

# UC Berkeley

## UC Berkeley Previously Published Works

### Title

Supported Dendrimer-Encapsulated Metal Clusters: Toward Heterogenizing Homogeneous Catalysts.

### Permalink

<https://escholarship.org/uc/item/1m83m5q4>

### Journal

Accounts of chemical research, 50(8)

### ISSN

0001-4842

### Authors

Ye, Rong  
Zhukhovitskiy, Aleksandr V  
Deraedt, Christophe V  
et al.

### Publication Date

2017-08-01

### DOI

10.1021/acs.accounts.7b00232

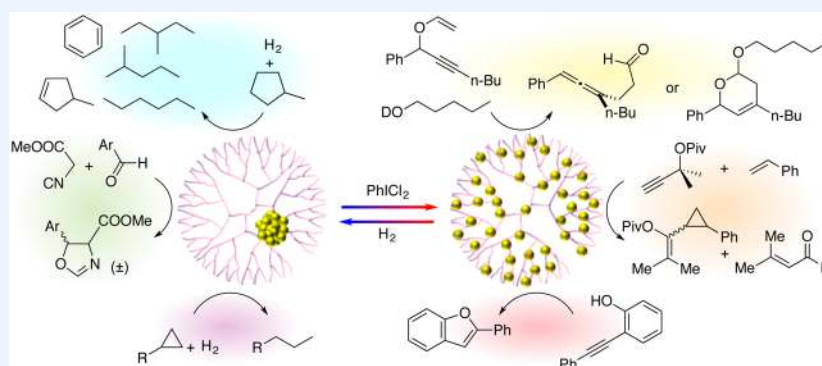
Peer reviewed

## Supported Dendrimer-Encapsulated Metal Clusters: Toward Heterogenizing Homogeneous Catalysts

Rong Ye,<sup>†,‡,§</sup> Aleksandr V. Zhukhovitskiy,<sup>†</sup> Christophe V. Deraedt,<sup>†,§</sup> F. Dean Toste,<sup>\*,†,§</sup> and Gabor A. Somorjai<sup>\*,†,‡,§</sup>

<sup>†</sup>Department of Chemistry, <sup>‡</sup>Kavli Energy NanoScience Institute, University of California, Berkeley, Berkeley, California 94720, United States

<sup>§</sup>Chemical Science Division, Lawrence Berkeley National Laboratory, 1 Cyclotron Road, Berkeley, California 94720, United States



**CONSPECTUS:** Recyclable catalysts, especially those that display selective reactivity, are vital for the development of sustainable chemical processes. Among available catalyst platforms, heterogeneous catalysts are particularly well-disposed toward separation from the reaction mixture via filtration methods, which renders them readily recyclable. Furthermore, heterogeneous catalysts offer numerous handles—some without homogeneous analogues—for performance and selectivity optimization. These handles include nanoparticle size, pore profile of porous supports, surface ligands and interface with oxide supports, and flow rate through a solid catalyst bed. Despite these available handles, however, conventional heterogeneous catalysts are themselves often structurally heterogeneous compared to homogeneous catalysts, which complicates efforts to optimize and expand the scope of their reactivity and selectivity. Ongoing efforts in our laboratories are aimed to address the above challenge by heterogenizing homogeneous catalysts, which can be defined as the modification of homogeneous catalysts to render them in a separable (solid) phase from the starting materials and products. Specifically, we grow the small nanoclusters in dendrimers, a class of uniform polymers with the connectivity of fractal trees and generally radial symmetry. Thanks to their dense multivalency, shape persistence, and structural uniformity, dendrimers have proven to be versatile scaffolds for the synthesis and stabilization of small nanoclusters. Then these dendrimer-encapsulated metal clusters (DEMCs) are adsorbed onto mesoporous silica. Through this method, we have achieved selective transformations that had been challenging to accomplish in a heterogeneous setting, e.g.,  $\pi$ -bond activation and aldol reactions. Extensive investigation into the catalytic systems under reaction conditions allowed us to correlate the structural features (e.g., oxidation states) of the catalysts and their activity. Moreover, we have demonstrated that supported DEMCs are also excellent catalysts for typical heterogeneous reactions, including hydrogenation and alkane isomerization. Critically, these investigations also confirmed that the supported DEMCs are heterogeneous and stable against leaching.

Catalysts optimization is achieved through the modulation of various parameters. The clusters are oxidized (e.g., with  $\text{PhICl}_2$ ) or reduced (e.g., with  $\text{H}_2$ ) in situ. Changing the dendrimer properties (e.g., generation, terminal functional groups) is analogous to ligand modification in homogeneous catalysts, which affect both catalytic activity and selectivity. Similarly, pore size of the support is another factor in determining product distribution. In a flow reactor, the flow rate is adjusted to control the residence time of the starting material and intermediates, and thus the final product selectivity.

Our approach to heterogeneous catalysis affords various advantages: (1) the catalyst system can tap into the reactivity typical to homogeneous catalysts, which conventional heterogeneous catalysts could not achieve; (2) unlike most homogeneous catalysts with comparable performance, the heterogenized homogeneous catalysts can be recycled; (3) improved activity or selectivity compared to conventional homogeneous catalysts is possible because of uniquely heterogeneous parameters for optimization.

In this Account, we will briefly introduce metal clusters and describe the synthesis and characterizations of supported DEMCs. We will present the catalysis studies of supported DEMCs in both the batch and flow modes. Lastly, we will summarize the current state of heterogenizing homogeneous catalysis and provide future directions for this area of research.

Received: May 8, 2017

Published: July 13, 2017

## ■ INTRODUCTION

The term “cluster” was applied by Cotton in the 1960s to compounds containing metal–metal bonds.<sup>1</sup> Metal clusters contain countable numbers of atoms: anywhere between two and several hundred thousand (the upper limit is not precisely defined).<sup>2</sup> In the case of ultrasmall gold clusters, their diameters range from subnanometer to  $\sim 2.2$  nm (equivalent to  $\sim 10$ – $300$  atoms, often called nanoclusters).<sup>3</sup> Theoretical work by Nørskov’s group suggests the transition of surface chemical activity of Au clusters from molecular to bulk behavior to be around 560 atoms, corresponding to a diameter of  $\sim 2.7$  nm.<sup>4</sup> Above this size, the surface properties of two probe adsorbates, O and CO, are indistinguishable from those of an extended surface. Below that critical size, finite-size effects can be observed, and facets become small enough for the charge redistribution upon oxygen adsorption to reach the edge of the particle.<sup>4</sup>

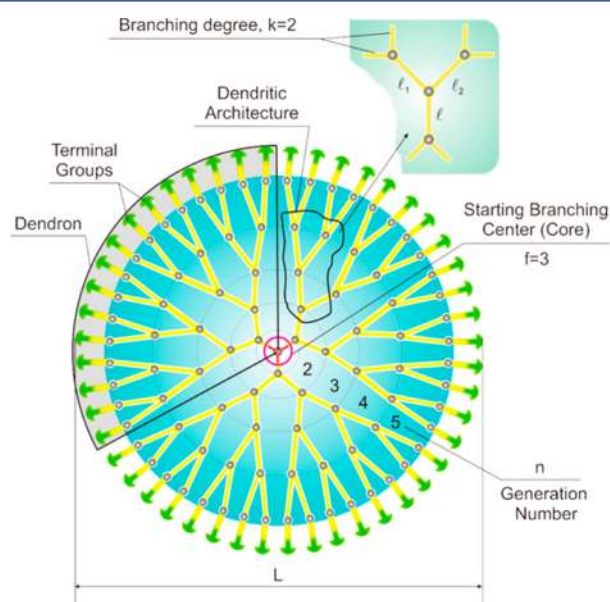
Clusters, in general, may have unusual catalytic properties. The high ratio of surface-to-bulk atoms in clusters facilitates both reactant activation and product desorption, offering new reaction pathways.<sup>5</sup> As the most active catalysts are usually made from precious metals, the use of clusters could also have significant economic impacts by increasing the turnover number and turnover frequency per metal atom. They can act as individual active sites, and minor changes in size and composition, e.g., the addition or removal of a single atom, can have a substantial influence on the activity and selectivity of a reaction.<sup>6</sup> Gates et al. reported that Ir<sub>4</sub> and Ir<sub>6</sub> clusters differ in catalytic activity both from each other and from metallic Ir particles.<sup>7</sup> Anderson’s group observed that the Pd 3d binding energy varied nonmonotonically with cluster size and that the changes correlate with strong size variations in CO oxidation activity.<sup>8</sup>

Control of cluster structural integrity (e.g., size, geometry) during their preparation and throughout a cluster-catalyzed transformation is critical to achieve the desired reactivity profile. However, in the pursuit of cluster stabilization through surface modification with ligands, catalyst activity is often compromised. Judicious ligand design is critical to balance cluster structural integrity and catalytic performance. One reliable and modular method to synthesize the metal clusters is through the use of dendrimers.<sup>9–12</sup> Dendrimer–cluster multivalent interactions protect the cluster from aggregation or leaching; meanwhile, the weak nature of individual interactions with surface sites preserves the catalyst activity.<sup>13</sup> Dendrimer-encapsulated metal clusters (DEMCs) generally exhibit high catalytic activity in homogeneous reactions, e.g., Heck, Suzuki, and Sonogashira cross-coupling, often superior to classical homogeneous catalysts.<sup>14,15</sup> The latter are, however, not readily recyclable and are unstable at high temperatures, giving rise under reaction conditions to “cocktails” of catalytically active species: metal complexes, clusters and nanoparticles.<sup>16</sup> Furthermore, these same catalysts display mediocre performance in traditionally heterogeneous transformations, e.g., hydrogenation of pyrrole. After applying the supported DEMCs in the hydrogenation of pyrrole,<sup>17</sup> we sought to further develop this platform of active, selective, recyclable, and air-stable catalysts for academically and/or industrially important transformations. Besides improved thermal stability and enhanced recyclability, supported DEMCs resist cluster aggregation (and therefore retain high activity) in all solvents even though unsupported DEMCs aggregate in low-polarity solvents. The key function of dendrimers in supported DEMCs is to ensure stability against not only aggregation but also metal leaching, particularly in reactions which require modification of the metal oxidation state. In our laboratories,

we have utilized the dendrimer-stabilization approach to prepare clusters and load them onto mesoporous supports for heterogeneous catalysis. Note that the clusters discussed in this account are confined within individual dendrimers, which is critical for their resistance to leaching; larger clusters stabilized by multiple dendrimers, are covered elsewhere.<sup>15</sup> This Account will focus on the investigations and developments of supported DEMCs on catalytic reactions performed in our groups. The synthesis and characterizations of supported DEMCs will be covered, followed by catalysis studies in the batch and flow modes. After a summary of the current knowledge, future directions will be discussed.

## ■ SYNTHESIS AND CHARACTERIZATION

DEMCs were synthesized adapting the method developed by Crooks and Zhao.<sup>18</sup> The synthesis procedure can be applied to Rh, Pd, Pt, and Au with generation 4 OH-terminated polyamidoamine (PAMAM) dendrimer (henceforth referred to as G4OH). Dendrimer generation is the number of branching nodes along a single path from the center of the dendrimer to the periphery (Figure 1).<sup>19</sup> A dendrimer stock solution was mixed



**Figure 1.** Schematic representation of a classical dendrimer molecule. Reprinted with permission from ref 19. Copyright 2012 American Chemical Society.

with a metal precursor for the complexation between these components. An excess of freshly prepared NaBH<sub>4</sub> solution was added dropwise with vigorous stirring. After the metal was reduced, the solution was purified via dialysis in cellulose dialysis tubing against an excess of deionized water. The DEMCs were immobilized onto mesoporous silica, e.g., SBA-15 (SBA stands for Santa Barbara),<sup>20</sup> via sonication. The deposition and anchoring of the DEMCs on the mesoporous support resulted from the hydrogen bonding between the terminal hydroxyl groups of G4OH and the surface of the SiO<sub>2</sub> support.<sup>17</sup> This interaction prevented the detachment of DEMCs from the mesoporous support, even under liquid-phase reaction conditions or at elevated temperatures. The supported DEMCs displayed no detectable leaching, and in this regard functioned as true heterogeneous catalysts. However, the tunable oxidation state of the surface metal atoms in DEMCs rendered these catalysts effective in a variety of transformations (vide infra).

The DEMCs were characterized by various techniques before and after loading, as well as during and after the completion of the catalyzed transformation. Transmission electron microscopy (TEM) offered direct visualization of the morphology of the DEMCs (Figure 2). The DEMCs possessed reproducibly uniform size and shape due to templation and stabilization by the dendrimer. These cluster parameters did not appear to change upon loading onto the SBA-15 support. The sizes of DEMCs ranged from 1 to 2.7 nm, depending on the metal and the metal-to-dendrimer molar ratio. These sizes fell within the aforementioned critical size range, in which the clusters exhibited finite-size effects. Inductively coupled plasma optical emission spectrometry (ICP-OES) enabled quantification of the metal content in the supported samples and the extent of metal leaching during the catalytic reactions. X-ray photoelectron spectroscopy (XPS) was utilized to determine the oxidation states of the metal atoms within DEMCs. For the as-synthesized Rh or Pt DEMCs, multiple oxidation states were observed. The oxidized portion was proposed to arise from incomplete reduction of metal salts during the DEMC synthesis or air exposure of the XPS sample.<sup>17</sup>

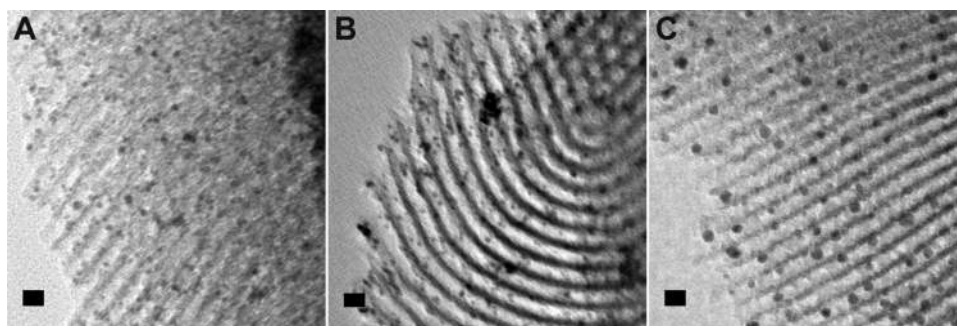
The oxidation states and coordination environment of Pt DEMCs were monitored in situ via near edge X-ray absorption fine structure (NEXAFS) and extended X-ray absorption fine structure (EXAFS).<sup>21</sup> As evidenced in Figure 3, reduction of Pt via an H<sub>2</sub> treatment led to high Pt–Pt and low Pt–Cl or Pt–O coordination numbers derived from EXAFS data. The addition of PhICl<sub>2</sub>, a hypervalent iodine oxidant, into the reaction solution generated Pt(II) and Pt(IV), as shown by EXAFS and NEXAFS analysis. The reduction and oxidation cycle could be repeated.<sup>21</sup> These powerful techniques provide valuable molecular insight into catalysts' operation under reaction conditions, even though currently their scan rate is in the order of minutes and thus cannot capture faster transformations.

## ■ CATALYSIS IN BATCH REACTORS

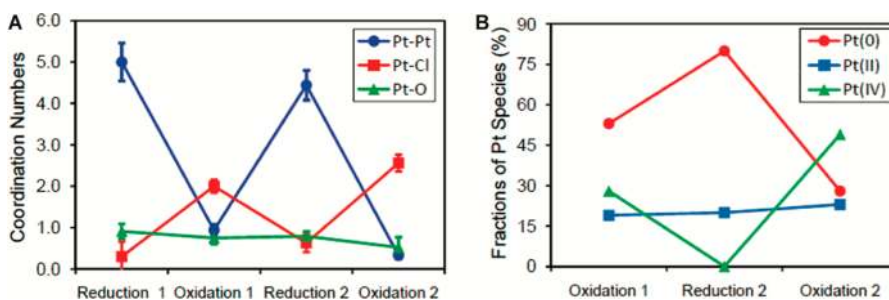
One of the first examples of supported DEMCs was reported by Chandler's group.<sup>22</sup> Pt DEMCs were deposited onto a commercial high surface area silica support. A pretreatment of O<sub>2</sub>/He at 300 °C followed by H<sub>2</sub> flow at 300 °C was used to remove the dendrimer. No significant change in clusters was observed by TEM. This catalyst was used for the oxidation of CO and the hydrogenation of toluene. Interestingly, the clusters obtained from the DEMCs were more active than a classic Pt/SiO<sub>2</sub> catalyst.<sup>22</sup> Simultaneously, Amiridis and colleagues investigated Pt DEMCs for catalytic CO oxidation.<sup>23</sup> Later on, applications of supported DEMCs included the selective hydrogenation of 3,4-epoxy-1-butene by the Williams group,<sup>24</sup> and the *trans*-2-butene conversion by Zaera and co-workers.<sup>25</sup>

In our groups, DEMCs supported on SBA-15 were active for a variety of reactions, and unlike particles capped with polyvinylpyrrolidone (PVP) or other agents, calcinations or equivalent manipulations of the DEMCs was unnecessary to uncover the active sites. In addition to permitting the catalyst to be recycled, deposition of the DEMCs on SBA-15 imparted additional thermal stability against aggregation. Furthermore, while unsupported DEMCs with PAMAM dendrimers were typically dispersible only in protic solvents or solvent mixtures, DEMCs supported on SBA-15 resisted aggregation in aprotic organic solvents (and in fact were more active in them).

We utilized supported DEMCs for the functionalization of  $\pi$ -bonds, which had previously been the realm of mainly homogeneous catalysts. Our initial studies focused on a hydroalkoxylation reaction, in which an electrophilic Pt catalyst activated an alkyne toward nucleophilic attack by an alcohol functionality (Figure 4). Initial attempts with 1.0 nm Pt<sub>40</sub>/G4OH/SBA-15 generated only 10% yield of product. (Pt<sub>40</sub> represents the molar ratio of Pt/G4OH is 40/1 in the synthesis.) This result was most



**Figure 2.** Representative TEM images of DEMCs supported in SBA-15. Rh<sub>40</sub>/G4OH/SBA-15 (A), Pt<sub>40</sub>/G4OH/SBA-15 (B), and Au<sub>40</sub>/G4OH/SBA-15 (C). Scale bars are 10 nm.



**Figure 3.** (A) Average coordination numbers of Pt atoms in the supported Pt catalyst after a sequence of hydrogen reduction and PhICl<sub>2</sub> oxidation treatments in the toluene derived from EXAFS analysis. (B) Fractions of Pt(0) and Pt(II) and Pt(IV) chloride species of the Pt catalyst derived from NEXAFS analysis. Reprinted with permission from ref 21. Copyright 2011 American Chemical Society.

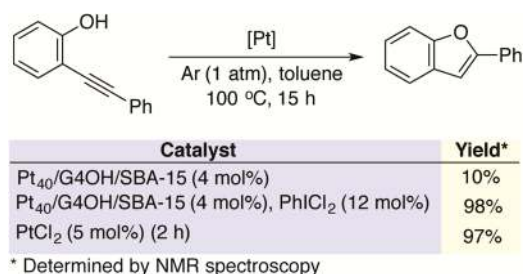


Figure 4. Hydroalkoxylation reaction with Pt catalysts.

likely due to the presence of catalytically inactive Pt oxide species on the Pt surface: indeed, XPS revealed that >70% of Pt were Pt(II) in Pt<sub>40</sub>/G4OH/SBA-15. Crooks and Zhao demonstrated the reduction of Pt(II) in the synthesis of Pt<sub>40</sub>/G4OH,<sup>18</sup> so the presence of Pt(II) in the supported clusters is likely due to surface oxidation in the loading and drying process. Oxidized Pt sites were not deemed intrinsically inactive—rather the oxide form of Pt was unreactive. Indeed, treatment of H<sub>2</sub>-pretreated Pt<sub>40</sub>/G4OH/SBA-15 with PhICl<sub>2</sub> resulted in 98% yields.<sup>26</sup> In this case, PhICl<sub>2</sub>, an oxidant, generated Pt chloride rather than oxide surface species and thereby transformed the Pt clusters' surface into a catalytically active one.

Another critical consideration was the nature of the catalytically active species: namely, did the oxidized Pt ions leach out from DEMCs and catalyze the reaction in a homogeneous fashion? We sought to address this question for the DEMC system in situ under optimal performance conditions. A three-phase test<sup>27</sup> was used with Wang resin-bound substrate (Figure 5A). Homogeneous PtCl<sub>2</sub> provided 26% conversion of resin-bound substrate to product. However, a negligible conversion (<2%) was observed for Pt<sub>40</sub>/G4OH/SBA-15 oxidized with PhICl<sub>2</sub>. A filtrate transfer test was conducted with a Pt<sub>40</sub>/G4OH/mesoporous silica pellet. A solution of starting material, PhICl<sub>2</sub>, and solvent (toluene) were added to the catalyst pellet in a reactor (step *i* in Figure 5B). After 42% yield was achieved, the reaction solution was transferred to another vessel without the heterogeneous catalyst (step *ii* in Figure 5B). A fresh solution of starting material was subsequently added to the original reaction vessel with the remaining oxidized catalyst pellet (step *ii* in Figure 5B). Both vessels were next subjected to otherwise identical reaction conditions (step *iii* in Figure 5B);

product was again generated in the vessel with the catalyst pellet, while in the vessel without it no further conversion took place, and product yield remained unchanged. Reactivity due to any leached homogeneous species could thus be ruled out; the active catalyst was in fact heterogeneous. Moreover, ICP-OES confirmed that Pt species did not leach from the Pt<sub>40</sub>/G4OH/SBA-15 catalyst when it was isolated after the reaction, and the concentration of Pt in the supernatant of the reaction solution was below the instrument's detection limit (1 ppm). Finally, the catalyst before and after reaction did not show any appreciable morphology change in TEM images.<sup>26</sup> This observation underscores the stability and recyclability of our supported DEMC catalyst system.

The stability of DEMCs against leaching is a key property of heterogenized homogeneous catalysis. When toluene, a nonpolar solvent, was used in combination with a polar solid phase (the mesoporous SiO<sub>2</sub>, the dendrimer, and the metal ions), metal ions formed by PhICl<sub>2</sub> oxidation tended to reside inside the dendrimer and their dissociation of from the polar support into the nonpolar solvent was unfavorable, even at a high temperature. However, for a more polar solvent (such as MeNO<sub>2</sub>), capable of strong coordination with metal ions and strong interaction with the dendrimer, dissociation of the metal ions (or dendrimers carrying the metal ions) became more pronounced, and leached metal ions were detected in the liquid phase.<sup>28</sup>

One of the long-term goals of this ongoing research program is to leverage heterogenized homogeneous catalysis to facilitate a broad spectrum of complex chemical transformations. During the past 10 years, we and others have already demonstrated that, in addition to intramolecular  $\pi$ -bond activation reactions, DEMCs were excellent catalysts for several other classes of transformations, including C–C bond activation and C–C bond formation. Elucidation of the C–C bond activation mechanism is essential for the selective production of hydrocarbons in the petroleum industry. Ring-opening reactions of cyclopropane derivatives were used as a model to investigate C–C bond activation with supported DEMCs (Figure 6). While homogeneous rhodium catalysts showed little or no activity even at elevated temperatures toward the ring opening of cyclopropylbenzene, Rh<sub>40</sub>/G4OH/SBA-15 showed a turnover frequency (TOF) of 2.24 h<sup>-1</sup> at room temperature, and the DEMCs were recyclable. The products of the DEMCs catalyzed reactions were 100% linear, in contrast to homogeneous counterparts that

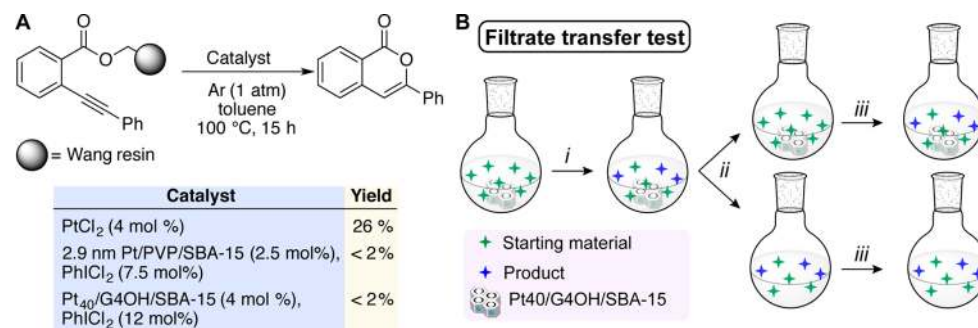
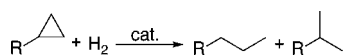


Figure 5. Catalyst heterogeneity tests. (A) Three-phase test to determine the presence of a homogeneous catalyst by leaching or release and capture. Yields were determined by NMR versus internal standard. (B) A filtrate transfer test. (*i*) To the reaction vessel charged with a substrate was added a pellet of Pt<sub>40</sub>/G4OH/mesoporous silica catalyst, toluene, and PhICl<sub>2</sub> oxidant. The mixture was stirred and the yield monitored. (*ii*) When the reaction reached 42% yield, the solution was removed and placed into a new vessel. A fresh solution of starting material was added to the original vessel with the catalyst pellet. (*iii*) Both vessels were then stirred and monitored. The yield was determined by gas chromatography versus internal standard. All transfers and reactions were conducted under Ar at 100 °C. The catalyst pellet was pre-reduced under H<sub>2</sub> atmosphere at 100 °C for 36 h before reaction. Adapted with permission from ref 26. Copyright 2010 Nature Publishing Group.



**Figure 6.** Catalytic ring opening reactions of cyclopropane derivatives.

produced the branched products, likely because of different reaction mechanisms. The reaction mechanism with the rhodium DEMCs was investigated. Reactants with electron-donating groups on the three-member ring exhibited a high reaction rate, probably due to a more stable cationic transition state in the rate-limiting step on the rhodium surface. Larger cluster size led to higher TOF and smaller reaction activation energy, probably because the stronger metallic character of the larger clusters favors the hydrogen chemisorption. The capping agent of the clusters affected both the reaction rate and the activation energy, analogous to ancillary ligand effects observed in homogeneous catalysts. The study revealed the above-mentioned fundamental factors controlling catalytic C–C bond activation activity and selectivity.<sup>29</sup>

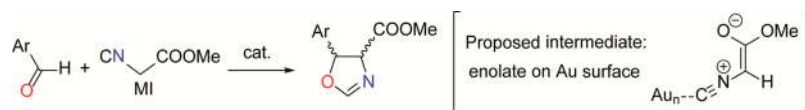
The Hayashi–Ito aldol reaction of methyl isocyanoacetate (MI) and benzaldehydes, a classic homogeneous Au(I)-catalyzed reaction, aptly demonstrated the excellent catalytic activity and controlled selectivity of supported DEMCs (Figure 7).<sup>30</sup> Au<sub>40</sub>/G4OH/SBA-15 showed higher activity and diastereoselectivity toward the *trans* product than DEMCs of Pd, Rh, or Pt, and the homogeneous analogues. Au DEMCs were stable for at least six cycles without apparent deactivation. The activation energy was insensitive to the size of Au DEMCs or the support pore profile. However, larger pore sizes of the support increasingly favored the *trans* product. Our speculation was that the *trans* product was more sterically demanding, so when the pore was small and the space was limited, kinetic control led to an increase in the *cis:trans* product ratio. Infrared (IR) spectroscopy suggested a strong interaction between MI and the gold catalyst,

implying the formation of an enolate ion intermediate from MI (Figure 7). The Hammett plot of benzaldehyde with various substituents was linear with a positive slope, indicating an increased electron density on the carbonyl carbon atom in the transition state of the rate-limiting step. These evidence supported our hypothesis that the rate-limiting step involved a nucleophilic attack of the aldehyde by the enolate formed from the deprotonated MI.<sup>30</sup>

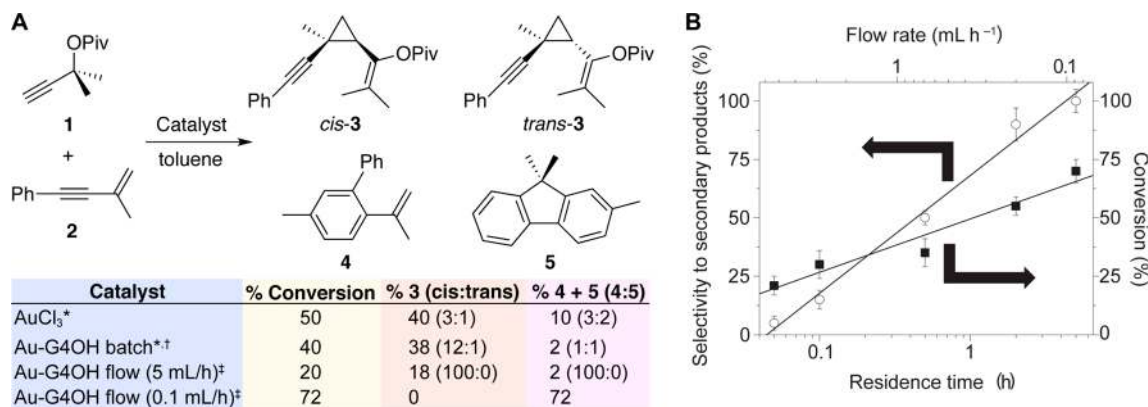
## ■ CATALYSIS IN FLOW REACTORS

To take full advantage of the heterogeneous nature of the supported DEMCs, we also studied the hydroalkoxylation reaction (shown in Figure 4) in a fixed bed plug flow reactor in a continuous flow mode. In this case, Pd<sub>40</sub>/G4OH/SBA-15 were used, as they were highly active and could provide a full conversion of reactants to products at room temperature. Separating the catalyst from reaction medium or any further purification of the product was obviated in this operation mode. In addition, the activity of Pd<sub>40</sub>/SBA-15 at different reaction temperatures could be conveniently measured in a flow reactor, and the apparent activation energy was determined to be 20.0 kcal/mol. In comparison, multiple reactions must be repeated at different temperatures to measure the activation energy in a batch mode. Thus, any operational error in the batch mode would generate inaccuracy in the activation energy. However, all reaction parameters could be controlled precisely and reproduced easily in a flow reactor.<sup>31</sup>

Applications of supported DEMCs in complicated reactions, e.g. a cascade reaction, highlight the scope of our DEMC system. A cascade rearrangement of propargyl pivalate **1**/cyclopropanation of enyne **2** was investigated with AuCl<sub>3</sub> and Au DEMCs (Figure 8A, B). The primary product **3** can rearrange under the reaction conditions into two secondary products, **4** and **5**. Homogeneous AuCl<sub>3</sub> at room temperature gave a 40% yield of



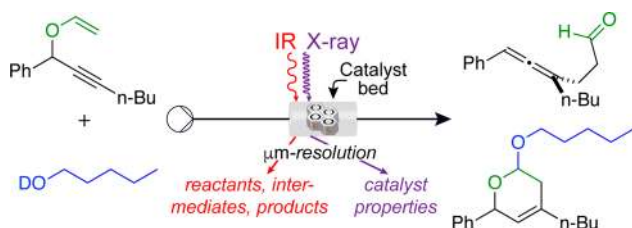
**Figure 7.** Hayashi–Ito aldol reaction of methyl isocyanoacetate (MI) and benzaldehydes and the proposed intermediate.



**Figure 8.** (A) Gold-catalyzed cascade cyclopropanation rearrangement in a batch reactor and a flow reactor, respectively. Reaction yield and selectivity were measured by <sup>1</sup>H NMR integration. <sup>\*</sup>Reaction run for 20 h at r.t. with 2 mol % catalyst. <sup>†</sup>6 mol % oxidizer was added. <sup>‡</sup>Total yield and selectivity were measured after 4 h of reactant flow at r.t. Reactant and oxidizer concentrations were 0.15 and 0.015 M, respectively. (B) Flow measurements of the conversion and selectivity of the cascade cyclopropanation-rearrangement reaction as a function of reactant residence time. With 2.0 ± 0.3 nm Au-G4OH/SBA-15 as the catalyst, the catalytic conversion (filled squares) and selectivity (open circles) toward the formation of secondary products **4** and **5** at room temperature increased as a function of the residence time of the reactants. The reactant and oxidizer concentrations were 0.15 and 0.015 M, respectively. Error bars represent up to ±6% differences in reproducibility. Adapted with permission from ref 28. Copyright 2012 Nature Publishing Group.

cyclopropane **3**, with a *cis:trans* ratio of 3:1, accompanied by a 10% yield of products **4** and **5** (in a 3:2 ratio) formed by the rearrangement of the product *cis*-**3**. However, Au-G4OH/SBA-15 in the batch mode led to a *cis:trans* ratio of 12:1 for **3** and only a small amount of the rearrangement products **4** and **5** (1% each). Another advantage of using supported DEMCs in a flow mode is that chemoselectivity was tuned by modifying the residence time of the reactants. Using the same catalyst in a flow reactor with a flow rate of 5 mL/h, an 18% yield of *cis*-cyclopropane **3** was measured (*cis:trans* ratio of 100:0), along with 2% of secondary products **4** and no measurable **5**. Reducing the flow rate to 0.1 mL/h and thereby increasing the residence time, increased the conversion to 72% and an exclusive selectivity for the rearrangement product **4** was obtained. A linear increase in the reactivity coupled with a linear enhancement in the selectivity toward the rearrangement product **4** was observed when the residence time of the reactants was modified continuously.<sup>28</sup> In the cascade reaction above, increasing the flow rate would shorten the residence time of the intermediate to prevent further rearrangements. Conversely, the final rearrangement product was favored by increasing the residence time. Such method of tuning chemoselectivity would be an advantage untenable in a batch reaction mode as well as in traditional homogeneous catalysis.<sup>28</sup>

Analysis of catalytic organic transformations in flow reactors and detection of short-lived intermediates are essential for optimization of these complex reactions. Spectral mapping of the organic phase and metallic catalyst during the multi-step formation of a dihydropyran in a flow microreactor was achieved through micrometer-sized synchrotron-based IR and X-ray beams with a spatial resolution of 15  $\mu\text{m}$  (Figure 9).

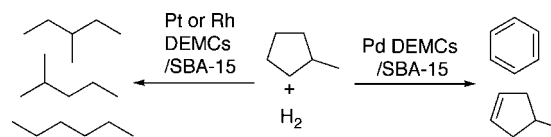


**Figure 9.** Schematic representation of a cascade reaction catalyzed by Au/G4OH/SBA-15 characterized in situ by synchrotron-sourced IR microspectroscopy and  $\mu\text{m}$ -NEXAFS spectroscopy.

Au/G4OH/SBA-15 activated the cascade reaction with high yield under continuous flow conditions. In situ synchrotron-sourced IR microspectroscopy detected the evolution of the reactant, a substituted propargyl vinyl ether, into the primary product, allenic aldehyde, which was then further isomerized to the acetal, the secondary product. The kinetic evolution of the organic reaction and the essential role of the primary product as an intermediate were analyzed via in situ IR microspectroscopy. Direct correlation was obtained between the catalytically active areas along the flow reactor, as detected by IR, to local high concentrations of the catalytically active species, Au(III), as analyzed by  $\mu\text{m}$ -NEXAFS spectroscopy. These measurements indicated that the oxidation state of the catalyst and, as a consequence, its catalytic properties were altered along the flow reactor. Mapping of the gradual evolution of this multistep catalytic process afforded a deeper mechanistic understanding of the kinetic role of the intermediates in this study.<sup>32</sup>

The DEMCs also worked well in a gas flow reactor at temperatures in the range of 150–250  $^{\circ}\text{C}$  (Scheme 1). Pt DEMCs were

### Scheme 1. Methylcyclopentane Hydrogenative Isomerization Catalyzed by Supported DEMCs



highly active for the hydrogenation of the methylcyclopentane (MCP) at 200–225  $^{\circ}\text{C}$ , with TOF up to 334  $\text{h}^{-1}$ , higher than other catalysts reported in the literature. The selectivity of 99.6% was achieved for the ring opening isomerization at high conversion (94%). Rh and Pd DEMCs brought different product selectivity. The deactivation of the catalysts began at temperatures above 250  $^{\circ}\text{C}$ , which could be attributed to the decomposition of the dendrimer and agglomeration of the clusters. The broad applications and wide operation conditions of DEMCs in catalysis were demonstrated.<sup>35</sup>

### CONCLUSIONS

The reactions that have been studied with supported DEMCs in our groups are summarized in Table 1. Advantages of supported

**Table 1.** List of Transformations Studied with Supported DEMCs in Our Groups

reaction type	DEMC metal	ref
hydrogenation and ring opening	Pt or Rh	17, 29
hydroalkoxylation reaction	Pt or Pd	21, 26, 31
Hayashi–Ito aldol reaction	Au	30
cascade cyclopropanation rearrangement	Au	28
cascade dihydropyran formation	Au	32
hydrogenative isomerization	Pt, Pd, or Rh	33

DEMCs as heterogenized homogeneous catalysts include the following: (1) the catalysts have the activity equivalent to homogeneous catalysts, which conventional heterogeneous catalysts lack, (2) the heterogenized homogeneous catalysts are recyclable in contrast to homogeneous catalysts with comparable performance, and (3) enhanced activity or selectivity compared to conventional homogeneous catalysts is enabled by exclusive heterogeneous handles for optimization.

### OUTLOOK

Besides the reactions shown in Table 1, we expect that a board range of transformations will benefit from supported DEMCs as heterogenized homogeneous catalysts. To expand the reaction scope, supported DEMCs more resistant to harsh reaction conditions are desired. In the cases described above, the formation of stable heterogeneous catalysts took advantage of the weak interactions between preformed DEMCs and a support. The fixation of dendrimer onto a support via covalent bonds can also be performed before the synthesis of DEMCs via two strategies. The first strategy is to end-link the dendrimer or dendron (usually contains a single chemically addressable group) to the support (convergent synthesis).<sup>34</sup> The second strategy consists of dendrimer growth, generation-by-generation, at the surface of the support (divergent synthesis). Interestingly, Astruc's group showed that the resultant catalysts synthesized via these two different routes could have different activity.<sup>35</sup> These synthesis methods might offer DEMCs with higher stability against deactivation or leaching in harsh conditions.

We have demonstrated that heterogenized homogeneous catalysis is achieved via DEMCs. However, with the exception of Ag and Cu, the main elements used as the active catalysts were limited to precious metals, i.e., Pt, Au, Pd, and Rh. Catalysis with other elements, particularly the more affordable and abundant first-row transition metals, like Fe, Co, and Ni, has few precedents.<sup>36</sup> These metals are prone to aggregation due to their ferromagnetism in the metallic state generated during the synthesis of clusters. Furthermore, they are vulnerable to oxidation when exposed to air, which complicates the formation of clusters. These intrinsic detriments account for their limited applications in the heterogenized homogeneous catalysis. It is highly desirable to broaden the cluster catalysis via incorporating earth-abundant metals in DEMCs.

Despite its broad utility, the supported DEMCs catalysts presently lack a modular handle to tune reaction outcomes. Yet, rapid optimization of catalyst performance metrics such as enantio-, diastereo-, regio-, and chemoselectivity would greatly advance the sophistication and scope of transformations catalyzed by metal clusters. Ancillary ligands, commonly utilized in transition metal catalysis to tune catalyst selectivity, were a logical choice of the desired modular handles to be added to metal clusters.<sup>37</sup> We expect to achieve product enantioselectivity using this strategy.

Rapid developments of characterization tools, especially synchrotron-based instruments,<sup>38</sup> would allow further understanding of structure–property relationship of the metal clusters. This knowledge would facilitate the development of the next-generation clusters catalysts.

## AUTHOR INFORMATION

### Corresponding Authors

\*E-mail: [fdtoste@berkeley.edu](mailto:fdtoste@berkeley.edu).

\*E-mail: [somorjai@berkeley.edu](mailto:somorjai@berkeley.edu).

### ORCID

Rong Ye: [0000-0002-4171-5964](https://orcid.org/0000-0002-4171-5964)

Aleksandr V. Zhukhovitskiy: [0000-0002-3873-4179](https://orcid.org/0000-0002-3873-4179)

Christophe V. Deraedt: [0000-0002-9347-7726](https://orcid.org/0000-0002-9347-7726)

F. Dean Toste: [0000-0001-8018-2198](https://orcid.org/0000-0001-8018-2198)

Gabor A. Somorjai: [0000-0002-8478-2761](https://orcid.org/0000-0002-8478-2761)

### Notes

The authors declare no competing financial interest.

### Biographies

**Rong Ye** was born in Dongguan, Guangdong, China. He received his B.E. degree from Sun Yat-sen University (Guangzhou, China) in 2011 after conducting research with Prof. Xiaoming Chen. He received his M.Sc. degree in Chemistry from UCLA in 2012. Currently, he is pursuing his Ph.D. degree with Professors Somorjai and Toste at the University of California, Berkeley and Lawrence Berkeley National Laboratory. His research interests encompass the synthesis, characterization, and reaction mechanistic studies of various catalytic materials.

**Aleksandr V. Zhukhovitskiy** was born in Dnepropetrovsk, Ukraine. He completed his undergraduate studies at Northwestern University in 2011 and earned his Ph.D. in Chemistry under the supervision of Professor Jeremiah A. Johnson at the Massachusetts Institute of Technology. Currently, Zhukhovitskiy is a Life Science Research Foundation Merck Postdoctoral Fellow in the laboratory of Professor Dean Toste in the Department of Chemistry at University of California, Berkeley. Zhukhovitskiy's graduate work advanced the surface chemistry of persistent carbenes and merged supramolecular cage chemistry with

polymer networks. In the Toste group, Zhukhovitskiy is focused on the development of new gold-catalyzed transformations.

**Christophe V. Deraedt** received his master's degree in nanoscience, life science, and chemistry in 2011 at the University of Bordeaux I. He worked on the synthesis and uses of green nanoreactors (dendrimers and polymers) for catalysis of reactions including C–C bond formation and transformation, CuAAC “click” reactions, and hydrogenation chemistry for his Ph.D. with Prof. Didier Astruc. In 2016, he started a postdoctorate in the Somorjai group on the heterogenization of homogeneous catalysts. His main work involved synthesis and use of metallic nanoparticles stabilized by dendrimers and supported on silica for C–C, C–H bond activation, and dehydrogenation reactions.

**F. Dean Toste** was born in Terceira, Azores, Portugal in 1971, but soon moved to Toronto, Canada. He obtained a B.Sc. and M.Sc. from the University of Toronto and his Ph.D. from Stanford University in 2000 from Professor Barry M. Trost. Following postdoctoral research at the California Institute of Technology in the laboratory of Professor Robert H. Grubbs, he joined the faculty at the UC Berkeley, in 2002. His research interests are in catalysis, in particular homogeneous catalysis, and its application to chemical synthesis.

**Gabor A. Somorjai** was born in Budapest, Hungary in 1935. He was a fourth-year student of Chemical Engineering at the Technical University in Budapest in 1956 at the outbreak of the Hungarian Revolution. He received his Ph.D. in Chemistry from UC Berkeley in 1960. He joined the IBM research staff in Yorktown Heights, New York until 1964. He joined the faculty at UC Berkeley in 1964. His research interest is in the fields of surface science and catalysis.

## ACKNOWLEDGMENTS

We acknowledge support from the Director, Office of Science, Office of Basic Energy Sciences, Division of Chemical Sciences, Geological and Biosciences of the US DOE under Contract DEAC02-05CH11231. A.V.Z. is a Merck Fellow of the Life Sciences Research Foundation. We are grateful to our current and former colleagues who have contributed to this work and whose efforts and creativity are cited and highlighted in this Account.

## REFERENCES

- (1) Bertrand, J. A.; Cotton, F. A.; Dollase, W. A. The Crystal Structure of Cesium Dodecachlorotrirhenate-(III), a Compound with a New Type of Metal Atom Cluster. *Inorg. Chem.* **1963**, *2*, 1166–1171.
- (2) Mason, M. G. Electronic structure of supported small metal clusters. *Phys. Rev. B: Condens. Matter Mater. Phys.* **1983**, *27*, 748–762.
- (3) Jin, R.; Zeng, C.; Zhou, M.; Chen, Y. Atomically Precise Colloidal Metal Nanoclusters and Nanoparticles: Fundamentals and Opportunities. *Chem. Rev.* **2016**, *116*, 10346–10413.
- (4) Kleis, J.; Greeley, J.; Romero, N. A.; Morozov, V. A.; Falsig, H.; Larsen, A. H.; Lu, J.; Mortensen, J. J.; Dulak, M.; Thygesen, K. S.; Nørskov, J. K.; Jacobsen, K. W. Finite Size Effects in Chemical Bonding: From Small Clusters to Solids. *Catal. Lett.* **2011**, *141*, 1067–1071.
- (5) Corma, A.; Concepción, P.; Boronat, M.; Sabater, M. J.; Navas, J.; Yacaman, M. J.; Larios, E.; Posadas, A.; López-Quintela, M. A.; Buceta, D.; Mendoza, E.; Guiler, G.; Mayoral, A. Exceptional oxidation activity with size-controlled supported gold clusters of low atomicity. *Nat. Chem.* **2013**, *5*, 775–781.
- (6) Tyo, E. C.; Vajda, S. Catalysis by clusters with precise numbers of atoms. *Nat. Nanotechnol.* **2015**, *10*, 577–588.
- (7) Xu, Z.; Xiao, F. S.; Purnell, S. K.; Alexeev, O.; Kawi, S.; Deutsch, S. E.; Gates, B. C. Size-dependent catalytic activity of supported metal clusters. *Nature* **1994**, *372*, 346–348.



- (8) Kaden, W. E.; Wu, T.; Kunkel, W. A.; Anderson, S. L. Electronic Structure Controls Reactivity of Size-Selected Pd Clusters Adsorbed on TiO<sub>2</sub> Surfaces. *Science* **2009**, *326*, 826–829.
- (9) Buhleier, E.; Wehner, W.; Vogtle, F. "Cascade"- and "Nonskid-Chain-like" Syntheses of Molecular Cavity Topologies. *Synthesis* **1978**, *1978*, 155–158.
- (10) Newkome, G. R.; Yao, Z.; Baker, G. R.; Gupta, V. K. Micelles. Part I. Cascade molecules: a new approach to micelles. A [27]-arborol. *J. Org. Chem.* **1985**, *50*, 2003–2004.
- (11) Hawker, C. J.; Frechet, J. M. J. Preparation of polymers with controlled molecular architecture. A new convergent approach to dendritic macromolecules. *J. Am. Chem. Soc.* **1990**, *112*, 7638–7647.
- (12) Crooks, R. M.; Zhao, M.; Sun, L.; Chechik, V.; Yeung, L. K. Dendrimer-Encapsulated Metal Nanoparticles: Synthesis, Characterization, and Applications to Catalysis. *Acc. Chem. Res.* **2001**, *34*, 181–190.
- (13) Gomez, M. V.; Guerra, J.; Velders, A. H.; Crooks, R. M. NMR Characterization of Fourth-Generation PAMAM Dendrimers in the Presence and Absence of Palladium Dendrimer-Encapsulated Nanoparticles. *J. Am. Chem. Soc.* **2009**, *131*, 341–350.
- (14) Rahim, E. H.; Kamounah, F. S.; Frederiksen, J.; Christensen, J. B. Heck Reactions Catalyzed by PAMAM-Dendrimer Encapsulated Pd(0) Nanoparticles. *Nano Lett.* **2001**, *1*, 499–501.
- (15) Deraedt, C.; Astruc, D. Homeopathic" Palladium Nanoparticle Catalysis of Cross Carbon–Carbon Coupling Reactions. *Acc. Chem. Res.* **2014**, *47*, 494–503.
- (16) Kashin, A. S.; Ananikov, V. P. Catalytic C–C and C–Heteroatom Bond Formation Reactions: In Situ Generated or Preformed Catalysts? Complicated Mechanistic Picture Behind Well-Known Experimental Procedures. *J. Org. Chem.* **2013**, *78*, 11117–11125.
- (17) Huang, W.; Kuhn, J. N.; Tsung, C.-K.; Zhang, Y.; Habas, S. E.; Yang, P.; Somorjai, G. A. Dendrimer Templated Synthesis of One Nanometer Rh and Pt Particles Supported on Mesoporous Silica: Catalytic Activity for Ethylene and Pyrrole Hydrogenation. *Nano Lett.* **2008**, *8*, 2027–2034.
- (18) Crooks, R. M.; Zhao, M. Dendrimer-Encapsulated Pt Nanoparticles: Synthesis, Characterization, and Applications to Catalysis. *Adv. Mater.* **1999**, *11*, 217–220.
- (19) Rebrov, E. A.; Leshchiner, I. D.; Muzafarov, A. M. Synthesis of Carbosilane Dendrimers with Variable Distance between Branching Nodes. *Macromolecules* **2012**, *45*, 8796–8804.
- (20) Zhao, D.; Feng, J.; Huo, Q.; Melosh, N.; Fredrickson, G. H.; Chmelka, B. F.; Stucky, G. D. Triblock Copolymer Syntheses of Mesoporous Silica with Periodic 50 to 300 Angstrom Pores. *Science* **1998**, *279*, 548–552.
- (21) Li, Y.; Liu, J. H.-C.; Witham, C. A.; Huang, W.; Marcus, M. A.; Fakra, S. C.; Alayoglu, P.; Zhu, Z.; Thompson, C. M.; Arjun, A.; Lee, K.; Gross, E.; Toste, F. D.; Somorjai, G. A. A Pt-Cluster-Based Heterogeneous Catalyst for Homogeneous Catalytic Reactions: X-ray Absorption Spectroscopy and Reaction Kinetic Studies of Their Activity and Stability against Leaching. *J. Am. Chem. Soc.* **2011**, *133*, 13527–13533.
- (22) Lang, H.; May, R. A.; Iversen, B. L.; Chandler, B. D. Dendrimer-Encapsulated Nanoparticle Precursors to Supported Platinum Catalysts. *J. Am. Chem. Soc.* **2003**, *125*, 14832–14836.
- (23) Deutsch, D. S.; Lafaye, G.; Liu, D.; Chandler, B.; Williams, C. T.; Amiridis, M. D. Decomposition and Activation of Pt-Dendrimer Nanocomposites on a Silica Support. *Catal. Lett.* **2004**, *97*, 139–143.
- (24) Liu, D.; López-De Jesús, Y. M.; Monnier, J. R.; Williams, C. T. Preparation, characterization, and kinetic evaluation of dendrimer-derived bimetallic Pt–Ru/SiO<sub>2</sub> catalysts. *J. Catal.* **2010**, *269*, 376–387.
- (25) Albiter, M. A.; Morales, R.; Zaera, F. Dendrimer-based synthesis of Pt catalysts for hydrocarbon conversion. *Appl. Catal., A* **2011**, *391*, 386–393.
- (26) Witham, C. A.; Huang, W.; Tsung, C.-K.; Kuhn, J. N.; Somorjai, G. A.; Toste, F. D. Converting homogeneous to heterogeneous in electrophilic catalysis using monodisperse metal nanoparticles. *Nat. Chem.* **2010**, *2*, 36–41.
- (27) Rebek, J. Mechanistic studies using solid supports: the three-phase test. *Tetrahedron* **1979**, *35*, 723–731.
- (28) Gross, E.; Liu, J. H.-C.; Toste, F. D.; Somorjai, G. A. Control of selectivity in heterogeneous catalysis by tuning nanoparticle properties and reactor residence time. *Nat. Chem.* **2012**, *4*, 947–952.
- (29) Ye, R.; Yuan, B.; Zhao, J.; Ralston, W. T.; Wu, C.-Y.; Unel Barin, E.; Toste, F. D.; Somorjai, G. A. Metal Nanoparticles Catalyzed Selective Carbon–Carbon Bond Activation in the Liquid Phase. *J. Am. Chem. Soc.* **2016**, *138*, 8533–8537.
- (30) Ye, R.; Zhao, J.; Yuan, B.; Liu, W.-C.; Rodrigues De Araujo, J.; Faucher, F. F.; Chang, M.; Deraedt, C. V.; Toste, F. D.; Somorjai, G. A. New Insights into Aldol Reactions of Methyl Isocyanacetate Catalyzed by Heterogenized Homogeneous Catalysts. *Nano Lett.* **2017**, *17*, 584–589.
- (31) Huang, W.; Liu, J. H.-C.; Alayoglu, P.; Li, Y.; Witham, C. A.; Tsung, C.-K.; Toste, F. D.; Somorjai, G. A. Highly Active Heterogeneous Palladium Nanoparticle Catalysts for Homogeneous Electrophilic Reactions in Solution and the Utilization of a Continuous Flow Reactor. *J. Am. Chem. Soc.* **2010**, *132*, 16771–16773.
- (32) Gross, E.; Shu, X.-Z.; Alayoglu, S.; Bechtel, H. A.; Martin, M. C.; Toste, F. D.; Somorjai, G. A. In Situ IR and X-ray High Spatial-Resolution Microspectroscopy Measurements of Multistep Organic Transformation in Flow Microreactor Catalyzed by Au Nanoclusters. *J. Am. Chem. Soc.* **2014**, *136*, 3624–3629.
- (33) Deraedt, C.; Melaet, G.; Ralston, W. T.; Ye, R.; Somorjai, G. A. Platinum and Other Transition Metal Nanoclusters (Pd, Rh) Stabilized by PAMAM Dendrimer as Excellent Heterogeneous Catalysts: Application to the Methylcyclopentane (MCP) Hydrogenative Isomerization. *Nano Lett.* **2017**, *17*, 1853–1862.
- (34) Gilbertson, J. D.; Vijayaraghavan, G.; Stevenson, K. J.; Chandler, B. D. Air and Water Free Solid-Phase Synthesis of Thiol Stabilized Au Nanoparticles with Anchored, Recyclable Dendrimer Templates. *Langmuir* **2007**, *23*, 11239–11245.
- (35) Deraedt, C.; Wang, D.; Salmon, L.; Etienne, L.; Labrugère, C.; Ruiz, J.; Astruc, D. Robust, Efficient, and Recyclable Catalysts from the Impregnation of Preformed Dendrimers Containing Palladium Nanoparticles on a Magnetic Support. *ChemCatChem* **2015**, *7*, 303–308.
- (36) Wang, H.; Rempel, G. L. Bimetallic Dendrimer-encapsulated Nanoparticle Catalysts. *Polym. Rev. (Philadelphia, PA, U. S.)* **2016**, *56*, 486–511.
- (37) Yasukawa, T.; Miyamura, H.; Kobayashi, S. Chiral Ligand-Modified Metal Nanoparticles as Unique Catalysts for Asymmetric C–C Bond-Forming Reactions: How Are Active Species Generated? *ACS Catal.* **2016**, *6*, 7979–7988.
- (38) Wu, C.-Y.; Wolf, W. J.; Levartovsky, Y.; Bechtel, H. A.; Martin, M. C.; Toste, F. D.; Gross, E. High-spatial-resolution mapping of catalytic reactions on single particles. *Nature* **2017**, *541*, 511–515.