively at the olefin moiety (Table 3, entries 2–5). The olefin moiety of an α,β-unsaturated carboxylic acid (**1g**) was also successfully reduced when the solvent was changed to THF to inhibit the formation of an ester in the presence of EtOH (Table 3, entry 6). A benzyl ester (**1h**), which is a common protecting group for carboxylic acids, was not deprotected through the selective reduction of olefin moiety (Table 3, entry 7). Furthermore, primary (**1i**), secondary (**1j**), and tertiary (**1k**) amides all were well tolerated under the optimized conditions (Table 3, entries 8, 9 and 10, respectively). Compounds bearing alkyl substituents at both ends of the α,β-unsaturated carbonyl moiety did not inhibit the reaction (Table 3, entries 11 and 12). Unfortunately, the selective mono-reduction of diene system proved difficult and both the olefins were eventually completely reduced without any loss of the carbonyl group (Table 3, entries 13 and 14). The selective reduction of an α,β-unsaturated aldehyde proved to be a more challenging reaction.[14] When the optimized conditions were applied to the α,β-unsaturated aldehyde (**1p**), both the olefin and carbonyl groups were reduced to give a mixture of the aldehyde (**2p**) and the corresponding alcohol (Table 3, entry 15). It has been reported that the solvent can control the chemoselectivity,[15] therefore, various solvents were examined (See ESI†). Pleasingly, the chemoselectivity of the process could be enhanced by adding *N*,*N*-dimethylacetamide (DMA) to give **2p** in high yield (Table 3, entry 16).

We then investigated the potential for further expanding the substrate scope of the selective olefin reduction process. Given that GO is hydrophilic, it was envisaged that substrates bearing polar or ionic functional groups would show a high level of affinity for the catalyst (Table 4). D-Glucal (**3a**), possessing three hydroxy groups, was successfully reduced under the optimized conditions without any loss of its hydroxy groups nor deactivation of the catalyst (Table 4, entry 1). An imidazolium salt (**3b**), which represents a framework widely employed in ionic liquids, was also reduced without any deactivation of the catalyst (Table 4, entry 2). In addition, a diastereoselective reduction was achieved when (−)-terpinen-4-ol (**3c**) was employed as a substrate (Table 4, entry 3), likely because of a hydrogen bonding interaction with an oxygen-containing functional group on the GO. The application of commercial Pd/C catalyst under the same conditions produced a 6 : 4 mixture of diastereomers.

Table 4 Expanded substrate scope of the Pd/GO-catalyzed reduction[a]

$$\text{Substrate} \xrightarrow[\text{50\% aq. EtOH, rt, 12 h}]{\text{H}_2\text{ (1 atm)}\ \ \text{Pd-GO (Pd: 0.1 mol\%)}} \text{Reductant}$$

Entry	Substrate	Product	Yield (%)[b]
1	 **3a**	 **4a**	96
2	 **3b**	 **4b**	98
3[c]	 **3c**	 **4c**	100 (85 : 15)[d]

[a] General conditions: Pd (0.1 mol%), **3** (0.3 mmol), H_2O (1.5 mL), and EtOH (1.5 mL) were mixed and stirred under a H_2 atmosphere (1 atm). [b] Isolated yield. [c] 0.5 mol% of Pd was added. [d] The ratio of diastereomers was determined by GC.

Conclusions

We have achieved the preparation of a reactive, selective, and recyclable Pd/GO precatalyst for the reduction of α,β-unsaturated carbonyl compounds. The active catalyst species, Pd(0) nanoparticles on rGO, is formed during the catalytic reaction, and can be recycled without any leaching or aggregation of the Pd species. The existence of minimal essential amounts of oxygen functionalities on graphene would effectively coordinate to Pd species, enhancing the chemoselectivity and stability of Pd nanoparticles.

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