

Highly Active, Selective, and Recyclable Water-Soluble Glutathione-Stabilized Pd and Pd-Alloy Nanoparticle Catalysts in Biphasic Solvent

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Glutathione-protected Pd, PdAu and PdPt nanoparticles (NPs) show greatly increased reactivity and stability towards the hydrogenation/isomerization of allyl alcohol in a biphasic organic/aqueous solvent mixture compared to single-phase alkanethiol-protected Pd-based NPs. NPs synthesized under aerobic conditions have higher activity compared to those synthesized under nitrogen, with the highest TOF of 676 mole product/mole metal/hour for 75:25 PdAu NPs at 20 mL/min H₂ flow. 75:25 PdAu NPs prepared under nitrogen have a

Introduction

Recent developments in nanotechnology have led to the synthesis of advanced materials with desirable reactivity as well as optical and electronic properties that have use in many applications, such as H₂ storage, drug delivery, sensing, and catalysis.^[1-3] The unique electronic structure and properties of nanoparticles (NPs) are largely due to the high surface area-tovolume ratio along with low coordination number of the surface atoms of NPs. This leads to size-dependent properties very different from the bulk materials. These properties brand NPs as a suitable candidate for the catalysis of a variety of organic reactions. The key issue is to obtain maximum catalytic efficiency by controlling the NP size, shape, composition and functionality, which can be accomplished by using various organic stabilizers, such as polymers,^[4] dendrimers,^[5] peptides,^[6] and ligands.^[7] The big challenge is to find a protecting stabilizer that prevents irreversible aggregation under the reaction conditions, but also allows high catalytic activity and controlled selectivity.

Transition metal NPs in solution have been frequently used over a solid support for catalyzing a variety of organic and inorganic reactions.^[8–10] While it is easy to separate the catalyst

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maximum TOF of 507 at 20 mL/min H_2 flow, but can be recycled 4 times (9 times at 8 mL/min H_2 flow). Ethyl acetate is a better organic phase solvent compared to dichloromethane and chlorobenzene in terms of TOF and recyclability. All of the NPs studied show >80% selectivity for the isomer product (propanal). The branched, open structure of the glutathione and use of the biphasic solvent provides high catalytic activity, high selectivity, and easy removal of the products in the organic phase for good recyclability of the water-soluble catalysts.

from the reaction products, heterogeneous systems often suffer from low turnover frequency (TOF), limited lifetime and poor selectivity, primarily due to the principle of diffusion and the involvement of two different phases in the catalytic system.^[11] Also, their complex method of preparation and poor particle morphological control^[1,12] has redirected studies on homogeneous systems. Homogeneous systems have recently drawn great interest due to their potential for higher activity and selectivity.^[13,14] Some of the current problems include leaching of delicate core metals and imperfect recycling and recovery. Homogeneous NPs with weak stabilizers often have high activity but become unstable in solution, leading to changes in size and morphology, dissolution, aggregation, or precipitation.

These stability issues can be addressed by synthesizing metal NPs with dendrimers, polymers or surfactants.^[15,16] Another option is the use of organic ligand stabilizers, such as thiols,^[7] phosphines,^[17] amines^[18] or ammonium salts.^[19] The ligands usually form a monolayer coating on the NP surface and provide control over the core size of the NPs^[20] and the solubility and catalytic activity.^[21] The NPs are usually highly stable and can be stored as solid powders, but often suffer significantly from lower catalytic activity due to the blocking of reactive sites.^[22] Crooks and co-workers reported the synthesis and substrate size-selective catalytic activity of various Pd NPs encapsulated within poly(amidoamine) dendrimers of different generations and different end groups.^[23] Steric crowding on the dendrimer periphery led to lower TOF for larger substrates. Also, PdPt and PdAu dendrimer-encapsulated alloy NPs had higher catalytic activity (TOF = 200-1500 mole H₂/mole metal/ hour) than dendrimer-encapsulated Pd, Au, or Pt single metal NPs (TOF = 0-800 mole H_2 /mole metal/hour) for the hydrogenation of allyl alcohol. The work of Sadeghmoghaddam et al. represents an example of thiol ligand-stabilized Pd NPs for catalysis, where they focused on understanding the mechanism and regioselectivity of hexanethiolate- and dodecanethiolate-



capped Pd NPs in different environments. They found that both hydrogen and the type of solvent are essential for the catalytic isomerization reaction.^[24] Shon and co-workers reported the synthesis of dodecanethiolate-capped Pd NPs, by employing a Bunte Salt precursor, for the hydrogenation of allyl alcohol.^[20] They showed that alkanethiolate-coated Pd and PdAu NPs selectively catalyze the isomerization of allyl alcohol over hydrogenation, where the reaction was 80% complete after one hour.^[25,26] Our group showed the same result of high isomerization selectivity but low reactivity for hexanethiolatecoated Pd NPs.^[18] In comparison, long chain alkylamine stabilizers were much more active, but less stable and more difficult to separate from the products.^[18] More recently, Shon and co-workers investigated the water-soluble ω -carboxyl-1hexanethiolate-capped (PdNP-1) and ω-carboxyl-1-octanethiolate-capped (PdNP-2) Pd NPs as micelle biphasic catalysts for hydrogenation and isomerization of 1-octen-3-ol, which showed a TOF of 1.43 site ${}^{-1}h^{-1}$ based on the active site of PdNP-1.^[27] Recyclability studies for PdNP-1 showed similar activity and 63-73% hydrogenation selectivity for up to 3 cycles. These examples show that strong stabilizing ligands on the Pd NPs surface leads to fairly stable NPs, but often give modest TOFs due to their metal-ligand interactions.

Here we describe the synthesis of Pd and Pd-alloy (PdAu and PdPt) NPs coated with glutathione (Glu) ligands for use in catalyzing the hydrogenation/isomerization of allyl alcohol as a model system. We hypothesized that the more open and branched Glu structure would improve the accessibility to the Pd surface, improving the catalytic activity, while the strong Pdthiol interaction would provide stability and isomerization selectivity as observed for other non-polar alkanethiol-coated Pd NPs. While the Glu ligand has not been as widely studied as other thiols, there are examples of Glu-stabilized $Au^{[28]}$ and $Pt^{[7]}$ NPs for homogeneous^[7] and heterogeneous^[28] catalysis. In the case of Pt, use of the Glu stabilizer did not lead to a higher TOF compared to alkanethiols.^[7] Glu-stabilized Pd NPs have been specifically studied previously for use as a homogeneous catalyst for the hydrogenation of nitroarenes in the aqueous phase^[29] and for the synthesis of heterogeneous NPs anchored onto metal oxides, such as ZnO and TiO2.[30] Chen and coworkers used Glu-stabilized PdAu NPs supported on carbon sheets as an oxygen reduction reaction (ORR) electrocatalyst after calcination while Niu et al. combined Glu Pd NPs with carbon microspheres for methanol oxidation electrocatalysis. Guan et al. combined Glu Pd NPs with hydrogels to improve the activity of a heterogeneous porous catalyst. In our work, we use a single-phase synthesis of Glu Pd, PdAu, and PdPt NPs under both inert and oxygen conditions.[31] Control was further explored by varying the composition of different metals to synthesize bimetallic alloy NPs. Furthermore, the catalytic properties of Pd and Pd-alloy NPs were studied in different biphasic solvent systems to obtain further insights into the role of solvent and ligand structure on the stability, activity and selectivity of these NPs. We also studied the recyclability of Glucoated NPs synthesized under inert and oxygen conditions. This research provides insight into factors that control the optimum catalytic performance, in terms of activity, selectivity, and recyclability, of Pd NPs stabilized with open, branched thiols operating under biphasic solvent conditions.

Results and Discussion

Pd Nanoparticle Synthesis and Characterization. To design a catalyst with high stability, efficiency and recyclability, we synthesized Pd and Pd alloy NPs by co-reduction of Pd with Au or Pt salts in different metal compositions [Pd:(Au or Pt) in 90:10, 75:25 and 50:50 ratios] in the presence of glutathione (Glu) under both inert and oxygen atmosphere as shown in Scheme 1. Sharma et al.[31] showed that Pd NPs synthesized under oxygen causes expansion in their lattice parameter from 3.88 Å to 4.12 Å due to the incorporation of oxygen. We hypothesized that the presence of oxygen in the lattice might result in different catalytic behavior due to different substrate or hydrogen binding properties caused by different metal-metal distance and potential electronic effects. All NPs were characterized using ¹H NMR and FTIR spectroscopy to show the attachment of ligands to the metal core of the NPs. TGA analysis of Pd-Glu (Inert) NPs, for example, gave a 25.6% organic composition and 74.4% Pd metal. The diameter of Pd-



Scheme 1. Single-phase synthesis of water-soluble glutathione-coated Pd and Pd-alloy NPs.

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Glu NPs was 1.8 ± 0.3 nm and 2.6 ± 0.5 nm for inert and oxy NPs, respectively, based on TEM analysis while the (50:50) Pd:Au-Glu NPs were 2.3 ± 0.5 nm and 2.1 ± 0.6 nm for inert and oxy NPs, respectively (Figure S1 and S2, supporting information), consistent with the literature.^[31] The exact composition of the alloy NPs was not determined. We assumed that bimetallic alloy NPs formed with a composition similar to the synthesis ratio based on the different catalytic activity for the pure Pd and Pd alloy NPs and based on previous results of Pd alloy NPs synthesized by co-reduction.^[18,32-34]

Hydrogen stability of glutathione-coated Pd NPs. Since hydrogen is one of the reactants in the hydrogenation/isomerization reaction of allyl alcohol, it was important for the NPs to be stable under a hydrogen atmosphere. Molecular hydrogen gets reversibly adsorbed on the surface of Pd where it rapidly dissociates into atomic hydrogen and then diffuses into the metal lattice and occupies octahedral interstitial sites.^[35] This increases the lattice constant. At low hydrogen partial pressure, α -phase PdH_x forms, which undergoes a phase transition into β phase PdH_x at higher hydrogen partial pressure.^[36,37]

We determined the stability of the aqueous solutions of Pd-Glu (Inert) and Pd-Glu (Oxy) NPs by monitoring the UV-Vis absorbance spectra of their solutions from 200–900 nm as a function of exposure time to pure hydrogen bubbling through the solution at a flow rate of 19.9 ± 0.7 mL/min as shown in Figure 1. Due to the strong binding of Glu ligands with Pd NPs, the NPs showed a very similar spectrum for at least 2 hours, confirming that they were stable against hydrogen-induced aggregation. Interestingly, the same trend was observed for Pd-alloy NPs with Au and Pt with different ratios confirming that Glu ligands provide stability against hydrogen-induced aggregation (data not shown). The UV-Vis spectra of these small Glu-coated Pd NPs shows an exponential decay in absorbance with an increase in wavelength and lack any surface plasmon resonance bands.

We also studied the stability of Pd-Glu (Inert) NPs and Pd-Glu (Oxy) NPs against hydrogen-induced aggregation under the biphasic condition of chlorobenzene and nanopure water in the presence of allyl alcohol at 19.9 ± 0.7 mL/min H₂ flow rate for 0, 5, 15, 30, 60, 120, 240 minutes using UV-Vis spectroscopy as shown in Figure S3 in the Supporting Information. UV-Vis spectra show Pd-Glu (Inert) NPs to be comparatively more stable than Pd-Glu (Oxy) NPs based on the lower overall absorbance at 250 nm and appearance of a fairly well-defined peak in this region for the latter, which is due to chlorobenzene, propanal, Pd(II)-thiolate species, or some combination (Figure S4 of supporting information shows their UV-vis spectra). The peak is better defined in this area due to greater instability of the Pd-Glu (Oxy) NPs by aggregation, precipitation, or Pd(II) formation, all of which would decrease the absorbance from the original NPs in the region. In both Pd-Glu NP samples, the absorbance at high wavelengths drops to some degree, but the overall stability is fairly good, although better for Pd-Glu (inert) NPs.

Biphasic catalysis with glutathione-coated NPs. We monitored the homogeneous biphasic liquid-liquid catalysis and selectivity for the hydrogenation/isomerization of allyl alcohol

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Figure 1. UV-Vis plots of absorbance vs. wavelength for exposure time 0– 120 min to 100% hydrogen bubbling through solutions of Pd-Glu (Inert) (A) and Pd-Glu (Oxy) NPs (B). Insets shows pictures of solutions without hydrogen at 0 minute and with hydrogen after 120 minutes.

(Scheme 2) with various Glu-coated Pd- and Pd-alloy NPs and compared them to previous work by others and our lab.^[18,20,25-27,32] The set-up is shown in Figure S5 of supporting information. Figure 2 shows several GCs of the aqueous and organic phase at different times up to 25 min during the reaction of allyl alcohol with H₂ (19.9 \pm 0.7 mL/min) catalyzed by Pd-Glu (Oxy) NPs. In the aqueous phase, the peak corresponding to allyl alcohol with a retention time (t_r) of 4.4 minutes decreased with time, eventually disappearing by 25 minutes, whereas the peaks corresponding to propanal and 1-propanol at t_r of 1.5 and 3.6 minutes, respectively, increased with time. In the organic phase, the peak heights for both products also increased with time as the allyl alcohol peak height decreased and eventually vanished completely by 25 minutes.

Qualitatively, the data clearly show that the catalyst is highly selective to the isomerization product, propanal, based on the much higher intensity for that peak in the GC compared to the peak for 1-propanol. A comparison of the peak intensities of the aqueous versus the organic phases shows that the products favor the organic phase more, which makes it easy to separate the products from the aqueous-soluble catalyst. This allows



Scheme 2. Illustration shows the biphasic catalytic reaction of allyl alcohol with hydrogen using various glutathione-coated nanoparticles.



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Figure 2. Example of biphasic catalysis using Pd-Glu (Oxy) NPs with 2 mL nanopure water and 2 mL chlorobenzene using 19.9 ± 0.7 mL/min H₂ flow rate for 25 minutes. GC-FID chromatograms of the aqueous phase (A) and organic phase (B) after 0, 5, 10, 15, 20 and 25 minutes as indicated.

easy recovery and reuse of the catalyst for several cycles. Control experiments using UV-vis and GC show that we can extract all 1-propanol and propanal from the aqueous phase into the organic phase for easy product separation (Figure S5 and S6).

Table 1 shows the turnover frequencies (TOF) for all synthesized Pd and Pd-alloy NPs at 19.9 ± 0.7 mL/min H₂ flow rate using chlorobenzene as the organic solvent along with the aqueous phase. The catalytic activities of Pd:Au NPs are higher

than Pd NPs at all compositions, generally increasing TOF with an increasing amount of Au in the NP. For Pd:Pt NPs, the activity is smaller than Pd for 10% Pt, about the same for 25% Pt, and higher for 50% Pt. Also, the alloy Pd:Au and Pd:Pt NPs synthesized under oxygen atmosphere showed higher catalytic activity than the same NPs synthesized under inert conditions. In the case of pure Pd NPs, the activity was about the same for those synthesized under oxygen or inert conditions. The presence of other metal helps to increase the rate of the reaction, especially for oxygen synthesized Pd-alloy NPs. Pd:Au-Glu (Inert/Oxygen) NPs in all ratios showed higher TOFs than Pd:Pt-Glu (Inert/Oxygen) NPs with the same ratio. We believe the higher electronegativity of Au (2.54) compared to Pt (2.28) is the main reason for the bigger improvement in the overall catalytic activity compared to Pd only (2.20). Increased electronegativity of the second metal makes the Pd more electropositive and can improve substrate binding through the olefin group.^[34] Also, the addition of the second metal may alter the geometry of the crystal lattice, allowing for more active sites to be available for catalysis that provides multiple binding/ interacting points with the substrate and/or hydrogen, increasing the rate of product formation.^[33,34] All NPs showed a high selectivity of >80% for the isomerized product. (75:25) Pd:Au-Glu (Oxy) NPs showed the highest TOF of 590 moles of product/mole metal/hour. It is interesting that the water-soluble Glu ligand leads to high selectivity for the isomerization product as previously shown for organic-soluble alkanethiols^[18] but the TOF is 2-6 times higher, likely due to the open structure of the Glu ligands compared to alkanethiols.

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Role of different hydrogen flow rates on TOF and selectivity of the catalytic reaction. It is important to study the effect of flow rates of hydrogen on the TOF and the selectivity of the overall reaction in order to better understand the reaction and optimize the turnover. We used 3 different flow rates of 100% hydrogen (8.0 ± 0.2 , 19.9 ± 0.7 and 39.9 ± 0.3 mL/min) and chlorobenzene/aqueous biphasic solvent system for Pd-Glu (Inert/Oxygen) NPs. It was observed that the TOF increased from 8.0 ± 0.2 to 39.9 ± 0.3 mL/min as shown in Table 2, whereas the selectivity didn't change.

We also studied the kinetics of the catalytic reaction for Pd-Glu (Inert) NPs by observing the total percentage completion of the reaction with time (minutes) at different hydrogen flow rates $(8.0\pm0.2, 19.9\pm0.7 \text{ and } 39.9\pm0.3 \text{ mL/min})$ using chlor-



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Table 1. Table of turnover frequencies (TOF) in mole product/mole total metal/hour and selectivity towards hydrogenated and isomerized products for all synthesized Pd and Pd-allov NPs under inert/oxygen conditions at 19.9 ± 0.7 mL/min H₂ flow rate using chlorobenzene organic solvent with aqueous phase.

Synthesiz		i a anoy i	i s unaci n	icit/oxygei	i contaition	15 at 19.9 ±	0.7 1112/11	111112 11	Sw fate usi	ing chilorob	chizene org	unic solven	e with aque	ous phuse.
	50:50 Pd:Pt- Glu (Oxy)	50:50 Pd:Pt- Glu (Inert)	75:25 Pd:Pt- Glu (Oxy)	75:25 Pd:Pt- Glu (Inert)	90:10 Pd:Pt- Glu (Oxy)	90:10 Pd:Pt- Glu (Inert)	Pd- Glu (Inert)	Pd- Glu (Oxy)	90:10 Pd:Au- Glu (Inert)	90:10 Pd:Au- Glu (Oxy)	75:25 Pd:Au- Glu (Inert)	75:25 Pd:Au- Glu (Oxy)	50:50 Pd:Au- Glu (Inert)	50:50 Pd:Au- Glu (Oxy)
Hyd TOF	36	20	26	31	30	7	14	11	20	56	22	66	29	39
lso TOF	216	215	186	150	142	95	191	189	398	435	305	524	380	510
Overall TOF	252	235	212	181	172	102	205	200	418	491	327	590	409	549
Hyd % Iso %	17 83	10 90	13 87	22 78	16 84	11 89	10 90	7 93	9 91	15 85	8 92	16 84	9 91	10 90

Table 2. Effect of flow rates of 100% hydrogen (8.0 ± 0.2 , 19.9 ± 0.7 and 39.9 ± 0.3 mL/min) on turnover frequencies (TOF) in mole product/mole Pd/hour and selectivity of the overall catalytic reaction using Pd-Glu (Inert/Oxygen) NPs.

Hydrogen flow-rates [mL/min]	8.0 ± 0.2		19.9±0.7		39.9±0.3		
Nanoparticles	Pd-Glu (Inert)	Pd-Glu (Oxy)	Pd-Glu (Inert)	Pd-Glu (Oxy)	Pd-Glu (Inert)	Pd-Glu (Oxy)	
Hydrogenation TOF	5	9	14	11	13	20	
Isomerization TOF	152	183	192	120	291	293	
Overall conversion TOF	157	192	206	201	304	313	
Hydrogenation [%]	5	8	10	7	6	9	
Isomerization [%]	95	92	90	93	94	91	

obenzene/aqueous biphasic solvent system. It clearly showed that at 8.0 ± 0.2 mL/min flow rate, it took 5 minutes for the NPs to become catalytically active as compare to higher flow rates which showed activity from the beginning of the reaction as shown in Figure S7 in the Supporting Information. While increased H₂ flow rate increased the TOF for the pure Pd NPs, it became clear that the stability is compromised for the higher flow rates, reducing the potential for recyclability. For this reason, we did not test all of the alloy NPs at the higher flow rates.

Solvent effects in the biphasic mixture. We studied dichloromethane (DCM), chlorobenzene (Clben) and ethyl acetate (EtOAc) as organic solvents for the biphasic solvent mixture to optimize the reaction using the (75:25) Pd:Au-Glu (Inert/Oxy) NPs as our model catalysts at a H₂ flow rate of 19.9 \pm 0.7 mL/min as shown in Table 3. Preliminary experiments indicated that the (75:25) Pd:Au-Glu NPs were highly active and among the most stable and most recyclable NPs at low to medium flow rates, which is the rationale for using these NPs for optimization of the solvent. TOF values showed that the

ethyl acetate solvent [TOF = 507/676 for (75:25) Pd:Au-Glu (Inert/Oxygen) NPs] is the best organic solvent in terms of activity compared to dichloromethane (TOF = 388/451) and chlorobenzene (TOF = 327/590). All solvents favored > 80%isomerized product (propanal). The TOF values were higher with Pd-Glu (Oxy) NPs compared to Pd-Glu (Inert) NPs for all three organic solvents in general, but the difference was much less for dichloromethane. We believe that the activity could depend on the aromaticity and polarity index of the organic solvent. As the solvent polarity decreases, the stability of the NPs increases likely due to greater H₂ solubility in the organic phase, which prevents NP instability caused by too much H₂ adsorption on the Pd NPs. The non-aromatic solvents may be better as they do not directly interact with the Pd surface as well as aromatics. These trends are pure speculation, however, as we didn't explore it further. More work will be needed to better understand these trends.

Recyclability of glutathione-coated Pd and Pd-alloy NPs. Due to their good stability, we compared the catalytic recyclability of (75:25) Pd:Au-Glu (Inert) NPs for hydrogena-

Table 3. Effects of organic solvent (dichloromethane	, chlorobenzene and ethyl acetate) on turnover frequencies (TOF) in mole product/mole to	tal metal/
hour and selectivity of the overall catalytic reaction at	19.9 ± 0.7 H ₂ flow rate using (75:25) Pd:Au-Glu (Inert/Oxygen) NPs.	

Organic Solvent used	Dichloromethane		Chlorobenzene		Ethyl acetate	
Nanoparticles	(75:25) Pd:Au-Glu (Inert)	(75:25) Pd:Au-Glu (Oxygen)	(75:25) Pd:Au-Glu (Inert)	(75:25) Pd:Au-Glu (Oxygen)	(75:25) Pd:Au-Glu (Inert)	(75:25) Pd:Au-Glu (Oxygen)
Hydrogenation TOF	47	66	22	66	73	102
Isomerization TOF	341	385	305	524	434	574
Overall conversion TOF	388	451	327	590	507	676
Hydrogenation [%]	12	16	8	16	16	15
Isomerization [%]	88	84	92	84	84	85

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tion/isomerization of allyl alcohol in various organic (chlorobenzene, ethyl acetate and dichloromethane)/aqueous biphasic solvent systems for 7–9 cycles at 19.9 ± 0.7 mL/min H₂ flow rate using UV-Vis spectroscopy as shown in Figure S8 in the Supporting Information. UV-Vis spectra for NPs in the presence of allyl alcohol and H₂ showed stability for 7 cycles with ethyl acetate, 5 cycles with dichloromethane, and 3 cycles with chlorobenzene, where each cycle reaction went until completion. We only counted cycles where full conversion of the reactants occurred. The Pd:Au-Glu NPs with low recyclability showed low absorbance and a more defined peak near 250 nm in the UV-vis spectrum. We also compared the recyclability of single metal Pd-Glu (Inert) and Pd-Glu (Oxy) NPs for hydrogenation/isomerization of allyl alcohol for at least 6 cycles in chlorobenzene/aqueous biphasic solvent system by UV-Vis spectrometry as shown in Figure S9 in the Supporting Information. The data clearly show that Pd-Glu (Inert) NPs were stable for more cycles than Pd-Glu (Oxy) NPs, again based on the lower absorbance around 250 nm for the latter. Note the high recyclability is not possible with the same clusters used in a single phase aqueous reaction. As shown in Figure S10, the UVvis spectrum of Pd-Glu NPs in single phase versus biphasic solvent on the second cycle shows a large degree of aggregation on the second cycle for the former. The gas chromatogram in Figure S10 shows mostly non-transformed reactant (allyl alcohol) in the GC.

Our data reveal that the ethyl acetate solvent leads to the highest TOF and highest recyclability. In addition, NPs synthesized under oxygen exhibit higher TOF but lower recyclability, whereas inert synthesized NPs exhibit lower TOF but higher recyclability. These trends are clear in the TOF and recyclability data for (75:25) Pd:Au-Glu (Oxy) NPs compared to (75:25) Pd:Au-Glu (Inert) NPs as shown in Table 4, all of which were obtained at a H₂ flow rate of 19.9 mL/min.

Maximizing the recycling capacity of the catalysts decreases the overall production cost of the chemical products significantly at the industrial scale. Using a biphasic solvent system with nanopure water and an immiscible organic solvent makes it very easy to extract the products into the organic phase and separate them from the aqueous-phase catalyst, which can then be reused in another reaction. Figure 3 shows GC-FID results demonstrating the catalytic recyclability of (75:25) Pd:Au-Glu (Inert) NPs using dichloromethane as the organic solvent and a H₂ flow rate of 8.0 ± 0.2 mL/min. The chromatograms of the organic and aqueous phases show only the presence of the propanal and 1-propanol products for the first 9 cycles. Each cycle shows high selectivity for propanal with a





Figure 3. Example of recyclability using (75:25) Pd:Au-Glu (Inert) NPs showing 100% completion of the catalytic reaction for at least 9 times (checked 11 times) with dichloromethane at 8.0 ± 0.2 mL/min H₂ flow rate. GC-FID chromatograms of the organic phase (A) and aqueous phase (B) after each cycle as indicated.

minor decrease in the TOF with each cycle. We focused on the lowest flow rate for this study since that leads to the highest NP stability.

Table S1 of supporting information shows the recyclability of various other Pd and Pd-alloy NPs using ethyl acetate,

Table 4. Table showing turnover frequencies (TOF) in mole product/mole total metal/hour and recyclability correlation for (75:25) Pd:Au-Glu (Inert/Oxygen) NPs in ethyl acetate, chlorobenzene and dichloromethane organic solvents.							
Reaction Conditions		Nanoparticles	Turnover frequencies [TOF]	Recyclability			
Hydrogen at 19.9 \pm 0.7 mL/min using organic solvent	Ethyl acetate	(75:25) Pd:Au-Glu (Oxy)	676	2			
		(75:25) Pd:Au-Glu (Inert)	507	4			
	Chlorobenzene	75:25) Pd:Au-Glu (Oxy)	590	1			
		(75:25) Pd:Au-Glu (Inert)	327	3			
	Dichloromethane	75:25) Pd:Au-Glu (Oxy)	451	1			
		(75:25) Pd:Au-Glu (Inert)	388	3			

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chlorobenzene or dichloromethane organic solvents at different H_2 flow rates. Ethyl acetate is the best solvent in terms of activity and recyclability. High recyclability is also generally associated with low flow rate and NPs synthesized under inert conditions.

Stability comparison of glutathione-coated Pd NPs with previously reported alkanethiol- and alkylamine-coated Pd NPs. To compare the stability of Pd-Glu (Inert) NPs in biphasic solvent with C6S-Pd NPs synthesized previously in our lab and used in a monophasic organic solvent (dichloromethane),^[18] we studied the hydrogenation and isomerization turnover rates of allyl alcohol using Pd-Glu (Inert) NPs at 3 different H₂ flow rates $8.0\pm0.2,~19.9\pm0.7$ and $39.9\pm0.3~mL/min$ as shown in Figure S11 in the Supporting Information. Although both Pd-Glu (Inert) NPs and C6S-Pd NPs are stabilized by thiol-coated ligands, Pd coated with Glu in the biphasic solvent system showed greater stability even at 39.9 ± 0.3 mL/min flow rates. The C6S-Pd NPs became unstable and precipitated. Also, Pd-Glu NPs showed higher TOF of up to ~300 moles product/ moles Pd/hour as compared to a max TOF of 93 for C6S-Pd NPs. The selectivity for both NPs was the same. This confirms that Glu-coated Pd NPs in biphasic solvent are more stable and suitable for some catalytic applications. We have also synthesized Pd NPs stabilized with alkylamines of various chain lengths (C8NH₂, C12NH₂ and C16NH₂) previously in our lab and investigated the catalytic activity and selectivity for the hydrogenation/isomerization reaction of allyl alcohol.^[18] These studies showed a TOF of 120 mole product/mole Pd/hour for C8NH₂ Pd NPs, 194 for C12NH₂ Pd NPs and 719 for C16NH₂ Pd NPs with the selectivity of only 1:1 or 3:2 ratios towards the hydrogenation: isomerization products. The stability of the shorter chain alkylamine-coated NPs was poor due to weak interaction of the ligands with the Pd core and all alkylamines showed modest recyclability due to difficulty in separation of products. Clearly, with Glu as a stabilizing ligand and the biphasic solvent system as the reaction mixture, we have successfully prepared a catalytic system that is stable, highly active, and easily separated from the products for high recyclability.

Glu-coated Pd-containing NPs showed >80% selectivity towards the isomerized product, which is similar to other thiolmodified Pd, and Pd-alloy NPs described in the literature.[18,25,26] The isomerization reaction is an important one-pot transformation to carbonyl compounds that proceeds with high efficiency, selectivity and atom economy while avoiding the two-step sequential oxidation and reduction reactions. Selective formation of the isomerized product is therefore a desirable attribute. Sensitive substrates do not survive the conditions involving the use of toxic and/or expensive oxidation and reduction reagents, making catalytic redox isomerization under mild reaction conditions especially useful as shown here. Also, in terms of atom economy, no byproducts are formed. Only the saturated aldehyde or ketone are formed, which are valuable intermediates for various pharmaceuticals, agrochemicals and fine chemicals. $^{\scriptscriptstyle [38]}$ For all of these syntheses, Pd NPs stabilized with Glu ligands showed high catalytic activity, selectivity and recyclability.

Conclusions

In summary, we have described the successful synthesis of various water-soluble Pd and Pd-alloy NPs stabilized with Glu, which shows highly active catalytic performance for selective isomerization of allyl alcohol with good recyclability. We observed that oxygen synthesized NPs are catalytically more active but have lower recyclability than the inert ones. The catalytic activity increased in the order of PdAu>PdPt>Pd, with increasing activity as the amount of Au or Pt increased, except when a small amount of Pt was used. All Glu-coated Pd and Pd-alloy NPs showed >80% selectivity towards the isomerized product for $\rm H_2$ flow rates from 8.0 to 39.9 \pm 0.2 mL/ min and after multiple reaction cycles (at low flow rate). The ethyl acetate solvent showed higher TOFs than chlorobenzene and dichloromethane, but the reasons are not well understood. The best recyclability performance was that of the (75:25) Pd:Au-Glu (Inert) NPs, which showed 100% completion of the catalytic reaction for at least 9 cycles using water/dichloromethane and a slow 8.0 ± 0.2 mL/min H₂ flow rate. These studies help us to better understand the effect of monolayer ligand chemistry, metal composition, and solvent on metal NP catalysis in terms of activity, selectivity, and stability/recyclability.

Experimental Section

Chemicals. Dichloromethane (99.5%), ethanol (200 proof), methanol (99%), acetone (99%) and 2-propanol (99.9%) were purchased from VWR Scientific Products and used as received. Sodium borohydride (98%), potassium tetrachloroplatinate(II), reduced-L-glutathione, ethyl acetate (99%), allyl alcohol (99%), propyl alcohol (99.7%) and propionaldehyde (99%) were purchased from Aldrich Chemical Co. and used as received. Potassium tetrachloropalladate (II) (99%) and chlorobenzene (98%) were purchased from Alfa Aesar Co. and used as received. Hydrogen tetrachloroaurate(III) was synthesized in our lab. Deuterium oxide and chloroform-d were purchased from Cambridge Isotope Laboratories. Water was purified using Barnstead nanopure water (18.3 M Ω cm) and used for all aqueous solutions.

Synthesis of glutathione-coated Pd NPs under Inert condition. We followed the synthesis reported by Sharma et al.[31] In the synthesis of "Inert" glutathione-coated Pd NPs, 0.50 g (1.531 mmol) of K₂PdCl₄ was dissolved in 30 mL of nanopure water and nitrogen gas was purged for at least 1 hour. Separately, 0.165 g (0.536 mmol) of reduced-L-glutathione was dissolved in 5 mL of nanopure water and purged in nitrogen for 1 hour. The two solutions were then combined and stirred under nitrogen atmosphere until PdCl₄²⁻ formed a complex with glutathione as indicated by the change in color from yellow to wine red. The reaction mixture was further stirred at 360 rpm for another 1 hour, which was then cooled down using an ice-bath. Subsequently, a fresh aqueous solution of NaBH₄ was prepared by dissolving 0.58 g (15.31 mmol) of NaBH₄ in 5 mL of nanopure water that was already purged in nitrogen for 1 hour. This solution was immediately added to the reaction mixture under stirring, giving an immediate change in color from wine red to black, indicating the formation of Pd nanoparticles. The solution was further stirred for 4 hours from which Pd NPs were separated by adding an equal volume of methanol (40 mL), stirring for 15 minutes, and centrifuging at 4000 rpm for 10 minutes to obtain precipitates of the Pd NPs. The mother liquor was removed and the



precipitated Pd NPs were dissolved in nanopure water and transferred into a round bottom flask to remove the water using a rotary evaporator heated at 45 °C. The black NPs were suspended in 100 mL of methanol and collected by vacuum filtration on a glassfritted Büchner funnel. The NPs were then washed thoroughly with methanol, ethanol and acetone successively two times before thoroughly drying and collecting. These NPs are referred to as Pd-Glu (Inert) NPs.

Synthesis of glutathione-coated Pd NPs under oxygen condition. Pd NPs coated with glutathione ligands under "Oxygen" conditions were prepared similarly by performing the above experiment under air atmosphere without purging nitrogen gas and keeping the molar concentration of K_2PdCl_4 , reduced-L-glutathione and NaBH₄ the same. The only visible difference was the formation of an orange colored solution during the addition of glutathione solution to the Pd salt solution.

Synthesis of glutathione-coated Pd-alloy NPs under inert and oxygen conditions. Pd-alloy NPs with different ratios of Pt or Au were synthesized ranging from 90:10, 75:25 and 50:50 under both inert and oxygen conditions by co-reducing them using NaBH₄. Here, both K₂PdCl₄ and K₂PtCl₄ or HAuCl₄.3H₂O metal salts in their respective molar ratio were dissolved together in nanopure water and used for further synthesis as described above. All of the synthesized NPs were relatively stable as confirmed by comparing the catalytic activity using 2 years old synthesized (75:25) Pd:Au-Glu (Inert) NPs as catalyst for hydrogenation/isomerization of allyl alcohol at 19.9 ± 0.7 mL/min H₂ flow rate. The reactant was converted into products within 10 minutes as observed before. The only difference observed was that % hydrogenation (1-propanol formation) increased from 16% to 33% whereas % isomerization (propanal formation) decreased from 84% to 67%. The reason for this is unknown, but could be due to the loss of some ligands from the Pd surface with time.

Characterization. ¹H NMR spectra of metal NPs were recorded on a 400 MHz INOVA spectrometer with 64 scans from -2 to 18 ppm at room temperature and pressure. ¹H NMR spectroscopy gives information about the successful attachment of ligands onto the metal core of the synthesized NPs and confirms the removal of non-bound ligands. A residual solvent peak at δ 4.79 ppm of D₂O was used as an internal reference. ¹H NMR spectrum of pure glutathione showed proton resonances at δ 2.21 (–CH₂CHCOOH), 2.58 (-CH2CONH), 2.95 (-CH2SH), 3.84 (-CHNH2), 4.00 (-CH2COOH) and 4.59 (--CHCH2SH) ppm. Protons from carboxylic acid, amide and amine were exchanged with D_2O and therefore, couldn't be observed in the spectrum. ¹H NMR of Pd-Glutathione NPs differed from that of pure glutathione in that the peaks for the thiol-coated Pd NPs were all broadened relative to those of pure glutathione. The peak for the two protons α to the thiol group at 2.95 ppm wasn't observed in the glutathione-coated Pd NPs, due to the presence of Pd core that creates large inhomogeneity in the magnetic field around the local chemical environment. Also, a lack of any sharp peaks in the spectra confirmed the absence of any other impurities or free ligand. ¹H NMR spectroscopy showed similar results for glutathione-coated Pd-alloy NPs synthesized under inert and oxygen condition.

UV-Vis data were obtained using a Varian Cary 50 Bio UV-Visible spectrophotometer ranging from 200–900 nm. All aqueous solutions were placed in a quartz cuvette with an optical path length of 1 cm and each spectrum was corrected using the solvent spectrum. UV-Vis data were used to assess the NP stability in the presence of H_2 and throughout the conditions of the reaction. We also obtained the spectra of allyl alcohol, 1-propanol, propanal, the various solvents tested, and Pd(II) salts or thiolate complexes to correlate with the spectra obtained under the reaction conditions.

TGA analysis was conducted using a 2950 TGA HR V5.4 A instrument with a flow rate of 100 mL/min of N₂ over a temperature range of 25–800 °C at a heating rate of 20 °C/min using sample sizes from 5.0–11.4 mg. TGA data were used to observe the change in weight of NPs to calculate the organic percentage present on the metal core.

Transmission electron microscopy (TEM) images were obtained using a FEI Tecnai F20 operated in TEM mode with an acceleration voltage of 200 kV. TEM analysis was carried out using a digital micrograph software (version 3.11.0) and ImageJ software for particles size analysis. TEM samples of water-soluble Pd-Glu and (50:50) Pd:Au-Glu NPs were prepared by dissolving in water and then drop casting the aqueous solution onto a 400 mesh Formvar/ carbon-coated copper grid, letting it air-dry for at least 4 hours.

Catalytic Reactions. The catalytic reaction of allyl alcohol to either hydrogenated and/or isomerized product was performed by dissolving 6.0 mg of Pd or Pd alloy NPs in 2 mL of nanopure water in a 10 mL glass vial with an outlet for spent hydrogen gas passed through a glass pipette. 2 mL of organic solvent [Chlorobenzene (Clben), Dichloromethane (DCM) or Ethylacetate (EtOAc)] and 200 μ L of allyl alcohol were added, forming a biphasic reaction mixture as shown in Figure S12 in the Supporting Information. The reaction mixture was then stirred at 500–600 rpm at room temperature and atmospheric pressure. Hydrogen gas was purged at a given flow rate (8.0 ± 0.2 , 19.9 ± 0.7 or 39.9 ± 0.3 mL/min) through a glass pipette and 20 μ L aliquots were removed from both aqueous and organic phases at particular intervals of time. NPs in the aqueous phase aliquot were precipitated by adding THF solvent in 2-fold excess (40 μ L) and centrifuging at 4000 rpm for 15 min.

The progress of the catalysis reaction was followed by gas chromatography (GC) of samples before exposure to hydrogen and after addition of catalyst and exposure to hydrogen at different intervals of time. The GC data was recorded on a Buck Scientific model 910 GC equipped with a 1/8th inch packed column (10% Carbowax 20 M on silica 80/100 mesh, 6 foot) using a flame ionization detector (FID) and helium as the carrier gas. The method developed for GC includes injecting $1 \ \mu L$ of the reaction aliquot and varying temperatures from (a) 80 °C to 80 °C, holding for 2 min (b) 80 °C to 135 °C, ramp at 25 °C/min (c) 135 °C to 135 °C, holding for 1 min. The pressure varied from (a) 12 psi helium for 3 min (b) 14 psi helium for 2 min. The turnover frequency (TOF) of the products were calculated using the slope of the linear portion of >60% of the conversion of reactant to isomer and hydrogenated product in the plot of % hydrogenation and % isomerization versus time as described previously.^[18]

Catalytic Recyclability Studies. For recycling studies, the first cycle was the same as described for the catalytic reaction. The organic layer with most of the product was separated from the aqueous layer containing the catalyst. 2 mL of additional organic solvent was added again to extract the remaining product from the aqueous layer. The two organic fractions were added together and 1 μ L was anlyzed by GC-FID. A 20 μ L aliquot of the aqueous phase was removed and the NPs were precipitated by adding 40 μ L of THF and centrifuging for 15 minutes prior to analyzing 1 μ L of the supernatant by GC-FID. The NPs in the aqueous phase were used again as catalysts by adding organic solvent, adding allyl alcohol, and purging with hydrogen gas for another reaction cycle. The entire process was repeated until the reaction stopped going to completion.



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Conflict of Interest

The authors declare no conflict of interest.

Keywords: Biphasic · Glutathione · Selectivity · Homogeneous · Catalysis · Recyclability · Nanoparticles · Allyl Alcohol · Hydrogenation · Isomerization

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Protected nanoparticles: Glutathione-protected Pd, PdAu and PdPt nanoparticles (NPs) show greatly increased reactivity and stability towards the hydrogenation/isomerization of allyl alcohol in a biphasic organic/aqueous solvent mixture compared to single-phase alkanethiol-protected Pd-based NPs. The branched, open structure of the glutathione and use of the biphasic solvent provides high catalytic activity, high selectivity, and easy removal of the products in the organic phase for good recyclability of the water-soluble catalysts.



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Highly Active, Selective, and Recyclable Water-Soluble Glutathione-Stabilized Pd and Pd-Alloy Nanoparticle Catalysts in Biphasic Solvent