

Review

Evolution of Isolated Atoms and Clusters
in CatalysisLichen Liu¹ and Avelino Corma^{1,*}

Structural transformation and evolution of active metal sites can occur in metal-catalyzed reactions in both homogeneous and heterogeneous systems. Such structural changes have an important impact on the catalytic behavior, including activity, selectivity, and stability. Aiming to establish a link between homogeneous and heterogeneous catalytic systems, this review begins with a discussion on dynamic structural transformations of metal catalysts in homogeneous reactions and the corresponding implications. We then discuss the evolution of isolated metal atoms and clusters in heterogeneous catalysts during catalyst activation and under reaction conditions. Finally, strategies for stabilizing subnanometric metal species on solid supports are presented for potential industrial applications.

Structural Transformations in Catalysis

Since the 1960s, surface reconstruction or structural transformation of solid materials under chemical reaction conditions has been well established by surface science studies after the introduction of ultrahigh vacuum systems and the related measurement techniques [1,2]. Later, the dynamic structural transformation of solid catalysts containing nanoparticles has been intensively studied at the atomic and molecular levels with advanced electron microscopy and spectroscopy techniques [3,4]. These advances have shaped our understanding of the nature of active sites in heterogeneous catalysis and have contributed to the rational design of solid catalysts for practical applications [5,6]. The surface reconstruction of nanoparticles can be understood as the rearrangement of the atoms in response to a change in the environment, which is induced by the interaction between the surface atoms and the gas-phase/liquid-phase reactants and/or solvents [7].

Based on the significant development of advanced characterization techniques (e.g., aberration-corrected electron microscopy, advanced *in situ* spectroscopy) and new methodologies for catalyst preparation, research on the nature of the active sites in heterogeneous metal catalysts has shifted in focus from nanoparticles to subnanometric metal catalysts; namely, isolated single atoms and metal clusters consisting of only a few atoms [8–10]. The size of these small metal species matches the catalysts used in homogeneous catalysis (as well as the active sites in enzymes [11]), and the crucial roles of isolated metal atoms and metal clusters with a few atoms in some catalytic processes have been demonstrated in numerous heterogeneous systems [12–16].

However, it is a clear trend in the catalysis community to look for unified concepts that may decrease or even eliminate the boundaries between homogeneous and heterogeneous catalysis [17–19]. Although the catalysts, reaction conditions, and reaction scopes are diversely different among the disciplines, similarity in the atomic structures of the active sites can be found; this similarity can be a connection to unify the reaction mechanisms in different systems. To achieve

Highlights

Structural evolution of isolated metal atoms and metal clusters with low atomicity is commonly observed in both homogeneous and heterogeneous catalysis. This evolution is directly associated with the formation of the working active sites and deactivation mechanism of the catalyst.

Understanding the evolutionary behavior of subnanometric metal catalysts can help to stabilize the active sites under harsh reaction conditions. Regeneration of the deactivated metal catalyst also relies on atomic-level understanding of the dynamic structural transformation processes.

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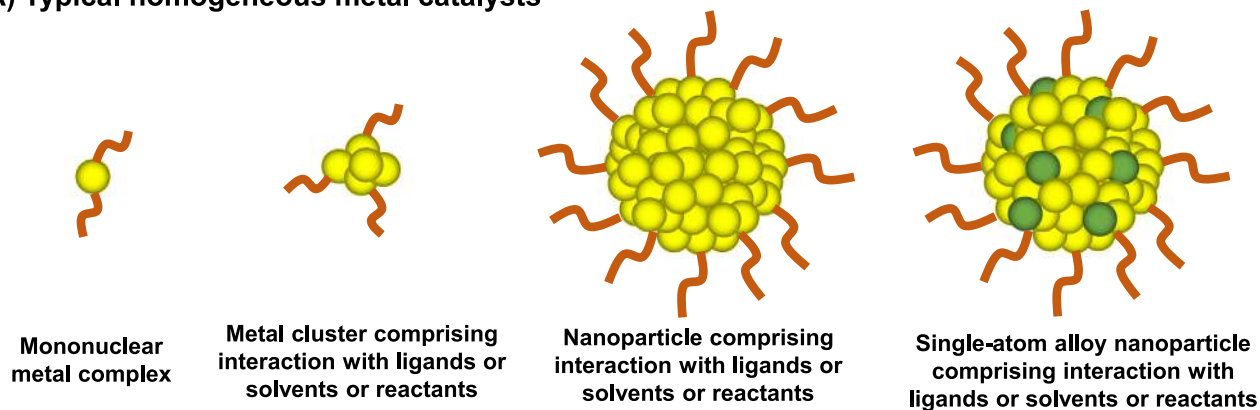
that unified mechanistic understanding, the dynamic structural transformation of the metal species will play a critical role, since such dynamic behavior exists commonly in both homogeneous and heterogeneous systems (Box 1).

In this review, we begin with a discussion of how molecular metal compounds or complexes may transform into metal clusters or nanoparticles in homogeneous catalytic systems. Implicated by the evolutionary behavior of molecular metal catalysts, we proceed to heterogeneous systems and discuss how the atomicity of the supported metal catalysts may change under reaction conditions, as well as discussing the corresponding implications for reactivity. Finally, perspectives on strategies for stabilization of the supported subnanometric metal catalysts, methods for catalyst regeneration, and relevant future research trends are presented.

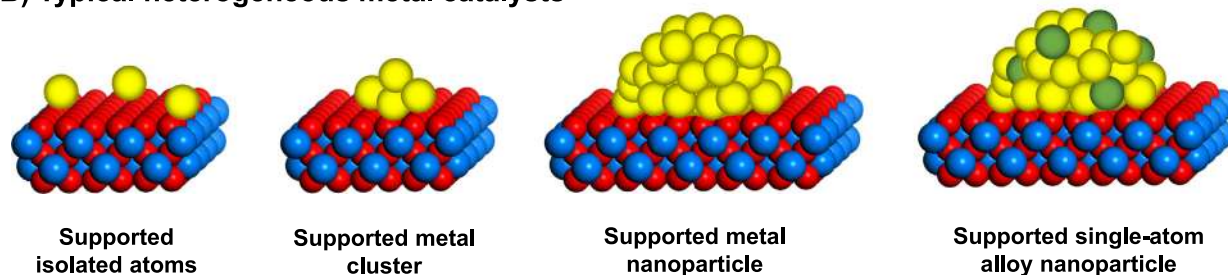
Box 1. The Structures of Typical Homogeneous and Heterogeneous Metal Catalysts

According to the size, chemical composition, and coordination environment, typical metal catalysts used in homogeneous and heterogeneous systems can be categorized into mononuclear metal complexes (supported isolated atoms), metal clusters, and nanoparticles. In Figure 1, the structures of the metal catalysts involved in this review are briefly illustrated. It should be noted that the atomic structure of a metal particle (either a cluster or a nanoparticle) will be quite complicated and highly dynamic under reaction conditions. Nevertheless, in many cases the ligands or coordination atoms to the metal sites should also be considered when discussing the structure of the active sites and the reaction mechanism.

(A) Typical homogeneous metal catalysts



(B) Typical heterogeneous metal catalysts



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Figure 1. Structures of Typical Homogeneous and Heterogeneous Metal Catalysts. (A) Illustrations of several types of metal catalysts used for homogeneous catalytic processes, including mononuclear metal complexes, metal clusters with a few atoms, metal nanoparticles, and single-atom alloy nanoparticles. (B) Illustrations of several types of supported metal catalysts containing isolated atoms, metal clusters with a few atoms, nanoparticles with tens or hundreds of atoms, and single-atom alloy nanoparticles containing isolated metal sites in a metal matrix. This review is focused on these metal catalysts and discusses how their structures will evolve under catalytic reaction conditions.

Homogeneous Catalytic Systems

Evolution of Molecular Metal Catalysts

Conventionally, active sites in homogeneous catalytic systems are usually associated with mononuclear metal complexes with ligands or reactants coordinating with the metal centers, which originate from metal complexes added in the reaction mixture. In some cases, binuclear or multinuclear metal species are also proposed to be the working active sites [20]; however, the detailed structural transformation, changes of the atomicity of the metal species in homogeneous catalysis, and the final active species formed are rarely studied.

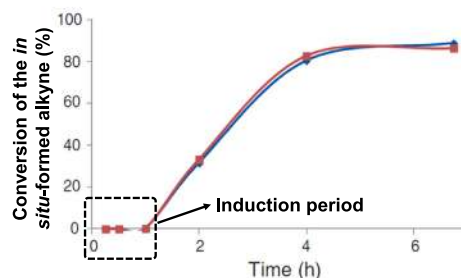
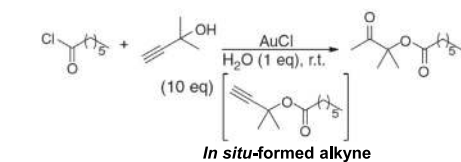
In 2012, Corma and colleagues reported the *in situ* generation of subnanometric Au clusters during the ester-assisted hydration of alkynes and bromination of *p*-dimethoxybenzene when using HAuCl_4 and AuCl compounds as the initial Au catalyst [21]. As shown in Figure 1A,B, it has been observed in both reactions that the initially introduced Au salts were not the active species, but rather the metal clusters formed during the reactions. Moreover, each reaction was better catalyzed by *in situ*-formed subnanometric Au clusters of different atomicity. Those observations are not exclusive for Au-catalyzed reactions but have also been observed in Pd-catalyzed C–C coupling reactions, Cu-catalyzed C–N, C–O, and C–N coupling reactions, and Pt-catalyzed hydrosilylation of alkynes (Figure 1C–E) [22–24]. In those examples, the formation of subnanometric metal clusters, as confirmed by fluorescence and matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF), can be associated with the initiation of product formation after an induction period (see the reaction kinetics graph in Figure 1A,B), indicating the critical role of metal clusters in these homogeneous catalytic processes.

The formation of subnanometric metal clusters from the metal compounds or complexes under reaction conditions could be caused by the reduction of metal precursors by the ligands or the reactants. In recent work, Rh_5 clusters have been found to be generated from organometallic mononuclear Rh complexes in the presence of H_2 , and the Rh_5 clusters serve as the working catalysts for homogeneous hydrogenation of *N*-heteroarenes [25]. By contrast, the transformation of organometallic complexes under reaction conditions can cause catalyst deactivation. This is shown with the evolution of a mononuclear Ir complex into Ir_6 clusters during the glycerol dehydrogenation reaction [26], which could be caused by the reduction of the mononuclear Ir complex by the product (H_2) or the reactant (glycerol).

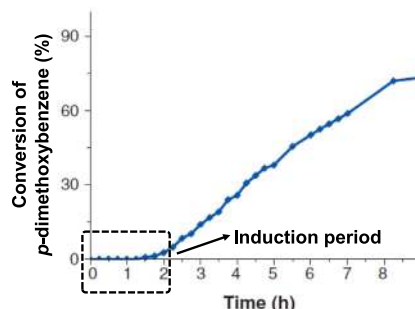
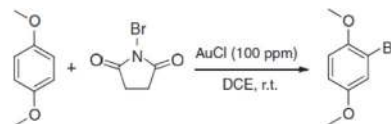
In homogeneous systems, the solvent can also play a role in the structural transformation of metal compounds. For example, when heating a mixture of CuCl and dimethyl sulfoxide (DMSO) in the presence of O_2 , CuCl can transform into CuOx clusters or nanoparticles [27]. Such a transformation has also been observed under the reaction conditions for CuCl-catalyzed oxidative coupling of terminal alkynes. Mechanistic and isotopic studies have shown that the *in situ*-formed CuOx nanoparticles (~2 nm in diameter) are the active species for oxidative coupling of terminal alkynes, which is also confirmed with heterogeneous CuOx/ TiO_2 catalysts. In the earlier case, the role of DMSO could be to promote the decomposition of CuCl and stabilize the resultant CuOx nanoparticles, while in some other cases solvents with weak reducibility [e.g., dimethylformamide (DMF)] can partially reduce the metal complex and stabilize the resultant metal clusters [28].

The growth of metal species from molecular precursors into metal clusters or nanoparticles during catalytic reactions can be treated as nucleation-growth processes, which have been intensively studied in the synthesis of colloid metal nanocrystals [29]. The solvent and reactants are the reducing agents that drive the transformation of the molecular metal catalysts into clusters or nanoparticles (Figure 2A) [30]. However, the concentration of the molecular metal precursor in the catalytic reactions is usually much lower than that for the wet-chemistry synthesis of

(A) Au-catalyzed ester-assisted hydration

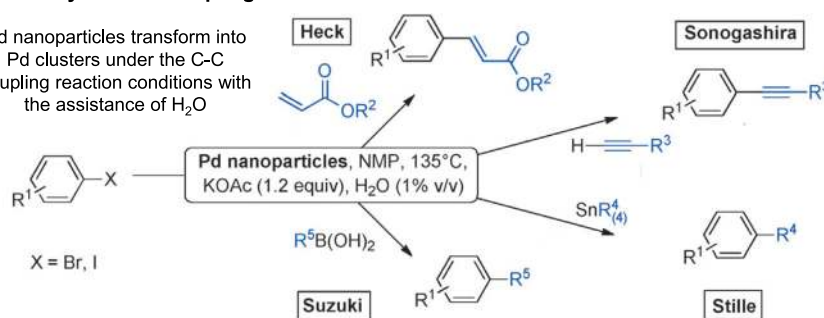


(B) Au-catalyzed bromination of arenes

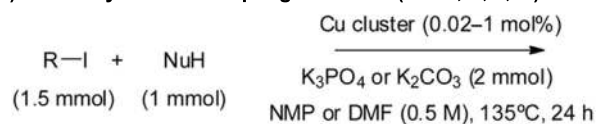


(C) Pd-catalyzed C–C coupling reactions

Pd nanoparticles transform into Pd clusters under the C–C coupling reaction conditions with the assistance of H₂O

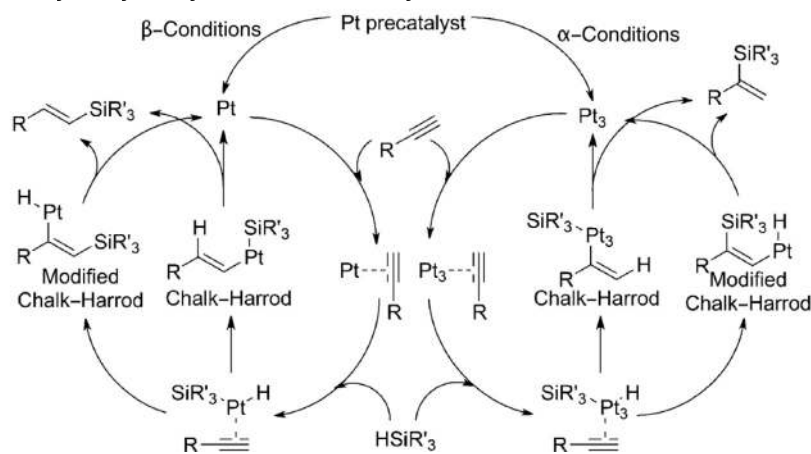


(D) Cu-catalyzed C–X coupling reactions (X = N, S, P, O)



NuH: amides, phenols, thiols, imidazoles, phosphines...

(E) Pt-catalyzed hydrosilylation of terminal alkynes



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metal nanoparticles, which makes the transformation between molecular metal species, clusters, and nanoparticles in liquid-phase reactions a dynamic process that depends strongly on the reaction conditions.

Evolution of Metal Clusters and Nanoparticles

As mentioned before, it has been reported that metal nanoparticles can disintegrate into smaller clusters or even single atoms in homogeneous systems [5,10]. A typical example is the leaching of Pd nanoparticles into Pd atoms and clusters during a C–C coupling reaction (Figure 2B). The oxidative addition of halide compounds to Pd nanoparticles is a critical step that causes the leaching of Pd species into solution [31–33]. This process is similar to oxidative etching in the synthesis and shape control of colloid metal nanoparticles [34]. It has been directly observed via transmission electron microscopy (TEM) that metal nanoparticles can be dissolved in solution under certain conditions as a consequence of oxidative etching [35,36]. The presence of nucleophilic molecules (e.g., water, amines) can promote the disintegration of Pd nanoparticles into Pd clusters under the reaction conditions for C–C cross-coupling reactions [21].

Due to the small size of the *in situ*-formed metal clusters and their flexible geometric structures, it is extremely difficult to resolve their atomic structures. The presence of metal clusters is usually confirmed by spectroscopy or mass spectrometry techniques. For example, Jiang and colleagues have isolated Pd₃ clusters coordinated with ligands that formed during Pd-catalyzed cleavage of both CS₂ carbon–sulfur bonds in the presence of HNO₃ [37]. The crystalline structure of the complex indicates that two S atoms are coordinated to Pd atoms in a bridged conformation, suggesting that the structure of the *in situ*-formed metal clusters interacts with the reactants and/or intermediates. Although the metal-catalyzed reaction usually occurs with the functional group in the substrate molecule, the interaction between the reactant and *in situ*-formed metal clusters can be related to the whole substrate molecule. Through experimental and theoretical studies, Cordon and colleagues have shown that medium to long alkyl/aryl side chains can stabilize smaller Au_n-alkyne intermediates than phenylacetylene for the hydration reaction of alkyne. Higher reactivity can be achieved due to the optimized Au⋯H–C and Au⋯π interactions [38].

Decomposition of metal agglomerates has also been observed in liquid-phase oxidation reactions. For instance, Au₂₅ clusters protected by thiol groups have been disrupted into Au(I) thiolates during the oxidation of styrene with *t*-butylhydrogenperoxide [39]. In this case, *t*-butylhydrogenperoxide should be the oxidant that drives the decomposition of the Au₂₅(SCH₂CH₂Ph)₁₈ clusters. The disintegration of Au particles has also been observed in Au/SiO₂ catalysts during the direct epoxidation of *cis*-cyclooctene with O₂. The *in situ*-formed subnanometric Au clusters from the leaching of Au nanoparticles are shown to be the working catalyst [40].

Figure 1. Evolution of Homogeneous Molecular Metal Catalysts under Reaction Conditions for Various Reactions. (A) Au-catalyzed ester-assisted hydration, (B) Au-catalyzed bromination of arenes, (C) Pd-catalyzed C–C coupling reactions, (D) Cu-catalyzed C–X (X = N, P, S, and O) coupling reactions, and (E) Pt-catalyzed hydrosilylation of alkynes. As can be seen the kinetic curves in (A,B), no conversion can be observed in the starting stage, implying that the starting Au complexes are not the working active species. ‘Induction period’ corresponds to the time between the starting of the catalytic reaction and the moment when measurable product is formed. After a certain induction period, products can be observed and the catalytic transformation is initiated. Similar induction periods have been observed in other reactions shown in (C–E). In (A,B,D,E), subnanometric metal clusters are *in situ* formed under reaction conditions from molecular metal complexes, while in (C) Pd clusters are formed from the disintegration of Pd nanoparticles with the assistance of H₂O. Adapted, with permission, from [21–24].

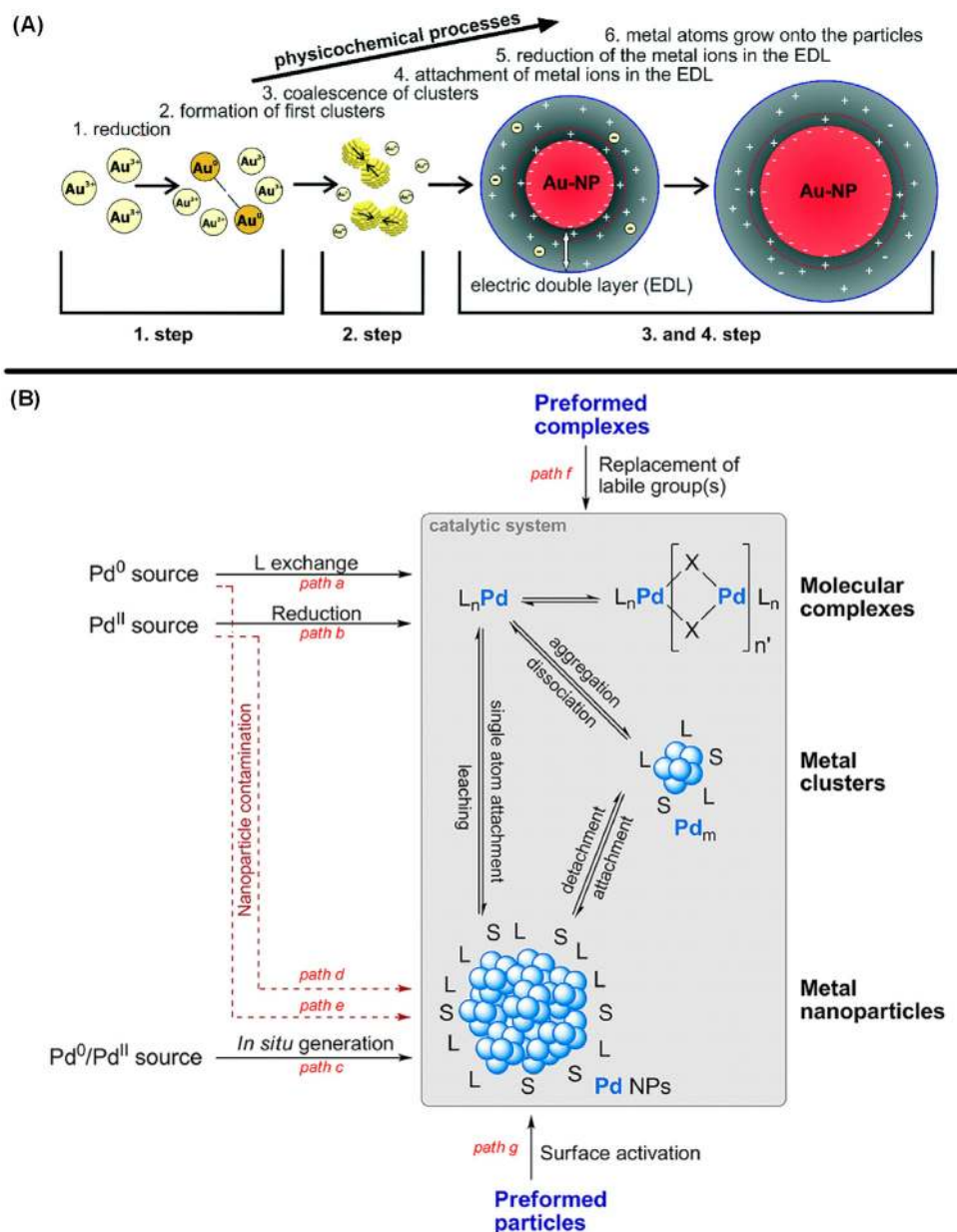


Figure 2. Illustration of the Formation of Metal Clusters and Nanoparticles from Molecular Complexes. (A) Growth of Au nanoparticles from atomic precursors in solution. Molecular Au complexes are reduced to metallic Au and form small Au clusters as nucleation sites. Through coalescence or the attachment of metal ions to the Au clusters, the size increases until the formation of Au nanoparticles. (B) Interchange between molecular Pd complexes, Pd clusters, and nanoparticles during catalytic reactions. The sintering and disintegration process can be highly dynamic and reversible, depending on the reaction conditions. Adapted, with permission, from [30,33].

It should be mentioned that one issue associated with the leaching of metal nanoparticles is the phantom reactivity observed in some organic catalytic reactions, which is caused by contamination with metal particles in magnetic stir bars [41]. Therefore, when using colloid metal clusters or nanoparticles for liquid-phase reactions, the leaching of metal species into solution is a critical

issue to be addressed before determining whether a reaction is classified as heterogeneous or homogeneous.

Heterogeneous Catalytic Systems

Evolution of Isolated Atoms

When isolated metal atoms are supported on solid carriers, the bonding interaction between the metal atoms and the support may not be strong enough to prevent sintering of the metal atoms (Box 2). One typical example is the structural evolution of supported isolated Pt atoms during the CO oxidation reaction. On the basis of an *in situ* X-ray absorption spectroscopy (XAS) study, the sintering of Pt atoms into Pt aggregates is associated with the reduction of positively charged Pt atoms by CO and further agglomeration caused by the higher mobility of the reduced Pt species [16,42]. However, when the support is changed from Al₂O₃ to CeO₂, the stability of isolated Pt atoms is greatly enhanced due to the stronger bonding interaction between Pt and CeO₂, resulting in the preservation of the dispersed Pt atoms [43,44]. Such CO-induced sintering of isolated Pt atoms has also been recently reported with Pt atoms supported on an MCM-22 zeolite during CO oxidation, the water–gas shift reaction, and a low-temperature CO+NO reaction [45,46]. As shown in Figure 3, the evolution of subnanometric Pt species depends strongly on the reaction conditions, exhibiting more flexible transformation than their nanoparticle counterparts under the same conditions. Despite the stability of Pt atoms supported on CeO₂ for the CO oxidation reaction, Pt atoms can transform into Pt nanoparticles of ~2 nm at >550°C when catalyzing the propane dehydrogenation to propylene [47]. These results indicate that the isolated metal atoms present in the as-prepared catalysts may not be the working active sites; rather, it is the *in situ*-formed metal clusters or nanoparticles.

The sintering of singly dispersed metal atoms into clusters and nanoparticles has also been observed with other metals. Followed by *in situ* extended X-ray absorption fine structure (EXAFS) spectroscopy, the atomically dispersed Au species in a fresh Au/CeO₂ sample transformed into Au nanoclusters under water–gas shift reaction conditions, even at 100–200°C [48]. The sintering of Au catalysts during the water–gas shift reaction has also been studied by TEM and the change in particle size can be associated with deactivation of the Au catalyst [49]. The sintering of Au atoms should be related to the reduction of cationic Au species into metallic Au by CO or H₂ produced in the water–gas shift reaction, since the sintering behavior is related to the CO/H₂O ratio in the feed gas. Although the sintering of isolated atoms is usually observed in the presence of reductive reactants, the addition of H₂ in the feed gases is beneficial for the stabilization of atomically dispersed Ir species on carbon support for heterogeneous methanol carbonylation to acetic acid [50]. The presence of H₂ can suppress the formation of volatile Ir (CO)₃ complexes and, therefore, avoid Ir leaching and sintering.

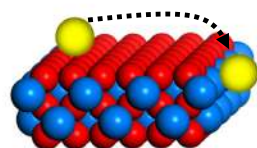
In other cases, the sintering of isolated metal atoms into clusters or nanoparticles can also be related to catalyst deactivation. This problem is observed in supported Au catalysts for hydrochlorination of acetylene. Hutchings and colleagues have demonstrated that singly dispersed Au atoms on carbon supports are the active sites for the hydrochlorination of acetylene to vinyl chloride monomer [51]. However, Au nanoparticles can form from the sintering of Au atoms under the reaction conditions, leading to catalyst deactivation [52]. This problem has been overcome by using Au complexes with S-containing ligands as the precursor for generating active and highly stable isolated Au atoms on the carbon support [53].

Another example to show the high mobility of atomically dispersed metal species under reaction conditions is the evolution of Cu cations confined in CHA zeolites during the NH₃-SCR

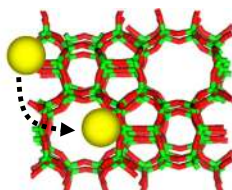
Box 2. Evolution of Supported Metal Catalysts under Reaction Conditions

Heterogeneous catalysts can show dynamic structural transformations during catalytic processes. The structural transformations will be reflected in the change of geometric and electronic structures. Several typical structural transformations are illustrated here in Figure 1. It should be noted that, for a given catalyst in a given reaction, the structure of the initial metal species may present several types of evolution behavior, such as surface migration, sintering, and redispersion, depending on the reaction conditions, the metal–support interaction, and other factors.

(A) Change of coordination environment

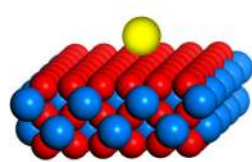


Migration on surface

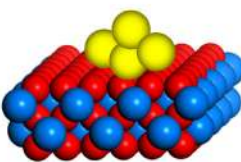
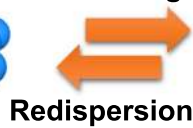


Migration in porous material

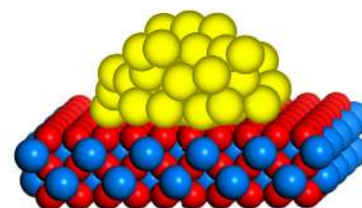
(B) Change of size

Supported
isolated atoms

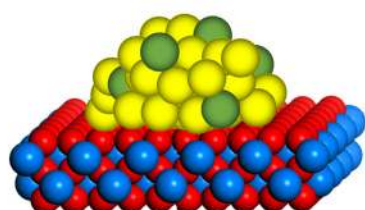
Sintering

Supported metal
cluster

Sintering

Supported metal
nanoparticleSupported metal
nanoparticle

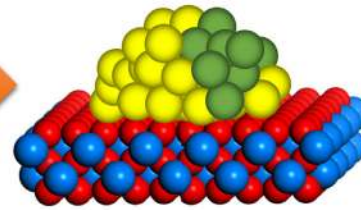
(C) Change of spatial distribution of the chemical compositions

Supported single-atom
alloy nanoparticle

Segregation



Redistribution

Supported bimetallic nanoparticle
with chemical segregation

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Figure 1. Several Types of Structural Evolution of Supported Metal Catalysts under Reaction Conditions. (A) An isolated metal atom may migrate from one type of binding site to another. When the support is a porous material like a metal–organic framework (MOF) or zeolite, the isolated atom may migrate from one site to another across the channel, pore, or cavity in the porous carrier material. (B) The atomicity of the metal species may change from isolated metal atoms to metal clusters with a few atoms to nanoparticles with tens or hundreds of atoms. The transformation can be reversible, depending on the reaction conditions and the physicochemical properties of the catalyst. (C) Potential structural transformation of supported single-atom alloy nanoparticles under reaction conditions. Due to the change of the atmosphere or environment, segregation may occur with single-atom alloy nanoparticles. By contrast, bimetallic nanoparticles with chemical segregation may be transformed into single-atom alloy nanoparticles under the proper conditions.

(selective catalytic reduction of NO_x by NH₃) reaction. In 2013, the migration and diffusion of Cu species from the surface of SAPO-34 zeolite crystallites to internal space during high-temperature activation in an O₂/N₂ atmosphere was observed by X-ray energy dispersive and X-ray photoelectron spectroscopy [54]. The migration mechanism of Cu species in this process has been studied in combined experimental and theoretical work (Figure 4A,B) [55].

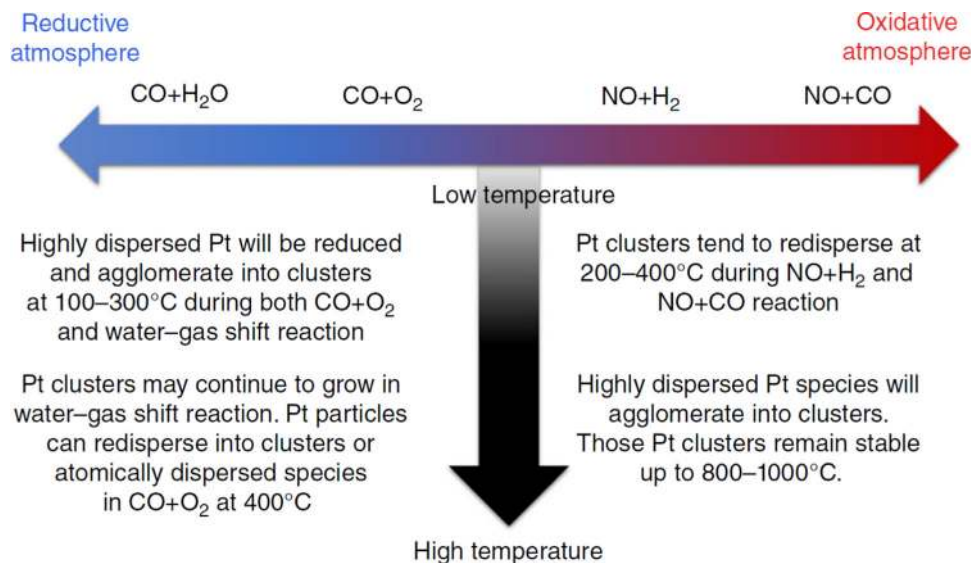
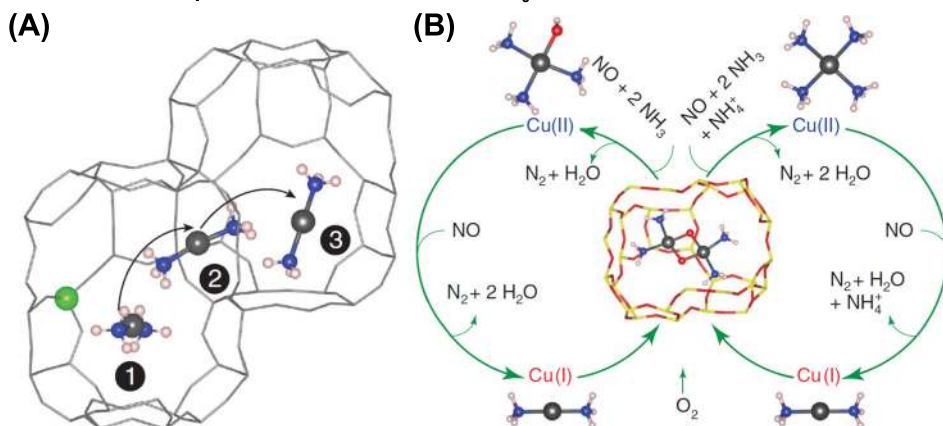
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Figure 3. Comparison of the Evolution of Pt Species under Different Reaction Conditions. The evolution of subnanometric Pt species is related to the reactants and reaction temperature. As summarized in this figure, the evolution is related to the chemical properties of the atmosphere. In a more reductive atmosphere, the sintering of the metal particles can be more favorable than that in an oxidative atmosphere. Nevertheless, the reaction temperature can also influence the state of the metal species. Redispersion of metal particles can occur when driven by thermal treatment. Such redispersion behavior could be related to the high mobility of metal atoms at high temperature. Adapted, with permission, from [46].

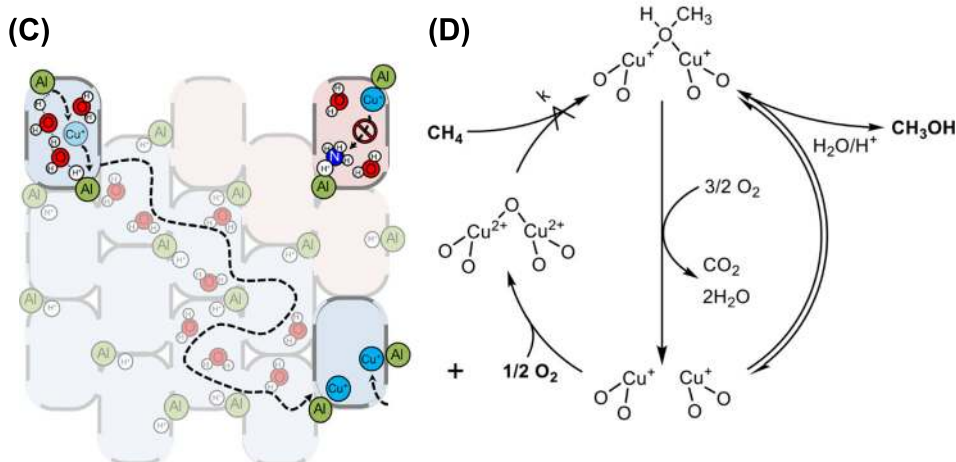
It is proposed that Cu atoms can migrate through the 8MR windows in the CHA zeolite and form dynamic Cu dimers that participate in an oxygen-mediated Cu(I)–Cu(II) redox cycle for the NH_3 -SCR reaction. Moreover, the migration of Cu has also been recently reported in the continuous partial oxidation of methane to methanol [56]. Through *in situ* spectroscopy techniques, Dinh and colleagues have shown that Cu(I) atoms can diffuse in CHA zeolites with the aid of $\text{H}^+/\text{H}_2\text{O}$ while inhabited by NH_3 under the conditions for the methane oxidation reaction (Figure 4C,D). These results indicate that the evolution of isolated atoms is strongly dependent on the reaction conditions (e.g., temperature, atmosphere).

Single-atom alloys are emerging materials containing isolated metal atoms in the matrix of another metal (Box 1), exhibiting unique reactivity compared with the corresponding monometallic counterparts [57]. Materials based on single-atom alloys have shown promising performance in various reactions, including selective hydrogenation, C–H activation in alkanes, and electrocatalytic reactions [58–60]. However, the stability of the isolated atoms in the metal matrix has rarely been studied, although metal segregation has been commonly observed in bimetallic nanoparticles under reaction conditions [61]. We speculate here that under some reaction conditions, either in reductive or oxidative atmospheres, the differing chemical potential between the two elements and reactants may cause the segregation of isolated metal sites.

In some cases, the structural evolution does not cause the sintering of isolated atoms and instead only the coordination environment is changed (Box 2). Such phenomena and associated implications for reactivity have been studied in both experimental and theoretical work [62–64]. Such influence can be interpreted since the electronic properties of the isolated metal species are directly related to their coordination environment. However, such structural evolution will be quite subtle and difficult to measure or characterize.

Evolution of Cu species in CHA zeolite under NH_3 -SCR reaction conditions

Evolution of Cu species in zeolite and its implication for methane oxidation reaction



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Figure 4. Evolution of Cu Species in Zeolites. (A,B) Illustration of the formation of paired Cu species under NH_3 -SCR reaction conditions and the corresponding reaction mechanism. Isolated Cu atoms can diffuse through the 8MR windows in the CHA zeolite structure and form Cu dimers, which catalyze the reaction between NH_3 and NO_x . (C,D) Depiction of hypothesized $\text{H}^+/\text{H}_2\text{O}$ -aided diffusion of Cu^+ within SSZ-13 to form Cu dimers, which are proposed to be the active sites for catalytic methane oxidation into methanol. However, the presence of NH_3 can inhibit the migration of isolated Cu species, which is not favorable for the methane oxidation reaction. In the reaction network (D), single O atoms may correspond to framework zeolite O atoms or coordinating H_2O molecules. Adapted, with permission, from [55,56].

In recent work, *in situ* transformation of isolated CuN_4 sites into subnanometric Cu clusters under the conditions for the electrocatalytic reduction of CO_2 into ethanol has been demonstrated [65]. Interestingly, the Cu clusters became redispersed into isolated Cu species following exposure to air. Considering the recent emerging interest in the applications of isolated metal atoms supported on carbon-based materials for various electrocatalytic reactions, it is necessary to study the potential structural transformations of metal species under electrocatalytic conditions and the impacts of the dopants and the morphology of the carbon support.

Evolution of Metal Clusters

During catalytic reactions, the growth of metal clusters into nanoparticles is usually driven by reductive reactants or a reducing atmosphere. As observed by high-resolution scanning

tunneling microscopy, sintering of Pd atoms and clusters can be induced by CO [66]. The continuous growth of mononuclear Ir species supported on zeolite Y to subnanometric Ir clusters in an intermediate step and finally to Ir nanoparticles has also been observed during the hydrogenation of cyclohexene to cyclohexane at 72°C [67]. In another example, subnanometric Au clusters supported on carbon nanotubes can agglomerate into Au nanoparticles of ~2 nm during the oxidation of thiophenol to corresponding disulfide and consequently cause catalyst deactivation [68]. The strong bonding between the thiol group and Au can account for the sintering of Au clusters. In an ultrahigh-vacuum system, sintering of subnanometric Au clusters (~0.5 nm) deposited on a TiO₂(110) surface was observed when exposed to a CO/O₂ mixture at 300 K. Interestingly, Au clusters remained stable in either CO or O₂, indicating the synergistic effect of CO and O₂ in initiating the Ostwald ripening of supported Au clusters [69].

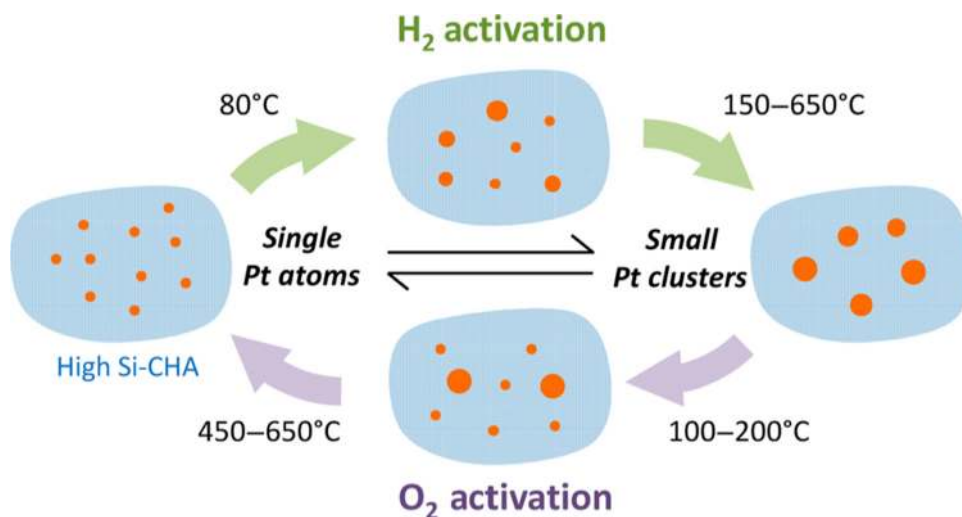
Accompanying the sintering of metal clusters, the reaction selectivity of the metal species can change accordingly. Subnanometric Ag₃ clusters deposited on alumina can sinter into Ag nanoparticles at >100°C, which caused increased selectivity to CO₂ in the direct epoxidation of propylene with O₂ [70]. The evolution of metal clusters may also occur during the post-reaction regeneration process. It is known that the C–H activation in alkanes is a structure-sensitive reaction, for which small Pt clusters are more active than the larger particles [71,72]. However, coke formed on small Pt clusters can block the active sites, requiring a high-temperature calcination-reduction treatment for regeneration, which may cause severe sintering of metal clusters. One potential strategy to overcome this issue is to stabilize subnanometric metal clusters in porous materials (discussed later).

Isolated atoms usually exhibit a stronger tendency towards sintering to reduce the surface energy [73]. From a thermodynamic viewpoint, sintering is related to the heat of adsorption of metal atoms/particles on a specific surface. For smaller metal entities, they have a stronger tendency for sintering to approach the lowest-energy state. Furthermore, the heat of adsorption of metal particles is also related to the surface structure and chemical composition. For instance, Ag particles are more stable on CeO_{2-x}(111) with oxygen vacancies than Ag particles of identical size but supported on an MgO(100) surface [74].

In principle, the electronic interaction between the metal and the support can be a descriptor to qualitatively or even semiquantitatively illustrate the stability of metal atoms/clusters on a given support. However, from a geometric viewpoint, only the metal atoms at the surface of metal nanoparticles can interact with reactants, while in the case of isolated atoms/clusters, almost all of the atoms can interact with the reactants. Therefore, isolated atoms and subnanometric clusters will be more sensitive to environmental changes while the structural disruption with large nanoparticles should be less favorable under the same conditions.

Redispersion of Supported Metal Aggregates into Isolated Atoms or Clusters

In the earlier sections, we discussed sintering of supported isolated atoms or metal clusters. The evolution can be bidirectional, however, meaning that metal clusters or even nanoparticles may evolve into isolated metal atoms after certain treatments or under reaction conditions. In some circumstances, the support can also provide the anchoring sites to facilitate the redispersion of metal aggregates. In 2016, Corma and colleagues reported the reversible transformation between Pt atoms and nanoclusters (~1 nm) in a high-silica CHA zeolite during oxidation–reduction treatments (Figure 5) [75]. When oxidizing Pt particles in air, metallic Pt can disintegrate and be captured by the zeolite framework [76]. The redispersion of metal aggregates into singly dispersed atoms can also be achieved in an inert atmosphere. Wei and colleagues have reported that Pd atoms were captured by N-doped carbon when the composite of Pd nanoparticles



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Figure 5. Reversible Transformation between Singly Dispersed Pt Atoms and Pt Nanoclusters (~1 nm) Confined in High-Silica CHA Zeolite during Reduction–Oxidation Treatments. Isolated Pt atoms can sinter into Pt nanoclusters of ~1 nm after being reduced by H₂ while the Pt nanoclusters can disintegrate into isolated Pt atoms after calcination in O₂. Adapted, with permission, from [75].

and N-doped carbon was heated at 900°C in argon [77]. In the case of non-noble metals, calcination in air may not be sufficient for the redispersion of particles into singly dispersed atoms due to the strong interaction between metal oxide particles and the support. To overcome this limitation, the presence of water can promote the redispersion of Cu nanoclusters into Cu atoms on alumina, which is likely to be due to the higher mobility of the copper hydroxide species [78]. Such an effect has also been reported with Cu-zeolite catalysts under NH₃-SCR conditions, and the higher mobility of the Cu hydroxide species than that of the CuOx species is supported by theoretical calculations [79].

In recent work, Cargnello and colleagues reported the deactivation of a Pd/Al₂O₃ catalyst caused by the disintegration of Pd nanoparticles into isolated Pd atoms during the methane combustion reaction [80]. An excess amount of O₂ was used for the methane combustion reaction and the oxidative atmosphere could be the driving force for the redispersion of Pd nanoparticles into isolated Pd atoms. Moreover, the deactivation of the Pd/Al₂O₃ catalyst also indicates that Pd nanoparticles are more active than Pd atoms for the methane combustion reaction when they are supported on Al₂O₃.

Since NO can be more reactive than O₂, one may consider that the redispersion of metal particles can be more favorable in the presence of NO. It has been reported in several NO-related reactions that NO can cause the oxidation of metal nanoparticles and therefore lead to the redispersion of metal particles on the support [81,82]. Related theoretical work indicates that the formation of metal-nitrosyl complexes plays a key role in the disintegration of metal nanoparticles [83].

It has been observed that Pt nanoparticles formed from sintering of Pt atoms can disintegrate into small Pt clusters at high temperature in a CO+O₂ atmosphere [46]. In another work on Rh species dispersed in zeolite Y, the agglomeration of a mononuclear Rh complex into Rh₄ clusters was observed under water–gas shift reaction conditions. Reversible redispersion of Rh₄ clusters into mononuclear Rh complexes occurred after treatment in helium flow [84].

Due to the high intrinsic stability of early transition-metal oxide species, the redispersion of those metal particles usually cannot be achieved by conventional calcination treatments. However, under some extreme conditions or in the presence of a suitable support, the redispersion of early transition-metal particles can be realized. Guo and colleagues have found that FeO_x nanoparticles supported on SiO₂ can be transformed into isolated Fe species with coordination to Si and C atoms during the direct nonoxidative conversion of methane into ethylene and aromatics at very high temperature (1173 K) [85]. In another work, Yang and colleagues reported the conversion of Ni nanoparticles into Ni atoms on N-doped carbon by a high-temperature annealing treatment [86]. These works indicate that the redispersion of early transition-metal nanoparticles into atoms may require high energy input and invoke other types of interaction such as metal–carbon or metal–nitrogen to replace the metal–oxygen bonding in the starting material.

The reactant-assisted disintegration of clusters or nanoparticles has been studied by theoretical calculations [87]. According to *ab initio* molecular dynamics simulations, Au atoms at the interface between Au nanoparticles and CeO₂ can escape from the Au nanoparticle and be trapped by the CeO₂ support due to the strong affinity between cationic Au and CeO₂ in the presence of CO and O₂. Interestingly, the Au atoms may reintegrate into the Au nanoparticle once the catalytic cycle for the CO+O₂ reaction is complete. This work indicates that the structure of the active species could be dynamically transformed during the catalytic cycle in some reactions. If so, the active site will not be a specific type of metal entity but rather will transition between a couple of states.

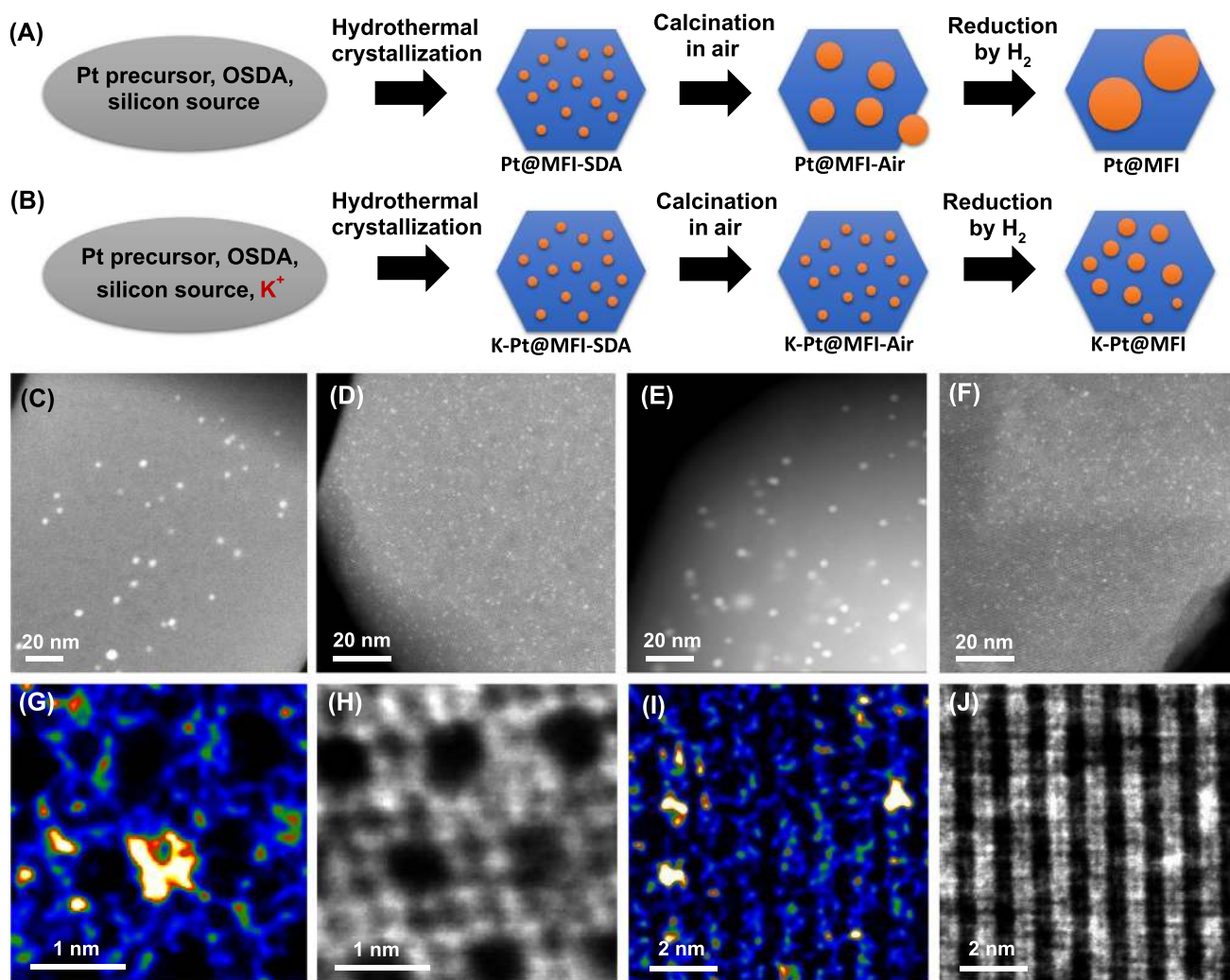
Recyclability is a key parameter to evaluate the potential of a catalyst for practical applications considering that catalyst deactivation is inevitable in some processes [88]. If catalyst deactivation is related to coke formation or the blockage of active sites caused by undesired product adsorption, a high-temperature calcination treatment in air is usually required to restore the exposure of active sites. However, when the metal species are supported on conventional nonporous solid carriers, severe sintering through Ostwald ripening or particle coalescence may occur in the consecutive high-temperature oxidation–reduction treatments. Then, additives could be added to accelerate the disruption of large metal nanoparticles into atoms or clusters. For instance, it has been found that treatment with CH₃I at 240°C can significantly transform Au nanoparticles supported on carbon, TiO₂, and Al₂O₃ into Au clusters or even Au atoms [89,90]. However, such redispersion is also related to the support, since treatment with CH₃I cannot effectively promote the redispersion of Au nanoparticles on SiO₂, which is potentially caused by the absence of anchoring sites for cationic Au species on SiO₂. The treatment of sintered Au catalyst with CH₃I has been shown to be an effective method to restore the activity of an Au/C catalyst for acetylene hydrochlorination reactions [91]. Synergistic effects have been observed in the reactant-induced disintegration of metal nanoparticles [92]. After treating carbon-supported metal nanoparticles (e.g., Ru, Rh, Pd) with a CH₃I/CO mixture, a volatile M(CO)_xI_y complex can be produced that can be captured and stabilized by the carbon support, resulting in the redispersion of metal nanoparticles into atomically dispersed species. The halide-promoted redispersion has been applied to some industrial catalysts used in light alkane dehydrogenation and reforming reactions [93].

Stabilization of Subnanometric Metal Species for Catalysis under Harsh Conditions

As discussed earlier, isolated metal atoms and metal clusters are quite sensitive to the environment. Responsive structural transformation may occur and cause catalyst deactivation, especially under high-temperature reaction conditions. In the case of catalyst deactivation caused by the redispersion of metal nanoparticles or clusters into isolated metal atoms, regeneration can be readily achieved by proper reductive treatment. However, regeneration may require harsh treatments when catalyst deactivation is caused by the sintering of isolated atoms or metal clusters into larger nanoparticles. In some cases, catalytic performance cannot be fully recovered due to the loss of

active metal component or structural disruption with the solid catalyst. In this context, it will be desirable to prepare solid catalysts in which the subnanometric metal entities are well stabilized and their reactivity can be easily recovered after facile regeneration treatments.

Generally, the stabilization of atoms and clusters on solid carriers can be achieved through either geometric constraints or chemical interactions between the metal species and the support. By choosing a suitable support that can introduce an appropriate metal–support interaction, the metal atoms or clusters can be strongly bonded to the solid carrier without ‘poisoning’ the active species. For instance, Al_2O_3 with penta-coordinated Al(III) sites are shown to be effective for



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Figure 6. Regioselective Generation of Subnanometric Pt Species in an MFI Zeolite. (A,B) Schematic illustration of the formation process of Pt@MFI and K-Pt@MFI samples by one-pot synthesis. Scanning transmission electron microscope (STEM) image of Pt-zeolite samples after reduction by H_2 at 600°C : K-free Pt-MFI (C), K-Pt@MFI (D), K-free PtSn@MFI (E), and K-PtSn@MFI (F). Identification of the location of subnanometric Pt clusters within the MFI structure. (G) High-resolution high-angle annular dark-field STEM (HAADF-STEM) image and (H) the corresponding integrated differential phase contrast (iDPC) image of the same area of the K-Pt@MFI sample in the [010] orientation. (I) HAADF-STEM image and (J) the corresponding iDPC image of the same area of the K-Pt@MFI sample in the tilted-[010] orientation. By correlating the paired HAADF-STEM and iDPC images, the location of the confined Pt clusters can be determined to be in the sinusoidal 10MR channels of the MFI zeolite. Adapted, with permission, from [98]. Abbreviations: OSDA, organic structure-directing agent; SDA, structure-directing agent.

stabilizing Pt atoms [94]. The use of coordinatively unsaturated binding sites for the stabilization of metal atoms has also been shown with other supports, such as CeO_2 and heteroatom-doped carbon materials [95]. In recent work, the addition of CeO_2 into an Au/C catalyst was reported to significantly promote the lifetime of supported Au catalysts for the hydrochlorination reaction of acetylene [96]. Redispersion of metallic Au nanoparticles on CeO_2 can occur in the atmosphere for acetylene hydrochlorination, which should be related to the redox cycles of Ce(IV)/Ce(III) and the strong interaction between atomically dispersed Au species with the CeO_2 support. The redispersion can occur in a wide range of $\text{C}_2\text{H}_2/\text{HCl}$ ratios, suggesting the flexibility of the Au/ CeO_2 catalyst.

The stabilization effect of defective sites on open-structure solid carriers may not be strong enough to preserve the high dispersion of subnanometric metal species under harsh reaction conditions, especially in reductive atmospheres at high temperature ($>500^\circ\text{C}$). In those circumstances, another strategy is to encapsulate subnanometric metal species into nanoporous materials, which can provide a constrained environment to protect the metal species from sintering into large nanoparticles while the reactants can still have access to the metal sites [97,98]. In this context, the well-matched pore size and rigid framework structure make zeolites ideal materials to host the singly dispersed metal atoms and small clusters. By post-synthesis treatment, isolated Pt atoms and Pt clusters can be introduced into a pure-silica MWW zeolite during the transformation of a 2D structure into a 3D [99]. The majority of the isolated Pt atoms and clusters are captured by the 12MR supercages in the final MCM-22 zeolite. Furthermore, it has been demonstrated that, subnanometric Pt clusters can be regioselectively generated in the sinusoidal channels of MFI zeolite instead of the intersectional void or the straight channels (Figure 6) [100]. This strategy can be extended to other metal-zeolite systems, and the location of metal species could be modulated by tuning the structure-directing agents.

In principle, the two strategies described can be combined by introducing anchoring atoms (e.g., Ce, Ti, Sn) in the framework of zeolites to stabilize the subnanometric metal species in the extra-framework positions [101]. The interaction between the anchoring sites and the metal species may cause synergistic effects for catalytic application. It has been reported that the small Au particle ($<2\text{ nm}$) confined TS-1 zeolite can work together with the framework Ti species to achieve the direct epoxidation of propylene to propane oxide with H_2 and O_2 [102]. To the best of our knowledge, precise control of the location of two functional components in zeolites has not been achieved yet and we expect advances in that direction will be made in the near future.

Concluding Remarks

As discussed in this review, the evolution of metal atoms and clusters is a common phenomenon in both homogeneous and heterogeneous systems. Understanding and elucidating the mechanism of the evolution of singly dispersed metal atoms and clusters can provide valuable information on the real active sites and how the catalyst is activated and deactivated during the entire catalytic process. In principle, for a specific type of metal species under given conditions, the tendency towards sintering or disintegration can be determined by the chemical interaction/potential between the metal species and the reactants, which can be studied by theoretical calculations. However, such calculations may be too complex and expensive under current conditions but may be achieved in the future on the basis of more powerful computing resources and better calculation methodologies (see Outstanding Questions).

Tracking the evolution of subnanometric metal species under the reaction conditions introduces great challenges in characterization, especially for homogeneous systems. The development of liquid TEM offers the opportunity to directly observe the evolution of metal catalysts under the

Outstanding Questions

Can the evolution of molecular catalysis in homogeneous and heterogeneous systems be tracked by electron microscopy and spectroscopy in real time?

Is it possible to establish a model and calculation methodology to predict the evolution behavior of supported isolated metal atoms by considering the metal-support interaction and the reaction conditions?

In bimetallic or multimetallic catalysts, how do the subnanometric metal domains evolve over time?

Can the isolated metal sites in single-atom alloys remain preserved under reaction conditions?

Can a synthesis methodology be developed for the regioselective generation of isolated metal atoms or clusters in specific locations within microporous systems?

How does the metal-support interaction evolve over time during the catalytic reaction?

reaction conditions for organic reactions, although the resolution is still not fine enough to view the atoms [103]. Other spectroscopic techniques (EXAFS, IR, XPS, UV-vis, and fluorescence) and mass spectroscopy also offer direct observation of the real-time evolution of subnanometric metal species under *in situ* or *operando* conditions. By combining the information obtained from different techniques, it is possible to depict the whole structural transformation process from the activation stage ('birth') to the deactivation ('death') stage [5,104].

Despite the recent emerging interests in the application of atomically dispersed metal catalysts for electrocatalysis, the evolution of metal species under electrocatalytic conditions has not been fully addressed and should be investigated systematically. Considering the more complicated reaction medium and reactor design compared with that of conventional thermal catalysis, more advanced *in situ* characterization techniques should be developed and the structure–reactivity correlation of the electrocatalyst should be established from the reaction initiation to the catalyst deactivation.

As discussed in this review, metal species may show dynamic structural transformations that are strongly dependent on the reaction conditions, and numerous factors including the temperature, reactants, pressure, support, metal loading, and particle size can influence their evolution. To establish a unified understanding of the evolution of metal catalysts, we have to directly compare the experimental results and rationalize the chemistry behind the phenomena. With that information in hand, catalyst development can be achieved in a more rational way [6,105]. In the case that the active species are *in situ* formed during the reaction, the direct generation of active sites in the starting catalyst can lead to a decrease in reaction time and an improvement in process efficiency. Since the *in situ*-formed metal species may be a mixture with various atomicities, modulations could be performed to improve the yield of the most active or suitable species with a narrow size distribution. In the case that the active species deactivate due to undesired structural transformation, deactivation could be alleviated or suppressed by adding components that can stabilize the active species. The regeneration efficiency could also be improved by choosing a suitable methodology for catalyst regeneration, which is based on the fundamental understanding of the evolution of subnanometric metal species in various environments.

Acknowledgments

We are grateful for financial support from the EU through the European Research Council (grant ERC-AdG-2014-671093, SynCatMatch) and the Spanish government through the 'Severo Ochoa Program' (SEV-2016-0683).

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