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A metal nanoparticle-based supramolecular approach for aqueous biphasic reactions†

Shilpa C. Mhadgut,[a] Kumaranand Palaniappan,[a] Muralidhara Thimmaiah,[a] Stephen A. Hackney,[b] Béla Török*[a] and Jian Liu*[a]

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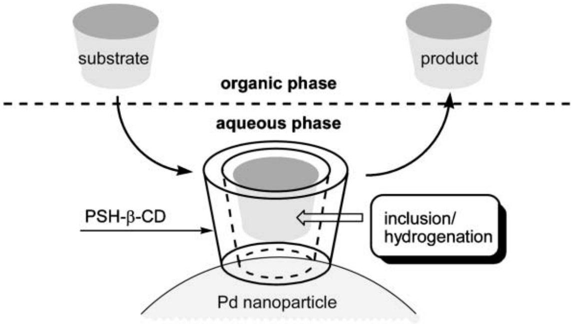
β-cyclodextrin immobilized on Pd nanoparticles was successfully employed as an efficient phase-transfer catalyst in aqueous biphasic hydrogenation reactions.

Aqueous/organic biphasic catalytic hydrogenations[1] have received much attention due to increased economic and environmental concerns on chemical production. A major problem encountered in these systems is the lack of phase-transfer efficiency of hydrophobic substrates to the catalytic species in aqueous media. In addition, the catalysts are currently limited to the water-soluble organometallic species. In recent years, dispersed metal nanoparticles were successfully used as a new type of catalyst[2] for various reactions in mono- or biphasic systems.[3] However, aqueous biphasic reactions catalyzed by metal nanoparticles have not been fully explored. Here, we report a new concept of using artificial host immobilized on metal nanoparticle as an efficient phase transfer catalyst for aqueous biphasic reactions. In particular, this proof-of-concept model system was demonstrated by water-soluble, β-cyclodextrin-modified Pd nanoparticles (β-CD/Pd) in biphasic hydrogenation reactions. We expect that this study may serve as a showcase in the development of new generation of multifunctional metal catalysts by the combination of the best features of supramolecular chemistry (molecular recognition) and nanoparticles (high surface-to-volume ratio).

It has already been shown that metal nanoparticles[4] can act not only as functional components in various nanomaterials, but also as scaffolds for the construction of molecular structures on their surfaces. Self-assembly of molecular receptors on particle surfaces leads to supramolecular structures capable of engaging in molecular recognition at the interface between the solution and particles.[5] Cyclodextrins (CDs)[6] are well-known molecular hosts capable of including small hydrophobic molecules inside their cavities in aqueous media, which leads to many applications in the food and pharmaceutical industries. It was observed that self-assembly of CDs on nanoparticles would bring these nanoscale entities the ability to hold hydrophobic molecules on their surfaces.[7] In this sense, inverse phase transfer of hydrophobic molecules from organic phase onto the surface of nanoparticles in aqueous media would be possible. Consequently, aqueous biphasic reactions with water-insoluble substrates catalyzed by CD-modified metal nanoparticles would be facilitated (Scheme 1). We selected β-CD/Pd as a model catalyst to test our hypothesis.



Scheme 1 Catalytic inverse phase transfer/hydrogenation of hydrophobic substrate in aqueous biphasic system

These nanoparticles were prepared by the attachment of PSH-β-CD[8] (Chart 1) to the surface of Pd particles during the particle formation (ESI†). The surface coverage of β-CD on these particles (3 nm in diameter) is estimated as 50% (elemental analysis).

3,3,5-Trimethyl-2-cyclohexenone (isophorone) was used as the first substrate for the hydrogenation of the carbon–carbon bond in aqueous media (Scheme 2) since we investigated this reaction recently in the presence of different catalysts in organic media.[9] For comparison, Pd-black (ESI†) was used as a reference catalyst in this study. Hydrogenation of isophorone was completed (Table 1) within two hours in the presence of β-CD/Pd in water (ESI†). In contrast, only 2% yield was achieved if 10 mg of Pd black was used as catalyst under identical conditions. Such difference was due to the aqueous medium and not the poor quality of Pd black. In fact, 100% yield was achieved for the hydrogenation of isophorone with same amount of Pd black in ethanol under the same reaction conditions, which was consistent

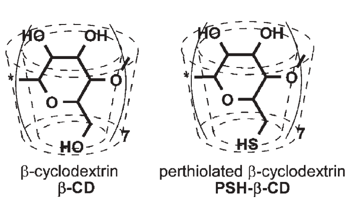
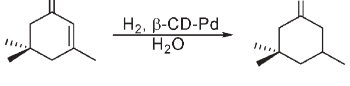


Chart 1 Structure of molecular hosts in this work.



Scheme 2 C=C double bond hydrogenation of isophorone in an aqueous biphasic system

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† Electronic supplementary information (ESI) available: details of β-CD/Pd preparation and characterization. Reaction conditions and characterization of hydrogenation reaction products. See http://www.rsc.org/suppdata/cc/b5/b502181b/

*btorok@mtu.edu and jianliu@mtu.edu (Béla Török)

Table 1 Catalytic C=C double bond hydrogenation of isophorone in the presence of β-CD/Pd or Pd black catalysts in aqueous and organic media[a]

entry	catalyst	solvent	additive	yield
1	β-CD/Pd	ethanol	-	25%
2	Pd black	ethanol	-	100%
3	β-CD/Pd	water	-	100%
4	Pd black	water	-	2%
5	β-CD/Pd	water	adamantane	45%
6	β-CD/Pd	water	1 mg β-CD	100%
7	β-CD/Pd	water	10 mg β-CD	100%

[a] reactions were performed in 5 mL of solvent under 20 bar hydrogen pressure at 25 °C for 2 hours.

with the results reported earlier.[9] The 25% yield provided by β-CD/Pd in ethanol was attributed to the partial block of active surface with surface-anchored β-CD. Thus a 250-fold increase (Fig. 1, entry A and B) in the reaction turnover frequency (TOF, h^{-1}) by β-CD/Pd was achieved in this aqueous biphasic system, as compared to Pd black. We propose that this enhancement originates mainly from an efficient transfer of hydrophobic organic substrate onto the surface of Pd nanoparticles by including these molecules inside the surface-attached β-CDs. Consequently; a more effective hydrogenation process is achieved.

We then selected adamantane (denoted as **AD**), an efficient guest molecule forming complex with β-CD in water, to test this hypothesis. Introduction of 1 mmol **AD**, (same amount as substrate), in the reaction mixture, including β-CD/Pd and isophorone, dramatically decreased the TOF and yield of hydrogenation under the same reaction condition (Table 1, entry 5 and Fig. 1, entry C). The adamantane molecules effectively competed with the substrate to the available CD binding sites on Pd particles resulting in a decrease in the hydrogenation rate. This experiment verified that the host–guest complexation of hydrophobic substrate with β-CD on Pd particles was the major driving force for the enhancement of catalytic efficiency. Such driving force was lost in an organic solvent as the reaction medium leading to a lower catalytic activity of β-CD/Pd, which was observed in the ethanol case.

We believe that the efficiency of hydrogenation was improved not only by the presence of β-CD, but also by the unique geometric arrangement of β-CD on Pd nanoparticle surfaces. The proximity of binding site (the cavity of β-CD) to the catalytic site (the surface of Pd nanoparticle) further enhanced the overall catalytic efficiency, which resembles the case of catalysis by natural enzymes. Addition of 1 mg free β-CD (Chart 1), (an approximately equivalent amount to the β-CD attached to Pd particles), to the reaction mixture of β-CD/Pd and isophorone in water did not change the TOF of the hydrogenation (Table 1, entry 6; Fig. 1, entry D). Introduction of 10 mg free β-CD only reduced the original TOF by 10% (Table 1, entry 7; Fig. 1, entry E). In a control experiment, the combination of free β-CD with Pd black in the same hydrogenation reaction did not provide the same enhancement in the TOF as observed in β-CD/Pd.‡ We suggest that the process of complexation and hydrogenation of substrate on β-CD/Pd particle surfaces was so efficient that the alternative path through the complexation of substrate with free β-CD and then diffusion to the surface of Pd nanoparticles was negligible. Direct complexation of substrate next to the catalytic site on particles eliminates the kinetic barrier of diffusing free β-CD/isophorone complex to the surface of Pd particles. Consequently, a synergistic effect between β-CD (phase transfer catalyst) and Pd nanoparticle (hydrogenation catalyst) on the overall catalytic process was achieved. As pointed out in the introduction, the major motivation to use aqueous biphasic systems for hydrogenation is to reduce the use of organic solvents. The catalyst reuse and/or regeneration are, however, also important questions in developing new applications. As such we have studied the recyclable character of our catalyst. The activity of our model catalyst has been tested during several cycles using the same test reaction (hydrogenation of isophorone, Scheme 1). It was found that after five consecutive reactions with the same catalyst, its activity remained the same.

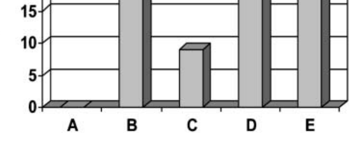


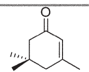
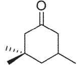
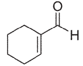
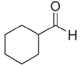
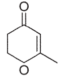
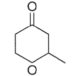
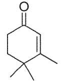
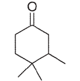
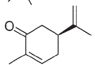
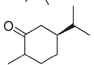
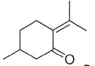
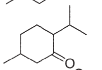
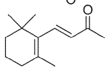
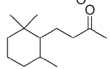
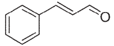
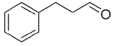
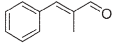
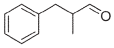
Fig. 1 Relative turnover frequency (TOF, h^{-1}) as compared with Pd black (A) for the hydrogenation of isophorone (1 mmol) in the presence of 10 mg of catalyst in aqueous biphasic media. (A) Pd black, 0.1 h^{-1}; (B) β-CD/Pd, 26 h^{-1}; (C) β-CD/Pd + 1 mmol of **AD**, 9 h^{-1}; (D) β-CD/Pd + 1 mg of free β-CD, 25 $\text{h}^{-1}$and (E) β-CD/Pd + 10 mg of free β-CD, 23 h^{-1}.

After the mechanistic study hydrogenation of two basic substrate groups were investigated such as selective C=C double bond hydrogenation of unsaturated carbonyl compounds and C=N double bond hydrogenation of imines. For the first part of the study several aliphatic and cyclic unsaturated carbonyl compounds have been selected. The hydrogenations have been carried out under the same experimental conditions used in Table 1. Table 2 summarizes the experimental results. Most substrates under this survey could be hydrogenated in excellent to good yields by β-CD/Pd within two hours in aqueous medium under mild reaction conditions. These results clearly indicate the generally applicable nature of our catalyst.

The results of hydrogenation of imines are tabulated in Table 3. As shown most amines readily underwent selective hydrogenation to form the expected secondary amines. The results indicate that the presence of strongly electron-withdrawing substituents lower the yields slightly. A comparison of the present results to another recent study on imine hydrogenation with supported Pd catalysts also highlights the activity of the β-CD/Pd catalyst.[10] As a limitation of the catalyst we mention that β-CD/Pd cannot catalyze C=O double bond hydrogenations. As these reactions normally do not occur on Pd catalysts our observation is in agreement with the literature.

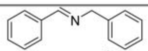
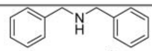
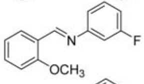
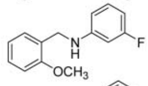
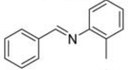
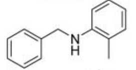
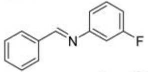
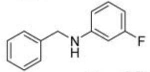
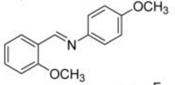
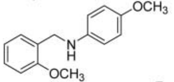
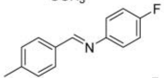
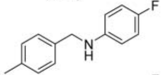
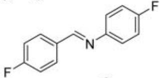
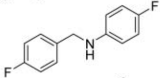
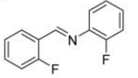
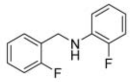
In summary, water-soluble, β-cyclodextrin(β-CD)-modified Pd nanoparticles (β-CD/Pd) were successfully used as a multifunational nanocatalyst for the hydrogenation of various hydrophobic substrates in an aqueous biphasic system. A unique feature of this catalytic system is that the aqueous phase serves as the only reaction medium. Thus, the water-soluble nanoparticle catalyst is not contaminated by organic substrates after the reaction and can be recycled for the next catalytic process. In addition, organic solvents are completely eliminated from the reaction mixture. The

Table 2 Catalytic C=C double bond hydrogenation of unsaturated carbonyl compounds in the presence of β-CD/Pd catalyst in aqueous medium[a]

entry	substrate	product	time (h)	Yield (%)
1			2	100
2			2	100
3			1	100
4			1.5	90
5			5	70
6			5	85
7			5	71
8			2	99
9			2	91

[a] reactions were performed in 5 mL of water by using 10 mg of β-CD/Pd catalyst and 1 mmol of substrate under 20 bar hydrogen pressure at 25 °C for the required time.

Table 3 Catalytic C=N double bond hydrogenation of imines in the presence of β-CD/Pd catalyst in aqueous medium[a]

entry	substrate	product	time (h)	yield (%)
1			1	100
2			1	100
3			1	100
4			3	71
5			1	81
6			1	72
7			1	82
8			1	85

[a] reactions were performed in 5 mL of water by using 10 mg β-CD/Pd catalyst and 1 mmol of substrate under 20 bar hydrogen pressure at 25 °C using for the required time. *products of secondary hydrogenolysis

second phase is actually composed of the organic substrate. Taken together, the elimination of the organic solvents from the reaction media and the no contamination of aqueous phase, this new approach is in line with the fundamental principles of green chemistry. It represents a new route for the development of efficient and sustainable catalytic processes. Most importantly, the concept of integration of molecular phase-transfer catalyst with metal nanoparticle catalyst into a dual-functional heterosupramolecular nanocatalyst represents a new approach in the development of nanoparticle-based catalysts for future applications.

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Shilpa C. Mhadgut,[a] Kumaranand Palaniappan,[a]
Muralidhara Thimmaiah,[a] Stephen A. Hackney,[b] Béla Török*[a] and Jian Liu*[a]
[a] *Department of Chemistry, Michigan Technological University, 1400 Townsend Drive, Michigan 49931, USA. E-mail: btorok@mtu.edu and jianliu@mtu.edu; Fax: 906-487-2061*
[b] *Department of Materials Science and Engineering, Michigan Technological University., 1400 Townsend Drive, Michigan 49931, USA*

Notes and references

‡ We thank one of the reviewers for this suggestion.

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